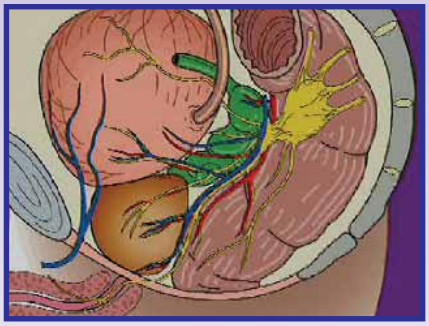
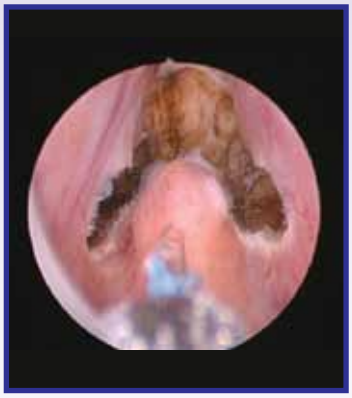
# MINIMALLY INVASIVE SURGERY IN UROLOGY

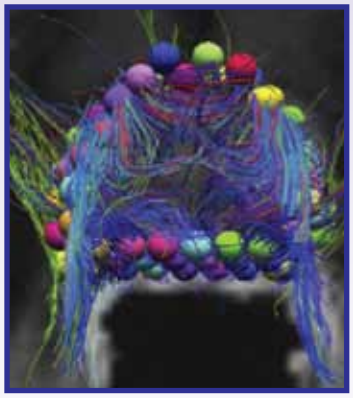

EDITORS

W. ARTIBANI - J. RASSWEILER

J. KAOUK - M. MENON





International Consultation on Minimally Invasive Surgery in Urology
Stockholm 2014

European Association of Urology

2015

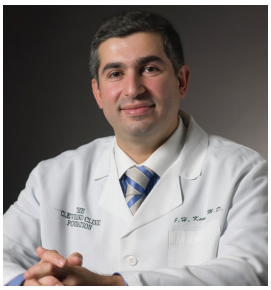
International Consultation on Urological Diseases

The great tragedy of science :
The slaying of a beautiful hypothesis by an ugly fact
Thomas Huxley (1825-1895)

**ISBN : 978-9953-493-22-0**

LAYOUT: SMART-DOT marketing & web consultants - www.smart-dot.com






*W. Artibani* *J. Rassweiler* *J. Kaouk* *M. Menon*

# Introduction

Over the past few decades, mini-invasive procedures have been applied more and more in any field of surgery, and particularly in Urology, which has been always at the front of innovation.

The pioneering vision and contributions of many have literally changed the approach to several urological diseases. Unfortunately, novel procedures have often been introduced in clinical practice without a proper evidence-based approach. The ideal process in this sense would have been the IDEAL stepwise structured approach (Innovation, Development, Exploration, Assessment, Long-term study), which was efficiently applied for example in the development of robotic kidney transplantation.

This e-book is the outcome of the commendable effort of a select group of clinicians who, under the input of the European Association of Urology (EAU) in cooperation with International Consultation on Urological Diseases (ICUD), met in Stockholm during the 29th annual meeting of EAU. By means of enthusiastic interactive collaboration, they critically revised the available evidence-based data, using standardised methodology. When evidence was missing, which is not uncommon, their personal experience and expertise filled the gap, providing an updated state-of-the-art overview in various topics related to mini-invasive surgery in urology.

The chapters follow the usual structure of ICUD consultations, with practical recommendations that cannot be intended to replace the conclusions and indications of EAU Guidelines. The aim is to provide an expert synopsis of the present knowledge.

Each section was enriched, whenever available, by a series of video clips showing in practice various operative techniques.

I would like to thank my co-chairs for their full commitment. All chairs and committees members deserve our and reader's appreciation, as they provided a highly informative overview of the present knowledge in the field, and a glimpse about the future.

Special thanks to Saad Khoury who was instrumental in implementing the final lay-out of the book.

This enterprise would have been impossible without the restless effort of the EAU central office, namely of Marian Smink and Loek Keizer.

I wish you an enjoyable journey across the various chapters.

Walter Artibani

# Contents

# EVIDENCE – BASED MEDICINE OVERVIEW OF THE MAIN STEPS FOR DEVELOPING AND GRADING GUIDELINE RECOMMENDATIONS.

## INTRODUCTION

The International Consultation on Urological Diseases (ICUD) is a non-governmental organization registered with the World Health Organisation (WHO). In the last ten years Consultations have been organised on BPH, Prostate Cancer, Urinary Stone Disease, Nosocomial Infections, Erectile Dysfunction and Urinary Incontinence. These consultations have looked at published evidence and produced recommendations at four levels; highly recommended, recommended, optional and not recommended. This method has been useful but the ICUD believes that there should be more explicit statements of the levels of evidence that generate the subsequent grades of recommendations.

The Agency for Health Care Policy and Research (AHCPR) have used specified evidence levels to justify recommendations for the investigation and treatment of a variety of conditions. The Oxford Centre for Evidence Based Medicine have produced a widely accepted adaptation of the work of AHCPR. (June 5th 2001 http://minerva.minervation.com/cebm/docs/levels.html). The ICUD has examined the Oxford guidelines and discussed with the Oxford group their applicability to the Consultations organised by ICUD. It is highly desirable that the recommendations made by the Consultations follow an accepted grading system supported by explicit levels of evidence.

The ICUD proposes that future consultations should use a modified version of the Oxford system which can be directly 'mapped' onto the Oxford system.

1. **1st Step: Define the specific questions or statements that the recommendations are supposed to address.**
2. **2nd Step: Analyse and rate (level of evidence) the relevant papers published in the literature.**

The analysis of the literature is an important step in preparing recommendations and their guarantee of quality.

***2.1 What papers should be included in the analysis?***

- Papers published, or accepted for publication in the peer reviewed issues of journals.
- The committee should do its best to search for papers accepted for publication by the peer reviewed journals in the relevant field but not yet published.
- Abstracts published in peer review journals should be identified. If of sufficient interest the author(s) should be asked for full details of methodology and results. The relevant committee members can then 'peer review' the data, and if the data confirms the details in the abstract, then that abstract may be included, with an explanatory footnote. This is a complex issue – it may actually increase publication bias as "uninteresting" abstracts commonly do not progress to full publication.
- Papers published in non peer reviewed supplements will not be included.

An exhaustive list should be obtained through:

I. the **major database**s covering the last ten years (e.g. Medline, Embase, Cochrane Library, Biosis, Science Citation Index)

II. the **table of contents** of the major journals of urology and other relevant journals, for the last three months, to take into account the possible delay in the indexation of the published papers in the databases.

It is expected that the highly experienced and expert committee members provide additional assurance that no important study would be missed using this review process.

***2.2 How papers are analysed?***

Papers published in peer reviewed journals have differing quality and level of evidence.

Each committee will rate the included papers according to levels of evidence (see below).

The level (strength) of evidence provided by an individual study depends on the ability of the study design to minimise the possibility of bias and to maximise attribution.

is influenced by:

**• the type of study**

The hierarchy of study types are:

- Systematic reviews and meta-analysis of randomised

controlled trials

- Randomised controlled trials
- Non-randomised cohort studies
- Case control studies
- Case series
- Expert opinion

**• how well the study was designed and carried out**

Failure to give due attention to key aspects of study methodology increase the risk of bias or confounding factors, and thus reduces the study's reliability.

The use of **standard check lists** is recommended to insure that all relevant aspects are considered and that a consistent approach is used in the methodological assessment of the evidence.

The objective of the check list is to give a quality rating for individual studies.

**• how well the study was reported**

The ICUD has adopted the CONSORT statement and its widely accepted check list. The CONSORT statement and the checklist are available at

http: //www.consort-statement.org

***2.3 How papers are rated?***

Papers are rated following a **«Level of Evidence scale»**.

ICUD has modified the Oxford Center for Evidence-Based Medicine levels of evidence.

The levels of evidence scales vary between types of studies (ie therapy, diagnosis, differential diagnosis/symptom prevalence study).

the Oxford Center for Evidence-Based Medicine Website: http://minerva.minervation.com/cebm/docs/ levels.html

***3. 3rd Step: Synthesis of the evidence***

After the selection of the papers and the rating of the level of evidence of each study, the next step is to compile a summary of the individual studies and the overall direction of the evidence in an **Evidence Table**.

***4. 4th Step: Considered judgment (integration of individual clinical expertise)***

Having completed a rigorous and objective synthesis of the evidence base, the committee must then make a judgement as to the grade of the recommendation on the basis of this evidence. This requires the exercise of judgement based on clinical experience as well as knowledge of the evidence and the methods used to generate it. Evidence based medicine requires the integration of individual clinical expertise with best

available external clinical evidence from systematic research. Without the former, practice quickly becomes tyrannised by evidence, for even excellent external evidence may be inapplicable to, or inappropriate for, an individual patient: without current bestevidence, practice quickly becomes out of date. Although it is not practical to lay our "rules" for exercising judgement, guideline development groups are asked to consider theevidence in terms of quantity, quality, and consistency; applicability; generalisability; and clinical impact.

**5. 5th Step: Final Grading**

The grading of the recommendation is intended to strike an appropriate balance between incorporating the complexity of type and quality of the evidence and maintaining clarity for guideline users.

The recommendations for grading follow the Oxford Centre for Evidence-Based Medicine.

The levels of evidence shown below have again been modified in the light of previous consultations. There are now 4 levels of evidence instead of 5.

The grades of recommendation have not been reduced and a "no recommendation possible" grade has been added.

**6. Levels of Evidence and Grades of Recommendation Therapeutic Interventions**

All interventions should be judged by the body of evidence for their efficacy, tolerability, safety, clinical effectiveness and cost effectiveness. It is accepted that at present little data exists on cost effectiveness for most interventions.

***6.1 Levels of Evidence***

Firstly, it should be stated that any level of evidence may be positive (the therapy works) or negative (the therapy doesn't work). A level of evidence is given to each individual study.

- **Level 1** evidence (incorporates Oxford 1a, 1b) usually involves meta-anaylsis of trials (RCTs) or a good quality randomised controlled trial, or 'all or none' studies in which no treatment is not an option, for example in vesicovaginal fistula.
- **Level 2** evidence (incorporates Oxford 2a, 2b and 2c) includes "low" quality RCT (e.g. < 80% follow up) or metaanalysis (with homogeneity) of good quality prospective 'cohort studies'. These may include a single group when individuals who develop the condition are compared with others from within the original cohort group. There can be parallel cohorts, where those with the condition in the first group are compared with those in the second group.
- **Level 3** evidence (incorporates Oxford 3a, 3b and 4) includes:

**good quality** retrospective 'case-control studies' where a group of patients who have a condition are matched appropriately (e.g. for age, sex etc) with control individuals who do not have the condition.

**good quality** 'case series' where a complete group of patients all, with the same condition/disease/therapeutic intervention, are described, without a comparison control group.

- **Level 4** evidence (incorporates Oxford 4) includes expert opinion were the pinion is based not on evidence but on 'first principles' (e.g. physiological or anatomical) or bench research. The Delphi process can be used to give 'expert opinion' greater authority. In the Delphi process a series of questions are posed to a panel; the answers are collected into a series of 'options'; the options are serially ranked; if a 75% agreement is reached then a Delphi consensus statement can be made.

***6.2 Grades of Recommendation***

The ICUD will use the four grades from the Oxford system. As with levels of evidence the grades of evidence may apply either positively (do the procedure) or negatively (don't do the procedure). Where there is disparity of evidence, for example if there were three well conducted RCT's indicating that Drug A was superior to placebo, but one RCT whose results show no difference, then there has to be an individual judgement as to the grade of recommendation given and the rationale explained.

- **Grade A** recommendation usually depends on consistent level 1 evidence and often means that the recommendation is effectively mandatory and placed within a clinical care pathway. However, there will be occasions where excellent evidence (level 1) does not lead to a Grade A recommendation, for example, if the therapy is prohibitively expensive, dangerous or unethical. Grade A recommendation can follow from Level 2 evidence. However, a Grade A recommendation needs a greater body of evidence if based on anything except Level 1 evidence
- **Grade B** recommendation usually depends on consistent level 2 and or 3 studies, or 'majority evidence' from RCT's.
- **Grade C** recommendation usually depends on level 4 studies or 'majority evidence' from level 2/3 studies or Dephi processed expert opinion.
- **Grade D** "No recommendation possible" would be used where the evidence is inadequate or conflicting and when expert opinion is delivered without a formal analytical process, such as by Dephi.

**7. Levels of Evidence and Grades of Recommendation for Methods of Assessment and Investigation**

From initial discussions with the Oxford group it is clear that application of levels of evidence/grades of recommendation for diagnostic techniques is much more complex than for interventions.

The ICUD recommend, that, as a minimum, any test should be subjected to three questions:

1. does the test have good technical performance, for example, do three aliquots of the same urine sample give the same result when subjected to 'stix' testing?
2. Does the test have good diagnostic performance, ideally against a "gold standard" measure?
3. Does the test have good therapeutic performance, that is, does the use of the test alter clinical management, does the use of the test improve outcome?

For the third component (therapeutic performance) the same approach can be used as for section 6.

**8. Levels of Evidence and Grades of Recommendation for Basic Science and Epidemiology Studies**

The proposed ICUD system does not easily fit into these areas of science. Further research needs to be carried out, in order to develop explicit levels of evidence that can lead to recommendations as to the soundness of data in these important aspects of medicine.

**CONCLUSION**

**The ICUD believes that its consultations should follow the ICUD system of levels of evidence and grades of recommendation, where possible. This system can be mapped to the Oxford system.**

**There are aspects to the ICUD system that require further research and development, particularly diagnostic performance and cost effectiveness, and also factors such as patient preference.**

**P. Abrams, S. Khoury, A. Grant 19/1/04**

# MINIMALLY INVASIVE SURGERY IN UROLOGY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## Committee 1

# Minimaly Invasive Radical Prostatectomy

### Chair

*C. Abbou (France)*

*B. Rocco (Italy)*

*V. Patel (USA)*

### Members

*T. Ahlering (USA)*

*A. Ali (USA)*

*A. Costello (Australia)*

*V. Ficarra (Italy)*

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*S. Pisipati (USA)*

*A. Tewari (USA)*

*J. Walz (France)*

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# Minimally Invasive Radical Prostatectomy

*C. Abbou, France, B. Rocco, Italy, V. Patel, USA*

*T. Ahlering, A. Ali, A. Costello, V. Ficarra, M. Graefen, G.K. Haines, M. Hruza, S. Joniau, J. Joseph, H. Lavery, R. Mandalapu, F. Montorsi, J. Peabody, S. Pisipati, A. Tewari, J. Walz*

## INTRODUCTION

Radical prostatectomy (RP) represents the standard for long-term cure of localised prostate cancer (PCa), with cancer-specific survival approaching 95% at 15 years after radical surgery [1]. Schuessler and colleagues described their initial experience with laparoscopic RP (LRP) and pioneered minimally invasive RP (MIRP) in 1992 [2]. In 1999, Guillonneau and Vallancien operated on a series of 40 patients with their technique of transabdominal descending LRP [3].

Abbou et al. in 2000 [334] and Binder and Kramer in 2001 [4] pioneered robot-assisted RP (RARP). When performed using the Da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA), RARP has been rapidly accepted as a safe and efficacious treatment option for localised PCa [5]. Over 80% of the RPs performed in the USA in 2011 used robot-assisted surgery [6].

RARP can be performed through a transperitoneal or subperitoneal approach, with more precision and choices for dissection as a result of the 3D vision of the Da Vinci system [6].

Indications for MIRP are the same of those for retropubic RP (RRP). According to the 2007 American Urological Association Guidelines (reviewed and validated in 2011) [7], low-, intermediate- and high-risk patients with localised PCa can undergo RP. The 2013 European Association of Urology (EAU) Guidelines [8] identify four categories of patients who should undergo RP: (1) patients with low- and intermediate-risk localised PCa and life expectancy > 10 years; (2) patients with stage T1a disease and life expectancy > 15 years or Gleason score (GS) 7; (3) selected patients with low-volume, high-risk localised PCa; and (4) highly selected patients with very-high-risk localised PCa (cT3b–T4 N0 or any T N1) in the context of multimodal treatment.

The aims of this issue are to give a comprehensive overview of the anatomical landmarks of MIRP, surgical technique, postoperative management, and short- and long-term outcomes, and then to establish expert guidelines.

## METHOD

A detailed search of the major medical databases (e.g., Pubmed and Scopus) was performed to retrieve original articles addressing various aspects of MIRP. Proceedings from the major conferences were also searched in some cases. The evidence was analysed using the Oxford method of assigning levels of evidence, and summary recommendations based on these levels of evidence were graded as advised by the Oxford Centre for Evidence-based Medicine, which are similar to the Grading of Recommendations Assessment, Development and Evaluation working group recommendations [9]. These recommendations are summarised in this issue.

## I. PREOPERATIVE CONSIDERATIONS

### A. ANATOMICAL ASPECTS OF THE PROSTATE AND SURROUNDING TISSUES

#### 1. SHAPE OF THE PROSTATE (figure 1)

The prostate is an ovoid gland that is normally 3 ´ 4 ´ 2 cm. The prostate gland is traversed by the prostatic urethra. Although ovoid, the prostate is referred to as having anterior, posterior and lateral surfaces, with an inferior narrowed apex and a superior broad base that is contiguous with the base of the bladder [335].

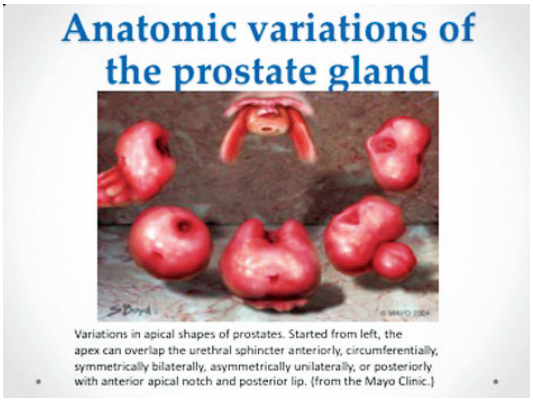



***Figure 1. Different aspects of the prostate gland (from the Mayo Clinic)***

## 2. CAPSULE

The structure often termed the “capsule” is the exterior stromal edge of the prostatatic parenchyma, which is formed by the transversely arranged fibromuscular layer of condensed smooth muscle, with relatively few glands in the outermost region of the prostate surface [26]. From a microscopic and pathological point of view, the correct term for this layer would be “condensed smooth muscle” or “outer edge” of the prostate. From a macroscopic and surgical point of view, a clearly defined, distinct outer edge of the prostate, reminiscent of a capsule, is grossly apparent, and it is used as a landmark for proper dissection

## 3. FASCIAE

The fasciae surrounding the prostate represent an essential anatomical structure for RP, in order to avoid positive surgical margins (PSMs) and preserve erectile function (EF).

Understanding the fasciae around the prostate is key to achieving the right degree of nerve sparing. Anatomical variations and the use of different nomenclature [48] may result in confusion.

The pelvic organs are covered by fasciae [10–12]. According to Terminologia Anatomica, there are essentially four fascial layers surrounding the prostate and neurovascular bundle (NVB). The endopelvic fascia has a parietal (levator ani fascia) and visceral component [13–15]. The parietal component covers the levator ani lateral to the fascial tendinous arch, and the visceral endopelvic fascia sweeps medially to cover the bladder and anterior prostate [10,16,17]. So, the prostatic capsule is covered by an outer endopelvic fascia (levator ani fascia) and inner fascia (prostatic fascia; PF). Posteriorly, Denonvilliers’ fascia surrounds the prostate [48].

All these fasciae are termed the periprostatic fasciae (PPFs) to signify that they are external to the prostatic capsule. The PPF covering the prostate can be divided into three basic elements according to location: anterior, lateral and posterior PPF [10,19,20,23,27,30–34] and seminal vesicular fascia (SVF; Denonvilliers’ fascia) [13,14,21,35–42].

During surgery, access to the lateral prostate may be gained by incision of the endopelvic fascia either medial or lateral to the arcus tendineous fasciae pelvis [12,14,21]. Avoiding incision of the endopelvic fascia might improve early recovery of urinary continence as well as postoperative EF [10,16,22].

## 4. BLADDER NECK

Surgical anatomy and role in maintaining continence and orgasmic function.

The bladder neck is the junction between the urinary bladder and the prostatic urethra, lying caudal to the apex of the trigone. The detrusor muscle at this level is differentiated into three layers of smooth muscle **(Figure 2)**: inner longitudinal, middle circular, and outer longitudinal [133,134]. In men, the radial fibres of the inner longitudinal layer pass through the internal urethral meatus to become continuous with the smooth muscle of the urethra. The middle layer of circular fibres forms a circular pre-prostatic sphincter that maintains continence at the level of the bladder neck. The verumontanum marks the distal limit of this internal (vesical) sphincter, making it possible to separate the prostate from the internal sphincter by blunt dissection [135]. The outer longitudinal detrusor fibres are thickened posteriorly to support the trigone and pass around the lateral wall of the bladder neck to meet anteriorly, forming a loop around the bladder neck that reinforces the circular pre-prostatic sphincter [133,134]. **(Figure 3)**

Tonic contraction of the bladder neck can maintain continence even if the striated urethral sphincter has been destroyed [133]. Three/four-dimensional multi-slice perineal ultrasonography has shown

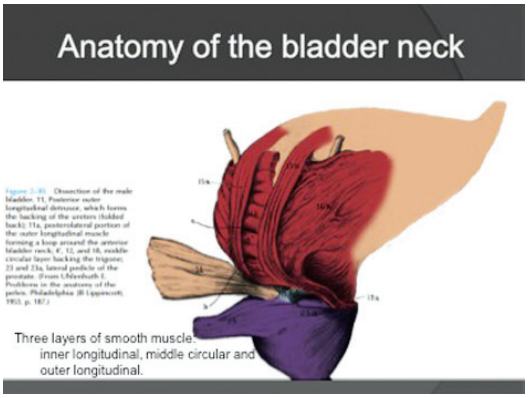



***Figure 2. Complexity of the posterior aspect of the bladder neck, 3 main muscular layers are involved playing a role for the continence and the ejaculation mechanism. The injury of the BN leads to “Climaturia”***

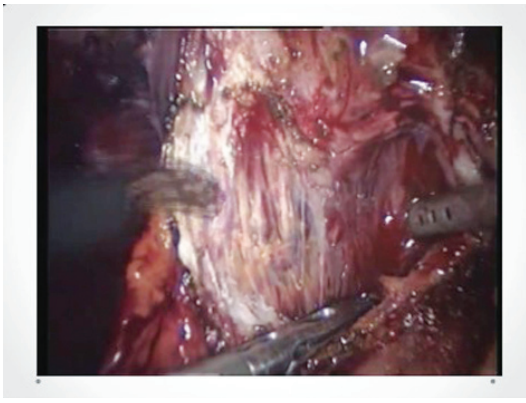


***Figure 3. Vision of the posterior layer of the bladder neck muscle after division of the BN***

***This muscle has been given the name of anterior Denonvilliers fascia or muscle***

that, post-prostatectomy, incontinent men differ from continent men mainly in the degree of hypermobility of the proximal urethra and funnelling of the bladder neck [136]. Urethral resistance and length proximal to the external sphincter are postulated to play a role in maintaining continence, and men who are continent after RP have a tubularised bladder neck **(Figure 4)** and functional proximal urethral length similar to the native anatomy [137,138]. The bladder neck is innervated by sympathetic fibres from the anterior portion of the pelvic plexus, causing α-1-mediated contraction of the bladder neck during orgasm.

## 5. ANATOMY OF THE APICAL REGION OF THE PROSTATE

The shape of the prostatic apex may vary substantially, directly influencing the length of the urethra after emerging from the apex [341]. The apex may overlap the urethral sphincter circumferentially, symmetrically bilaterally, asymmetrically unilaterally, anteriorly only, posteriorly only, or can bluntly end above the sphincter. Significant overlap makes preservation of the long and short urethral sphincters difficult, and should be considered during dissection and appropriate transection of the urethra at the apex. **(Figures 5-6-7-8)**

Furthermore, the position of the apex deep in the small pelvis, as well as its close connection to the dorsal vein complex, rectum and sphincter, makes dissection of the prostatic apex difficult in minimally invasive surgery [225].

The external urethral sphincter is an omega-shaped muscle consisting of an external striated part and an internal smooth muscle layer [48,226,227]. Its fibres surround the urethra, whose length is 1.5–2.4 cm. A considerable part of the urethral sphincter is located intraprostatically between the prostatic apex and the colliculus seminalis [228]. Pelvic magnetic resonance imaging has shown an increased risk of urethral shortening when the prostatic parenchyma covers the urethral muscle

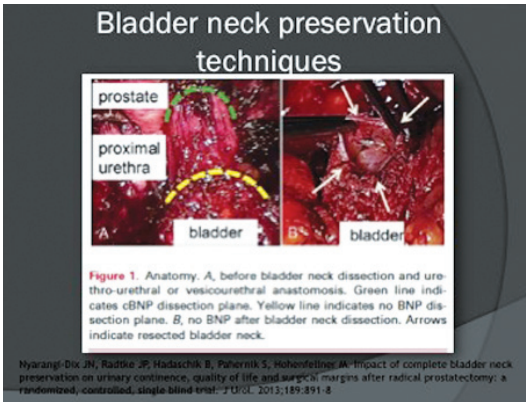



***Figure 4. Preservation and non preservation aspect of the bladder neck***

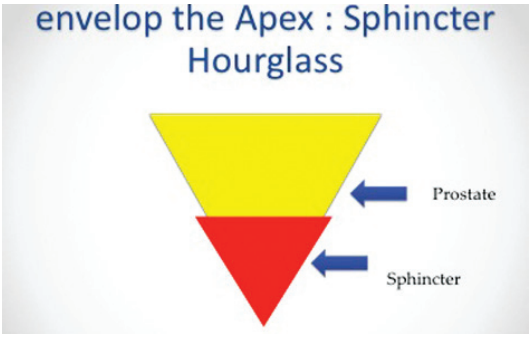



***Figure 5. Apex of the prostate inside a « sphincter hourglass »***

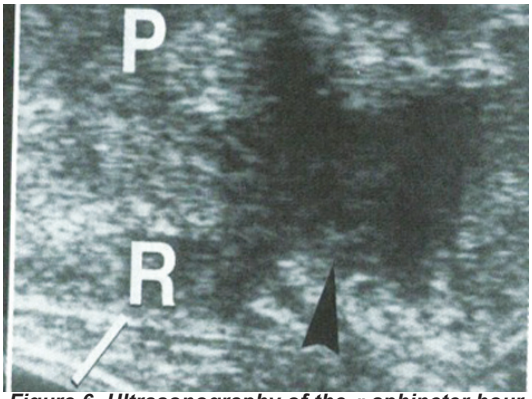



***Figure 6. Ultrasonography of the « sphincter hourglass »***

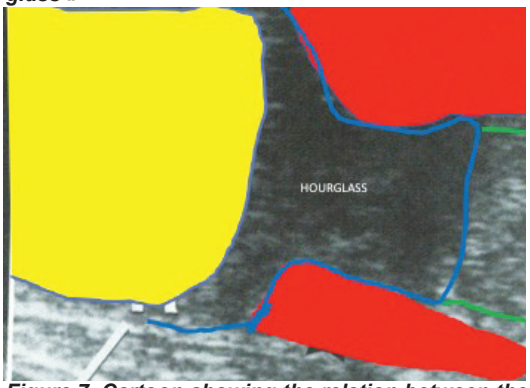



***Figure 7. Cartoon showing the relation between the prostate in yellow and the « sphincter hourglass ». Pelvic floor in red.***

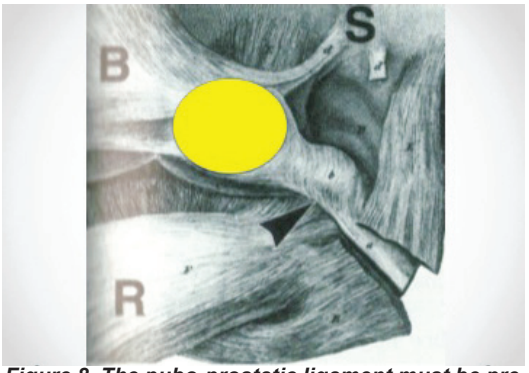



***Figure 8. The pubo-prostatic ligament must be preserved to spare the sphincter complex***

[229]. This may aggravate preparation of the full-length urethral sphincter during RP.

## 6. NEUROVASCULAR BUNDLES

### *a) Introduction*

Since the landmark discovery of the cavernous nerves by Walsh and Donker [54], which led to the development of nerve sparing prostatectomy, surgeons have become even more nuanced in their approach to the NVB at the time of RP. Our understanding of the NVB has increased greatly since 2000 with publications from several authors [10,23,55].

The advent of 10 times magnified vision, combined with a dry field in robotic surgery, has allowed urologists to identify the conduit bearing the structures that are called the NVB, including the cavernous nerves, and do as little damage as possible to these structures during the operation.

### *b) Neuroanatomy*

Sympathetic supply (T10–L2) is conveyed to the pelvis via the hypogastric nerves **(Figure 9)**, and the pelvic parasympathetic supply is derived from the pelvic splanchnic nerves (S2–S4). These autonomic fibres converge to form the pelvic plexus (also known as the inferior hypogastric plexus). The pelvic plexus is a fenestrated network of nerves that lies in a sagittal plane in the retroperitoneal space, lateral to the rectum. Caudal fibres of the pelvic plexus join with vessels branching from the inferior vesicle artery to form the NVB [23].

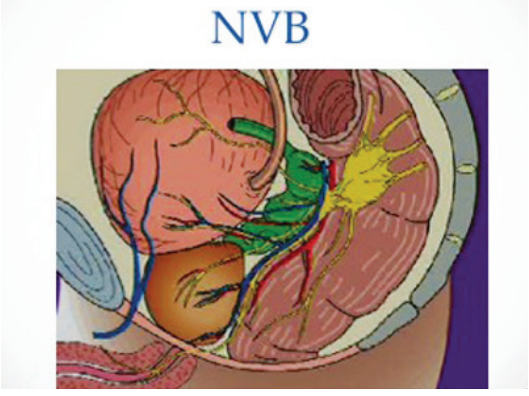



***Figure 9. Anatomy of the Hypogastric nerves***

#### 1. Cavernous nerves (Figure 10)

The NVB starts at the base of the prostate between 3 and 9 o'clock. It then runs outside the prostatic capsule, inferomedially to the apex. At the apex it projects anteriorly, where it is most likely to be damaged during surgery [23]. This damage can be caused by cutting the NVB, diathermal injury, or inadvertent suturing at this position. There is also concern regarding stretching of the NVB causing neuropraxia. Some surgeons promote a "high anterior release" or "veil of Aphrodite" nerve-sparing technique to prevent damage to anterior parasympathetic fibres [31].

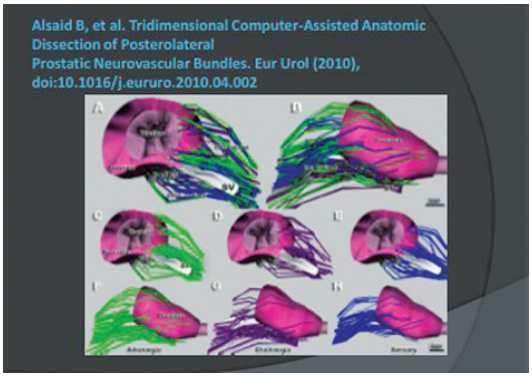



***Figure 10. Complexity of the NVB including adrenergic , sensitive and cholinergic nerves. The nerves surround the postero-lateral aspect of the prostate but some fibres covers the anterior aspect of the gland***

We have shown that only a minority of nerves in the anterior periprostatic region are functionally significant parasympathetic nerves [57].

Three fascial spaces functionally compartmentalise the NVB. Rectal neurovascular supply is generally in the posterior and posterolateral sections of the NVB, running within the leaves of Denonvilliers and pararectal fascia. Supply to the levator ani is in the lateral section, within the lateral pelvic fascia. The cavernosal nerves and prostatic neurovascular supply descend along the posterolateral surface of the prostate with the prostatic neurovascular supply most anterior. Functional organisation is not absolute and is less pronounced proximally at the levels of the seminal vesicle and prostatic base. The complexity of the NVB constituents means that the terms NVB and cavernosal nerves are not synonymous [57].

Distally, the cavernosal nerves pierce the urogenital diaphragm and run with the deep artery and vein of the penis to provide parasympathetic supply to the crura [58].

#### 2. Pudendal nerve

The pudendal nerve provides somatic innervation to the external urethral sphincter (rhabdosphincter). It is arises predominantly from the S2–S4 ventral rami, but occasionally receives contributions from S5 [59]. After exiting the pelvis, it runs in the lateral wall of the ischiorectal fossa within Alcock's canal. It then provides rhabdosphincter supply via its infralevator perineal [60,61] or dorsal [10,62] nerve branches.

Takenaka et al. found a mean distance of 5.5 mm from the lowest point of the endopelvic fascia to the point where the sphincteric branch of the pudendal nerve enters the rhabdosphincter [10]. Others have also found branches innervating the rhabdosphincter in close proximity to the prostatic apex [61]. Hence, care must be taken because these branches can potentially be injured during apical dissection of the prostate, or by inadvertent suturing or diathermy

deep in this region. Preservation of the levator ani fascia can help protect the levator ani muscle, rhabdosphincter and pudendal nerve branches to the rhabdosphincter [10].

Several studies have suggested that there are intrapelvic pudendal branches to the rhabdosphincter in some men [59,62] and these could be at risk during dissection of the NVB.

### *c) Vascular anatomy*

#### 1. Dorsal vascular complex

The dorsal vascular complex, also known as Santorini's plexus, comprises both veins and small arteries and lies on the ventral surface of the prostate [55]. Ligation of the dorsal vascular complex during radical prostatectomy minimises blood loss. However, since the introduction of laparoscopic and robotic-assisted surgery, some surgeons have advocated division of the dorsal vascular complex without prior ligation, as a means to maximizing urethral length and likelihood of achieving a negative apical margin. This technique is made possible due to the decreased venous blood loss afforded by increased intra-abdominal pressure from CO2 insufflation [63].

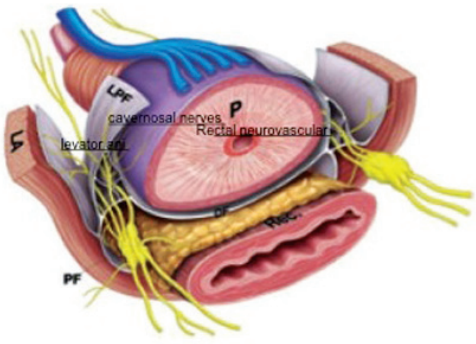
#### 2. Accessory pudendal artery

The accessory pudendal arteries are any arteries arising cranial to the pelvic diaphragm, and passing inferior to the pubic bone to enter the penile hilum. These most commonly have an intrapelvic origin but may also come from extrapelvic arteries. Reported prevalence of accessory pudendal arteries varies from 4 to 75% [64], and in some cases they may provide the only erectile arterial supply [65].

Arterial insufficiency post-prostatectomy may affect recovery of EF. Therefore, if possible, these arteries should be preserved during RP [66].

#### 3. Prostatic pedicle

Clegg described the prostatic arterial anatomy in 1955. According to his description, the gland was supplied by the prostatic branch of an artery that he named the prostato-vesical artery, a well-defined trunk of variable origin. Despite the name he gave to this artery, it had only prostatic branches or only small inferior vesical arteries in almost half of the cases. He noted that the prostatic artery had a trajectory obliquely downward, forward, and medially on the anteroinferior surface of the bladder toward the prostate gland, terminating in a division into anterior and posterior branches. Clegg also identified a typical morphology of the prostatic artery capsular branches that he named the "corkscrew pattern" [336–338].




NVB T Costello: three fascial spaces

***Figure 11. T Costello: The fascias determine three spaces real routes for the NVB***

Bouissou and Talazac were the first to describe the presence of two independent prostatic arteries on each pelvic side: one cranial artery they named the vesico-prostatic artery, supplying branches to the bladder base and the inner and cranial prostate gland; and one caudal artery that had a close relationship with the middle rectal artery and mostly supplied the peripheral and caudal gland [339].

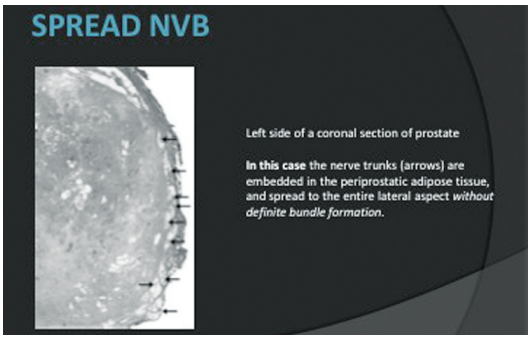
Ambrósio et al. described the variable origin of the prostatic artery: inferior vesical (41.5%), internal pudendal (26.4%), umbilical (15.1%), obturator (5.7%), inferiorgluteal (1.9%), and internal iliac (9.4%) arteries. After reaching the prostatic surface, the arteries penetrate the capsule in two anterolateral and two posterlateral quadrants [340].

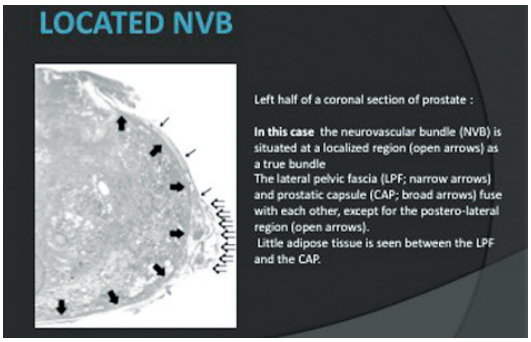
#### 4. Relationship between prostatic fascia and NVB

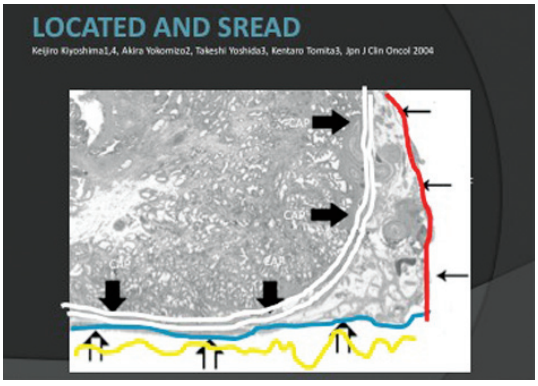
The relationship between the PF and NVB is controversial [32,35,42]. Several authors have stated that the NVB is located strictly between the prostatic capsule and either the visceral endopelvic fascia or posterior PPF/SVF) [19,20,23,43,44]. Kourambas et al. questioned this straightforward view and proposed that, in axial section, the posterior PPF/SVF is part of an H-shaped fascial structure flanking the prostate [32]. These findings were corroborated by others, who described the posterior PPF/SVF as almost merging into the NVB, or splitting at its lateral border into anterior and posterior leaves passing around the NVB **(Figure 11)**, binding it in a triangular fashion with the LAF [14,23,25,45] **(Figure 12,13,14).**

## II. SURGICAL STRATEGIES ALLOWED BY NVB ANATOMY

In performing a complete nerve-sparing procedure, surgeons must dissect between the prostatic capsule and prostatic fascia, being the fused endopelvic fascia. As the surgeon comes closer to the prostatic capsule, damage to the NVB is less likely. However, this also allows more opportunity for inadvertent capsular incision or leaving a positive surgical margin. Nerve sparing can be performed antero-inferiorly or in retrograde fashion, or even incrementally with some removal of the NVB tissue but not complete removal.




***Three different aspect of the NVB and the fascias***

***Figure 12. the prostate capsule, prostate fascia and LPF are stuck leaving no space for the NVB***

***Figure 13. NVB are well gathered in a postero lateral position***

***Figure 14. NVB are spead and located in a postero lateral position***

The multilayered character of the PPF allows the surgeon to vary the dissection between the nerves and prostatic capsule, with the aim of leaving a layer of tissue on the prostate as a safety margin. In cases with a low risk of extraprostatic extension, a closer dissection can be chosen, and in cases with a higher risk of extraprostatic extension, a wider dissection plane can be chosen. This approach is termed incremental nerve sparing [46,47]. The dissection can be intrafascial, interfascial or extrafascial [48] **(Figure 15)**.

## 1. INTRAFASCIAL DISSECTION

Intrafascial dissection of the NVB follows a plane on the prostatic capsule, remaining medial or internal to the PF at the antero- and posterolateral aspect of the prostate and remaining anterior to the posterior PPF/SVF [24,28,29,49,50]. In antegrade intrafascial dissection starting at the 6 o'clock position, one may find an easier plane of dissection because, at this level, the posterior PPF/SVF is thick and easily recognized as a single-layer structure. During a high lateral approach, the plane of dissection can be difficult to identify, due to the multi-layered appearance of the fasciae, especially at the posterolateral border of the prostate. Intrafascial dissection carries a high risk of inadvertent iatrogenic capsular penetration [18] **(Figure 16)**.

## 2. INTERFASCIAL DISSECTION

Interfascial dissection of the NVB is performed outside or lateral to the PF at the anterolateral and posterolateral aspects of the prostate, combined with dissection medial to the NVB at the 5 and 7 o'clock or 2 and 10 o'clock positions of the prostate in axial section. This is done by moving the intact NVB off the prostate so that the posterolateral prostate remains covered with fascia. This approach allows a greater tissue buffer to surround the prostate in contrast to intrafascial dissection, presumably resulting in an oncologically safer approach [12,14,24,29,49,50].

Recent studies have suggested subdividing interfascial dissection into closer and wider dissection planes. To define the extent of the prostatic tissue margin, a grading system has been proposed. Tewari et al. proposed four grades of dissection [46]. They also used vascular structures as landmarks for dissection but in their case the veins on the lateral aspect of the prostate are the landmark. Patel *et al.* **(Figure 17, 18)** proposed an inverse five-grade scale of dissection, where grade 5 represents full nerve sparing and grade 1 no nerve sparing. They used the prostatic vasculature as a possible landmark, with the "landmark artery" running on the lateral border of the prostate as either a prostatic or capsular artery [51,52].

Bearing in mind that neural anatomy may vary substantially, different dissection planes aim to achieve an incremental security margin on the prostate, to avoid a positive surgical margin than incremental nerve sparing. Incremental nerve sparing implies that the course and location of erectile nerve fibres can be reliably identified, which is not possible due to their microscopic nature and variable anatomy. The degree of nerve sparing with this technique is due to chance and the degree of nerve fibre preservation cannot reliably be controlled. In contrast, the amount of tissue that is left on the prostate to avoid a positive surgical margin can be controlled to achieve incremental tissue margins to cover the prostatic capsule and PCa if present. For this reason incremental se-

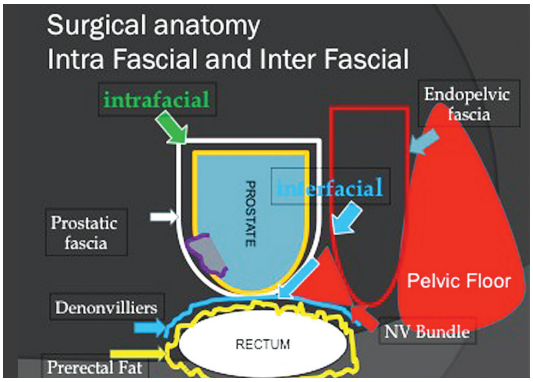



*Figure 15. Summary of the different route of the radical prostatectomy (CC Abbou)*

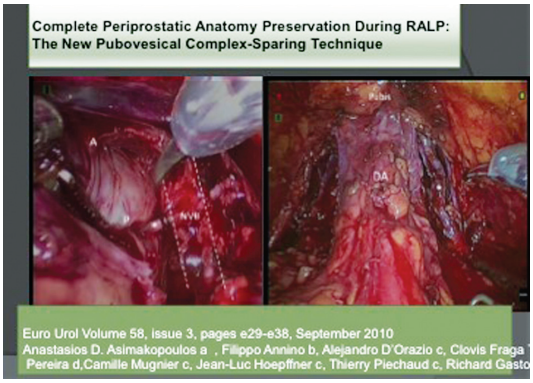



*Figure 16. Intrafascial dissection leaving intact the "bladder apron": the prostate is extracted from its cage thought 2 lateral incisions (R Gaston)*

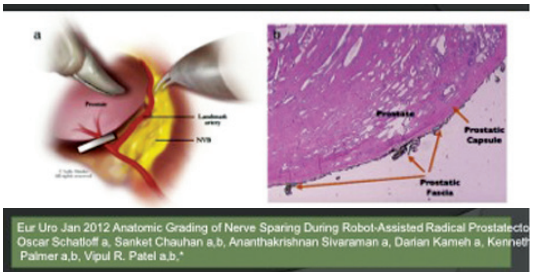



*Figure 17. Left figure The Landmark Artery Allows a safe dissection of the prostate leaving a security layer of prostate fascia*

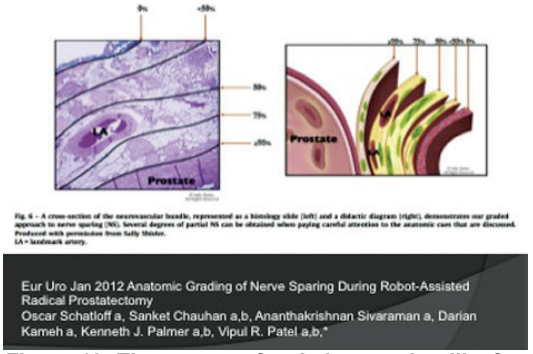



*Figure 18. The prostate fascia is an onion like fascia with multiple layers*

curity margin rather than incremental nerve sparing better reflects the true prostate anatomy and aim of the proposed technique [53].

### 3. EXTRAFASCIAL DISSECTION

Extrafascial dissection is performed lateral to the LAF and posterior to the posterior PPF/SVF. The NVB running along the posterolateral aspect of the prostate is completely resected but the LAF, PF and posterior PPF/SVF remain on the prostate. This is the most oncologically safe dissection method, but carries a risk of complete erectile dysfunction (ED) [14,29,50].

## III. SURGERY

### 1. TRANSPERITONEAL APPROACH

The transperitoneal approach is the most widely used for MIRP and gives unparalleled access to perform extended pelvic lymph node dissection (LND) [67].

#### *a) Patient positioning*

It is usual to place the patients' legs in stirrups, slightly flexed at the hips, for optimal access to the abdomen and perineum. Some surgeons opt for spreader bars so that the legs are straight, or nearly so, and spread to allow access to the penis, scrotum and perineum, and if necessary, the rectum. Care must be taken with either approach to avoid undue pressure or stretch on the nerves [68,69].

#### *b) Port placement*

An appropriate site for insufflation of the pneumoperitoneum for port placement can be safely achieved by placing a Hasson port or Veress needle just underneath the costochondral junction on the left. Once safe entry is achieved, it is important that after the first port is placed, the abdomen should be thoroughly inspected for blood, abnormal insufflation pattern, bowel injury, and other adhesions. Initial laparoscopic lysis of adhesions can safely be achieved if needed.

In general, the camera port site is midline, at or above the navel. This position is sufficiently cephalad to allow comfortable access to the entire pelvis, which is especially important for extended LND.

Most camera/extraction site incisions are vertical; however, many authors have stressed the importance and ease of transverse incision to avoid incisional hernias and improve cosmesis [70,71].

#### *c) Apex of the prostate, dorsal vein complex and anterior prostatic fat*

Eichel and associates gave the first detailed description of dissecting the anterior prostatic fat and stapling the dorsal vein to reduce PSMs at the apex [76]. Removing the anterior prostatic fat improves apical landmarks and visualization of the dividing line between the prostate and bladder during anteri-

or bladder neck transection. An unexpected finding is that this fat pad contains lymph nodes in ~15% of cases, and in 1–2% of cases it can be the only site of lymph node metastasis [77, 78].

## 2. EXTRAPERITONEAL APPROACH

Extraperitoneal RP simulates the gold standard technique of open RP. The entire procedure is performed in the retropubic space of Retzius. The following is a brief description of the technique [104].

***a) Extraperitoneal space creation and trocar configuration*** **(Figure 19 a,b)**

The instruments required to create the potential extraperitoneal space include an OMS-XB2 (Oval) ExtraviewTM balloon dilator trocar (Autosuture, Norwalk, CT, USA) (or a SpacemakerTM), a 0° laparoscope, two S-shaped retractors, and a 15-cm smooth trocar (12 mm 512 XD; Ethicon Endo-Surgery, Cincinnati, OH, USA) (Fig. 5). A separate scope is advised because the robotic camera and scope system are difficult to manoeuvre due to their weight.

Initial access is obtained via a 3-cm left periumbilical skin incision. The subcutaneous tissue is bluntly dissected to expose the anterior rectus sheath. A 1-cm incision is made in the latter and an S-shaped retractor is used to sweep the underlying rectus muscles laterally, to bring the posterior rectus sheath into view. Once the latter is visualised, the balloon dilator is inserted into the space of Retzius, with the scope placed inside the uninflated balloon [104]. The tip of the balloon should be angled upward and toward the midline, to avoid inadvertent injury to the posterior rectus sheath, or access to the peritoneal cavity. There should normally be some resistance from the linea alba until the balloon dilator is passed below the semicircular line of Douglas. With the start of balloon inflation, the space of Retzius and the retropubic fat are dissected, bringing the pubic symphysis into view. The other important landmarks are the inferior epigastric vessels (one artery and two veins), which are visualised on both sides. The balloon dilator is removed after deflation and replaced by a 15-cm smooth trocar, which creates the extra space required for trocar placement cephalad and laterally. CO2 insufflation of the extraperitoneal space is carried out through the same trocar up to a pressure of 15 mm Hg. Under direct vision, the space is enlarged by retracting the scope into the trocar and using the beveled tip of the trocar (insinuated under the inferior epigastric vessels) to sweep the peritoneum posterolaterally on either side. The movements necessary to develop the extraperitoneal space laterally widen the fascial opening, causing leakage of air around the trocar. To lessen air leakage, a Foam Grip Trocad (Covidien), balloon tip trocar, or a Vaseline gauze wrapped around the trocar can also be used for this.

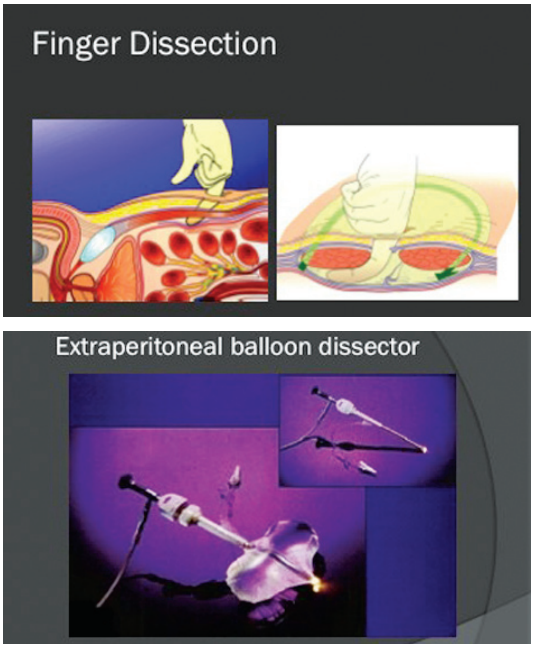



***Figure 19 a,b. Creation of the extraperitoneal space using the finger dissection followed by the balloon***

Robot-assisted procedures call for particular consideration in trocar placement to avoid robotic arm collision. Ten centimetres between all robotic working arm trocars is advised. Five to six trocars can be used in a "W" configuration during four-arm Da Vinci extraperitoneal robotic prostatectomy. Three 8-mm Da Vinci metal robotic trocars and two disposable assistant trocars (one 12-mm, 150-mm long trocar, and one 5-mm trocar) are used in addition to the 12-mm infraumbilical camera trocar. Once an adequate space is created, and the peritoneum pushed cephalad and laterally, the 12-mm right assistant trocar is introduced 5 cm medial to the anterior superior iliac spine, along a line joining this anatomical landmark to the umbilicus. The assistant trocars can be placed on either side, based on the surgical team's preference.

The trocar for the fourth robotic arm is placed opposite the assistant trocar (5 cm cephalad and medial to the anterior superior iliac spine) and guided toward the pubic symphysis under direct vision. We use a hypodermic needle to guide the site of insertion of the two remaining robotic working trocars on either side. They are generally placed 10 cm caudal and lateral to the umbilicus on either side, forming a triangle with the latter. The trocars for the robotic working arms are placed lateral to the respective epigastric vessels, at a more perpendicular angle to the abdominal wall to avoid robotic arm collision. Trocar tunnelling should be avoided, because it restricts trocar motion. For the remaining 5-mm assistant trocar that is placed 5–8 cm lateral to the umbilicus on the right side, the dissection is performed in a more medial and cephalad direction. The robot is docked once all the trocars are in place.

The subsequent steps of the procedure are similar to those of the transperitoneal approach, regardless of whether robotic assistance is needed.

***b) Advantages and disadvantages of the extraperitoneal approach***

There are several advantages of the extraperitoneal route. These include the need for less steep Trendelenburg positioning [104,105]. This is helpful in patients with poor pulmonary reserve. Diaphragmatic expansion is less compromised, facilitating ventilation and reducing possible complications. The limited Trendelenburg position also lessens the risk of position-related neuropraxia, which is more likely when body weight is shifted to the shoulders, with possible brachial plexus compression. The extraperitoneal route avoids all potential intraperitoneal adhesions. This approach gives rapid access to the target organ. The bladder takedown step is eliminated. The peritoneum acts as a natural barrier obviating the need for bowel retraction from the operative surgical field. This potentially lessens the incidence of paralytic ileus [105]. In addition, this route allows containment of bleeding or urine leakage in the confined extraperitoneal space.

Disadvantages of the extraperitoneal approach include: unfamiliarity with access and instruments; difficulty in spacing the trocars, especially with the use of the fourth arm; limited working space; and increased risk of lymphocoele formation following pelvic LND. If extended pelvic lymphadenectomy is indicated, the alternative transperitoneal approach may afford better exposure of the cephalad limits of the template of dissection. Tension on the anastomosis is often cited as a potential disadvantage of the extraperitoneal approach, given that the urachal attachments are unaltered. As with open retropubic prostatectomy, which is generally performed extraperitoneally, there is no meaningful tension on the anastomosis once completed. The initial sutures are indeed under some tension, which is quickly redistributed, or relieved with the placement of additional sutures. Approximating the posterior urethra to the posterior bladder neck is helpful in eliminating possible tension, facilitating anastomosis. The pressure in the working space can be decreased to 8 or 10 mm Hg to ease re-approximation of the bladder to the urethra. The application of perineal pressure is also helpful at this stage, lessening the risk of urethral tearing.

## 3. PELVIC LYMPH NODE DISSECTION

Lymph node status provides staging information that may guide further therapy. More than two positive lymph nodes at prostatectomy significantly affects prostate-cancer-specific survival [83]. LND may be beneficial in some patients [84–86]. A subset of patients may be cured, even with positive lymph node status [87,88]. Performing LND meticulously can reduce time to progression and prostate-cancer-specific mortality [89,90]. Despite these proposed benefits, LND does have significant limitations regarding long operative time and associated risks. Only one randomised single-centre trial has been performed comparing limited/standard to extended pelvic LND, leading to reduced biochemical recurrence in intermediate/high risk men at 74 months [91].

Risks of LND can include vascular, nervous and lymphatic complications [92]. With laparoscopic pelvic LND, incidence of bleeding complications was <1% [93]. Postoperative deep vein thrombosis and pulmonary embolism are associated with LND [94,95]. Obturator nerve injury has not been reported in studies of robotic prostatectomy, however, it remains a constant concern. Ureteral injury is also likely to be encountered during extended LND. The most frequently reported complication of LND is lymphocoele. Lymphocoele occurs in nearly half of the patients, but clinically significant cases are seen in a minority of patients (5–15%), depending on the number of lymph nodes removed [96–98]. The overall number of additional complications of LND is small and a recent systematic review noted that Clavien grade >3 complications occur in <2% of patients.

The major anatomical landmarks for pelvic LND include the internal and external iliac artery and vein, the obturator nerve and vessels, and the iliac bifurcation to the level of the ureter [95]. Some surgeons include super-extended LND to the presacral nodes [99,100]. Obturator only (limited) pelvic LND is not extensive enough to provide accurate staging information because many of the positive nodes are not in this region [99].

Omission of pelvic LND for low-risk PCa is described as safe and is recommended in guidelines [8,101]. The EAU guidelines recommend extended LND if the risk of lymph node involvement is >5% [8].

Thirteen to 20 lymph nodes are recommended as an adequate yield for accurate staging [8,102,103]. Extending LND to include the internal iliac lymph nodes increases nodal yield as well as the ability to detect positive lymph nodes [96,99].

## 4. SURGICAL DISSECTION OF THE PROSTATE AND SURROUNDING TISSUES USING THE DESCENDING TECHNIQUE

***a) Bladder neck preservation, reconstruction and anastomosis***

Twelve-month continence rates for open RRP, LRP and RARP vary between 60 and 93%, 66 and 95% and 84 and 97%, respectively [127].

Kojima et al. divided the surgical modifications intended to improve continence into three sub-categories: preservation of anatomical elements, such

as bladder neck, NVB and pubovesical complex; reconstruction of the urethral sphincter; and reinforcement of the bladder neck [132]. Resection of the bladder neck during RP contributes to incontinence and disrupts the closure mechanism of the bladder neck during orgasm, possibly leading to orgasm-associated incontinence (climacturia) [139–141].

Technical modifications have been proposed for bladder neck dissection in challenging circumstances: bladder neck reconstruction and Bladder Neck Preservation to hasten the return of continence and lower the incidence of urethrovesical anastomotic strictures, without compromising oncological control of the tumour.

In addition to its possible role in post-prostatectomy continence, bladder neck dissection may affect development of urethrovesical anastomotic leaks [142,143], bladder neck contracture/anastomotic stricture [144,145] and climacturia [139–141]. While bladder neck resection per se is not a predictive factor for anastomotic leakage, a large bladder neck defect may lead to a challenging urethrovesical anastomosis, which in turn is a known risk factor for anastomotic leakage [146]. RARP carried out be experts after a period of learning showed a urine leakage rate of 0.1–6.7% (mean 1.8%) [147]. Anastomotic leakage can precipitate uroperitoneum (especially with transperitoneal LRP/RARP), which if undetected, may cause serious complications [148]. Anastomotic leakage may be a risk factor for development of urethrovesical anastomotic stricture/bladder neck contracture [145,149,150], although a direct causal association is controversial [151]. Similarly, patients with anastomotic leakage may have delayed recovery of continence and even a high incidence of incontinence [145,149].

A difficult urethrovesical anastomosis, potentially resulting from a wide bladder neck defect, may be a risk factor for later bladder neck contracture [144,145]. Breyer et al. found that the incidence of post-prostatectomy bladder neck was 0.48–17.5% with open RRP and 0–3% with LRP/RARP, with weighted mean incidence rates of bladder neck contracture for open RRP, LRP and RARP of 5.1%, 1.1% and 1.4%, respectively [144].

Climacturia is involuntary urine leakage during orgasm [139]. It is a troublesome and under-reported consequence of RP [152], with rates varying between 20 and 93% [139,153–155]. Bladder neck damage and/or injury to sympathetic nerves may prevent closure of the internal sphincter, which when coupled with relaxation of the external sphincter at the time of orgasm, may precipitate urine leakage [141]. Manassero et al. have suggested the role of functional urethral length in addition to loss of bladder neck integrity in post-RP patients complaining of climacturia [140].

Bladder neck dissection in RP can be more challenging in men with enlarged median/lateral prostate lobes [156–160] or prior transurethral resection of the prostate (TURP) for benign prostatic hyperplasia [160–164]. RP in patients with large median lobes can leave a large bladder neck defect, injure the ureteric orifices, and cause ureteric obstruction during subsequent urethrovesical anastomosis. Concern about these factors may lead surgeons to dissect too close to the prostate, creating an inadvertent PSM at the prostate base or bladder neck [157]. Retracting the median lobe anteriorly may facilitate bladder neck dissection. This can be achieved via traction on the Foley catheter [158]; directly via an atraumatic grasper in the fourth robotic arm [160,165]; or passing a “rescue stitch” with a Hem-o-lok clip at the tail end through the enlarged intravesical prostate lobes [159]. Subsequent to posterior bladder neck transection, robot-assisted placement of 6 Fr double pigtail catheters [156] or double J stents [157] into the ureters to identify the ureteric orifices before performing urethrovesical anastomosis has been described in patients with median lobes or cancer protruding into the bladder neck. An enlarged prostate gland or a median lobe can significantly increase blood loss, length of hospital stay, requirement for bladder neck reconstruction, and operative time needed for bladder neck dissection and urethrovesical anastomosis, but there is no significant difference in urine leakage, bladder neck contracture, or continence rates [156–160,166,167]. There is no difference in overall PSM rates after RARP in men with or without median lobes (9.5–10% vs. 11–13.6%, respectively) [158,160]. RARP in men with a large prostate gland is associated with significantly lower PSM rates [166,168].

Men with prior TURP may have wide bladder necks and scar tissue present that can make identification of the ureteric orifices and bladder neck dissection challenging.

Prior TURP can lead to: higher overall PSM rates in men undergoing LRP [169] and RARP [170]; higher bladder neck [170,171] and prostate base margin positivity [160]; anastomotic stricture after LRP [162]; bladder neck contracture after open RRP [145,172]; greater need for bladder neck reconstruction and increased operative time in RARP [164]; and higher rates of anastomotic leak in LRP and open RRP [169,173]. Continence is not affected [162].

***b) Anterior versus posterior approach to the seminal vesicles (only for transperitoneal approach)***

In the initial nine cases of LRP [2], the intention was to reproduce open anatomical Walsh retrograde RP [72]. The bladder was released from the anterior abdominal wall and the prostate was released at the apex. The prostate and nerves were dissected in a retrograde manner and seminal

vesicle dissection was the final step in extricating the prostate. Subsequently, Guillonneau and Vallancien introduced the idea of starting the dissection by incising the peritoneum in the pouch of Douglas and accessing and freeing the seminal vesicles [73] **(Figure 20)**. Menon and Tewari [74], describing the Vattikuti Institute RARP, introduced the idea of early transection of the anterior and posterior bladder neck and then releasing the seminal vesicles.

With the posterior approach, dissection begins in the pouch of Douglas, and proponents claim easier identification and dissection of the vas deferens and seminal vesicles and easier transection of the posterior bladder neck. The most potent theoretical reason discouraging the posterior approach is that sympathetic hypogastric nerves in the line of dissection between the lateral borders of the SVs are transected. We know from testicular cancer that injury to the hypogastric plexus can affect bladder neck function and orgasmic sensation [75].

***c) Anterior bladder/prostate junction and anterior prostatic fat***

Removing the anterior prostatic fat can have three advantages: (1) reduce PSM at the apex; (2) improve visualisation of the dividing line between the prostate and bladder during transection of the anterior bladder neck; and (3) remove the lymph nodes on ~15% of occasions. In 1–2% of cases, these lymph nodes can harbour the only site of lymph node metastasis [76–79].

***d) Surgical technique for apical dissection***

Apical dissection of the prostate is performed after complete mobilisation of the prostate **(Figure 21)**. It may be useful to increase intra-abdominal pressure to 20 mmHg to prevent blood spillage from the dorsal vein complex [230]. Ligature of the dorsal vein complex is beneficial in avoiding blood loss from large vessels [231]. Another option is compression of large vessels with a sponge stick or the use of a bulldog clamp [232].

The prostate is separated from the urethral sphincter by blunt dissection and cut with scissors without cautery for maximal preservation of the NVB.

The tissue covering the prostatic part of the sphincter is gently pushed cranially **(Figure 21)** until the underlying longitudinal smooth muscle becomes visible. The longitudinal smooth muscle fibres are followed intraprostatically by blunt dissection and retraction of the apical tissue.

The anterior part of the urethra is transected until the transurethral catheter becomes visible. The catheter can be lifted toward the symphysis pubis. By external traction applied to the catheter, additional compression of the dorsal vein complex is achieved to minimise blood loss. The dorsal urethra is transected. For better visualisation of the apical region, Tewari et al. described an alternative technique, using a 30° upward-facing lens in combination with retraction of the prostate [233]. By using this technique it was possible to reduce the rate of PSMs from 4.4% to 1.4%.

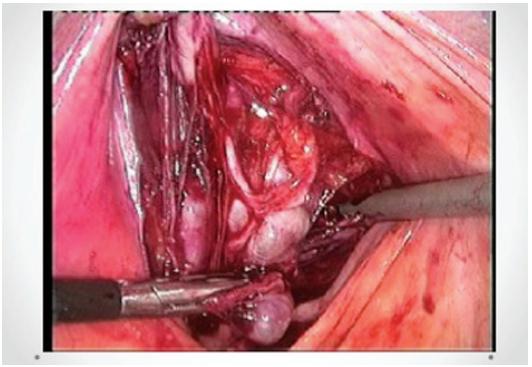


***Figure 20. Dissection of the seminal vesicle thought the Douglas pouch***

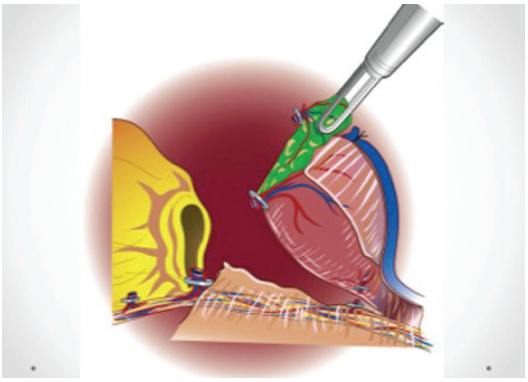


***Figure 21. Complete dissection of the posterior aspect of the prostate before apical dissection***

If the apical region of the prostate is suspicious for a PSM or residual tumour cells remain in the urethra, intraoperative frozen sections should be taken. Biopsies at the apex of the prostate as well as from the urethral resection site are helpful in predicting a positive surgical margin, but there are not many further surgical options in this area, because more aggressive treatment may result in a higher rate of urinary incontinence [234]. In particular, frozen sections can reduce PSM rate for preoperative high-risk tumours and when full functional length urethral sphincter preservation is intended [235].

## 5. RETROGRADE TECHNIQUE

This approach using the principles of open RRP became known as the Heilbronn technique [122].

***a) Control of the dorsal vein complex***

Retrograde dissection starts at the apex of the prostate with control of the dorsal vein complex. The

bladder is grasped using forceps via port 5 (right lateral port) and retracted cranially. The endopelvic fascia is incised and the apex is dissected bluntly. The puboprostatic ligaments are transected. The dorsal vein complex is secured with double suturing at the apex and bladder neck to provide adequate hemostasis. A 15-cm Vicryl 2/0 with MH needle is used for intracorporal suturing. The dorsal vein complex can be transected proximal to the apical suture. If minor bleeding occurs, it may be controlled with bipolar coagulation.

***b) Transection of the urethra***

The urethra is incised at the apex of the prostate. The Foley catheter is ligated to avoid deflation of the balloon, and then it is cut at the orifice of the urethra and pulled inside the abdomen to retract the prostate cranially with a grasper. Another 20 Fr Foley catheter is placed in the urethra from outside for better identification of the urethral stump. Finally, the urethra is transected completely.

***c) Control of the distal pedicles and sparing of the neurovascular bundles***

In case of non-nerve sparing LRP, both NVBs and the distal pedicles of the prostate are dissected. Denonvilliers´ fascia is incised and the dorsal plane of the prostate is separated from the rectum. When preservation of the NVBs is attempted, the space between the urethra and the NVBs is dissected bluntly until Denonvilliers´ fascia can be identified. The rectal balloon is inflated with 40–60 ml of air. The prostatic fascia is incised and the small branches to the NVBs are controlled using 5-mm titanium clips. Hem-o-lock clips are not used near the urethra, to avoid migration into the anastomosis, electric energy sources are not used near the NVBs, to avoid nerve damage.

***d) Transection of the bladder neck***

The apex of the prostate is pulled ventrally again using the cut Foley catheter as a retractor. The bladder neck is incised, followed by the descending part of the prostatectomy. After incision of the bladder over the blocked balloon of the Foley catheter, the balloon is deflated with a cut into the catheter distal to the ligature. The catheter can be grasped U-shaped and used again as a retractor for the prostate. The ureteral orifices are identified, and the bladder neck is cut completely. The next step is the dissection of the proximal pedicles of the prostate and the transection of the right and left vas deferens.

***e) Dissection of seminal vesicles***

Retrovesical access to the seminal vesicles is now accomplished, both seminal vesicles are completely exposed, and the seminal vesical arteries are transected after clipping.

### 6. COMPARISON OF RETROGRADE AND ANTEGRADE TECHNIQUE:

***a) Advantages of antegrade technique***

Early control of the proximal prostatic pedicle, resulting in reduced bleeding.

Early control of the arteries of the seminal vesicles.

Better working angle for the instruments

***b) Disadvantages of antegrade technique***

1. Suboptimal exposure of prostatic base during control of prostatic pedicles.
2. Later identification of the NVBs still covered by the levator fascia.

***c) Advantages of retrograde technique***

1. Early control/haemostasis at dorsal vein complex
2. Earlier identification of NVBs
3. Exposure of NVBs during every step

***d) Disadvantages of retrograde technique***

1. Late control of the proximal prostatic pedicle
2. Technically more difficult than antegrade technique

### 7. INGUINAL HERNIAS

An under-reported consequence and/or complication of RARP or LRP is inguinal hernia. The risk of inguinal hernia formation following LRP or RARP is lower than that with open RP and occurs in 5–6.4% of patients following RARP [79,82]. Repair of symptomatic hernias was recently endorsed in the Pasadena consensus [83]. Others have recommended repair of all inguinal hernias due to a low complication rate associated with the new synthetic meshes that do not need re-retroperitonealisation [84], but presently there is no high level of evidence supporting this.

### 8. SPECIMEN RETRIEVAL AND COMPLETION OF THE PROCEDURE

The fascial opening at the periumbilical camera trocar site is widened just enough to extract the specimen. Only closure of the anterior rectus sheath is necessary. Occasionally, a small opening is required in the posterior rectus sheath and peritoneum to release air trapped in the peritoneum, which should be suspected if tympany is noted with abdominal percussion. No fascial closure is necessary for the other trocar sites given their extraperitoneal location.

## IV. POSTOPERATIVE MANAGEMENT

Postoperative management of patients treated with RARP is influenced by several factors related to important differences in terms of national health care systems, personal habits, and cultural background. The aim of this chapter is to help with standardisa-

tion of postoperative management of patients treated with RARP.

## 1. HOSPITAL STAY

Typically, patients treated with RARP have rapid recovery immediately after the surgical procedure. In most studies from high-volume centres, patients were mobilised and allowed to drink clear liquid on the night of surgery [117,271].

The majority of patients are discharged on postoperative day 1 or 2 once they are ambulatory and tolerate food with minimal discomfort, after drain removal [295–297]. After RARP, most patients experience mild/moderate abdominal discomfort, which improves steadily over a few days. In cases of discomfort or pain, oral ketorolac or opiates are the preferred choices. However, there is a rapid decline in the average medication use that corresponds to the subjective improvement in pain symptoms [298].

## 2. PERIOPERATIVE OUTCOMES AND COMPLICATIONS

RARP can be performed routinely within a short time, with low risk of blood loss and low transfusion rates. The Pasadena systematic review of the literature demonstrated an overall mean operative time of 152 min (range: 90–291 min), mean blood loss of 166 ml (range: 69–534 ml), mean transfusion rate <2% (range: 0.5–5%), mean catheterization time of 6.3 days (range: 5–8.6 days), and mean hospital stay <1.9 days (range: 1–6 days) [Novara, 2012]. Obesity, large prostate volume, prior abdominal surgery, prior surgery for benign prostate hypertrophy, or presence of median lobe may make RARP more challenging, thus increasing operative time, blood loss, or catheterization time. Surgical experience (e.g., number of cases performed, or achieving a fellowship training in RARP) is associated with better perioperative outcomes.

Postoperative complications are uncommon after RARP. The overall mean rate is 9% (range: 3–26%). The mean rates of complications are: grade 1, 4% (range: 2–11.5%); grade 2, 3% (range: 2–9%); grade 3, 2% (range: 0.5–7%); grade 4, 0.4% (range: 0–1.5%); and grade 5, 0.02% (range: 0–0.5%). The most common surgical complications are: lymphocoele or lymphorrhoea (mean: 3.1%; range: 1.2–29%), urinary leakage (mean: 1.8%; range: 0.1–6.7%) and reoperation (mean: 1.6%; range: 0.5–7%) [Novara, 2012].

Several studies have compared perioperative outcomes and complications in RRP, LRP and RARP. With regard to RARP and RRP, Novara's meta-analysis showed significant differences for rates for blood loss [weighted mean difference (WMD): 582.77; 95% confidence interval (CI): 435.25–730.29; P<0.00001] and transfusion rate [odds ratio (OR): 4.85; 95% CI: 2.86–8.22; P<0.00001) in favour of RARP, whereas rates for operative time (WMD: −15.8; 95% CI: −68.65 to 37; P=0.56) and overall complications (OR: 1.1; 95% CI: 0.59–2.04; P=0.76) were similar for RARP and RRP [Novara, 2012]. Previous meta-analysis conclusions were confirmed by two more recent non-randomised comparative studies [Liu, 2013; Alemozaffar, 2014]. Using the National Surgical Quality Improvement Program database, Liu et al. compared 4036 MIRPs and 1283 open RPs. They observed significantly less perioperative blood transfusion (1.3% vs. 21%) and fewer major complications (5% vs. 9%) in the MIRP group in comparison with RRP [Liu, 2013]. Alemozaffar et al. compared 621 RRPs with 282 RARPs and found a significant difference in mean blood loss (852 vs. 207 ml; P<0.001) and transfusion rates (30.3% vs. 4.3%; P<0.001) in favour of RARP [Alemozaffar, 2014].

Conversely, rates for operative time (WMD: 34.78; 95% CI: −1.36 to 70.93; P=0.06), blood loss (WMD: 54.21; 95% CI: −75.17 to 183.59; P=0.41), and overall complications (OR: 1.24; 95% CI: 0.8–1.93; P=0.34) were similar in LRP and RARP. Only the transfusion rate (OR: 2.56; 95% CI: 1.65–3.96; P<0.00001) was significantly lower in RARP patients [Novara, 2012]. The equivalence of perioperative outcomes and complications between RARP and LRP was recently confirmed in a randomised controlled trial (RCT) [Porpiglia, 2013].

RARP can be performed routinely with a low risk of complications [level of evidence (LE) 2-3, grade of recommendation (GR) B]. Surgical experience, patient characteristics, and cancer characteristics may affect the risk of complications. RARP and LRP offer significant advantages in terms of transfusion rate and blood loss in comparison with RRP [LE 2, GR B]. No significant differences between the different approaches were observed in terms of postoperative complications [LE 2, GR B].

## 3. URETHRAL CATHETER REMOVAL

Postoperative urine drainage after vesicourethral anastomosis during RARP remains an integral part of the operation and has traditionally been maintained using a urethral catheter.

Depending on the surgeon's preference and individual patient considerations, urethral catheter removal takes place between postoperative days 4 and 10 after RARP [271,274,297,299]. In community settings, especially during the learning curve of RARP, a more conservative approach has been reported, with catheter removal around postoperative day 7 [8]. However, in referral centres with a high annual case load, urethral catheter removal is anticipated between postoperative days 2 and 4, without compromising urinary continence recovery or increasing the risk of postoperative complications [300,301]. However, early catheter removal, is associated with a higher rate of urinary retention (5–10%) [302,303].

If a watertight anastomosis has been achieved during RARP, voiding cystography before urethral catheter removal is not routinely recommended, because in most patients, urine leakage is absent [117]. In patients with evident urine leakage, the catheter should be left in place until a subsequent cystogram reveals resolution, typically 1 week later.

Some authors have questioned the need for urethral catheter placement during RARP. Urethral catheterisation may represent a significant source of discomfort following RARP, associated with physical limitations [304]. It has been argued that long-term catheterisation may play a role in enhancing postoperative inflammation, increasing the risk of bladder neck or urethral strictures [305].

Some authors suggest the use of a suprapubic tube to reduce catheter-related discomfort. The suprapubic tube is maintained in place for 5 days after RARP and then clamped. On postoperative day 7, if the residual urine volume is <50 ml per void, the suprapubic tube is removed [306]. However, a recent RCT demonstrated a lack of significant advantages of suprapubic tube placement in terms of pain, catheter-related problems, and treatment satisfaction [301].

## 4. PELVIC DRAINAGE REMOVAL

The use of a pelvic drain in patients treated with RARP with or without pelvic LND is controversial. The intended role of pelvic drain is the potential collection of urinary extravasation or prevention of symptomatic lymphocoeles when pelvic LND is performed. Most drains play little role in the postoperative course of men undergoing RARP and they are commonly removed within 24 h of patient discharge [16]. However, pelvic drainage is associated with high patient morbidity, infection, prolonged hospital stay, and high costs [307,308]. When the urethrovesical anastomosis is watertight, placement of a pelvic drain may be unnecessary, even if pelvic LND is performed [308,309].

To date, the decision about postoperative drain removal is usually taken at the surgeon's discretion, without the support of specific evidence-based guidelines regarding the ideal time for removal. Typically, the pelvic drain is removed if output is 100 ml/8 h within 24 h of discharge [117,271,308].

## 5. PENILE REHABILITATION AFTER RARP

Historically, ED after RP was a significant side effect with a negative impact on sexual health of patients treated for PCa. Despite the advantages of the robotic approach, a significant proportion of patients might still experience ED (6–46%) [274].

Management of post-RP ED is mainly by administration of pro-erectile drugs. The final therapeutic goal for postoperative ED is to achieve erections sufficient for satisfactory sexual intercourse. To this end, clinicians have several therapeutic options including phosphodiesterase type-5 (PDE5) inhibitors, intracavernous injection [310-313], urethral microsuppositories [314], vacuum devices, and penile implants [315].

Currently, PDE5 inhibitors represent the first-line therapy in patients undergoing nerve-sparing RARP, either unilateral or bilateral, even if there is no definitive evidence on the best treatment strategy [316,317].

Early penile rehabilitation prevents penile fibrosis development, which ultimately translate to veno-occlusive dysfunction in a time-dependent fashion after surgery [318,319].

In the clinical setting, the concept of penile rehabilitation after RP was pioneered by Montorsi et al. in 1997 [310]. Thirty patients treated with bilateral nerve-sparing (BNS)RP were randomised to receive intracorporeal injections of alprostadil early after surgery or no therapy. The rate of recovery of spontaneous erections in the groups receiving intracavernous injection was significantly higher than in those undergoing observation alone. Advent of PDE5 inhibitors has resulted in a shift toward oral treatment of postoperative ED. Sildenafil, tadalafil and vardenafil provide recovery of EF after open RP ranging from 35 to 75% among patients who undergo nerve-sparing surgery.

Padma-Nathan and colleagues published the first placebo-controlled multicentre RCT assessing the efficacy of daily sildenafil for treatment of post-RP ED in 76 men. However, the recovery of spontaneous erections was limited (27% vs. 4% for sildenafil vs. placebo) due to a high proportion of patients with preoperative EF impairment [320]. Bannowsky et al. evaluated the effect of low-dose sildenafil for rehabilitating EF after nerve-sparing RP. Forty-three sexually active patients were randomised to receive either placebo or sildenafil 25 mg/day at night. In the sildenafil group, 47% achieved and maintained an erection sufficient for vaginal intercourse at 1 year after surgery, compared with 28% in the control group [321].

Montorsi *et al.* evaluated 303 potent men treated with BNSRP and randomised to receive tadalafil 20 mg on demand or placebo. In patients treated with tadalafil, 71% reported an improvement in EF as compared to 24% of those treated with placebo ($P<0.001$). Tadalafil 20 mg achieved a 52% rate of successful intercourse, which was significantly higher than the 26%, obtained with placebo ($P<0.001$) [322]. Despite the encouraging results, to date the optimal treatment regimen after BSRP has still to be clearly defined. Only a few reports have compared the role of on-demand and daily

administration of PDE5 inhibitors after BNSRP. Montorsi et al. published a double-blind, double-dummy, multicentre, parallel-group study of 628 patients randomised to receive vardenafil nightly and vardenafil on-demand or placebo. Surprisingly, in contrast to the hypothesised prophylactic use of PDE5 inhibitors for penile rehabilitation, this study demonstrated higher EF recovery rates in patients randomised to the on-demand use of PDE5 inhibitor [323]. Similar results were obtained by Pavlovic et al. in a double-blind RCT of nightly versus on-demand 50 mg sildenafil after nerve-sparing MIRP. Again, the authors failed to demonstrate any significant differences in EF between treatments, after adjusting for potential confounding factors [324].

However, it has been hypothesised that the observed lack of superiority of rehabilitation may be related to the pharmacokinetic profile of the PDE5 inhibitors used in the trials. Sildenafil and vardenafil both have a short half-life, which may limit achievement of a continuous therapeutic dose with single daily administration. Therefore, Montorsi et al. investigated the effect of tadalafil 5 mg/daily and 20 mg on demand versus placebo on the rate of EF recovery after BNSRP in a double-blind, double-dummy, placebo-controlled RCT. Again, this study did not demonstrate superior efficacy of daily tadalafil as compared to on-demand administration [325].

In summary, none of the currently available PDE5 inhibitors showed greater efficacy when given daily as compared to on demand after BNSRP in well-designed, prospective, RCTs. These data suggest that on-demand use of PDE5 inhibitors is warranted for the prevention and treatment of ED in patients undergoing BNSRP, while daily administration is not supported by clinical evidence.

Briganti et al. proposed a group stratification to predict EF recovery in a series of patients who underwent bilateral nerve-sparing RRP [318]. They proposed a classification based on preoperative patients features according to the risk of postoperative ED: low risk [age ≤65 years, IIEF-EF ≥26, and Charlson Comorbidity Index (CCI) ≤1], intermediate risk (age 66–69 years, IIEF-EF 11–25, and CCI ≤1), and high risk (age ≥70 years, IIEF-EF ≤10, and CCI ≥2). Based on this classification, which was subsequently externally validated in a population treated with RARP [326], the same group analysed different treatment schedules according to risk categories. There was a significant improvement in the 3-year EF recovery related to daily therapy with PDE5 inhibitor as compared with on-demand administration, but only in patients with intermediate risk of ED after BNSRP (74% vs. 52%; P=0.02). On the contrary, no differences were noted between on-demand and daily treatment in patients with low or high risk of ED after surgery. It may be that in patients with more favourable preoperative characteristics, the probability of recovering EF is high, regardless of the type of PDE5 inhibitor administered, due to their excellent baseline profile [36]. Similarly, in patients with a high risk of postoperative ED, the potential benefit of rehabilitation is masked by the already compromised EF. Conversely, daily PDE5 inhibitor administration was more effective than on-demand administration in patients with intermediate risk of postoperative ED. The maximal effect of penile rehabilitation is obtained in men with partial impairment of preoperative EF. These results need to be confirmed in large, prospective RCTs [327].

### 6. PELVIC FLOOR REHABILITATION AFTER RARP

Urinary incontinence in patients treated with RARP ranges from 4 to 31% [129]. In most men, urinary incontinence progressively improves after RARP and spontaneous recovery may take as long as 1–2 years after surgery [269]. Pelvic floor muscle training may provide faster recovery of continence after RP [328-331].

Some authors advocate a potential role for preoperative pelvic floor muscle training, because it is associated with improvement in continence recovery. However, the presence of several biases (significant differences in terms of treatment regimens, continence definitions, and length of follow-up) and the limited number of patients reduced the reproducibility of those results [332].

In general, conservative management is advised as the main approach for urinary incontinence after RP. EAU guidelines state that men undergoing some form of pelvic floor muscle training, before or after RP achieve continence more quickly than untreated men do [333].

## V. OUTCOMES OF RARP

In 2012, four systematic reviews and meta-analyses summarised perioperative, oncological and functional (urinary continence and potency recovery) outcomes in case series and comparative studies published until August 2011 [Novara, 2012; Ficarra, 2012; Novara, 2012; Ficarra, 2012]. We performed an update of our previous systematic review to select the most relevant studies reporting RARP outcomes and published until February 2014.

### 1. ONCOLOGICAL OUTCOMES

Considering the long natural history of PCa and the available follow-up in RARP series, most of oncological data concerning RARP are still represented by surrogate end-points as well as the rate of PSMs and biochemical disease-free survival

(bDFS). Data on metastasis-free and cancer-specific survival are immature.

The Pasadena systematic review showed that the mean prevalence of PSMs after RARP was 15% (range: 6.5–32%). According to the pathological extension of primary tumour, the mean PSM rate was 9% (range: 4–23%) in pT2 cancers, 37% (range: 29–50%) in pT3 cancers, and 50% (range: 40–75%) in pT4 cancers. The most prevalent site of PSM after RARP was the apex in 5% (range: 1–7%) of cases, posterolateral surface in 2.6% (range: 2–21%), bladder neck in 1.6% (range: 1–2%), and anterior surface in 0.6% (range: 0.2–2%). Prostate volume, clinical T stage, biopsy Gleason score, presence of perineural invasion, and surgeons' experience were the most relevant predictors of PSMs after RARP [Novara, 2012].

More controversial is the impact of the extent of preservation of NVB dissection on PSM rates. In 2013, Srivastava et al. demonstrated that the use of an appropriate preoperative algorithm for a risk-stratified approach to nerve-sparing surgery does not compromise the oncological safety of the procedure [Srivastava, 2013]. Similarly, cancer control is not influenced by the antegrade or retrograde nerve-sparing technique during RARP. In 2013, Ko et al. published a matched pair analysis comparing 172 cases each that underwent antegrade nerve-sparing or retrograde nerve-sparing surgery. The overall PSM rate was 11.6% after the antegrade approach and 7% after the retrograde approach. A non-significant difference was detected after data stratification according to pathological stage. In pT2 tumours the PSM rates were 7.9% and 4.6% after the antegrade and retrograde approach, respectively.

Meta-analysis of available comparative studies revealed a non-significant difference in overall PSM rates following RRP and RARP [Novara, 2012].

Some studies comparing RARP and RRP were published after the previous meta-analysis [Silberstein, 2013; Pierorazio, 2013; Park, 2014; Thompson, 2014; Alemozoffor, 2014; Sooriakumaran, 2014] (Table 1). Most these studies confirmed the overlapping PSM rates between the open and robot-assisted approaches to RP [Silberstein, 2013; Park, 2014; Alemozaffar, 2014]. However, Pierorazio et al. analysed a large series of patients who underwent RP at Johns Hopkins University, Baltimore, USA. There was a higher overall PSM rate in the 1422 patients who underwent RARP in comparison with the 4950 who underwent RRP (18.1% vs. 13.2%; P<0.001). This difference in favour of open surgery was confirmed by analysing only pT2 cases (8.4% vs. 4.1%; P<0.001) [Pierorazio, 2013]. Conversely, a large multinational, multi-institutional study comparing 22,393 patients who underwent open RP, LRP or RARP showed lower PSM rates after minimally invasive procedures in comparison with open surgery. In detail, the overall PSM rates were 13.8% after RARP, 16.3% after LRP and 22.8% after RRP, respectively. Cox regression with propensity scores for adjustment and covariates confirmed the significant advantages in favour of MIRP in comparison with RRP [Sooriakumaran, 2014]. The potential impact of the learning curve on PSM rates after RARP has been analysed. In a prospective, single-surgeon study of 1552 consecutive cases treated in Australia from 2006 to 2012, Thompson et al. observed that in pT2 tumours, the PSMs after RARP became lower in comparison with RRP after 108 procedures and 55% lower after >860 procedures. Similarly, in pT3/4 cases, PSMs reached a plateau after 200–300 RARPs [Thompson, 2014].

An RCT comparing prevalence of PSMs after 60 RARPs with 60 LRPs showed overlapping results. Overall PSM rates were 20% and 26% after LRP and RARP, respectively. Similarly, PSM rates in pT2 cases were 16% and 13.5%, respectively [Porpiglia, 2013].

With regard to bDFS, only a few studies have reported data with acceptable follow-up. In 2010, Menon et al. reported 1384 patients at a median follow-up of 60 months. The 3-, 5- and 7-year bDFS rates were 90%, 87% and 81%, respectively, with 95.5% cancer-specific survival [Menon, 2010]. Similar results were reported by Sooriakumaran et al. in ~1000 patients evaluated at a median follow-up of 6.3 years [Sooriakumaran, 2012]. More recently, Ficarra et al. analysed bDFS in 183 consecutive patients with a minimum follow-up of 5 years after RARP. The 3-, 5- and 7-year bDFS was 96.3%, 89.6% and 88.3%, respectively [Ficarra, 2013]. In 2014, the Vattikuti Urology Institute published the largest report of oncological outcomes to date, analysing long-term follow-up of 4803 patients who underwent RARP between September 2001 and December 2010 and who were followed up until April 2011. The actuarial 8-year bDFS, metastasis-free survival and cancer-specific survival were 81%, 98.5% and 99.1%, respectively [Sukumar, 2014].

Meta-analysis of comparative studies published in 2012 revealed no significant differences in bDFS between RRP and RARP (hazard ratio: 0.9; 95% CI: 0.7–1.2; P=0.526) or between LRP and RARP (hazard ratio: 0.5; 95% CI: 0.2–1.3; P=0.141) [Novara, 2012]. Three recent studies comparing bDFS in RARP and RRP confirmed these results. [Silberstein, 2013; Park, 2014; Alemozaffar, 2014].

In agreement with the Pasadena consultation and the recent recommendations of the EAU guidelines, we can conclude that RARP offers positive surgical margin rates at least equivalent to those of RRP and LRP [LE 2, GR B]. Preliminary data from large series show that high-volume robotic surgeons can achieve progressively superior results in comparison with traditional open surgery [LE 2, GR B]. Several large case series have shown good long-term prostate-specific antigen (PSA)-free survival of pa-

tients treated with RARP [LE 3, GR B]. Some non-randomised comparative studies have confirmed the equivalence between RARP and RRP in terms of bDFS [LE 3, GR B]. However, the median follow-up of these studies is not yet adequate for definitive conclusions. Finally, significant data on metastasis-free survival and cancer-specific mortality are not currently available.

## 2. URINARY CONTINENCE

The Pasadena systematic review showed that 12-month urinary incontinence rates following RARP ranged from 4% to 31% (mean: 16%) in studies adopting the continence definition of "no pad". In studies using "no pad or safety pad" as the continence definition, 12-mo urinary incontinence rates ranged from 8% to 11% (mean: 9%) [Ficarra, 2012]. Ficarra et al. reported functional outcomes in patients with long-term follow-up. Continence rates were 39% at 1 month, 73% at 3 months, 87% at 6 months and 91% at 12 months. The median time to reach continence was 2 months and no other patients became continent after 12 months [Ficarra, 2013]. Beyond the well-known concerns about study quality and methodological issues due to different definitions and methods used for data collection, some patient characteristics such as age, high body mass index (BMI), large prostate volume, and surgical experience can affect recovery of urinary continence after RARP. Similarly, several surgical aspects can influence continence rates – anterior and posterior anastomosis reconstruction techniques being the most relevant.

A 2013 survey showed that 52% of urologists routinely performed posterior musculofascial plate reconstruction, 20% sometimes, and 28% never [Ficarra, 2013]. The role of posterior reconstruction in early recovery of continence is still controversial. Although two RCTs showed negative results, two meta-analyses showed a small advantage in favour of posterior reconstruction for continence recovery at 1 month after RARP. Conversely, posterior reconstruction showed no advantage for continence at 3 and 6 months after RARP over the standard approach [Ficarra, 2012; Rocco, 2012]. Similarly, total (anterior and posterior) reconstruction was evaluated in a few comparative studies and cumulative analysis showed a small significant difference in favour of total reconstruction at 1 month after RARP (OR: 0.40; 95% CI: 0.16–0.96; P=0.04) [Ficarra, 2012].

Another controversial issue is the role of nerve-sparing procedures in early and late recovery of urinary continence. In fresh cadaveric models, Takenaka et al. observed that the NVB followed a straight proximal-to-distal course along the urethra, but histological analysis revealed that these nerves adopted either a frontal, sagittal or axial course. These nerves either traversed through the connective tissue that is interposed between the rhabdosphincter and levator ani muscle, or travelled ventromedially in the pararectal space. Thick myelinated and thin non-myelinated fibres from nerve bundles originating from the splanchnic nerve were identified. Takenaka et al. believed that these thick myelinated fibres accounted for the motor innervation of the rhabdosphincter, thus supporting the theory that the fibres responsible for continence course along the cavernous nerve. Hence, it is believed that preservation of the cavernous nerve safeguards the adjoining continence fibres (Hollabaugh RS, Steiner MS, 2001) [Takenaka UROLOGY 65: 136–142, 2005] Takenaka Tewari, 2007, J. Urol **Figure 1**) and Hinata N, Murakami G, Urology 2014). Two papers published after the Pasadena meta-analysis analysed this aspect [Srivastava, 2013; Tewari, 2013]. Srivastava et al. analysed the impact of different grades of nerve-sparing techniques on early return of continence in 1417 patients who underwent RARP from December 2008 to October 2011 by a single surgeon. Using no pad as the definition of urinary continence, the authors reported a 3-month urinary continence rate of 71.8% in the grade 1 group, 54.7% in grade 2, 45.7% in grade 3, and 43.5% in grade 4 (P<0.001). The favourable impact of grade of cavernous nerve preservation on early recovery of urinary continence was confirmed in a multivariate analysis [Srivastava, 2013]. The same team published a second case series of 1335 patients who underwent RARP between January 2005 and December 2010 by a single surgeon. Patients included in this retrospective analysis were preoperatively continent and potent and were followed up for ≥1 year. The 1-year continence rates were 98% in grade 1, 93.2% in grade 2, 90.1% in grade 3, and grade 4 in 88.9% (P<0.001). This study confirmed the independent predictive role of nerve-sparing extension on 1-year continence recovery [Tewari, 2013].

In 2014, Hinata et al. investigated the impact of NVB preservation on recovery from sphincter fatigue symptoms following RARP [Hinata 2014]. In a cohort of 11 patients who underwent RARP, overall continence rates of 42.2%, 58.3% and 79.1% were reported at 1, 3 and 6 months, respectively. A significant difference in the continence rates was observed between the patients who underwent bilateral NS, unilateral NS or a non-nerve-sparing procedure at 1 (P=0.0045) and 3 months (P=0.0343), but not at 6 months (P=0.9615). The continence rates at 1 and 3 months were 54.3% and 68.6% for the BNS group, 50.0% and 64.1% for the unilateral NS group, and 28.6% and 47.6% for those who had non-nerve-sparing RARP. Similarly, the frequency of sphincter fatigue symptoms at 1 and 3 months were reported to be 43.8% and 36.4% for the bilateral NS group, 52.2% and 66.7% for the unilateral NS group, and 83.3% and 77.3% for the non-NS group, thus demonstrating a significant difference among the three groups at 1 (P=0.0004) and 3 (P=0.0326) months postoperatively, but not at 6 months (P=0.4316) [Hinata J Urol 2014; 84 (1): 144 – 148].

The Pasadena systematic review retrieved eight studies comparing RARP and RRP and eight comparing RARP and LRP. With regard to RARP and RRP, meta-analysis showed that absolute risk of 12-month urinary incontinence was 11.3% after RRP and 7.5% after RARP. Therefore, the absolute risk reduction was 3.8% in favour of RARP (OR: 1.53; 95% CI: 1.04–2.25; P=0.03). In 2014, Thompson et al. investigated the impact of the learning curve for RARP on recovery of urinary continence in comparison with that for RRP. They showed that early urinary incontinence scores for RARP surpassed RRP after 182 procedures and increased to a mean difference of 8.4 points (95% CI: 2.1–14.7), reaching a plateau at 700–800 cases [Thompson, 2014].

Similarly, with regard to RARP and LRP, the Pasadena systematic review demonstrated significant advantages in 12-month continence rates in favour of RARP (OR: 2.39; 95% CI: 1.29–4.45; P=0.006) [Ficarra, 2012]. These results were recently confirmed by an RCT comparing 60 RARP with 60 LRP procedures performed by a single surgeon with expertise in both techniques. Porpiglia et al. also categorised as continent patients using a safety pad, and reported a 12-mo urinary continence recovery of 95% after RARP and 83% after LRP (P=0.04) [Porpiglia, 2013].

We conclude that RARP offers high rates of early and late continence recovery [LE 3, GR B]. The prevalence of urinary incontinence can be influenced by preoperative patient characteristics, surgeons' experience, surgical technique, and methods used to collect and report data. Posterior musculofascial reconstruction has a slight advantage in terms of 1-month urinary continence recovery [LE 2–3, GR C]. The grade of cavernous nerve preservation correlates with the rate of early and 12-month recovery of urinary continence [LE 3, GR C]. Non-randomised comparative studies showed a significant advantage in favour of RARP in comparison with RRP in terms of 12-month recovery of urinary continence [LE 2–3, GR B]. A recent RCT confirmed that RARP is better than LRP in terms of recovery of urinary continence [LE 2, GR B].

***a) Anterior suspension***

In a prospective comparative study of 331 patients, Patel et al. found a significant advantage in terms of early recovery of continence at 3 months using a single anterior suspension stitch to the pubic bone (83% vs. 92.9%; P= 0.013) [342].

The aim of this technique is stabilisation of the urethra, thus avoiding urethral retraction and facilitating urethral dissection. Patel et al. used a large needle with a non-braided absorbable suture such as Polyglytone or Caprosyn on a large CT1 needle. The needle is held about two-thirds back at a downward angle and placed in the visible notch between the urethra and dorsal vascular complex. The needle is pushed straight across at 90° and then the wrist is turned to curve around the apex of the prostate. The suture strength needs to be sufficient to allow the needle holders to pull up tight and perform a slip knot, which prevents the suture from loosening as it is tied. A second suture is placed to suspend the urethra to the pubic bone and secondarily ligate the dorsal vascular complex. The dorsal vascular complex is encircled and then stabilised against the pubic bone along with the urethra.

***b) Posterior musculofascial plate reconstruction***

In 2006, Rocco et al. proposed a technique for restoration of the posterior aspect of the rhabdosphincter, which aimed to shorten the time to continence in patients undergoing RRP [343]. In 2007, Rocco et al. described the posterior reconstruction technique for transperitoneal LRP [344]. In 2008, Coughlin et al. applied posterior reconstruction of the rhabdosphincter to RARP, with some minor technical modifications [345]. The technique was further modified in 2011 [346].

The reconstruction is performed using two 3-0 poliglecaprone sutures (on RB-1 needles) tied together, with each individual length being 12 cm. Ten knots are placed when tying the sutures to provide a bolster. The free edge of the remaining Denonvillier's fascia is identified after prostatectomy and approximated to the posterior aspect of the rhabdosphincter and the posterior median raphe using one arm of the continuous suture. As a rule, four passes are taken from the right to the left and the suture is tied. The second layer of the reconstruction is then performed with the other arm of the suture approximating the posterior lip of the bladder neck (full thickness) and the vesicoprostatic muscle, as described by Walz et al. [347], to the posterior urethral edge and to the already reconstructed median raphe. This suture is then tied to the end of the first suture arm.

One of the key steps for appropriate reconstruction is preservation of Denonvillier's fascia when dissecting the posterior plane between the prostate and the rectal wall. If this dissection is performed at the perirectal fat tissue, Denonvillier's fascia is not adequately spared, precluding posterior reconstruction.

A systematic review in 2012 showed that reconstruction of the posterior musculofascial plate improves early recovery of continence within the first 30–45 days after RP. Furthermore, a trend towards lower leakage rates has been found in patients who underwent posterior reconstruction [348].

## 3. POTENCY OUTCOMES

### *a) RALP versus RRP and LRP*

NS RALP is increasingly being adopted to improve functional outcomes. In a systematic review by Ficarra et al. [274], cumulative analysis of four prospective studies [127,275-277] comparing RALP and RRP (LE 3) and a further three historical control series [278-280] (LE 4) revealed the prevalence of ED to be 47.8% and 24.2% after RRP and RALP, respectively. This demonstrates significant advantages in terms of 12-month recovery of potency in favour of RALP. The superiority of RALP over LRP in terms of potency was confirmed more recently by Ploussard et al. in a comparison (LE 4) of 1377 extraperitoneal LRPs and 1009 extraperitoneal RARPs. In a systematic review of 31 studies reporting the potency rates after RARP, Ficarra et al. [274] reported that 12- and 24-month potency rates were 54–90% and 63–94%, respectively, following NS RALP. Their report confirmed the lower risk of ED after RALP with bilateral preservation of the cavernous nerves.

## 4. POTENCY RECOVERY

The Pasadena systematic review showed that potency recovery rates after RARP were 50% (32–68%), 65% (50–86%), 70% (54–90%), and 79% (63–94%) after 3, 6, 12 and 24 months, respectively. Considering only the studies with high methodological quality (according to the Mulhall criteria), the mean 3-, 6-, 12- and 24-month potency rates were 48% (32–68%), 68% (50–86%), 76% (62–90%), and 82% (69–94%), respectively. [Ficarra, 2012]. Similarly to the urinary continence evaluation, the adopted definition of potency and methodological differences can explain the wide variance among the studies. Several predictors can affect potency rates following RARP, including patient age, preoperative potency status, comorbidity, BMI and extent of the nerve-sparing procedure.

Studies including both unilateral and bilateral nerve-sparing procedures showed 3-, 6-, 12-, and 24-month potency rates of 32%, 53%, 69% (62–90%) and 63%, respectively, whereas the same rates for full BNS surgery were 56%, 69% (50–86%), 74% (62–90%), and 82% (69–94%), respectively. Preoperatively potent patients who underwent BNS RARP needed a median 6 months to recover potency. After 12 months, few patients further improved their potency status [Ficarra, 2013].

With regard to the comparison between RARP and RRP, a recent systematic review and meta-analyses demonstrated that the prevalence of ED, according to different definitions, was 47.8% after RRP and 24.2% after RARP, with a significant absolute risk reduction of 23.6% (OR: 2.84; 95% CI: 1.48–5.43; P=0.002). Thompson et al. estimated the number of RARP cases that were needed to achieve sexual results that were better than those with traditional RRP. Using the EPCIC quality of life questionnaire, they calculated that RARP sexual function scores surpassed RRP scores after 99 procedures, and increased to a mean difference of 11.0 points after 861 cases, reaching a plateau at 600–700 RARPs.

Comparative studies have shown that the prevalence of ED was 55.6% after LRP and 39.8% after RARP, with an absolute risk reduction of 14.8% (OR: 1.89; 95% CI: 0.70–5.05; P=0.21) [Ficarra, 2012]. This last meta-analysis included only three poor quality, retrospective comparisons using historical controls and only one RCT. This last study demonstrated a significant advantage in favour of RARP in terms of 12-month recovery of potency. At 1 year after surgery, 32% of patients were potent after LRP and 77% after RARP [Asimakopoulos, 2011]. These data were confirmed by another RCT in 2013. The authors compared 35 patients who received monolateral or bilateral nerve-sparing LRP with 35 who received the same procedure robotically. The 12-month potency rates were 54% in the LRP arm and 80% in the RARP arm (P=0.02).

In conclusion, methodological issues significantly influence the prevalence of potency recovery after RARP. With this limitation, bilateral, cautery-free, retrograde nerve-sparing techniques are associated with a higher percentage of potency recovery than unilateral, cauterising, antegrade techniques [LE 2–3, GR C]. More extended (full) nerve-sparing offers a higher probability of preserving the cavernous nerves and obtaining better functional outcomes [LE 3, GR C]. RARP is associated with significantly better results in comparison with RRP [LE 2–3, GR B] and LRP in terms of potency recovery [LE 2, GR B].

## 5. TRIFECTA

In 2003, Salomon et al. proposed combining oncological and functional outcomes in a single score [1]. In 2005, Bianco et al. suggested combining bDFS, urinary continence, and sexual potency recovery rates into the trifecta outcome to identify patients who achieved an optimal result after RP [2]. In 2012, Ficarra et al. performed a systematic review to analyse all the studies reporting outcomes as trifecta. Only five studies reported the trifecta for RARP. Trifecta can be reached in 44–83% of evaluated patients. Potency recovery is the most relevant outcome with a negative effect on the trifecta rate. Continence, potency and bDFS rates were 80–98%, 60–97% and 88–96%, respectively [Ficarra, 2012].

In 2013, Ficarra et al. reported combined outcomes of RARP using the Survival, Continence and Potency (SCP) system. In patients who were preoperatively continent and potent, who underwent a nerve-sparing technique and did not require any adjuvant therapy, combined oncological and continence outcomes were attained in 80% of cases. In

the subgroup of patients not evaluable for potency recovery, oncological and continence outcomes were reached by 68.7% of cases [Ficarra, 2013].

The SCP system was also used by Porpiglia et al. in a comparison of RARP and LRP. The system allowed us to show that P0 patients overlapped between the two compared techniques, and the main difference concerned the percentage of patients able to reach IIEF-5 score >17 with the use of PDE5 inhibitors [Porpiglia, 2012].

## VI. CONCLUSIONS

### 1. ANATOMY

| | Grade of recommendation |
|---|---|
| The parietal endopelvic fascia covers the medial aspects of the levator ani muscle, and the visceral component of the endopelvic fascia covers the pelvic organs, including prostate, bladder and rectum. | |
| The periprostatic fascia consists of the anterior, lateral and posterior prostatic fascia and seminal vesicular fascia (Denonvilliers' fascia). | |
| The structure often termed prostate capsule is not a capsule from an anatomical point of view but the exterior stromal edge of the prostate parenchyma formed by condensed smooth muscle with few glands. From a surgical point of view, a surgical capsule is visible as a clear and distinct outer edge of the prostate, reminiscent of a capsule during RP. | |
| At the posterolateral aspect of the prostate, the lateral prostatic fascia and Denonvilliers' fascia virtually merge into the NVB to split into several anterior and posterior leaves passing around the bundle to bind it in a triangular fashion with the levator ani fascia. | |
| Different dissection planes are possible during a nerve-sparing procedure. The amount of tissue that is left on the prostate can be controlled to achieve incremental tissue margins and avoid PSMs. The term incremental security margin instead of incremental nerve sparing does better reflect the true aim of the technical variation. | |
| Intrafascial dissection of the NVB follows a plane on the prostatic capsule, remaining medial or internal to the PF at the antero- and posterolateral aspect of the prostate and also remaining anterior to the posterior prostatic fascia and seminal vesicles fascia. | |
| Interfascial dissection of the NVB is performed outside or lateral to the PF at the anterolateral and posterolateral aspects of the prostate, combined with dissection medial to the NVB at the 5 and 7 o'clock or 2 and 10 o'clock positions of the prostate in axial section. | |
| Extrafascial dissection is carried out lateral to the levator ani fascia and posterior to the posterior prostatic fascia and seminal vesicular fascia. The NVB running along the posterolateral aspect of the prostate is completely resected. | |
| Surgical principles regarding sparing the NVB at RP relate to understanding its complexity and variability. | |
| A clear understanding of the neurovascular anatomy and its variations is compulsory for surgeons performing RP. | |
| There are essentially four fascial layers surrounding the prostate and NVB. | |
| The endopelvic fascia has a parietal (levator ani fascia) and visceral component. The parietal component covers the levator ani lateral to the fascial tendinous arch, and the visceral endopelvic fascia sweeps medially to cover the bladder and anterior prostate. The prostatic capsule is covered by an outer levator ani fascia and inner prostatic fascia. Posteriorly, Denonvilliers' fascia surrounds the prostate. | |
| The NVB starts at the base of the prostate between 3 and 9 o'clock. It then travels outside the prostatic capsule, inferomedially to the apex. At the apex it projects anteriorly.<br>Surgeons should understand significant inter-individual variation of NVB anatomy. | |
| In performing a complete nerve-sparing procedure, surgeons must dissect between the prostatic capsule and the periprostatic fascia, namely, the fused endopelvic fascia. | |
| The advent of 10× magnified vision with the Da Vinci system allows surgeons to see the neurovascular structures optimally. | |
| Nerve sparing can be performed antero-inferiorly or in retrograde fashion or even incrementally with some removal of the NVB tissue but not complete removal. | |
| Anatomical dissection of the NVB shows that the most likely place for damage to the cavernous nerves is at the apex. | |

## 2. TRANSPERITONEAL APPROACH

| | Grade of recommendation |
|---|---|
| The transperitoneal approach is the most widely used for RP and gives unparalleled access to perform extended pelvic LND. | C |
| Meticulous padding and avoiding hyperextension during patient positioning are essential to prevent neuropathy. | |
| Obtaining an appropriate site for insufflation of the pneumoperitoneum for port placement can be safely achieved by placing a Hasson port or a Veress needle just underneath the costochondral junction on the left. | |
| Transverse incisions compared to vertical can lead to reduction of wound complications with fewer hernias, less pain, and superior cosmesis. | B |
| Posterior approach advantages are: potentially easier to dissect the seminal vesicles, and simplification of posterior transection of the bladder neck. | |
| Posterior approach disadvantage is the potential partial transection of the hypogastric nerve, which can affect bladder neck function and orgasmic sensation. | |
| Removal of anterior prostatic fat reduces apical margins, improves visual landmarks during transection of the bladder neck, and identifies and removes metastatic lymph nodes in ~2% of cases. | C |
| Assessment of risk of nodal involvement is essential to determine necessity and extent of pelvic LND. | |
| Extended pelvic LND provides important information for prognosis, which cannot be matched by any other current procedure. Studies have recommended that 13–20 nodes are adequate for accurate staging. | C |
| Inguinal hernia repair is recommended in men when symptomatic and is a consideration in asymptomatic hernias due to low risk and its potential to prevent future need of hernia surgery. | C |

## 3. EXTRAPERITONEAL APPROACH

| | Grade of recommendation |
|---|---|
| Extraperitoneal RP simulates the gold standard open RP technique. | C |
| Extraperitoneal approach requires less steep Trendelenburg positioning. | C |
| Extraperitoneal route avoids all potential intraperitoneal adhesions and eliminates the bladder takedown step. | C |
| Significantly fewer bowel-related complications such as ileus, hernias, and intestinal injury are reported when using the extraperitoneal approach. | C |
| Avoiding bowel handling lessens the incidence of paralytic ileus, providing relatively faster recovery. | C |
| Extraperitoneal route allows containment of bleeding or urine leakage. | C |
| Extraperitoneal approach makes it difficult to space the trocars and provides limited working space, which may be inappropriate if extended lymphadenectomy is indicated. | C |
| Extraperitoneal approach carries an increased risk of lymphocoele formation following pelvic LND. | C |
| Fenestration of the peritoneum adjacent to the LND site is recommended to mitigate the incidence of lymphocoele when using the extraperitoneal approach. | C |
| Anastomotic tension is often cited as a potential disadvantage of the extraperitoneal approach, which may be relieved by posterior musculofascial plate reconstruction. | C |
| Functional outcomes of extraperitoneal RARP are equivalent to the transperitoneal approach. | C |
| Extraperitoneal RARP can be performed in patients with obesity, with pelvic kidneys, and kidney transplantation. | C |
| The only contraindication to the extraperitoneal approach is in patients who have had the extraperitoneal space created during a previous procedure, such as in mesh herniorraphy, especially where bilateral meshes are anchored to the pubic symphysis. | C |

## 4. BLADDER NECK PRESERVATION

| | Grade of recommendation |
|---|---|
| Urethral resistance and urethral length proximal to the external sphincter are postulated to play a role in maintaining continence. | C |
| Men who are continent after RP have tubularised bladder neck and functional proximal urethral length similar to the native anatomy. | C |
| A large bladder neck defect may lead to a more challenging urethrovesical anastomosis, which is a known risk factor for anastomotic leakage. | C |
| A difficult urethrovesical anastomosis, potentially resulting from a wide bladder neck defect, may be a risk factor for later bladder neck contracture. | C |
| Bladder neck dissection can be more challenging in men with enlarged median/lateral prostate lobes or prior transurethral resection of prostate for benign prostatic hyperplasia. | C |
| Patients with enlarged median/lateral prostate lobes or prior transurethral resection of prostate are more likely to need bladder neck reconstruction. | C |
| During RARP, in case of large bladder neck defect, anterior bladder neck plication may be performed; also to shorten time to recovery of continence. | C |
| During RARP, bladder neck preservation may shorten time to recovery of continence and improve quality of life. | A |
| Bladder neck preservation does not seem to increase the rate of PSMs. | C |
| A key concern in bladder neck preservation is the likelihood of leaving residual benign prostate tissue at the bladder neck, which may cause elevated PSA in the post-prostatectomy patient and mimic malignant biochemical recurrence. A negative bladder neck biopsy may not conclusively rule out the absence of benign prostate tissue at the bladder neck. | C |

## 5. APICAL DISSECTION

| | Grade of recommendation |
|---|---|
| The position of the prostate apex deep in the small pelvis as well as the close connection to the dorsal vein complex, rectum, and sphincter makes its dissection a difficult step during minimally invasive surgery. | |
| Some methods to facilitate apical dissection are: increasing intra-abdominal pressure to 20 mmHg to prevent blood spillage from the dorsal vein complex; ligature of the dorsal vein complex; and compression of larger vessels with a sponge stick or use of a bulldog clamp. | C |
| Using a 30° upward-facing lens in combination with retraction of the prostate can achieve better visualisation of the apical region. This technique can reduce the rate of PSMs. | C |
| In preoperative high-risk tumours and when full functional-length urethral sphincter preservation is intended, intraoperative frozen sections of the prostate apex and/or urethral resection can reduce PSM rate. | C |
| Currently, there is neither standardisation nor a recommendation to perform or omit frozen sections in RP. | C |
| A PSM can lead to increased biochemical recurrence. | C |
| Many factors can influence PSM: preoperative high-risk features (PSA >20 ng/ml, Gleason score ≥8, higher clinical stage); high BMI; enlarged prostate or with a narrow pelvic space. | C |
| Another factor that may influence PSM is the performance of nerve-sparing RP. | C |
| A high operative volume and surgeons beyond their learning curve can reduce the rate of PSMs significantly. | C |
| Currently, there are two different treatment options for patients with a PSM: immediate (adjuvant) postoperative external irradiation, or delay of salvage radiotherapy until local recurrence. | B |
| The best management of a positive surgical margin is striving to avoid it. | |

## 6. RETROGRADE APPROACH

| | Grade of recommendation |
|---|---|
| Minimally invasive RP with a retrograde approach can be performed with a trans- and extraperitoneal approach. | C |
| Advantages of the retrograde technique include early control of the dorsal vein complex, early identification of NVBs, and exposure of NVBs during every step. | C |
| The retrograde technique is technically more difficult than the antegrade approach and provides late control of the proximal prostatic pedicle. | C |
| Retrograde nerve sparing may improve post-prostatectomy potency. | C |

## 7. POTENCY

| | Grade of recommendation |
|---|---|
| RARP offers better 12-month potency rates when compared to RRP. | B |
| RARP offers better short-term and intermediate-term potency rate when compared to LRP. | B |
| Nerve-sparing RARP is associated with better potency outcome. | B |
| Athermal dissection during nerve sparing is supposed to result in better potency outcome. | C |
| With the limited amount of data available, traction-free nerve sparing during RARP results in early recovery of potency. | C |
| Intrafascial nerve sparing is associated with improved potency rates when compared to the interfascial nerve-sparing approach, but this can be at the expense of an increased rate of PSMs. | C |
| Cavernosal nerve preservation is a graded phenomenon and not an "all-or-nothing" concept. | C |
| Higher degree of nerve sparing is associated with better sexual outcomes. | C |
| Retrograde nerve sparing is associated with better potency outcome at 3, 6 and 9 months. | C |
| Nerve sparing during RARP results in better urinary function and continence outcomes. | C |
| Intrafascial nerve sparing is associated with early return to continence and better short-term continence rates. However, this may be associated with higher rates of PSMs. | C |
| Better degree of nerve sparing is associated with early return of continence. | C |

## 8. POSTOPERATIVE MANAGEMENT

| | Grade of recommendation |
|---|---|
| In most high-volume centres, patients are mobilised and allowed to drink clear liquid on the night of surgery. | C |
| Most patients are discharged on postoperative day 1 or 2, after drain removal (if positioned). | C |
| In case of discomfort or pain, oral ketorolac or opiates are the preferred choice. | C |
| Catheter removal has been reported between postoperative days 4 and 10. | B |
| In high-volume centres, catheter removal is anticipated between postoperative days 2 and 4, without compromising recovery of urinary continence or increasing the risk of postoperative complications. | B |
| If a watertight anastomosis is obtained, voiding cystography before catheter removal is not routinely recommended. | C |
| In patients with urine leakage, the catheter should be left in place until a subsequent cystogram reveals resolution, typically 1 week later. | C |
| A suprapubic tube can be used instead of the catheter. However, this does not bring significant advantages in terms of pain, catheter-related bother, and satisfaction when compared with early catheter removal. | A |
| The role of a pelvic drain to manage potential collection of urine or lymph is controversial. Pelvic drains are associated with higher patient morbidity, infection, prolonged hospital stay, and increased costs. When the urethrovesical anastomosis is watertight, the placement of a pelvic drain may be considered unnecessary, even if LND is performed. | C |
| Pelvic drain is typically removed if output is 100 ml/8 h within 24 h of discharge. | C |
| Despite the advantages of the robotic approach, a significant proportion of patients might still experience ED (6–46%), with different degrees of severity. | C |
| The final goal of treatment of postoperative ED is to achieve erection sufficient for satisfactory sexual intercourse. Therapeutic options include PDE5 inhibitors, intracavernous injections, urethral microsuppositories, vacuum devices, and penile implants. | B |

| | Grade of recommendation |
|---|---|
| PDE5 inhibitors represent first-line therapy in patients who undergo nerve-sparing RARP, either unilateral or bilateral. | C |
| There is evidence for early penile rehabilitation prior to penile fibrosis development. | C |
| Tadalafil, low-dose sildenafil and vardenafil can be used for penile rehabilitation. | A |
| The used of a vacuum erection device together with PDE5 inhibitors can have a beneficial effect. | C |
| Vardenafil on demand shows better recovery rates compared to vardenafil nightly. | A |
| No significant difference was found between the use of sildenafil nightly or on demand. | A |
| No significant difference was found between the use of tadalafil 5 mg nightly or 20 mg on demand. | A |
| In patients with more favourable preoperative characteristics, the probability of recovering EF is high, regardless of the type of PDE5 inhibitor administered. | C |
| In most men, urinary incontinence shows progressive improvement after RARPand spontaneous recovery may take as long as 1–2 years after surgery. | C |
| Pelvic floor muscle training can shorten time to continence and improve the severity of incontinence, voiding symptoms and pelvic floor muscle strength 12 months postoperatively. | A |
| Pre- and postoperative pelvic floor muscle training does not improve continence when compared with postoperative training only. | A |

## 9. OUTCOMES

| Oncological outcomes | Grade of recommendation |
|---|---|
| RARP offers positive surgical margin rates at least equivalent to those of RRP and LRP. | B |
| Preliminary data from large studies show that high-volume robotic surgeons can achieve progressively superior results in comparison with traditional open surgery. | B |
| Available large case series have shown good long-term PSA-free survival of patients treated with RARP. | B |
| Non-randomised comparative studies have confirmed the equivalence between RARP and RRP in terms of bDFS. | B |
| Significant data on metastasis-free survival and cancer-specific mortality are not currently available. | |

| Urinary continence outcomes | Grade of recommendation |
|---|---|
| RARP offers high early and late continence rates. | B |
| Posterior musculofascial reconstruction seems to offer a slight advantage in terms of 1-month recovery of urinary continence. | C |
| The grade of cavernous nerves preservation correlates with the percentage of early and 12-month recovery of urinary continence. | C |
| Non-randomised comparative studies have shown a significant advantage in favour of RARP in comparison with RRP in terms of 12-month recovery of urinary continence. | B |
| A recent RCT has confirmed that RARP is better than LRP in terms of recovery of urinary continence. | B |

| Potency recovery | Grade of recommendation |
|---|---|
| Recovery of potency after RARP is significantly influenced by methodological issues. With this limitation, bilateral, cautery-free, retrograde nerve-sparing techniques are associated with greater recovery of potency. | C |
| More extended (full) nerve-sparing surgery offers a greater probability of preserving cavernous nerves and achieving better functional outcomes. | B |

| Perioperative outcomes and complications | Grade of recommendation |
|---|---|
| RARP can be performed routinely with a relatively small risk of complications. | B |
| Surgical experience, patient characteristics, and cancer characteristics may affect the risk of complications. RARP and LRP offer significant advantages in terms of transfusion rate and blood loss in comparison with RRP. | B |
| There are no significant differences in postoperative complications between the different approaches. | B |

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## Committee 2

# Minimal Invasive Adenomectomy

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# Minimal Invasive Adenomectomy

*R. Sotelo, H. John*

*Sascha Ahyai, Alexander Bachmann,*
*C. Fiori, T. Herrmann, D-V. Matei, M. Mirandolino, L. Nuñez,*
*F. Porpiglia, R. Scarpa, M. Seitz*

## I. INTRODUCTION

Transurethral resection of the prostate (TURP) has b een the gold standard for the surgical management of benign prostatic obstruction (BPO) for >70 years. However, in the past few years, several minimally invasive treatments have been developed as alternatives to TURP. Therefore, updated clinical recommendations for minimally invasive adenomectomy are mandatory.
The efficacy of TURP has been improved by the introduction of continuous-flow resectoscopes as well as bipolar resection technology. Transurethral microwave thermotherapy has been proposed, as well as transurethral needle ablation of the prostate, holmium and thulium laser technology, and photoselective vaporisation of the prostate. For large glands, laparoscopic prostatectomy and robotic simple prostatectomy are alternatives, in addition to open simple prostatectomy and transurethral enucleation. These alternative surgical techniques and the increase in medical therapy with a-blockers, 5-a-reductase blockers, anticholinergics, and their combinations have led to a progressive decrease in the use of TURP.

Patient selection and comorbidity may influence the choice of surgical technique to decrease infravesical obstruction. Efficacy and safety profiles are mostly similar between the different transurethral approaches. A urological department should offer at least one alternative to conventional monopolar TURP, for example, bipolar TURP or a laser technique. Currently, the decision to make is whether to resect, vaporise or encucleate. Finally, no new technology can ever replace a trained surgeon and optimal results with new technologies can only be achieved with an expert-controlled learning curve.

## II. LASER TECHNOLOGIES

### 1. INTRODUCTION

Albert Einstein has discovered the physical principals of lasers in 1917. Thirty years later, Gordon Gould introduced the acronym LASER (light amplification by stimulated emission of radiation). Laser light consists of one wavelength and, in contrast to ordinary light, it is monochromatic, unidirectional and coherent. With the invention of the “ruby”, the first laser, on May 16, 1960 by Theodore Maiman, the search began for its clinical application alias, “solution looking for a problem”. The first laser in urology to be investigated as a minimally invasive alternative to transurethral resection of the prostate (TURP) was the neodynium: yttrium aluminium garnett (YAG) and the diode laser in the early 1990s. Regardless of whether it was applied as interstitial laser coagulation (ILC), contact laser vaporisation (CLV) or visual laser ablation of the prostate (VLAP), this first enthusiasm for laser ended in disappointment. Despite the efficacy and durability shown in some randomised controlled trials (RCTs), the Nd:YAG laser was abandoned for various reasons that could not be explained by the existing data [1]. One possible reason was that the results with its extended use could not match the published data. As a result of the deep penetration of these first lasers when applied to benign prostatic enlargement (BPE), patients suffered secondary urethral sloughing of necrotic prostatic tissue, needing prolonged suprapubic catheter provision or reoperation [2]. Currently, new laser techniques have gained a leading role in the surgical treatment of benign prostatic obstruction (BPO). Due to their haemostatic properties, morbidity, catheter time and length of hospital stay (LOS) are less compared to TURP or simple open prostatectomy (OP). The current and future challenges are in patients with lower urinary tract symptoms (LUTSs) secondary to BPE who are

generally older, have more comorbidity, are more often taking anticoagulants or anti-platelet medication, and have larger prostates due to increased use of simultaneous medical treatment for LUTSs at the same time. As more high-risk patients are treated and laser therapies are becoming more popular [3], urologists inevitably have to deal with these novel technologies and devices. Currently, there are four lasers used as minimally invasive alternatives to the reference standards of TURP and simple OP: [1] holmium: YAG; [2] potassium titanyl phosphate (KTP) or lithium triborate (LBO; GreenLight); [3] thulium; and [4] diode. Their application on the prostate may comprise an inside-out technique of laser resection of the prostate (LRP) and laser vaporisation/ ablation of the prostate (LAP), or an outside-in technique of laser enucleation of the prostate (LEP). With different types of lasers, it is possible to perform the various procedures listed in **Table 1**. However, all four lasers have distinct tissue interaction characteristics when applied to transurethral BPO surgery. This is explained by their specific wavelength and/ or mode of operation. Apart from that, there are differences in the quantity and quality of published papers, level of evidence (LE) and follow-up data among these lasers and their techniques (**Table 2)**. Although some lasers are not updated, patients are happy because they are nevertheless being treated with a laser.

In the following text, each of the lasers and its predominant surgical technique to treat BPO is described according to the specific physical properties, historical background, surgical technique, LE and potential drawbacks. Finally, comparative trials between the different lasers are discussed.

## 2. HOLMUIM: YTTRIUM ALUMINIUM GARNETT (HO:YAG) LASER

### *a) Physical background*

The Ho:YAG laser is a pulsed solid laser with a wavelength of 2140 nm. The laser energy is invisible within the infrared area and is mainly absorbed by cellular water. In other words, the penetration depth of the Ho:YAG laser in water and (prostatic) tissue is probably ~0.4 mm. At the end of the laser fibre, vapor bubbles are formed that rapidly expand and destabilise molecules with which they come in contact. Depending on the distance between the laser fibre end and tissue, there may be no effect (distance ≥ 3 mm), blanching and haemostasis (< 3 mm), or (in direct contact) cutting and fragmentation. Thus, by the means of reusable flexible quartz fibre, an exact incision of prostatic tissue can be achieved **(figure)**, and at the same time, vessels can be coagulated by defocusing the laser fibre. This pulsed thermo-mechanical effect can also be used for stone fragmentation.

### *b) History*

In transurethral prostatic surgery, the Ho:YAG laser was first used by its pioneers Gilling and Fraundorfer to remove small pieces of prostatic tissue, so-called holmium laser resection of the prostate (HoLRP) [4]. Despite HoLRP showing more favourable results than TURP in an RCT [5], HoLRP was soon abandoned and substituted by the more efficient holmium laser enucleation of the prostate (HoLEP); the results of which were published for the first time in 1998 [6]. Holmium laser ablation of the prostate (HoLAP) using a vaporising side-firing technique never gained widespread use in clinical practice. This is most likely explained by the limited tissue ablation and reduction in prostate-specific antigen

***Table 1. Laser and laser techniques for the surgical treatment of BPE***

| Laser | Resection | Vaporisation | Enucleation |
|---|---|---|---|
| Holmium | HoLRP | HoLAP | HoLEP |
| GreenLight | PVPLRP | PVP | GreenLEP |
| Thulium | ThuVARP | ThuVAP | ThuLEP |
| Diode | DiLRP | DiLAP | DiLEP |

*DiLRP, diode laser resection of the prostate; DiLAP, diode laser vaporization; DiLEP, Diode laser enucleation of the prostate; GreenLEP, photoselective enucleation of prostate; HoLAP, holmium laser ablation of the prostate; HoLEP, holmium laser enucleation of the prostate; HoLRP, holmium laser resection of the prostate; PVP, photoselective vaporisation of the prostate; PVPLRP, photoselective laser resection of the prostate; ThuLEP, Thulium laser enucleation of the prostate; ThuVAP, thulium laser vaporisation; ThuVAR, thulium laser vaporisation.*

*Table 2. Laser Techniques: characteristics.*

| Laser | Holmium (Ho) | KTP SHB Nd:YAG<br>LBO SHB Nd:YAG[a] | Thulium | Diode |
|---|---|---|---|---|
| Surgical technique | Enucleation | Vaporisation | Vaporisation<br>Vaporesection<br>Vapoenucluation | Vaporisation<br>Enucleation |
| Acronyms | HoLEP<br>HoLAP<br>HoLRP | PVP | ThuVAP<br>ThuVARP<br>ThuVEP<br>ThuLEP | DiLEP<br>Enucleation |
| Fibre | End-firing | Side-firing | Front-firing | Side-firing<br>Front-firing |
| Wavelength (nm)<br>Operating mode | 2140 nm<br>Pulsed | 532 nm<br>quasi-continuous | 2013 nm<br>continuous | 940–1470 nm<br>continuous |
| RCTs vs. TURP | Yes | Yes | Yes | No |
| RCTs vs. OP | Yes | Yes | No | No |
| Longest follow-up RCTs | 7 years | 3 years | 18 months | NA |

*Both types of GreenLight laser.*

(PSA) achieved by HoLAP, resulting in retreatment rates of 15–20% [7, 8]. Since HoLEP became feasible, it has remained the preferred surgical technique when using the Ho:YAG laser for BPO.

### *c) Surgical technique of HoLEP*

For HoLEP, the prostatic lobes are detached retrograde from the surgical capsule using the laser fibre and the shaft of the laser resectoscope like the index finger in OP. After their enucleation, the prostatic lobes are fragmented (morcellated) within the bladder or prostatic fossa and evacuated.

Traditionally, as described by Gilling *et al*. as a first step, the laser is used to make two incisions from the lip of the bladder neck at the 5 and 7 o'clock positions to the verumontanum. These incisions are deepened to the surgical capsule, which is optically identified. Subsequently, a third horizontal incision just in front of the verumontanum connects the apical ends of the first incisions. Gently lifting the middle lobe with the shaft of the laser resectoscope, the laser fibre follows the anatomical plain between the prostatic tissue and the surgical capsule, until the lip of the bladder neck is reached and the retrograde enucleation of the middle lobe is completed. Detaching the remaining tissue from the bladder neck, the prostatic lobe can float into the bladder. As a second step, the apical bottom edges of the side lobes are mobilised with semicircular incisions following the surgical capsule, starting at the 6 o'clock position. Simultaneous to the enucleation, small to medium-sized vessels of the surrounding tissue are coagulated by the scattering energy of the laser fibre, ensuring instant haemostasis and good vision for the surgeon **(Figure 1)**. Accordingly, this step is repeated starting from the 12 o'clock position, mobilising the upper part of the side lobes. Subsequently, the lower and upper incisions are connected, extending them laterally and following the surgical capsule until the lip of the bladder neck is reached and the side lobe again is pushed into the bladder. After that, the prostatic cavity is wide and allows a clear view of the surgical capsule. The defocused laser fibre can be used to coagulate any residual bleedings from the surgical capsule. As a final step, the enucleated prostatic lobes floating in the bladder lumen have to be removed using a morcellator device. The lobes are sucked to the tip of the morcellator blades **(Figure 2)**, cut into pieces small enough to pass through the inner hollow morcellator blade and tube into a collector, and removed for histopathological examination **(Figure 3)** [9]. During the morcellation process, it is essential to keep the bladder lumen filled with irrigation fluid, to prevent bladder injury. After morcellation and final inspection of the surgical field, a three-way catheter, allowing further irrigation, should be placed.

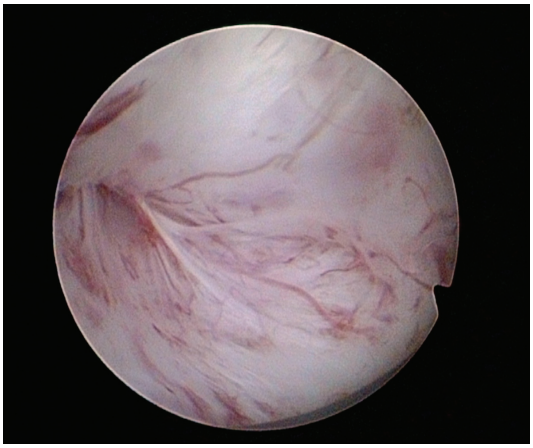

***Figure 1. Apical enucleation: surgical capsule – right side lobe.***

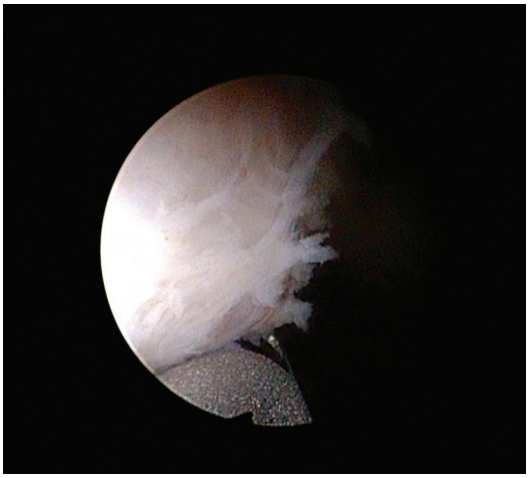

*Figure 2. Morcellation*

*Figure 3. Morcellated prostatic lobes: HoLEP specimen.*

Variations of the original technique described above have evolved. In contrast to the traditional technique, we have found enucleation of the side lobes easier when turning the instrument upside down after the surgical plane is found **(Figure 4)**. Furthermore, our lateral mobilisation of the side lobes is continued up to the 12 o'clock **(Figure 5)**. By these means, the lobes are only attached to a small bridge of urethral mucosa and tissue, when the anterior commissure is incised.

***d) Scientific evidence***

Entering HoLEP as a search item in PubMed resulted in 162 hits between 1998 and 2013. These hits included six RCTs comparing HoLEP with monopolar TURP in small to medium-sized prostates, with up to 7 years follow-up [10–15], and three RCTs comparing HoLEP with OP in large prostates, with up to 5 years follow-up [16–18]. All RCTs demonstrated that HoLEP is independent of prostate size, with at least equal efficacy to TURP and OP in short-, medium- and long-term follow-up, but it has lower (specifically perioperative) morbidity and significantly shorter catheter time and LOS (LE 1) **(Tables 3 and 4 a,b,c)**. Generally, the types of complications resemble those of TURP. However, due to its haemostatic properties, HoLEP has fewer bleeding complications (LE 1), which are the main drawback of TURP and OP. For example, in contrast to TURP and OP, there was no requirement for blood transfusion after HoLEP in any of the RCTs **(Table 4b)**. Haemostasis during HoLEP arises because the radial blood vessels need to be coagulated only once at the level of the surgical capsule and most are immediately sealed during the enucleation process. The "sealing effect" plus the use of isotonic saline as irrigation fluid excludes the risk of TUR syndrome, which to date has never been reported in HoLEP (LE 1). Late complications after HoLEP,

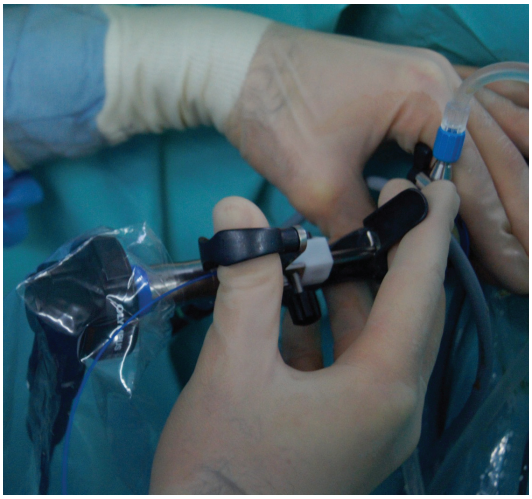

*Figure 4. "Up-side down technique".*

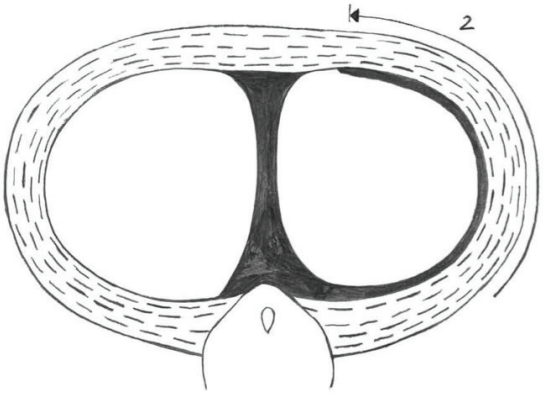


*Figure 5. Modified "Hamburg Technique".*

***Table 3. Summary of RCTs comparing HoLEP with TURP***

| RCT | Comparators | Follow-up (months) | No. of Patients | Main results |
|---|---|---|---|---|
| Gilling *et al*. (34) | HoLEP vs. TURP | 84 | 120 | HoLEP is at least equivalent to TURP in the long term with fewer reoperations being necessary. |
| Ahyai *et al*.(10) | HoLEP vs. TURP | 36 | 200 | HoLEP results in significantly better micturition parameters and less perioperative morbidity. |
| Montorsi *et al.* (15) | HoLEP vs. TURP | 12 | 100 | Similar effectiveness and complication rate after HoLEP and TURP. HoLEP associated with shorter catheterisation time and hospital stay. |
| Eltabay *et al*. (35) | HoLEP vs. TURP | 12 | 80 | Shorter catheterisation time and hospital stay, lower haemoglobin loss, and greater improvement of voiding function after HoLEP compared to TURP. |
| Mavuduru *et al.(14)* | HoLEP vs. TURP | 9 | 30 | Comparative effectiveness and safety with the advantage of reduced intraoperative haemorrhage and perioperative morbidity. |
| Chen *et al.* (36) | Bipolar TURP | 24 | 280 | HoLEP: less risk of haemorrhage, decreased bladder irrigation and catheterisation times, and reduced hospital stay. |
| Kuntz *et al*. (37) | OP | 60 | 120 | HoLEP and OP equally effective for removal of large prostatic adenomas. Less perioperative morbidity after HoLEP. |
| Naspro *et al*. (17) | OP | 24 | 80 | Similar functional results 2 years after HoLEP or OP. Reduced catheterisation time, hospital stay, and blood loss after HoLEP. |

***Table 4a: Functional outcome data after HoLEP***

| Therapy | Com-parator | Study | LE | HoLEP No. of pts. | Mean FU (yr) | Mean age (yr) | Mean TRUS (ml) | Mean PSS preop | Mean QOL preop | Mean Qmax preop (ml/s) | Mean PVR preop (ml) | Mean operation time (min) | Mean tissue retrieved (g) | Mean catheter time (d) | Mean LOS (d) | Mean IPSS postop | Mean QOL postop | Mean Qmax postop (ml/s) | Mean PVR postop (ml) | Increase PCa (%) | PSA drop (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| HoLEP | TURP | Ahyai (10) | 1b | 100 | 3.0 | 68.0 | 53.5 | 22.1 | | 4.9 | 238.0 | 94.6 | 35.9 | 1.0 | 2.0 | 2.7 | | 29.0 | 8.4 | 3.0 | |
| HoLEP | OP | Kuntz (16) | 1b | 60 | 5.0 | 69.2 | 114.6 | 22.1 | | 3.8 | 280.0 | 135.9 | 93.7 | 1.3 | 2.9 | 3.0 | | 24.3 | 10.6 | 5.0 | |
| HoLEP | TURP | Wilson (42) | 1b | 60 | 2.0 | 71.7 | 77.8 | 26.0 | 4.8 | 8.4 | | 62.1 | 40.4 | 0.7 | 1.2 | 6.1 | 1.3 | 21.0 | | | 87.0 |
| HoLEP | OP | Naspro (17) | 1b | 41 | 2.0 | 66.3 | 113.3 | 20.1 | 4.1 | 7.8 | | 72.1 | 59.3 | 1.5 | 2.7 | 7.9 | 1.5 | 19.2 | | 4.8 | |
| HoLEP | TURP | Briganti (43) | 1b | 60 | 2.0 | 65.2 | 73.3 | 21.1 | 4.4 | | | | | | | | | | | | |
| HoLEP | TURP | Montorsi (44) | 1b | 52 | 1.0 | 65.1 | 70.3 | 21.6 | 4.6 | 8.2 | | 74.0 | 36.1 | 1.3 | 2.5 | 4.1 | 1.4 | 25.1 | | 11.5 | |
| HoLEP | TURP TUVRP | Gupta (13) | 1b | 50 | 1.0 | 65.8 | 57.9 | 23.4 | | 5.2 | 112.0 | 75.4 | 17.2 | 1.2 | | 5.2 | | 25.1 | 20.0 | | |
| HoLEP | N/A | Gilling (45). | 3 | 71 | 6.1 | 69.1 | 58.5 | 25.7 | 4.9 | 8.1 | 105.0 | 47.0 | 27.0 | 1.9 | 1.0 | 8.5 | 1.8 | 19.0 | 33.0 | 2.8 | 61.0 |
| HoLEP | N/A | Kuo (46) | 3 | 206 | 1.6 | 70.5 | | | | | | 133.6 | 68.2 | | 1.1 | | | | | 9.7 | |
| HoLEP | N/A | Elzayat (47) | 3 | 225 | 2.6 | 73.7 | 126.0 | 18.7 | 3.7 | 8.0 | 325.4 | 117.0 | 86.5 | 1.3 | 1.2 | 3.9 | 0.8 | 26.2 | 29.7 | 2.2 | 90.0 |
| HoLEP | N/A | Elzayat (30) | 3 | 118 | 4.1 | 76.5 | 59.3 | 17.3 | 3.3 | 6.3 | 232.0 | 124.0 | 30.0 | 1.3 | 1.5 | 5.6 | 1.2 | 19.1 | 46.6 | 3.4 | 67.2 |
| HoLEP | N/A | Vavassori (48) | 3 | 330 | | 66.0 | 62.0 | 24.0 | 5.2 | 9.0 | | 74.8 | 40.0 | 1.0 | 2.0 | 0.9 | 0.1 | 26.0 | | 3.6 | 80.4 |
| HoLEP | N/A | Shah (49) | 3 | 280 | 3.0 | 65.9 | 54.6 | 21.1 | | | 179.6 | 61.3 | 29.8 | | | 4.9 | | 17.6 | 19.1 | 1.1 | |

*FU, follow-up; IPSS, International Prostate Symptom Score; N/A, not applicable; PCa, prostate cancer; PVR, post-voiding residual urine; Qmax, maximum urine flow; QOL, quality of life; TRUS, transrectal ultrasound.*

such as urethral stricture, bladder neck sclerosis or reoperation due to recurrence of prostatic adenoma, are as rare as in TURP [10, 12, 19] **(Table 4c).** Similar to OP, HoLEP leads to an anatomically correct and maximal tissue ablation, demonstrated by PSA reductions > 80% [20], and excellent and lasting functional outcome [16] **(Table 4a)**. Tan *et al*. demonstrated in pressure flow studies that HoLEP leads to better removal of prostatic obstruction than TURP does, which is probably best explained by the greater amount of tissue retrieved by HoLEP [15, 20]. Higher tissue retrieval rates may lead to longer operating time when HoLEP is compared to TURP. However, in trained hands, tissue retrieval rates seem comparable between HoLEP and TURP, and HoLEP and OP [21].

To date, HoLEP represents the most rigorously analysed laser technique. Meta-analyses have

***Table 4b: Perioperative complication rate (%) after HoLEP***

| Therapy | Com-parator | Study | LE | Mucosal bladder injury | Capsular perforat-ion | Ureteric orifice injury | Incomplete morcellation | Intraop bleeding | Conv-ersion | Trans-fusion | sec Coagu-lation | Re-catheter isation | sec rese-ction | Clot retention |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| HoLEP | TURP | Ahyai (10) | 1b | | | | | 0 | 0 | 0 | 1.0 | 0 | 0 | |
| HoLEP | OP | Kuntz (16) | 1b | | | | | 0 | 0 | 0 | 5.0 | 3.0 | 3.3 | |
| HoLEP | TURP | Wilson.(42) | 1b | 0.0 | 0 | | | 0 | 0 | 0 | 0 | 16.6 | 0 | |
| HoLEP | OP | Naspro (17) | 1b | 7.3 | | | | | | 0 | 2.4 | 12.1 | | |
| HoLEP | TURP | Briganti (43) | 1b | | | | | | | | | | | |
| HoLEP | TURP | Montorsi (44) | 1b | 18.2 | | | | | 0 | 0 | 1.7 | 5.3 | 0 | |
| HoLEP | TURP TUVRP | Gupta (13) | 1b | 4.0 | 2.0 | | | 0 | 0 | 0 | 0 | 2.0 | 0 | |
| HoLEP | N/A | Gilling (45). | 3 | 0.0 | 0 | | | 0 | 0 | 0 | 0 | 0 | 0 | |
| HoLEP | N/A | Kuo (46) | 3 | 1.9 | 2.0 | | 1.9 | | | 1.0 | | 7.8 | | 2.4 |
| HoLEP | N/A | Elzayat (47) | 3 | 1.0 | | | | | 3.5 | 1.0 | | | | 0.5 |
| HoLEP | N/A | Elzayat (30) | 3 | 0.8 | | | | | 0 | 1.7 | 0 | 1.7 | 0 | 1.7 |
| HoLEP | N/A | Vavassori (48) | 3 | 5.7 | | | | | 0 | 0 | 2.4 | 5.1 | | 1.2 |
| HoLEP | N/A | Shah (49) | 3 | 3.9 | 9.6 | 2.1 | | | 2.9 | 1.4 | | 3.9 | | 0.7 |

***TUVRP, transurethral vapor resection of the prostate.***

***Table 4c: Late complication rate (%) after HoLEP***

| Therapy | Comp-arator | Authors | LE | Meatal urethral stricture | BNC | BPH recurrence | Transient dysuria | Urge inconti-nence | Stress inconti-nence | Mixed inconti-nence | Retrograde ejaculation | Potency |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| HoLEP | TURP | Ahyai (10) | 1b | 4.1 | 3,1 | 0,0 | | | 1.0 | | 74.0 | |
| HoLEP | OP | Kuntz (16) | 1b | 3.3 | 1,7 | 0,0 | | | 0 | | | |
| HoLEP | TURP | Wilson (42) | 1b | 3.3 | 0,0 | 0,0 | | | 3.0 | | 75.0 | |
| HoLEP | OP | Naspro (17) | 1b | | | 7,3 | | 3 mo=34<br>12 mo=5.4<br>24 m=0 | 0 | | | IIEF no change |
| HoLEP | TURP | Briganti (43) | 1b | | | | | | | | 78.3 | IIEF-EF no change, orgasmic domain significant decrease |
| HoLEP | TURP | Montorsi (44) | 1b | 1.7 | 0,0 | | | 1 mo=44 | 1.7 | | | IIEF-EF no change, orgasmic domain significant decrease |
| HoLEP | TURP & TUVRP | Gupta (13) | 1b | 2.0 | | | 10.0 | | 6 mo=2 | | | |
| HoLEP | % | Gilling (45). | 3 | 0 | 0,0 | 2,6 | | 7.9 | 2.6 | 10.5 | | |
| HoLEP | % | Kuo (46) | 3 | 2.4 | 3,9 | | | | | | | |
| HoLEP | % | Elzayat (47) | 3 | 1.3 | 0,4 | | 9.3 | 1.8 | 1.8 | | | |
| HoLEP | % | Elzayat (30) | 3 | 2.0 | 2,0 | 8,0 | 11.0 | | 2.5 | | | |
| HoLEP | % | Vavassori (48) | 3 | 3.3 | 0,6 | 2,7 | 28.0 | | 0.6 | | | |
| HoLEP | % | Shah et al.(49) | 3 | 4.6 | 0,4 | | 10.7 | | 0.7 | | | |

BNC, bladder neck contracture; BPH, benign prostatic hyperplasia; postop, postoperative; preop, preoperative; pts, patients.

shown that it has the highest LE to be a minimally invasive and cost-effective alternative to TURP and OP, and it is recommended accordingly by the EAU Guidelines (LE 1, GR A) [22–25].

***e) Drawbacks***

The major drawback of HoLEP seems to be its shallow learning curve. At least for surgeons trained in transurethral resection, the technique and laser equipment used for HoLEP seem not to be intuitive. There is a problem with a lack of mentors and training models, which makes anatomical enucleation of the prostate a challenge for every self-taught HoLEP learner. In contrast, when compared to TURP, the intraoperative vision during HoLEP is improved due to less bleeding. At the same time, prolonged operating times at the beginning of the learning curve do not expose the patient to the risk of TUR syndrome. Several mostly retrospective publications (LE 3) on the learning curve of HoLEP imply that: [1] similar to other surgical procedures, ≥ 20 procedures are necessary to become familiar with the technique [26, 27]; [2] during the learning curve, complications such as transient urgency and urinary incontinence might be more prevalent [27]; and [3] complication rate seems to decrease after ~50 procedures [28]. General recommendations include being an endoscopically skilled surgeon, starting with prostates of moderate size [29], and ideally, performing the first HoLEP procedures under supervision of an experienced mentor. Given these conditions, HoLEP seems to provide durable results and a low rate of complications and reoperation, even during the learning process [30] (LE 3).

***f) Conclusion***

The efficacy data for HoLEP, especially when looking at its evidence level, are self-explanatory. So far, HoLEP is the most rigorously investigated laser technique for surgical treatment of BPE. For several years it has been recommended as a minimally invasive alternative to TURP and OP (LE 1, GR A), and today, it probably represents the new reference standard for at least large prostates and all other transurethral, open or laparoscopic enucleation techniques.

***g) Transurethral innovative techniques – what is the future?***

The current laser technologies discussed here have demonstrated their specific scientific LE and clinical indications to treat BPO. Despite the ongoing need for further research and follow-up data for these new techniques, TURP and OP are no longer the sole techniques used for prostatectomy [22]. According to the current EAU Guidelines, patient selection with respect to age, comorbidity, medication and prostate size should be the key issue in "instrumental technique decision making", when treating BPO surgically [25]. Future RCTs comparing holmium, thulium and GreenLight laser techniques and bipolar TURP (as a minimally invasive alternative to monopolar TURP) are necessary to identify the new reference standard for small to medium-sized prostates. However for the treatment of medium-sized to large prostates, there are sufficient LE 1 data that patients might benefit from enucleation techniques when compared to (bipolar) TURP **(Table 5)**. When comparing different transurethral enucleation approaches, safety and efficacy profiles are similar, which has been shown in two RCTs comparing HoLEP versus plasmakinetic enucleation of prostate (PKEP) with 1 year follow-up, and HoLEP versus thulium laser enucleation of the prostate (ThuLEP) with 18 months follow-up [31, 32]. The ongoing changes in practice patterns could lead to deciding whether to resect, vaporise or enucleate, rather than debating the technology or energy of the different devices. In a recent RCT comparing (photoselective) vaporisation (PVP-120 W) and (holmium laser) enucleation of prostates > 60 ml, the latter demonstrated a superior efficacy and safety profile [33]. Despite a potential bias because the authors are known as HoLEP rather than photoselective vaporization of the prostate (PVP) surgeons, a preoperative cut-off of prostate volume > 60 ml might be reasonable for selecting patients for transurethral enucleation. New technology can never replace a good surgeon, therefore, mentoring programmes led by experts are needed to guarantee optimal outcome outside clinical trials and referral centres.

***Table 5. RCTs comparing enucleation techniques of different technology with bipolar TURP***

| RCT bTURP | Comparator/mean TRUS | Conclusion |
|---|---|---|
| Chen *et al*. [4] (24 months follow-up) | HoLEP/57 g | HoLEP has less bleeding and shorter catheterisation time and hospital stay. |
| Yang *et al*. [39] (18 months follow-up) | ThuLEP/72 g | ThuLEP has less bleeding and shorter catheterization time and hospital stay. |
| Zhu *et al*. [41] (60 months follow-up) | PKEP/113 g | PKEP has less bleeding and shorter catheterization time and hospital stay. |
| Lusuardi *et al*. [25] (6 months follow-up) | ELEP/59 g | ELEP has less bleeding and shorter catheterisation time and hospital stay. |

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## 3. THULIUM:YTTRIUM-ALUMINIUM-GARNET (TM:YAG) LASER

In Tm:YAG lasers, energy is emitted at a wavelength of 2013 nm in a continuous-wave fashion [1–4]. Tm:YAG lasers have almost the same absorption characteristics as holmium lasers in water and tissue. Being a continuous-wave laser with consequent continuous energy output, it has intrinsic superior properties for ablation in soft tissue surgery, as do all contemporary continuous-wave vaporising lasers. Due to the slightly shorter wavelength compared with Ho:YAG, the depth of penetration is decreased to 250 μm.

The wavelength is close to the absorption peak of water. Due to its short penetration, its high-energy density leads to rapid vaporisation of water and tissue. In contrast to the tearing effect of Ho:YAG caused by the pulsed energy emission, Tm:YAG allows smooth vapo-incision of tissue by continuous-wave laser energy output. Unlike KTP, LBO the thermostable chromophore water provides constant ablative conditions for tissue interaction. In contrast to Ho:YAG with pulsed emission mode, Tm:YAG with continuous emission does not allow lithotripsy [1].

### *a) Physical properties* (table 1)

In this model, continuous-wave Tm:YAG showed the shallowest coagulation depth. In contrast to KTP and LBO, bleeding rate and tissue necrosis remained stable with elevated tissue ablation rate at an energy output raised to 120 W [5, 6].

### *b) History*

The Tm:YAG laser was introduced into clinical practice in 2005. The 2013-nm laser was the most commonly used laser in published studies, although two other thulium-based generators with slightly different wavelengths exist. The "2 micron" laser has excellent vaporisation features [2], and the Wendt–Nordahl [4]development of the technique moved to vaporesection. The first English-language publication on vaporesection or ThuVARP using an 80-W device was published in 2007 [5]. Internationally, Xia et al. published their

***Table 1 The physical properties of Tm:YAG at different energy levels.***

| Study | Bach *et al*. (2) | | Heinrich *et al*. (4) | |
|---|---|---|---|---|
| Laser type | Thulium | | KTP | LBO |
| Wavelength (nm) | 2013 | 2013 | 532 | 532 |
| Power setting (W) | 70 | 120 | 80 | 120 |
| Tissue ablation rate (g/10 min) | 9.80 ± 303 | 16.41 ± 5.2 | 3.99 ± 0.48 | 7.01 ± 1.83 |
| Bleeding rate (g/min) | 0.11 ± 0.03 | 0.15 ± 0.09 | 0.21 ± 0.07 | 0.65 ± 0.064 |
| Tissue necrosis (mm) | 1.09 ± 0.14 | 1.09 ± 0.09 | 0.667 ± 0.064 | 0.835 ± 0.073 |

*Thulium Tm:YAG, KTP Kalium-Titanyl-Phosphate (Greenlight), LBO (Lithium-Borat, Greenlight HPS 120). As experimental organ model, perfused porcine kidney model (PPKM) was used.*

initial results on "Tangerine"-technique vaporesection with a 50-W device in 2005 in Chinese [6]. Further technical refinements towards enucleation were pioneered by groups in Hamburg–Barmbek (vapoenucleation; ThuVEP) [7] and Hannover (transurethral anatomical enucleation of the prostate with Tm:YAG support; ThuLEP) [8]. Bach et al. published a study on ThuVEP in 2009, and most of the literature on ThuVEP originates from that group. Herrmann et al. described ThuLEP in 2010, which served as a prototype approach for blunt enucleation of the prostate, with the sparing use of laser only for incision and precise coagulation in order to preserve the intact surface of the surgical capsule for anatomical orientation throughout the whole procedure, unlike in ThuVEP. This technique has served as a blueprint for other laser techniques [9,10]. To overcome the numerous abbreviations and acronyms for the four different approaches, a consensus paper was published in 2010 [11] and was later accepted in the EAU Guidelines on laser and technologies in 2012 [12].

## THULIUM LASER TECHNIQUES [11]

1) Tm:YAG vaporisation of the prostate (ThuVAP);

2) Tm:YAG vaporesection (ThuVARP);

3) Tm:YAG vapoenucleation (ThuVEP);

4) Tm:YAG laser enucleation of the prostate (ThuLEP)

***c) Scientific evidence*** **(Table 2)**

Entering "thulium", "2 micron" and "prostate" as search terms in PubMed resulted in 89 hits between 2005 and 2014. Those publications contained only one that dealt with vaporisation, that is, ThuVAP in a prospective study [13]. The best evidence exists for ThuVARP. Eight RCTs have compared ThuVARP with monopolar [14,15,19,21,22], bipolar or plasmakinetic [16–18,20] TURP, and one with electrovaporisation [19]. Ther was one meta-analysis from 2013 [23]. The techniques most commonly used in ThuVARP are the Tangerine technique (thulium laser resection of the prostate), described by Xia et al. [24] and ThuVARP described by Bach et al. [5](like HoLRP). The longest follow-up was 4 years in on RCT [15] and 5 years in a prospective single treatment arm study [25]. In addition ThuVARP has been evaluated for treatment of acute urinary retention [32] and large prostates [33], coagulation disorders, and high-risk patients [21, 34].

For ThuVEP, no RCTs have been carried out, but prospective single arm studies have been published on treatment of urinary retention [26], large volume prostate [27], coagulation disorders [28], impotence [29] of the pioneering group with a follow-up of 4 years [30, 31].

One RCT has compared ThuLEP and HoLEP, with 18 months follow-up [35], and another has compared ThuLEP and TURP, with 3 months follow-up [36]. Furthermore one prospective non single treatment arm study has been reported [37].

All the above RCTs [ThuVARP [14–22] and ThuLEP [35,36] displayed equivalence in comparison to the standard treatment arm. Procedural time tended to be longer. Perioperative safety was in favour of the Tm:YAG treatment arm.

With regard to ablation rate, PSA decreased by ≤ 82% for ThuVARP [16], 88% for ThuVEP [27], and 83% for ThuLEP [8].

Long-term complications were comparable to standard treatment [15,25,35], or very low in single arm prospective studies [30,31].

*Table 2. Transurethral plasmakinetic prostatectomy (TUPKP)*

| Study | Study type | Year of publication | Technique | Follow-up | No. of patients | Main finding |
|---|---|---|---|---|---|---|
| Vargas et al. (13) | Prospective single centre | 2014 | ThuVAP | 6 | 55 | Safe and effective, low perioperative and late complications |
| Yang et al. (20) | RCT | 2013 | ThuVARP vs. TURP plasmakinetic | 18 | 158 | Technique falsely labelled as ThuLEP. ThuVARP and PKRP equal with regard to symptomatic and urodynamic parameters. |
| Peng et al. (18) | RCT | 2012 | ThuVARP vs. TUPKP | 3 | 100 | ThuVARP is superior to TUPKP in terms of safety, blood loss, recovery time and complication rate, and is equivalent for improvement of functional and symptomatic parameters. Operation duration significantly longer than for ThuVARP. |
| Cui et al. (15) | RCT | 2013 | ThuVARP vs. TURP | 48 | 96 | No significant difference in terms of functional and symptomatic parameters. Lower perioperative morbidity and equally low occurrence of late adverse effects in favour of ThuVARP |
| Xia et al. (14) | RCT | 2008 | ThuVARP | 12 | 96 | ThuVARP significantly superior to TURP in terms of catheterisation time, hospital stay, and haemostasis. Equivalence in urodynamic and symptomatic parameters. Late complications were also comparable. |
| Swiniarski et al. (36) | RCT | 2012 | ThuLEP vs. TURP | 3 | 106 | No significant difference in terms of functional and symptomatic parameters. |
| Zhang et al. (35) | RCT | 2012 | ThuLEP vs HoLEP | 18 | 133 | No significant difference for urodynamic and symptomatic parameters. Superior with regard to blood loss; inferior with regard to operation time. |
| Netsch et al. (28) | Single arm prospective study | 2014 | ThuVEP | 48 | 124 | ThuVEP is a safe, efficacious, and durable procedure for the treatment of BPO. The incidence of late complications with ThuVEP was low. |

### *d) Surgical technique*

#### 1. ThuVARP

The basic technique of ThuVARP is similar to HoLRP, but in contrast, it is more effective, given the vaporising nature of the mode of action (continuous-wave laser). Techniques vary between chip-like resection of the prostate [5] or structured approaches that target the surgical capsule, such as the Tangerine technique [24]. In the latter, the surgical capsule is exposed at the 6 o'clock position, the verumontanum is preserved, and then incisions are made at the 5 and 7 o'clock positions at the bladder neck, followed by resection of the middle lobe. The lateral lobes are resected in a retrograde fashion. The lobe is cut at the 1 and 3 o'clock and 9 and 11 o'clock positions. The lobe is morcellated in situ by resecting small pieces, targeting the surgical capsule. The full technique is described in detail by Xia et al. [24].

#### 2. ThuVEP

The technique of ThuVEP is comparable to the three-lobe enucleation technique of HoLEP [38]. The principle of the technique was developed from ThuVARP and involves gradually resecting larger areas of the transitional zone as the learning curve progresses. The final technique is a vapo-incising technique that vapo-dissects in between the transitional and peripheral zones, so that the whole enucleated bed of the transition zone is covered by a coagulation seam

[39]. No detailed teaching manual has been published so far depicting the steps in detail.

### 3. ThuLEP (Figure 1 - 4)

ThuLEP has primarily been designed with the aim of reproducibility [8]. The key point of this technique is to maintain an untouched surgical capsule throughout the procedure by blunt exposure of the dissection layer and avoiding obscuring the anatomy by charring and coagulation. This allows better anatomical orientation during the procedure, especially when undertaking transurethral enucleation. The procedure was described in detail by Herrmann et al. in 2010 [8], as an adaption of vapo-enucleation to blunt enucleation [38].

The adenoma is widely and bluntly dissected, as in OP. Incisions are made at the prostatic apex and bladder neck, the nutrifying vessels from the peripheral to the transition zones are punctiformly coagulated, leaving the capsule largely untouched.

### 4. Drawbacks

The main drawback for ThuVAP is the sparse availability of data. A possible reason for this is that vaporisation alone is almost exclusively dominated by PVP (photoselective vaporisation of the prostate by KTP or LBO lasers). Until now, the focus has been on resection and enucleation techniques. Although ThuVARP is relatively easy to implement like TURP, bipolar vaporisation is still an inside-out technique with familiar intraoperative boundaries, and ThuVEP is a paradigm shift like any other enucleating technique, being an outside-in technique. The high vaporisation capacity of Tm:YAG allows the surgeon to move gradually from resection of small pieces of tissue (ThuVARP) to large pieces (ThuVEP). Mentor-based approaches are not commonly available, but where they are, 8–16 cases [28] are sufficient to master the approach. However, as in HoLEP, structured teaching programmes are missing and most centres use a self-taught learning curve after initial workshop attendance. For ThuVEP, there has been no RCT, but the data available has demonstrated the efficacy of the technique at up to 4 years follow-up. Two RCTs have investigated ThuLEP but the follow-up was short [36] or short to intermediate [35].

Demonstrating similar effectivity and safety like in HoLEP within 18month, results most likely will match HoLEP in long term FU, as both are anatomical enucleations using the same reproducible planes.

### *f) Conclusion*

Tm:YAG-based techniques have shown efficacy and safety for ThuVARP in intermediate- and long-term RCTs. ThuVEP has evolved into a technique that provides results that can be found with other enucleating techniques, although RCTs are missing. ThuLEP has shown efficacy and safety in RCTs in the intermediate and short term. Most interesting is the direct comparison with HoLEP that showed no clinical relevant difference.

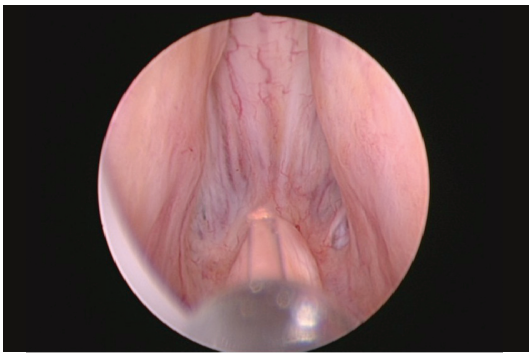

***Figure 1. Situs at the verumantonum***

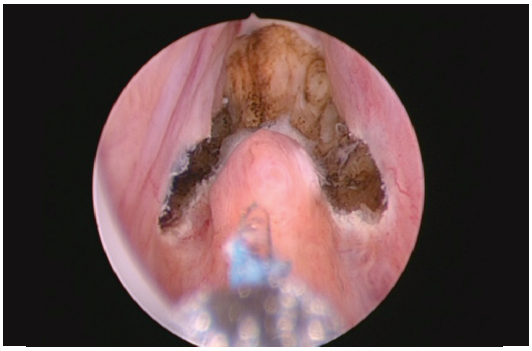

***Figure 2. Inverted U-shaped vapo-incisions around the verumontanum onto the base of the side lobes (ThuLEP)***

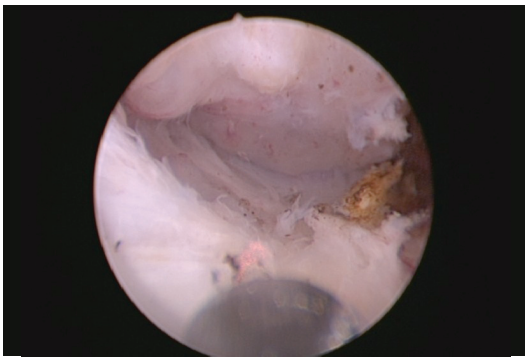

***Figure 3. Blunt exposure of the surgical capsule (ThuLEP)***

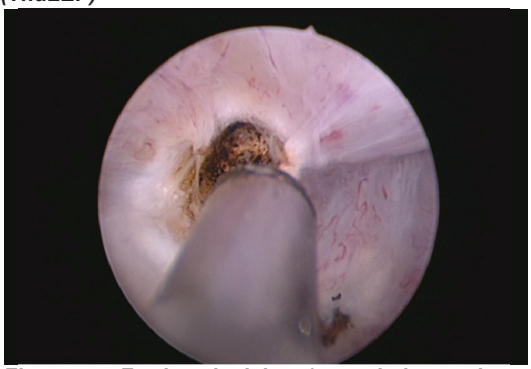

***Figure 4. Further incisions/coagulation only at points of adherence or perforating nutrifying vessels (ThuLEP)***

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## 4. DIODE LASER VAPORISATION OF THE PROSTATE

### *a) Physical background*

Diode lasers for the treatment of BPO are continuous-wave lasers and are currently available at different wavelengths. Previously, low-power diode lasers between 805 and 850 nm were used for interstitial laser coagulation [1–6]. Currently, diode lasers emitting light at 940, 980, 1320 and 1470 nm are being tested and in clinical use for vaporisation of the prostate [7–12] in side-fire and end-fire (bare fibre) techniques [13]. In general, the lower the wavelength of the light emitted by the laser (805–980 nm), the higher is the coagulation zone. In contrast, the higher the wavelength is, the more effective are the cutting and vaporisation capabilities.

In preclinical studies with an ex vivo autologous blood-perfused porcine kidney model, diode lasers (> 50 W) at 940, 980 and 1470 nm show higher tissue ablation capacity in comparison to the KTP laser at 80 W and similar haemostasis. In contrast, the coagulation zones at 50 W differ significantly. Diode lasers emitting light at 940 and 980 nm show a coagulation depth of 8–10 mm in the kidney model, indicating deeper tissue penetration and greater tissue damage [9, 11–13]. With a penetration depth of 3.4 mm, the diode laser at a wavelength of 1470 nm seems to be more favourable. It is questionable whether the results from an ex vivo kidney model reflect the condition in the human prostate in every aspect. However, evaluation in human cadaver prostates showed similar results to the porcine model. The ablation effect of the diode laser at 980 nm (100–200 W) is 2–3 times greater than the vaporisation zone of the KTP laser (80 W) or diode laser at 1470 nm (50 W). In human cadaver prostates, diode lasers at 980 nm demonstrate deeper coagulation (2–3.4 times) than the KTP laser at 80 W or diode laser at 1470 nm (50 W)9. Therefore, the diode laser can combine high tissue ablation with the benefit of excellent haemostasis due to deep coagulation. However, the deep coagulation zones of the laser in the 940- and 980-nm generators may cause damage to the underlying structures such as the neurovascular bundles and external sphincter, which may cause erectile dysfunction (ED) and incontinence [11]. Unfortunately, the value of the human cadaver prostates is limited, because there is no blood perfusion, which is one of the main absorbers at wavelengths of 500–1000 nm. Therefore, in vivo studies on canine prostates were carried out to evaluate the diode lasers. At 940 nm, the dog prostate tissue was treated with a generator output level of 200 W. The mean extension of the coagulation zone was 4.31 mm and the ablation capacity was estimated at ≤1500 mm3/min [11]. In contrast, the diode laser at 1470 nm produced a coagulation rim of 2.3 mm and the tissue removal ability reached ~400 mm3/min [12, 13].

### *b) History*

The first reports of diode laser treatment of prostate enlargement began in the early 1990s. The low-power generators available in those days led to a focus on interstitial laser coagulation14. In 2007, the first study was published on a diode laser prostatectomy side-fire technique with promising results, while the first case of diode laser enucleation of the prostate (DiLEP) was reported in 201115.

### *c) Surgical technique*

The commonly used techniques of diode laser vaporisation of the prostate (DiLAP) and DiLEP use the principle of GreenLight laser vaporisation and HoLEP.

### *d) Scientific evidence*

Only a small number of studies have investigated the clinical applications of diode laser prostatectomy with a maximum follow-up of 1 year. All studies have shown high intraoperative safety and excellent haemostatic properties, however, reports on long-term durability and safety are inconsistent [13]. **(Table 1)**

#### 1. DiLAP (Figure 1)

In a preliminary clinical study of 10 patients, the diode laser at 1470 nm improved the International Prostate Symptom Score (IPSS) after 12 months from 16.3 to 5.0, and the quality of life (QoL) score fell from 3.3 to 0.9. Maximum urine flow (Qmax) increased from 8.9 ml/s preoperatively to 22.4 ml/s after the operation, but reoperation rates were 20% due to failure of laser treatment of a prominent midlobe [8]. A 200-W high-power diode laser at 980 nm was compared with a 120-W GreenLight laser at 532 nm in a single-centre prospective study of 117 patients. Both lasers provided rapid tissue ablation; the high-power diode laser at 980 nm was more favourable in terms of haemostasis during and after surgery. The higher rates of urinary retention (20%), urgency (24%), urge incontinence (7%), bladder neck strictures (15%), stress incontinence (9%) and tissue necrosis after diode laser ablation of the prostate are indications of deep tissue damage. The authors found that data for high-power diode laser vaporisation of the prostate at 980 nm were not sufficiently mature for treating LUTS secondary to BPO [11]. In a subsequent study of 52 patients, the diode laser at 980 nm and 100 W with 0.1-s pulse length and 0.01-s pulse interval resulted in significant durable improvements in Qmax, post-voiding residual urine (PVR) and IPSS QoL score. In that single-centre, single-surgeon series, no severe complications were reported, such as urinary incontinence, significant irritative symptoms, retrograde ejaculation, or worsening erectile function [11]. A subsequent investigation on diode laser vaporisation at 980 nm in 47 patients revealed a distinct improvement in IPPS and QoL. There was no deterioration in erectile function. The most common postoperative complications were retrograde ejaculation (31.7%) and irritative symptoms (23.4%) [16]. Following the development of new laser fibre geometry, Shaker *et al.* [17] compared high–power, 980-nm DiLAP with a conventional side-fire probe in 120 patients with LUTSs suggestive of BPO, with follow-up of ≥ 6 months. DiLAP is associated with some drawbacks such as prolonged irritative symptoms and tissue sloughing. The quartz head contact fibre can achieve similarly good outcomes in ablating the prostate compared to the side-firing conventional fibre, with fewer complications and side effects [13, 17].

#### 2. DiLEP

Yang et al. compared an end-firing continuous-wave diode laser at 980 nm with TURP for enucleation of

***Table 1. Overview of diode lasers with different wavelengths compared to the 532-nm GreenLight laser***

| Wavelength | Absorbers | Ablation | Coagulation | Advantages | Disadvantages |
|---|---|---|---|---|---|
| 800–900 nm<br>low power | Tissue +++<br>Haemoglobin +++<br>Water + | (+) | +++ | Good coagulation and deep tissue penetration, e.g. for ILC | No sufficient ablation |
| 940–980 nm<br>high power | Tissue +++<br>Haemoglobin +++<br>Water ++ | +++ | +++ | Very good ablation at > 100 W | Deep tissue penetration |
| 1320/1470 nm | Tissue +<br>Water ++++ | +++ | ++ | Good ablation, moderate cutting ability at 80–100 W; moderate tissue penetration = good haemostasis | Lack of studies |
| | | | | | |
| 532 nm | Tissue +++<br>Haemoglobin ++++<br>Water + | +++ | +++ | Very good ablation; small to moderate tissue penetration, moderate cutting ability | |

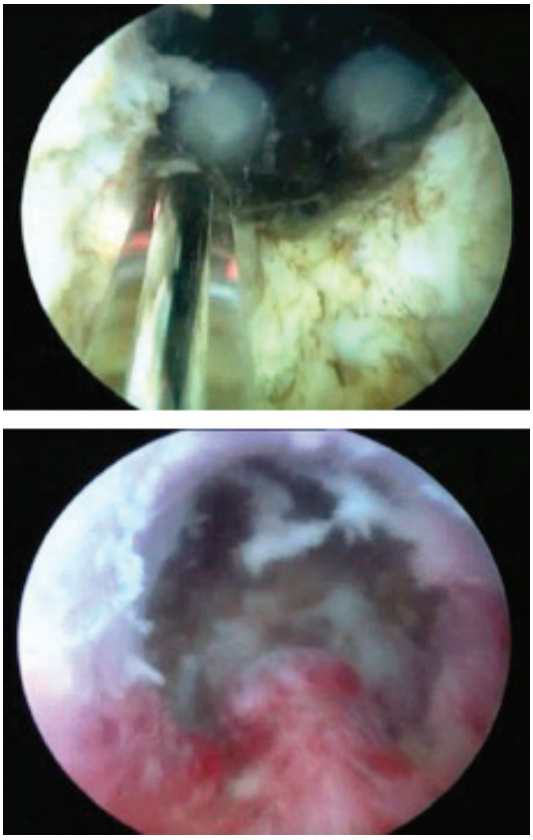

***Figure 1. Post-treatment status after 1470 nm DiLAP (basal and apical aspect of the prostate)***

the prostate for treatment of BPO. Inclusion criteria were significant BPO and a total prostatic weight of ≥ 40 g (74 patients treated with DiLEP and 52 with TURP). DiLEP resulted in a significantly lower drop in haemoglobin level, shorter catheterisation time, and shorter postoperative stay. Delayed postoperative sloughing of necrotic tissue was not observed in the DiLEP group. Improvements in voiding parameters were comparable between the groups, and were sustained during ≤ 1 year follow-up [18].

***a) Drawbacks***

Diode laser prostatectomy is feasible. Nevertheless, despite its favourable intraoperative safety, long-term follow-up and large trials are needed to evaluate the technique fully. From the clinical point of view, diode laser vaporisation with generators emitting light at 900–1000 nm should be used with caution due to their deep penetration that might lead to damage of underlying structures such as the neurovascular bundle, rectum, bladder neck or external sphincter. In contrast, diode lasers at 1470 nm have good vaporisation ability as well as a reasonable and safe tissue penetration depth. This might offer a side-fire operation technique but also a HoLEP-like (DiLEP) procedure with a high safety profile.

***f) Conclusion***

On the basis of current research, diode laser surgery for treatment of BPO lacks a high level of evidence and therefore should be reserved for clinical trials.

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## 5. GREENLIGHT: POTASSIUM TITANYL PHOSPHATE OR LITHIUM TRIBORATE

### *a) Physical background*

The GreenLight laser is a quasi-continuous, diode-pumped, frequency-doubled, solid-state laser with a side-fibre technique, and beam wavelength of 532 nm. Compared to other lasers, the 532-nm wavelength of GreenLight is selectively absorbed in tissue haemoglobin and is not impeded by the procedural irrigant. These unique properties allow the GreenLight laser to vaporise prostatic tissue (PVP) efficiently and rapidly. The temperature of the haemoglobin increases and dissipates the heat into the surrounding tissue. The water in the tissue is heated until pockets of steam or vapour bubbles form. The vapour bubbles create pressure in the connective tissue and then burst. This vaporisation process is repeated throughout the various layers of prostatic tissue until there is complete debulking of the prostatic tissue. GreenLight is absorbed by oxyhaemoglobin 40 times greater than by a diode laser and 100 times greater than by a thulium and Ho:YAG laser. The depth of tissue coagulation by GreenLight, irrespective of the power level (80–180 W) used, does not exceed 1–2 mm, with an optical penetration depth of only 0.8 mm, because most of the thermal energy is consumed and carried away by the highly efficient vaporisation effect. As a result of the photoselectivity, the vascular adenoma tissue, is evaporated, and typically not the stromal fraction. This coral- or fibre-like mesh is repelled and urine is excreted. This fact does not correspond to the familiar sloughing of necrotic material by other laser and minimally invasive procedures. Cystoscopy controls of the prostatic fossa 4 weeks postoperatively showed mostly lodges with smooth walls with only scattered fibrous coatings [1].

### *b) History*

PVP involving the 60-W GreenLight KTP laser was first introduced at the Mayo Clinic, Rochester, USA in 1998 [2]. The GreenLight Laser System is manufactured by American Medical Systems, Minnetonka, MN, USA, which became a wholly owned subsidiary of Endo Pharmaceuticals in June 2011. After its commercial launch in 2003, this system has evolved over the past decade from the 80-W KTP laser to the so-called HPS (high-power system) incorporating an LBO crystal with a maximum power output of 120 W in 2006 to the current 180-W LBO GreenLight XPS laser involving a new liquid-cooled MoXy fibre that aims to improve efficacy, especially in patients with larger prostate glands.

The first, preliminary clinical results in 10 patients were reported in 2003 [3]. In further clinical evaluations of the 80-W KTP laser, Swiss hospitals were importantly involved. In 2004, the first European results from 65 patients were reported by Sulser et al. from University Hospital Basel, Switzerland [4]. An extended series of patients from the German-speaking area, with 6 months follow-up, was reported by Bachmann et al. from the Ludwig Maximilian University of Munich in the same year [1]. In 2005, the efficiency of the 80-W KTP laser vaporisation was documented for the first time in a larger study population of 108 patients and a longer follow-up period of 12 months by the working group of Sulser and Bachmann et al. [5]. Up to that time, there was still no comparative study with the gold standard for treatment of BPO, TURP. Therefore, prospective comparison of KTP laser vaporisation in 64 patients from University Hospital Basel with TURP in 37 patients from Kantonsspital Baden created much interest [6]. With comparable baseline parameters in both groups, the TURP group had a shorter operation time. The decreases in haemoglobin and serum sodium concentrations were significantly higher in the TURP group. In terms of voiding speed and IPSS, no significant differences were found 6 months postoperatively. The first prospective randomised study published in 2006, comparing PVP with TURP, showed similar results after a follow-up period of 12 months [7]. The costs of hospital stay in the laser group, despite the high cost of disposable fibres for the KTP laser, remained 22% below the costs of TURP. Subsequent studies with the higher-powered laser (GreenLight HPS) operating at 120 W with a new fibre design reported beneficial outcomes after long-term follow-up [8,9].

The International GreenLight Users (IGLU) Group, founded 2006, is an independently formed collaboration of physicians and researchers from nine centres around the world with extensive experience in PVP laser therapy. The Group was established to research, share and present information on the optimal use and outcomes of PVP. They have published pooled data on patients treated with the 80-W KTP and 120-W HPS laser systems [10–12].

Historically, operating on prostates > 80 mL in volume was considered by some users to be too slow with the 80-W KTP or 120-W HPS GreenLight laser. The manufacturer claims that, to improve operating speed, the rate of vaporisation has been increased through 50% increases in power and laser beam area with the newest 180-W XPS GreenLight laser (0.44 mm2 vs. 0.28 mm2 for the HPS 120 W laser). These increases were achieved using the MoXy fibre with active cooling cap technology utilising saline flow to minimise tip devitrification, which is said to reduce power degradation significantly throughout the procedure. The actual depth of vaporisation and coagulation in the tissue remain the same as in the 120-W HPS system [13].

The first results of the latest and largest study (Goliath) comparing XPS PVP with TURP were published in European Urology in November 2013. In a prospective randomised controlled trial at 29 centres in nine European countries involving 281 patients with BPO, it was proven that XPS GreenLight laser vaporisation is comparable to TURP in terms of early subjective and objective efficiency parameters. It was shown that recovery parameters are superior with XPS. Early re-intervention rate after 1 month is three times higher after TURP but similar to XPS after 6 months [14].

***c) Surgical technique***

Developing a standardised, methodical approach to treatment of the prostate gland using the GreenLight laser system is an integral part of developing positive experiences and ensuring positive patient outcomes.

One can find different surgical techniques in the literature [15] depending on the prostate size, prostate configuration, and type of technique (Malek technique [16], Basel technique [15], vaporisation incision technique [17], spiral technique, and anterior start technique [15]).

A special 22.5–26.0-Ch laser cystoscope (30° optic) with continuous flow of liquid (sterile 0.9% NaCl) should be used to insert and control the laser fibre. An additional suprapubic bladder trocar is not necessary. The laser beam is deflected at the top of the laser fibre obliquely to the polished surface of the fibre axis, and is laterally radiated at an angle of 70° (side-fire fibre). A special filter is placed between the optic and the video camera to obtain a visible yellow–red laser beam, with a circular area of ~0.44 mm2 (XPS MoXy fibre) at ~2 mm from the fibre tip, thus permitting localised and efficient non-contact side-firing vaporisation.

The surgical procedure is similar to the TURP technique. The Basel technique is explained in the following paragraph.

Once the physician has determined the amount of tissue that needs to be removed, lasing may begin at the bladder neck as the first step. Using an 80-W laser setting around the bladder neck is recommended to avoid inadvertent damage to important structures (ureteral orifices or trigone). As the physician progresses in this procedure, the power setting can be adjusted up to 120 W to achieve efficient vaporisation. The second step is removal of the lateral lobes. The lateral lobes are systematically vaporised from the bladder neck to the verumontanum (first one side and then the other, or alternatively, symmetrically). The objective is to create a concave surface. The procedure is started high at the bladder neck using a sweeping motion downward. In this manner, the surgeon should become accustomed to a structured, line-like vaporisation to achieve a uniform effect. To avoid mucous membrane bleeding due to a high-energy effect, the mucosa should be lasered initially with 80–120 W, followed by a gradually increased laser performance up to 180 W to achieve the greatest possible removal. For smaller glands, a maximum power of 120–160 W is probably sufficient. Removal of the median lobe is the third step. This is started at the bladder neck by slowly rotating the fibre side-to-side (so-called sweeping), by no more than 30–40°. Lasing is continued at the bladder neck until capsular fibres are visualised before progressing towards the apex and verumontanum. For larger median lobes, it is advisable to form a channel at the 5 and 7 o'clock position in the lithotomy position, with establishment of an intermediate portion of tissue for better control of tissue removal. If it is desired, the channels can be lasered down to the capsule with removal of the entire intervening tissue to achieve maximum desobstruction, either by vaporisation, or for the experts, also by partial enucleation of the median lobe. The enucleated median lobe does not need to be pushed into the bladder, but can be vaporised at its base at the bladder neck. Treatment of anterior tissue is at the discretion of the physician. Anterior apical tissue should be vaporised with caution, while maintaining awareness of the sphincteric position and capsule. Finally, the apical parts of the prostate enlargement are vaporised, including the paracollicular area. For protection of the external urethral sphincter, laser energy should be limited to 120–140 W. For expert operators, an ejaculation-protective vaporisation technique is possible.

The continuous formation of vaporisation bubbles indicates a sufficient vaporisation effect. A sweeping distance to the tissue surface of 0.5–3 mm (maximum distance, one fibre diameter) and an average sweeping speed of 0.5–1.0 sweeps/s (2–4 mm/s) guarantees a continuously high vaporisation performance [18–20]. Increasing the sweeping distance, angle or speed leads to a lower vaporisation effect by higher tissue absorption. This effect can be used in rare cases of bleeding for coagulation of the tissue. Additionally, with the XPS GreenLight laser system, an extra coagulation mode, using pulsating light to cauterise ruptured vessels, is available for better control of aberrant bleeding and for rapid suppression of bleeding.

To achieve sufficient haemostasis, the GreenLight laser offers the opportunity to treat patients without stopping oral anticoagulants such as phenprocoumon or platelet aggregation inhibitors such as clopidogrel. Even in rare cases of persistent vessel bleeding, untreatable by vaporisation or coagulation, the use of 0.9% NaCl rinsing liquid facilitates coagulation of the bleeding vessel by bipolar electricity. When using compatible transurethral equipment, even a change of the laser cystoscope is avoidable, which makes the procedure comfortable and safe.

As a result of the immediate coagulation with vascular occlusion during the vaporisation procedure, there is no risk for TUR syndrome in GreenLight laser surgery [21].

In conclusion, the increased power of the XPS system, with the modified MoXy fibre, gives the opportunity to treat larger prostate glands (> 80 ml), even in the case of anticoagulation.

***d) Scientific evidence***

One hundred and forty articles can be retrieved in PubMed with the search terms "greenlight and prostate". The first article from 2004 reports the feasibility and efficiency of first-generation 80-W KTP laser vaporisation [4]. The final article from November 2013 reports the initial results of the largest and most recent prospective multicentre RCT, the Goliath study, which presents safety and efficiency data for comparison of 180-W XPS GreenLight laser vaporisation and TURP [14]. Most of the other recently published articles on GreenLight laser vaporisation of the prostate are based on data from KTP and HPS lasers. Only a few studies are available for the XPS system [22–26]. Among these articles are seven RCTs comparing PVP [only one for XPS (Goliath study)] with TURP in small to middle size prostates with up to 3 years follow-up; one RCT comparing PVP and HoLEP [27]; one RCT comparing PVP and OP [28]; and two RCTs comparing PVP and diode laser [29,30].

In all prospective randomised studies comparing TURP with PVP, the average operation time with 80-W KTP or 120-W HPS PVP is 20 min longer than with TURP, and the catheterisation time is 1.9 days shorter and the hospital stay is 2.1 days shorter after PVP [31,32]. The rate of blood transfusion after surgery with the GreenLight laser is significantly lower (0.3% vs. 6.9%) [31,32]. In meta-analyses, there was no significant difference between TURP and PVP in terms of postoperative urinary retention rate, urinary tract infection, haematuria, urethral stenosis, urethral stricture, or bladder neck sclerosis [31,32]. In terms of improvement of maximum urine flow (Qmax) and IPSS, as well as reduction of PVR, no difference between the two techniques occurred in all seven RCTs [9,14,33–37], as shown in **Table 1**.

In the study with the longest postoperative follow-up, there was a significantly higher reoperation rate after surgery with the 120-W HPS laser for re-TURP/PVP (11% vs 1.8%), with all patients in the PVP group having a prostate volume > 80 ml [9].

The only available study comparing 80-W KTP PVP with OP in patients with prostate volume < 80 ml showed comparable reoperation rates, increase in Qmax and reduction of PVR. Perioperative transfusion rate after OP was 13.3% and 0% in the PVP group. The reduction in QoL and prostate volume was significantly greater after OP [28].

One study with a maximum follow-up of 3 months in 33 patients with prostate volume > 120 ml showed that postoperative voiding symptoms can be improved significantly in larger prostate glands [38].

A prospective randomised trial comparing HoLEP with 120-W HPS PVP in patients with prostate volume > 60 ml showed comparable results in terms of operation time and improvement of IPSS and QoL, while Qmax, PVP, PSA and prostate volume were significantly more reduced by HoLEP. Twenty-one percent of the PVP cases were converted to TURP due to intraoperative bleeding, while none of the HoLEP cases was; probably as a result of the intention to vaporise to the capsule in all PVP cases [27].

Due to the strong haemostatic properties of the GreenLight laser, it is particularly suitable for patients receiving oral anticoagulation or antiplatelet therapy. In a study of 162 patients treated with warfarin (19%), aspirin (62%), clopidogrel (12%) or ≥ 2 anticoagulants (7%), no severe intraoperative complications were seen. Within 30 days of intervention, postoperative bleeding occurred in 4% of patients, necessitating surgical revision in 2% of patients and blood transfusion in 1%. Remarkably, blood transfusion and surgical re-intervention were only necessary in patients receiving warfarin or ≥ 2 anticoagulants [39]. The safety and efficiency of PVP in anticoagulated patients was also proven in other studies [40,41].

Some recent studies of the newest XPS GreenLight laser have been published. Comparison of the older 120-W HPS and 80-W KTP systems with the new 180-W XPS GreenLight system shows that the latter has higher efficiency and comparable intraoperative safety and postoperative results [22–26].

In the next few years, the most important publication will be the follow-up results of the Goliath study [14], because of its power with > 100 patients in each group. In the initial 6 months follow-up, XPS was comparable to TURP in terms of IPSS, Qmax and proportion of patients free of complications. XPS resulted in a lower rate of early re-intervention but there was a similar rate after 6 months.

**In conclusion**, the results of prospective randomised comparisons of PVP and TURP show evidence of lower perioperative morbidity (especially bleeding) of PVP and comparable functional results, but according to evidence levels, data are missing for long-term follow-up.

**Table 1** ***Major studies of TURP***

| RCT | Year of publication | Comparators | Follow-up (months) | No. of patients | Main results |
|---|---|---|---|---|---|
| Bachmann et al. [14] | 2013 | 180-W XPS vs. TURP | 6 | 135 vs. 133 | • First and largest multicentre RCT comparing XPS PVP with TURP<br>• Update of European user experience of PVP and TURP<br>• XPS was comparable to TURP in terms of IPSS, Qmax and proportion of patients free of complications.<br>• XPS results in a lower rate of early reinterventions, but has a similar rate after 6 months<br>• Adverse events, including storage symptoms are comparable |
| Xue et al. [33] | 2013 | 120-W HPS vs. TURP | 36 | 100 vs. 100 | • Equivalent improvement in Qmax, IPSS, PVR and QoL<br>• LOS, LOC and operation time shorter for PVP<br>• Intraoperative complications lower in PVP group |
| Lukacs et al. [34] | 2012 | 120-W HPS Vs. TURP | 12 | 69 vs. 70 | • First multicentre RCT comparing PVP with TURP<br>• Equivalent improvement in Qmax, IPSS, PVR and QoL<br>• Complications comparable in both groups<br>• Median duration of procedure longer in PVP group (71 vs. 55 min)<br>• LOS shorter in PVP group (1 vs. 2.5 days) |
| Capitan et al. [35] | 2011 | 120-W HPS vs. TURP | 24 | 50 vs. 50 | • PVP is as effective as TURP in symptom reduction and improvement of QoL<br>• No difference in the response of storage and voiding symptoms<br>• Complication rate is the same in both procedures<br>• Reduced LOS and LOC for PVP<br>• Ejaculation better preserved by PVP |
| Al-Ansari et al. [9] | 2010 | 120-W HPS vs. TURP | 36 | 60 vs. 60 | • Mean operating time significantly shorter for TURP<br>• Significant reduction in haemoglobin and serum Na levels at the end of TURP only<br>• No major intraoperative complications in the PVP group<br>• Transfusion rate 20%, TUR syndrome rate 5% in TURP group, 0 in PVP group<br>• Equivalent improvement in Qmax, IPSS and PVR<br>• Reduced LOS and LOC for PVP<br>• No difference in postoperative bladder neck contracture<br>• Repeat procedure was required in one TURP and six PVP patients |
| Bouchier-Hayes et al. [36] | 2010 | 80-W KTP vs. TURP | 12 | 59 vs. 50 | • Equivalent improvement in Qmax, IPSS and PVR<br>• Reduced LOS (1.09 vs. 3.6 days) and LOC (13.0 vs. 44.7 h) for PVP<br>• Adverse events less frequent in PVP group |
| Horasanli et al. [37] | 2008 | 80-W KTP vs. TURP | 6 | 39 vs. 37 | • Early functional results (IPSS, Qmax and PVR) of TURP are superior to PVP in patients with enlarged prostates > 70 ml<br>• Reduced LOS and LOC for PVP<br>• Reduced operation time for TURP |
| Bachmann et al. [6] | 2005 | 80-W KTP vs. TURP | 6 | 64 vs. 37 | • Prospective two-centre study (not randomised)<br>• Operating time shorter in TURP group<br>• Decrease of serum haemoglobin and Na greater after TURP<br>• LOC shorter for PVP<br>• Outcome of Qmax and IPSS similar in both groups within 6 months<br>• Sort of perioperative complications different in both groups, however overall cumulative perioperative morbidity comparable (PVP 39.1% vs.TURP 43.2.1%) |

*IIEF-5, International Index for Erectile Function-5 questionnaire; LOC, length of catheterisation; LOS, length of stay; OP, open prostatectomy.*

**Table 1** *Major studies of TURP (continued)*

| RCT | Year of publication | Comparators | Follow-up (months) | No. of patients | Main results |
|---|---|---|---|---|---|
| Elmansy et al. [27] | 2012 | 120-W HPS vs. HoLEP | 12 | 37 vs. 43 | • Subjective functional results, such as IPSS and QoL are equal for HPS PVP and HoLEP<br>• Early objective functional results (Qmax, PVR) of HoLEP appear to be superior<br>• 22% HPS PVP cases converted due to bleeding (intention to vaporise to the capsule in all cases) |
| Chiang et al. [30] | 2010 | 120-W HPS vs. 200 W diode laser (980 nm) | 12 | 84 vs. 55 | • No difference in IPSS, Qmax, QoL and PVR between HPS and diode laser<br>• Higher postoperative irritative symptoms after diode laser<br>• Superior haemostatic properties for diode laser<br>• Higher reoperation rate due to bladder neck sclerosis and necrotic tissue |
| Skolarios et al. [28] | 2008 | 80-W KTP vs. OP | 18 | 65 vs. 60 | • Inclusion criteria: prostate volume > 80 ml<br>• PVP with longer operation time (80 vs. 50 min), shorter LOS (48 vs. 144 h) and LOC (24 vs.120 h)<br>• No difference in IPSS, Qmax, PVR, IIEF-5 and reoperation rate<br>• At 3 months, prostate volume was significantly lower in OP (10 vs. 50 ml)<br>• Better QoL for OP after 6 and 12 and 18 months<br>• 13% transfusion rate in OP group, 0% in HPS PVP group |

*IIEF-5, International Index for Erectile Function-5 questionnaire; LOC, length of catheterisation; LOS, length of stay; OP, open prostatectomy.*

***e) Drawbacks***

There is some concern regarding the long-term reoperation rate after PVP. Scientifically, there is still a lack of long-term follow-up of the functional outcome and reoperation rate in patients treated with GreenLight PVP compared to TURP. The study of Al-Ansari et al. from 2010, with the longest available follow-up (3 years), comparing 120-W HPS PVP with TURP, showed a higher reoperation rate for PVP (11% vs. 1.7%), but all reoperation cases had an initial prostate size > 80 ml [9]. There have been a few other long-term studies of 80-W KTP, but not in the setting of a randomised trial. Ruszat et al. published a 3-year retreatment rate of 6.8% with 80-W KTP PVP. Urethral and bladder neck strictures were observed in 4.4% and 3.6% of patients, respectively [42]. Bachmann et al. compared 80-W KTP PVP with TURP (not randomised) and reported reoperation rates of 6.7 vs. 3.9% due to insufficient tissue removal, 4.5 vs. 3.1% due to urethral strictures, and 4.5 vs. 2.4% due to bladder neck strictures [43]. One of the reasons for higher reoperation rates is insufficient tissue removal. The RCTs listed in **Table 1** showed significantly less removal of prostate tissue by PVP compared to TURP. This is certainly due to the lower power of the KTP and HPS system compared to the XPS system using the MoXy fibre. Comparison of the efficiency of the three systems concluded that the XPS system is more favourable with regard to reduced operation time, fibre use and PSA reduction, suggesting more cost-effective tissue removal [22,24,25]. In conclusion, the higher vaporisation speed of the XPS system probably eliminates this disadvantage of the previous systems. If we consider again the Goliath study, TURP remains the faster technique (39.3 vs. 49.6 min), but XPS achieves the same reduction in prostate size measured by postoperative transrectal ultrasound. Using PSA reduction as surrogate parameter for prostate volume reduction, TURP was still better (XPS: –34%, TURP: –43.2%) [14].

Many vaporisation techniques are used. Studies comparing the different techniques regarding functional outcome and vaporisation effects/efficiency are missing. A frequently underestimated problem is the learning curve for GreenLight vaporisation. An international group of experts recommends 30–50 procedures as a minimal requirement to become familiar and safe with the technique [15]. Tissue factors such as fibrotic adenoma, prostate stones, and bleeding vessels may interfere with vaporisation. Other problems of the PVP laser technique can be explained by its biophysical characteristics. At a fibre–tissue distance > 3 mm, energy density already drops, with the result that tissue coagulation increasingly occurs instead of vaporisation. However, the coagulated tissue can be a vaporisation barrier, which limits the vaporisation effect. Maintaining

an optimal tissue distance is sometimes hindered due to anatomical conditions and limited visibility through the development of vaporisation bubbles. These facts underline that the technique and the power of the system itself influence the tissue removal and adverse effects. The experience of the surgeon using the GreenLight laser and knowing the physical characteristics of the system are important in achieving patient satisfaction, good functional outcome, and a low rate of adverse effects.

### *f) Conclusion*

Currently, there are three GreenLight systems: 80 W KTP, 120 W HPS and 180 W XPS. They have all been used in clinical studies with similar results and complications when compared with other minimally invasive techniques in short- and medium-term follow-up. Due to the strong haemostatic properties of the GreenLight laser, it is particularly suitable for patients under oral anticoagulation or antiplatelet therapy. Some recent studies have found that XPS has greater efficiency with comparable intraoperative safety and postoperative results.

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# III. TURP AND BIPOLAR TURP

## 1. INTRODUCTION

For more than seven decades, TURP has been the reference surgical treatment for management of LUTSs due to BPO because of its well-documented long-term efficacy [1].

In recent years, the role of TURP has been challenged by the introduction of various minimally invasive treatments such as transurethral microwave thermotherapy (TUMT) or transurethral needle ablation of the prostate, and particularly, laser procedures such as HoLEP and ThuLEP and PVP [2, 3, 4]. The extended use of medical therapy, together with the introduction of more minimally invasive treatments, has led to a progressive decline in the number of TURP procedures performed in western countries [5].

There has been significant improvement in the technical aspects of TURP, such as the introduction of continuous-flow resectoscopes and incorporation of bipolar technology aimed to improve the efficacy of the procedure and reduce its morbidity [6, 7].

The goals of this chapter are to review the current role of TURP in the management of BPO and to compare the clinical results of monopolar TURP (mTURP) and bipolar TURP (bTURP).

## 2. DIAGNOSTIC WORK-UP

Systematic diagnostic work-up should be done by history; validated symptom questionnaires (e.g., IPSS); physical examination; urine and blood analysis; prostate, bladder and kidney ultrasound uroflowmetry; and ultrasound measurement of PVR. The systematic work-up should exclude relevant diseases or conditions that also cause LUTSs, other than BPO [4]. None of the current guidelines recommends routine pressure flow tests before surgery [2]. Nevertheless, filling cystometry and pressure–flow measurement are indicated before surgical treatment in men who: [1] cannot void > 150 ml; [2] have a maximum flow rate > 15 ml/s; [3] are < 50 or > 80 years of age; [4] can void but have PVR > 300 ml; [5] are suspicious of having neurogenic bladder dysfunction; [6] have bilateral hydronephrosis; and [7] have undergone radical pelvic surgery or previous unsuccessful (invasive) treatment [4].

## 3. INDICATIONS

The most frequent indication (50–60%) for TURP is moderate to severe LUTSs refractory to medical treatment [2] in patients with < 80 ml prostate volume (Section 3.1). Strong indications for invasive treatment irrespective of symptoms are: [1] acute urinary retention; [2] BPE-related haematuria; [3] recurrent urinary tract infection (UTI) caused by bladder outlet obstruction; [4] bladder diverticula; [5] bladder stones; and [6] renal insufficiency caused by BPO [2, 4, 8].

### *a) Prostate size*

In recent guidelines, TURP is indicated as the gold standard treatment for LUTSs secondary to BPO in prostates between 30 and 80 ml [4]. TURP can be successfully performed even in patients with small prostates (< 30 ml) but it can be safely replaced by transurethral incision of prostate, and this is particularly true for small prostate glands without a median lobe [4]. On the contrary, the upper prostate volume limit is still a matter of debate. Traditionally, a prostate volume exceeding 100 ml is considered an indication for OP or HoLEP, because several trials have demonstrated that HoLEP prostatectomy achieves the same results as simple OP, with lower invasiveness [4, 9]. However, there is no strong evidence in the literature regarding the upper size limit of the prostate suitable for TURP: the suggested threshold depends on the surgeon's experience, resection speed, and resectoscope size [4]. Moreover, with the introduction of bipolar technology (Section 7), this limit seems to have been overcome as a result of the favourable safety profile of bipolar TURP, even in cases with long operating times [4, 10, 11, 12].

## 4. OPERATIVE AND PERIOPERATIVE ASPECTS

### *a) Antibiotic prophylaxis*

UTIs should be treated before performing TURP [4, 13]. Antibiotic prophylaxis before TURP has been investigated in several RCTs [14–16]. All three of these suggested the routine use of antibiotic prophylaxis because it significantly reduces bacteriuria, fever and sepsis after TURP. The optimal antibiotics and method of administration are still a matter of debate, even though Berry et al. concluded that a significant reduction in postoperative UTI can be achieved with a wide range of antibiotics, including quinolones, cephalosporins and co-trimoxazole [14]. They also suggested that short courses of antibiotics may be more effective than single-dose regimens [14].

### *b) Neoadjuvant therapy with 5α-reductase inhibitors (5-ARIs)*

Different RCTs have investigated the role of 5-ARIs in decreasing perioperative bleeding associated with TURP [17, 18]. Although no systematic review or meta-analysis is available, the majority of papers suggest that 5-ARIs (finasteride or dutasteride) decrease the risk of bleeding [17, 18]. In these studies, the 5-ARI was administered 2–6 weeks before surgery but the optimal route of administration has not yet been determined.

### *c) Instruments*

Traditionally, TURP has been performed by monopolar diathermy, which involves an electrical current flow from an active electrode to the prostate and through the body, before exiting via a return electrode placed on the skin [19]. Modern generators produce high-frequency current with a maximum cutting power of 200 W [7]. A microprocessor-controlled electrical unit with an active electrode that transduces permanent signals to the processor allows real-time power adjustment [8]. Peak powers in the millisecond range may reach 230 W, but the total power for TURP is lower than that of earlier generators. The use of hypo-osmolar irrigation fluids (i.e., glycine, sorbitol or mannitol solutions) that are molecularly inert, optically clear and nonconductive is required. The introduction of bipolar devices represents an important technical improvement (Section 7.1).

During recent decades, technical refinements have improved the TURP procedure. The introduction of video-TURP has improved ergonomic aspects of the procedure and the quality of the endoscopic field of vision [8, 20, 21], and has facilitated teaching of the procedure, which is of paramount importance, especially in academic centres.

The introduction of continuous-flow resectoscopes (i.e., Iglesias' resectoscope) has accelerated the procedure (no need for bladder voiding) and has provided a low irrigation pressure that reduces the risk of fluid reabsorption [22]. The main drawback of these resectoscopes is the larger diameter (≥ 26 F) with respect to other ones and this may lead to urethral injuries [8].

Introduction of the suprapubic trocar represents another step in the direction of low irrigation pressure [23]. The system achieves further improvement of the quality of vision because the irrigation fluid (with blood and prostatic chips) flows from the resectoscope to the suprapubic trocar, maintaining a clean prostatic fossa. Although it is not widely used by urologists, some authors recommended the use of a suprapubic trocar when a large gland (> 60 ml) has to be approached [7, 8].

### *d) Resection technique*

Different approaches to prostate resection have been proposed. With the Nesbit technique, resection starts at the level of the ventral parts of the gland (between 11 and 1 o'clock), followed by both lateral lobes, the median lobe, and finishing with the apex [24]. Flocks and Culp started with the median

lobe then segmented the lateral lobes at 9 and 3 o'clock [25]. Mauermayer [26] divided the procedure into four steps: mid-lobe resection, resection of lateral lobes and ventral parts, and apical resection. There is no evidence about the best technique, and the choice depends on the surgeon's preference.

We now describe the Mauermayer technique in more detail. The procedure starts with early median lobe resection. The lobe is resected down to the point where circular bladder neck fibres are encountered. At the end of median lobe resection, the bladder neck and prostatic fossa are flat with the bladder floor that extends from the trigone. Overresection of this area may undermine the bladder neck and should be avoided. Once the median lobe is resected, the resection continues at 6 o'clock until the verumontanum, which is the limit of the resection and should be respected. In this way, a large working channel is created and this helps further steps of the procedure. Then, the lateral lobes are treated. The left lobe is treated from 5 o'clock, anticlockwise. The resectoscope is rotated without advancing or withdrawing the scope after each loopful. On small prostates this may be the entirety of the prostate, but large prostates may require multiple loop lengths. In that case, once this is done to near appropriate depth, one can progress more distally. The character of the prostatic tissue usually changes when the surgical capsule is encountered: the foamy prostate tissue becomes more stromal and fibrous. Resection of the lateral lobe reaches the verumontanum. During this phase, it is important to avoid coagulating small bleeding vessels in tissue that will soon be resected. The same procedure is done on the right side.

Attention can then be turned to the anterior prostate: resection begins just inside the bladder neck and continues distally. During resection of the anterior prostate, at the apex, the verumontanum should be carefully checked to avoid external sphincter damage.

Finally, resection of the apex is refined. The resectoscope is gently withdrawn distal to the verumontanum to visualise exactly the edge of the existing resected tissue. The scope is placed at the proximal aspect of the verumontanum and, without moving the resectoscope in or out, the apex is resected by rotating the scope.

At the end of resection, the bladder is irrigated with an Ellik evacuator to remove the prostatic chips. This process usually triggers mild bleeding. A few minutes of coagulation of the small bleeding vessels are well spent, and attention should be paid to the bladder neck and anterior tissue. Usually, haemostasis is checked after interruption of the irrigating fluid flow [26, 27].

After the procedure a large (20–22 Fr) three-way catheter is left in place. A balloon is blocked in the prostatic fossa (volume of balloon = resection weight) or left in the bladder (volume of balloon + resection weight + 20 ml), depending on the surgeon's preference and on immediate postoperative haematuria [8].

***e) Radical versus limited resection***

Only a few studies have assessed the roles of radical (i.e., resection down to the surgical capsule) versus minimal TURP. Aagaard et al. have reported 10 years of follow-up data from 167 patients treated by radical or minimal TURP [28]. The decrease in urinary symptoms and improvements in Qmax and PVR were similar in the two groups, but the treatment failure rate within 10 years was higher in the minimal (23% vs. 7%, $P < 0.05$) TURP arm [28]. In a similar RCT, the authors concluded that functional results of minimal and standard TURP were comparable [29]. Notwithstanding any firm conclusions, these studies suggest that radical TURP is not mandatory in all patients.

***f) Postoperative care***

Immediately after the procedure, continuous bladder irrigation with saline solution is started and remains until the first postoperative day or depending on postoperative haematuria. The diet is resumed 12 h after the procedure, according to the patient's acceptance. Mobilisation of the patients is allowed on postoperative day 1.

Different protocols are used in the clinical practice for catheter removal. Such protocols include prolonged catheterisation in cases with larger prostates, catheter removal as soon as urine is completely cleared, completely clear urine after 24 h without irrigation, and removal on a fixed postoperative day [30]. In general, the catheter is removed after 1–4 days [31, 8].

## 5. EFFICACY

***a) Symptoms***

TURP provides excellent and stable clinical outcomes, as demonstrated by several studies with long-term follow-up (≥ 20 years). Madersbacher et al. reviewed 29 RCTs published between 1986 and 1998 [5] and found that the overall decrease in symptom score was 70.6%.

In a recent revision of 25 RCTs with a TURP arm published between 1996 and 2006 (1144 men), Marszalek et al. reported an overall American Urological Association (AUA)/ IPSS decrease of 62% and a consistent improvement in QoL [2].

***b) Peak flow and post-void residual volume***

Qmax and PVR volume are currently used to evaluate the clinical results of TURP. In the study of Madersbacher et al. [5], the mean increase in Qmax was 9.7 ml/s, (+120%) with respect to baseline. Similarly, Marszalek et al. reported an increase of Qmax from 8.3 at baseline to 20.7 ml/s (+149%) [2].

We analysed the data of a recent systematic review and meta-analysis of the clinical effectiveness of mTURP versus bTURP [19]. Considering the data of 579 patients in the monopolar arm, the mean (unweighted) improvement of Qmax 12 months after surgery was +12 ml/s (+183%).

In the systematic review on 2434 patients, Lourenco et al. compared TURP and other minimally invasive treatments for BPH and concluded that TURP was more effective than other treatments [laser coagulation, TUMT and transurethral needle ablation (TUNA] in terms of symptom score and increase in urine flow rate [32].

In the study of Madersbacher et al. [5], the PVR volume decreased by 60.5% after TURP, whereas, in a recent meta-analysis, Mayer et al. reported a mean reduction of 90 ml after prostate resection [31]. We analysed the data of the meta-analysis of Ahyai et al. [33] about functional outcomes and complications after transurethral procedures for BPH, and we found a mean (unweighted) decrease of PVR volume of 71%.

## 6. MORBIDITY

### *a) Intraoperative complications*

#### 1. Bleeding

The main intraoperative complication during TURP is still bleeding, even if it has decreased significantly in recent years. Studies from the 1970s to the 1990s have reported a transfusion rate < 20%, while in 1999, Madersbacher et al. reported that mean transfusion rate was 8.6% [2, 5]. In 2008, Reich et al. found that the transfusion rate for > 10 000 procedures was 2.9% [34]. In 2012, Mayer et al. reviewed data from 67 studies on 3470 patients treated with mTURP (1997–2007) and reported a transfusion rate of 4.4% [31].

Risk factors for arterial bleeding are preoperative infection or urinary retention because of a congested prostate gland, while venous bleeding generally occurs because of capsular perforation and venous sinusoid openings. Overall, the amount of intraoperative bleeding may be related to gland size [8, 35].

Rassweiler et al. have reported the technical aspects of prevention and treatment of bleeding during and after TURP. In case of significant bleeding, the catheter balloon can be inflated up to 70–80 ml and put under traction to compress the prostatic fossa. Digital rectal compression for 5–10 min may be useful [8].

#### 2. TUR syndrome

TUR syndrome is characterised by mental confusion, nausea, vomiting, hypertension, bradycardia, and visual disturbances. It is caused by dilutional hyponatremia (serum sodium < 125 mEq/l) due to irrigating fluid reabsorption. When untreated, TUR syndrome may lead to cerebral or bronchial oedema [8].

The incidence of this life-threatening syndrome has decreased during recent decades. In the study of Mayer et al., TUR syndrome rate was 1.8%, and in a recent meta-analysis comparing mTURP and bTURP, TUR syndrome occurred in 35/1375 patients in the mTURP group (2.5%) [31].

The main risk factor for TUR syndrome is early perforation of prostatic capsular veins or sinuses during the procedure. Other factors are prolonged operation time, large prostate, and past or present nicotine abuse [36]. Early diagnosis controlling serum electrolytes is mandatory. Immediate suspension of the procedure and infusion of furosemide and hypertonic NaCl are the therapies of choice [8].

The introduction of bipolar technology has further decreased the rate of this complication (Section 8.3.2).

#### 3. Other complications

Extravasation of irrigating fluid occurs when the prostatic capsule is injured or the bladder neck is divided. Even if the rate of capsular perforation ranges from 0.9 to 4%, [37, 38] poor data are available in systematic reviews and meta-analyses.

Rectal injury during TURP is a rare complication, and the vast majority of reported cases have occurred in patients who required re-TURP or who had radiotherapy to either the prostate or rectum. If a small rectal injury occurs, an initial trial of non-operative therapy with urethral drainage, bowel rest, and antibiotic therapy is reasonable. If a persistent fistula develops or when major injury occurs, fistula repair and colostomy should be considered [27].

Injury of the ureteral meatus is a possible intraoperative complication that occurs more frequently in patients with a large median lobe. Reports on these complications are anecdotal [8].

### *b) Postoperative complications*

#### 1. Clot retention

Postoperative bleeding may result in clot formation and a bladder tamponade that require evacuation or, less frequently, re-intervention (1.3–5%) [8].

In their meta-analysis and critical comparison of three decades of mTURP, Mayer et al. reported a clot retention rate of 1.3–7.3% [31].

Unknown coagulation disorders or chronic use of antiplatelet or anticoagulant drugs may increase the risk of bleeding [39]. Evacuation of clots and balloon traction at the bedside, or (when these manoeuvres are not successful) reoperation, are the treatments of choice [8]. If surgical intervention remains unsuccessful, percutaneous superselective embolisation is an option [40].

**2. UTIs**

Rate of UTI after TURP ranges widely from 4% up to > 20% [8]. Mayer et al. reported that the rate of UTI after mTURP varied from 2.3 to 7.9% and it was significantly higher in more recent series [31]. The authors suggested that this may be related to greater antibiotic resistance. Rassweiler et al. identified the following conditions as risk factors for UTI: [1] preoperative bacteriuria; [2] procedure duration > 70 min; [3] postoperative stay > 2 days; and [4] discontinuation of catheter drainage (clot evacuation) [8].

Antibiotic prophylaxis is recommended (Section 4.1) before TURP.

**3. Failure to void**

Failure to void after catheter removal occurs in 3–9% of patients treated with TURP. In the meta-analysis of Lourenco et al., this rate reached 4.5% (significantly lower than TUMT, TUNA and laser ablation) [32] and in the study of Mayer et al. it reached 6.8% [31]. The authors explained these data with detrusor hypo-contractility after prolonged BPO. Other authors agree that detrusor hypocontractility is the primary cause of urinary retention after TURP [37, 41]. In light of this, urodynamic evaluation before re-TURP seems to be mandatory [8, 2].

***c) Long-term complications and retreatment***

**1. Incontinence**

Although early urge incontinence due to detrusor overactivity (pre-existing or related to healing of prostatic fossa or UTI) may occur in up to 40% of patients treated with TURP [8], and can be managed with anticholinergics and non-steroidal anti-inflammatory drugs, incontinence that persists for > 6 months requires attention. A diagnostic work-up including urodynamic and endoscopic evaluation should be done. Rassweiler et al. reported different causes for long-term incontinence, such as sphincter incompetence (30%) or detrusor instability (20%). The incidence of stress urinary incontinence ranges from 0.5% to 2.2% [4, 8]. In a recent meta-analysis of mTURP and bTURP, incontinence occurred in 6/392 (1.5%) cases in the mTURP arm [19].

Treatment includes pelvic floor rehabilitation, biofeedback, drugs (duloxetine) and surgery (bulking agents, pro-ACT, slings, and artificial urinary sphincter) [2].

**2. Bladder neck stenosis and urethral strictures**

The two major late complications are urethral strictures and bladder neck contractures. Despite improvements in surgical techniques, lubricants, instruments, and electrical technology, the incidence of urethral strictures is still remarkable (2.2–9.8%) [8]. In the study of Mayer et al., the incidence was 4.1% [31], while in the meta-analysis of Omar et al., urethral strictures occurred in 34/994 (3.4%) cases [19]. Some authors have highlighted the multifactorial causes of urethral strictures, depending on surgical technique, duration of intervention, technology, instrument size, and antibiotic regimen [8].

Treatment includes endoscopic urethrotomy or laser incision.

Bladder neck stenosis usually occurs after resection of small prostates (< 30 ml) and its incidence ranges from 0.3 to 9.2% [8]. In the recent literature, the rate is ~3% [31]. Transurethral incision of the prostate should be considered when this kind of prostate has to be managed.

Treatment includes electrical, or preferably, laser incision of the bladder neck [42].

**3. Sexual dysfunction**

Two major issues arise when this topic is discussed: loss of ejaculation and ED after the procedure.

Loss of ejaculation (retrograde ejaculation) is due to resection/destruction of the bladder neck and is reported in 65% of cases [2, 5]. Lourenco et al. reported loss of ejaculation in 196/408 patients (48%) in the TURP arm of their meta-analysis [32]. Some authors suggest that retrograde ejaculation can be avoided if the prostatic tissue around the verumontanum is spared during the procedure [8]; nevertheless, this risk should be kept in mind when a young patient has to be treated.

ED has been reported in 3.4–32% of cases [5, 8]. In an analysis of 29 RCTs, the incidence of ED following TURP was 6.5% [5], and Lourenco et al. reported ED in 60/477 (12%) of patients after TURP [32]. Nevertheless, there is a longstanding debate about the impact of TURP on ED. The most cited article on this topic is an RCT by Wasson et al. that compared ED in patients treated with TURP and watchful waiting for moderate symptoms of BPH. There were comparable ED rates in both arms (19% and 21%, respectively) after 2.8 years of follow-up [43]; thus, high rates of postoperative ED reported by some authors seem more likely to have been caused by confounding factors (such as age and comorbidity) rather than TURP.

**4. Retreatment**

Traditionally, retreatment rate after TURP ranges from 3 to 14% [5]. Lourenco et al. reported retreatment in 2% of TURP procedures [32] and Mayer et al. reported a rate of 5% [31]. Previously, some authors have suggested that the reoperation rate is higher after TURP than OP. Roos et al. found a reoperation rate within 8

years of 12–15% versus 1.8–4.5% for TURP and OP, respectively [44]. Semmens et al. reported a reoperation rate of 6.6% versus 3.3%, respectively [45]. The main cause of reoperation is incomplete resection [8].

One should note that retreatment rate after TURP is lower than that after other minimally invasive treatments [5, 32].

***d) Mortality***

**1. Perioperative mortality**

Mortality following TURP has decreased constantly and significantly during the past few decades, and in the majority of recent series, has ranged from 0.1 to 0.71% [5, 8, 44]. For example, in an analysis of 10 564 men who underwent TURP, mortality during the first 30 days was only 0.1% [34].

**2. Long-term mortality**

In the most cited paper about this topic, Roos et al. reported that mortality after TURP was higher (relative risk: 2.5) than after OP [44]. The authors correlated this difference with the higher rate of myocardial infarction in the TURP arm. Nevertheless, these results have never been confirmed [46]. In a study of > 25 000 men, Madersbacher et al. compared mortality rate after TURP (20 671 procedures) and OP (2452 procedures) and showed that the 8-year incidence of myocardial infarction was identical after TURP (4.8%) and OP (4.9%), and mortality rates at 90 days and 1, 5 and 8 years were almost identical [47].

## 7. MODIFICATIONS OF TURP: BIPOLAR TRANSURETHRAL RESECTION OF THE PROSTATE

One of the most important technical refinements of TURP is the incorporation of bipolar technology.

***a) Technology and instruments***

As defined by the International Electrotechnical Commission, a bipolar electrode has two active electrodes attached to a single support, with a structure that allows high-frequency electric current to pass through these two electrodes when electrified [7].

During the past decade, different manufacturers (Gyrus, VISTA-ACMI, Olympus, and Karl Storz) incorporated bipolar technology in endoscopic instruments for TURP.

High-frequency electric power (≤ 400 W) passes through the conductive irrigation solution (0.9% NaCl) resulting in a vapour layer (plasma) containing energy-charged particles, which induce tissue disintegration through molecular dissociation [7]. Once the cut is initiated, due to the lower impedance, the power required for tissue resection is significantly reduced to 90–120 W.

Bipolar devices differ with respect to the shape of the loop and the technical solution of bTURP (i.e., active and return electrode). The different devices can be distinguished by the way in which the active and passive electrodes are arranged: [1] two different loops (parallel or opposite) (Vista ACMI – withdrawn from the market in 2006 and Karl Storz); [2] using the distal end of the resection loop [Gyrus]; and [3] using the working element of the resection shaft (Olympus).

Theoretically, only the instruments with two loops with two different wires to conduct the current path (active and passive/neutral electrodes) fulfil all criteria of bipolar technology, while other devices should be called almost bipolar.

The other technical aspects of the bipolar resection (Sections 4.3–4.6) such as instruments, resection technique and postoperative care are the same as for mTURP.

***b) Potential pro and cons of bipolar TURP***

Bipolar technology allows the use of saline solution (0.9%) as irrigating fluid and this plays a basic role in reducing morbidity of the procedure. The use of physiological NaCl for irrigation virtually eliminates the risk of hyponatremia of TUR syndrome.

Bipolar systems lead to a lower resection temperature than that of monopolar systems, thus, theoretically, thermal damage to surrounding tissue is reduced.

As emphasised by Rassweiler et al. [7], bipolar technology should reduce the risk of prostatic capsular lesions as a result of lower electrical stimulation of the pelvic floor and better endoscopic orientation due to the reduced coagulation depth in the resected prostatic tissue.

bTURP technology presents some drawbacks. Paradoxically, initiation of the cut (microseconds) requires high electrical power (≤ 480 W) that may result in electrical or thermal injury of the surrounding tissues. The technical modifications of bTURP may also play an important role. For example, the use of a metal sheath or single loop as a neutral electrode may lead to conductive trauma of the urethra in the case of insufficient low-conductive lubrication [48]. Some authors have reported an inferior handling quality of the bipolar loops [7].

## 8. BIPOLAR VERSUS MONOPOLAR TURP

There have been several randomised trials comparing clinical results of bTURP and mTURP and at least three meta-analyses have been published [12, 31, 49]. In the first meta-analysis, the “Quality Health Ontario” group dedicated a section of important evidence-based analysis to mono- and bipolar TURP [49]; in the second one, Mamou-

lakis et al. analysed the data of 17 RCTs (1406 patients) [12]; and in the recent one, Omar et al. revised data of 24 RCTs (2744 patients) [19].

In the next two sections we briefly revise the evidence in the current literature, focusing on meta-analysis data.

### *a) Perioperative data*

#### 1. Operative times

One of the potential drawbacks of bTURP is its long operating times [50,51]. On the contrary, Rassweiler et al., in a non-systematic literature review [7] did not find any differences in terms of resection speed (0.4–0.75 g/min monopolar vs. 0.3–0.6 g/min bipolar). Meta-analyses that compared operating times of the two techniques confirmed that were no differences [12, 49].

#### 2. Blood losses

Several data are available about post-procedural transfusion rate (Section 8.3.1). However, only a few papers report mean decreases in haemoglobin levels that may reflect the physiological blood loss during the procedure. Overall, the mean decrease in haemoglobin after bTURP is lower [52, 53], or equal [54] to that of mTURP, and none of the RCTs reviewed showed a higher haemoglobin loss for bTURP.

#### 3. Duration of irrigation

Mamoulakis et al. analysed data of six trials that reported the duration of irrigation [12]. Overall, duration was longer in the mTURP arm and pooled analysis confirmed this result (weighted mean difference: 8.75 h; 95% confidence interval: 6.8–10.7 h).

#### 4. Catheterisation time

Comparison of catheterisation time among studies is difficult because of the different protocols for catheter removal (Section 4.6). Nevertheless, two meta-analyses have focused on this point. In the study of Mamoulakis et al., mean catheterisation times ranged from 31.9 to 108 h in the mTURP arm and from 18.4 to 96 h in the bTURP arm [12]. These results were confirmed by another meta-analysis (bTURP vs. mTURP: 32.2 vs.57.5 h) [49].

#### 5. Postoperative stay

Several trials have reported that length of hospital stay after bTURP is shorter (≤ 48 h) or equal to that of mTURP. Unfortunately, due to the large heterogeneity of the pooled data, analysis was not possible [12]. In the report of the Health Quality Ontario Group, the pooled reduction in postoperative stay was 0.9 days [49].

### *b) Efficacy*

The literature does not demonstrate significant differences between bTURP and mTRUP in terms of symptom relief, QoL, Qmax improvement and PVR reduction. In other words, the two techniques are equally effective in treating symptoms and improving urinary flow [12, 19, 49].

The meta-analysis of Omar et al. adds some new information to the current literature. For the first time in a meta-analysis, postoperative Qmax (ml/s) was higher in the bTURP arm at 3 months (3.04 ml/s), 6 months (2.14 ml/s) and 12 months (1.30 ml/s). Although these differences were significant, the authors concluded that no clinically significant differences were found and highlighted that the meta-analysis showed evidence of heterogeneity [19].

### *c) Morbidity*

Several RCTs have focused on the safety of bTURP and all meta-analysis have reported data on procedural morbidity.

The literature confirms the excellent safety profile of bTURP and demonstrates that this approach is associated with fewer adverse events than mTURP is [12, 19, 49].

#### 1. Bleeding

The RCT of Omar et al., including 136 patients, focused specifically on perioperative bleeding. The decline in postoperative haemoglobin and bleeding requiring transfusion was significantly greater in mTURP than bTURP [51]. In the meta-analysis of Mamoulakis et al., the need for blood transfusion in the mTURP group was twice that in the bTURP group (3.5% vs. 1.8 %) but the difference was not significant [12]. This trend reached statistical significance in the meta-analysis of Omar et al., in which the blood transfusion rate was 4.3 and 2.2%, respectively [19].

#### 2. TUR syndrome

One of the main potential advantages of bipolar technology is the disappearance of TUR syndrome. However, this technology does not prevent fluid reabsorption and subsequent complications such as pulmonary oedema [7]. The literature confirms that TUR syndrome is negligible during bTURP. Mamoulakis et al. reported no case of TUR syndrome in 0/681 patients in the bTURP arm versus 13/681 (1.9%) in the mTURP arm [12]. The same results emerged more clearly in the study of Omar et al. (bipolar 0/1401 vs. monopolar 35/1375; 2.5%) [19].

#### 3. Clot retention

As previously stated, clot retention is one of the more frequent perioperative complications. Current data confirm that clot retention is less frequent after bTURP than mTURP. Clot retention rate after

bTURP was 2.8% versus 8.7% after mTURP [12] and 2.7% versus 5.8% [19]; both differences were significant.

#### 4. UTIs

There were no differences between the bTURP and mTURP groups for postoperative UTIs in the eight trials considered by Omar et al. [19].

#### 5. Failure to void

Six RCTs compared failure to void after mTURP and bTURP. Overall, 18/484 cases (3.7%) in the bTURP group and 21/488 (4.3%) in the mTURP group were recorded [19].

#### 6. Incontinence

Postoperative stress incontinence was analysed in six RCTs, and no differences were recorded between the mTURP and bTURP groups. Incontinence rate was 1% in the bTURP group and 1.5% in the mTURP group, and in three of the trials, no incontinence was recorded [19].

#### 7. Urethral strictures

One of the most important concerns about bTURP was the high rate of urethral strictures reported in the past [55–57].

Larger resectoscope diameter (27 Fr), higher ablative energy peak used, and electric current return (leakage) via the resectoscope sheath have been proposed as risk factors for urethral strictures [8, 12].

In a recent RCT involving 518 patients that focused on urethral strictures, incidence was 1.5% in the bTURP group and 2.4% in the mTURP group [58]. In the study of Mamoulakis et al., incidence was 2.1% and 2.7% [12], and in the study of Omar et al., the incidence was 3.3% and 3.4% in the bTURP and mTURP groups, respectively (not significant in both cases) [19].

Notwithstanding the initial doubts, the current literature demonstrates that bTURP does not increase the risk of urethral strictures with respect to mTURP.

#### 8. Sexual dysfunction

Several RCTs focused specifically on sexual function after mTURP and bTURP. In a study involving 295 patients, IIEF scores, orgasmic function, sexual desire, intercourse satisfaction, and overall sexual satisfaction did not differ significantly between the techniques during follow-up [59]. Similarly, in an RCT involving 286 patients, Akman et al. reported data of 188 patients with regular sexual activity. ED worsened in 32 (17.0%) patients, improved in 53 (28.2%), and remained unchanged in 103 (54.8%). Changes in IIEF scores during follow-up were similar between the bTURP and mTURP groups [60].

Although bipolar technologies have demonstrated no electric current passage through the periprostatic tissues to stimulate or damage the surrounding nerves, a double-blinded RCT evaluating ED is still awaited, and perhaps it reveals yet another potential advantage of bipolar technology, that is, not endangering erectile function which is up to now not clearly evident [mamu new gold standard]

#### 9. Retreatment

Few papers report data on retreatment after bTURP. In the RCT of Autorino et al., one of 31 (3.2%) patients in the mTURP group and one of 32 (3.1%) in the bTURP group underwent reoperation for BPH recurrence after 4 years [61]. In an international multicentre RCT, the midterm results at up to 3 years follow-up showed that the retreatment rate was 4.3% and did not differ between the bTURP and mTURP groups [30]. In an RCT with 5 years follow-up, Xie et al. reported retreatment in 3 of 110 (2.7%) patients in both groups. Thus, the midterm results of bTURP are at least comparable with those of mTURP [62].

## 9. CONCLUSIONS

mTURP is the current surgical standard procedure for men with moderate-to-severe symptoms due to BPH and prostate 30–80 ml in volume. It provides subjective and objective improvement with acceptable complication rates. Technical improvements such as video-TURP and introduction of continuous-flow resectoscopes have made the procedure safer and have facilitated ergonomics and teaching possibilities. Functional results are stable after long-term follow-up, which is not the case for other transurethral procedures.

bTURP shares similar clinical efficacy with mTURP and has an improved safety profile, allowing minimal bleeding risk and eliminating the risk of TUR syndrome. Irrigation and catheterisation time are significantly shorter with bTURP than mTURP, even if it is unclear if this translates into shorter postoperative stay. Although mid-term results suggest that bTURP has a stable outcome, further data are needed to confirm these findings.

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# IV. LAPAROSCOPIC SIMPLE PROSTATECTOMY

## 1. INTRODUCTION

Prostatic adenomectomy is the surgical procedure perfomed to treat BPO. It is described by various nomenclatures such as enucleation of the prostatic adenoma, OP, benign prostatectomy, and simple prostatectomy. It is possible to perform prostatic adenomectomy by different approaches, including perineal, prevesical, retropubic or suprapubic, transvesical or combined.

The first interventions for correction of urinary retention resulting from enlarged prostate were performed via the perineal approach. In 1639, Covillard was probably the first to resect a hypertrophied median lobe, after conducting perineal cystolithotomy [1]. Subsequently, Gouley in 1873 and Goodfellow in 1891 described the systematic adenomectomy of lateral and median lobes during perineal prostatectomy [2,3].

In 1827, Amussat was the first to perform prostatectomy via the suprapubic transvesical approach for partial resection of a hypertrophied median lobe while performing suprapubic cystolithotomy [4].

Belfield5 in 1890 and Fuller6 in 1895 advocated the enucleation of all the obstructive prostatic tissue by suprapubic access, combined or not with the perineal approach. However, it was Freyer [7] in 1912 that popularised the technique, describing the results of > 1000 patients operated upon by transvesical suprapubic prostatectomy.

In 1909, van Stockum [8] published the first report of prevesical or retropubic prostatic adenomectomy through an incision directly over the anterior surface of the prostate; a technique defined by Millin [9] with modifications in 1947.

In the following decades, the transurethral endoscopic approach replaced open surgery for treatment of most cases of BPH.

Patients with a bulky prostate weighing > 80 g benefit from open adenomectomy [10-12]. Laparoscopic adenomectomy was described by Mariano et al.[13] in 2002, and in 2004, Nadler et al.[14] described the extraperitoneal approach for prostate adenomectomy. When compared with conventional surgery, the laparoscopic approach has several benefits: less intraoperative blood loss; better postoperative respiratory function; improved cosmetic appearance; shorter period of bladder irrigation and catheterisation; and reduced hospital stay and recovery time, despite the longer intraoperative time [15-18].

Sotelo et al. described robotic prostatic adenomectomy in 2008, with the aim of reducing the operating time and facilitating dissection of the adenoma through articulated instrumentation [19,20].

## 2. METHODS

A literature search was done in PubMed from 2002 to 2014, limited to studies in the English language. The key word used were “laparoscopy”, “benign prostatic hypertrophy”, “adenomectomy”, and “simple prostatectomy”. A total of 113 citations were extracted. After screening the titles, 18 studies were included in the final analysis.

The studies were rated according to the level of evidence (LE) and grade of recommendation (GR) using International Consultation on Urological Diseases (ICUD) standards.

## 3. OPERATIVE TECHNIQUE

Laparoscopic simple prostatectomy was originally carried out through a transperitoneal approach. Subsequently, many surgeons have preferred an extraperitoneal approach; probably to avoid communication between the abdominal cavity and urine. The surgical approach to prostatic adenoma varies, with the most common being the transvesical and transcapsular approaches.

We describe both the trans- and extraperitoneal approaches.

### *a) Indications*

Laparoscopic prostate adenomectomy is indicated for patients with urinary tract obstruction and prostates > 80 g. The indications for laparoscopic or open access are the same [10,11]. Patients in need of concomitant surgical treatment for large bladder diverticulum or bladder urolithiasis also have indications for laparoscopic surgery [10,11,21].

### *b) Contraindications*

The presence of small or fibrous glands, prostate cancer, untreated UTI, or history of previous pelvic surgery or radiotherapy can limit the laparoscopic approach for prostatic adenoma [10,11,21].

### *c) Preparation and patient positioning*

All patients receive a preoperative evaluation that includes a complete medical history and physical examination. They must respond to the IPSS or another QoL questionnaire to assess the degree of voiding impairment. If there are lumps on rectal examination or elevation in serum PSA, prostate biopsy guided by transrectal ultrasonography, should be performed to rule out the presence of cancer.

Ultrasound evaluates impairment of the upper urinary tract, identifies bladder pathology, estimates prostate volume, and quantifies the residual urine volume after voiding.

Patients with suspected urethral stricture, haematuria, or bladder stones or diverticulum are recommended to undergo urethrocystoscopic evaluation. This is also useful for planning the prevesical retropubic approach for prostate adenomectomy, assessing the presence of a large median lobe, and where bladder neck incision will facilitate the procedure.

Uroflowmetry is useful to estimate Qmax.

All patients give signed informed consent for the proposed procedure. Patients go to the hospital on the day of surgery, with 8 h fasting and colonic hygiene performed at home. Blood typing and reservation for transfusion are performed routinely. Antibiotic prophylaxis must be started at anaesthesia induction to prevent infections. Pelvic surgery and laparoscopic procedures are risk factors for venous thrombosis, therefore, prophylaxis with low-molecular-weight heparin is essential.

Patients are placed in the supine position, with their arms along the body, with shoulder pads. The legs are protected by bands or elastic stockings and a venous return pump, placed in leggings to allow

access to the perineum during the procedure and to facilitate approach of the monitor. Patients are fixed on the table using seat belts. The procedure is conducted under general anaesthesia with tracheal intubation and controlled ventilation to protect the airway, control of PaCO2, and assist surgical exposure.

The surgical table is positioned in the Trendelenburg position (Lloyd–Davies position) to retract the bowel from the pelvic operating field.

Povidine–iodine solution is used as an antiseptic agent for skin preparation. After placement of surgical draping, an 18 Fr Foley catheter is introduced to empty the bladder, allowing its aseptic handling during the procedure. The surgeon stands at the head of the operating table, the first assistant on the right side of the patient, the second auxiliary on the left side, and the surgical technician at the side of the patient's feet **(Figure 1).**

***d) Transperitoneal access***

The trocars are introduced using the transperitoneal approach. The first incision, at the umbilical level, is held open for insufflation of CO2 for pneumoperitoneum, and introduction of the 11-mm trocar for the zero-degree optic. A purse-string suture using non-absorbable number two sutures prevents loss of CO2 and fixes the trocar. After inspecting the cavity, three additional trocars are inserted under direct vision: one 6-mm trocar for suction and another two 11-mm trocars on each side of the abdomen on the pararectal external line, between the umbilicus and anterior superior iliac spine to be used by the main surgeon **(Figure 2).**

A transverse incision is performed in the anterior parietal peritoneum, as cranially as possible to avoid bladder injury. The incision is extended caudally in the form of an inverted U. The areolar tissue from the space of Retzius is dissected in an anterior and caudal direction until identification of the pubic symphysis.

***c) Extraperitoneal access***

To access the extraperitoneal space, a transverse incision is needed, 1 cm below the umbilicus, including the skin, adipose tissue and anterior rectus abdominal aponeurosis, with 1 cm to each side of the median raphe. The rectum is elevated with an S retractor. Using gauze on the tip of a long haemostat, the rectum is separated from the posterior rectus aponeurosis with circular movements against the aponeurosis, freeing the junction of the anterior aponeurosis, with the posterior aponeurosis on the side of the rectus abdominal muscle. The same manoeuvre is performed on both sides, leaving only the median raphe that is bisected with scissors. Dissection of the preperitoneal space is then completed with the aid of the laparoscope and insufflation.

**Approach for prostatic adenoma:** after dissection of the fibroadipose tissue covering the prostate and bladder, the endopelvic fascia is opened and the cephalic portion of the prostate is identified. Haemostatic suturing is performed at 4 to 8 o'clock positions, and optionally, a suture on the dorsal vein complex can be used. A longitudinal incision is performed on the anterior surface of the prostate, extending up to the anterior bladder neck **(Figure 3).**

Monopolar or bipolar electrocautery controls bleeding from the superficial vessels of the dorsal venous plexus. Repair points with zero polyglactin sutures with rectified needles are introduced through the abdominal wall into the cavity, and positioned on each side of the incision to allow better exposition of the dissection planes.

**Enucleation of the adenoma:** electrocautery is used to make a circular incision around the urethral meatus, with direct vision of the ureteral meatus. The incision is continued until whitish and firm prostate adenoma is identified.

The hypertrophic prostate tissue is dissected in a relatively avascular plane between the adenoma and the periphery of the prostate, in the circumferential caudal direction, using a combination of suction, forceps traction and prostate manipulation **(Figure 4)**.

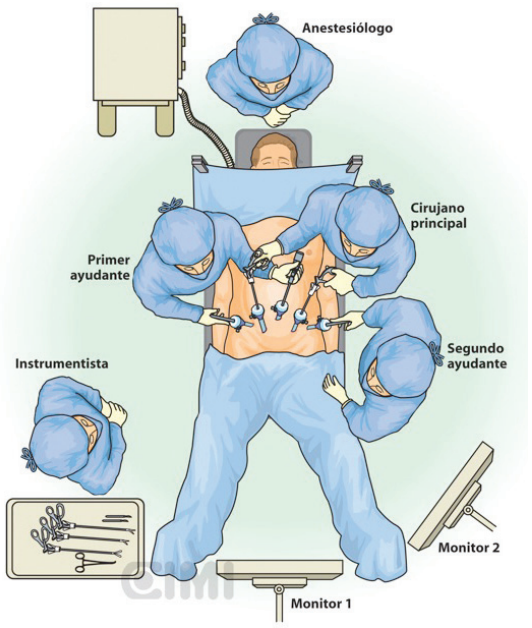


***Figure 1. Position of the surgical team.***

Prostatic adhesions or perforating vessels can be controlled by monopolar, bipolar or ultrasonic shears coagulation. In the prostatic apex, the urethra is sectioned, proximal to the verumontanum, avoiding excessive traction and injury to the sphincter muscle fibres. After complete removal of the adenoma, in single or separate lobes, it is attached to the abdominal wall with a suture, out of the field of view.

At the end of the procedure, the adenoma is morcellated and removed. An inspection is carried out to ensure complete resection of prostatic adenoma, and adequate haemostasis. Residual nodules can be removed by blunt or sharp dissection. Bleeding points must be controlled by electrocautery (mono- or bipolar) or suturing.

**Reconstruction of vesical trigone:** the bladder neck is reconstructed through simple interrupted suturing with polyglactin, between the bladder mucosa and floor of the posterior prostatic space. The alternative method is to suture the posterior bladder wall directly into the urethra, similar to that performed in radical prostatectomy.

A 22 Fr catheter is inserted through the urethra into the bladder, for bladder drainage and saline irrigation. Cystostomy is not usual. Closure of the prostatic capsule and bladder incision is achieved with 2-0 polygalactin sutures.

Prostate and bladder incisions are tightly sutured with continuous points of 2-0 polygalactin sutures. Leaking is tested with 200 ml of saline solution, repeatedly irrigating the bladder. If there is a saline leak or any perforation, the site is closed with a simple suture.

**Extraction of the specimen and cavity drainage:** the prostatic adenoma is extracted with a morcellator that uses a rotary blade to cut the prostate tissue in cylinders that can pass within its sheath. This manoeuvre is done repeatedly until there is no more tissue within the cavity. An alternative is the use of an EndoBag (AutoSuture; TycoHealthcare Group LP, Norwalk, CT, USA), which is introduced via the lateral 10-mm port, and the fragmented adenoma is placed inside.Adrain is positioned through one of the port incisions and is attached to the skin with a zero silk suture. The other ports are closed with 2-0 polyglactin sutures, and the skin with 4-0 polyglactin sutures.

Immediately after the procedure, continuous bladder irrigation is started with saline solution and continues until the first postoperative day or when haematuria ceases. The diet is resumed 12 h after the procedure, according to patient acceptance. The drain can be removed when the drainage volume is < 80 ml/day. Patients are discharged with the urinary catheter, which is removed in the clinic at 3–10 days after surgery.

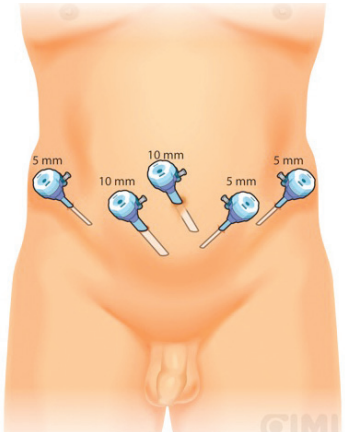


*Figure 2. Trocar positioning.*

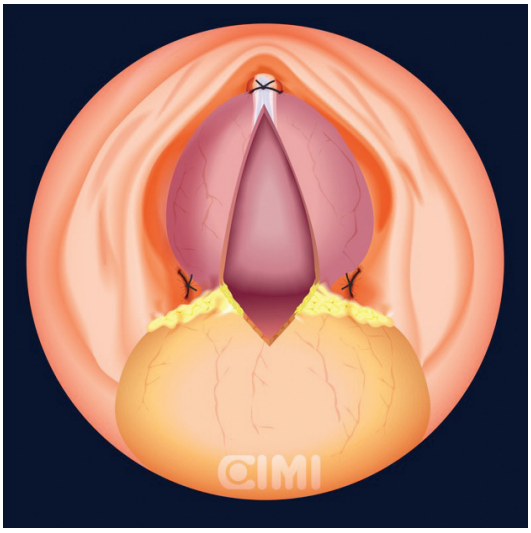

*Figure 3. Haemostatic sutures to prevent bleeding during dissection.*

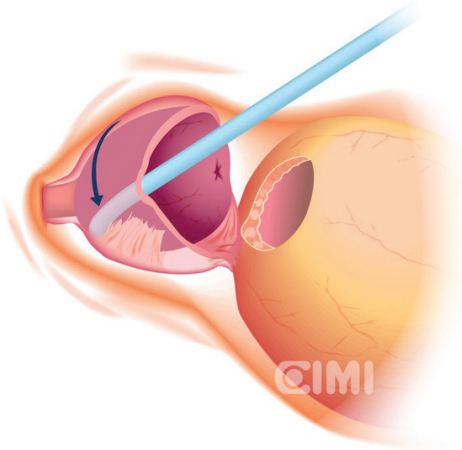

*Figure 4. Enucleation of adenoma with manipulator.*

## 4. DISCUSSION

The EAU guidelines [11] recommend that OP is the first-choice surgical treatment in men with drug-refractory LUTSs secondary to BPO, and prostate size > 100 ml, in the absence of Holmium lasers. However, even though OP has the most favourable and durable outcomes, it is also considered the most invasive surgical treatment for BPH and is associated with high morbidity and complication rates.

Laser technology appears to be a good alternative for treatment of large BPH. Some studies have advocated that laser technology has similar outcomes to OP for prostates > 80 ml in volume, and with lower complication rates. Nevertheless, the long learning curve and costs are the main factors that have limited widespread diffusion of the technique [39,40].

The laparoscopic approach to BPH treatment aims to combine the durable outcomes of OP with its limited invasiveness and lesser morbidity. Since the first publication by Mariano et al.[13], various other techniques have been developed **(Table 1).**

Five studies [15,17,18,28,29] comparing laparoscopic versus open techniques for treatment of BPH all found that the former techniques were favourable in terms of catheter duration, hospital stay, blood loss and irrigation time. The mean operating time was significantly longer for the laparoscopic than the open approach. Most studies have found that the procedure is more time consuming. The use of a finger for adenoma enucleation reduces the operating time. Hoepffner et al.[30] and Chlosta et al.[37] reported a mean operating time of 66.34 and 55 min, respectively, with finger manipulation, compared with an average time of 117.64 min without finger assistance [33]. In terms of complications, McCullough et al.[17] found significant differences in UTIs (1% in laparoscopic group vs. 9.8% in open group) and urosepsis (0% in laparoscopic group vs. 4.9% in open group) in favour of the laparoscopic group.

Asimakopoulos et al. [33] found in a systematic review that the most common complication for laparoscopic simple prostatectomy was bleeding requiring transfusion (5.6%), followed by urinary retention requiring recatheterisation because of haematuria (3%). In contrast, for simple OP, the need for transfusion due to severe bleeding was 3.3–36.8% and the overall prevalence of complications was 17.3%40.

Some authors [12,18,21] have noted a reduction in operating time for laparoscopic adenomectomy, perhaps because of the technical improvement and experience acquired by the surgeon over time.

The most important disadvantages of laparoscopic adenomectomy are: long learning curves; two-dimensional vision; limited freedom of instrument movement; and uncomfortable position for surgery [15-19,22-31].

## 5. CONCLUSION

Laparoscopic simple prostatectomy is an effective alternative for treatment of large-volume prostates, with similar and durable outcomes to open surgery, as well as the advantages of being minimally invasive.

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*Table 1. Laparoscopic adenomectomy in the literature*

| First author | Year | LE | No. of patients | Mean operating time (range or SD) min | Mean blood loss (ml) | Mean Foley duration (days) | Mean LOS (days) | Mean TRUS vol. (ml) | IPSS mean preop | IPSS mean postop | Mean resected tissue (range or SD) (ml) | Mean resected tissue (%TRUS vol) | Transfusion rate n (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Van Velthoven** | **2004** | 3 | 18 | 145 [32.5] | 192 [178] | 3 [2] | 5.9 [5.] | 95.1 [28.1] | N/A | N/A | 47.6 [30] | 50 | 1 |
| **Rey** | **2005** | 3 | 5 | 95 | N/A | 3 | 4 | N/A | N/A | N/A | N/A | N/A | 0 |
| **Sotelo** | **2005** | 3 | 17 | 156 [88.37] | 516 | 6.3 [1.3] | 2 [1.1] | 92 [50-150] | 24.5 | 9.9 | 93 | 100 | 5 |
| **Porpiglia** | **2006** | 3 | 20 | 107.2 [34.9] | 411.6 | 6.13 [3.7] | 7.8 [4.1] | 94.2 [19.6] | 20.9 [7] | 10 [14] | 70.7 | 75 | 2 |
| **Mariano** | **2006** | 3 | 60 | 138.48 [23.4] | 330.98 | 4.6 [1.2] | 3.46 [0.98] | 144.5 [41.7] | 28.3 [4.75] | 5.1 [2.5] | 131 [68-398] | 90 | 0 |
| **Baumert** | **2006** | 3 | 30 | 115 [30] | 367 | 4 [1.7] | 5.1 [1.8] | 122 [39] | 22.4 [6.9] | 5.7 [3.6] | 77.2 [2.4] | 63 | 1 |
| **Barret** | **2006** | 3 | 60 | 113 | 595 | 4.9 | 6.2 | 110 | 13 | N/A | N/A | N/A | [13] |
| **Peltier** | **2006** | 3 | 51 | 149 | 100 | 2 | 5 | N/A | N/A | 3 | 46 | N/A | N/A |
| **Hoepffner** | **2007** | 3 | 100 | 66.34 | 250 | 3.17 | 4.3 | 97.1 [18.5] | 24.2 [5.1] | 3 [1.6] | 68.2 [5.5] | 70 | 0 |
| **Massoud** | **2007** | 3 | 20 | 109 | 347 | 3.6 | 4.9 | N/A | N/A | N/A | 128 | N/A | 0 |
| **McCullogh** | **2009** | 3 | 96 | 95.1 [32.9] | 350 | 5.2 [2.6] | 6.3 [1.9] | 111.3 [35.3] | N/A | N/A | N/A | N/A | [15.8] |
| **Zhou** | **2009** | 3 | 45 | 105.4 [26.5] | 360.1 [165.4] | 4.6 | 6.3 | 85.4 [15.1] | 25.5 [2.4] | 6.2 [2.1] | 78.2 [16.3] | 91 | 3 |
| **Ramon** | **2010** | 3 | 10 | 112.5 [80–135] | 150 [100-300] | 7 [3–21] | 3.5 [2-5] | 104 [63–147] | 24 [19-33] | 5 [0–9] | 62 [40–93] | 60 | 0 |
| **Yun** | **2010** | 3 | 11 | 191.9 [132-276 | 390.9 [200–800] | 5.6 [4–8] | 6.5 [5-9] | 109.3 | 26.9 | 4.2 | 72.4 [58-103] | 66 | 2 |
| **Porpiglia** | **2011** | 3 | 78 | 103 [31] | 333 [321] | 3.5 [1.4] | 5.4 [1.5] | 96 [15] | 18.5 [5.8] | 7 [6] | 70 [18] | 73 | 2 |
| **Chlosta** | **2011** | 3 | 66 | 55 [45–85] | 200 [100-250] | 7.3 [6–9] | 5.2 [5-10] | 85.5 [70-100] | 29.5 [2.5] | 5.8 [5-8] | 85.5 [65-98] | 100 | 0 |
| **Castillo** | **2011** | 3 | 59 | 123 [90–180] | 415 [50-1500] | 4.2 [3–7] | 3.5 [2-7] 7] | 108.5 [75-150] | 18 [12-26] | N/A | 95.2 [40-150] | 88 | 4 |
| **Oktay** | **2011** | 3 | 16 | 133 [75–210] | 134 [50-300] | 6.3 [6–7] | 3.9 [2-7] | 147 [80-200] | 9.2 | 25.4 | N/A | N/A | 1 |

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# V. ROBOTIC SIMPLE PROSTATECTOMY

## 1. INTRODUCTION

### *a) Surgical approach in BPO*

BPE is a highly prevalent condition among older men, affecting nearly 6.5 million white men aged 50–79 years [1]. The most common therapeutic approach for symptomatic BPE is oral medication. Nevertheless, in cases of failure or refusal of pharmacological treatment or stable urinary retention, surgery has to be considered. For many years, open simple prostatectomy (OSP) has been the primary treatment option for patients with BPO [2-7].

The reproducibility and low invasiveness of TURP resulted in a worldwide expansion of this technique, limiting the indications for OP to adenomas > 100 $cm^3$, especially in the presence of coexistent pathological conditions (e.g., calculi and diverticula). For these patients, OSP seems to be more effective and safer than TURP [8] (LE 1b).

The need for a lower midline incision with subsequently longer hospitalisation and convalescence than for transurethral techniques, added to higher blood loss and transfusion rates commonly reported for OSP [3,8,9], drove the effort to develop minimally

invasive approaches, which should reflect the robust and durable results of the open surgical approach.

### *b) Robotic approach*

The robotic approach has supplanted the open approach for radical prostatectomy as the surgical treatment of choice wherever robots are available [10]. However, radical prostatectomy is not the only procedure in robot-assisted (RA) urological surgery. A robot is only an instrument that allows an improvement in surgical performance. As a result, it should prove useful for many other urological procedures [11]. Even though RA surgery has advantages over other minimally invasive approaches, especially in procedures including complex extirpative (partial nephrectomy, and lymphadenectomy) and/or reconstructive (anastomoses and parenchymal raphies) phases, the accuracy and ease of dissection make this approach potentially ideal for simple prostatectomy too.

### *c) Article extraction for literature review*

A systematic literature review was performed in MEDLINE using PubMed and in Scopus database: we retrieved citations using combinations of the titles 'robot/robotic simple prostatectomy', 'robot/robotic prostate adenomectomy' and titles NOT 'cancer' and NOT 'radical'. The search results were successively filtered to select only case reports, original articles, reviews and systematic reviews. Finally, hand searches of references identified in electronically abstracted articles were carried out. A total of 45 English-language publications were identified using PubMed and nine in Scopus, which were screened by title and abstract. These papers were peer reviewed to exclude duplicates, editorial replies, and letters to the editor: a total of 11 papers were eligible for inclusion in this review (**Table 1** [11–15,18–24]). The LE using ICUD standards is also reported.

## 2. SURGICAL TECHNIQUE

### *a) Procedure description* (Figure 1)

Robot-assisted simple prostatectomy (RASP) was first described by Sotelo *et al*. [12]. With the patient under general anaesthesia and positioned in the steep (25°) Trendelenburg position, pneumoperitoneum is obtained using a Veress needle inserted in the left hypocondrium, where the risk of bowel adhesions is low and the parietal peritoneum is more adherent to the posterior layer of the rectus muscle sheath. A transperitoneal approach is used with a port configuration similar to that described by Patel [25] for the daVinci radical prostatectomy, excluding the 5-mm assistant port and using only five trocars: 12 mm for the optic, two (if Standard System is used: Cases 1–21) or three (if the 4S System was used) 8-mm robotic trocars and a 12-mm assistant port in the suprailiac right position. If the daVinci Standard System is used instead of the left suprailiac robotic port, a 5-mm assistant port is placed. We use the 0° optic, one monopolar scissors, one plasmakinetic forceps (or Maryland bipolar dissector), and one large needle driver. If the daVinci 4S System is available, an additional Cadiere forceps is used.

After incision of the urachus and umbilical arteries, the bladder is detached from the abdominal wall and the space of Retzius is developed until the anterior surface of the prostate is cleaned from overlying fatty tissue. A horizontal cystotomy incision is performed immediately proximal to the junction of the bladder and prostate, several millimetres cranially with respect to the incision commonly performed during radical prostatectomy. The bulging prostatic lobes (with or without a median lobe) are thus visualised. A circular incision on the bladder mucosa overlying the prostate lobes at the level of the bladder neck is carried out as in the open approach, to find and develop the cleavage plane of the adenoma. A stitch placed into the median lobe may be useful to help traction during dissection (using a needle driver from the left 5-mm assistant port if the daVinci Standard System is used, or the Cadiere grasper on the third arm in the case of the daVinci 4S System). The adenoma is freed from the prostatic pars periferica by using a combination of electrocautery and blunt dissection. Any perforating blood vessels may be controlled with the plasmakinetic or Maryland bipolar forceps, or monopolar coagulation. After freeing the apex of the prostate, the urethra is incised clearly proximal to the external sphincter to avoid its damage. The prostatic fossa is then trigonised (according to the technique described by Sotelo et al. [12] by suturing the posterior edge of the bladder neck mucosa to the posterior edge of the urethra. If bleeding at the level of the prostatic fossa persists, haemostatic matrix agents (Floseal or Tacoseal) may be used by placing them in contact with the prostatic pars periferica. A 24 Ch silicon or silicon-coated, double-lumen catheter is inserted with the balloon into the bladder. The horizontal cystotomy incision is closed in a watertight manner using a 2-0 monofilament running suture and the bladder is irrigated to assess repair integrity. A drain is inserted. The prostate adenoma should be extracted using an EndoCatch bag from the median port (for example).

### *b) Postoperative course*

No continuous irrigation of the catheter should be needed at least until significant postoperative haematuria is seen (≤ 20%) [11]. Short-term antibiotic prophylaxis (cephazolin 2 g, 30 min preoperatively and 1 g 12 h postoperatively) is usually given. Patients may be dismissed on Day 2 after surgery with an indwelling catheter without drainage. The catheter is removed on Day 3–7.

### *c) Surgical variants*

Besides this classic variation (proposed by Sotelo et al. [12]), other surgical technique modifications have been proposed for RASP. For example, Coelho et al. [13] has proposed plication of the posterior prostatic capsule to decrease perioperative blood loss.

*Table 1. Robot-assisted simple prostatectomy series: operative data*

| Author | Yr | LoE | Patients | Mean age | Mean oper.T | Mean op BL | Mean Foley duration | Mean LoS | Mean TRUS vol. | Mean IPSS | | Mean PSA | Mean resected tissue | | Transfusion rate |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Yr | LoE | (n) | (yr) | (min) | (ml) | (d) | (d) | (ml) | preop | postop | ng/ml | (ml) | (% of TRUS vol) | n(%) |
| Sotelo *et al.* (12) | 2008 | 3 | 7 | 64.7 | 195 | 382 | 7.5 | 1.3 | 77.7 | 22 | 7.25 | 12.51 | 50.5 | 64.99 | 1(14.3) |
| Yuh *et al.* (18) | 2008 | 3 | 3 | 76.7 | 211 | 558 | - | 1.3 | 323 | 17.7 | - | 25.1 | 301 | 93.19 | 1(33) |
| John *et al.* (19) | 2009 | 3 | 13 | 70 | 210 | 500 | 6 | 6 | - | - | - | - | 82 | - | 0 |
| Uffort *et al.* (20) | 2010 | 3 | 15 | 65.8 | 128.8 | 139.9 | 4.6 | 2.5 | 70.9 | 23.9 | 8.13 | 5.17 | 46.4 | 65.44 | 0 |
| Sutherland *et al.* (21) | 2011 | 3 | 9 | 68 | 183 | 206 | 13 | 1.3 | 136.5 | 17.8 | 7.8 | 17.4 | 112 | 82.05 | 0 |
| Coelho *et al.* (13) | 2012 | 3 | 6 | 69 | 90 | 208 | 4.8 | 1.4 | 157 | 19.8 | 5.5 | 6.96 | 145 | 92.36 | 0 |
| Vora *et al.* (22) | 2012 | 3 | 13 | 67.1 | 179 | 219 | 8.8 | 2.7 | - | 18.2 | 5.3 | 12.3 | 163.3 | - | 0 |
| Matei *et al.* (11) | 2012 | 3 | 35 | 65.2 | 186 | 121 | 7.4 | 3.2 | 106.6 | 24 | 5 | 5.44 | 87 | 81.61 | 0 |
| Dubey *et al.* (15) | 2012 | 3 | 3 | - | 220 | 160 | 3 | 3.5 | - | - | - | - | - | - | 0 |
| Banapour *et al.* (23) | 2013 | 3 | 16 | 68.4 | 228 | 197 | 8 | 1.3 | 141.8 | 22 | 7 | 12.8 | 94.2 | 66.43 | 0 |
| Clavijo *et al.* (14) | 2013 | 3 | 10 | 71.7 | 106 | 375 | 8.9 | 1 | 81 | 18.8 | 1.67 | 5.81 | 81 | 100.00 | 0 |

Clavijo et al. recently advocated intrafascial simple prostatectomy [14], described as complete prostatectomy, performed by preserving the puboprostatic ligaments, periprostatic fascia and seminal vesicles. Finally, Dubey and Hemal reported their experience with complete urethrovesical reconstruction [15].

## 3. DISSERTATION

### *a) Background*

The benefits of the robotic approach in urological surgery are mainly advocated for radical prostatectomy. Extending the indications for this approach to simple prostatectomy might encounter resistance, mainly due to the worldwide expansion of endoscopic TURP (a strong competitor) [16] and the high costs of robotic procedures [17]. Nevertheless, some considerations may overcome these problems.

A structured literature review performed to extract information useful for comparison of OSP and RASP [11] selected 14 papers published from 1995 to 2011. Despite the well-recognised advantages of the open procedure [i.e., optimal functional results, short operation time [average 82.3 min), low reoperation rates, and no TURP syndrome], not insignificant disadvantages have been reported, such as: longer catheterisation time (5.76 days), longer catheter irrigation time, higher blood loss requiring transfusion (average: 11.3%, range: 4.4–17.9%), resulting in longer hospital stay (average: 7.61 days) and longer convalescence.

As far as large (> 80 ml) prostatic hyperplasia is concerned Ou et al. [8] showed that OSP is superior in terms of effectiveness and safety over endoscopic TURP) (LE 1). AUA and EAU guidelines suggest

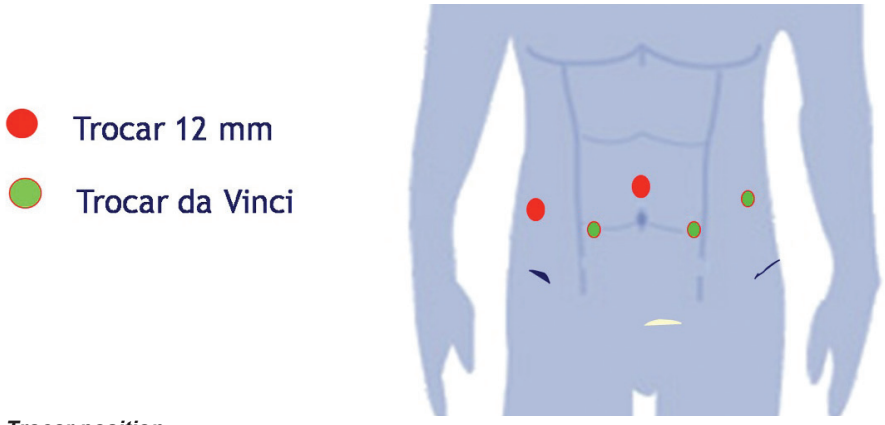


*Figure 1. Trocar position*

avoiding the endoscopic approach when prostate volume is > 80 ml (LE 1b, GR A). Even when considering bTURP, which allows a higher speed of resection, it seems that the higher the prostate volume, the lower the percentage of prostatic tissue removed (71.2% if < 80ml, 69% if 80–99 ml, and 66.5% if > 99 ml) [11]. Similar data (64.75% of removed tissue) were reported by Zhu et al. [17] in 52 patients (out of 132) with prostate volume > 80 ml (average: 101.6 ml) and Ou et al. [8] in the previously mentioned randomised trial (53.2% of resected prostatic tissue). In the RASP series [11], the average reported relative amount of removed tissue was 81.2%.

If TURP is not an optimal choice for large volume obstructive prostates [8,24], then other minimally invasive procedures have to be promoted in this setting of large (> 80 ml) obstructive BPE, such as RASP.

***b) RASP in the literature***

As far as RASP is concerned, all 11 studies selected and included in the final review were non-comparative case series (LE 3) ranging in size from three to 35 patients and reporting a total of 130 cases of RASP from 2008 to 2013 [11–15,18–23]. Indications for RASP included acute urinary retention (n = 60), persistent obstructive symptoms (n = 59), failure of medical management (n = 9) and frequent UTIs (n = 2). The mean ages ranged from 65 to 77 years. The mean LOS was 1–6 days, with eight studies reporting a mean LOS < 3 days. The two earliest series from 2008 reported one patient receiving perioperative transfusion, with no transfusion in the remaining series. The mean resected prostate weight was 51–301 g **(Table 1)**, amounting to 65–100% (median: 81.8%) of the total prostatic volume at TRUS. There was one case of intraoperative conversion to OSP due to an insurmountable deadlock during the procedure and excessive blood loss [21], and one case of epigastric arterial injury [12]. There were seven cases of incidental (T1) prostate carcinoma [11,13,23].

Postoperative complications included urinary leak managed with extended postoperative catheterisation [22], prolonged haematuria [23] that required hospital readmission, and postoperative incarcerated inguinal hernia associated with a concomitantly performed inguinal herniorraphy that required surgical management [20].

***c) Advantages of RASP***

The superiority of RASP in terms of haemostasis is mainly related to two factors: [1] the almost bloodless field due to pneumoperitoneum; and [2] improved vision due to the optic system magnification and the in-line visual angle that enables selective coagulation of the perforating vessels and excellent control of the surgical capsule (pars periferica) haemostasis [11].

This improved bleeding control seldom requires catheter irrigation (as often emphasised [11,13–15]) and the low pain level profile of the postoperative course results in shorter LOS and faster convalescence (average time to return to work of 13 days) according to John et al. [19]. Use of analgesic drugs is reduced compared with the open approach, even if no uniformity is seen in reporting these data (mg/patient, days of analgesic therapy, use or not of opioids) [11].

Hence, by shortening the convalescence and back-to-work time [19], the social impact (i.e., cost savings) of RA surgery might be significantly more relevant even if, in the case of RASP, they are more difficult to quantify.

Beyond these considerations the magnification and dexterity afforded by the robot and the confidence from familiarity with the prostate and periprostatic anatomy contribute significantly to enabling the surgeon to perform RASP [14]. As for many other diseases with lower incidence rates than prostatic cancer (such as high-volume prostatic hyperplasia), the possibility to see the procedure (and in this context, Youtube has become an unexpected and useful tool), read a description of it, or see drawings describing the main stages, may be of importance [11].

The costs of robotic procedures and the need for a learning curve may be inconveniences [14] that result in centralisation of RASP candidates at high-volume robotic surgery centres; a phenomenon seen over the past decade for prostate cancer surgery [26]. High-volume robotic surgery centres guarantee a high level of relevant expertise and the possibility to diversify the surgical repertoire (thus including simple prostatectomy) based upon an economy of scale policy.

This may explain why the reported RASP series were published by working groups with a high level of expertise in robotic surgery.

***d) Conclusions***

RASP is a feasible and reproducible procedure.

The accuracy and ease of dissection, improved bleeding control, low level of postoperative pain, and low rate of complications, leading to a shortening of hospital stay, faster convalescence and return to work, are known advantages of robotic surgery. As a result, the RA approach is worth consideration in cases of high-volume prostate adenoma.

Unfortunately, only small and non-comparative studies are available in the literature. Despite the lack of RCTs (LE 1) or comparative cohort studies (LE 2) necessary to validate the promising published results and yield higher LEs, the published data do suggest that RASP offers comparable clinical outcomes to OSP but with decreased risks of perioperative haemorrhage and transfusion, shorter LOS, and decreased risk of postoperative complications.

The incidence of high-volume obstructive prostate adenoma is low, therefore, the use of RASP needs good robotic skills and the possibility to diversify the surgical repertoire based upon an economy of scale policy; both features that characterise high-volume and thus high-expertise robotic surgical centres.

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## VI. LESS ADENOMECTOMY

### 1. INTRODUCTION

BPE is the most common cause of LUTSs in elderly men. Surgical intervention is appropriate for patients with moderate-to-severe LUTSs and for patients who develop acute urinary retention or any complication related to BPH [1,2].

Despite the advances in endourological treatments for BPO, OP is the surgical treatment of choice for men with prostates ≥ 80 ml, especially with concomitant pathology (i.e., calculi or diverticula). [1,2,5–7]

Open simple prostatectomy can be performed by either the suprapubic or retropubic approach. Suprapubic or transvesical simple prostatectomy consists of enucleation of the adenoma through an incision of the lower anterior bladder wall. It was popularized by Freyer, who described his

first 1000 cases in 1912 [3]. In retropubic simple prostatectomy, enucleation of the adenoma is achieved through a direct incision of the anterior prostatic capsule; an approach that was popularised by Millin [4].

OP is the most invasive but also the most effective and durable procedure for treatment of LUTSs. Efficacy is maintained after long-term observations of > 5 years. Perioperative complications include mortality (<0.25% in contemporary series) and blood transfusion (7–14%). Long-term complications are urinary incontinence (10%) and bladder neck stenosis or urethral stricture (~6%) [5–7].

In 2002, Marino and associates described the first laparoscopic prostatectomy, which was reproduced with some modifications and then performed with robotic assistance [8]. Laparoscopic simple prostatectomy utilises the same surgical steps previously described in OP (Millin or Freyer techniques) and a magnified laparoscopic view, which allows for improved haemostasis [9]. The functional outcomes of the procedure seem promising and comparable to those obtained with OP. Moreover, the studies comparing laparoscopic and open simple prostatectomy demonstrated a global advantage of laparoscopic simple prostatectomy in terms of blood loss, hospital stay, and catheterisation time [9–12].

Laparoendoscopic single site surgery (LESS) was first suggested as a consensus nomenclature suggested by the Urologic NOTES Working Group in 2008. LESS is now widely accepted as a general term for all new surgical procedures using one skin incision for access of the camera and instruments, with or without an additional port with a maximum size of 5 mm [13,14].

The concept of LESS is based on minimisation of the skin incision necessary to gain access to the abdominal or pelvic cavities to perform surgical procedures. This concept might translate into a benefit for patients in terms of port-related complications, recovery time, pain, and cosmesis [14]. Different procedures have been performed in urology with LESS: simple, radical and partial nephrectomy, kidney cryotherapy, donor nephrectomy, pyeloplasty, nephroureterectomy, cystectomy, radical prostatectomy, diverticulectomy, and simple prostatectomy, and some of them with robotic assistance.

A systematic literature review was performed in PubMed with the following combination of search terms: single-port, laparoendoscopic, transvesical, enucleation, prostate, and adenomectomy. A total of 52 English-language publications were identified, which were screened by title and abstract. After peer review and exclusion of duplicates, editorial replies, and letters to the editor, seven were eligible for inclusion in this review. The studies were rated according to LE and GR using ICUD standards.

## 2. SURGICAL TECHNIQUE

LESS adenomectomy can be performed by placing a single-port device in the umbilicus with a transperitoneal approach as described by Sotelo *et al*. [15] in 2009, but this is challenging, because the bladder must be dropped and the finger cannot be used to assist the enucleation. They reported a 67-year-old man with acute urinary retention, in whom they performed LESS adenomectomy using an R-port, and no extra skin incisions were made. The total operating time was 2 h, estimated blood loss was 200 ml, and hospital stay was 2 days. There were no intraoperative or postoperative complications. Specimen weight was 95 g. At 3 months follow-up, AUA symptom score was 3/35. Additionally, at the end of surgery, the cystotomy incision was closed laparoscopically in a water-tight fashion. With the new double-bend instruments, this method has been made easier, but it is still inherently difficult to carry out.

Another alternative is the one described by Desai *et al*. [16] in 2008, the so-called single-port enucleation of the prostate (STEP), which they used in three patients with BPH. The R-Port device was introduced percutaneously into the bladder through a 2.5-cm incision. After establishing pneumovesicum, the adenoma was enucleated in its entirety transvesically and it was extracted through a solitary skin and bladder incision. Mean operating time was 200 min and mean blood loss was 500 ml. They removed a mean 86% of prostate tissue, the mean duration of hospitalisation was 1 day, and the Foley catheter was removed after a mean 7.3 days. All patients were voiding spontaneously without a significant PVR volume and were fully continent. The mean postoperative peak urinary flow rate after catheter removal was 46.6 ml/s. Using this technique, the bladder does not need to be dropped. Also, the finger can be used to assist the enucleation. At the end of surgery, the cystotomy closure can be done in a standard open fashion. The following papers continue using this technique **(Table 1).**

## 3. SURGICAL STEPS

All procedures were performed under general anaesthesia with the patient in a modified low-lithotomy position. Initially, cystoscopy was performed and the prostate was evaluated endoscopically. The bladder was filled with normal saline. The

proposed site of the skin incision was marked, and an approximately 2.5-cm skin incision was carried down to the rectus fascia. The incision was located two finger-breadths above the symphysis pubis **(Figure 1)**. The bladder wall was identified and cleared of any prevesical fat, and two stay sutures of 2-0 Vicryl were placed. The bladder wall was entered sharply between the stay sutures, and the inner ring of the multiport was inserted into the bladder and deployed with the help of the introducer. The inner and outer rings were approximated by removing the slack on the plastic sleeve, thus cinching the abdominal and bladder wall between the rings of the multiport in an airtight seal **(Figure 2)**. The valve of the multiport was inserted and the bladder was insufflated with $CO_2$ to create the pneumovesicum. The insertion and deployment of the R-Port was monitored cystoscopically. A U-shaped incision was made over the bladder mucosa immediately overlying the adenoma from 3 to 9 o'clock through the 6 o'clock position. Typically, a reddish zone of mucosa is present immediately lateral to the internal meatus that serves as a reliable guide for creating the mucosal incision. The horizontal limb of the U incision was made first using a hook electrode and cutting current to reach the adenoma. The whitish prostatic adenoma was readily identified, and the plane between the surgical capsule and the adenoma was created using the hook and suction cannula. The two limbs of the U incision were created, followed by completion of the circumferential mucosal incision **(Figure 3)**. A 2-0 Vicryl suture on a CT-1 needle with a Hem-o-lok at the end of the suture was placed through the adenoma for retraction purposes, which was exteriorised percutaneously with a Carter–Thomason device. Small perforating vessels and tissue strands between the surgical capsule and adenoma were systematically divided using ultrasonic shears, enabling enucleation to proceed in a relatively avascular plane **(Figure 4)**. The adenoma was thus enucleated until only the urethral mucosal attachment remained. For the large prostate gland, a finger was introduced through the multiport ring to expedite the distal part of the enucleation. The urethral mucosa was divided sharply using cold endoshears. Trigonisation was performed with an interrupted 2-0 Vicryl suture, and tied down with an extracorporeal knot pusher **(Figure 5)**. The prostatic adenoma was extracted through the multiport ring after dividing it intravesically into two or three pieces **(Figure 6).** Haemostasis was confirmed, and a 20 Fr three-way Foley catheter was inserted with the balloon inflated to 40 ml. The catheter was irrigated to confirm a clear and free return. A suprapubic catheter can be inserted through the inner ring of the Triport **(Figure 7).** The bladder opening was sutured using 3-0 Vicryl, and the fascia and skin were closed in a standard fashion [16–20].

Desai *et al*. [17] updated their previous work with 34 patients with a TRUS prostate volume ≥ 60 ml, and any patient who was otherwise being considered for open or standard laparoscopic enucleation was considered for STEP. They used a three-channel TriPort in 30 patients and a four-channel single-port device Quad-Port in four patients. They used the same surgical technique as described above. Finger assistance was used to expedite enucleation of the distal apical portion in 19 (55%) cases. There were complications during STEP in three patients: one death in a Jehovah's Witness who developed a severe haematuria with coagulopathy and refused blood transfusion; one enterotomy during the TriPort insertion in a patient with a previous laparotomy where the port was inserted more cephalad towards the umbili-

***Table 1. LESS adenomectomy evidence***

| Authors | No. of cases | Prostate volume (ml) | Operating time (min) | EBL (ml) | Days of stay | Foley catheter removal (days) | Digital assistance (%) | Excised prostate (%) | Complication rate (%) | Conversion rate (%) | Decrease of IPSS | Increase of Qmax (ml/s) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Desai *et al.*** | 34 | 102.5 | 116 | 460 | 3 | 6 | 19 (55) | 66.3 | 8 (23) | 2 (5.9) | 16 | 36.2 |
| **Oktay *et al.*** | 3 | 102.5 | 105 | 190 | 4 | 6 | 0 (0) | 79.1 | 0 (0) | 0 (0) | 16 | 14.8 |
| **Lee *et al.*** | 7 | 100.8 | 191.8 | 600 | 3.1 | 5.29 | 0 (0) | 53.7 | 3 (42.9) | 0 (0) | 12 | 10.4 |
| **Oh and Park** | 32 | 73 | 109.4 | 177 | 3 | 5.31 | 32 (100) | 76.7 | 0 (0) | 0 (0) | 23 | 30.4 |
| **Wang *et al.*** | 9 | 83.8 | 161 | 419 | 7.1 | 8.6 | 0 (0) | 64.6 | 3 (33.3) | 1 (11.1) | 21 | 12.9 |
| **Fareed *et al.*** | 9 | 146.4 | 228 | 584.4 | 6 | 15 | 0 (0) | 53.4 | 3 (33.3) | 1 (11.1) | 11.07 | 13.7 |

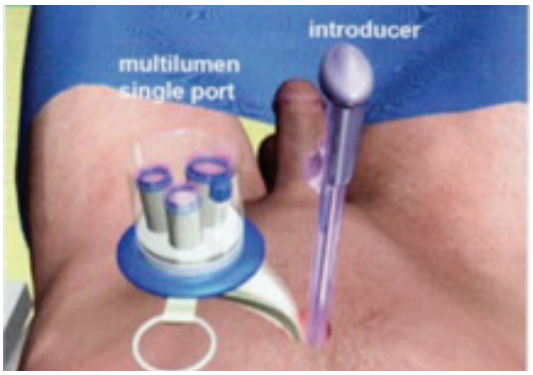


***Figure 1. Position of the multichannel port in the patient.***

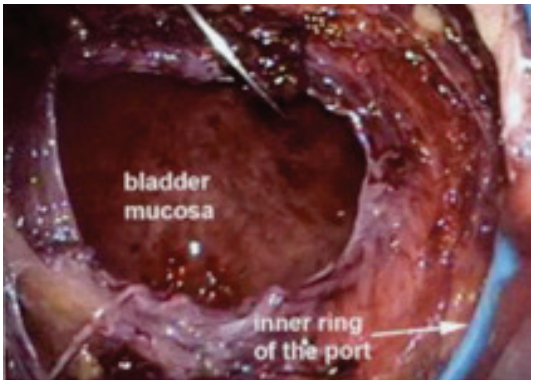


***Figure 2. External view of the positioned multichannel port***

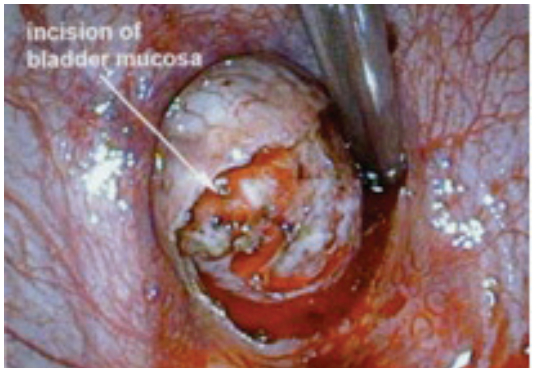


***Figure 3. Incision of bladder mucosa around the adenoma***

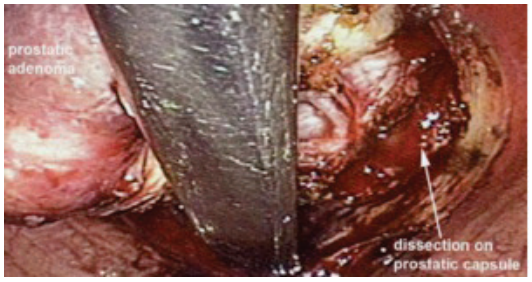


***Figure 4. Enucleation of adenoma.***

cus; and one patient with bleeding. There were complications in five patients after STEP: four bleeding, and one UTI. They noticed that the transvesical approach provides direct access to the large prostatic adenoma with no need for peritoneal violation; pneumovesicum also provides effective tamponade of venous channels facilitating the surgery.

Two Korean authors reported LESS adenomectomy with home-made single-port devices. Lee *et al*. [18] included seven patients with prostates > 80 ml on TRUS. No digital assistance was necessary in any of the cases, with a mean operating time of 191.8 min, a mean 53.7% of prostate tissue excised, a decrease of 12 points in the IPSS score, and a mean increase of 10.4 of Qmax, which were the lowest values among all the studies. Oh and Park [19] performed STEP in 32 patients, which was finger assisted with a similar home-made single-port device. These patients were compared with a group of 67 who received TURP. Both groups had similar preoperative characteristics. The postoperative IPSS (4.00 vs. 8.77), Qmax (36.19 vs. 22.03 ml/min), and IPSS recovery period (5.54 vs. 10.88 weeks) were significantly improved in the STEP group compared with the TURP group. The mean operating time and catheterisation time were significantly longer. Weight of the extracted specimen was greater in the STEP than TURP group (48.35 vs. 29.85 g).

Wang *et al.* [20] performed STEP in eight patients with moderate-to-large obstructive prostates with a TriPort device. No digital assistance was necessary in any case. The follow-up time was 1 year, which was the longest time in all the studies, and all of the postoperative parameters (e.g., IPSS and Qmax) improved.

Recently, Fareed *et al*. [21] performed RA STEP in nine patients using a Gelport as a LESS device. One had to be converted because the Gelport could not be placed. Despite demonstrable improvement in uroflowmetry and IPSS parameters after surgery, the operating time was longer than for other surgical options for BPH, and three patients had severe complications.

The advantage of LESS adenomectomy is in avoiding the abdominal cavity, even the pre-peritoneal space, by performing the surgery directly as an intraluminal procedure. This is important in patients with multiple previous operations by using a single incision and avoiding the potential complications associated with multiple trocars (e.g., bleeding and incisional hernia).

Even with the evolution of the instruments and technology, the step of enucleation is technically

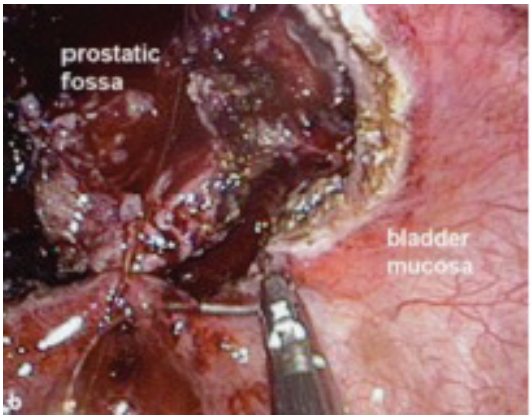


*Figure 5. Trigonisation of the bladder to the urethra.*

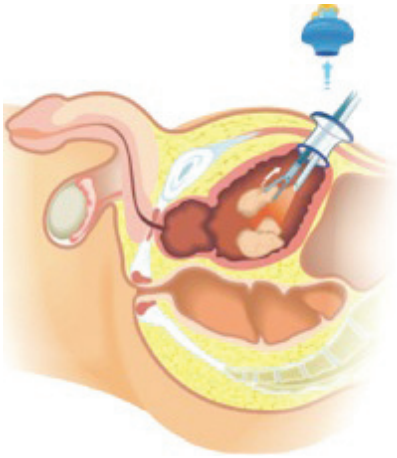

*Figure 6. Extraction of adenoma through the open multichannel port.*

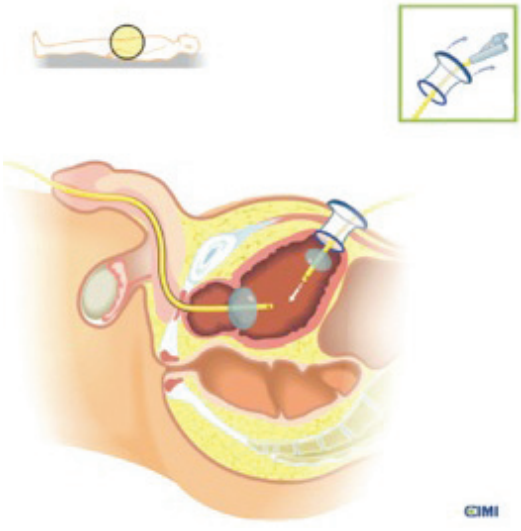

*Figure 7. Insertion of Foley catheter.*

demanding for most surgeons. Nevertheless, the results have shown that the extracted prostate volumes are similar between open and LESS adenomectomy.

Most studies did not use finger assistance for enucleation. The studies with more cases did, and recognised it as an advantage for larger prostates. They also noted the importance of placing the trocar nearest to the pubis to facilitate the use of the finger.

A future direction is to evaluate the use of laser technology through single-site trocars for BPH surgery, or different combinations to minimise complications and improve visualisation and the working space.

## CONCLUSIONS

LESS adenomectomy for BPO can provide an alternative surgical approach in experienced hands. However, it is technically demanding and has no proven benefits over standard laparoscopy or other minimally invasive approaches. Additional studies with a larger number of patients are required to validate this approach and compare it to other approaches.

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## VII. RECOMMENDATIONS

### 1. HOLMIUM LASER

HoLEP is a prostate size-independent procedure with at least equal efficacy as TURP and OP but with longer operating time. (LE 1)

HoLEP has lower – specifically perioperative – morbidity, and statistically significantly shorter catheter time and hospitalisation compared to TURP and OP. (LE 1)

The major drawback of HoLEP seems to be its learning curve. (LE 2)

HoLEP is the new reference standard for all enucleation techniques (i.e., transurethral, open or laparoscopic). (LE 1)

### 2. GREENLIGHT LASERS

The GreenLight systems have demonstrated similar results and complications when compared to other minimally invasive techniques in short-term and medium-term follow-up. (LE 1)

Due to the strong haemostatic properties of the GreenLight laser, it is particularly suitable for patients taking oral anticoagulation or antiplatelet therapy. (LE 2)

In a recent RCT with a short 6-month follow-up period, XPS showed non-inferiority (comparable) to TURP. (LE 1)

### 3. THULIUM LASER

Thulium laser techniques are minimally invasive treatments for BPO, which have shown efficacy and durability during short-term and intermediate follow up compared to other minimally invasive treatments. (LE 2)

Complications are comparable to those of standard treatments. (LE 2)

### 4. DIODE LASER

A limited number of studies have investigated the clinical applications of diode laser prostatectomy, showing improvements in voiding parameters but with more morbidity compared to GreenLight and holmium lasers. (LE 4)

Although several studies have shown a high level of intraoperative safety and excellent haemostatic properties, reports on long-term durability and efficacy are inconsistent. (LE 3)

### 5. TURP

TURP is the reference treatment for BPO in prostates between 30 and 80 ml. (LE 1)

TURP is more effective than other treatments (ILC, TUMT and TUNA) in terms of increase in urine flow rate. (LE 2)

TURP provides excellent and stable clinical outcomes with low morbidity, transfusion rates and retreatment rates. (LE 1)

### 6. BIPOLAR TURP (BTURP)

bTURP is equally effective as mTURP in treating symptoms and improving urinary flow rates. (LE 1)

bTURP is associated with fewer adverse events than mTURP is, with shorter irrigation and catheterisation times. (LE 2)

bTURP has a rate of retreatment that is similar to that of mTURP. (LE 2)

## 7. LAPAROSCOPIC ADENOMECTOMY

Laparoscopic simple prostatectomy is an effective alternative for treatment of BPO, with durable outcomes that are similar to those of open surgery, but with less morbidity. (LE 2)

Laparoscopic simple prostatectomy is more time consuming than OP, but finger assistance during the enucleation can greatly reduce the disparity. (LE 3)

Laparoscopic simple prostatectomy should be reserved for surgeons with extensive laparoscopic experience. (LE 3)

## 8. ROBOT-ASSISTED SIMPLE PROSTATECTOMY (RASP)

RASP is a feasible and reproducible procedure. (LE 3)

RASP may offer comparable clinical outcomes to OP but with decreased risks of perioperative haemorrhage and transfusion, shorter length of hospitalisation, and decreased risk of postoperative complications. (LE 3)

High costs and the need to overcome a significant learning curve may dictate centralisation of RASP at high-volume robotic surgery centres. (LE 3)

## 9. LESS ADENOMECTOMY

LESS adenomectomy has shown improvement in IPSS and Qmax at short follow-up. (LE 3)

LESS adenomectomy for BPO can provide an alternative surgical approach in experienced hands. (LE 3)

LESS adenomectomy is technically demanding and has no proven benefit over other minimally invasive approaches. (LE 3)

## Committee 3

# Minimally Invasive Radical Cystectomy

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# Minimally Invasive Radical Cystectomy

*K. Guru, P. Wiklund*

*P. Agarwal, M. Annerstedt, R. Boris, F. Gaboardi, E. Kauffman, J. Palou, S. Raza, M. Saar, M. Stockle, G. Thalmann*

## I. NEOADJUVANT CHEMOTHERAPY

### 1. INTRODUCTION

Although radical cystectomy is considered the gold standard treatment for clinically localized muscle-invasive bladder cancer, nearly 50% of patients develop metastases within 2 years [1]. Once locally advanced or metastatic, prognosis remains poor. Therefore, perioperative chemotherapy is critical to improve survival outcomes in high-risk patients. Current guidelines recommend neoadjuvant chemotherapy (NAC) for patients with cT2–4a cN0 cM0 urothelial carcinoma [2], leading to an overall survival (OS) benefit of 5% after 5 years [3]. In contrast, cisplatin-based adjuvant chemotherapy to date has not consistently shown significant benefit in randomised trials. Adjuvant therapy is therefore only advised in clinical trials [2], high-risk patients who have perivesical tumor extension (Stage ≥ 3) and/or regional lymph node metastasis and did not receive NAC [4].

### 2. RATIONALE FOR NEOADJUVANT CHEMOTHERAPY

NAC is believed to have the potential to eradicate micro-metastases prior to surgery, especially if the recommended dose and duration of treatment are tolerated [3, 5–11]. Surprisingly, improved survival with NAC has not been compromised by treatment-related deaths or adverse events that prevent radical cystectomy [12]. Nevertheless, NAC is presently underutilised. Even though the National Cancer Database reported an increase in overall chemotherapy from 27% in 2003 to 34.5% in 2007 [13], and a recent analysis identified an overall increase in the use of NAC from 7.6% in 2006 to 20.9% in 2010 [14], administration rates are still as low as 11% in patients with pT4 disease, even at high-volume tertiary centres [15]. Factors that negatively influence receipt of NAC are increasing age, low patient income, and treatment at a non-academic institution. A multidisciplinary approach at an academic centre improved utilisation of NAC to > 50% [16]. NAC does not increase the risk of complications or death, which should encourage its use perioperatively [17, 18].

### 3. MINIMALLY INVASIVE CYSTECTOMY AND NEOADJUVANT CHEMOTHERAPY

Robot-assisted radical cystectomy (RARC) has comparable operative, pathological and short-term clinical outcomes to the open approach [19, 20]. Favourable operative results include lower intraoperative blood loss, earlier return to bowel function, less pain and quicker postoperative convalescence [21, 22]. RARC is as an independent predictor of fewer overall and major complications [23]. In a large series from the International Robotic Cystectomy Consortium (IRCC) of 939 patients who underwent RARC, 138 received postoperative NAC. On multivariate analysis, NAC independently predicted overall and high-grade complications at 90 days after surgery, while it did not affect mortality (OR (95%CI) 1.91 (0.86-4.28) p=0.114) [24]. In a more recent univariate analysis, the IRCC found that NAC was significantly associated with 90-day mortality in pT4 patients, but NAC was not an independent predictor of complications [25].

### 4. ADJUVANT CHEMOTHERAPY

One disadvantage of adjuvant chemotherapy has been the ineligibility for cisplatin-based chemotherapy after cystectomy. Age, comorbidity, severity of renal failure and patient reluctance each affect eligibility and completion of adjuvant chemotherapy. Grade 2–5 complications typically prohibit initiation of adjuvant chemotherapy [10]. On the contrary, RARC has been shown to decrease complications, using the same stan-

dardised methodology [26], and is associated with an ~50% lower risk of all complications [23]. In a recent study, patients with advanced bladder cancer (pT4) showed similar complication rates as those with pT ≤ 3 disease after RARC [25]. Therefore, a minimally invasive approach might increase the number of patients eligible for adjuvant chemotherapy. To maximise the opportunity for timely adjuvant chemotherapy, rapid recuperation from surgery is crucial [27]. For patients who are willing to start treatment and avoid time-consuming complications within 90 days postoperatively, the real benefit from adjuvant chemotherapy might be even higher than the presumed 9% benefit in 3-year OS [28].

## 5. COMPLIANCE

Multidisciplinary approaches have improved compliance to NAC from 10.8% to 55% over a 1-year period [16]. Coordination of service with stringent consultation criteria for medical oncology evaluation of newly diagnosed patients improves compliance and evaluation for NAC, without surgeon bias towards early RARC.

## 6. CONCLUSION

Minimal invasive radical cystectomy reduces complication rates following radical cystectomy (level of evidence; LE 2). Although perioperative chemotherapy is known to prolong survival in high-risk patients (LE 1), it suffers from overtreatment, especially for NAC. The low risk profile of minimal invasive cystectomy provides higher feasibility for adjuvant chemotherapy to reduce the number of patients being overtreated with chemotherapy and to increase the benefit from cytostatic therapy (LE 4). Better postoperative outcomes from the minimally invasive approach motivate incorporation of adjuvant chemotherapy **(Table 1)**.

## 7. RECOMMENDATIONS

| | Grade |
|---|---|
| • Cisplatin-based combination NAC shows a marginal overall survival benefit | **B** |
| • In patients with pT3/4 or N+ disease, who have not received NAC, adjuvant chemotherapy with a cisplatin-based regimen should be considered | **B** |
| • Better postoperative outcomes after minimal invasive cystectomy facilitate adjuvant chemotherapy | **C** |
| • Multidisciplinary approach improves compliance and likelihood of receiving NAC | **C** |

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# II. IMMEDIATE ONCOLOGICAL OUTCOMES

## 1. SURGICAL MARGINS

Despite the advantages of robotic surgery, including 10´ magnification, 3D vision and endo-wrist technology, lack of tactile feedback raises concerns about adequacy of excision for advanced disease. Positive soft-tissue surgical margins (STSMs) after radical cystectomy are associated with local recurrence and decreased OS [1, 2]. Based on a 2004 consensus attempting to standardise outcomes of surgical treatment for invasive bladder cancer, acceptable positive STSM rate for radical cystectomy was < 10% and < 15% for bulky disease (T3/T4) [3 ].

Data from the International Laparoscopic Cystectomy Registry (ILCR) demonstrated an STSM rate of 2% [4]. The IRCC reported an overall STSM rate of 6.8% in 513 patients undergoing RARC [5]. Advancing T stage, positive lymph nodes, and increasing age were independently associated with a higher likelihood of STSMs, while case number and institution volume were not found to be predictive [5]. For every increase in pathological T stage above pT2, there was a five times higher chance of a positive STSM ($P < 0.001$). In a series of 121 patients, Snow-Lisy et al. reported a positive STSM rate of 6.6% [6]. Similar to the IRCC data, that group noted that positive STSMs were more likely to occur in patients with extravesical extension, although they were unable to discern the exact location of the positive margin from an additional retrospective review of pathological specimens. Mmeje et al. reported a an STSM rate of 2% in a study of 275 RARC patients from two institutions, with a 6% local recurrence rate after a mean follow-up of 3.5 years [7]. A recent review of 11 studies with 230 patients reported a 2.6% rate of STSMs in patients undergoing RARC [8]. Overall, RARC provides adequate soft-tissue margins comparable to those for open surgery [1, 9]. These findings suggest that STSMs are associated with infiltration of the soft tissue boundaries of the bladder, rather than learning curve and surgical error. In patients with large tumours and/or suspected extravesical disease, wide dissection of the perivesical tissue is recommended to reduce STSM rates [10].

Although a learning curve has been shown to affect STSMs during robot-assisted radical prostatectomy, it is controversial whether a similar relationship is present with RARC. Hellenthal et al. reported that sequential RARC case volume served as a surrogate for a learning curve and no difference in STSMs was noted in sequential volume compared to the initial 10 procedures [5]. In the IRCC database, positive STSM rates at centres with > 50 RARC procedures were no different than those of centres performing ≤ 50 procedures. In contrast to these findings, other studies support a decrease in

positive STSM rates with increased surgical experience [11–13].

## 2. LYMPH NODE YIELD

An experienced robotic surgeon can perform high-quality extended pelvic lymph node dissection (LND) at the time of RARC. Although measurement of successful primary tumour extirpation is straightforward, defining the adequacy of LND is a challenge. Davis *et al*. performed a second-look open LND (expert surgeons) after completion of robotic pelvic LND [14]. They reported that > 80% of patients had no residual tissue or tissue without identification of any lymph nodes. Robotic LND in this series took an average 117 min to complete. Second-look open LND added an additional 60 min to the operation. The authors concluded that LND was complete in 93% of cases and should allay concern that the technique itself limits completeness of the dissection.

Current consensus on appropriate e-PLND should include all lymph nodes between the aortic bifurcation and common iliac vessels (proximally), genitofemoral nerve (laterally), circumflex iliac vein and lymph nodes of Cloquet (distally), and internal iliac vessels (posteriorly), including the obturator fossa and presacral lymph nodes anterior to the sacral promontory [15]. In some cases, additional extension superior to the level of the inferior mesenteric artery has been performed [16]. The area of historical concern regarding robotic pelvic LND has been related to the cephalad extension of anatomical dissection. This was a legitimate concern with the standard da Vinci system, but more cephalad port placement and the longer reach of the updated da Vinci S and Si systems have together corrected this limitation. Sagalovich *et al*. have shown that for robotic extended pelvic LND for high-risk prostate cancer, the camera can be rotated behind the lateral aspect of the external iliac vessels with gentle medial retraction to allow for LND in the triangle of Marcille [17].

The incidence of positive nodes at the time of radical cystectomy is > 20% [2]. The inclusion of pelvic LND at the time of cystectomy provides both prognostic information and potential therapeutic benefit [18, 19]. Accurate pathological staging may identify patients best suited for adjuvant therapy. Some node-positive patients will achieve long-term disease-free survival after surgery alone [20]. Lymph node yield alone is suggested to have prognostic significance [3, 18]. The 2004 consensus study by Herr *et al*. that attempted to standardise outcomes of surgical treatment for invasive bladder cancer identified 15 lymph nodes as the minimal acceptable yield for this surgery [3]. The ability to remove a minimal number of lymph nodes using robotic assistance was initially challenged by opponents of minimally invasive approaches [3, 21].

In 2008, Guru *et al*. reported on the feasibility and safety of performing adequate robot-assisted LND, demonstrating a higher lymph node yield with increasing case volume [22]. Wang and colleagues found no difference in the number of lymph nodes retrieved via open or robotic approaches (20 vs. 17) [23]. Pruthi *et al*. reported a mean 19 lymph nodes removed (range: 8–40) in their first 100 patients undergoing RARC, surpassing the minimum acceptable nodal yield proposed for open surgery. A recent prospective, randomised, non-inferiority study by Nix *et al*. demonstrated a mean lymph node yield of 19 in the RARC group versus 18 in the open radical cystectomy group [24]. Collaborative evaluation by the IRCC recently evaluated 765 patients treated with RARC [25]. Fifty-eight percent underwent extended pelvic LND, 40% standard pelvic LND, and 2% did not undergo pelvic LND. Overall, 27% of patients had positive lymph nodes at the time of surgery. In extended pelvic LND, the mean lymph node yield was 21 and for standard pelvic LND, the mean yield was 13. Performance of extended pelvic LND was significantly associated with sequential case number, surgeons, and institutional volume. On multivariate analysis, institutional volume and sequential case number remained significant predictors of extended pelvic LND. High-volume centres (> 100 cases) were 3.5 times more likely to perform extended pelvic LND. In addition to reports on the adequacy of pelvic LND among RARC patients, Mmeje *et al*. published oncological outcomes for node-positive patients receiving RARC, with a mean follow up of 3.5 years [7]. Recurrence-free survival (RFS) and OS were comparable to those for open surgery. Lymph node density < 20% was predictive of improved survival. Hence, there is now convincing evidence that a robotic approach achieves acceptable lymph node yields and positive lymph node rates during extended pelvic LND.

## 3. CONCLUSION

Positive STSM rates and total lymph node yields for RARC are acceptable based on proposed standards for radical cystectomy, and are in accordance with contemporary series using an open approach. Surgical volume and experience with RARC play some role in the improvement of STSM rates and lymph node yields. Maximising the performance, impact, and interpretation of pelvic LND during radical cystectomy is dependent on many variables, including lymph node viability, method of submission (*en bloc* or separately) [26], pathological processing [27], anatomical extent (extended vs. standard template) [15], and surgical dedication and skills. RARC does not appear to preclude thorough dissection or the possibility of complete clearance of nodal tissue within intended anatomical boundaries. Many studies have demonstrated maintenance of adequate LND while advancing the goal of reducing morbidity for patients requiring radical cystectomy for high-grade T1 tumours refractory to intravesical therapy and invasive bladder cancer.

## 4. RECOMMENDATION

Minimizing STSMs during RARC is imperative to maximise good oncological outcome for muscle invasive bladder cancer (Grade of recommendation; GR B)

Learning curve may not directly improve STSM rates in RARC, however, proper patient selection remains important during early surgical adoption of MIS techniques (GR C)

Extended pelvic LND during RARC is critical for appropriate bladder cancer staging and may provide a potential therapeutic benefit (GR B)

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# III. COMPLICATIONS

## 1. INTRODUCTION

Radical cystectomy is a complex and potentially morbid operation even among high-volume surgeons from centres of excellence. Until recently, there has been a dearth in standardised reporting of complications after radical cystectomy. Only 2% of reports (73 open series and 36 minimally invasive series) from 1995 to 2005 met at least nine of the critical reporting elements in surgical outcomes according to Donat [1]. Complication reports may be limited by reporting and selection bias for healthier patients. Standardised reports on complications after open radical cystectomy using the validated Clavien reporting system reveal disappointingly high complication and mortality rates ranging from 26 to 64% and 1 to 7%, respectively [2–5]. Readmission rates are as high as 27% with bowel, urinary and infectious complications being the most common reasons [6]. Transfusion rate in one series was ~66%, with a median estimated blood loss of 1 L for 1142 consecutive open radical cystectomies [4]. Some data confirm that robotic minimally invasive approaches potentially lower complication rates after radical cystectomy, based on recent studies evaluating complications in a standardised fashion, including in comparison with open series, as summarised here.

## 2. INSTITUTIONAL SERIES

A recent report by Xylinas *et al*. measured complications in 175 consecutive patients undergoing RARC. The median age of patients was 73 years and median estimated blood loss was 400 mL (interquartile range: 250–612 mL) with a transfusion rate of 17%. Early complication (<30 days) and late complication (30–90 days) rates were 42% and 34%, respectively. Overall, the perioperative mortality rate in this series was 2.8% [7]. A more sobering multi-surgeon report from City of Hope (Pasadena, USA) suggests that complication rates are much higher. In that analysis of 209 consecutive patients, 77.5% experienced any complication and 32% experienced a major (Clavien grade 3–5) complication within 90 days of surgery. However, in contrast to other studies, transfusions were considered a complication in this series. On multivariate analysis, patients with an ileal conduit urinary diversion had a decreased risk for complications compared to continent urinary diversions. Overall, 90-day perioperative mortality rate was 5.3% [8].

Early adopters of RARC for bladder cancer have explored robotic-assisted intracorporeal urinary diversions. Azzouni and colleagues from Roswell Park Cancer Institute analysed outcomes after the first 100 consecutive RARC cases with intracorporeal ileal conduit urinary diversions. The 90-day overall complication rate was 81%. Infections were the most common complication and accounted for 31% of all complications. Overall, only 15% of the complications were major complications (Clavien grade 3–5) [9]. The Karolinska Institute in Stockholm examined the results of 70 patients undergoing RARC with an intracorporeal continent neobladder urinary diversion by one of two surgeons [10]. The overall 90-day complication rate was 58.5%. Mortality rate was only 1.4% at 90 days but the series had notable limitations, including selection bias favouring healthier patients, retrospective study design, and small cohort size. These reports suggest that intracorporeal urinary diversions are complex procedures and complications are still significant even in the hands of experts.

## 3. MULTI-INSTITUTIONAL SERIES

The IRCC reported data from 939 patients from 16 institutions. The median estimated blood loss was 400 mL with a 15% intraoperative transfusion rate. The 30- and 90-day complication rates were 41% and 48%, respectively. At 90 days, the mortality rate was 4.2% and the readmission rate was 20% [11]. Variables associated with major complications (Clavien grade 3–5) on multivariate analysis included age at surgery, increased body mass index, NAC, current smoking, and intraoperative transfusion. In their most recent report featuring data from 935 patients treated at 18 centres, the 90-day complication rate was 41% and 49% for intracorporeal versus extracorporeal urinary diversion, respectively [12].

## 4. COMPARISON BETWEEN OPEN CYSTECTOMY AND RARC

Several small prospective single-institution studies have evaluated complications between open cystectomy and RARC. These studies all demonstrated similar complication rates between the two approaches, or trends towards fewer complications in the RARC cohorts. Ng and colleagues treated 187 consecutive patients (104 open cystectomy and 83 RARC) and found a higher 90-day complication rate in the open cystectomy group (62% vs. 48% for RARC, which was not a significant difference. However, there was a significant difference in the rate of major (Clavien grade 3–5) complications in the open cystectomy versus robotic group (30.8% vs. 16.9%) [13]. Robot-assisted surgery was an independent predictor of fewer overall and major complications. Musch *et al.* found in a prospective cohort study of 142 consecutive patients (100 RARC and 42 open cystectomy) a reduced rate of overall (59% vs. 93%) and major (24% vs. 43%) complications at 90 days [14].

One prospective randomised controlled trial compared open cystectomy [20] with RARC [21]. Although the study was designed as a non-inferiority study in terms of lymph node retrieval between the

two surgical approaches, it also reported no difference in complications between the two groups. This conclusion is tempered by the fact that this endpoint was underpowered to define this relationship [15]. Preliminary results from a randomised trial at Memorial Sloan Kettering Cancer Center of 109 patients revealed no difference in overall complications (61% RARC vs. 62% open cystectomy) [16]. Ultimately, the results of this ongoing trial and a randomised, multicentre prospective trial of open cystectomy versus RARC, NCT01157676, will address the issue of perioperative complications more definitively. The latter study is designed to measure perioperative outcomes, and initial results after ~40 patients reveal no difference in Clavien grade ≥ 2 complications [17].

## 5. RECOMMENDATIONS

RARC is associated with significant morbidity and mortality as seen with the open radical approach. It is critical to collect and report outcomes in a standardised fashion with at least 3 month data.

Institutional series reveal that RARC has similar complication rates to previously published open RC series level (LE 1b, 4; GR C).

Transfusion and estimated blood loss is significantly lower in the RARC group (LE 4; GR C).

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# IV. FUNCTIONAL OUTCOMES AND QUALITY OF LIFE

## 1. INTRODUCTION

No randomised controlled studies comparing conduit diversion with neobladder or continent cutaneous diversion have been performed. Consequently, almost all studies used in this report are of level 3 evidence. Therefore, the recommendations given here are grade C only, based on expert opinion without formal analysis.

## 2. QUALITY OF LIFE

There remains a lack of good data evaluating quality of life (QoL) in patients after RARC. Yuh *et al*. have investigated the effect of RARC on QoL after surgery [1]. All 34 patients had RARC with extracorporeal urinary diversion. Functional Assessment of Cancer Therapy-Bladder (FACT-BL) questionnaires were administered preoperatively and 6 months postoperatively. Patients undergoing chemotherapy were not excluded. Initially, there were significant decreases in the physical and functional domains, with improvements in the emotional domain. Total FACT-General and FACT-BL scores decreased in the initial period after RARC and then progressively improved. There was no significant difference in total scores at 3 months after surgery; meanwhile at 6 months follow-up, total FACT-BL scores exceeded those before RARC. It was concluded that QoL appears to return promptly to, or exceeds, baseline levels by 6 months after RARC. Short-term improvement might lead to greater patient satisfaction and more rapid initiation of adjuvant chemotherapy.

Poch *et al*. have studied short-term health-related QoL (HRQoL) after RARC with extracorporeal urinary diversion using the Bladder Cancer Index (BCI) and European Organisation for Research and Treatment of Cancer (EORTC) Body Image Scale (BIS) [2]. They found a decline in the urinary domain at up to 1 month after RARC, but this returned to baseline by 1–2 months. There was a decline in the bowel domain at 0–1 month and 1–2 months after RARC, but this returned to baseline by 2–4 months. The decline in BCI scores was greatest for the sexual function domain, but this returned to baseline by 16–24 months after RARC. Body image perception using BIS showed no significant change after RARC except at 4–10 months. Thus, based on BCI and BIS scores, HRQoL after RARC shows recovery of urinary and bowel domains at ≤6 months. Longer follow-up with a larger cohort of patients will help refine HRQoL outcomes.

Aboumohammed *et al*. [3] have compared HRQoL outcomes between RARC and open cystectomy groups, in a multi-institutional setting. Utilising the BCI and BIS questionnaires, the study reported no difference in HRQoL outcomes at up to 30 months postoperatively. A similar trend was noted when the cohort was stratified according to the type of diversion (open vs. robotic extracorporeal vs. robotic intracorporeal). Over time, improvement of sexual function was better in the open cystectomy group.

## 3. CONTINENCE

There are limited published data on urinary continence in patients with orthotopic neobladders after RARC **(Table 2)**. The number of patients receiving continent urinary diversions is variable and depends on institutional experience and patient preference. Continence results in the literature are difficult to compare between studies because of a lack of consensus, variability in definition, inconsistent follow-up, and unstructured/non-stan-

***Table 2. Summary of studies of robot-assisted intracorporeal neobladder***

| Author and year | Patients | Functional outcomes at 1 year |
|---|---|---|
| **Tyritzis *et al*. 2013 (4)** | 70 | Daytime continence, 88%<br>Night-time continence, 72%<br>66% of men received nerve-sparing surgery with<br>58% potent post-surgery |
| **Goh *et al*. 2012 (5)** | 8 | Daytime continence, 75%<br>Night-time continence, NR |
| **Canda *et al*. 2011 (6)** | 25 | Daytime continence, 64.7%<br>Night-time continence, 17.6% |
| **Sala *et al*. 2006 (7)** | 1 | Daytime continence, 100%<br>Night-time continence, 0% |

*NR, not reported.*

dardised data collection. Few studies have used a validated anonymous questionnaire to evaluate continence. One of the largest series [4] showed that most patients achieved daytime continence after surgery. Urinary continence was defined as the use of no or one safety pad. Incontinence was defined as the use of one, two or more pads. Daytime continence at 12 months ranged between 65 and 90% in both men and women with orthotopic bladder substitution. Increasing age has a negative impact on functional outcomes, including daytime continence. This is an important factor to take into consideration when evaluating functional outcomes in bladder cancer. Attempted nerve sparing improves daytime continence, and increasing age worsens it in open cystectomy. Men with type 2 diabetes achieve daytime continence more slowly than controls and are less likely to achieve nighttime continence.

## 4. SEXUAL FUNCTION

Results of the largest RARC series published show that male and female patients remain sexually active after surgery [4]. It is evident that increasing age has a negative impact on achieving successful postoperative sexual function. This is an important factor to take into consideration when evaluating functional outcomes in bladder cancer, because cystectomy patients have a mean age of ~70 years [8]. Postoperatively, patients were followed up at 6 weeks; at 3, 6, 12, 18 and 24 months; and thereafter once a year. Postoperative functional outcome regarding potency rates were assessed. The International Index of Erectile Function (IIEF)-5 score was used and patients were defined as potent if their IIEF-5 score was ≥ 17, or if they could perform intercourse more than half the times it was attempted, with or without a phosphodiesterase inhibitor. The 1-year potency rate was 80–90% in preoperatively potent men that underwent a nerve-sparing procedure.

Only a few studies have examined the postoperative sexual function of women undergoing cystectomy and urinary diversion [9–13]. Results suggest that sexual dysfunction is common and may be improved by leaving the uterus intact when possible and preserving the autonomic nerves lateral to the vagina [11–15].

## 5. CONCLUSIONS

Experience with RARC demonstrates acceptable functional outcomes regarding QoL, urinary continence, and recovery of erectile function, supporting this approach as a valid alternative to open cystectomy. However randomised trials addressing functional outcomes after cystectomy are still needed for confirmation. Based on predominantly level 3 evidence, recommendations given here are grade C only based on expert opinion without formal analysis.

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## V. SURVIVAL OUTCOMES OF ROBOT-ASSISTED RADICAL CYSTECTOMY AND LYMPH NODE DISSECTION

### 1. INTRODUCTION

Justification of RARC requires demonstration of comparable oncological outcomes to those of open cystectomy. Durable cure can be achieved with open cystectomy in the absence of NAC in ~60% of patients [1]. Given the recent advent of RARC, the scarcity of long-term oncological outcomes has been a primary limitation to its widespread adoption. Currently, one meta-analysis and three randomised clinical trials (RCTs) have compared robotic and open approaches to cystectomy in terms of immediate perioperative outcomes [2–5]. The ongoing RAZOR trial [6] aims to report 2-year progression-free survival as its primary outcome, providing a high level of evidence. This section summarises the published literature on survival outcomes of RARC.

### 2. SURVIVAL OUTCOMES

Data on long-term survival outcomes are currently scarce due to the limited number of studies with >5 years follow-up **(Table 3)**. Early reports of survival outcomes were subject to selection bias, potentially restricting the interpretation of feasibility of RARC in patients with advanced disease. Although a few

**Table 3.** ***Intermediate to long-term oncological outcomes following RARC (includes minimum 2 years mean or median follow-up)***

| Authors/year | No. of patients | Follow-up (months) | ≤T2 (%) | Margin rate | LN+ rate | RFS | CSS | OS | Survival estimates |
|---|---|---|---|---|---|---|---|---|---|
| Yu *et al.*, 2014 (7) | 162 | 52 | 67.6 | 4.3 | 21.6 | 74 | 80 | 54 | 5 years |
| Raza *et al.*, 2014 (8) | 99 | 73[e] | 48.5 | 8.1 | 30.2 | 53 | 68 | 42 | 5 years |
| Snow *et al.*, 2013 (9) | 17 | 67 | 35 | NR | NR | NR | 69 | 39 | At last follow up |
| Khan *et al.*, 2013 (10) | 14 | 60 | 71 | 0 | 0 | 50 | 75 | 64[d] | NR |
| Mmeje *et al.*, 2013 (11) | 50[a] | 42[b] | 34 | 2 | 100 | 43 | NR | 55 | 3 years |
| Xylinas *et al.*, 2013 (12) | 175 | 36 | 65.1 | 5 | 17.1 | 63 | 66 | NR | 5 years |
| Tyritzis *et al.*, 2013 (13) | 70 | 30 | 81.4 | 1.4 | 14.3 | 80 | 89 | 89 | 2 years |
| Collins *et al.*, 2013 (14) | 113 | 25 | 73.5 | 5.3 | 20 | NR | 67 | 67 | 5 years |
| Martin *et al.*, 2010 (15) | 59[c] | 21/25[b] | 38.9 | NR | 34 | 71 | NR | 72 | 3 years |
| Jonsson *et al.*, 2011 (16) | 45 | 25 | 77 | 2 | 20 | 84 | 86 | NR | 3 years |

randomised studies have compared RARC and open cystectomy, their intermediate and long-term survival outcomes have not yet been reported. Current understanding of survival of RARC patients is based largely on retrospective series.

A few recent retrospective case series have provided initial reports of 5-year survival, although limited by small numbers of patients. Snow *et al*. reported long-term outcomes for 121 minimally invasive radical cystectomies, with only 17 patients being treated with RARC [9]. Sixty-five percent had extravesical disease and demonstrated cancer-specific survival (CSS) and overall survival (OS) rates of 69% and 39%, respectively, meanwhile recurrence-free survival (RFS) was not reported for the RARC group. The study observed significantly better OS and CSS in organ-confined, margin-negative and lymph-node-negative disease, however, the results were not separately reported for RARC. Similarly, Khan *et al*. reported 43% RFS and 55% OS in 14 patients with median follow-up of 5 years, however, the cohort had 71% patients with organ-confined disease [10]. Raza *et al*. reported outcomes of 99 consecutive patients with a minimum 5 years follow-up at a single institution [8]. With an STSM rate of 8.1% and lymph node positive rate of 30%, the 5-year RFS and CSS were 52% and 68%, respectively. Higher tumour and lymph node stage were independent predictors of RFS, CSS and OS, while positive margins and Charlson Comorbidity index (CCI) were associated with worse CSS and OS. In a study of 162 patients, Yu *et al*. reported 74%, 80% and 54% 5-year RFS, CSS and OS, respectively, over a median follow-up of 52 months [7]. The predictors of OS and CSS included lymph node density, pathological stage, and CCI. These outcomes compare with those reported for open cystectomy. Stein *et al*. reported 5-year RFS and OS of 68% and 66%, respectively, in 1054 patients [3]. The RFS estimates compare well with those reported by Yu *et al*., however, OS remains better for open cystectomy. Similar to the findings of Raza *et al*., Dotan *et al*. reported an independent association of positive STSM with worse disease-specific survival [17]. Disease-specific survival for both studies was similar (68% RARC vs. 71% open cystectomy at 5 years), despite a lower STSM rate (4%) and higher rate of organ-confined disease (54%) compared to RARC. However, comparison of retrospective studies remains subject to selection bias.

Several studies of RARC have provided survival outcomes at intermediate follow-up of 2–3 years. Although this abbreviated follow-up may miss late recurrence, most cases of post-cystectomy cancer recurrence occur within 12–18 months of surgery. Therefore, 3-year post-cystectomy data still provide critical information for assessment of oncological efficacy of RARC. Xylinas *et al*. reported outcomes in 175 patients with a median follow-up of 3 years, including 17 patients with at least 5 years follow-up [12]. Thirty-five percent had extravesical and 17% had lymph-node-positive disease, and positive STSM rate was 5%. The estimated 5-year RFS and CSS rates were 63% and 66%, respectively. Collins *et al*. reviewed the outcomes of 113 patients with median follow-up of 25 months [18]. With a 5% positive STSM rate and 20% lymph-node-positive disease, they estimated a 67% 5-year CSS and OS in their cohort, and 74% of patients had organ-confined disease. Martin *et al*. reported 3-year RFS and OS rates of 71% and 72%, respectively, with 39% organ-confined disease [15]. Thirty-four percent of patients had lymph-node-positive disease with an unreported margin status. Similar to other reports, poorer outcomes were associated with extravesical node-positive disease.

The ongoing RCT comparison of open and robotic approaches for radical cystectomy, with progression-free survival as the primary outcome remains of great interest for understanding the oncological efficacy of RARC. Until such data are available, information for understanding oncological outcomes of RARC needs to be extracted from retrospective reports.

## 3. CONCLUSION

Long-term survival outcomes are limited by the small number of case series and require follow-up data from the few reported RCTs to reach a definitive conclusion (LE 3, GR C).

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## Committee 4

# Minimally Invasive Nephrectomy (Laparoscopic and Robotic)

### Chair

*A. Alcaraz (Spain)*

*A. Hemal (USA)*

### Members

*R. Abaza (USA)*

*M. Allaf (USA)*

*C. Bahler (USA)*

*M. Ball (USA)*

*N. Buffi (Italy)*

*L. Dorairajan (India)*

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*R. Kumar (India)*

*F. A. Mistretta (Italy)*

*M. Musquera (Spain)*

*L. Peri (Spain)*

*F. Petros (USA)*

*P. Singh (India)*

*C. Sundaram (USA)*

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# Minimally Invasive Nephrectomy (Laparoscopic and Robotic)

*A. Alcaraz, A. Hemal*

*R. Abaza, M. Allaf, C. Bahler, M. Ball, N. Buffi, L. Dorairajan, Z. Gordon, R. Kumar, F. A. Mistretta, M. Musquera, L. Peri, F. Petros, P. Singh, C. Sundaram*

## A. LAPAROSCOPIC & ROBOTIC SIMPLE AND COMPLEX NEPHRECTOMY FOR BENIGN INDICATIONS (ONLY TRANSPERITONEAL APPROACH)

## I. INTRODUCTION AND HISTORY

Urological laparoscopy began with the first laparoscopic nephrectomy by Dr. Clayman and his team [1]. Once it was proven to be feasible, there was an exponential growth in the range of procedures, the number of each procedure performed, and the number of urologists performing the procedures, and now laparoscopy has become adopted worldwide by urological surgeons. Laparoscopic urological surgery has become a standard technique in the urologist's armamentarium. Historically, laparoscopic urological procedures have developed by urologists attempting to push back the frontiers as wells as by refinement of instrumentation and technological innovations. These have included the Harmonic Scalpel, radiofrequency vessel sealing, articulating instruments, locking plastic clips, barbed sutures, and haemostatic agents. Other innovations include miniature laparoscopes of 5 mm diameter, high-definition camera systems, and visual obturators and morcellators. Morcellators have helped maintain the minimally invasive nature of ablative urological procedures, although their use has not been popular and their utility has been questioned [2]. Another innovation is hand-assisted laparoscopic nephrectomy (HALN), which started as a bridge in the learning curve of pure laparoscopic surgery but is now used for facilitating performance of complex nephrectomy in conditions such as xanthogranulomatous pyelonephritis (XGP) and autosomal dominant polycystic kidney disease (ADPKD). This chapter discusses the current indications for laparoscopic nephrectomy in benign conditions, the techniques of transperitoneal laparoscopic surgery, and the outcomes as compared to those of open surgery.

## II. STUDY METHODS

Open, laparoscopic or robot-assisted laparoscopic nephrectomy encompasses a wide range of indications and complexity. Although simple nephrectomy for indications such as non-functioning symptomatic hydronephrotic kidney, and unilateral nephrectomy for secondary hypertension due to renal artery stenosis, are simple due to the lack of adhesions, nephrectomy for inflammatory conditions such as XGP, renal tuberculosis, chronic perinephric abscess, and previously operated cases can be challenging. Each case presents with its own challenges, making head to head comparison between different modalities in small case series difficult. As a result, studies of high quality in the form of well-conducted randomised clinical trials (RCTs) are not available. Most of the evidence is low level in the form of case series, heterogeneous cohort studies or non-randomised case–control or cohort studies. Hence, the recommendations contained in this article are based on such low-level evidence and expert opinions.

A PubMed search with the search string "laparoscopic nephrectomy NOT partial NOT donor" identified 2334 items. When filters "Human and English" were used, there were 1737 items. The titles of these articles were scrutinised and studies confined to malignancies, as well as editorials and debates were excluded. Thereafter, abstracts were studied and relevant articles were selected. There was no RCT of good quality or a meta-analysis exclusively restricted to the use of different technologies and treatment modalities for nephrectomy for benign diseases. In a small RCT from the UK, which included an inhomogeneous group of patients undergoing nephrectomy for benign and malignant diseases, the authors found that recruiting patients had become increasingly difficult [3]. There were ethical dilemmas in conducting the study and they could recruit only 45 patients from 2001 to 2004 who consented to participate, that

is, 20% of eligible patients. There was initial reluctance to participate because of concerns about safety, but later, patients were seeking laparoscopy because of its perceived advantages. Hence, large single- or multicentre cohorts and comparative studies (all of level 3 evidence) were included in this systematic review.

## III. INDICATIONS AND CONTRAINDICATIONS OF LAPAROSCOPIC NEPHRECTOMY FOR BENIGN DISEASES

### 1. INDICATIONS FOR NEPHRECTOMY FOR BENIGN CONDITIONS

1. The indications for nephrectomy for benign conditions include:
    - Symptomatic non-functioning kidney caused by:
    - Pelviureteral junction or ureterovesical junction obstruction
    - Renal or ureteral calculus
    - Multicystic dysplastic kidney
2. Infections and inflammatory conditions such as:
    - Renal tuberculosis
    - Renal echinococcosis
    - XGP
    - Emphysematous pyelonephritis or renal carbuncle not resolving with conservative management
    - Perinephric abscess not responding to conservative management such as percutaneous drainage
3. Non-functioning or poorly functioning scarred kidney, or renal artery stenosis with functioning contralateral kidney causing uncontrolled secondary hypertension
4. Pre-transplant nephrectomy

### 2. CONTRAINDICATIONS

The absolute contraindications to laparoscopic surgery include:

1. Pregnancy
2. Uncontrolled coagulopathy
3. Active peritonitis
4. Extensive adhesions
5. Severe cardiopulmonary disease

Relative contraindications include:

1. Severe obesity
2. Renal anomalies such as pelvic kidney
3. Reoperative surgery
4. ADPKD
5. XGP
6. Lack of surgical expertise

These relative contraindications are related to the level of surgical expertise.

## IV. TECHNIQUE OF LAPAROSCOPIC NEPHRECTOMY FOR BENIGN DISEASES

### 1. TECHNIQUE OF STANDARD LAPAROSCOPIC NEPHRECTOMY

The procedure is typically performed under general anaesthesia. The patient is positioned in a modified flank position with the ipsilateral side elevated by 30–45° using a sandbag or a gel roll. The bottom leg is slightly flexed at the hip and the knee, and the top leg is kept straight. A pillow is placed between the legs as a cushion. The ipsilateral hand is secured on the chest as a modified sling or placed on a raised arm rest. The opposite arm is secured on an arm board. The patient is strapped to the table with 7–10-cm wide tapes at the shoulder and hip levels. Pneumatic sequential compression devices should be placed on the lower extremities. Upper and lower body warming blankets must also be placed. An orogastric or nasogastric tube is placed and the bladder is catheterised with a Foley catheter. The surgical site is prepared from the nipples to the pubis and the patient is draped. Pneumoperitoneum is established using a Veress needle, visual obturator, or an open technique.

A 12-mm camera port is placed lateral to the umbilicus. Another 12-mm port is placed below the xiphoid. A 5-mm port is placed subcostally in the mid-clavicular line. The 12-mm sub-xiphoid port may be used as the camera port so that the working hands do not straddle the telescope. The standard steps include mobilising the colon and duodenum (for right nephrectomy) or the spleen (for left nephrectomy). The anatomical landmarks are identified, namely, the psoas muscle, gonadal vein, and ureter. The ureter is mobilised, retracted and traced up to the renal hilum where the renal vein and artery are dissected out. On the left side, usually the lumbar and gonadal veins may have to be secured with titanium clips and divided. The renal artery and vein are usually divided with a laparoscopic endoGIA stapler. Alternatively, the renal artery may be secured with Hem-o-lok clips. The kidney is completely mobilised. The ureter is usually divided at the end and the specimen is entrapped in a lap sac. The specimen may be morcellated within the bag and retrieved through one of the 12-mm ports or retrieved intact by a Pfannensteil incision.

### 2. TECHNIQUE OF HAL NEPHRECTOMY (HALN)

The hand-assist port is placed at the umbilicus through a 7-cm incision. The right hand is inserted through this port for left-sided nephrectomy and the left hand is used for right-sided nephrectomy. In addition, a 12-mm was placed in the mid-clavicular line subcostally and another port is placed below the xiphoid. An additional 5-mm port may be placed laterally for retraction. A left-sided 12-mm port at the level of the umbilicus placed laterally may facilitate the use of the left hand through the hand-assist device for a right-handed surgeon and the right hand can be used through this 12-mm port. Placing the hand-assist port in the midline is particularly useful when bilateral nephrectomy is planned, as in the case of pre-transplant patients. The steps of nephrectomy are the same as for pure laparoscopic nephrectomy. The specimen after entrapment in the bag is retrieved through the incision made for the hand-assist device.

## V. ANALYSIS OF OUTCOMES MEASURES OF STUDIES ON LAPAROSCOPIC NEPHRECTOMY FOR BENIGN DISEASES

### 1. LIMITATION OF ANALYSIS

The techniques of measurement of the usually studied variables such as estimated blood loss (EBL), operating time, postoperative analgesic requirement, hospital stay, and return to work are not defined in most studies or standardised. Hence, comparison of one study with another in this regard was difficult. Pooling of results from cohort studies has been done keeping in mind that the results yielded may not be completely reliable. Non-randomised or case–control studies in which open and laparoscopic techniques have been compared may provide better comparison because the technique for measurement of a variable would be similar in the two groups. Data of comparative studies have been pooled on this assumption and the results analysed **(Table 1).**

### 2. ESTIMATED BLOOD LOSS

Data from various studies show that blood loss in laparoscopic nephrectomy is less to that with open nephrectomy. The reasons for this difference include: pressure due to pneumoperitoneum reducing capillary oozing and venous bleeding; and the meticulous haemostasis necessary to maintain a clean field of vision for carrying out a laparoscopic procedure. Nevertheless, selection bias could also explain the difference because most urologists, especially in the early stages of learning, choose simpler cases.

### 3. TRANSFUSION RATE

Although the EBL has been consistently less in laparoscopic nephrectomy compared to open nephrectomy in most studies, the transfusion rate has varied among studies. In one large study, the blood transfusion rate was higher for the laparoscopic than open procedure [8].

### 4. OPERATING TIME

The operating time also varies among studies. Most studies define this time from incision to skin closure, but some studies measure from the time the patient enters the operating theatre to the time he/she is shifted to the recovery room [4]. As a result, there is variability in the measurement of operating time between different cohorts.

It is also expected that in the initial stage of learning, the time taken for laparoscopy will be longer [4]. This confounding factor is exemplified in the study by Kerbl et al. [4], in which there was a significant difference in the operating time between the laparoscopic and open surgery groups, but more recent studies indicate similar operating times for laparoscopic and open techniques [6].

### 5. TIME TO RESUME FEEDING

Most studies comparing laparoscopic with open nephrectomy show that the former facilitates early resumption of feeding. Although the range and mean time to resumption of feeding shows variation depending on the indication for nephrectomy, in general, the studies show ≥1 day earlier resumption of feeding in favour of laparoscopic over open nephrectomy.

### 6. HOSPITAL STAY

In most studies, hospital stay has been shorter for laparoscopic compared with open procedures. However, it must be borne in mind that discharge policies differ among hospitals and geographic regions. Furthermore, over the past two decades when laparoscopic surgery has developed, hospital stay even for open surgery has shown a decreasing trend. Hospital stay has changed from several days ~20 years ago to several hours in many centres, making comparison between studies and pooling of estimates difficult.

The difference in the minimum hospital stay in the initial series is wider than in later studies, indicating the trend towards early discharge even after open surgery. It should also be noted that the maximum hospital stay has progressively increased; possibly because for both laparoscopic and open surgery, there has been a trend towards treating more complex cases. Hospital stay may also be increased by the influence of selection bias, especially for open cases.

***Table 1. Pooled estimates of operative outcomes of studies comparing transperitoneal laparoscopic and open nephrectomy for benign conditions***

| | | | | Operating time (min) | | | EBL (ml) | | | Hospital stay (days) | | | Return to work (days) | | | Feeding resumption (days) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Study no. | Study ref. | Group | No. of cases | Min | Max | Mean | Min | Max | Mean | Min | Max | Mean | Min | Max | Mean | Min | Max | Mean |
| 1 | (4) | Lap | 20 | 125 | 515 | 355 | 50 | 500 | 200 | 1 | 11 | 3.68 | 1.7 | 21 | 6.43 | 0 | 3 | 1.4 |
| | | Open | 25 | 60 | 345 | 165 | 50 | 1500 | 332 | 5 | 12 | 7.35 | 5.6 | 28 | 17.36 | 1 | 6 | 3 |
| 2 | (5) | Lap | 12 | 105 | 360 | 145 | 50 | 200 | 140.7 | 2 | 6 | 3.5 | 10 | 21 | 16 | | | |
| | | Open | 13 | 60 | 240 | 156.6 | 75 | 750 | 295 | 3 | 16 | 8 | 35 | 84 | 32.6 | | | |
| 3 | (6) | Lap | 131 | 41 | 210 | 90 | 40 | 750 | 200 | 2 | 46 | 4 | 8 | 144 | 24 | 1 | 5 | 1.33 |
| | | Open | 118 | 30 | 240 | 90 | 50 | 1800 | 250 | 2 | 79 | 10 | 10 | 160 | 36 | 1 | 4 | 2 |
| 4 | (Inflammatory conditions only)(7) | Lap | 84 | NA | NA | 170 | NA | NA | 156 | NA | NA | 4.3 | NA | NA | NA | NA | NA | NA |
| | | Open | 94 | NA | NA | 148 | NA | NA | 155 | NA | NA | 8.1 | NA | NA | NA | NA | NA | NA |
| Total Lap | | | 247 | (Weighted mean) | | 141 | (Weighted mean) | | 182 | (Weighted mean) | | 182 | (Weighted mean) | | 21.2 | (Weighted mean) | | 1.34 |
| Total Open | | | 250 | (Weighted mean) | | 123 | (Weighted mean) | | 225 | (Weighted mean) | | 225 | (Weighted mean) | | 32.7 | (Weighted mean) | | 2.18 |

***All studies with level 3 evidence.***

***Lap, laparoscopic nephrectomy; Max, maximum; Min, minimum; NA, information not available; Open, open nephrectomy.***

### 7. CONVALESCENCE OR RETURN TO WORK

Return to work yields similar results as duration of hospital stay. There is a trend towards early return to work even after open surgery. However, there has been a progressive increase in mean time for return to work from the early small series to the recent larger ones. This has likely been influenced by the increasingly complex cases being treated, especially by laparoscopic techniques. Nevertheless, most cases show a difference of 10 days to 2 weeks in favour of laparoscopic surgery over open nephrectomy.

## VI. COMPLICATIONS OF LAPAROSCOPIC NEPHRECTOMY

Two large multicentre studies have shown similar spectra of complications for laparoscopic urological surgery **(Table 1)**. Pooled data from studies assessing laparoscopic simple nephrectomy alone indicate that the most common complications are vascular and visceral injuries followed by haematoma, and bleeding and wound infections at the trocar or specimen retrieval incision sites. Pulmonary complications such as pneumonia and atelectasis, and urinary tract infection (UTI) were the predominant medical complications. Conversion is recorded as a complication in some studies [9], but in many circumstances, it may be the best decision in the patient's interest. Thus, conversion rates may serve as a benchmark for expertise or quality of service and should not be viewed as a complication. Occasionally, conversion may actually be in patient's best interest when progress is not being made especially in the case of laparoscopic simple nephrectomy for benign inflammatory diseases such as XGP. Intraoperative complications and conversion rates decrease with increasing experience but postoperative complications such as wound infection and medical complications remain the same

[10. The overall complication rate in large series for all urological laparoscopic procedures ranged from 4.4% [11] to 6.9% [9]. Reoperation rate was 0.8% and mortality rate ranged from 0.08% to 0.09%. Complication rates for transperitoneal and retroperitoneal nephrectomy and other procedures were similar in the studies of Soulie *et al*. [9] and Gill *et al*. [12]. There have been few studies with adequate numbers of cases to compare complication rates for laparoscopic and open procedures exclusively performed for benign renal disease. In a systematic review of complications in 300 laparoscopic simple nephrectomy procedures, major complication rate was 13.7% and minor complication rate was 5.7%, compared to 10.7% and 3.3%, respectively, for laparoscopic radical nephrectomy, and 10.6% and 0.5%, respectively, for laparoscopic donor nephrectomy [13]. Conversion to open surgery was highest for laparoscopic simple nephrectomy (3.7% vs. 2.5% for laparoscopic radical nephrectomy and 1.5% for laparoscopic donor nephrectomy), indicating the difficulties in laparoscopic simple nephrectomy. Minor complications included wound infection, ileus, and subcutaneous emphysema, with an overall complication rate of 9.5%. One comparative study has shown a higher absolute in cases in wound infection in open surgery [8]. Comparative studies of open and laparoscopic surgery have not shown a higher rate of respiratory complications, although laparoscopy, by virtue of it being less painful, is expected to help reduce pulmonary complications.

## VII. LAPAROSCOPIC NEPHRECTOMY IN COMPLEX BENIGN CONDITIONS

There were several confounding variables in comparative studies for laparoscopic and open surgery for benign conditions. These include diverse conditions ranging from non-functioning congenitally hydronephrotic kidney and renal artery stenosis, in which the surgical field is pristine and poses little challenge to the urologist, to non-functioning kidneys in inflammatory conditions such as XGP, renal tuberculosis or calculus disease, in kidneys that have undergone prior open or endoscopic surgery, in which dense and extensive adhesions can make dissection difficult and distort anatomical landmarks. Thus comparative studies that are robust enough to provide reliable evidence are lacking.

This is in contrast to studies comparing laparoscopic and open procedures in conditions such as T1 renal tumour, low-stage upper tract tumor, or living donors for renal transplantation, in which the subjects are more homogeneous and randomised studies, or at least case-controlled studies of reasonable quality have been published.

Laparoscopy has progressed from laparoscopic nephrectomy for simple benign diseases to radical nephrectomy for T1 renal tumours, and finally, after acquiring substantial experience, to complex inflammatory conditions such as XGP and renal tuberculosis. These conditions were initially considered as a contraindication [14] but are now considered as feasible in experienced hands [15].

### 1. BENIGN COMPLEX CONDITIONS THAT MAY REQUIRE NEPHRECTOMY

Difficult cases include simple nephrectomy for: inflammatory non-functioning kidney; previously operated cases; XGP; and ADPKD.

### 2. LAPAROSCOPIC NEPHRECTOMY IN INFLAMMATORY NON-FUNCTIONING KIDNEY

Inflammatory conditions such as previous pyonephrosis, perinephric abscess, and renal tuberculosis can cause significant perinephric adhesions that make laparoscopic simple nephrectomy technically demanding. The challenges include anatomical distortion; inability to visualise the essential anatomical landmarks; fibrous tissue and adhesions making visibility of vascular anatomy difficult, especially at the renal hilum; and greater risk of adjacent organ injury, such as to the diaphragm, spleen, pancreas, liver and bowel due to adhesions. These conditions were initially suggested as contraindications for laparoscopic nephrectomy [16], but with acquisition of greater expertise, these have been shown to be feasible.

Recent reports on laparoscopic nephrectomy for inflammatory conditions such as chronic pyelonephritis and tuberculous non-functioning kidney are from centres and surgeons with considerable experience. These report show that laparoscopic nephrectomy can be safely performed with all the benefits of minimal access surgery accruing to the patient at the cost of a marginal increase in operating times [7, 17, 18]. Thus, it is reasonable to state that laparoscopic nephrectomy in these conditions is safe and efficacious when performed by urologists highly skilled in laparoscopic surgery.

### 3. LAPAROSCOPIC SIMPLE NEPHRECTOMY IN PREVIOUSLY OPERATED CASES

Laparoscopic nephrectomy in patients who have undergone previous abdominal surgery can be difficult owing to development of adhesions, anatomical distortion, and fixation of viscera to the anterior abdominal wall, making access and dissection difficult. A retrospective review of 64 simple nephrectomies showed that there was no significant difference in patients with and without previous surgery, with regard to conversion rate, complication rate, blood loss, operating time and hospital stay [19]. Only the blood transfusion rate was significantly higher in the group with previous surgery. The authors attributed this higher transfusion rate to the greater proportion of older patients and patients with comorbidity in the previously operated group. They also noted longer operating time and hospital stay if the patient had undergone abdominal surgery at the same site rather

than another site. Aminsharifi and Goshtasbi compared the outcomes of laparoscopic simple nephrectomy in patients who had previous renal surgery with those who had previous percutaneous surgery [20]. There was no significant difference in operating time, complication rates, blood loss, and mean time to oral intake. However, there was only a combined total of 38 cases. They noted that both groups had significant perirenal adhesions. One patient in each group had injury to the diaphragm that was managed laparoscopically. They also noted higher transfusion rates and longer operating times in the group with prior open renal surgery, although this did not reach statistical significance.

These studies indicate that laparoscopic simple nephrectomy can be performed in cases that have had previous renal surgery, but the transfusion rate, operating time and hospital stay are likely to be higher than in patients who have not had any previous surgery.

### 4. LAPAROSCOPIC SIMPLE NEPHRECTOMY FOR ADPKD

Unilateral laparoscopic simple nephrectomy for ADPKD was first described in 1996 [21], and bilateral laparoscopic nephrectomy for ADPKD in 2001 [22]. Simple nephrectomy for ADPKD is typically required as a pre-transplant procedure in cases in which the kidney extends into the right iliac fossa, preventing graft placement. The other indications include severe hypertension, persistent infection in the cysts, recurrent or persistent bleeding, and persistent significant pain.

If a Veress needle is used for establishing pneumoperitoneum, it must be placed caudal to the lower pole of the kidney. Sometimes an extra 5-mm port may be required in the posterior axillary line for retraction. If the indication for nephrectomy is an infected cyst, the cyst should not be ruptured, to prevent the contents from spilling into the peritoneal cavity. If spillage occurs, it should be quickly aspirated. In uninfected kidneys, large cysts may be aspirated to facilitate dissection but one should avoid spillage of cyst fluid into the peritoneal cavity. It is believed that some toxins are present in the fluid because spillage causes significant pain in the postoperative period and prolongs postoperative ileus [23, 24]. Renal cysts can be ruptured during specimen extraction once a portion of the specimen is outside the body, so that the fluid does not spill into the peritoneal cavity. At the same time, rupturing the cyst outside the body helps to reduce the size of the specimen, which helps in delivering the specimen out through a smaller incision. Morcellation may facilitate extraction of the kidney via a smaller incision [25].

Study results are summarised in **Table 2**. These studies show that all the advantages of laparoscopic nephrectomy in other conditions such as reduce blood loss, lower transfusion rate, lower postoperative analgesic requirement, and shorter hospital stay are all realised for laparoscopic simple nephrectomy for ADPKD.

### 5. LAPAROSCOPIC SIMPLE NEPHRECTOMY FOR XGP

XGP is a chronic severe inflammation of the kidney usually due to longstanding calculus disease or ureteral obstruction. The affected kidney has poor function. There is often extensive adhesion of the kidney to the abdominal wall and adjacent viscera. In the early experience with laparoscopic nephrectomy, Bercowsky et al. concluded that laparoscopic nephrectomy does not confer any advantage in cases with XGP [16]. Data from seven studies analysed are shown in **Table 3.**

Complications were seen in up to 67% of patients in different series. There was no significant difference in blood loss between open and laparoscopic surgery. The operating times were 2 h longer for laparoscopy on average, and the conversion rate was ~20%. As in other laparoscopic procedures, the conversion rate for laparoscopic nephrectomy for XGP also decreased. In one of the largest series, there was a conversion rate of 12% [37]. Rosoff et al. have proposed that conversion to a HAL procedure may be a useful alternative to formal open conversion. They had four conversions out of 10 to a hand-assisted procedure but none underwent open conversion [34].

### 6. OVERCOMING DIFFICULTIES IN LAPAROSCOPIC SIMPLE NEPHRECTOMY IN COMPLEX CASES

Technical innovations that may facilitate nephrectomy include performing extrafacial (radical) nephrectomy [36] or subcapsular nephrectomy [40]. Conversion rates to open surgery are higher than laparoscopy performed for most other procedures [13]. The reason for conversion in most cases is attributed to non-progression due to adhesions, anatomical distortion, and vascular or visceral injury. Conversion to a hand-assisted procedure instead of a formal open procedure may preserve the benefits of minimal access surgery in many circumstances (HALN). Most studies on HALN originate from developed rather than developing countries, perhaps due to the high cost of hand-assist devices.

## VIII. ROBOT-ASSISTED LAPAROSCOPIC NEPHRECTOMY

Robot-assisted procedures have only recently started in most institutions. Therefore, studies on nephrectomy for benign indications may have been conducted during the learning curve phase.

***Table 2. Outcome of laparoscopic and HAL nephrectomy compared to open nephrectomy for ADPKD***

| | | | | Operating theatre time- (min) | | | EBLML | | | Hospital stay (days) | | | Complications | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Study no. | Study ref. | Group | No. of cases | Min | Max | Mean | ML | Max | Mean | Min | Max | Mean | No. | % |
| Studies on HAL bilateral nephrectomy in ADPKD | | | | | | | | | | | | | | |
| 1 | (26) | HALS-B/L | 10 | NA | NA | 194 | | | 203 | NA | NA | 4.7 | 2 | 20 |
| 2 | (27) | HALS-B/L | 34 | NA | NA | 226 | NA | NA | NA | NA | NA | 4.6 | 9 | 26 |
| | Total no. and weighted mean | | 44 | NA | NA | 219 | NA | NA | 203 | NA | NA | 4.6 | 11 | 25 |
| Study on HAL unilateral nephrectomy in ADPKD | | | | | | | | | | | | | | |
| 1 | (27) | HALS-U/L | 24 | NA | NA | 173 | NA | NA | NA | NA | NA | 4 | 4 | 16.7 |
| Studies on laparoscopic bilateral nephrectomy in ADPKD | | | | | | | | | | | | | | |
| 1 | (28) | Lap-B/L | 24 | NA | NA | 270 | NA | NA | 125 | NA | NA | 3 | 9 | 37.5 |
| 2 | (29) | Lap-B/L | 15 | 278 | 424 | 372 | 150 | 700 | 300 | 3 | 7 | 5 | 8 | 53 |
| 3 | (29) | Lap-B/L | 22 | 240 | 568 | 345 | 175 | 1400 | 300 | 4 | 12 | 7 | 9 | 41 |
| | Total no. and weighted mean | | 61 | 240 | 568 | 322 | 150 | 1400 | 231 | 3 | 12 | 4.9 | 26 | 43 |
| | | | | Operating theatre time | | | EBL | | | Hospital stay | | | Complications | |
| Studies on laparoscopic unilateral nephrectomy in ADPKD | | | | | | | | | | | | | | |
| 1 | (30) | Lap-U/L | 16 | 95 | 233 | 167 | 10 | 200 | 76 | 2 | 11 | 4 | 3 | 18.75 |
| 2 | (31) | Lap-U/L | 21 | 90 | 310 | 180 | 0 | 700 | 154 | 3 | 11 | 5.2 | 7 | 33 |
| 3 | (28) | Lap-U/L | 18 | NA | NA | 180 | NA | NA | 50 | NA | NA | 3 | 1 | 5.6 |
| 4 | (32) | Lap-U/L | 11 | NA | NA | 6.3 | NA | NA | 135 | NA | NA | 3 | 8 | 73 |
| 5 | (33) | Lap-U/L | 22 | 95 | 415 | 255 | 100 | 5000 | 400 | NA | NA | 4 | 4 | 18 |
| 6 | (23) | Lap-U/L (14 cases, 20 procedures) | 20 | 90 | 360 | 190 | 50 | 500 | 192 | NA | NA | 4.86 | 4 | 20 |
| | Total no. and weighted mean | | 108 | 90 | 415 | 178 | 0 | 5000 | 180 | 3 | 11 | 4.12 | 27 | 25 |
| Studies on open unilateral nephrectomy in ADPKD | | | | | | | | | | | | | | |
| 1 | (29) | Open-U/L | 19 | 100 | 170 | 128 | 10 | 500 | 222 | 5 | 24 | 8.3 | 12 | 63 |
| | | | | Operating theatre time- (min) | | | EBLML | | | Hospital stay (days) | | | Complications | |
| Study no. | Study ref. | Group | No. of cases | Min | Max | Mean | ML | Max | Mean | Min | Max | Mean | No. | % |
| 2 | (21) | Open -U/L | 14 | NA | NA | 157 | NA | NA | NA | NA | NA | 9.26 | 4 | 29 |
| 3 | (25) | Open -U/L | 12 | NA | NA | 147.1 | NA | NA | NA | NA | NA | 5.9 | 2 | 16.7 |
| | Total no. and weighted mean | | 45 | 100 | 170 | 142 | 10 | 500 | 222 | 5 | 24 | 8 | 18 | 40 |

B/L, bilateral; HALS, hand assisted laparoscopic nephrectomy; U/L, unilateral.

***Table 3. Outcome of laparoscopic nephrectomy in XGP***

| Study no. | Study ref. | Group | No. of cases | Technique | Mean Operating time (min) | Mean blood loss (ml) | Mean hospital stay (days) | Mean post-operative narcotic use | Complications No. of cases | Complications (%) | Complication types and no. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | (16) | Lap | 5 | Lap TP 3, RP 2 | 360 | 260 | 6 | 57 | 3 | 60 | Conversion 1, pulmonary embolism 1, ileus 2, abscess 1 |
| | | Open | 4 | | 154 | 438 | 5.7 | 62 | | | |
| 2 | (34) | Lap | 11 | Lap TP 11 single centre; conversion to HALS 4; no open conversion | | 217 | 2.4 | | 4 | 36 | Ileus 2, renal fossa abscess 1, fever 2 total 4 complications |
| 3 | (35) | Lap | 10 | Lap TP 10, 2 open conversion | 228 | 385 | 3.8 | | 3 | 30 | Diaphragmatic injury 1, ileus 2 |
| | | Open | 15 | Open | 155 | 350 | 8.2 | | 6 | 40 | Liver 1, colon1, faecal fistula 1, UTI 1, ileus 2 |
| 4 | (36) | Lap | 6 | HALS 2; conversion to open 1 | 301 | 775 | 4.8 | 57 | 3 | 50 | Haemorrhage needing conversion, pleural injury, jaundice and pleural effusion |
| | | Open | 6 | | 168 | 642 | 11.2 | 130 | 2 | 33 | Duodenal injury 1 and death 1 |
| 5 | (37) | Lap (Extrafacial) | 66 | | 133.8 | 204.2 | 2.4 | | 3 | 5 | Colonic injury 1, wound infection 2, conversion 8 |
| 6 | (38) | Lap (Extrafacial) | 19 | | 284 | 220 | 4.4 | 150 | 3 | 16 | Conversion 5, vascular injury 1, diaphragmatic injury 1 |
| 7 | (39) | Lap Extrafacial | 9 | | 228 | 300 | 3 | | 6 | 67 | Diaphragmatic injury 1, serosal bowel injury 2, sepsis 1, retroperitoneal haematoma 1, empyema 1 |
| | | Open | 10 | | 261 | 900 | 11 | | 5 | 50 | Serosal bowel injury 1, empyema 1, deep vein thrombosis 1, sepsis 1, wound infection 1 |
| Total Lap | | | 126 | | 176 | 258 | 3.1 | 57 | 25 | 20 | |
| Total open | | | 35 | | 187 | 567 | 9.2 | 103 | 13 | 37 | |

*All studies of level 3 evidence.*
*RP, retroperitoneal; TP, transperitoneal.*

The patient is positioned as described for transperitoneal laparoscopic nephrectomy. Three ports are placed in the mid-clavicular line; the central 12-mm port is for the camera and the two 8-mm robotic ports are for the robotic instruments. Another 12-mm port is placed immediately adjacent to the umbilicus at the level of the camera port for an assistant to insert instruments for suction and retraction, apply staplers or clips, and introduce a laparoscopic specimen extraction bag. The fourth robotic arm is used by placing the robotic trocar 4–5 cm inferior to the caudal robotic instrument port. A dual-blade retractor or Prograsp retractor is used as the fourth arm instrument.

Following standard steps of mobilising the colon and duodenum (for right nephrectomy) or spleen (for left nephrectomy), the ureter is identified in the retroperitoneum, mobilised, retracted and followed up to the renal vessels. The renal vessels can be clipped using a robotic Hem-o-lok clip applier. Alternatively, a laparoscopic stapler or clip applier can be introduced by the assistant at the patient's side. The specimen can be retrieved by enlarging the umbilical incision.

There is only one small case series for robot-assisted laparoscopic nephrectomy for benign conditions [41]. Although this study has demonstrated the feasibility, efficacy and safety of robot-assisted nephrectomy, no advantage has been shown over pure laparoscopic procedures. Some studies have shown a longer operating time for robot-assisted nephrectomy; probably due to the time required for docking and de-docking the robot.

The complication rates of robot-assisted nephrectomy (RAN) are similar to those of pure laparoscopic nephrectomy. RAN has longer operating times than laparoscopic nephrectomy; probably due to the learning curve and the robotic docking time. Other perioperative outcomes are similar. Thus, RAN appears to give no advantage over laparoscopic nephrectomy. The European Association of Urology guidelines panel have stated that the only use may be to provide an opportunity for training [41, 42] towards acquiring skills for robot-assisted partial nephrectomy.

## IX. RECOMMENDATIONS

1. Laparoscopic nephrectomy can be performed for most benign conditions with many benefits to the patient such as less postoperative pain; earlier recovery, discharge from hospital and return to work; less blood loss; and better cosmetic results. The procedure should be offered to patients whenever such expertise is available [Grade of recommendation (GR) B].

2. The complication rates of laparoscopic surgery when performed for benign conditions are similar to those for open surgery in expert hands (GR B).

3. Nevertheless, laparoscopic simple nephrectomy is a misleading term when performed for complex conditions such as reoperation, XGP, renal tuberculosis and ADPKD. Laparoscopic simple nephrectomy in the above-mentioned conditions is feasible but must be attempted only by experienced laparoscopic urologists. Hence, cases should be referred to centres where such expertise is available (GR B).

4. Patients with the above-mentioned conditions who are being prepared for laparoscopic simple nephrectomy should be counselled about the higher rate of complications and higher probability of conversion to HALS or to an open procedure (GR C).

5. In difficult laparoscopic simple nephrectomies, the plane of dissection can be outside Gerota's fascia, as in radical nephrectomy, or in the subcapsular plane (GR C).

6. HALS should be considered as an option in certain circumstances such as reoperation, XGP and ADPKD, either deliberately or in case of difficulty in carrying out pure laparoscopic nephrectomy as an alternative to conversion to an open procedure. This preserves most of the benefits of pure laparoscopic procedures to a great extent (GR C).

7. Conversion rate may be used as a benchmark for skill or quality of service and should not be viewed as a complication, especially in laparoscopic simple nephrectomy for inflammatory benign renal disease (GR C).

8. Laparoscopic simple nephrectomy is associated with higher complication and conversion rates compared to laparoscopic radical nephrectomy or donor nephrectomy. However, the complication rates are comparable to those of open nephrectomy for similar indications (GR C).

9. Laparoscopic simple nephrectomy even in complex cases such as ADPKD, reoperation, and renal tuberculosis, but not XGP, offers most of the benefits of laparoscopic surgery, such as shorter hospital stay, less postoperative pain, lower blood loss and transfusion rate, early return to work, and superior cosmesis (GR C).

10. Laparoscopic simple nephrectomy in XGP has high complication and conversion rates. It offers the benefit of shorter hospital stay but operating time is substantially higher, except in rare high-volume referral centres. Hence, it cannot be recommended for routine practice at the current level of knowledge (GR C).

## X. FUTURE DIRECTIONS

- Country- and region-specific cost–benefit analysis is required.
- Disease-specific data should be collected on the outcomes of laparoscopic surgery.

## XI. CONCLUSIONS

Laparoscopic nephrectomy for benign diseases encompasses a wide spectrum of conditions. Experience with laparoscopic nephrectomy for benign inflammatory diseases of the kidney is limited. There is a lack of high-quality studies due to such indications for nephrectomy being uncommon. Laparoscopic nephrectomy in such cases is associated with a higher complication rate and more frequent conversion. Such procedures must be done only by highly skilled laparoscopic urologists.

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# B. LAPAROSCOPIC AND ROBOTIC SIMPLE AND COMPLEX NEPHRECTOMY FOR MALIGNANT INDICATIONS

Laparoscopic and Robotic Simple and Complex Nephrectomy for Malignant Indications

## I. INTRODUCTION

Kidney cancer is the 12th most common cancer worldwide, with 338,000 new cases diagnosed in 2012 [1]. It is the third most common genitourinary cancer in the US, with >65,000 estimated new cases and >13,500 deaths in 2013 [2]. Renal cell carcinoma (RCC) accounts for the majority of all renal malignancies, and clinical stage T1 RCC tumours (≤7 cm) comprise the bulk of incidentally detected renal masses [3]. Despite increased detection of incidental renal masses, 20–30% of all patients are still diagnosed with metastatic disease [4].

Radical nephrectomy (RN) is the standard of care for clinically localised RCC when nephron-sparing surgery (NSS) is not possible [5–12]. After the first nephrectomy was performed in the 1860s, and Robson's description of RN for malignancy in 1963, open RN (ORN) became the mainstay of treatment for renal masses [13,14]. Until the advent of minimally invasive surgery, nephrectomy required relatively large abdominal or flank incisions, regardless of procedural complexity. The selection of surgical approach depends upon multiple factors, including tumour size and location, body habitus, prior abdominal surgery, and surgeon's preference. However, the prevalent use of cross-sectional imaging has led to earlier diagnosis of smaller incidental renal masses such that the need for ORN is less likely [15].

## II. LAPAROSCOPIC NEPHRECTOMY

### 1. INTRODUCTION

Since its introduction in 1991 [16], laparoscopic nephrectomy (LN) has become an accepted minimally invasive alternative to ORN for renal extirpation of masses that are not eligible for NSS [17]. LN has demonstrated comparable cancer control to ORN, as well as quicker convalescence, reduced estimated blood loss (EBL), and superior cosmesis, with an acceptable complication rate [18–23].

The literature reveals numerous large laparoscopic case series, including for large and/or complex tumours. Gill *et al.* performed radical LN in 100 patients with a mean tumor size of 5.1 cm and 1.6 days of hospitalisation **(Table 1)**. Surgical margins were negative for malignancy in all 100 patients, therefore, the authors concluded that LN with intact specimen extraction should be the standard of care for patients with T1-3aN0M0 renal masses measuring ≤12 cm [20]. Steinberg *et al.* reported the feasibility of LN in 231 patients; 65 of whom had cT2 tumours with a mean size of 9.2 cm. Compared to the 166 patients with cT1 tumours, those with cT2 tumours were younger and had greater EBL (200 vs. 100 ml, $P$<0.001). Importantly, operating time, analgesic requirements, hospital stay, time to convalescence, and complication rates were comparable between these two LN groups [24]. The technique for LN continues to evolve and can be performed safely with good perioperative outcome for the management of clinical stage T2 and T3 disease [25]. Nevertheless, the decision to alter the surgical procedure should be considered when either oncological control or patient safety is a concern [25].

### 2. LAPAROSCOPIC VERSUS OPEN NEPHRECTOMY AND ONCOLOGICAL OUTCOME

In the study by Gill et al. described above, the 100 radical LN cases were compared to a contemporary cohort of 40 patients who underwent ORN for a mean tumour size of 5.4 cm [20]. Compared to LN, ORN had a trend towards longer operating time (175 vs. 185 min, P=0.40), significantly higher EBL (187 vs. 670 ml, P<0.001), and significantly longer hospital stay (1.5 vs. 5.6 days, P<0.001). Baseline clinical and oncological features were comparable between the radical LN and ORN groups. Surgical margins were negative for malignancy in all 40 ORN patients as well as all 100 LN patients. At a mean follow-up of 16.1 months, there were no local or port-site recurrences. Two patients, both with pT1N0M0 tumours and dialysis-dependent renal

*Table 1. Summary of studies of outcomes of LN and RN*

| Study ref. | No. of patients | Tumour size (cm) | p stage (%) | Operating time (min) | EBL (ml) | Trans-fusion (%) | Conver-sions *n* (%) | PSM (%) | LOS (days) | Complications (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| **Laparoscopic series** | | | | | | | | | | |
| (20) | 100 | 5.1 | pT1 (76)<br>pT2 (8)<br>pT3 (14.5)[a]<br>pT4 (1.3) | 168 | 212 | NM | 2 (2) | None | 1.6 | Periop 14 |
| (24) | 65 | 9.2 | pT2 (57.9)<br>pT3 (40.4)[a]<br>pT4 (1.7) | 180 | 200 | None | None | 3.1 | 1.6 | Intraop 7.7<br>Postop 21.4 |
| (57) | 63 | 5.4 | pT1(84)<br>pT2 (4)<br>pT3 (9)[a]<br>pT4 (2) | 168 | 179.1 | NM | None | 1.5 | 1.4 | Postop 7 |
| (58) | 11 | 12.4 | pT2 (45.5)<br>pT3 (45.5)[a]<br>pT4 (9.0) | 155.8 | 154.5 | None | None | None | 3.1 | Postop 18.2 |
| (59) | 37 | 6 | pT3[a] | 190 | 200 | 16 | 1 (2.7) | 5 | 3 | Periop 19 |
| (25) | 247 | 7.76 | pT2 (8.8)<br>pT3(12.2)[a] | NM | 198 | 7.3 | None | None | 3.6 | Intraop 16.4<br>Postop 32.7 |
| (26) | 88 | 9.2 | cT2 | 241.5 | 493 | NM | 4 (4.5) | NM | NM | Intraop 10.2<br>Postop 17 |
| (27) | 200 | 9.0 | pT2a (45.5)<br>pT2b (17.5)<br>pT3a (36.0)<br>pT4 2 (1.0) | 188 | 320 | 8.1 | 12(5.7) | 3.5 | 3.4 | Intraop 3.8<br>Postop 19[b] |
| (60) | 94 | 9.0 | pT3 (98)[a]<br>pT4 (2) | 145 | 200 | NM | 6 (6.4) | NM | 6 | Postop 38[c] |
| (28) | 222 | 8.5 | pT2 (64)<br>pT3(36)[a] | 180 | 280 | 19 | 12 (5.4) | None | | Periop 28.8 |
| **Robotic series** | | | | | | | | | | |
| (44) | 5 | 66 $cm^3$ | pT1a (25)<br>pT1b (50)<br>pT3 (25)[a] | 321 | 150 | NM | 1(20)[d] | NM | 3 | None |
| (45) | 6 | 4.5 | pT1a (40)<br>pT1b(40) | 345 | 125 | 16 | 1(16.7)[d] | None | 3 | Periop 18 |
| (46) | 42 | 5.1 | pT1a (28.6)<br>pT1b (45.7)<br>pT2 (8.6)<br>pT3(14.3)[a] | 294 | 223 | NM | None | None | 2.4 | Periop 2.6 |
| (48) | 15 | 6.7 | pT1a (33.3)<br>pT1b (40)<br>PT2 (26.6) | 221 | 210 | 15 | 1 (6.7) | NM | 3.5 | Intraop 13.3<br>Postop 20 |
| (49) | 13 | 4.8 | NM | 168 | 100 | NM | 1(7.7)[d] | NM | 2 | Periop 30.7 |

[a]*Stages readjusted to 2010 AJCC standards (7th edition AJCC Cancer Staging Manual)*
[b]*Clavien grade III–V (including one death) occurred in 10.4%*
[c]*Clavien grade III–V (including one death) occurred in 4.3%*
[d]*Conversion to hand-assisted or standard LN*
*Intraop, intraoperative; NM, not mentioned; Periop, perioperative; Postop, postoperative; PSM, positive surgical margin; LOS: length of stay.*

failure, developed distant metastases. One of these patients, who also had multi-organ tumours (bilateral RCC, synchronous transitional cell carcinoma of the bladder, and prostate adenocarcinoma), died at 11 months postoperatively, giving an overall mortality rate of 1%. Gill et al. concluded that LN provides an encouraging surrogate alternative with technical and oncological efficacy comparable to ORN [20].

Steinberg et al. also compared their LN series described above to a comparable cohort of 34 patients who had undergone ORN for a mean tumour size of 9.9 cm. Compared to ORN, both LN groups achieved lower EBL (500 ml), and reduced operating time, quicker hospital discharge and more rapid recovery occurred in the cT2 LN group. There were no significant differences in histopathological criteria or complications between the ORN and LN groups; however, long-term oncological follow-up data were not available [24].

In a retrospective multi-institutional study, Jeon et al. analyzed 255 patients with large renal tumours and 88 and 167 patients underwent LN and ORN, respectively. All patients had pT2 tumours with a comparable size of 9.2 and 9.8 cm, respectively. Although operating time was significantly greater in the LN group compared to the ORN group (241.5 vs. 202.7 min, P<0.001), EBL was significantly lower in the LN group (439 vs. 604 ml, P=0.006). With median follow-up of 19 months for the LN group and 25.8 months for the ORN group, there was no difference in local recurrence or distant metastasis, mortality rate, 2-year overall survival (92.7 vs. 94%), or 2-year cancer-specific survival (90.1 vs 93.7%) between the two groups. Thus, the authors concluded that radical LN achieves comparable cancer control to ORN with short-term follow-up [26].

## 3. COMPLICATIONS OF LAPAROSCOPIC NEPHRECTOMY

Gill et al. reported a complication rate for LN of 14%, including major complications in 3% and minor complications in 11%. Two patients required conversion to open surgery due to bleeding, and all minor complications resolved spontaneously without additional intervention [20]. Although there was no significant difference in intraoperative complication rates between the LN and ORN groups in the study of Steinberg et al., there was a trend towards higher vascular complications/haemorrhage with ORN. There were similar postoperative complication rates between the groups [24]. Jeon et al. reported a 4.5% open conversion rate among 88 patients with cT2 tumours; three were due to vascular injury and one was secondary to mechanical CO2 insufflator failure [26]. Among 247 patients who underwent LN for a mean tumour size of 7.7 cm, Bird et al. reported transfusion and complication rates of 7.3% and 49.1%, respectively, and both rates were significantly higher for pT2–3 patients [25].

Similarly, Pierorazio et al. also found the rate of open conversion to be significantly greater for larger tumours. In their series of 200 LN patients, the conversion rate was 13.8% for tumours >10 cm [27]. Luciani et al. reported a conversion rate of 5.4% in their multicentre study of 222 LN patients and found a significant difference in tumour diameter between those that were converted to open surgery and those who completed laparoscopic surgery (11.9 vs. 8.5 cm, P=0.001). Moreover, multivariate analysis revealed pathological stage to be the only independent predictor of conversion to open surgery [28].

## 4. LAPAROSCOPIC NEPHRECTOMY AND HYBRID TECHNIQUES FOR INFERIOR VENA CAVA THROMBUS

**Table 2** summarises studies of minimally invasive nephrectomy and intervention for management of inferior vena cava (IVC) thrombus between 2002 and 2010. Case reports and small case series have been reported with most accomplished via a hybrid surgical approach using hand-assisted laparoscopy or an open incision for IVC thrombus extraction [29–34]. Romero et al. successfully performed a purely laparoscopic nephrectomy for a 7.5-cm renal mass with a small thrombus not requiring cross-clamping of the IVC [32].

***Table 2. Summary of studies of LN with intervention for management of IVC thrombus***

| **Variables** | Sundaram[29] | Varkaraki[30] | Disanto[31] | Romero[32] | Martin[33] | Hoang[34] |
|---|---|---|---|---|---|---|
| No. of IVC cases | 1 | 4 | 1 | 1 | 4 | 7 |
| Mean tumor size (cm) | 12.5 | 9.0 | 9.0 | 7.5 | 7.3 | 9.1 |
| Mean operating time (min) | None | 248 | 105 | 143 | 140 | 240 |
| IVC thrombus level | II | I | II | II | II | II-III |
| Surgical method | Hand-assisted | Hybrid open | Hybrid open | Pure lap | Hand assisted | Hybrid open |
| LOS (days) | Expired on 3 | 6.2 | 6 | 2 | 2.9 | 5 |
| Conversion | None | None | None | 0 | 1 | 1 |
| Complications | Death | 0 | Postop hypotension required transfusion | 0 | PE in one patient | ATN, AFib in one patient. COPD exacerbation, NSTEMI in other patient |

# III. ROBOTIC NEPHRECTOMY FOR RENAL MALIGNANCY

## 1. INTRODUCTION

The introduction of the da Vinci surgical system (Intuitive Surgical, Sunnyvale, CA, USA), expanded the application of laparoscopic surgery to various complex renal procedures, including pyeloplasty [35], partial nephrectomy [36–39], and donor nephrectomy [40]. It is also suggested that the robotic platform may permit surgeons to offer an alternative minimally invasive intervention for complex renal masses, which would otherwise typically require an open approach. Although not a fundamentally different approach compared with LN, robotic technology adds integrated 3D vision and meticulous instrumentation to standard laparoscopic techniques. Since the initial report in 2001 of robotic nephrectomy in a 77-year-old woman with a non-functioning right kidney [41], the literature regarding robotic nephrectomy has remained sparse but includes studies evaluating feasibility, safety and oncological outcomes of robot-assisted LN (RALN). The role of robotic technology in conventional laparoscopy is still unclear. This is partly due to the additional cost, because standard LN is achievable in the majority of patients requiring renal extirpation [42,43].

## 2. MAJOR ROBOTIC RADICAL NEPHRECTOMY STUDIES IN THE LITERATURE

There are only a few published reports of RALN, with small numbers of patients. An early report from 2005 describes the feasibility of RALN is five cases from a single institution, with a median operating time of 321 min, tumour size of 66 $cm^3$, and EBL of 150 ml [44]. Despite one conversion to hand-assisted laparoscopy because of bleeding, the authors concluded that RALN is feasible and a viable option for RN. A later report by Nazemi *et al.* compared RALN (6 cases) to ORN (18 cases), LN (12 cases), and hand-assisted LN (21 cases) by a single surgeon. They found no significant difference in perioperative or postoperative complication rates between groups other than significantly higher EBL, postoperative analgesic use, longer hospital stay and shorter operating time in the ORN group compared to the other approaches [45]. The longer operating time in the RALN group was attributed to the learning curve of the evolving technique, port placement, and robot docking time. Importantly, although operating theatre costs were significantly greater in the robotic and laparoscopic groups, there was no significant difference in overall hospital charges between the four groups in this series.

Rogers *et al.* described their experience with RALN for benign and malignant diseases in a large cohort of patients [46]. In their two-surgeon experience, among 42 patients who underwent nephrectomy, 35 underwent radical RALN and the remainder simple RALN. These nephrectomies were performed via a transperitoneal (34 radical and 5 simple) or retroperitoneal (1 radical and 2 simple) approach. The overall mean operating time was 294 min, EBL was 223 ml, tumor size was 5.1 cm, and hospital stay was 2.4 days. There were no open conversions in this series, and all patients had negative surgical margins. Compared to the RALN group reported by Nazemi *et al.*, this RALN group had lower operating time (294 vs. 345 min) and lower complication rate (2.6 vs 18%) [45]. In addition, Rogers *et al*. demonstrated the safety and feasibility of RALN in an obese patient population with a body mass index (BMI) of up to 44 $kg/m^2$ [46].

## 3. ROBOTIC RADICAL NEPHRECTOMY VERSUS STANDARD OR HAND-ASSISTED LAPAROSCOPY

The steep learning curve with LN compared to RALN [47] has resulted in studies comparing the two approaches. A prospective non-randomised study compared the perioperative outcome of 15 patients undergoing RALN with a contemporary 15 patients undergoing radical LN. All cases were performed for clinical stage T1–2N0M0 renal masses by a single surgeon experienced in laparoscopy and robotic surgery [48]. The authors found no significant difference in patient demographics, tumor characteristics, or perioperative variables. The only notable difference was longer operating time in the RALN group, which was explained on the basis of a learning curve. There were no differences in open conversion, complication rate or histopathological features of tumours between the approaches. With short-term follow-up, this small study failed to reveal any observable benefit of RALN over LN for localised RCC. However, it did demonstrate comparable safety and oncological efficacy for RALN and LN. Similar results were found in another small retrospective comparison of patients who underwent LN (*n*=46), hand-assisted LN (*n*=20) and RALN (*n*=13) for benign and malignant disease [49].

## 4. ROBOTIC NEPHRECTOMY FOR COMPLEX CASES

Critics of RALN assert that the additional cost of robotic technology is not justified due to a lack of perceived benefit over LN [45,48,49]. Nevertheless, proponents of RALN suggest that it enables more complex nephrectomy to be performed in a minimally invasive fashion in settings where standard laparoscopy has yet to be reported, which has been observed for other complex procedures performed robotically but never laparoscopically [50–52]. RALN has been successfully applied for tumours with extensive ICV thrombi requiring cross-clamping of the vein, without the need for an open incision for venous manipulation [53,54]. The first such series included five patients who underwent RALN with IVC tumour thrombectomy, including one patient with two IVC thrombi in each of two renal veins. Mean BMI was 36.6 $kg/m^2$. There were no complications, transfu-

sions, or re-admissions. Since this initial report, other institutions have performed this procedure [55], and a multi-institutional study is currently underway.

RALN has also been reported for tumours with local invasion into contiguous organs, including the liver, pancreas and duodenum [56]. The additional cost of RALN remains controversial and one study of 150 nephrectomies found that robotic surgery is no more costly than LN when a robot is already available [42].

## IV. CONCLUSIONS

ORN has traditionally been considered standard management for renal extirpation when NSS is not possible. LN has emerged as an accepted alternative with oncological efficacy comparable to that of ORN, yet with shorter recovery, decreased morbidity, and improved cosmesis. RALN may broaden the application of LN by overcoming some of the technical challenges of laparoscopy, particularly for complex nephrectomy.

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# C. LAPAROSCOPIC & ROBOTIC RETROPERITONEOSCOPIC NEPHRECTOMY

## I. INTRODUCTION

One of the arguments against the use of laparoscopy for renal surgery is that the transperitoneal approach violates the abdominal cavity for a procedure that is traditionally performed through the retroperitoneal route. Open nephrectomy, for both benign and malignant conditions, is usually performed through a flank incision that does not transgress the peritoneum. The theoretical advantage of this approach is that it minimises bowel handling, injury and contamination from an inadvertent spill. Laparoscopically, however, retroperitoneal access is considered relatively difficult because the space is limited, has to be created by dissection of the alveolar tissue, and is unfamiliar to most surgeons. Several innovations, devices and techniques have been developed to allow retroperitoneoscopic access to the kidney for nephrectomy. Over the past 20 years when transperitoneal laparoscopy was established

in urology, parallel development of retroperitoneal laparoscopy has ensured a steady stream of studies on retroperitoneoscopic nephrectomy (RPN).

## II. METHODS

A Pubmed/Medline search was performed for articles using the key words “laparoscopy, kidney, retroperitoneal, retroperitoneoscopy, and nephrectomy” in various combinations. Guidelines published by major urological associations were reviewed and cross-referenced articles from the above searches were accessed. Six hundred and five abstracts of articles relevant to the subject were reviewed and the full text was retrieved for abstracts related to RPN. These were reviewed for history, indications, outcomes, comparisons, and donor surgery.

## III. HISTORY

The first report of retroperitoneal laparoscopic surgery using insufflation of gas for urological disease was in 1979 [1]. There was limited interest in this approach over the next decade and most of the developments focused on transperitoneal access, driven by the revolution in laparoscopic cholecystectomy. In 1992 and 1993, Gaur reported the use of a balloon to spread the retroperitoneal alveolar tissue and create space for nephrectomy of the native kidney in a patient scheduled for renal transplantation [2,3]. This was a catalytic development for retroperitoneal and extraperitoneal urological surgery, and balloon dissection, with various modifications, remains the cornerstone of this approach.

Subsequent to this report, Kerbl et al. reported an experimental study on six pigs followed by a single case of RPN in a 48-year-old man [4]. They highlighted the restricted working space and possibility of pneumothorax. Mandressi et al. tried this approach in four patients and named it the retro-extraperitoneal approach [5]. Under fluoroscopy, they inserted a Veress needle into the perirenal space to localise the kidney and concluded that this approach is less traumatic, less painful, and has a shorter hospital stay than open surgery. In 1994, Rassweiler et al. described the first major modification of the dissecting balloon; they used a balloon on a trocar that allowed simultaneous visualisation during dissection [6]. They reported six nephrectomies with no complications. This modification remains the prototype on which most commercial devices available today are fashioned. In the same year, McDougall et al. reported using balloon dissection for RPN in 12 patients and highlighted the potential advantages of this route in avoiding peritoneal breach [7]. Valdivia et al. called this approach “lumboscopy” and used the Gaur technique for dissection to perform three nephrectomies [8].

The use of $CO_2$ under high pressure in the retroperitoneum has generated some concern, and in 1995, Shiozawa *et al*. performed gasless RPN in eight kidneys in four pigs [9]. In the same year, Diamond *et al*. described this approach in three children and highlighted the advantage of easy conversion to the open approach without changing patient position, early control of the renal artery, and avoidance of peritoneal breach [10].

## IV. SURGICAL TECHNIQUES

The first use of surgeon-controlled robotic arms to manipulate instruments during laparoscopic nephrectomy was reported by Partin *et al*. in 1995 [11]. The robotic arms held the camera and a retractor, which were controlled by the surgeon, who performed conventional laparoscopy through additional ports. These initial reports laid the foundation for further development of RPN.

General anaesthesia with intubation and neuromuscular blockade are used, and the stomach and urinary bladder are continuously drained. The patient is placed in the full lateral decubitus position at 90° to the table. Elevation of the kidney-bridge or placement of a rolled bolster under the dependent flank is optional, but helps increase the working space between the costal margin and iliac crest, for creation of the primary port.

Creation of an adequate retroperitoneal space is the first and, probably, the single most important surgical step in this procedure. While the Veress technique of closed insufflation has been previously described [5], the preferred approach is to make a 1.5-cm incision below the tip of the 12th rib into the retroperitoneum. Once the lumbodorsal fascia is breached and the psoas muscle is felt, blunt finger dissection is performed, followed by balloon dissection using commercially available or indigenously designed devices [2]. The plane of dissection is outside Gerota’s fascia (for malignancies) or inside it (for benign pathology). A self-retaining port is then placed into this incision and $CO_2$ is insufflated to maintain the space. Additional ports **(Figure 1)** are placed under direct vision, taking care to avoid peritoneal breach with the anterior port. Appropriate port placement is crucial in retroperitoneoscopy because of the limited space available. Gill *et al*. have suggested that placement of the balloon dissector within Gerota’s fascia, with a longitudinal incision in

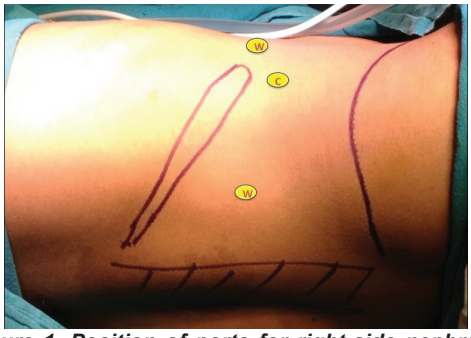


***Figure 1. Position of ports for right-side nephrectomy. C, camera port; W, working port.***

the fascia, allows rapid access to the renal hilum [12,13]. Although this lateral approach is the most common means of access, a posterior approach in the prone position has also been described, particularly for children [14].

**SUMMARY OF RECOMMENDATIONS**

- The 90° lateral position allows maximal access to the retroperitoneal space. Unlike transperitoneal procedures, an oblique tilt hampers access to the posterior spine and this could limit manoeuvrability (Grade C).
- Every effort should be made to create a wide space before beginning surgery. This could include finger dissection, balloon inflation, or sweeping away the peritoneum under direct vision. Open primary port placement with additional ports placed under vision is probably the safest approach. The ports should be placed as far apart as possible to allow maximal movement of the instruments (Grade B).
- Peritoneal breach with loss of pneumo-retroperitoneum is a common problem and may necessitate conversion if not properly handled. The breach may be occluded with a retractor or cotton pad, vented with an intraperitoneal needle, or widened to normalise pressure (Grade B).
- If there is difficulty identifying structures, fixed landmarks such as the psoas muscle, gonadal vein, and ureter should be used as a guide. For right-side lesions, it is important to identify clearly the renal vein and differentiate it from the gonadal vein and the vena cava before ligation (Grade B).

Blunt dissection should be used to identify anatomical planes. In large hydronephrotic kidneys, drainage of fluid or extracorporeal retraction may be used (Grade B)

## V. INDICATIONS AND OUTCOMES

Virtually all nephrectomies can be performed through a retroperitoneoscopic route. This includes treatment of benign as well as malignant tumours.

### 1. SIMPLE NEPHRECTOMY FOR BENIGN CONDITIONS

Many reports show the feasibility and safety of simple nephrectomy for benign renal diseases in children and adults [20–26]. Rassweiler et al. reported their experience of 200 retroperitoneoscopic procedures including 78 RPNs [26]. They classified simple nephrectomy [65] and nephroureterectomy [11] as difficult procedures and radical nephrectomy [2] as a very difficult procedure with increasing complications and conversion rates. Similarly, Hemal and colleagues reported 185 RPNs for various indications including ureteropelvic junction obstruction, kidney stone disease, tuberculosis (TB), ectopic ureters, ureterocele, renovascular hypertension, and vesicoureteric reflux [27]. They described a 10% conversion rate to open surgery, primarily in cases with stone disease, and a 4% major complication rate that was not influenced by the learning curve. Gupta et al. reported 505 patients who underwent RPN for benign non-functioning kidneys [28]. The mean operative time, blood loss, and hospital stay were 85 min, 110 ml, and 3 days, respectively. Blood transfusion rate was 0.5%, and 5.7% of patients required open conversion, including six with pyonephrosis.

Simple nephrectomy has also been described for removal of native kidney in transplant recipients. In a series of 36 RPNs in 15 transplant recipients and 17 non-transplant patients, Doublet et al. reported a mean operating time of 95±38 min (35–180 min), which was shorter for transplant recipients compared to patients with other indications [23]. The authors considered retroperitoneoscopy to be the first-line approach for transplant recipients. This becomes even more relevant in patients scheduled to receive peritoneal dialysis because the procedure does not breach the peritoneum [29].

Additional indications for which retroperitoneoscopy is feasible include obesity, heminephrectomy for horseshoe kidney with stone disease, ectopic pelvic kidney, and polycystic kidney [30–33]. Challacombe et al. used the retroperitoneoscopic approach for giant hydronephrotic kidneys [34]. They modified their technique by performing balloon dissection in two directions and used extracorporeal retraction, which contributed to a decrease in operating time. By expanding the indications, Hemal et al. explored the feasibility of simple nephrectomy in 52 patients with pyonephrosis; 46 of whom had previously been on percutaneous drainage [35]. Although six (11.5%) patients required conversion to open surgery due to bowel injury or non-progress of the procedure, the mean operating time and mean blood loss were only 110 min and 95 ml, respectively. The current indications are summarised in **Table 1.**

For simple nephrectomy, the reported conversion rate to open surgery is 0–16% and complication rate is 5–45% [36,37]. The most common causes for conversion are failure to progress with the operation, bleeding, and limited surgical experience with poor case selection [38]. A more detailed discussion on these issues is presented in the sections on comparative outcomes later in this chapter.

Kidneys with extensive perinephric adhesions, such as those with xanthogranulomatous pyelonephritis, TB, and pyonephrosis may pose a potential difficulty in creating the retroperitoneal space and dissection [39]. Inflammatory pathology involving adjacent organs is also a relative contraindication.

***Table 1. Indications for retroperitoneoscopic simple nephrectomy***

Poorly or non-functioning kidneys:

- obstruction (stone, or pelviureteric junction obstruction)
- reflux nephropathy
- infection
- cystic disease
- dysplasia
- renal artery stenosis

Pre-transplant nephrectomy:

- grade 4 or 5 hydronephrosis
- stone disease
- significant proteinuria
- recurrent pyelonephritis

***a) Summary of recommendations***

1. Retroperitoneoscopic simple nephrectomy is feasible for most cases of benign non-functioning kidneys. The commonest indications are ureteropelvic junction obstruction and kidney stone disease (Grade B).
2. Retroperitoneoscopy may be a preferred approach for patients receiving peritoneal dialysis (Grade C)
3. Outcomes improve with surgical experience and there is a learning curve associated with the procedure (Grade B)
4. Patients should be counselled about a ≤10% rate of conversion to open surgery (Grade C)

***b) Evidence table***

| Refs | Key question/outcome | Level of evidence |
|---|---|---|
| (21) | Safety in children, 18 patients, various benign diseases | Positive, 3 |
| (22) | Safety in adults, 20 patients, various benign diseases | Positive, 3 |
| (23) | Safety in adults for transplants recipients (19) and other indications (17) | Positive, 3 |
| (24) | Safety in children, 31 patients, various benign diseases | Positive, 3 |
| (26) | Safety in adults and learning curve (76), various benign diseases | Positive, 3 |
| (27) | Safety in 185 retroperitoneoscopic nephrectomy including 53 patients with nonfucntioning kidney due to stone disease, pyonephrosis, TB, Xanthogranulomatous pyelonephritis | Positive, 3 |
| (34) | Safety in large hydronephrotic kidneys, 11 procedures | Positive, 3 |
| (39) | Description of early vascular control, 150 cases, various benign diseases | Positive, 3 |
| (28) | 505 procedures, varied indications, safe | Positive, 3 |
| (35) | Safety in pyonephrosis, 52 cases: 46 nephrostomy, 6 conversions to open surgery, 6 subcapsular nephrectomy | Positive, 3 |
| (29) | Safety in children on dialysis, 14 procedures, small contracted kidneys | Positive, 3 |

## 2. RADICAL NEPHRECTOMY

Malignant tumours localised to the kidney (T1 and T2) are amenable to retroperitoneoscopic radical nephrectomy (RPRN). After establishing the feasibility of RPRN, this approach was extended to managing renal tumours, and in 1998, Gill et al. suggested that this may be a safe approach for renal tumours <8 cm [40]. In 2000, they reported one of the first large series treated with RPRN [41]. They performed 53 radical nephrectomies on patients with a mean tumour size of 4.6 cm (range: 2–12 cm). The mean operating time was 2.9 h (range: 1.2–4.5 h), with estimated blood loss of 128 ml. Seventeen percent of patients had minor complications and 4% required open conversion. Similarly, Yoshimura et al. reported 23 RPRNs from July 2000 to May 2002 [42]. Their mean operating time and mean blood loss was 203 min (range: 129–314 min) and 113 ml, respectively. One patient required open conversion and it was suggested that understanding the anatomy of the perirenal fascia was an important step in making this procedure safe.

The oncological validity of RPRN has been established in several studies **(Table 3)**. There is no reported increased risk of port site or local recurrence, and disease-free survival (DFS) rates are comparable with those of the open approach for renal tumours <5 cm [43,44]. Silva et al. performed RPRN for T1–T2 tumours in 50 patients with a mean tumour size of 5.3 cm (range: 3–13 cm). One patient had port site recurrence and it is suggested that this approach should be chosen carefully for large tumours as enough space may not be available in the retroperitoneum for manipulation and may cause iatrogenic breach in the tumor[45].

Fan et al. have suggested that T3, T4 tumour, presence of lymph nodes, venous thrombi, and adjacent organ involvement may require wider exposure and dissection that is allowed by the retroperitoneoscopic approach is limited and not an ideal procedure [50]. However, data from other centres suggest that the tumour size limit may not be inviolable. Larre et al. evaluated the intermediate oncological results for 146 renal tumours, including 41 that were T2 or higher [48]. The mean follow-up was 35.4 months and DFS at 5 and 10 years was 87.3 and 73.2%, respectively. Hetet et al. retrospectively analysed the results of 42 RPRNs for which the mean tumour size was 12 cm (range: 6–17 cm) [46]. A total of 16.7% of patients required conversion to open surgery because of technical difficulties: five had venous injuries and one had an arterial injury. With a mean follow-up of 15 months (range: 1–64 months), four patients died of metastatic disease.

***Table 3. Perioperative and oncological outcomes following RPRN for renal tumours***

| Refs | No. of procedures | Mean tumour size, cm (range) | Mean operating time (min) | Mean blood loss (ml) | Mean hospital stay (days) | Complications | Conversion rate | Mean follow-up, months (range) | Oncological outcomes |
|---|---|---|---|---|---|---|---|---|---|
| (41) | 53 | 4.6 (2–12) | 174 | 128 | 1.6 | 17% minor, 4% major | 4% | NR | NR |
| (44) | 50 | 3.8 (2–9) | 139 | 149.78 | 6 | 2 major, 1 minor | 6% | NR | 2 disease progression |
| (42) | 23 | NR | 203 | 113 | NR | 0% | 4.3% | NR | NR |
| (46) | 42 | 4.6(1.5–9) | 132 | 120 | 8.3 | NR | 16.7% | 15 (1–64) | NA |
| (47) | 52 | 5±2.0 (2–10.2) | 150± 54.3 | 242±402.2 | 44.9± 30.8 hrs | 7.7% | NR | 13.5±11.9 | 2% recurrence |
| (45) | 50 | 5.3(3–13) | 150 | 130 | 2.2 | 4% major 8% minor | 2% | | 2 recurrences |
| (48) | 146 | NR | NR | NR | NR | NR | NR | 35.7 (1-137) | DFS at 5 and 10 years: 87.3% and 73.2%, Cancer-specific survival 96.2% and 92.0 % |
| (49) | 108 | 4.2±2.1 T1–2 | 211.5±59.6 | 340.7± 221.5 | NR | NR | NR | Median:35.6 | 5-year overall survival: 94.5%, Recurrence-free survival: 96.2% |

***NR, not recorded.***

Body habitus of the patient may affect the operative difficulty in this retroperitoneoscopic approach. Akaihata et al. have correlated anthropometric measurements with operative difficulties [50]. Although body mass index (BMI) was not associated with operative difficulties, anterior perirenal fat and the distance from the 12th rib to the iliac crest correlated with operating time. However, RPRN is feasible even in obese and super-obese patients. Abreu et al. reported successful RPRN for a 12-cm tumour in a patient with BMI 77 kg/m2, with an operating time of 3 h and no complications [51]. Although posteriorly located tumours appear to be easier to remove with in the retroperitoneoscopic approach, hilar tumours are associated with more blood loss, longer operating time and difficult pedicle dissection [52].

As for simple nephrectomy, early control of the renal hilum seems to be advantage with this approach. In their first 60 cases, Yang et al. mobilized the kidney before controlling the hilum, while in their next 40 cases, they controlled the renal pedicle first [53]. They found that blood loss, operating time and hospital stay were lower with the latter approach, even though the conversion and complication rates remained the same.

***a) Summary of recommendations***

1. RPRN is feasible for most renal tumours (Grade B)
2. T2 tumours may also be amenable to retroperitoneoscopic surgery (Grade C)
3. Posterior tumours may be better suited to this approach (Grade C)
4. Vascular injuries are the most common major complications and may require conversion to open surgery (Grade B)

## 3. DONOR NEPHRECTOMY

There are several recent reports on pure retroperitoneal laparoscopic live donor nephrectomy [54–64]. Abbou et al. reported the feasibility of this approach and in a subsequent report, Kadam et al. compared CO2 absorption in 30 transperitoneal donor nephrectomies and 30 retroperitoneoscopic donor nephrectomies [56,57]. They found no difference in the two procedures. Modi et al. reported 100 retroperitoneoscopic procedures, including 25 for right kidneys, four cases with two renal arteries, and two with two renal veins [60]. The mean ischaemic time was 4.9 min (range: 2.96–8 min), with no graft loss. For the right-sided donors, they used a vascular stapler with a single line of fire on the vena cava to obtain a venous cuff. They expand this experience to 217 cases in a more recent study of laparoscopic renal transplantation [61]. The retroperitoneoscopic approach may be particularly suited to the right kidneys. Saito et al. found a higher frequency of right-sided donors in this approach in comparison with the transperitoneal approach [62]. Kohei et al. performed 425 procedures over 8 years and reported success in all but one [64]. The warm ischaemic time was 4.8 min and 1-year graft survival was 98%. Most studies on retroperitoneoscopic donor nephrectomy are restricted to a few centres, with greater numbers being performed transperitoneally or using hand-assisted devices [65,66].

**a) Summary of recommendations**

1. Retroperitoneoscopic donor nephrectomy is safe and feasible (Grade B)
2. It may be advantageous for right kidneys (Grade C)

***b) Evidence table***

| Refs. | Key question/outcome | Level of evidence |
|---|---|---|
| (41) | 53 procedures, maximum 12-cm tumour, 68% discharged in 23 h, 4% conversion, 13% complications; all less than open surgery | Positive, 2 |
| (44) | 41 radical nephrectomies, all margins free, no port site recurrence, 91% survival at 54 months | Positive, 3 |
| (46) | 42 procedures, maximum 9-cm tumour, 10 pT3 tumours, 6 vascular complications | Positive, 3 |
| (45) | 50 procedures, maximum 13-cm tumour, 4% major and 8% minor complications; local and port recurrence in T3a disease | Positive, 3 |
| (48) | 146 consecutive surgeries, 41 pT2/T3 tumours, 2 margins positive, no port recurrences, 96% cancer-specific, 5-year survival | Positive, 3 |

# VI. COMPARATIVE STUDIES

## 1. RETROPERITONEOSCOPY VERSUS OPEN SURGERY

Following the initial reports of RPRN, in 1996, Doublet et al. retrospectively compared 19 patients undergoing RPN with 10 cases of open nephrectomy [58]. The operating time for RPRN was 115 min compared to 110 min for open surgery, and the hospital stay was shorter for the RN cases. In 1998, Rassweiler et al. compared clinical outcomes between transperitoneal, retroperitoneoscopic and standard open nephrectomy for benign diseases [67]. They concluded that while operating time was shorter for open surgery, analgesic requirement was lower and hospital stay was shorter for the laparoscopic group, with most patients being discharged within 2 days. Convalescence time was lowest in the retroperitoneoscopy group, and they concluded that this approach had the lowest perioperative morbidity. RPN has also been evaluated in comparison with open surgery for complicated benign pathology. Hemal et al. retrospectively reviewed data for nine patients undergoing RPN for tuberculous kidneys and another nine undergoing open nephrectomy [59]. The first two cases of RPN had to be converted to open surgery, and the operating time was longer for RPN but the recovery data were superior. They recommended early hilar control while performing RPN for TB. Similarly, Zhang et al. compared 22 patients with tuberculous kidneys undergoing RPN or open surgery and found similar operating times with less blood loss and shorter hospital stay in the RPN group [39,60]. Technical feasibility and success have also been demonstrated for pyonephrosis. Gupta et al. compared 505 RPNs with 112 open nephrectomies performed over the same period [28]. Twenty-five patients required conversion to open surgery, primarily in the initial part of their experience. The mean operative time was 85 minutes (range 45-240 min) in the retroperitoneoscopic group and 70 minutes (range 35-120 min) in the open group. The mean blood loss was 110 mL (range 30-600 mL) in the retroperitoneoscopic group and 170 mL (range 70-500 mL) in the open group. Four (0.8%) patients in the retroperitoneoscopic group needed a blood transfusion, whereas 5 (4.5%) patients in the open group had a blood transfusion. The hospital stay in the retroperitoneoscopic group was 3 days (range 1-7 d) and was 5 days (range 3-12 d) in the open group.

While comparing retroperitoneoscopy with open surgery for malignant lesions, Goel et al. evaluated 18 patients undergoing RPRN and 11 undergoing open radical nephrectomy [68]. The operating time was longer in the first group but analgesic requirement was lower and hospital stay and time to return to normal activities were shorter. Similar findings have been reported in other studies [42,69,70]. Wang et al. allocated patients with T1 renal tumours for RPRN (185 cases) or open radical nephrectomy (167 cases) [71]. They found no significant difference in operating time but lower blood loss, shorter hospital stay, and lower analgesic requirement in the RPRN group.

### *a) Summary of recommendations*

1. RPN has favourable outcomes over open surgery in terms of blood loss, hospital stay, and return to work (Grade B)
2. Operating time is longer for retroperitoneoscopy (Grade B)

### *b) Evidence table*

| Refs. | Key question/outcome | Level of evidence |
|---|---|---|
| (58) | 19 RPN including 10 transplanted kidneys versus 10 open, no conversions, similar operating time and complications | Positive, 2 |
| (59) | 9 RPN for TB versus 9 open, 2 conversions, longer operating time, lower blood loss, and shorter recovery in RPN | Positive, 3 |
| (39) | 22 RPN for TB versus 22 open, similar operating time, lower blood loss, and shorter recovery in RPN | Positive, 3 |
| (72) | 23 RPN for T2 tumours versus 25 matched open surgery, no conversion or complication, shorter hospital stay, and lower blood loss and pain in RPN | Positive, 3 |
| (60) | 23 RPN for pyonephrosis versus 23 open, lower blood loss and shorter recovery in RPN | Positive, 3 |
| (71) | 352 patients, T1 renal cell carcinoma, randomised to RPN or open, similar operating time, lower blood loss, lower recovery period with RPN | Positive, 2 |

## 2. RETROPERITONEOSCOPY VERSUS TRANSPERITONEAL LAPAROSCOPIC NEPHRECTOMY

With the existence of a competing approach in transperitoneal nephrectomy (TPN), it is essential that comparative data for the two techniques be rigorously evaluated. In one of the first studies comparing transperitoneal with retroperitoneal nephrectomy, Ono et al. reported shorter operating time, lower blood loss, and no conversions for retroperitoneoscopy in six cases, while three of 28 transperitoneal procedures needed conversion to open surgery [73]. Similar outcomes have been reported in terms of morbidity and hospital stay but with some advantage in operating time and analgesic requirement for retroperitoneoscopy, possibly due to direct access [74,75].

Hemal et al. compared RPN with TPN for giant hydronephrotic kidneys in 18 patients. There was no open conversion or complications, and they concluded that radical nephrectomy was feasible despite the large space occupied by giant hydronephrotic kidneys [76,77]. In a prospective comparison of RPN with TPN in extremely obese patients with BMI ≥40kg/m2, patients undergoing RPN had lower blood loss, shorter operating time, greater specimen weight, lower risk of conversion, and shorter hospital stay [78]. A comparison of haemodynamic parameters between the two approaches found fewer haemodynamic changes and a lesser adverse effect on ventilatory functions with RPN [79].

Lorenzo et al. compared RPN and TPN in children and found that the mean operating time for RPN was 85 min compared with 126 min for TPN [80]. The mean blood loss and hospital stay were similar for both groups. Kim et al. systematically reviewed the data on RPN and TPN among children [81]. Out of 689 nephrectomies, 401 were performed by the retroperitoneoscopic approach. The mean age of the children was 4.8 and 5.4 years, respectively, in the RPN and TPN groups, and the mean operating time was 129 and 154 min. Complications in both groups were similar and the authors concluded that because the cases in the two groups were not matched, the lower operating time for RPN may not be significant.

Nambirajan et al. reported the first randomised controlled trial (RCT) comparing transperitoneal radical nephrectomy (TPRN) and RPRN in 40 cases [82]. Both approaches were similar in terms of perioperative parameters and technical difficulties with zero conversion rate. Desai et al. randomised 102 patients with renal tumours into two groups [47]. Fifty patients underwent TPRN and 52 underwent RPRN. RPRN was associated with shorter time to renal artery control (91 vs. 34 min) and renal vein control (98 vs. 45 min) and shorter total operating time (207 vs. 150 min). Blood loss, hospital stay and convalescence time were similar. However, these advantages in operating time have not been supported by other studies [83,84]. On the issue of oncological validity, a multi-institutional study compared 472 TPRN with 108 RPRN procedures at 23 institutions from January 1997 to December 2007. The 5-year overall survival and recurrence-free survival were similar in both groups [49].

Fan et al. reported a systematic review and meta-analysis comparing TPRN and RPRN [50]. They reviewed 12 studies including three RCTs and nine retrospective studies. The operating time was non-significantly shorter for the retroperitoneoscopic approach, while blood loss, hospital stay, and analgesic requirement were similar in both groups. Intraoperative complication rate was lower in the RPRN group but postoperative complications and blood transfusion rates were similar, as were oncological outcomes. The authors concluded that RPRN may be a faster approach, especially for posterior tumours.

While comparing the outcomes in patients undergoing donor nephrectomy, Troppmann et al. reported that they were able to complete 87% of the 52 procedures planned retroperitoneoscopically, whereas seven were switched to transperitoneal laparoscopy [85]. A comparison of the 45 successful cases with 45 planned and executed transperitoneal procedures showed similar warm ischaemic time and donor outcomes.

### *a) Summary of recommendations*

1. Both retroperitoneoscopic and transperitoneal nephrectomy have similar outcome parameters (Grade B)
2. Operating time may be shorter for retroperitoneoscopy (Grade B)

***b) Evidence table***

| Refs | Key question/outcome | Level of evidence |
|---|---|---|
| (82) | 40, T1/T2 tumours, randomised, no difference in any parameter, occasional delayed oral intake in RPRN | Positive, 2 |
| (47) | 102 renal tumours, randomised, tumours ≤15 cm, earlier vascular control and shorter operating time in RPN | Positive, 2 |
| (78) | 51 obese (BMI >40 kg/m$^2$) patients, RPN had non-significant advantages in blood loss, operating time, conversion rate, and recovery time | Positive, 3 |
| (85) | 45 RPN versus 45 TPN for donor nephrectomy, no difference in outcomes | Positive, 3 |

## VII. ROBOT-ASSISTED SURGERY

There are few data on the use of robotic assistance for RETROPERITONEOSCOPIC simple or radical NEPHRECTOMY RPN or RPRN. One of the reasons for this could be that there is little added advantage of robotic assistance for ablative procedures such as nephrectomy. Another reason might be the limited space available for placement of robotic ports in the retroperitoneum. Rose et al. reported the first case of robot-assisted retroperitoneoscopic nephroureterectomy in two patients; one with a symptomatic non-functioning hydronephrotic kidney with a megaureter, and the other with a lower ureteric tumour [86].

## VIII. CONCLUSIONS

RPN or RPRN is an established surgical option for benign and malignant diseases. It has similar surgical and oncological outcomes as transperitoneal laparoscopic surgery. It may potentially allow quicker access to the renal hilum and earlier vascular control, which in turn, may translate into shorter operating time. This is, however, is not uniformly documented. To make it more popular, greater opportunities for training and expansion with the use of robotic assistance may be necessary. The development of simulators and virtual training, mentored training opportunities, and standardised programmes could help increase the pool of trained surgeons.

## IX. RESEARCH RECOMMENDATIONS

1. There are no RCTs comparing RPN or RPRN with open surgery or TPN for long-term oncological outcomes in renal malignancy
2. RPN and TPN should be compared for their learning curve because one of the potential criticisms of RPN is the difficult orientation
3. RPN for tumours greater than T2 is not established. This should be evaluated in prospective studies.
4. Long-term surgical complications of RPN versus TPN have not been compared and should be evaluated
5. Use of simulators and virtual training should be evaluated to increase the pool of trained surgeons
6. Use of robotic platforms needs evaluation

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# D. NOTES AND HYBRID NOTES FOR RENAL SURGERY

## I. DEFINITION

The terms used to describe minimally invasive surgical techniques are continually evolving due to continuous changes in the procedures. There is no worldwide accepted consensus on how to name these procedures. In this consultation, we use the terms proposed by the Urologic NOTES Working Group in 2007 [1] [level of evidence (LE) 4; grade of recommendation (GR) C]:

- NOTES: surgical procedure that utilises one or more patent natural orifices of the body, with the intention of puncturing a hollow viscera to enter an otherwise inaccessible body cavity. These orifices include the mouth, nostrils, anus, vagina and urethra. The hollow viscera that may be punctured include the bladder, vagina, colon, stomach and oesophagus.

- Hybrid NOTES: surgical procedure in which >75% of the procedure is performed via the instrumentation inserted via a natural orifice, but some instruments or ports are passed transabdominally.

- NOTES-assisted: surgical procedures in which a natural orifice is used as an additional port during laparoscopic surgery for insertion of an instrument or an endoscope for visualisation.

Endoscopic procedures such as cystoscopy, transurethral resection or ureteroscopy are not considered NOTES procedures, although they are performed through a natural orifice.

## II. EXPERIMENTAL STUDIES

The first experimental application of NOTES was accredited to Kalloo *et al.* [2]. Using an endoscope, they performed 12 successful transgastric peritoneoscopies. After that, five procedures with 2 weeks survival were successfully carried out, with negative peritoneal cultures and no complications found during follow-up.

The first successful experimental application of NOTES in urological surgery was described in 2002, when Gettmann *et al*. developed a porcine model of transvaginal nephrectomy [3]. Six nephrectomies in four pigs were performed, with five of them requiring an additional abdominal port to complete the procedure. With a mean operating time of 210 min, the authors experienced technical difficulties due to the anatomy of the animal and the laparoscopic instrumentation available at that time.

Since then, several different studies have been published; all of them showing the feasibility of NOTES nephrectomy using different approaches, but most of them requiring additional ports to complete the procedure.

- **TRANSVAGINAL:** this is the most widely used approach. Different groups have proven the viability of this route of access for radical and partial nephrectomy. The transvaginal approach offers an easy way to remove large specimens and easy closure of the incision. Haber et al. performed 10 hybrid transvaginal procedures (partial and radical nephrectomy, robotic pyeloplasty), combining NOTES with an umbilical port, and did not report any intra- or postoperative complications [4]. Aminsharifi et al. submitted 10 dogs to left or right hybrid transvaginal nephrectomy (combined with an umbilical port) with a mean operating time of 101 min [5]. The human cadaver model has also been used by other groups. Aron et al. performed four nephrectomies using a multichannel laparoscopic port in the vagina, combined with a three-channel R-port in the umbilicus to monitor the transvaginal procedure. They completed three procedures but had to abandon one because of dense pelvic adhesions [6]. All these studies have reported the feasibility of hybrid NOTES nephrectomy in animal and human cadaver models using standard laparoscopic instruments, although difficulties related to instrumentation and organ retraction are reported. (LE 3)

- **TRANSGASTRIC:** no model of pure transgastric renal surgery has been reported. Some groups have combined the transgastric approach with another NOTES approach to perform a NOTES procedure using multiple ports of entry. Lima *et al*. carried out a non-survival study combining transgastric and transvesical approaches in a pig nephrectomy model, although no removal of the specimen was done [7]. Isariyawongse *et al*. described one case of NOTES transvaginal bilateral nephrectomy combined with a NOTES transgastric approach [8]. Visceral wound closure is difficult with the transgastric approach. The transgastric approach lacks the possibility to retract intra-abdominal structures to perform nephrectomy comfortably. (LE 3).

- **TRANSRECTAL:** this approach offers the possibility of easy specimen removal, although wound closure is difficult; also, it has a lack of organ retraction capability and a risk of peritoneal infection. The latter has been investigated in animal survival models using different access and sterilisation techniques, with promising preliminary results and good healing of the colonic incision sites [9,10]. Bazzi et al. were able to complete three nephrectomies in three female pigs using a dual-channel gastroscope through the rectum and assisted by a 5-mm umbilical trocar [11]. They translated their experience in the porcine model to human cadavers, in which they performed four nephrectomies with a mean operating time of 175 min; again, using a transrectal dual-channel gastroscope and assistance of an umbilical trocar for visualisation [12]. A non-survival study comparing transvaginal and transrectal NOTES partial nephrectomy in pigs showed similar operating times in both groups, with no difference in technical difficulty between the two techniques [13].

- **TRANSURETHRAL:** in this section we do not include transurethral resection or cystoscopy, because they are not laparoscopic techniques. The transurethral port in renal surgery has been used in combination with other approaches. Metzelder *et al*. performed eight nephroureterectomies in piglets, combining a specially designed transurethral port that worked through the bladder dome with a 12-mm transumbilical device [14]. Baldwin *et al*. reported three simple nephrectomies performed through the urethra and ureter with the assistance of two abdominal trocars. After dilating the ureter, they changed the ureteral sheath using a 12-mm bariatric trocar, which allowed entry of instruments and was the exit for the previously sliced surgical specimen [15]. Nadu *et al*. reported their experience with six porcine nephrectomies using a transurethral approach with umbilical assistance, although they did not remove the specimen pieces [16]. All these experimental case series have reported the need for specially designed instruments if this surgery is to be completed safely, and showed the need for morcellation of the surgical specimen.

- **PURE NOTES:** in relation to instrumentation and technology, the only currently available model for pure NOTES renal surgery is with a transvaginal approach. Some reports describe the feasibility of the pure NOTES procedure in animal models, but not in human cadavers. Haber *et al*. performed five pure transvaginal NOTES right nephrectomies in pigs using a gastroscope, and an Endo-Gia stapler inserted simultaneously through two incisions in the posterior fornix of the vagina. The stapler was used as a retractor during kidney dissection and for pedicle section and the operative time decreased progressively as a result of the learning curve [17]. Perretta *et al*. described an animal model of pure NOTES transvaginal retroperitoneal nephrectomy. With the animal in the supine position, they opened the vagina postero-laterally and created a retroperitoneal space that was expanded using $CO_2$ insufflation. Nephrectomy was performed using a two-channel endoscope, and they were able

to finish 10 cases (right and left nephrectomy) with a mean operating time of 50 min and no complications. They have also described an attempt to perform the same technique in two formaldehyde-preserved human cadavers, but the stiffness of the tissue prevented dissection of the kidneys [18]. Laydner *et al*. have published two reports of robotic retroperitoneal transvaginal NOTES nephrectomy in cadavers placed in the prone jacknife position [19].

### 1. SUMMARY

The experimental studies with NOTES report the feasibility of renal surgery in different animal models with different natural orifices. The main difficulties reported are related to:

Access to the peritoneal cavity. In surgery performed through the peritoneum, it is mandatory to avoid any injury to abdominal viscera. In some cases, this means that direct visualisation from another point is required when entering the NOTES port.

Organ retraction. This seems to be the main problem in renal surgery. As long, flexible and versatile instrumentations are required, the use of endoscopes does not offer sufficient strength to retract the organs to perform the operation comfortably.

Infection. The laparoscopic entrance through the intestinal tract can lead to infection in both the entrance site and the peritoneal cavity if adequate preventive measures are not taken.

Wound closure. The transvaginal approach offers an easy view to close the entry orifice. The other natural orifices require the use of specific devices to close the viscera properly.

Pure renal NOTES surgery has only been achieved using the transvaginal approach. Some groups have shown that combination of two NOTES approaches allows this surgery to be performed without any abdominal incision.

### 2. CONCLUSION

Animal and human cadaver models of NOTES surgery have demonstrated the feasibility of these procedures. These models are useful to develop new instrumentation and for training. The Committee recommends the use of these models before translating them into clinical practice. (LE 3, GR C).

## III. CLINICAL STUDIES

The only currently feasible NOTES approach in human renal surgery is the transvaginal one. No human cases of other approaches have been published; probably related to the lack of safety due to the instrumentation available [20].

Before the concept of NOTES was defined, at the beginning of the laparoscopic era, Breda *et al*. performed the first laparoscopic nephrectomy in Italy in 1993. Once the kidney was detached from its lumbar site, they brought it to the pelvic cavity and removed it via posterior colpotomy [21]. The next report of a NOTES-like procedure was in 2002, when Gill *et al*. performed 10 laparoscopic nephrectomies and extracted the tissue pieces through the posterior fornix of the vagina [22]. Although these cases show a clear direction towards the ideal of non-scar surgery, they cannot be considered NOTES because the natural orifice was only used as an exit route for surgical specimens and not as an entrance port for surgical tools.

In 2008, Branco *et al*. performed the first hybrid NOTES nephrectomy: simple nephrectomy for a dysfunctional kidney, which was removed from a 23-year-old woman using two 5-mm trocars in the abdomen and a transvaginal port [23]. In the same year, Alcaraz *et al.* performed the first radical nephrectomy [30]. Two years later, Allaf *et al.* carried out the first laparoscopic nephrectomy with vaginal extraction, considering the transvaginal approach as a viable alternative to open and laparoscopic surgery for living kidney donation [24]. Also in 2010, Sotelo *et al*. combined the transvaginal approach with a multi-channel access port in the umbilicus, resulting in an hybrid NOTES procedure with only one incision in the navel [25]. Since the first hybrid NOTES nephrectomy, we have found some case reports describing hybrid NOTES procedures for simple, radical and living donor nephrectomy [24–29]. Alcaraz *et al*. published their series of 14 cases of hybrid NOTES transvaginal nephrectomies for renal tumor, atrophic kidneys and nephrolithiasis [30]. First, they placed a trocar in the navel and created a pneumoperitoneum. After that, a second abdominal trocar and the vaginal port were placed under direct vision. A deflectable camera was inserted through the vagina, offering vision similar to that for commonly used laparoscopic nephrectomy, and surgery was performed using the two abdominal trocars **(Figure 1)**. With this technique, all the cases were finished by removing the kidney through the vagina. Colonic injury was seen in one patient with multiple previous operations, which was noticed on postoperative day 2 [30]. Georgiopoulos *et al*. have published their series of 38 hybrid NOTES transvaginal nephrectomies combining a multi-instrument port in the navel and a vaginal port, with the use of specially designed extra-long, pre-bent straight instruments through the vagina. The use of these specially designed instruments improves the limitations associated with transvaginal access [31].

Alcaraz *et al*. have described their experience with hybrid NOTES radical nephrectomy for living donor nephrectomy, using three abdominal trocars and a transvaginal one, which was used for organ retraction during the operation and as an ex-

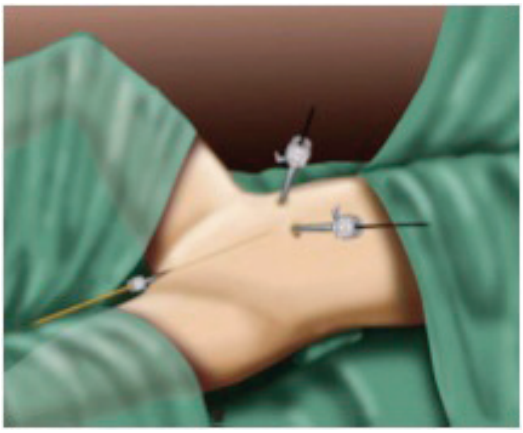

***Figure 1. Position of the patient for hybrid NOTES radical nephrectomy. A bariatric-surgery trocar is placed through the posterior vaginal cul-de-sac under direct vision and a deflectable camera is inserted through it. Two abdominal trocars are used as entry ports for common laparoscopic instruments to perform nephrectomy.***

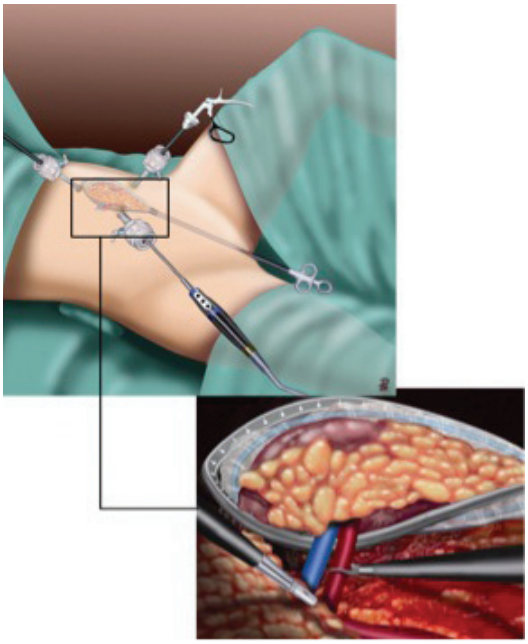

***Figure 2. Position of the trocars for transvaginal assisted NOTES for living donor nephrectomy. One trocar is placed in the navel and two others in the abdominal wall, while the transvaginal port is used for organ retraction during surgery.***

traction channel **(Figure 2)**. They published their first 20 cases of transvaginal assisted NOTES living donor nephrectomy and compared them to a matched, paired group of cases undergoing laparoscopic hand-assisted living donor nephrectomy. The procedure was completed in all cases and operative variables were similar between the groups, except that warm ischaemia time was longer in the transvaginal group (4.98 vs. 2.60 min). They also assessed the sexual function of those women that had donated their kidney transvaginally, describing no change before and 4 months after surgery [32].

Regarding pure NOTES, there is only one case published in the literature. In 2010, Kaouk *et al*. performed pure transvaginal NOTES nephrectomy for atrophic kidney in a women aged 58 years. Surgery took 420 min and the kidney was removed through a 3-cm posterior colpotomy. The authors reported difficulties with securing the port position, organ retraction, and fatigue due to the length of the operation. They claim that pure NOTES nephrectomy may be feasible in selected cases, although ports and instrumentation require further modification for NOTES urologic surgery to be practical [33].

## 1. SUMMARY

- The only NOTES approach for kidney surgery currently available is the transvaginal approach.
- Hybrid and assisted NOTES nephrectomies are feasible in selected patients.
- It remains to be established what benefit this surgical approach offers over conventional laparoscopy, because no prospective comparative study has been published.
- There is a need for better instrumentation to make NOTES urological surgery practical.
- Pure NOTES nephrectomy, although feasible, must be considered an experimental procedure until new evidence is provided.

## 2. CONCLUSION

In human renal surgery, the vagina is the only natural orifice that can be realistically considered for NOTES surgery. Hybrid and transvaginal assisted NOTES nephrectomies are feasible. Pure NOTES nephrectomy, although feasible, must be considered an experimental operation until better instrumentation is designed. (LE 3, GR C).

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# E. SILS/LESS/NEEDLESCOPIC KIDNEY SURGERY

## I. INTRODUCTION

Laparoscopy has significantly affected urological surgery. Since the first report of laparoscopic nephrectomy by Clayman *et al*. in 1991 [1]. this technique has gained worldwide acceptance. Laparoscopic surgery has been established as the gold standard for nephrectomy [2]. Although laparoscopy is less invasive than open surgery, it still requires several incisions, each at least 1–2 cm in length. Each incision carries potential morbidity risks of bleeding, pain, hernia, and/or internal organ damage, and may incrementally decrease cosmesis [3,4]. Cosmesis is particularly important in paediatric patients and is demanded by many adults [5]. Alternatives to conventional laparoscopy are single-incision laparoscopic surgery (SILS) [6], laparoendoscopic single-site surgery (LESS), and needlescopic surgery [7]. The panel members have analysed papers on SILS, LESS, and needlescopic kidney surgery. The following definitions are used in this manuscript:

- SILS: this is a single-incision (~20 mm) laparoscopic procedure, usually at the level of the umbilicus, where different trocars are inserted [8].
- LESS: single-incision access to the abdominal cavity using a single multichannel trocar, inserted in a small-length incision, through which different laparoscopic tools pass simultaneously to perform a complete surgical procedure [9].
- Needlescopic surgery: this is a laparoscopic procedure performed using 2- and 3-mm rigid endoscopes, ports, and instruments [10].

## II. DATA ACQUISITION

### 1. MEDLINE SEARCH

The literature search was carried out using Pubmed and Scopus. We analysed papers including SILS, LESS and needlescopic nephrectomy.

### 2. PAPER SELECTION

Case reports, congress proceedings, editorials and letters to the editor were not included. Publications reporting from the same institution and cohorts were limited to the most recent or largest study.

### 3. QUALITY OF EVIDENCE

There is still an on-going learning curve with these techniques. It was therefore difficult to draw strong conclusions from the data currently available for analysis. There is a lack of multicentre, randomised controlled studies producing conclusive evidence supporting the different techniques. In the absence of high-quality data, the expert panel came to the conclusion that providing guidance on the use of these techniques is important.

## III. ANALYSIS OF THE CURRENT LITERATURE

Papers published in peer-reviewed journals have been evaluated by the committee using the levels of evidence **(Table 1)** and guideline recommendations have been graded according to the Oxford Centre for Evidence-based Medicine Levels of Evidence **(Table 2)** [11]. Aims were graded to provide transparency between the underlying evidence and the recommendation given. It should be noted that when recommendations are graded, the link between the level of evidence and grade of recommendation is not linear. Data were extracted and the primary outcomes that were analysed included perioperative complication rates, conversion rates, postoperative pain, and cosmetic satisfaction. If sufficient data were available, perioperative complications were subdivided into intraoperative complications and postoperative complications within 30 days of surgery. Postoperative complications were classified according to the Clavien–Dindo grading system [12]. Conversion in the LESS and SILS groups was defined as follows: (1) addition of one 5- or 12-mm trocar, (2) conventional laparoscopy (addition of more than one trocar), or (3) open surgery [13,14]. The secondary outcomes were operating time, estimated blood loss (EBL), postoperative time to oral intake, length of stay (LOS), and time of convalescence.

## IV. SILS/LESS/NEEDLESCOPIC KIDNEY SURGERY

### 1. SILS KIDNEY SURGERY

Laparoscopy developed with the intent to replace open surgery in order to achieve a less-invasive approach. Although the improvements have been significant, conventional laparoscopy still requires several incisions, each at least 1–2 cm in length, with intrinsic morbidity risks of internal organ damage, bleeding, herniation, and pain, and a decrease in cosmetic results for each incision. An alternative to traditional laparoscopy is SILS **(Figure 1)**.

To overcome the clash among the trocars, SILS utilises bent and articulated instrumentation introduced through either adjacent conventional trocars.

First experiences in nephrectomy conducted with this revolutionary approach were published between 2007 and 2008 [6,15–17], followed by studies describing the safety and feasibility of single access in other urological surgical procedures, for example,

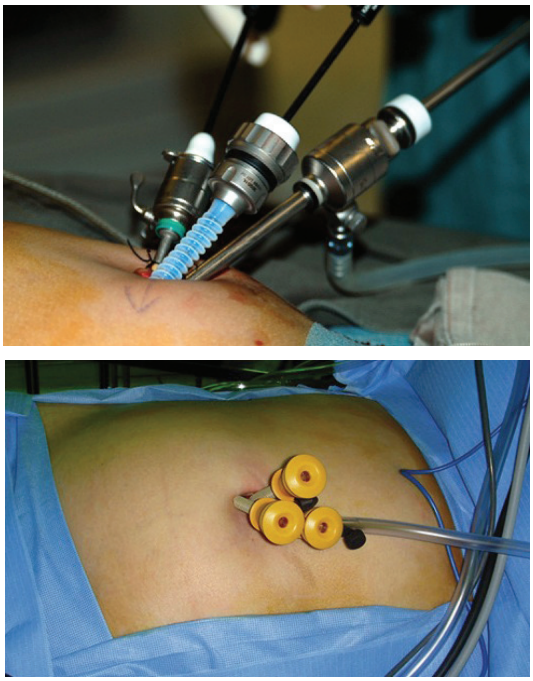

*Figure 1. SILS*

renal cryotherapy [18], pyeloplasty, adrenalectomy, varicocelectomy and sacrocolpopexy [19–21].

To the best of our knowledge, systematic reviews and meta-analyses of randomised controlled trials, simple randomised controlled trials, or non-randomised cohort studies have not been published comparing conventional laparoscopic nephrectomy with SILS.

After a first experience of SILS nephrectomy in a wet laboratory porcine model [15], Raman *et al.* published their first report of a case–control study in 2008, which compared the perioperative outcomes between the two techniques [22]. In the latter study, there were no differences in operating time, narcotic analgesic use, transfusion requirement, complication rate, surgical margin status, or LOS between SILS and conventional laparoscopic in 33 nephrectomies performed (22 using conventional laparoscopy and 11 using SILS).

Among all the operative records comparing SILS and conventional laparoscopy, there was only a statistically significant difference in EBL (higher in conventional laparoscopy), but this difference was not clinically significant, considering the absence of any difference in changes in haemoglobin between the two groups.

The data emphasise that SILS nephrectomy is safe, feasible, and equally efficacious to conventional laparoscopic nephrectomy, without compromising surgical or postoperative outcomes.

Moreover the analgesic requirement is increased by the necessity to enlarge the umbilical incision, up to 4–6 cm, in nephrectomy for renal tumours. This necessity blunts any demonstrable difference between the two groups. More significant results with respect to postoperative analgesic requirement could be achieved in non-extirpative surgery such as renal cryotherapy, pyeloplasty, and varicocelectomy, in which lengthening an incision for specimen extraction is not necessary.

## 2. LESS KIDNEY SURGERY

Raman *et al.* published their first report on laparoscopic single-site surgery for nephrectomy in pigs in 2007 [15].

LESS procedures are performed via a single, umbilical or extraumbilical, skin and fascial incision, through which a single multichannel access platform is introduced (single port; **Figure 2**).

Compared to other innovative laparoscopic approaches, LESS overcomes all the limitations intrinsic to a single incision, for example, lack of true triangulation and instruments clashing, due to technological progress, such as new laparoscopic access devices, optics, and specifically designed instrumentation, which are still evolving [23].

To date, the LESS approach has been applied in several urological surgical procedures, including simple, partial, radical, and donor nephrectomy, nephroureterectomy, adrenalectomy, pyeloplasty, transvesical simple prostatectomy, transperitoneal laparoscopic and robotic radical prostatectomy, and robotic cystectomy [18, 24–28].

In initial studies all the investigators carefully selected patients to undergo LESS; in particular, patients with T1 kidney tumours. More recently, Ponsky *et al*. described LESS radical nephrectomy for a tumour mass of 8 cm, and accomplished the procedure removing the specimen intact [16].

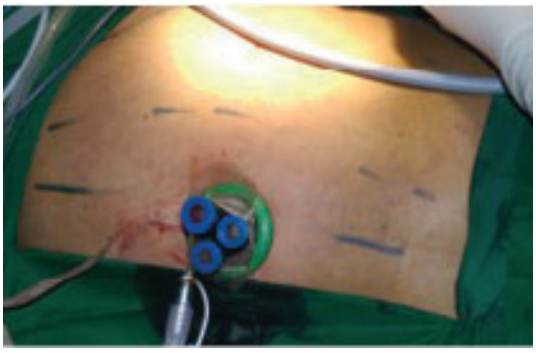

*Figure 2. Single port*

In a systematic review and meta-analysis of comparative studies, Fan *et al*. showed the evidence regarding the efficiency, safety, and potential advantages of LESS nephrectomy compared with conventional laparoscopy. Out of 690 studies identified, the authors chose two randomised controlled trials and 25 retrospective studies with a total of 1094 cases. All data were extracted and summarised independently by two authors, and any disagreement was resolved by the adjudicating senior authors, and the manuscript was rated by the Centre for Evidence-Based Medicine (Oxford) criteria.

Assuming that appropriate patient selection is mandatory, LESS nephrectomy is described as safe and feasible, with shorter LOS, significantly reduced postoperative pain, lower analgesic requirement, shorter recovery time, and better cosmetic outcome when compared to the conventional laparoscopic approach. There were no significant differences in peri- or postoperative complications, EBL, warm ischaemia time, or postoperative serum creatinine levels of recipient grafts for the donor nephrectomy subgroup. However, the operating time was longer and the conversion rate to open surgery was significantly higher for LESS than conventional laparoscopy. However, no significant difference was found between the two groups if only open conversions were analysed [29].

During the past few years laparoscopic donor nephrectomy has evolved and two innovative minimally invasive approaches, both LESS, have been proposed.

In 2008, Gill *et al*. reported the first successful single-port transumbilical live-donor nephrectomy [30], and in 2009, Rais-Bahrami *et al.* described the first LESS donor nephrectomy through a Pfannenstiel incision [31].

The first case series of live-donor nephrectomy showed the safety and feasibility of the LESS approach, with a mean ischaemia time of 5–7 min, without major complications [30, 32, 33].

Two studies have compared LESS Pfannenstiel and transumbilical incision donor nephrectomy with contemporary series of conventional laparoscopic donor nephrectomies. Although both studies were retrospective, therefore susceptible to inherent bias, and with small sample sizes, the results highlighted no significant difference between the two groups in terms of LOS and total analgesic requirement, and faster convalescence for the LESS group. The authors concluded that the advantages of LESS nephrectomy when compared with conventional laparoscopy are limited to cosmetic outcomes [34, 35].

## 3. NEEDLESCOPIC KIDNEY SURGERY

Although the needlescopic approach **(Figure 3)** is the oldest among the three techniques, the literature about its use in nephrectomy is poor and out-dated.

Needlescopic surgery was initially conceived as a diagnostic laparoscopic mini-invasive approach, and was first used therapeutically in the gynaecological field. The first reports of the technique for urological applications is attributed to Gill's group at the end of 1990s [10].

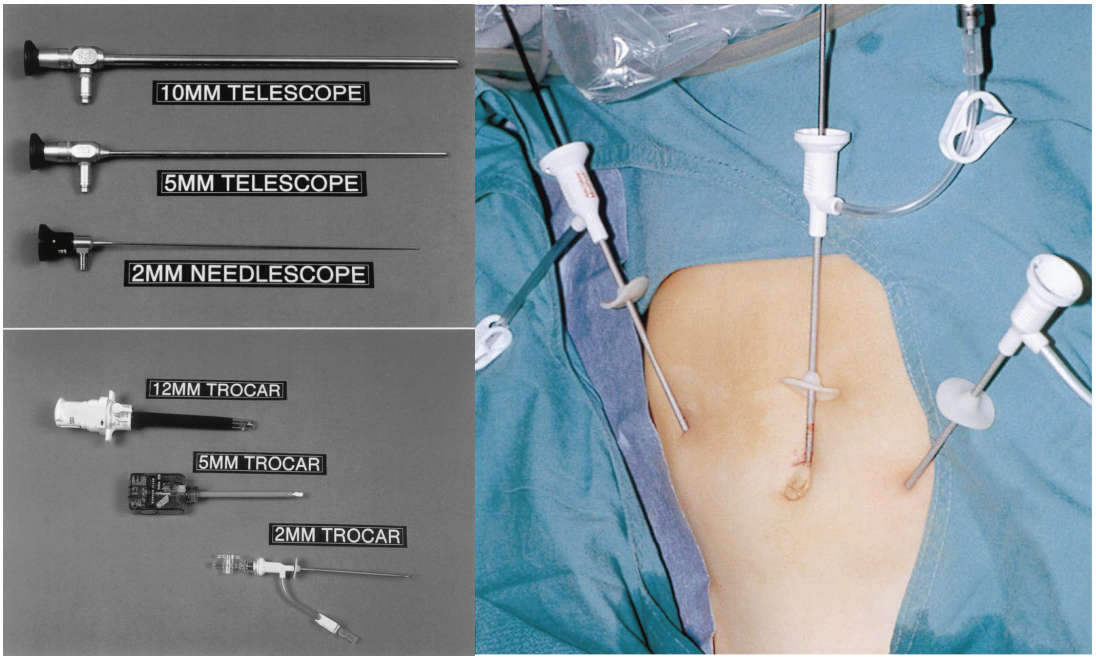


***Figure 3. Needlescopic surgery***

After the first study that described the safety and feasibility of the technique, in 2001, Gill *et al*. reported a more complete analysis with longer follow-up and a larger population, which in the end consisted of 65 patients [36]. The authors described most of the urological conditions for which needlescopic techniques can be exploited, with the most common being adrenalectomy. As far as we are aware, a codified needlescopic approach for nephrectomy has not yet been described. Gill *et al*. described only their new variant of nephroureterectomy, in which they applied the needlescopic tools to retrieve the distant ureter and bladder cuff, but nephroureterectomy was concluded using the classic laparoscopic retroperitoneal technique.

To the best of our knowledge, no more studies have been conducted on the topic. In our opinion, although needlescopic surgery brings intrinsic advantages in relation to cosmesis, less pain, shorter LOS with faster recovery, and lower comorbidity, the disadvantages, in particular, the limited number of specific instruments, lack of versatility and durability, and smaller window for the laparoscopic camera, restrict this technique to highly skilled laparoscopic surgeons. Moreover the necessity to have a larger incision for specimen removal limits the use of needlescopic surgery to reconstructive applications.

## V. CONCLUSIONS AND RECOMMENDATIONS ON SILS/LESS/NEEDLESCOPIC KIDNEY SURGERY

To date, experience of needlescopic, SILS and LESS approaches for kidney surgery is limited. Few high-volume centres are using these challenging techniques, which require highly skilled laparoscopic surgeons. Technical difficulties, such as interference among the trocars inserted through a single incision and the limited number of specific instruments, and lack of versatility and durability, were the major challenges experienced by the first pioneers. However, surgical technology has progressed in the field of miniaturisation, and good results are now available in particular for the LESS approach.

In surgical procedures that require removal of large specimens, for example, nephrectomy, approaches such as the needlescopic technique have been left behind. However, in our opinion, the needlescopic approach, for its reconstructive surgical applications, could have a role in kidney surgery and urology in general.

Our literature review shows that most studies comparing these innovative techniques with conventional laparoscopy for radical nephrectomy are case–control series, based on small populations, with an absence of high-quality data. This could be explained by the on-going learning curve with these techniques.

In our opinion, further prospective randomised studies are required to evaluate the real potentials of these approaches.

Therefore, according to the literature, we recommend the application of these surgical procedures only in high-volume centres, performed by highly skilled laparoscopic surgeons, and after careful patient selection (low body mass index, low comorbidity, and not advanced stage tumours). Moreover, the use of minimally invasive techniques should not compromise nephron-sparing surgery in tumours at stages lower than T1b.

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# F. LAPAROSCOPIC & ROBOTIC DONOR NEPHRECTOMY

## I. INTRODUCTION

The incidence of end-stage renal disease (ESRD) (115,000 per year) is higher than that of all urological malignancies except for prostate cancer (230,000 per year) and more people die from ESRD than any single urological malignancy in the US [1–3]. Globally, the number estimated to be on renal replacement therapy is 220,000 [4]. Treatment by renal transplantation results in mortality rates that are significantly less than those on the transplant waiting list [5]. Efforts to expand renal transplantation have included both living donation and extended criteria deceased donors (age >60 years, hypertension, death from cerebrovascular accident, terminal creatinine >6.

Living donation represents a growing treatment option for ESRD with ~27,000 such procedures being performed globally, representing 39% of all kidney transplants. More than 40 countries have seen a ≥50% increase in living donation in the past decade [6]. The US has the most living donations per year, which reached a plateau in 2002 at ~6,000, representing nearly one-third of all donations. Graft survival rates are higher in living compared to deceased donors (10 years: 58 vs. 46%) [7]. In 1995, laparoscopic donor nephrectomy was introduced to increase the pool of available donors [8]. While the number of kidneys transplanted has increased by 48% since the introduction of laparoscopic nephrectomy, the percentage coming from living donors (34%, 5,732/16,893) has remained steady in the US [9].

## II. METHODS

This review was based on a systemic literature search over 10 years (January 2004 to January 2014) in Medline and Embase. The primary search terms used were: ("kidney" OR "kidney transplantation") AND ("donor" OR "living donors") AND "laparoscopy*" OR "nephrectomy*"). All fields including MeSH terms were searched. The search was limited to human subjects and the English language. Additional searches were done in the Web of Science and the Cochrane Library, with a focus on systemic reviews, meta-analyses, and randomised trials. Abstracts from major transplantation and urology meetings were reviewed from the previous 3 years. Guideline statements from the European Association of Urology (EAU), British Transplant Society and Renal Association, and US Organ Procure-

ment and Transplant Network (OPTN) were also reviewed [10–12].

Medline returned 1106 articles and Embase 412. These 1,518 articles were individually evaluated for relevance, and 784 were excluded due to being non-clinical, paediatric, or not minimally invasive. The 734 included in the study were organised into the following categories: donor safety (266), donor selection (60), kidney selection (148), surgical approach (92), surgical technique (90), and future perspectives (60). Overall, there were 35 randomised controlled trials (RCTs), 12 systemic reviews, and 12 meta-analyses. Studies were assessed for level of evidence (1–4) and recommendations were graded (A–D) according to a modified version of the Oxford system as previously described [13].

## III. DONOR SAFETY

More articles were related to donor safety (270, 35%) than any other topic, and more RCTs, meta-analyses, and systemic reviews were dedicated to assessing the safety and efficacy of laparoscopic donor nephrectomy than any other topic. A study based on the OPTN database of >80,000 live donors in the US found 25 deaths within 90 days of surgery (3.1 per 10,000), but found long-term risk of death was no different than age- and comorbidity-matched controls that had no contraindications for kidney donation [14]. An analysis of ~70,000 living kidney donors in the US showed an overall complication rate of 8%, while a separate study showed major complications were <5% [15,16].

Numerous studies have shown the equivalence of laparoscopic donor nephrectomy to open surgery. In four meta-analyses and three RCTs, the open technique consistently had a shorter warm ischaemia time (WIT) and operating theatre time, while the laparoscopic group consistently had lower analgesic requirements, shorter hospital stay, and shorter time to return to work [17–23]. Complications and short- and long-term graft function were similar between the groups. One population-based study of 2509 patients found major complications were the same between open and laparoscopic surgery, and a second study of 601 patients found that complications, perioperative death, and survival >35 years did not differ from those in healthy controls [15,24].

In the largest population-based study of this review (>192,000), the rates of ESRD were estimated at 90 per 10,000 for kidney donors, 326 per 10,000 for the general population, and 14 per 10,000 for matched healthy controls without contraindication for donation [25]. Two other population-based studies estimated the rate of ESRD between 34 and 54 per 10,000 [26,27].

Studies evaluating hypertension after kidney donation have shown mixed results. Two meta-analyses evaluated hypertension and proteinuria after kidney donation, but few prospective studies were available for inclusion. Donors had small increases in urinary protein, but no accelerated loss in glomerular filtration rate (GFR) after donation up to 15 years in one analysis [28]. However, the other analysis found a 5-mm Hg increase in systolic blood pressure in kidney donors compared to controls [29]. In a population-based study, hypertension increased from 2.6% to 27.1% at 5 years but no control group was available [30]. Also, a recent prospective study found some early signs of chronic kidney disease (CKD) (e.g., 23% greater parathyroid hormone, 4% decreased haemoglobin, 24% greater homocysteine). However, blood pressure and proteinuria were unchanged after donation compared to matched donors [31].

### 1. SUMMARY OF RECOMMENDATIONS

1. Kidney donors should be informed that perioperative complications occur in ~8% of patients with <5% being major complications (Grade B).
2. Laparoscopic donor nephrectomy should be considered equivalent to open donor nephrectomy for graft function and complications (Grade A).
3. Kidney donors should be informed that perioperative mortality is estimated at 3.1 per 10,000 cases, and rates of ESRD are higher in kidney donors when compared to matched controls but lower than in the general population (Grade B).

### 2. FURTHER RESEARCH

1. Contemporary rates of major and minor complications as new technologies are introduced.
2. Donor safety should be assessed in donors with diabetes, hypertension or obesity, in elderly donors, or in those with other medical diagnosis that might increase risk of long-term renal failure.

**3. EVIDENCE TABLE,** ***Studies on the safety and efficacy of laparoscopic donor nephrectomy compared to open donor nephrectomy***

| Study type | First author, year, reference | Subjects | Study question | Critical findings | Rating of evidence |
|---|---|---|---|---|---|
| Meta-analyses and systemic reviews | | | | | |
| | Yuan *et al*., 2013 (17) | 1900 | How do short-term outcomes compare between open and laparoscopic surgery? | Compared with open, laparoscopic surgery showed shorter hospital stay and time to return to work, and less intraoperative blood loss without an increase in intraoperative and postoperative complications or compromise of recipient graft function. | 1, positive |
| | Wilson *et al*., 2011 (18) | 596 | Cochrane review: how do outcomes compare between open and laparoscopic surgery? | Laparoscopic surgery was associated with less analgesia, shorter hospital stay, and faster return to normal physical functioning, while not experiencing increased complications or graft loss. WIT was longer for laparoscopy. | 1, positive |
| | Greco *et al*., 2010 (19) | 8364 | How do outcomes compare between open and laparoscopic surgery? | Laparoscopic surgery resulted in less postoperative pain and blood loss with shorter hospital stay, while postoperative graft function was not inferior to that with open surgery. WIT was longer for laparoscopy. | 1, positive |
| | Nanidis *et al*., 2008 (20) | 6594 | How do outcomes compare between open and laparoscopic surgery? | The open surgery group had shorter WIT and operating theatre time, while the laparoscopy group had shorter length of stay and return to work. Graft function and complications were similar between the groups. | 1, positive |
| 5 | Garg *et al*., 2006 (28) | 428 | What are the long term changes in proteinuria and GFR for kidney donors? | Donors had small increases in urinary protein, but no accelerated loss in GFR after donation up to 15 years. | 2, positive |
| | Boudville *et al*., 2006 (29) | 357 | Is there an increased risk of elevated blood pressure after donation? | There was a 5-mm Hg increase in systolic blood pressure in kidney donors compared to controls. | 2, negative |
| RCTs | | | | | |
| | Simforoosh *et al*., 2012 (21) | 200 | How do outcomes compare between open and laparoscopic surgery? | WIT was longer for laparoscopic vs. open surgery, but there were no differences in delayed graft function or 5-year graft survival. | 1, positive |
| | Nicholson *et al*., 2010 (22) | 84 | How do outcomes compare between open and laparoscopic surgery? | Laparoscopic surgery had increased WIT, but improved analgesic requirements, hospital stay, return to employment, and complications. The graft survival was similar between the groups. | 2, positive |
| | Dols *et al*., 2010 (23) | 100 | How do long-term outcomes compare between open and laparoscopic surgery? | Blood pressure, GFR, quality of life (SF-36), fatigue (MFI-20) and graft survival were all similar between the open and laparoscopic groups at a minimum follow-up of 5-years. | 2, positive |
| Prospective | | | | | |
| 10 | Kasiske *et al*., 2013 (31) | 399 | Are there any short-term signs of CKD in donors compared to matched non-donors? | GFR declined by 28% and there were some early signs of CKD (23% greater parathyroid hormone, 4% decreased haemoglobin, 24% greater homocysteine). However, blood pressure and proteinuria were unchanged after donation. | 2, negative |
| Population based case control | | | | | |
| | Muzaale *et al*., 2014 (25) | 192,434 | Is the lifetime risk of ESRD higher in donors than a matched cohort free from contraindications for donation? | The estimated lifetime risk of ESRD was 90/10,000 for donors, 326/10,000 for unscreened non-donors (general population), and 14/10,000 for healthy non-donors. | 2, positive |
| | Mjoen *et al*.,2010(30) | 908 | What is the affect of kidney donation on hypertension and GFR? | Hypertension increased from 2.6% to 27.1% at 5 years. GFR increased between 1 and 5 years. No control group. | 3, negative |
| | Okamoto *et al*., 2009 (24) | 601 | How does survival compare between kidney donors and a matched population group? | No perioperative deaths and only 3 (0.5%) serious complications. Overall survival was better than in an age- and sex-matched cohort from the general population >35 years. | 3, positive |
| | Garg *et al*., 2008 | 7637 | Are there any differences in cardiovascular events and hypertension between kidney donors and healthy controls? | There were no differences in death or cardiovascular events between groups in the first decade after donation. Donors were more frequently diagnosed with hypertension (16.3 vs. 11.9%), but were also more frequently seen by a primary care physician. | 3, positive |
| 15 | Hadjianastassiou *et al*.,2007(15) | 2509 | How do major complication compare between open and laparoscopic donor nephrectomy? | Major complications were the same between laparoscopic (4.5%) and open (5.1%). | 3, positive |

*Limited to the 15 most relevant references.*
*MFI-20, 20-Item Multidimensional Fatigue Inventory; SF-36, 36-Item Short Form Health Survey*

# IV. DONOR SELECTION

Due to long waiting lists for kidney transplantation, expanding the criteria for living donors has been performed in many transplant centres. Patient factors such as age (>60 years), body mass index (BMI; >30), hypertension, and diabetes have excluded numerous potential donors. In two meta-analyses evaluating age >60 years, few prospective studies were evaluated. Recipient renal function was worse with older donors, but donor renal function was not [32,33]. Although graft survival tended to be worse for the older group (relative risk: 0.88, 95% confidence interval: 0.72–1.07) it was not statistically significant, and this association was less prominent in studies performed after the 1980s [32]. Even if the 12% decrease in graft survival were significant in contemporary studies, it may be an acceptable alternative to dialysis for many patients.

Two prospective studies reported older donors had similar quality of life and graft survival as younger donors [34,35]. In one matched retrospective study, older donors (≥60 years) had similar operative outcomes and complications, improved analgesic requirements, similar postoperative creatinine values, and recipient creatinine at 6–12 months was not significantly different clinically [36]. Other retrospective studies showed a mix of positive [37,38] and negative [39,40] outcomes for older donors.

The EAU, UK, and United Network for Organ Sharing (UNOS) guidelines for living kidney donation state that age alone is not an absolute contraindication, but that >60 years increases perioperative risks for the donor and may increase long-term risk of graft compromise [10–12].

Obesity was evaluated by one meta-analysis, but few prospective studies were available. In the meta-analysis, increased BMI was associated with conversion to open surgery and longer operating theatre times, but other short-term outcomes including GFR loss for donors were equivalent [41]. One population-based study of 5304 donor nephrectomies found a higher rate of perioperative dialysis in the group with BMI >35, but similar rates of re-admission, re-operation, graft failure and mortality across all BMI ranges [42]. A retrospective study found no differences in postoperative GFR or microalbuminuria for those with BMI >35 compared to <25 [43]. Obesity is a relative contraindication in the EAU, UK and UNOS living kidney donation guidelines, with BMI 30–35 requiring additional counselling about perioperative and long-term health risks. The guidelines recommend donors with BMI >35 should be discouraged from donation [10–12].

Few studies have assessed the appropriateness of accepting donors with a diagnosis of diabetes or hypertension. A recent prospective study found no difference in postoperative GFR (1 year) or blood pressure (5 years) when comparing donors with and without hypertension [44]. Another retrospective study found those with diabetic or impaired glucose tolerance on oral glucose tolerance test had equivalent survival to 20 years [45]. A retrospective report studied patients with metabolic syndrome [≥3 of the following: truncal obesity, high low-density lipoprotein (LDL), low high-density lipoprotein (HDL), diabetes mellitus, or hypertension) and found a declining GFR postoperatively [46]. The UK and UNOS guidelines state that mild to moderate hypertension that is controlled with one or two medications, where there is no evidence of end-organ damage, can still be considered for donation [11,12]. Diabetes and pre-diabetes are considered contraindications for kidney donation.

## 1. SUMMARY OF RECOMMENDATIONS

- Healthy patients ≥60 years old should be considered for live donor nephrectomy, especially if the recipient is ≥60 years old (Grade B).
- Healthy patients with isolated obesity (BMI 30–35) should be considered for live donor nephrectomy (Grade C).

## 2. FURTHER RESEARCH

- Are patients with isolated medical diagnosis (e.g., hypertension, diabetes, or elevated LDL) safe candidates for donation?
- Are patients who have received surgical treatment for obesity safe candidates for donation?

**3. EVIDENCE TABLE,** ***Studies on expanded criteria donors including advanced age, BMI, hypertension, and diabetes***

| | First author, year, reference | n | Study question | Critical findings | Rating of evidence |
|---|---|---|---|---|---|
| Meta-analyses and systemic reviews | | | | | |
| | Lafranca *et al*., 2013 (41) | 6019 | Does BMI affect outcomes during donor nephrectomy? | The high BMI group (>30) had a higher risk of conversion and longer operating theatre duration, but was otherwise no different than the low BMI group. | Positive 2 |
| | Iordanous *et al*., 2009 (32) | 2450[a] | Does age affect outcomes during donor nephrectomy? | Recipient GFR was lower in the >60-years group, but graft and recipient survival were not significantly different. | Negative 2 |
| | Young *et al*., 2008 (33) | 918 | Does age affect outcomes during donor nephrectomy? | Older donors had similar operating times, blood loss and length of stay, but had decreased GFR loss. | Positive 2 |
| Prospective | | | | | |
| | Klop *et al*., 2013 (34) | 501 | Does age affect quality of life after donor nephrectomy? | Older donors (≥60 years) had better physical function scores at 1 and 3 months and worse scores at 6 and 12 months. | Positive 2 |
| | Tent *et al*.,2012 (44) | 141 | Are outcomes similar between a hypertensive and non-hypertensive group after kidney donation? | There were no differences in pre- and posto-perative nuclear medicine GFR assessments, 1-year donor blood pressure and GFR, 5-year donor blood pressure and GFR outcomes between a hypertensive and non-hypertensive group. | Positive 2 |
| | Minnee *et al*., 2008 (35) | 105 | Are outcomes similar for older donors after kidney donation? | Older donors (≥55 years) had similar complication rates and quality of life as younger donors except the postoperative pain scores were lower for older donors. | Positive 2 |
| Population-based case–control | | | | | |
| | Reese *et al*., 2009 (42) | 5304 | OPTN database: are outcomes similar between normal and high BMI groups after kidney donation? | All outcomes were similar between normal and high BMI groups except delayed graft function was higher in the very obese (BMI >35) group. | Positive 2 |
| Retrospective | | | | | |
| | O'Brien *et al*., 2012 (37) | 383 | Are outcomes similar between obese, elderly, and standard donors after kidney donation? | No difference was observed in operating time, blood loss, complications, and GFR at up to 2 years between obese, elderly, and standard donors. | Positive 3 |
| | Mjøen *et al*., 2011 (39) | 721 | Are outcomes similar between obese, elderly, and standard donors after kidney donation? | Age, male sex, and BMI were all associated with eGFR at 1 year. | Negative 3 |
| | Cuevas-Ramos *et al*., 2011 (46) | 140 | Are outcomes similar between standard donors and donors with metabolic syndrome after kidney donation? | Those with metabolic syndrome (≥3 of truncal obesity, high LDL, low HDL, diabetes mellitus, or hypertension) were at increased risk of eGFR decline. | Negative 3 |
| | Young *et al*., 2011 (40) | 1260 | Do older donors have similar outcomes to normal age donors after kidney donation? | For older donors (≥60 years), graft loss tended to be higher but not significantly, death-censored graft loss was no different, & death in recipients was higher when compared to younger donors. | Negative 3 |
| | Facundo, *et al*., 2011 (38) | 192 | Do older donors have similar outcomes to normal age donors after kidney donation? | Older donors had similar complications and length of stay and there were no recipient graft losses from older donors. The 1-year GFR was lower in recipients of older donors. | Positive 3 |
| | Okamoto *et al*., 2010 (45) | 444 | Do donors with diabetes or impaired glucose toler- ance have similar survival to normal kidney donors? | Those with diabetes or impaired glucose tolerance on oral glucose tolerance test had equivalent survival to 20 years. | Positive 3 |
| | Heimbach, *et al*., 2005 (43) | 553 | Do obese donors have similar outcomes to normal BMI donors after kidney donation? | No difference was observed in any outcome except minor perioperative complications between obese (≥35) and BMI <25. | Positive 3 |
| | Jacobs *et al*., 2004 (36) | 84 | Do older donors have similar outcomes to normal age donors after kidney donation? | Older donors (≥60 years) had similar operative outcomes and complications, improved analgesic requirements, and worse recipient creatinine at 6–12 months. | Positive 3 |

*Limited to the 15 most relevant studies.*
*[a]Only two studies were prospective and none were RCTs.*
*eGFR, estimated glomerular filtration rate.*

## V. KIDNEY SELECTION

Efforts to improve renal imaging and leave donors with the healthiest kidney have resulted in >150 articles over the past 10 years. Seventy-eight of the articles have analysed preoperative imaging protocols [e.g., computed tomography (CT) or magnetic resonance imaging (MRI)] to assess arteries, veins, the collecting system, and renal stones. The two other main categories for donor selection compare right to left sided donation and donation with vascular anomalies. There were only two RCTs related to kidney selection, with one finding right donation equivalent to left, and the other finding lower-voltage CT scans (lower radiation dose) equivalent to higher voltage for determining arterial anatomy [47,48].

Based on the International Commission on Radiological Protection, the EU recommends a maximum 1-year dose for occupational exposure of 50 mSv and 100 mSv for 5 years [49]. However, recommendations for medical exposure of patients should be based on balancing the risks and benefits of the exposure [50]. The average per capita radiation exposure is estimated to be 6.2 mSv in the US and 0.7–2 mSv in Europe [51,52]. A typical triphasic CT scan produces ~10 mSv or approximately 3 mSv per phase [53].

Numerous prospective studies have found equivalent or superior sensitivity of CT over MRI for detecting arterial and venous branching [54–57]. Comparison of MRI to selective angiography or to intraoperative findings has yielded mixed results, with some studies finding decreased sensitivity for accessory arteries for MRI [58–61]. Most MRI studies have used 1.5-Tesla machines. One abstract compared a 3-Tesla MRI with CT angiography and found equivalent detection of vascular and collecting system anatomy [62].

The ability of CT scans to assess accessory arteries, venous anomalies or collecting system anatomy was uniformly positive [63–66]. One prospective study found that four-phase CT was effective at detecting lumbar veins, and another found that a single phase was accurate for detection of arterial and venous anatomy [63,65]. The use of 3D-CT reconstruction and volume calculation to preferentially leave the larger kidney with the donor has shown mixed results in retrospective studies. A recent study found the volume of the retained kidney was associated with postoperative GFR [67]. However, a second abstract analyzing donors with a >10% discrepancy in volume, from whom the smaller kidney was removed, did not find a significant improvement in postoperative donor function [68]. Another recent study found that CT volume analysis was sufficiently correlated with nuclear medicine studies for determining asymmetry and selective use of nuclear scan based split renal function allows careful selection for kidney donation [69].

Studies of right-sided kidney donation were uniformly positive. The single RCT showed shorter operating time for right-sided nephrectomy and equivalent complications and graft survival [47]. Two additional prospective studies demonstrated equivalence between right and left kidney donation [70,71]. One population-based study showed a small but clinically insignificant difference in 90-day graft survival [72]. Working closely with the transplant team is imperative for successful right-sided donation due to the shorter length of the renal vein.

Vascular anomalies were common, with one study finding nearly 25% of 820 donor nephrectomies had vascular anomalies [73]. More than 30 studies looked at the effects of multiple renal arteries on donor and recipient outcomes, but all were retrospective in nature. Nearly all of the studies reported equivalent perioperative complications and long-term graft survival for multiple renal arteries [74–76]. However, one study found worse long-term graft survival [77]; one study showed increased short term dialysis [78]; and one study showed increased ureteral complications [79]. Two studies showed worse recipient outcomes when ≥3 arteries were present, but equivalent outcomes for two compared to one artery [80,81]. The UK guidelines on kidney donation state that multiple arteries or anatomical anomalies are not absolute contraindications [11].

There were no prospective studies evaluating the effects of donating a kidney with a renal stone or cyst, but numerous retrospective studies investigated stones and one investigated cysts. In general, the stones were ~4 mm and did not cause complications when they were donated with the kidney [82–84]. There were also studies documenting successful removal of stones ex vivo prior to implantation [85,86]. The UK and UNOS kidney donor guidelines recommend against donation in cases of metabolic stone disease, recurrent stones, multiple or bilateral stones, or struvite stones. However, a solitary stone or small calcifications (1–2 mm) should not be considered a contraindication [11,12]. The kidney with the stone should be donated or the stone should be removed from the donor. A study of 25 kidneys donated with simple cysts demonstrated there were no cyst-related complications or adverse effects on graft function [87].

Few studies evaluated imaging of the collecting system or effects of donating a kidney with complete ureteral duplication. Ureteral duplication is seen in ~1% of kidneys [88]. One paper reported favourable results of 12 kidneys donated with complete duplication and no functional impairment or graft loss [89]. A second paper also reported 12 kidneys transplanted with complete duplication, and concluded that it was safe, although four of the cases had temporary urinary fistulae [90]. Delayed abdominal plane film radiography after contrast CT has been reported as a means of detecting urinary duplications, while avoiding the extra radiation of a delayed CT phase [91].

## 1. SUMMARY OF RECOMMENDATIONS

1. Multi-detector CT scans with at least an arterial phase should be considered the gold standard for preoperative imaging (Grade B).
2. Right-sided kidney donation should be considered safe and effective with appropriate training and coordination with the transplant team (Grade B).
3. Kidneys with two arteries should be considered safe and effective with appropriate training and coordination with the transplant team (Grade C).

## 2. FURTHER RESEARCH

1. Decreasing CT voltage (e.g. 100 kVp) and eliminating non-contrast, venous, and delayed phases should be further studied as a way to decrease radiation exposure.
2. The ability of 3-Tesla MRI angiograms to replace CT scans for detecting accessory arteries should be further studied as a means of decreasing radiation exposure.
3. Further studies should assess the effect of volume-based kidney selection on donor renal function outcomes.
4. Further studies should assess outcomes related to double and triple artery kidneys for donation.
5. Further studies should assess the safety of kidney donation with small nephrolithiasis.

## 3. EVIDENCE TABLE, *Studies on preoperative imaging*

| Study type | First author, year, reference | n | Study question | Critical findings | Rating of evidence |
|---|---|---|---|---|---|
| RCTs | | | | | |
| | Sahani *et al*., 2007 (47) | 62 | Can lower radiation doses result in equivalent sensitivity for detecting arteries? | Each technique had 100% sensitivity compared to intraoperative findings for arterial anatomy, and subjective scoring of visibility of branching arteries was similar. The 120 kilovoltage (kVp) dose was only 68% of the 140 kVp dose, and the 100 kVp was only 48% of the 140 kVp dose | Positive, 1 |
| | Minnee *et al*., 2008 (48) | 60 | Do those randomised to right nephrectomy have similar outcomes as those randomised to left donor nephrectomy? | Right kidney donation was shorter in duration than left. All other outcomes were equivalent with 1-year graft survival >93% for both right and left kidney donation | Positive, 1 |
| Prospective | | | | | |
| | Sameh *et al*., 2013 (54) | 89 | Does CT have sufficient ability to find accessory arteries, early branching, and renal vein anomalies? | Multi-detector CT found 7/14 accessory arteries, all 5 cases of early branching of the main renal artery, and 3/6 venous anomalies. | Negative, 2 |
| | Liefeldt *et al*., 2012 (55) | 48 | Does 1.5-T MRI have similar outcomes as 120 kPv CT for identifying accessory arteries, venous anomalies, and ureteral anomalies in the same patients? | Both imaging modalities were similar in their ability to detect venous and ureteral anomalies, but CT was better at detecting accessory arteries than MRI. | Negative, 2 |
| 5 | Gulati *et al*., 2012 (62) | 30 | Does 3-T MRI have similar outcomes as CT for identifying accessory arteries, venous anomalies, and ureteral anomalies in the same patients? | Both imaging modalities were similar in their ability to detect vascular and collecting system anomalies. | Positive, 2 |
| | Hoda *et al*., 2011 (70) | 91 | Do left and right kidney donation have similar WIT, complications, and graft survival? | All outcomes were equivalent between right and left kidney donation and 1-year graft survival was >97% for both. | Positive, 2 |
| | Kang *et al*., 2009 (63) | 51 | Does a single arterial phase CT have the ability to detect arterial and venous anomalies? | Six of eight renal anomalies were diagnosed by arterial phase CT and 9/11 accessory arteries. | Positive, 2 |

***Evidence table. Studies on preoperative imaging (ctd)***

| | | | | | |
|---|---|---|---|---|---|
| | Gluecker *et al*., 2009 (56) | 42 | Does 1.5-T MRI have similar outcomes as 120 kPv CT for identifyingaccessory arteries, venous anomalies, and ureteral anomalies? | Both CT and MRI found 5/6 accessory arteries and all 3 venous anomalies. | Positive, 2 |
| | Neville *et al*., 2008 (58) | 53 | Does 1.5-T MRI have similar outcomes as selective angiography in identifying accessory arteries in the same patients? | MRI detected 7/11 accessory arteries while selective angiography detected 6/7. | Negative, 2 |
| 10 | Kim *et al*., 2007 (59) | 40 | Does 1.5-T MRI have similar outcomes as selective angiography for identifying accessory arteries in the same patients? | MRI detected all main renal arteries and both accessory arteries. | Positive, 3 |
| | Kramer *et al*., 2007 (60) | 14 | Does 1.5-T MRI have the ability to identify arterial and venous anatomy correctly? | MRI correctly identified 13/14 of the venous and 13/14 of the arterial anatomy. | Positive , 3 |
| | Schlunt *et al*., 2007 (64) | 70 | Does CT have the ability to detect arteries, veins, and ureters? | CT was 97%, 100% and 96% sensitive at detecting arteries, veins and ureters, respectively. | Positive, 2 |
| | Schlunt *et al*., 2006 (65) | 65 | Does four-phase CT scan have the ability to detect lumbar arteries? | Four-phase CT scan had 97% sensitivity for detecting lumbar vessels >3 mm. | Positive, 2 |
| | Bhatti *et al*., 2005 (57) | 31 | Does 1.5-T MRI and CT have similar abilities to identify accessory arteries and venous anomalies? | Both MRI (97%) and CT (100%) were successful at identifying veins, but MRI detected only 1/5 accessory arteries while CT detected all 5. | Negative, 2 |
| 15 | Kock *et al*., 2005 (61) | 42 | Does 1.5-T MRI and digital subtr-action angiography have similar abilities to identify accessory arteries in the same patients? | MRI found more accessory vessels than did digital subtraction angiography. | Positive, 2 |
| | Lewis *et al*., 2004 (66) | 40 | Does CT have the ability to find accessory arteries and venous anomalies? | CT was 97%, 100% and 96% sensitive at detecting arteries, veins and ureters, respectively. | Positive, 2 |
| | Abrahams *et al*., 2004 (71) | 300 | Is right-sided donor nephrectomy equivalent to left-sided? | Operating times were shorter for right-sided donor nephrectomy than left. Complications and graft survival was equivalent. | Positive, 2 |
| Population based | | | | | |
| | Davis *et al*., 2012 (72) | 5391 | UNOS database: does right-sided donor nephrectomy result in increased graft failure rates? | Right-sided nephrectomy had a small decrease in 90-day graft failure when compared to left (4.8 vs 5.7%), but had equivalent overall graft survival. | Positive, 2 |
| Retrospective | | | | | |
| | Roth *et al*., 2014 (68) | 223 | Does volume-based kidney selection have the ability to improve donor renal function after kidney donation? | GFR was not improved when comparing the volume screened group with the non-volume screened group, and was also not significantly improved when comparing those who gave a smaller kidney to those who gave a larger kidney. | Negative, 3 |
| 20 | Yakoubi *et al*., 2013 (67) | 140 | Is the volume of the retained kidney associated with donor GFR? | Preoperative GFR, age, and the volume of the retained kidney were all associated with donor GFR at 1-year. | Positive, 3 |

*Limited to the 20 most relevant articles.*
*CT scan was multi-detector (16 or 64) unless specified otherwise.*
*CT and MRI were performed with appropriate intravenous contrast agent with timing consistent with the angiographic phase of imaging.*

## VI. SURGICAL APPROACH

Numerous minimally invasive surgical approaches have been studied including laparoscopic, laparoscopic hand-assisted, and robotic. These approaches have been studied for both transperitoneal and retroperitoneal surgery. Over 25 articles comparing hand-assisted to pure laparoscopy were identified and generally demonstrated equivalence in clinically relevant outcomes.

One meta-analysis reported that hand-assisted nephrectomy had similar donor and recipient complications as pure laparoscopic nephrectomy, but improved WIT, operating time, and blood loss [92]. Three RCTs compared hand-assisted retroperitoneal to pure laparoscopic transperitoneal donor nephrectomy and found similar in-hospital costs, overall complication rates, quality of life, and graft outcomes [93–95]. WIT was shorter in the hand-assisted group.

A fourth RCT compared hand-assisted transperitoneal to pure laparoscopic transperitoneal donor nephrectomy and did not find any significant differences in measured outcomes, although the sample size was small [96]. WIT tended to be lower in the hand-assisted group. Numerous other retrospective studies showed equivalent outcomes between hand-assisted and pure laparoscopy [97–100].

Aside from the above-mentioned RCTs, only one prospective study evaluated the retroperitoneal approach showing favorable results [101]. Numerous other retroperitoneal studies generally found equivalent donor and recipient outcomes between the retroperitoneal and transperitoneal approaches [102–104].

There were no prospective studies evaluating robotic-assisted donor nephrectomy and retrospective studies showed mixed results. A population-based study of 4305 donors found robot-assisted nephrectomy to be associated with higher hospital charges ($48,639 vs $37,019) [105]. Few studies had control groups, but in general, studies assessing robotic assistance found equivalent blood loss, complications, length of stay, and graft function as pure laparoscopic donor nephrectomy [106–108].

### 1. SUMMARY OF RECOMMENDATIONS

1. The decision on whether to use a pure, hand-assisted, or robotic laparoscopic approach should be based on the experience and training of the surgeon and operating theatre team (Grade B).
2. The decision on whether to use a transperitoneal or retroperitoneal approach should be based on the experience and training of the surgeon and operating theatre team (Grade B).

### 2. FURTHER RESEARCH

1. Further studies should evaluate the additional cost of the robot-assisted approach.

### 3. EVIDENCE TABLE, *Studies evaluating hand or robotic assistance*

| Study type | First author, year, reference | n | Study question | Critical findings | Rating of evidence |
|---|---|---|---|---|---|
| Meta-analyses and systemic reviews | | | | | |
| 1 | Kokkinos *et al*., 2007 (92) | 276 | Does hand-assisted laparoscopic donor nephrectomy compare favourably to pure laparoscopic donor nephrectomy? | Hand-assisted surgery had similar donor and recipient complications, but improved WIT, operating time, and blood loss. | Positive, 2 |
| RCTs | | | | | |
| | Klop *et al*., 2014 (93) | 40 | Does hand-assisted retroperitoneal laparoscopic donor nephrectomy compare favourably to transperitoneal pure laparoscopic donor nephrectomy for right-sided donations? | Quality of life, complication rate, pain, and hospital stay were the same between the groups, while WIT was shorter and EBL was greater for the hand-assisted retroperitoneal group. | Positive, 2 |
| | Dols *et al*., 2014 (94) | 190 | Does hand-assisted retroperitoneal laparoscopic donor nephrectomy compare favourably to transperitoneal pure laparoscopic donor nephrectomy? | Length of stay, postoperative complications, quality of life and graft complications did not differ between the groups, while the hand-assisted retroperitoneal group had shorter WIT and operating time, and fewer intraoperative complications. | Positive, 1 |
| | Klop *et al*., 2013 (95) | 186 | Is hand-assisted retroperitoneal laparoscopic donor nephrectomy cost effective compared to transperitoneal pure laparoscopic donor nephrectomy? | The in-hospital costs were equivalent between procedures with $8935 for the hand-assisted retroperitoneal approach and $8650 for the laparoscopic approach. | Positive, 1 |

***Studies evaluating Hand or robotic assistance (ctd)***

| | | | | | |
|---|---|---|---|---|---|
| 5 | Bargman *et al*., 2006 (96) | 40 | Does hand-assisted laparoscopic donor nephrectomy compare favourably to pure laparoscopic donor nephrectomy? | Complications, graft function, and quality of life were equivalent, while WIT and blood loss tended to be lower in the hand-assisted group. Postoperative analgesic requirements tended to be higher in the hand-assisted group. | Positive, 2 |
| Prospective | | | | | |
| | Wadström *et al*., 2005(101) | 75 | Were outcomes acceptable when using a hand-assisted retroperitoneal laparoscopic nephrectomy approach for consecutive donors? | EBL, complications, and graft function were similar to published studies of laparoscopic kidney donation. | Positive, 3 |
| Population based | | | | | |
| | Monn *et al*., 2013 (105) | 4305 | Does robot-assisted laparoscopic donor nephrectomy cost the same as laparoscopic donor nephrectomy? | Robot-assisted cases cost more than pure laparoscopic cases ($48,639 vs $37,019) and had longer hospital stays. Complications were similar between groups. | Negative 3 |
| Retrospective | | | | | |
| | Lucas *et al*., 2013 (97) | 153 | Does hand-assisted laparoscopic donor nephrectomy compare favourably to pure laparoscopic donor nephrectomy? | Complications and graft outcomes were the same between the groups, but WIT and operating time were shorter for the hand-assisted group. | Positive, 3 |
| | Hotta *el al*., 2013 (102) | 404 | Does retroperitoneal laparoscopic donor nephrectomy compare favourably to hand-assisted transperitoneal laparoscopic donor nephrectomy? | Complications, delayed graft function, and graft survival did not differ between the groups. Blood loss was less in the retroperitoneal group and WIT was less in the hand-assisted transperitoneal group. | Positive, 3 |
| 10 | Cohen *et al*., 2013 (106) | 120 | Does robot-assisted laparoscopic donor nephrectomy compare favourably to pure laparoscopic donor nephrectomy? | Quality and safety metrics did not differ between the groups | Positive, 3 |
| | Akin *et al*., 2012 (103) | 351 | Does hand-assisted retroperitoneal laparoscopic donor nephrectomy compare favourably to hand-assisted transperitoneal laparoscopic donor nephrectomy for right-sided donations? | Both groups had similar rates of complications, length of stay, and graft function | Positive, 3 |
| | Hubert *et al*., 2011 (107) | 100 | Is robot-assisted laparoscopic donor nephrectomy safe and effective? | Complications and graft function were similar to studies published for the pure laparoscopic group. | Positive, 3 |
| | Troppmann *et al*., 2010 (104) | 90 | Does retroperitoneal laparoscopic donor nephrectomy compare favourably to transperitoneal laparoscopic donor nephrectomy? | Both groups had similar rates of complications, WIT, and graft function. | Positive, 3 |
| | Kocak *et al*., 2007 (100) | 800 | Does hand-assisted laparoscopic donor nephrectomy compare favourably to pure laparoscopic donor nephrectomy? | Complications and graft function were similar between groups, but conversion rates and length of stay were improved with the hand-assisted approach | Positive, 3 |
| 15 | Gorodner *et al*., 2009 (108) | 209 | Were outcomes acceptable when using robot-assisted laparoscopic donor nephrectomy for complex vascular anatomy? | EBL, complications, length of stay and graft function were equivalent between normal and complex vascular anatomy. The WIT was slightly shorter in the normal vascular anatomy group. | Positive, 3 |

*Limited to the 15 most relevant articles.*

*EBL, estimated blood loss.*

## VII. SURGICAL TECHNIQUE

The most focused upon area within the category of surgical technique was pain management with three RCTs related to this topic. There was also a meta-analysis and an RCT assessing the effect of ureteral stents on stricture rates. Another RCT was related to positive pressure insufflation. Other areas such as WIT and hilar control techniques have rarely been studied in the past decade.

Two of the RCTs studied transversus abdominis plane blocks and found decreased pain in the short-term, long-term, or both [109,110]. A retrospective study also found continuous infusion of local anaesthetic to the retroperitoneal cavity and the pre-rectus abdominis space resulted in improved pain scores and morphine equivalents [111]. Another RCT looked at continuous intravenous infusion of ketorolac and found pain scores from 16 to 24 h were significantly lower or nearing significance for the ketorolac group and that time to ambulation was shorter. Urine output and haemoglobin scores were lower in the ketorolac group but this was felt to be clinically insignificant [112].

Maintaining a low insufflation pressure during laparoscopic kidney donation generally resulted in improved outcomes. One RCT found that 7 mm Hg versus 14 mm Hg resulted in increased urine output and lower overall, deep, and referred pain scores. However, lower pressures also resulted in increased operating theatre times [113]. A prospective study of positive pressure insufflation found that cardiac stroke volume was decreased at a pressure of 20 mm Hg but not at a pressure of 12 mm Hg. However, the long-term affects of this are unknown [114].

Both ureteral stents and preservation of the gonadal vein with the kidney specimen were studied with mixed results on recipient ureteral stricture rates. In a meta-analysis of five RCTs, the odds of ureteral complications associated with stent placement was only 0.24 when compared to no stent [115]. In contrast, a separate RCT showed no patients in the stented or non-stented groups developed a stricture at a median of 10 months. Urinary tract infection rates were higher in the stented group [116]. Two retrospective studies looking at gonadal vein preservation with the specimen did not find an improvement in stricture rates [117,118].

A prospective and retrospective study looked at WIT and graft function and did not find any association with the majority of WITs being <10 min [119,120]. A retrospective study with longer WITs found worse graft function for total WIT >45min (harvest and transplantation) [121].

Several studies evaluated the safety of polymer-locking clips, with mixed results. Retrospective studies of >2000 kidney donors found no vascular accidents while using polymer-locking clips to secure the renal artery or arteries [122,123]. However, a report on securing the renal hilum during laparoscopic kidney donation in the Manufacturer and User Facility Device Experience database (MAUDE) found that both deaths reported were in the locking clip group. The estimated failure rate was 1.7% for locking clips, 4.9% for titanium clips, and 3% for staplers [124].

A second report based on survey results of members of the American Society of Transplant Surgeons found that clips were associated with the greatest risk of vascular complications after donor nephrectomy [125]. At least six deaths worldwide have been attributed to polymer-locking clips, with ≤2 clips being used in each case [126]. The manufacture of the the Weck Hem-o-Lok clip (Teleflex) specifically lists donor nephrectomy as a contraindication for living donor nephrectomy [127], which has been supported by UNOS. Mortality rates from clips are low and they are preventable. However, clip failure is an event with a high risk of death. Therefore, polymer-locking clips should be avoided or used in a manner that eliminates any risks of failure such as using multiple clips on the aortic side of the artery (with a cuff of arterial wall distal to the clip), or used in addition to the Endo TA stapler.

Finally, two retrospective studies investigated whether heparinisation improved graft outcomes. Both concluded that heparinisation did not result in improved graft outcomes, and therefore it was safe to omit during laparoscopic kidney donation [128]. Mannitol has been used to limit kidney injury during warm ischaemia, although no comparative studies have been found. A survey of 17 high-volume urology centres performing donor nephrectomy found that 65% used mannitol [129]. Similarly, no human studies assessing the effects of periarterial papaverine in donor nephrectomy have been found. Ensuring adequate urine output form the divided ureter is a common practice prior to ligating the artery, but the effect of this practice has not been well studied.

### 1. SUMMARY OF RECOMMENDATIONS

1. The use of a local anaesthetic injection (surgeon or anaesthetist) should be considered superior to not using a local injection (Grade B).
2. Lower insufflation pressures (<14 mm Hg) should be considered superior to higher pressures (Grade B).
3. Polymer-locking clips are contraindicated for donor nephrectomy by the manufacturer and should not be used without disclosure to the donor and additional techniques to eliminate the risk of clip migration off the artery.

### 2. FURTHER RESEARCH

1. What are the optimal local anaesthetic and postoperative pain regimens?
2. Does insufflation pressure affect long-term graft survival?
3. Does mannitol affect long-term graft survival?

**3. EVIDENCE TABLE,** ***Studies looking at technical modifications to improve graft survival and patient's outcome***

| Study type | First author, year, reference | n | Research question | Critical findings | Rating of evidence |
|---|---|---|---|---|---|
| Meta-analysis | | | | | |
| | Mangus *et al*., 2013 (115) | 796 | Does stenting of extravesical ureteroneocystostomy during recipient transplantation lead to decreased complications? | The odds ratio for ureteral complications was less in stented patients in both the RCTs (odds: 0.24) and the case-series groups (odds: 0.58). | Positive, 1 |
| RCTs | | | | | |
| | Warlé *et al*., 2013 (113) | 20 | Does low insufflation pressure (7 mm Hg) vs. standard (14 mm Hg) result in decreased pain scores postoperatively? | Lower pressures resulted in increased urine output and lower overall, deep, and referred pain scores. Lower pressures also resulted in increased operating theatre times. | Positive, 2 |
| | Parikh *et al*., 2013 (109) | 60 | Do ultrasound-guided TAP blocks improve pain in retroperitoneal laparoscopic donor nephrectomy? | The TAP group had lower pain scores, longer duration till first pain medication, and lower total pain medication consumption in the first 24 h. | Positive, 1 |
| | Hosgood *et al*., 2013 (110) | 46 | Do ultrasound-guided TAP blocks improve pain in laparoscopic donor nephrectomy? | Pain scores in the TAP group were lower in the first 2, but not the 3rd postoperative day. Morphine equivalents were lower in the TAP group at 6 h, but were equivalent for overall hospitalisation. | Positive, 1 |
| 5 | Grimsby *et al*., 2012 (112) | 111 | Does continuous infusion of ketorolac safely improve pain in laparoscopic donor nephrectomy? | Pain scores from 16–24 h were significantly lower or nearing significance for the ketorolac group although morphine equivalents at 24 h and discharge did not differ. Time to ambulation was shorter in the ketorolac group. Urine output and haemoglobin were lower and creatinine tended to be higher in the ketorolac group. | Positive, 1 |
| | Osman *et al*., 2005 (116) | 100 | Do ureteral stents reduce the incidence of ureteral stricture during transplantation of a live donor kidney? | Ureteral stent placement was not associated with ureteral strictures or vesicoureteral leaks, but was positively associated with urinary tract infections. | Negative, 2 |
| Prospective | | | | | |
| | Mertens Zur Borg *et al*., 2004 (114) | 22 | Does positive pressure insufflation affect haemodynamic responses? | Stroke volume was decreased at a pressure of 20 mm Hg but not at a pressure of 12 mm Hg. | Positive, 2 |
| | Simforoosh *et al*., 2006 (119) | 100 | Is WIT associated with graft outcome? | Categorical WIT (4–6, 6–10, >10 min) was not associated with delayed graft function, graft loss, median serum creatinine). | Negative, 2 |
| Retrospective | | | | | |
| | Biglarnia *et al*., 2011 (111) | 100 | Does continuous infusion of local anaesthetics into the retroperitoneal cavity and the pre-rectus abdoninus space result in improved pain scores? | Those with continuous infusion had lower morphine equivalent usage, shorter stay in the postoperative area, less nausea, and a shorter length of stay. | Positive, 3 |
| 10 | Friedersdorff *et al*., 2011 (128) | 119 | Does systemic heparinisation lead to decreased postoperative graft complications? | Overall 1-year graft survival rate was 97% and no different between the groups. | Negative, 3 |
| | Kocak *et al*., 2010 (117) | 800 | Does laparoscopic kidney dona- tion with a technique that does not preserve the gonadal vein with the specimen lead to acceptable ureteral stricture rates? | There was only 1 ureteral stricture found in the recipients. | Positive, 3 |
| | Hsi *et al*., 2009 (124) | 92 | Are locking-polymer clips free from adverse events for securing the renal hilum during nephrectomy in the FDA database? | The estimated failure rate was 1.7% for locking clips, 4.9% for titanium clips, and 3% for staplers. Only 2 deaths were reported and both were in the locking clip group. | Negative, 3 |

*Studies looking at technical modifications to improve graft survival and patient's outcome (ctd)*

| | | | | | |
|---|---|---|---|---|---|
| | Ponsky *et al*., 2008 (122) | 1695 | Are locking-polymer clips free from adverse events for securing the renal hilum during nephrectomy? | Not a single clip failed to control the renal artery. | Positive, 3 |
| | Simforoosh *et al*., 2006 (123) | 341 | Are locking-polymer clips free from adverse events for securing the renal hilum during nephrectomy? | No vascular accidents occurred. | Positive, 3 |
| 15 | Soulsby *et al*., 2005 (120) | 52 | Is WIT associated with graft outcome? | Categorical WIT (<3, >3 or 0–5, 5–10, >10 min) was not associated with short or long-term graft outcome. | Negative, 3 |

*Limited to the 15 most relevant articles.*
*TAP, transversus abdominis plane.*

## VIII. FUTURE PERSPECTIVES

Sixty articles were located related to laparoendoscopic single-site surgery (LESS), natural orifice transluminal endoscopic surgery (NOTES), or techniques to increase the supply of kidney donors. Two RCTs, a prospective study, and two matched prospective studies evaluated the safety and results of LESS. Both RCTs found some improvement in pain scores or time to full recovery for the LESS group, while reporting similar complications, operative results, and graft outcomes [130,131]. The prospective study reported that LESS is safe and feasible [132].

All three retrospective matched studies showed positive results for LESS. One study showed that obese donors had similar outcomes to non-obese donors during LESS [133]. Another study showed increased operating theatre time, but improved patient-reported time to complete recovery [134]. The final matched study showed operating time and WIT were longer, but graft function was similar and patient-reported convalescence was faster in the LESS group [135].

In a survey of 49 previous laparoscopic kidney donors (mean age 51 years), 51% said they would consider NOTES if they could be reassured it was as safe as conventional laparoscopy. Ninety percent said they were not unhappy with their scars after their previous surgery and 33% had fears of NOTES negatively affecting their sexual function [136]. One prospective study and one matched retrospective study reported positive outcomes for transvaginal extraction (NOTES) after laparoscopic kidney donation. The prospective study reported that pain scores and return to normal activities were improved in NOTES. However, 19% of attempted NOTES procedures were converted to transabominal procedure [137]. The matched retrospective study showed that WIT was longer in NOTES but that other outcomes including graft function were similar after short-term follow-up [138].

Over 25 articles were identified that looked at ways to increase the supply of live kidney donation with an emphasis on kidney paired donation, educational programmes, donor incentives, and the use of kidneys removed for small renal masses. One RCT investigated a structured educational programme for recipients and did not find a significant increase in live donation [139]. Multiple small retrospective studies of kidney donation after removal of a small enhancing renal mass from the donated kidney demonstrated positive outcomes without tumor recurrence up to 10 years [140,141]. There was local recurrence of transitional cell carcinoma in the ureter of a donated kidney [140].

Several studies have reported favourable outcomes with kidney paired donation, which is of particular interest when a patient has a willing but incompatible donor [142,143]. The OPTN operates a national kidney paired donation system in the US [144]. Kidney paired donation has been estimated to significantly shorten the waiting time for kidney waiting list candidates [145].

### 1. SUMMARY OF RECOMMENDATIONS

1. LESS donor nephrectomy has similar outcomes to conventional laparoscopic nephrectomy in experienced hands and may result in improved pain scores or return to full activities (Grade B).
2. National kidney paired donation programs should be encouraged as a means to increase the supply of available donors (Grade C).

**2. EVIDENCE TABLE,** ***Study using LESS technique or measure to improve patient's outcome***

| Study type | First author, year, reference | n | Research question | Critical findings | Rating of evidence |
|---|---|---|---|---|---|
| RCTs | | | | | |
| | Richstone *et al*., 2013 (130) | 29 | Does LESS result in improved pain scores compared to conventional laparoscopy? | LESS resulted in improved pain scores on postoperative day 1, but not day 0. Operative time, EBL, length of stay, WIT, and graft function were similar between the groups. 2/15 patients were converted from LESS to conventional surgery. | Positive, 2 |
| | Lee *et al*., 2013 (131) | 100 | Does LESS result in improved recovery compared to conventional laparoscopy? | Operative time, EBL, length of stay, and graft survival were similar between the groups. Overall satisfaction was the same between the groups but more LESS patients said they were fully recovered at 2 months (97% vs. 80%). | Positive, 2 |
| | Barnieh *et al*., 2011 (139) | 100 | Does a structured educational session with ESRD patients increase the likelihood of living donation? | Two in the control group and 4 in the education group had a potential donor contact the transplant programme. | Negative, 2 |
| Prospective | | | | | |
| | Gimenez *et al*., 2011 (132) | 40 | Is LESS safe for kidney donation? No comparison group provided. | The procedure was safe with WIT 4 min and length of stay 1.8 days. Two were converted to hand-assist laparoscopic surgery. | Positive, 3 |
| 5 | Kishore *et al*., 2013 (137) | 67 | Is transvaginal extraction (NOTES) during conventional laparoscopic kidney donation safe and feasible compared to a transabdominal approach? | 30/37 attempted transvaginal extractions were successful. There were no differences in WIT, EBL, length of stay, complications or graft function. Pain scores and return to normal activities were improved in the transvaginal approach. | Positive, 2 |
| Retrospective | | | | | |
| | Afaneh *et al*., 2012 (133) | 64 | Does LESS in obese patients result in similar perioperative donor outcomes and recipient graft function as LESS in non-obese patients in a matched cohort? | Operative time was longer for the LESS group while EBL, length of stay, and graft survival were similar between groups. | Positive, 3 |
| | Yoshihide *et al*., 2012 | 5 | Are kidneys after nephrectomy for small renal cell carcinoma safe to use for transplantation? | There was no cancer recurrence in the recipients. | Positive, 2 |
| | Afaneh *et al*., 2011 (134) | 100 | Does LESS result in improved recovery compared to conventional laparoscopic in a matched cohort? | Operative time was longer for the LESS group while EBL, length of stay, and graft survival were similar between groups. Patient reported time to complete recovery was improved with LESS. | Positive, 3 |
| | Alcaraz *et al*., 2011 (138) | 60 | Is transvaginal extraction (NOTES) during conventional laparoscopic kidney donation safe and feasible compared to a transabdominal approach in a matched comparison? | There was no difference in EBL, operating theatre time, length of stay, complications or graft function. WIT was longer in the NOTES group (5 vs 2.6 min). | Positive, 3 |
| 10 | Canes *et al*., 2010 (135) | 35 | Does LESS result in improved recovery compared to conventional laparoscopic in a matched cohort? | WIT was longer for the LESS group while EBL, length of stay, and graft survival were similar between groups. Patient-reported convalescence was faster in the LESS group. | Positive, 3 |

*Limited to the 10 most relevant articles.*

## IX. CONCLUSION

The laparoscopic approach has become the gold standard for living kidney donations and represents >92% of all living kidney donations in the US [146]. Safety for those willing to donate should be the top priority of future research with a goal to decrease the estimated perioperative mortality (3.1 per 10,000 cases) to zero. Long-term rates of ESRD were higher in kidney donors when compared to healthy matched controls but lower than in the general population. Research to define the risk of ESRD in extended criteria risk donors is important for obtaining appropriate informed consent moving forward.

Imaging efforts to prepare for surgery and identify the healthiest kidney to leave with the donor should at the same time minimise the risk of ionising radiation and long-term malignancies in donors. Operative technique should above all safely secure the renal hilum to eliminate future donor deaths. New techniques such as LESS and local anaesthetic adjuvants offer promising advances in postoperative care and recovery. Finally, kidney paired donation programmes and other efforts to increase the supply of living donors should continue with the knowledge that living kidney donation provides the best solution for the thousands of people currently on a kidney waiting list.

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# G. LAPAROSCOPIC AND ROBOTIC ADRENALECTOMY

## I. INTRODUCTION

Adrenal tumors are common entities, with incidentalomas found in 3.4–7% of patients in imaging studies [1]. After appropriate imaging and endocrine workup, most functional adrenal masses, those measuring >4 cm, and those with radiographic features of concern, are candidates for surgical resection. Recently published guidelines from the American Association of Clinical Endocrinologists and the American Association of Endocrine Surgeons [2] include recommendations for diagnostic workup of adrenal lesions that is beyond the scope of the present guidelines. We sought to grade the evidence supporting the role of minimally invasive adrenalectomy for treatment of adrenal pathology and develop guidelines for its use.

## II. DATA ACQUISITION

This review was based on a systematic literature search in Medline and Embase from January 2004 to January 2014. The primary search terms used were ("adrenal" OR "adrenalectomy" AND ("laparoscopic" or "robotic" or "minimally-invasive". All fields including MeSH terms were searched. The search was limited to human subjects and the English language. Additional searches were done in the Web of Science and the Cochrane Library with a focus on systematic reviews, meta-analyses and randomised trials. Abstracts from major urological meetings were reviewed from the previous 3 years. Guideline statements from the Society of American Gastrointestinal and Endoscopic Surgeons [3], American Association of Clinical Endocrinologists and American Association of Endocrine Surgeons [2] were also reviewed. Studies were assessed for level of evidence [1–4] and recommendations were graded (A–D) according to a modified verison of the Oxford system. [4]

## III. LAPAROSCOPIC ADRENALECTOMY

Laparoscopic adrenalectomy was initially described by Gagner *et al*. in 1992 [5]. Since its introduction, it has become the gold standard for surgical treatment of benign adrenal neoplasms and is increasingly used for malignant tumours [6–9]. Multiple retrospective and prospective series have demonstrated decreased pain, lower blood loss, faster convalescence, less ileus, and shorter hospital stays for laparoscopic adrenalectomy [7, 10–17]. Regardless of underlying pathology, the best outcomes for adrenalectomy are associated with high-volume surgeons [18]. Although most studies have focused on outcomes in adults, recent literature also supports safety and feasibility of a laparoscopic approach in children [19, 20].

Several studies have analysed the role of laparoscopy for specific adrenal tumours. In patients with symptomatic primary hyperaldosteronism, laparoscopic adrenalectomy is associated with few postoperative complications, shorter hospital stay, and equivalent improvement of hypertension and hypokalemia compared to patients treated with an open approach [10, 21]. Similarly, resection of pheochromocytomas, which is thought to be more difficult due to catecholamine release during manipulation, and increased vascularity, is aided by a laparoscopic approach.

Compared to open surgery, laparoscopy is associated with less blood loss [22–25] and shorter length of stay (LOS) [14, 22, 23, 26–28]. Additionally, episodes of intraoperative hypertension or hypotension are less [23, 28] or similar during laparoscopic procedures. **Table 1** summarises the results of studies comparing laparoscopic and open approaches for benign tumours.

### 1. Recommendations

- Laparoscopic surgery should be considered as first-line therapy for benign renal masses requiring surgical resection [Grade or recommendation (GR) B]
- Laparoscopic surgery should be considered as first-line therapy for patients with pheochromocytoma (GR B)
- The use of laparoscopy for adrenocortical carcinoma (ACC) is debated. Although no prospective comparative series have been reported, retrospective series have reported increased peritoneal carcinomatosis, positive margins, and local recurrence rates for laparoscopic compared to open surgery [29–33]. Conversely, in a matched comparison of laparoscopic and open adrenalectomy for ACC <10 cm, no difference in cancer-specific survival, tumour capsule violation, or carcinomatosis was noted [34]. Although a laparoscopic approach may be feasible for select cases of ACC without adjacent organ invasion, an open surgical approach remains the gold standard.

### 2. Recommendation

For cases of known or suspected ACC, open surgical resection should be performed (GR C)

Laparoscopic resection of large adrenal masses is not well studied, due to inconsistency about what size constitutes a large mass, and a dearth of studies addressing this question. It is well established,

***Table 1. Comparison of laparoscopic and open adrenalectomy studies***

| Study type | No. of patients | First author, year | Critical findings | Rating of evidence |
|---|---|---|---|---|
| Retrospective | | | | |
| | 108 | Lang, 2008 | Laparoscopic surgery has less EBL, and shorter LOS and operating time than open surgery | Positive, 3 |
| | 100 | Thompson, 1997 | Laparoscopic surgery has shorter LOS and lower morbidity, but increased operating time than open surgery | Positive, 3 |
| | 66 | Brunt, 1996 | Laparoscopic surgery has less EBL, shorter LOS, but longer operating time than open surgery. | Positive, 3 |
| | 669 | Lee, 2008 | Laparoscopic surgery has less EBL, and shorter LOS and operating time than open surgery | Positive, 3 |
| | 172 | Barreca, 2003 | Laparoscopic surgery has shorter LOS but similar EBL and operating time compared to open surgery | Positive, 3 |
| | 486 | Kwan, 2007 | Laparoscopic surgery has less EBL, shorter LOS and similar operating time compared to open surgery | Positive, 3 |
| | 80 | Chotirosnramit, 2007 | Laparoscopic surgery has less EBL, shorter LOS and longer operating time compared to open surgery | Positive, 3 |
| | 67 | Wu, 2006 | Laparoscopic surgery has less EBL, shorter LOS and similar operating time compared to open surgery | Positive, 3 |
| | 70 | Hallfeldt, 2003 | Laparoscopic surgery has less EBL, shorter LOS and longer operating time compared to open surgery | Positive, 3 |
| | 54 | Tanaka, 2000 | Laparoscopic surgery has shorter LOS and similar EBL and operating time compared to open surgery | Positive, 3 |
| | 80 | Imai, 1999 | Laparoscopic surgery has less EBL, shorter LOS and similar operating time compared to open surgery | Positive, 3 |
| | 80 | Shen, 1999 | Laparoscopic surgery has less morbidity compared to open surgery | Positive, 3 |

*EBL, estimated blood loss*

however, that size is correlated with risk of ACC. Using a size cut-off of 4 cm, the sensitivity for ACC is 93%, although the specificity is only 42% [35]. As previously described, tumours with preoperative concern for ACC are safely resected by an open approach. For benign tumours, however, most studies have described similar outcomes across size ranges, with similar morbidity [27, 36, 37]. However, resection of adrenal masses >8 cm is associated with longer operating time, increased blood loss, and longer hospital stay [37]. Moreover, larger tumours may be associated with a higher risk of open conversion [38]. For larger tumours found to be locally invasive, most authors recommend open conversion [39, 40]

**Recommendation**

Large adrenal tumours without preoperative or intraoperative concern for ACC may be safely resected via a laparoscopic approach; however, open conversion is warranted if ACC is suspected (GR C).

## IV. LAPAROSCOPIC SURGICAL APPROACHES

Multiple surgical approaches have been described to access the adrenal gland, but the two most common approaches are lateral transabdominal adrenalectomy (LTA) and posterior retroperitoneoscopic adrenalectomy (PRA). Less common approaches include anterior transabdominal adrenalectomy and lateral retroperitoneoscopic adrenalectomy.

### 1. LATERAL TRANSABDOMINAL ADRENALECTOMY (LTA)

LTA is the most common transperitoneal approach. This approach allows greater working space than the retroperitoneal approach, which can be beneficial for larger tumours and obese patients [41]. The patient is placed in the flank position with the side of the tumour facing up, allowing gravity to retract the abdominal contents medially. Ports are placed to allow triangulation to the adrenal gland of interest. Left-sided tumours often require three ports, while right-sided tumours require an additional port for liver retraction.

### 2. POSTERIOR RETROPERITONEOSCOPIC ADRENALECTOMY (PRA)

PRA is the most common retroperitoneal approach [42]. This approach allows one to avoid entering the peritoneal cavity, which may be beneficial in patients with prior abdominal surgery. However, there is often less working room and anatomical landmarks may be unfamiliar compared to the transperitoneal view. Access to the retroperitoneum is gained inferolateral to the tip of the 12th rib by perforation of the dorsal lumbar fascia, placing a balloon trocar and inflating the retroperitoneal space.

A systematic review and meta-analysis comparing LTA and PRA found no difference in operating time, blood loss, time to ambulation, oral intake, or complication rate among techniques, with equivocal findings for LOS and convalescence time [43]. A more recent meta-analysis found no difference in any perioperative outcome, including operating time, blood loss, LOS, time to oral intake, overall and major morbidity, and mortality [44].

**Recommendation**

Both transperitoneal and retroperitoneal approaches to laparoscopic adrenalectomy are safe. The approach should be chosen based on surgeon training and experience (GR A).

### 3. LAPAROENDOSCOPIC SINGLE-SITE SURGERY

Laparoendoscopic single-site surgery (LESS), single-incision laparoscopic surgery, or single-port laparoscopic surgery is a laparoscopic procedure performed through a single multi-channel port rather than separate ports. Compared to traditional laparoscopy, LESS may be more challenging to perform because of loss of instrument triangulation [45]. Several case–control studies have demonstrated similar outcomes for LESS and traditional laparoscopic techniques when performed by experienced surgeons [46]. A systematic review and meta-analysis of LESS versus conventional adrenalectomy, comprised entirely of retrospective studies, showed no difference in blood loss, time to oral intake resumption, or LOS [47]. There were no differences in the perceived advantages of LESS, including cosmesis, recovery time, or port-related complications.

**Recommendation**

LESS adrenalectomy should be considered an experimental procedure that requires further study (GR C).

## V. ROBOTIC ADRENALECTOMY

Robotic surgery is increasingly utilised as an alternative to laparoscopic surgery. Several feasibility studies have demonstrated the safety and feasibility of robotic adrenalectomy [48–54]. The perceived advantages of robotic over traditional laparoscopy include stereoscopic vision, improved magnification, and greater range of motion [55]. A recent systematic review and meta-analysis, including one randomised clinical trial and eight observational studies, demonstrated lower blood loss and shorter hospital stay in robotic cases, and similar operating times, conversion rates, and complication rates. Both transperitoneal and retroperitoneal robotic approaches have been described, but no comparative series have been reported.

**Recommendation**

Robotic adrenalectomy may be considered an alternative to laparoscopic adrenalectomy but requires further study (GR B).

## VI. SUMMARY OF RECOMMENDATIONS

1. Laparoscopic surgery should be considered as first-line therapy for benign renal masses requiring surgical resection (GR B)
2. Laparoscopic surgery should be considered as first-line therapy for patients with pheochromocytoma (GR B)
3. For cases of known or suspected ACC, open surgical resection should be performed (GR C)
4. Large adrenal tumours without preoperative or intraoperative concern for ACC may be safely resected via a laparoscopic approach; however, open conversion is warranted if ACC is suspected (GR C).
5. Both transperitoneal and retroperitoneal approaches to laparoscopic adrenalectomy are safe. The approach should be chosen based on surgeon training and experience (GR A).
6. LESS adrenalectomy should be considered an experimental procedure that requires further study (GR C)
7. Robotic adrenalectomy may be considered an alternative to laparoscopic adrenalectomy but requires further study (GR B)

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## Committee 5

# Nephron-sparing Surgery

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*I. Gill (USA)*

*A. Mottrie (Belgium)*

### Members

*S. Campbell (USA)*

*B. Challacombe (United Kingdom)*

*V. Ficarra (Italy)*

*R. Houston-Thomson (USA)*

*A. Minervini (Italy)*

*G. Novara (Italy)*

*P. Russo (USA)*

*R. Uzzo (USA)*

*H. Van Poppel (Belgium)*

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# Nephron-sparing Surgery

*I. Gill, A. Mottrie*

*S. Campbell, B. Challacombe, V. Ficarra, R. Houston-Thomson, A. Minervini, G. Novara, P. Russo, R. Uzzo, H. Van Poppel*

## A. EMERGING EVIDENCE OF DECREASING KIDNEY CANCER MORTALITY

### I. INTRODUCTION

Kidney cancer incidence rates have significantly risen in the US and in many countries across the world [1,2]. This trend is likely due to widespread axial imaging, leading to increased diagnosis of incidental kidney cancers, and from increasing incidence of obesity, which might have an aetiological role [3,4]. Earlier reports suggested that overall kidney cancer mortality rates have continued to rise despite an increase in kidney cancer surgery. More contemporary reports, however, indicate that kidney cancer mortality has now begun to decrease, both in the US and Europe [1,5]. However, it is unclear whether this decrease is due to improved treatment of localised or advanced cancers, because the benefits from curative treatments for localised kidney cancers, and innovations in the treatment of advanced cancers (through surgery and targeted systemic therapies) may contribute towards the decrease in population mortality from kidney cancer. Analysis of the Surveillance, Epidemiology, and End Results (SEER) dataset provides contemporary data on kidney cancer incidence, mortality and survival trends in the US between 1988 and2010.

#### 1. INCIDENCE

From 1988 to 2008, kidney cancer incidence increased from 11.6 cases to a peak of 18.4 cases per 100,000. Although the incidence decreased somewhat between 2008 and 2010, overall from 1988 to 2010, the annual percent change (APC) in incidence rate increased significantly (+2.46; P<0.0001). According to American Joint Committee on Cancer (AJCC) stage, age-adjusted incidence of stage I kidney cancers increased from 4.3 to 10.4 cases per 100,000 from 1988 to 2010 (APC +5.35; P<0.0001). Stage II cancers increased modestly from 1.2 to 1.4 cases per 100,000 (APC

+1.43; P<0.0001) and stage III cancers were unchanged at 2.4 cases per 100,000 (APC +0.26; P=0.26). Stage IV cancers decreased significantly from 2.6 to 2.2 cases per 100,000 (APC –0.58; P=0.01). Cancers of unknown stage also decreased from 1.2 to 0.7 cases per 100,000 (APC –2.98; P<0.0001).

#### 2. MORTALITY

Overall, kidney cancer mortality initially increased between 1988 and 1998 from 4.0 to 4.6 deaths per 100,000 (APC +1.61; P=0.02) and then

decreased between 1998 and 2010 from 4.6 to 3.6 deaths per 100,000 (APC –1.32; P=0.0006). Over the entire study period, mortality did not significantly change (APC –0.33; P=0.13). According to AJCC stage, mortality due to Stage I/II cancers, while accounting for only a minority of overall deaths, increased steadily over the study period (0.2 to 0.6 deaths per 100,000 for stage I cancers, APC +5.32; P<0.0001 and 0.1 to 0.3 deaths per 100,000 for stage II cancers, APC +4.40; P<0.0001). When considering the entire study period between 1998 and 2010, stage III cancer deaths remained unchanged from 0.6 to 0.7 deaths per 100,000 (APC +0.36; P=0.54); however, during the more recent period between 1994 and 2010, stage III cancer deaths decreased significantly from 0.9 to 0.7 deaths (APC –1.08; P=0.006). Stage IV cancers, which accounted for the majority of deaths, also did not change over the entire study period (1.9 to 1.8 deaths per 100,000; APC –0.45; P=0.10). However, during the more recent period between 1998 and 2010, stage IV cancer deaths decreased from 2.4 to 1.8 (APC –1.48; P=0.007). Deaths from cancers with unknown stage decreased significantly over the study period (1.3 to 0.3 deaths per 100,000, APC –6.47; P≤0.0001).

#### 3. CANCER-SPECIFIC SURVIVAL (CSS)

Overall 1-year and 5-year CSS for all years was 82.4% and 69.8%, respectively; median survival was not reached. According to AJCC stage, 5-year kidney CSS for all stages improved significantly from 62.7% in 1988 to 75.8% in 2005; the last study year with 5-year follow-up data (P<0.0001). CSS for stage I cancers remained unchanged from 93.9% to 94.5% (P=0.57). CSS was also unchanged for stage II cancers, from 82.6% to 87.2% (P=0.13). In contrast, survival improved significantly for more

advanced Stage III and IV cancers, at 63% to 73% (P=0.0007), and 7.9% to 12.8% (P=0.01), respectively. Survival worsened significantly for cancers of unknown stage from 61.6% to 52.1% [95% confidence interval (CI): 45.7–58.2%; P=0.08].

Over the past two decades, three notable trends have emerged in the US population-based kidney cancer landscape: (1) cancer incidence has increased significantly; driven almost exclusively by an increase in the diagnosis of localised stage I cancers and to a lesser extent by Stage II cancers, while Stage IV and unknown stage cancers have decreased; (2) cancer mortality decreased significantly after a peak of 4.6 deaths per 100,000 persons in 1998 to a low of 3.6 per 100,000 in 2010 (P=0.0006); and (3) 5-year CSS significantly improved overall from 62.7% to 75.8%, with by-stage improvements seen only for the more advanced stage III and IV cancers.

When taken in conjunction with the observed increases in kidney cancer treatment volumes during this same time period [6], these data suggest two things: (1) improved mortality rates are primarily a result of curative treatment-driven stage down-migration of kidney cancer in the US population towards stage I cancers, which have excellent survival; and (2) to a lesser extent, improvements in the quality-of-care and treatment outcomes for more advanced stage III and IV cancers.

Improvements in 5-year survival for the more advanced stage III/IV cancers pre-dated the 2005 introduction of multi-kinase inhibitors in the US, indicating that other factors contributed. This analysis indicates that for stage III cancers (including venous/nodal involvement) this trend first started around 2001,and for stage IV cancers (locally advanced/metastatic), this trend first started around 1997. The adoption of improved surgical techniques for excising caval tumour thrombi [7], immunotherapy for metastatic disease [8], or cytoreductive nephrectomy for metastatic disease [9] may have facilitated these trends. In a Swedish cohort of patients treated before and after the introduction of tyrosine kinase inhibitors, median overall survival among patients presenting with metastatic kidney cancer improved from 9.6 to 12.4 months, and was associated with a prescription for a tyrosine kinase inhibitor, prior nephrectomy, and female sex [10]. Improved stage IV treatments, while meaningful to individual patients, are less likely to affect overall population mortality, given that modest improvements in survival are on average <6 months [11].

A prior study evaluating US data up to 2002 indicated increasing kidney cancer mortality despite increased treatment rates. The authors concluded that small renal masses were being over-diagnosed and over-treated [12]. This more contemporary study, which updates data up to 2010, provides new evidence that treatment may indeed be starting to provide demonstrable benefit. The lag-time for population effects of treatments to become evident is likely due to the slow growth rate and low initial malignant potential of many kidney cancers. These findings support the continued treatment of kidney cancers, including small renal masses in appropriately selected patients. Although a small renal mass is highly unlikely to be metastatic at diagnosis, a sizable percentage (70–80%) of these small tumours will eventually increase in size [13] and potentially become more likely to metastasise; a process that is typically not predictable.

One important point to note is that this analysis included cancers of unknown stage. Excluding these unknown stage cases would artificially skew the results by not accurately representing overall population-based data. Incorporating these cases more accurately reflects kidney cancer incidence and mortality trends in the US population overall. Missing tumour size accounted for the majority of these unknown stage cases; notably, the survival outcomes of these unknown stage cancers were intermediate between those of stage III and IV cancers, suggesting that they primarily represent cancers that are more advanced at presentation.

## 4. CONCLUSION

Despite increased kidney cancer incidence, mortality has recently decreased and 5-year survival has improved. Kidney cancer treatments, including curative surgery for small cancers and, to a lesser extent, therapies for more advanced cancers, appear to be helping reduce cancer mortality.

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## II. SIGNIFICANCE OF CHRONIC KIDNEY DISEASE

Renal function is now recognised as a major concern for cancer survival for patients with localised renal cell carcinoma (RCC). Many such tumours have limited oncological potential and the greatest threat to long-term health may relate more to renal functional decline associated with the intervention rather than oncological sequelae. Several studies have shown that many patients with renal cancer have pre-existing chronic kidney disease (CKD), or will be at risk for *de novo* CKD after renal surgery; particularly if radical nephrectomy (RN) is performed [1–3]. In general, more profound levels of CKD are associated with progressively increased risk of morbid cardiovascular events and compromised survival, even after confounding factors such as diabetes and hypertension are taken into account [4,5]. Hence, there has been a strong consensus to preserve nephrons in an effort to avoid CKD and optimise renal function whenever reasonable, and this basic precept has been emphasised in the most recent American Urological Association (AUA) and European Association of Urology (EAU) guidelines [6,7]. In these documents, the primary focus is on small renal masses (clinical stage T1a), and most agree strongly with this precept in this setting, because RN would represent therapeutic overkill in most such cases.

Over the past 5–10 years multiple retrospective studies have studied this, suggesting an advantage for partial nephrectomy (PN) over RN, even for larger tumours (clinical stage T1b/T2a) [8–11]. A meta-analysis of such studies [12] has revealed an apparent advantage for PN in terms of better renal function (61% risk reduction for severe CKD) and improved overall survival (19% risk reduction in all-cause mortality). However, almost all studies in this analysis were retrospective and thus potentially affected by selection bias. This meta-analysis also demonstrated a 29% improvement in cancer-specific survival associated with PN, which can only be explained by selection bias, because it is highly unlikely that PN is a better oncological intervention than RN [13]. A recent study by Shuch and colleagues also strongly suggests that selection bias is an important contributor to the results of these studies [14]. These data should be viewed in light of the only randomised controlled study of PN versus RN, which targeted a patient population that would have been most likely to benefit from PN, namely, patients with relatively small renal tumours (<5.0 cm). This trial failed to demonstrate a survival advantage for PN, even though there was less CKD in this group [15]. Although there were some flaws in this trial, the results are provocative and suggest that the renal functional advantage related to PN may not be as beneficial as previously thought [13].

One way to reconcile these findings is to postulate that CKD primarily due to surgical removal of nephrons (CKD-S) may not have the same deleterious implications as CKD due to medical causes (CKD-M). In reality, most of the previous data about CKD were derived from population-based studies in which medical aetiology predominated, and some of the conclusions from these studies may not apply to patients with CKD-S [4,5,13]. One recent study explored this hypothesis, looking at ~4000 patients with renal cancer managed with surgery from a single academic centre [16]. Almost 1200 of these patients had CKD prior to surgery (CKD-M), >900 had CKD only after surgery (CKD-S), and another 2000 had no CKD even after surgery. For the group as a whole, survival was compromised in patients with an annual decline of renal function >4.0%. The annual decline of renal function after surgery was 4.7% in the CKD-M group, and only 0.7% in the CKD-S group, suggesting that renal function is much more stable in this setting. In addition, the overall survival of patients with CKD-S was substantially improved when compared to patients with CKD-M, and approximated that of patients with no CKD even after surgery **(Figure 1)**.

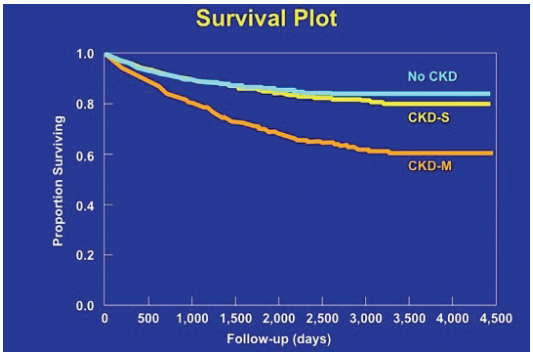


***Figure 1. Overall survival related to postsurgical CKD status and aetiology of CKD. Recent data suggest that the favourable outcomes in the CKD-S group are likely restricted to patients with new baseline eGFR >40 ml/min/1.73m2. Modified from Lane and colleagues (16), reprinted with permission of Journal of Urology, Elsevier B.V.***

However, these data have limitations because they did not control for the potential impact of comorbidity or new baseline glomerular filtration rate (GFR), and they did not include a control group of patients with pure CKD-M [16]. A follow-up study addressed all of these concerns in a comprehensive manner and confirmed that CKD-S is more stable and has less impact on overall survival than CKD-M; particularly if new baseline GFR is >40 ml/min/1.73m$^2$ [17].

The most recent guidelines for classification of CKD from our nephrology colleagues emphasise the importance of level of renal function (estimated GFR; eGFR), evidence of structural damage to the nephron (e.g. proteinuria), and aetiology of CKD as important factors for prognostic assessment of the risk of progressive decline of renal function. Of these parameters, the least studied is aetiology of CKD [18]. Recent studies in patients with renal cancer suggest that CKD primarily due to surgical removal of nephrons correlates with relatively low risk of progressive decline in renal function, and has less impact on overall survival than medical aetiology, as long as the new baseline eGFR is ≥40 ml/min/1.73m$^2$. Further studies with long-term follow-up are needed to refine our understanding of these important issues.

## RECOMMENDATIONS

1. Patients with small renal masses (clinical stage T1a), pre-existing CKD, or with an abnormal contralateral kidney (anatomically or functionally) should be managed with nephron-sparing approaches whenever feasible, to optimise new baseline GFR after intervention. Grade A (highly recommended); level of evidence: 2 (good quality prospective cohort studies about: (1) adverse outcomes related to degree of CKD; and (2) effects of PN versus RN on new baseline GFR).
2. Patients with larger renal masses and a normal contralateral kidney may be managed with either nephron-sparing approaches or RN based on individual patient and tumour characteristics. Grade D (no recommendation possible); level of evidence: 4 (conflicting evidence).

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## III.DESCRIPTIVE AND PREDICTIVE ROLE OF PADUA SCORE

According to international guidelines, clinical tumour size and surgical feasibility are the two parameters usually considered when planning partial nephrectomy (PN) [1]. However, other anatomical features of the renal tumour are routinely considered in the nephron-sparing surgery decision-making process. In this scenario, in 2006 urologists and anatomists from the University of Padua, Italy started a project that aimed to define and standardise some anatomical and topographical renal tumour characteristics that predict the surgical complexity of PN. The PADUA classification was initially described in 2009. As reported in the original description, the following seven parameters were included: (1) face location; (2) longitudinal polar location; (3) rim location; (4) degree of tumour deepening into the parenchyma; (5) renal sinus involvement; (6) upper collecting system involvement; and (7) clinical maximal diameter of the tumour. PADUA score must be assigned using magnetic resonance imaging or 3D computed tomography to define clinical stage and anatomical characteristics of the tumours. Anatomical landmarks and related scores are reported in detail in the original publication [2].

### 1. PREDICTIVE ROLE

After the identification and definition of each feature included in the PADUA classification, Ficarra *et al*. tested prospectively this system in a series of 164 consecutive patients who underwent open PN (OPN) for cT1 renal tumours between January 2007 and December 2008. This study demonstrated the ability of the PADUA classification to subdivide patients who underwent OPN into three groups with significantly different risks of perioperative complications [2]. Specifically, according to univariate and multivariate analyses, the authors proposed to stratify patients into three different categories: low-risk group (score 6 or 7); intermediate-risk (score 8 or 9) and high-risk (score ≥10). In particular, multivariate analysis showed that PADUA score ranging from 8 to 9 identified a group of patients with a 14-fold higher risk of overall complications compared to those patients reporting scores of 6 to 7. Patients with a score ≥10 had a 30-fold higher risk of complications compared to those with scores of 6 or 7. Stratifying by anterior or posterior tumour site, PADUA score retained a statistically significant power in both locations [2].

In the following years, PADUA classification was widely used and validated in traditional laparoscopic, single-site laparoscopic PN (LPN), and robot-assisted PN (RAPN), as well as in OPN and ablative laparoscopic or percutaneous techniques.

More interestingly, numerous studies tested the ability of PADUA score to predict perioperative outcomes in patients who underwent LPN and RAPN. Specifically, more complex cases in which the risk of long warm ischaemia time (WIT), and/or complications are higher can be accurately identified, improving preoperative counselling and selection criteria for patients suitable for PN with different approaches. Waldert *et al*. performed the first external validation of PADUA score in a series of 240 consecutive tumours treated with OPN or LPN. PADUA score turned out to be an independent predictor of complication rate. Moreover, ischaemic time correlated with the PADUA score and was significantly higher in patients with high-risk tumours [3]. In 2012, Tyritzis *et al*. performed an external validation of PADUA score evaluating 74 consecutive OPNs. Using the threshold of 8, PADUA score was able to predict complications with a sensitivity of 90.9% and specificity of 77.8% (area under the curve: 0.89). Also in that study, PADUA score was an independent predictor of the risk of complications. PADUA score ≥8 identified a group of patients with an ~20-fold higher risk of complications [4]. In the same year, Kruck *et al*. reported higher haemoglobin loss and longer hospital stay in 81 patients with tumours with PADUA score >8 who underwent LPN [5].

Mottrie *et al*. performed the first external validation of PADUA score in a series of 62 consecutive patients who underwent RAPN during the learning curve period. PADUA score (6/7 vs. 8–11) was significantly correlated with WIT, console time, blood loss, percentage of pelvicaliceal repair, and overall complications. PADUA score was the only variable that could predict the risk of overall complications and turned out to be an independent predictor of WIT >20 min in multivariate analysis, after adjusting for the surgeon's experience [6]. Previous results were confirmed in a subsequent multicentre, international RAPN series. In a large series of 347 cases treated in four European and US robotic centres from September 2008 to September 2010, all multivariate models confirmed that PADUA score was an independent predictors of WIT >20 min, together with surgeons' experience and upper collecting system repair. Similarly, the score turned out to be an independent predictor of overall complication rates [7].

In 2013, Porpiglia *et al*. evaluated the predictive role of PADUA score on the Margin, Ischemia and Complication (MIC) system in a series of 206 patients who underwent LPN. The MIC rate was influenced mainly by LPN and PADUA score. Specifically, MIC rate increased with surgeons' experience and decreased when complex lesions were treated [8]. Recently, Minervini *et al*. performed an external validation of PADUA score in a series of 244 patients treated with simple enucleation. Again, PADUA score turned out to be an independent predictor of overall complications, surgical complications and major postoperative complications (Clavien grade 3/4) [9]. Greco *et al.* demonstrated that PADUA score was an independent predictor of WIT duration and postop-

erative complications in a series of 190 patients who underwent single-site LPN for renal tumour. Notably, on multivariable analysis, PADUA score was the only predictor of a favourable outcome [low vs. high score: odds ratio (OR): 4.99; *P*<0.001], with patients with low PADUA score tumours considered as ideal candidates for single-site PN [10]. In the same series of patients, Springer *et al*.demonstrated that PADUA score was the only factor predicting the significant increase of serum creatinine and significant decrease in estimated glomerular filtration rate 6 months after the procedure [11].

Few studies have compared PADUA score with other nephrometry systems. In 2011, Hew *et al*. tested the PADUA and RENAL systems in a series of 134 PNs. Both systems predicted complications in univariable analysis. In multivariable analyses, PADUA score ≥10 (OR: 3.98, *P*=0.01), RENAL score ≥9 (OR: 4.21, *P*=0.02), tumour size (OR: 1.35, *P*=0.02) and age (OR: 1.04, *P*=0.04) were independent predictors of complications. Both scores were able to predict WIT, and showed a substantial reproducibility with an intraclass correlation coefficient of 0.73 for

PADUA and 0.70 for RENAL scores [12]. In 2012, Bylund *et al*. evaluated the association of tumour size, tumour location, RENAL score, PADUA score and centrality index score with perioperative outcomes and postoperative renal function. Both PADUA and RENAL systems outperformed tumour size and location for prediction of perioperative outcomes [13]. In 2014, Zhang *et al*. tested PADUA and RENAL scores in a series of 245 Chinese patients with renal neoplasms undergoing LPN. In that retrospective study, both scores were able to predict the percent change in estimated glomerular filtration rate on multivariable analysis. The data from that study confirmed the substantial reproducibility of the PADUA and RENAL scores, according to concordance values ranging between 0.69 and 0.89 for the various components of the PADUA score and between 0.67 and 0.89 for RENAL nephrometry [14].

## 2. CONCLUSIONS

The use of nephrometry systems must be recommended in clinical practice to improve patient counselling and to stratify patients suitable for PN. The use of these classifications can improve the comparability between different series and approaches. Data from the literature demonstrate that PADUA score is able to predict perioperative outcomes such as ischaemia time, blood loss, and intra- and postoperative complications regardless of the approach used to perform PN.

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## IV. RENAL NEPHROMETRY DESCRIPTIVE AND PREDICTIVE ROLES

There are multiple measures of risk that must be considered and managed in the treatment of localised renal tumours. These include tumour risk, which encompasses the inherent biology of the tumour and, to the surgeon charged with excision or ablation, the anatomical complexity of the tumour.

In 2008, the first system to measure the anatomical complexity of tumours was published. This system, known as the RENAL nephrometry score is a points-based system that objectifies differences in the anatomical variations of a renal mass for the purpose of improving risk stratification, standardising reporting, and allowing meaningful comparisons between published reports. Subsequently, similar (PADUA) and distinct (c-INDEX) systems to measure tumour anatomical complexity (nephrometry) have been described and investigated. Each system seeks to quantify the anatomical complexity of renal tumours by measuring similar aspects including size, endo/exophycity, proximity to relevant hilar structures, and location. The anticipated result is a more meaningful comparison of treatment choices, complications, pathology, and outcomes (both functional and survival).

Since their advent, investigators have evaluated these three nephrometry scoring systems independently, collaboratively and comparatively **(Table 1)**, assessing their ability to provide insight into multiple descriptive and predictive outcome variables **(Table 2)**. This chapter provides a brief review of the published results of nephrometry scores relevant to the management of renal masses.

### 1. DESCRIPTIVE ROLE OF NEPHROMETRY

Tumour complexity (nephrometry) measures have been used to describe clinically relevant, treatment-specific parameters such as operative approach, operating time, warm ischaemia, and even the complexities of treatment decision making **(Table 2)**. Investigators have associated each of the three nephrometry scoring systems with surgical approaches including the use of elective nephron-sparing surgery (NSS), radical nephrectomy (RN), and robotic or open techniques. Additionally, several investigations have used these systems to describe variations in operative and warm ischaemia times, thereby ascribing temporal objectivity to complexity **(Table 2)**. Summary data from these reports suggest that increasing complexity is associated with greater use of nephrectomy and/or open approaches than partial nephrectomy, with correspondingly longer operating and ischaemic times.

One of the more robust descriptive uses of nephrometry measures has been in correlating tumour complexity with complications of tumour excision or

***Table 1. Number of publications utilising nephrometric scoring systems independently or collaboratively***

| RENAL Nephrometry | PADUA | C-Index |
|---|---|---|
| Bruner *et al*. (1), Hayn[2], Weight[3], Mufarrij[4], Liu[5], Simhan[6], Kutikov[7], Satasivam[8], Wang[9], Gorin[10], Rosavear[11], Broughton[12], Stroup[13], Tobert[14], Tomaszewski[15], Mayer[16], Altunrende[17], Sisul[18], Okhunov[19], Schmit[20], Kopp[21], Chang[22], Reyes[23], Matsumoto[24], Jung[25], Khalifeh[26], Canter[27], Montgomery[28], Simhan[29] (n=30) | Tyritzis[30] Porpiglia[31], Minervini[32], Greco[33] (n=4) | Samplaski[34] |
| | | |
| Lagerveld[35], Kruck[36] | Kobayashi[37], (n=3) | |
| | | Esen[38] (n=1) |
| Okhunov[39], | Bylund[40], | Lavallee[41] (n=3) |

***Table 2. Evidence and recommendation grade for descriptive and predictive uses of anatomic tumor complexity (nephrometry) systems***

| Nephrometry | LE | GR | Refs |
|---|---|---|---|
| | | | |
| Descriptive role (Nephrometrics can describe …) | | | |
| Treatment specific: | | | |
| Treatment type or approach | 3 | C | Canter[27], Broughton[12], Esen[38], Rosavear[11], Stroup[13], Tobert[14] |
| Operating and ischaemic times | 3 | C | Tomaszewski[15], Lavallee[41], Mayer[16], Altunrende[17], Okhunov[19], Bylund[40], Porpiglia[31], Kruck[36] |
| Complications: | | | Bylund[40], Simhan[6], Rosavear[11] |
| Post NSS (MIS or open) | | | Hayn[2], Weight[3], Mufarrij[4], Liu, Ellison, Minervini, Tyritzis, Porpiglia |
| Urine leakage focus | 3 | C | Bruner |
| Haemorrhage focus | 3 | C | Jung, Kruck |
| Conversion to RNx | 3 | C | Kobayashi |
| Post RFA | 3 | C | Chang, Schmit, Reyes |
| Post cryotherapy | 3 | C | Sisul, Lagerveld, Okhunov, Schmidt |
| | | | |
| Predictive role | | | |
| (Nephrometrics can predict …) | | | |
| Surgical outcome: | | | |
| Prolonged hospital stay | 3 | C | Kruck |
| Pathology | 3 | C | Kutikov, Satasivam, Gorin, Wang |
| Surgical margins | 3 | C | Khalifeh, Porpiglia |
| Survival | 3 | C | Kopp |
| Tumor growth rate | 3 | C | Matsumoto |
| Renal function | 3 | C | Bylund, Kruck, Okhunov, Simplaski |

***GR, grade of recommendation; LE, level of evidence; RFA, radiofrequency ablation; RN, .***

ablation. Investigators have described predominantly surgical complications associated with these objective measures; most commonly bleeding, urinary leakage, or conversion to RN, during or following NSS and ablative therapies. Simhan *et al*. assessed the risks characterised by nephrometry scores detailing complications by organ system as well as clinical diagnosis in 390 patients undergoing open or minimal invasive NSS [6]. The published data uniformly demonstrate a positive correlation primarily between urinary leakage, perioperative blood loss, transfusion risk and tumour complexity, although other less-commonly reported surgical and medical complications have also been shown to be related. Unfortunately each of the aforementioned studies, while largely case controlled, were single-centre or limited multi-institutional retrospective assessments of the uncontrolled results of several surgeons with varied skill sets and levels of experience. Currently, there are no level 1 data assessing the descriptive role of nephrometry systems leading to homogeneously low levels of evidence and recommendation grades **(Table 2)**. Although the collective experience with nephrometry scoring systems is still growing and inter-observer variability appears good, the systems are only now being incorporated into prospectively designed clinical trials.

## 2. PREDICTIVE ROLE OF NEPHROMETRY

Although the anatomical complexity of a tumour is associated with the extent and complexity of renal surgery or ablation, descriptive correlations such as operating time and complications are not unexpected. Included in these findings is the related metric of hospital length of stay, which is positively correlated with the complexity of the tumour being treated **(Table 2)**. However, an unanticipated role of nephrometry scoring systems is their potential role in predicting oncological and functional outcomes. Several investigators have published primarily single-institutional retrospective series using nephrometry to predict tumour pathology. These data suggest that more anatomically complex lesions tend to be more biologically aggressive as measured by stage, grade and type. One multi-institutional study has correlated nephrometry with a risk of upstaging after robotic partial nephrectomy [10]. Conversely less-complex lesions have been correlated with more indolent pathology [8]. At least two studies used nephrometry scores to predict postoperative margin status following MIS NSS [26,31]. If tumour complexity predicts indolent versus aggressive disease, it would follow that it may be able to predict survival outcomes as well. At least one group has used their data to suggest that there is a relationship between tumour complexity and survival outcomes following radical or partial nephrectomy for cT2 tumours [21]. Similarly, if complexity predicts ischaemic time, then it may also predict overall renal function following partial nephrectomy.

Several investigators have published their experience with nephrometry scores predicting renal function. They have noted a correlation between declines in renal function and higher complexity indices [19,36,40]. Finally, in patients under active surveillance (AS), tumour complexity has been shown to predict radiographic growth rates [24].

## 3. CONCLUSIONS

Predictive markers of various outcome measures are the focus of intensive research in the field of localised kidney cancer. Over the past 5 years, objective measures of tumour complexity, including the RENAL nephrometry score, PADUA score and C-Index have been developed and investigated for their descriptive and predictive roles. The data all remain fundamentally limited in that there have been no prospective clinical trials to evaluate their clinically utility. Instead, they represent low-level case-controlled series that have related tumour complexity to management complexity and related outcomes. More surprisingly are the growing number of data that appear to correlate higher complexity to more aggressive biology, faster growth rates, and lower survival. Although the field remains in its infancy, these data provide a provocative look at how objectifying relatively simple measures such as tumour size and location can consolidate reporting structures, make for improved comparisons, and bring forward potentially unanticipated correlations.

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# B. PARTIAL NEPHRECTOMY

## I. INTRODUCTION

### 1. PARTIAL VERSUS RADICAL NEPHRECTOMY

Historically, radical nephrectomy (RN) has been considered the gold standard for localised renal cell carcinoma (RCC). Partial nephrectomy (PN) was initially reserved for absolute indications such as patients with bilateral RCC or a solitary kidney, and relative indications such as impaired renal function in the contralateral kidney [1]. Current treatment guidelines are informed mainly by observational studies suggesting that PN provides oncological outcomes equivalent to those seen with RN, and is associated with a reduced risk of subsequent chronic kidney disease (CKD) and cardiovascular events compared with RN [2,3]. This reasoning has yielded widespread acceptance of PN as the preferred treatment for most clinical T1 renal masses (diameter ≤7 cm), whenever technically feasible, even in those with a normal contralateral kidney (elective indications). It was hypothesised that in these patients, PN may offer comparable oncological control to that of RN, but with better preservation of renal function, leading to improved overall survival (OS). To test this hypothesis, the European Organisation for Research and Treatment of Cancer (EORTC) designed a phase III randomised trial to compare PN and RN in 541 patients with a small (≤5 cm) solitary renal mass and a normal contralateral kidney [4]. The results of the EORTC 30904 study (5,6) conflict with previous observational studies. This prompted us to reconsider the current paradigms. A comprehensive review of the Medline literature from January 1, 2009 to February, 18, 2014 regarding RN and PN for renal tumours was conducted.

### 2. IMPACT ON SURVIVAL

In a recent meta-analysis of 20 observational studies in patients with small renal masses (T1a and selected T1b), OS was better after PN compared with RN with a pooled hazard ratio (HR) of 0.80 [95% confidence interval (CI): 0.74–0.87; *P*<0.001) [7]. However, the evidence of the available data suggesting a survival benefit for PN is of low quality considering the observational nature of the studies, resulting in a risk of selection bias and statistical heterogeneity. Several additional observational studies were published, reporting better OS with PN [8–11] or equivalent oncological outcomes [12–14] compared with RN. PN for tumours >7 cm was associated with higher mortality than RN (HR=5.3, *P*=0.025) and equivalent cancer-specific survival (CSS) rates were recorded after PN and RN in patients with Fuhrman grades III/IV or pT3a histology [15]. In highly selected patients with locally advanced RCC, PN was safe and provided oncological outcomes equivalent to patients treated with RN [16]. A recent study using the Surveillance, Epidemiology, and End Results (SEER) Medicare-linked database showed that some elderly patients (≥75 years) and/or those with multiple comorbidities at diagnosis may not benefit from PN with respect to other-cause mortality [17]. Another recent study reported that elective PN is not associated with an increased risk of recurrence and cancer-specific mortality in T1 renal tumours [13]. In contrast to what was expected, the EORTC 30904 trial – the only randomised trial of RN versus PN for renal tumours ≤5 cm – demonstrated a survival benefit for those treated with RN (vs. PN). With a median follow-up of 9.3 years, 18% of RN and 25% of PN patients had died, with an HR of 1.50 (95% CI: 1.03–2.16, *P*=0.03). Kidney cancer mortality occurred in 3.0% of PN and 1.5% of RN patients (*P*=0.23) [5].

### 3. IMPACT ON RENAL FUNCTION

In a meta-analysis of 10 observational studies, PN correlated with a 61% risk reduction in severe CKD (HR 0.39, 95% CI: 0.33–0.47, *P*<0.0001). The definition of severe CKD varied substantially between the studies, ranging from an estimated glomerular filtration rate (eGFR) <60 ml/min/1.73m$^2$ to the need for dialysis [7]. In the EORTC 30904 study, over a median follow-up of 6.7 years, and compared with RN, PN substantially reduced the incidence of at least moderate stage A (eGFR <60 ml/min/1.73m$^2$) and stage B (eGFR <45 ml/min/1.73m$^2$) renal dysfunction, although the incidence of advanced kidney dis-

ease (eGFR <30 ml/min/1.73m$^2$) was relatively similar in the two treatment arms, and the incidence of kidney failure (eGFR <15 ml/min/1.73m$^2$) was nearly identical. The beneficial impact of PN on renal function did not result in improved survival in this study population, with a median follow-up of 9.3 years, for all-cause mortality (HR: 1.50; 95% CI, 1.03–2.16 in favour of RN, as previously reported). Although many patients may develop moderate renal dysfunction after RN (85.7% vs. 64.7% for PN), they are not likely to progress to kidney failure (1.5% vs. 1.6% for PN) [6], and it seems that RN has a minimal adverse impact on OS (81.1% vs. 75.7% for PN) [5,18]. In patients with preoperative CKD due to medical causes, lower postoperative eGFR was recently associated with increased mortality independent of age and comorbidity. However, in patients with normal renal function prior to surgery, postoperative eGFR was not an independent predictor of survival [19]. Two recent studies have reported superior renal function after PN compared to RN in patients with T1 renal tumours [20,21], even when performed with extended ischaemia (>30 min) [21]. However, the impact of improved renal function with PN on OS remains controversial. Data from a retrospective study including 442 patients with benign renal masses suggest that renal preservation with PN may be associated with improved survival compared with RN, after excluding the confounding effect of malignancy [8].

## 4. PERIOPERATIVE MORBIDITY AND QUALITY OF LIFE

It is widely accepted that PN is a technically more complex operation than RN. In particular, the risk of complications increases with tumour anatomical complexity. PN achieves better health-related quality of life than RN due to better preservation of renal function and avoidance of end-stage renal disease and dialysis [22]. The EORTC 30904 study demonstrated that PN is associated with a higher complication rate than after RN. Re-operation for perioperative complications was necessary in 4.4% of PN and 2.4% of RN patients [4]. Lowrance *et al*. also found a higher complication rate for patients undergoing PN compared with RN (20% vs. 14%). Elderly patients did not experience a proportionally higher complication rate than young patients [23]. It should be noted that the contemporary modifications in surgical technique and the introduction of laparoscopic and robot-assisted techniques used for PN in large centres of excellence have further reduced the morbidity of the PN procedure.

## 5. CONCLUSION

Based on the whole body of literature, PN is recommended for the treatment of T1 renal masses whenever technically feasible, even in patients with a normal contralateral kidney (level of evidence 3, grade of recommendation C). However, based on the EORTC 30904 study, and compared with PN, only a small and similar percentage of RN patients progress to kidney failure, and RN is associated with an equal or even better OS (level of evidence 1). Therefore some patients with a normal contralateral kidney are probably better managed with an uncomplicated RN; that is, those with locally advanced tumour growth, unfavourable tumour location, large (>7 cm) or complex renal tumour, or extension into the inferior vena cava or renal vein, those with significant deterioration of general health, and those for whom long-term benefits of PN are uncertain, such as some elderly and infirm patients. PN must always be weighed against the risk of acute surgical morbidity and the risk of local recurrence due to incomplete resection, or tumour multifocality. Laparoscopic RN is the standard of care for patients with T2 tumours and renal tumours not treatable by PN. Patient performance status, surgical expertise, and careful patient selection are important factors in the treatment decision process. To investigate further the impact of PN relative to RN on OS and quality of life in patients with localised RCC, another randomised trial may be needed.

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## II. ONCOLOGICAL OUTCOMES: PN VS RN FOR T1A, T1B, T2 TUMORS

### 1. Management of Positive Surgical Margins

A paradigm shift from radical nephrectomy (RN) for all renal tumours, regardless of size, to the expanded use of elective partial nephrectomy (PN) began 20 years ago and continues today. The vast majority of the literature is driven by single-institutional and non-randomised surgical series subject to all of the usual concerns regarding heterogeneity of the data and treatment selection biases. Despite that, emerging understanding of the variable threats from renal cortical tumours (nearly 50% are benign or indolent in nature), evidence for oncological non-inferiority of PN from a randomised trial, and emerging concerns for the adverse impact of iatrogenic chronic kidney disease (CKD) have fuelled this paradigm shift. Skilled surgeons utilise techniques derived from complex stone, trauma, vascular, and donor transplantation surgery to address fundamental concerns regarding perioperative bleeding and urinary fistula, to improve PN outcomes [1]. During this time, surgical oncologists moved away from Halsteadian radical surgical approaches toward organ- and limb-preserving procedures breast cancer, sarcoma) which maintained quality of life without sacrificing local tumour control or long-term survival. The stage was set for an expansion of elective PN [2]. The initial nephron sparing patient pool comprised patients with tumours <4 cm. In an initial 1993 report of 241 patients, only two experienced local recurrence and there was 95% survival after 3 years of median follow-up [3]. Ten-year follow-up indicated that these results were durable [4], with other centres providing confirmatory data [5]. Contemporary reports from major centres in the US and Europe with a commitment to kidney surgery continued to support the oncological efficacy of PN for T1a (<4 cm) renal tumours across all of the newly described histological subtypes of renal cortical tumours [6–10].

Despite the accumulating evidence supporting PN for small renal masses, scepticism remained regarding the safety and effectiveness of PN. The only phase 3 randomised trial to address the PN versus RN question, EORTC 3094, was initiated in 1992 as an intention to treat (ITT), non-inferiority trial. Patients with renal cortical tumours ≤ 5 cm were randomised to RN or PN with a goal of accruing 1300 patients. Remembering that in 1992, PN was not a widely performed procedure and real expertise was concentrated in only a few major centres worldwide, 45 centres, first in Europe and later in the US and Canada, were enlisted but accrual was poor, and in 2003, the study was closed with only 541 patients randomised. For a variety of reasons, including missing pathology, higher stage pathology, tumour multi-focality, 81 patients randomised

to RN and 73 randomised to PN were deleted from the study, leaving the remaining 71% of patients for analysis. In addition, 55 (14.1%) randomised patients switched treatment arms, 39 patients from PN underwent RN (14.9%) and 16 patients from RN underwent PN (5.9%). Also, 53 patients (13.5%) were lost to follow-up, yet statistical analysis was conducted with the assumption that they had died from unknown causes. The ITT analysis was published in 2011 after a median follow-up of 9.3 years and revealed that only 12/117 (10.3%) deaths in the study were attributed to renal cancer. ITT analysis revealed a significant 10-year overall survival advantage of 81% for RN versus 75.7% for PN, but a significant difference did not persist when renal cancer patients were analysed alone. The authors provided no details or information regarding the number of operations performed at each centre, the complexity of the operations performed, the estimation of residual preserved kidney function in the patients undergoing PN, whether renoprotective measures were used, and the ischaemia times. Despite the obvious limitations in this randomised trial that began 22 years ago and ended 11 years ago, just as the rationale for kidney-sparing approaches was being developed and increasing expertise in PN was being acquired, the results indicate that PN did not compromise renal cancer control in patients with small renal masses [11].

Encouraged by the above results, when surgeons were faced with larger tumours located in a polar location, they began considering PN in that setting, and hence the rationale for expanding PN to larger renal cortical tumours of 4–7 cm was articulated [12]. Initial single-institutional reports seemed to support PN for larger tumours whenever technically feasible [13–15]. Combining the Mayo Clinic and Memorial Sloan Kettering Cancer Center (MSKCC) databases, investigators evaluated 1159 patients with renal tumours 4–7 cm treated with RN (*n*=873, 75%) and PN (*n*=286, 25%), and demonstrated no significant difference in survival between the groups [16]. Reports of extension of PN to even larger tumours and those of higher stage (T2, T3a), nearly 20% of which turned out to be benign on final pathology, continued to confirm an oncological efficacy for selective use of PN for larger tumours [17,18]. The principles of elective kidney-sparing surgery described above, derived largely from open surgical experience, have been largely confirmed in the more technically challenging laparoscopic and robot-assisted approaches to PN [19–21]. There is no question that the execution of PN, by any technique, requires a combination of surgical judgment and skill to achieve complete resection with negative surgical margins. The ultimate oncological outcome is driven by interplay between tumor biology and patient host factors. The utilisation of PN whenever technically feasible is endorsed by various guideline committees [22].

## 2. IMPACT OF POSITIVE MARGINS

A historical criticism of PN relates to the need for a 1–2-cm surgical margin of healthy tissue surrounding the tumour. Although this belief is felt to be founded in the basic principles of surgical oncology, no firm data exist to support this view. This issue is relevant particularly when surgeons pursue endophytic tumours and peri-hilar renal tumours, or renal tumours abutting the collecting system that would all be effectively excluded from PN if there were strict adherence to a 1-cm margin rule. Also, uncertain pathological factors relating to the handling of the tumour specimen and fractures in its capsule may lead to an inked margin that is positive. In 2003, Sutherland and colleagues evaluated 44 PN specimens with a median tumour margin of 0.2 cm. No patient with a negative tumor margin developed local recurrence. Of three patients with a microscopically positive surgical margin, two did not develop local recurrence after 39 and 62 months of follow-up, and the third patient developed distant metastases and local recurrence. The authors concluded that the absolute margin depth was irrelevant to outcome [23]. MSKCC and Mayo Clinic investigators combined their data and analysed 1344 patients undergoing 1390 PN procedures from 1972 to 2005. Positive surgical margins were documented in 77 cases (5.5%) and were significantly associated with decreasing tumour size and presence of a solitary kidney. Experienced surgeons from both centres described small endophytic tumours – many of which were not palpable and located only by using intraoperative ultrasound – as difficult to find and resect, and often associated with close or positive surgical margins. All patients with positive surgical margins were managed expectantly with an overall 10-year probability of freedom from local recurrence and metastatic recurrence of 93%. There was no significant difference in either local or metastatic recurrence between the patients with positive or negative surgical margins [24]. Using the Ontario Cancer Registry, Finelli and colleagues reviewed 664 PNs from 1995 to 2004 and reported a 10.7% positive surgical margin rate. Overall and disease-specific survival did not vary according to margin status [25].

Marszalek and colleagues performed an exhaustive literature review of PN, including open, laparoscopic and robotic approaches, involving 27 studies and 11,024 patients. Positive surgical margins were reported in 0–7.0% of cases and they confirmed that the thickness of the non-neoplastic kidney surrounding the tumour specimen was irrelevant, and that most patients do not experience local or systemic recurrence. In patients who underwent complete nephrectomy because of a positive surgical margin, residual viable disease was rarely detected. Patients with higher-grade tumours or those undergoing imperative PN were more likely to develop recurrent local or systemic disease. The authors concluded

that careful surveillance alone is the most appropriate approach to a margin-positive pathology report after PN [26]. Breda and colleagues reported a survey of European and American surgeons from 17 centres, who treated 855 patients with laparoscopic PN. They reported positive surgical margins in 21 patients (2.4%); two-thirds of whom were treated with immediate complete nephrectomy [27].

**In general**, if the surgical resection is complete and there is no obvious tumour in the resection bed, most major centres advocate careful surveillance rather than complete nephrectomy as the next step. This approach depends on the fact that nearly 50% of small renal tumours have indolent or benign histology with low metastatic potential. When gross disease is left behind, the most appropriate next step is a secondary intervention (radical nephrectomy or a wider partial nephrectomy).

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## III. ENUCLEATIVE PARTIAL NEPHRECTOMY (SIMPLE TUMOR ENUCLEATION)

The treatment of small renal masses represents an area of increasing interest. At present, nephron-sparing surgery (NSS) can be performed either as standard partial nephrectomy (PN), defined as excision of the tumour and an additional margin of healthy peritumoral renal parenchyma, or as simple enucleation (SE)/enucleative PN.

### 1. SURGICAL TECHNIQUE AND APPROACH

SE consists of excising the tumour by blunt dissection following the natural cleavage plane between the peritumoral pseudocapsule and the renal parenchyma, without removing a visible rim of healthy renal tissue. It was first described as an open technique but it is also feasible with a laparoscopic or robotic approach [level of evidence (LE) 3; grade of recommendation (GR) C]. A matched-pair analysis of 392 patients treated with SE for T1a/T1b renal tumours, including 160 patients in the open group and 80 in the robotic group (Endoscopic Robot-Assisted Simple Enucleation (ERASE) ), showed that ERASE is a feasible technique with a positive surgical margin (PSM) rate comparable to that of the open technique [1]. The study showed warm ischaemia time (WIT) and complication rates similar to those of the open approach, along with the advantages of minimal invasiveness.

### 2. INDICATIONS

SE can be used for the elective treatment of sporadic renal masses regardless of tumour dimensions [2], as well as for patients with relative and absolute indications for NSS (LE 3; GR B) [2,3]. Possible advantages of SE have been reported, especially for tumours with unfavourable nephrometry (PADUA score ≥10; RENAL score ≥10, totally endorenal tumours, and cT1b tumours with endophytic growth into the medulla and close to the main intrarenal vessels and collecting system) (LE 4; GR C). However, most studies that have reported the perioperative results of SE have not analysed subgroups of patients with challenging tumours [4–6]. In a recent study, that did assess the perioperative results of SE in 244 patients, 21% had a PADUA score ≥10, thus confirming that SE might widen the indications of NSS, including the most challenging cases [7].

With the advent of nephrometric scores, it is important in the future to test further the efficacy of SE for the treatment of tumours with adverse nephrometric scores and to compare the results with those of standard PN [8,9].

### 3. EXCLUSION CRITERIA FOR SIMPLE ENUCLEATION

High Fuhrman grade (grade 4) can be a contraindication for SE (no recommendation possible). A recent paper from the SATURN (Surveillance and Treatment Update Renal Neoplasms, SATURN Project – LUNA Foundation, Florence, Italy) project showed that patients who underwent SE for Fuhrman grade 4 disease had significantly worse cancer-specific survival compared to those undergoing standard PN [2]. However, the number of patients was too small (20 standard PN vs. 4 SE) to make this observation anything more than a suggestion for future studies.

### 4. WARM ISCHAEMIA TIME, FUNCTIONAL OUTCOMES AND PERIOPERATIVE COMPLICATIONS

Some authors have hypothesised that SE might be associated with shorter WIT and protective against complications, such as major bleeding and urinary fistula, compared to standard PN [10]. In a single-centre prospective series, SE showed a low incidence of postoperative complications requiring re-intervention, urinary fistula, and ureteral stenting [5,7]. However, in a large multicentre, prospectively derived dataset (RECORd project), a matched-pair comparison of 396 patients showed that SE and standard PN were associated with similar WIT and overall, surgical and medical complications (LE 3; GR C) [6]. In the same study, SE was associated with shorter operating time and lower blood loss when compared to standard PN [6]. No comparative data on mid- and long-term functional outcomes between SE and standard PN have been reported to date (no recommendation possible).

### 5. SURGICAL MARGIN STATUS

The achievement of negative surgical margins (NSMs) is one of the major challenges of NSS. PSMs after NSS occur in 2–8% of patients. The presence of PSMs as a risk factor for disease recurrence after NSS is still a matter of debate, however, it should prompt more frequent and intensive surveillance. The incidence of PSMs has been consistently low for SE [11,12]. The protective effect of blunt enucleation towards the risk of PSMs has been demonstrated in a prospective pathological study of 90 patients with renal cell carcinoma. The study showed inflammatory tissue with a median thickness of 1 mm, which allowed NSMs for tumours extending microscopically beyond the tumor capsule [13]. This thin layer of normal tissue was present as “leopard spots” on the intact tumour capsule, and in cases with neoplastic penetration of the capsule into the kidney tissue [13]. A recent prospective study on 304 patients evaluated the prognostic effect of capsule penetration on local recurrence after SE [14]. At a median (range) follow-up of 52 months [12–96], there was no significant difference in progression-free survival (PFS) between patients with an intact tumour capsule and those who had neoplastic penetration of the capsule into the kidney tissue (5-year PFS 97.5% and 96.7%, respectively) [14]. In the latter group, the crude local recurrence rate was 3.2%. Two

recent multicentre studies showed a significantly lower incidence of PSMs after SE when compared to standard PN [2,6]. The first study compared the perioperative outcomes of SE versus standard PN in T1 renal tumours, and the incidence of PSMs was significantly lower in patients treated with SE and 4.7 times higher in patients undergoing standard PN [6]. The conclusion of the committee is that SE is at least non-inferior to standard PN for the risk of PSMs (LE 3; GR C). However, prospective randomised trials using a standardised classification of different NSS techniques are warranted to reach definitive conclusions regarding the risk of PSMs with different types of NSS.

## 6. ONCOLOGICAL OUTCOMES, FROM PATHOLOGY REPORTS TO MID- AND LONG-TERM FOLLOW-UP STUDIES

The oncological safety of blunt SE has been demonstrated by retrospective studies in which the width of the surgical margins was not associated with oncological prognosis, and by prospective pathological studies [13–15]. Several retrospective studies have confirmed good oncological results of SE and some of these studies have demonstrated similar local recurrence-free and cancer-specific survival between SE and standard PN, for renal tumours with a diameter of ≤7 cm [16–23]. One study has confirmed similar cancer-specific survival between SE and radical nephrectomy (LE 2 and 3; GR B).

Increased knowledge within the results of different renal cancer treatments strategies has resulted in advances in patients care, However, only a prospective randomised study will be able to defining the best technique for NSS and the parameters for surgical decision making between standard PN and SE.

The overall GR for the technique of enucleative partial nephrectomy is B, because it is based on consistent LE 3. Most of the evidence highlights the positive value of the technique.

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# IV. FUNCTIONAL OUTCOMES OF PARTIAL NEPHRECTOMY: QUALITY, QUANTITY, AND ISCHAEMIA

## 1. INTRODUCTION

With the rising incidence of small renal masses and concomitant down-staging of localised tumours, we have witnessed noteworthy changes in the treatment paradigm of kidney cancer over the past two decades [1,2]. Clinical guidelines currently recommend partial nephrectomy (PN) for cT1 renal tumours, if technically feasible [3,4], based on several observational studies suggesting a lower risk of chronic kidney disease, without compromising oncological outcome [5–10]. Several studies have reported that urological surgeons have begun to adapt their practice to higher rates of PN for patients diagnosed with localised renal tumours in the US [11–13]. It is therefore essential to have an understanding of the current evidence surrounding the relationship between PN and kidney function.

## 2. RENAL FUNCTIONAL OUTCOMES AFTER PN

The traditional description of the surgical technique for PN involves dissection of the renal hilum and clamping of the renal artery and vein in order to facilitate adequate and safe resection of the renal mass and minimise blood loss [14,15]. At issue is the amount of safe warm ischaemia time (WIT) during PN, which is of relevance because renal hilar clamping is considered the conventional approach for PN; in particular for robotic and laparoscopic approaches. A recent expert panel from the Society of Urologic Oncology (SUO) put forth a policy position that every minute matters in preserving renal function during PN, and that longer WIT may not be the ideal standard of care [16]. Supporting this position is a study from the Cleveland Clinic and Mayo Clinic of 362 patients with solitary kidneys who underwent PN with warm ischaemia. The results suggested that each minute of WIT was associated with a 6% [hazard ratio (HR): 1.06; $P$<0.001] greater risk of acute renal failure and 4% (HR: 1.04; $P$=0.03) greater risk of stage IV chronic kidney disease during follow-up [17]. Furthermore, the authors evaluated cut-off points of WIT and reported that 25 min was the best cut-off to distinguish between patients who did and did not develop short- and long-term renal functional consequences.

Subsequent to this study, Lane *et al*. reported a multi-institutional collaboration involving 660 patients with solitary kidneys treated with warm or cold ischaemia during PN [18]. This study was notable for several important findings. First, while patients treated with cold ischaemia had longer ischaemia times compared with patients treated with warm ischaemia (45 vs. 22 min; $P$<0.001), renal functional outcomes were similar, suggesting that longer periods of cold ischaemia and shorter periods of warm ischaemia protect renal function to an equivalent extent. Second, one of the strongest features associated with duration of ischaemia time was the amount of kidney removed, indicating that longer periods of ischaemia are intimately linked with larger tumours requiring more complex resection and reconstruction. Third, baseline renal function and percentage of healthy kidney preserved after PN, both termed non-modifiable, were the primary determinants of long-term renal function, with ischaemia time losing significance in a multivariable analysis incorporating these features.

In an attempt at validation, the solitary kidney warm ischaemia cohort, previously reported by the Mayo Clinic and Cleveland Clinic, was re-evaluated while incorporating the percentage of kidney preserved [19]. This updated analysis validated baseline renal function and percentage of kidney preserved as important determinants of short-and long-term renal function after PN. Additionally, WIT as a continuous variable was associated with short-term renal consequences, and longer WIT (>25 min) was associated with long-term renal function in multivariable analyses.

## 3. MODIFIABLE FEATURES AFFECTING RENAL FUNCTION

To address the possible deleterious effects of warm ischaemia on renal function, off-hilar-clamp PN has been recently assessed for open, laparoscopic and robot-assisted approaches. Another collaboration involving the Cleveland Clinic and Mayo Clinic compared the aforementioned 362 warm ischaemia patients with 96 patients treated without hilar clamping, with all PNs performed in the setting of a solitary kidney. The warm ischaemia group had significantly increased risks of acute kidney injury after surgery

and increased risks of new-onset chronic kidney disease during follow-up [20]. Supporting this, Kopp *et al*. observed that off-clamp surgery without hilar control had greater median estimated blood loss (300 vs. 200 ml; $P<0.001$) and lower incidence of long-term chronic kidney disease (12.5% vs. 24.4%; $P=0.05$) [21]. Several recent studies have begun to report their initial data on safety of robotic PN for smaller and modestly complex renal tumours, as determined by nephrometry scores [22,23].

Recently, Gill *et al*. have described a novel approach of zero ischaemia PN that involves anatomical microdissection of blood vessels that supply the renal tumour [24]. In that study of 59 patients with mean tumor size of 3.2 cm and mean nephrometry score of 7.0, treated surgically by laparoscopic or robotic PN, all patients were imaged with thin-slice computed tomography focused on the kidney, to define the renal vasculature supplying the tumour. During minimally invasive PN to achieve zero ischaemia, selective anatomical vascular dissection and clamping of the arterial supply to the renal tumour were performed with aneurysm micro-bulldog clamps. Although the transfusion rate was 19% in this initial series, there was only a decrease of 11.4% in estimated glomerular filtration rate (eGFR) at 4 months postoperatively. In a subsequent study from the University of Southern California comparing robotic or laparoscopic PN, with and without vascular microdissection to achieve zero ischaemia, Ng *et al.* found similar outcomes for median estimated blood loss, complications, and postoperative serum creatinine, despite the patients in the zero-ischaemia group having larger and more complex renal tumours (i.e. hilar) [25].

Although the concept of off-clamp PN, whether by open, laparoscopic or robotic approaches, is appealing, these initial studies have been limited by relatively small sample sizes or lack of a comparison group, and all studies were non-randomised and subject to selection bias. Thus, further studies of emerging surgical techniques that minimise WIT or eliminate the need for clamping of the renal hilum are needed. However, based on the current evidence regarding renal function after PN, it is reasonable to conclude the following main points. [1] The quality of kidney (as measured by preoperative eGFR) and quantity of kidney (amount of healthy/vascularised remnant kidney after PN) are primary determinants of renal function after PN. [2] Every minute of WIT predicts early postoperative renal damage and longer WIT (>25 min) is associated with long-term renal function impairment and should be avoided. [3] Cold ischaemia should be used if longer periods of ischaemia are anticipated, especially in the imperative setting. [4] PN without ischaemia (i.e. without hilar clamping) appears to have better renal functional outcomes compared with warm ischaemia for tumours that are amenable to this technically demanding approach.

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## V. EVOLVING INDICATIONS FOR PARTIAL NEPHRECTOMY

Oncological surgery has evolved. Once largely limited to reactive surgery to alleviate symptoms, most cancer surgery is now proactive, to prevent progression, pain and suffering. Surgeons have become less radical and less invasive for the treatment of nearly all tumours. This has been facilitated by survival metrics demonstrating that “more” is not consistently “better”, an increased awareness of the quantifiable morbidity associated with surgical interventions, an understanding of impaired quality of life associated with intervention, economic concerns, and improved MIS technologies. The management of localised kidney cancer has led many of these changes, given the crucial function of the kidneys. Robson’s initial description of radical nephrectomy [1] has been supplemented by excellent outcomes reported for nephron-sparing surgery (NSS), particularly for T1 renal tumours [2].

The contemporary literature on renal cell carcinoma (RCC) is replete with data evaluating the evolving indications for renal preservation, as well as the appropriate use of NSS and MIS to achieve the goals of cure and maintenance of renal function. These indications can be broadly defined as those that expand the indications for NSS and those that decrease the indications for NSS. These data are reviewed briefly here.

### 1. EXPANDING INDICATIONS FOR NSS

Once confined to absolute or relative renal functional impairment, the expanding indications for NSS are due to improvements in our understanding of biology, renal function, tumour anatomy, technology, and education.

### 2. EXPANDING INDICATIONS BASED ON BIOLOGY

Most small renal masses are now recognised as malignant [3] and most are often low grade [4]. In a review of >26 published reports representing >27,000 solid renal masses, Corcoran *et al*. reported that >85% of cT1 lesions were RCC, nearly 70% were clear cell carcinomas, and 74% of publications evaluating the relationship between size and malignant histology noted a positive correlation [3]. When evaluating tumour grade, Rothman *et al*. noted a similar association between size and grade in a Surveillance, Epidemiology, and End Results (SEER) analysis of ~20,000 renal tumours demonstrating that 80% of localised renal tumours were low grade and that size predicted grade [4]. These data provide a biological rationale for NSS for cT1a tumours and increasingly for cT1b and cT2 tumours [5].

In a comparative systematic review and meta-analysis, Kim *et al*. pooled data from 21 studies of ~32,000 patients, and noted a 20–30% risk reduction in all cause mortality and CSS for those undergoing NSS compared to radical nephrectomy [5]. Published reports have largely demonstrated equivalent oncological outcomes for NSS versus radical nephrectomy for cT1b lesions [6] and particularly in patients with localised cT2 lesions [7].

### 3. EXPANDING INDICATIONS BASED ON RENAL FUNCTION PRESERVATION

The significance of chronic kidney disease (CKD) and functional outcomes of NSS are independent topics in this EAU-ICUD publication. Evolution of the renal functional implications of renal surgery as a rationale for expanded indications for NSS is summarised briefly. A heightened awareness of the deleterious effects of CKD on the risk of death and cardiovascular disease has focused attention on renal preservation [8]. This was followed by a sentinel article documenting increased rates of CKD following radical nephrectomy [9]. Subsequent publications have confirmed [5] or challenged [10] the significance of these findings, separating medical from surgical forms of CKD [11], predictors of continued decline [12], and an inability to demonstrate improved survival based on prospective data [13]. This increased awareness of pre-existing and potentially progressive CKD has increased utilisation of NSS [14]. All these data have at least challenged clinicians to focus on understanding the significance of the functional changes and risks associated with various forms of surgical intervention.

## 4. EXPANDING INDICATIONS BASED ON RENAL TUMOR ANATOMY

The recent description and increased adoption of scoring systems that objectify tumour complexity (nephrometry) has led clinicians to make more meaningful comparisons of treatment choices, complications, pathology, and outcomes (both functional and survival). With expanded biological and functional indications for NSS, surgeons no longer use tumour anatomy as an absolute or even relative contraindication for NSS. Several studies have evaluated the increased use of NSS with increasing tumour complexity and the association of complexity with non-oncological clinical outcomes. Although this is the topic of a separate EAU-ICUD document, in summary NSS is increasingly being used in larger, more central, endophytic, hilar and more complex tumours, with associated higher but generally acceptable perioperative risks [15–17].

## 5. EXPANDING INDICATIONS BASED ON TECHNOLOGY AND EDUCATION

Technological advances have allowed more patients to benefit from minimally invasive approaches, further expanding the role of NSS. While pure laparoscopic NSS is technically challenging, in skilled hands it has proved largely equivalent to open NSS; although selection biases can adversely affect comparisons [18]. The high dissemination of robotics along with more standardised training [19] and improved optics/haptics compared to standard laparoscopy have led to wider adoption and expansion of the indications for MIS/NSS, with equivalent or improved outcomes including shorter ischaemic times [20]. The data from these studies are independent topics of this EAU-ICUD publication.

## 6. DECREASING INDICATIONS FOR NSS BASED ON ACTIVE SURVEILLANCE/ABLATION/COMPLICATIONS AND COMPETING RISKS DATA

Percutaneous thermal tissue ablation offers the possibility to decrease the role of NSS, although practice pattern data have not substantiated significant shifts toward ablation over the past 10 years [14]. Whether ablation alters the natural history of a localised renal tumour has been increasingly challenged by equally robust cancer-specific outcomes in active surveillance series [21]. Although few level 1 data exist regarding active surveillance, independent registry and pooled data demonstrate that truly localised renal cancers grow slower than previously recognised (median 3–5 mm/year), with a low risk of metastases at a median of 2–4 years (<5%) [21]. In elderly and infirm patients, competing risks often pose a greater threat to longevity than the small renal mass, arguing against the need for any surgical intervention [13,22,23]. Recent data recognising the need to balance the surgical risks of complex NSS [16] with the uncertain short/intermediate-term functional and overall survival benefits in patients with acceptable baseline estimated glomerular filtration rate are beginning to support the role of uncomplicated radical nephrectomy in well-selected elderly patients [13].

## 7. CONCLUSION

Evolving indications for more (or less) NSS in the management of localised RCC require critical reading of the literature and must be contextualised to the individual patient. Priorities must be established and ordered appropriately. First and foremost, excision must have the greatest chance for cure. Renal preservation and minimisation of complications are important secondary surgical goals. Given current data, the indications for NSS continue to evolve.

## 8. SUMMARY

| Evolving indications for NSS | Level of evidence | Grade of recommendation |
|---|---|---|
| **Expanding** Indications for NSS | | |
| - Biology | 3 | C |
| - Renal function | 2-3 | C |
| - Tumor anatomy | 3 | C |
| - Technology | 3 | C |
| | | |
| **Decreasing** Indications for NSS | | |
| - Active surveillance /competing risks | 3 | C |
| - Ablation/radical nephrectomy | 1-3 | C |

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# VI. ROBOTIC PARTIAL NEPHRECTOMY TECHNIQUES

## 1. CONVENTIONAL MULTIPORT VERSUS SINGLE-SITE ROBOT-ASSISTED PARTIAL NEPHRECTOMY

Single-site surgery has been developed in the past few years to yield fewer port-related complications, quicker recovery time, less pain, and better cosmesis due to minimisation of skin incision to gain access to the abdominal or pelvic cavities [1]. The technique has been limited to robot-assisted partial nephrectomy (RAPN) in selected cases and by experienced surgeons, with promising results [2]. Nevertheless, a recent comparative study of multiport versus single-port RAPN demonstrated significantly better outcomes for standard multiport RAPN in terms of operating time, warm ischaemia time (WIT), and postoperative estimated glomerular filtration rate, as well as achieving trifecta outcomes (WIT <25 min, negative surgical margins and no intraoperative or postoperative complications) [3]. These findings suggest that, at the present time, and with the currently available Da Vinci platform, a limited role for single-site surgery in RAPN [level of evidence (LE) 3; grade of recommendation (GR) C].

## 2. TRANSPERITONEAL VERSUS RETROPERITONEAL APPROACH

RAPN is more commonly performed through a transperitoneal approach. However, the retroperitoneal approach has been described in several

surgical series [4]. The main advantages of the retroperitoneal approach include avoiding bowel mobilisation, more direct access to the kidney and renal hilum, and potentially easier dissection of posterior tumours, with the potential to decrease operating time. Conversely, the main disadvantages are represented by the small working space, and presence of limited landmarks. Although comparative studies with transperitoneal and retroperitoneal RAPN are sparse, a recent systematic review and meta-analysis on laparoscopic PN demonstrated shorter operating time (weighted mean difference 48.85 min; *P*<0.001) and shorter length of hospital stay (weighted mean difference 1.01 days; *P*=0.001) in favour of the retroperitoneal approach [5] (LE 3; GR C). The validity of these figures for RAPN remains unclear and selection between the two approaches is mainly based of surgeons' preference and tumor location.

## 3. TUMOR IDENTIFICATION

Although not mandatory in the presence of predominantly exophytic tumours, margin identification and marking by intraoperative ultrasound is of particular use for neoplasms with large endophytic growth and/or hilar location. Robotic ultrasound probes are available, allowing direct control of the probe by the console surgeon [6].

## 4. HILAR CONTROL

The classic approach to RAPN includes clamping of the main renal artery to reduce blood loss and allow tumour resection in a bloodless field. Vascular clamping is typically removed at the end of cortical renorrhaphy. More recently, Gill *et al*. reported an early unclamping technique, where artery clamping is removed after closure of the inner medullary defect, allowing significant decrease in WIT [7].

Due to the increased relevance of WIT as a modifiable factor to reduce kidney injury and loss of renal function, alternative approaches have been reported. Off-clamp RAPN

has been described in selected cases with tumours of low complexity and large exophytic growth (e.g., low RENAL nephrometry or PADUA scores), demonstrating good perioperative results and preservation of renal function [8] (LE 3; GR C). More recently, a super-selective clamping of tertiary or higher-order arterial branches has been described by Gill *et al*. to provide tumour ischaemia without compromising blood flow in the remaining parenchyma in complex tumours

not suitable for off-clamp techniques [9,10]. Specifically, a detailed preoperative 3D

reconstruction of triphasic computed tomography (CT) images of the kidneys with 0.5-mm thick slices is performed to evaluate tumour and vascular anatomy in the most accurate way. Intraoperative, vascular microdissection of secondary, tertiary and quaternary branches is performed to identify specific vascular branches directly supplying the tumour, which are clip-ligated and divided. Conversely, tertiary or quaternary branches supplying the peritumoural parenchyma are selectively and transiently controlled with a neurosurgical microbulldog clamp during tumour excision. Intraoperative colour Doppler ultrasound is performed before tumour resection to confirm the lack of blood flow within the tumour, as well as a reduction in peritumoural blood flow [9,10]. Alternatively, near-infrared fluorescence imaging can also be adopted to demonstrate the efficacy of the super-selective clamping before tumour resection [11].

In the most recent publication by the same group comparing such a sophisticated technique with standard artery clamping, super-selective clamping was associated with longer median operating time (*P*<0.001), higher transfusion rates (24% vs. 6%, *P*<0.01) but similar perioperative complications (15% vs. 13%), and hospital stay. However, patients receiving super-selective clamping experienced a significantly smaller decrease in estimated glomerular filtration rate at discharge (0% vs. 11%, *P*=0.01) and at last follow-up (11% vs. 17%, *P*=0.03) as well as greater parenchymal preservation on postoperative CT volumetrics [12]. Although they are appealing, vascular microdissection and super-selective clamping are complex surgical techniques, whose reproducibility has not been extensively tested outside the centre that initially promoted them (LE 4; GR C).

Preoperative super-selective transarterial embolisation and intraoperative controlled hypotension [13, 14] are alternatives to minimally invasive PN without artery clamping in complex tumours, but both techniques have not been widely adopted (LE 4; GR D). Finally, cold ischaemia has also been adopted during RAPN by transarterial cold perfusion of the kidney, retrograde ureteral cooling or, more recently, by the use of ice slush to cover the kidney during ischaemia [15] (LE 4; GR D).

## 5. TUMOUR EXCISION

Tumour excision should ideally be performed cutting sharply with a rim of normal renal parenchyma, mainly using cold scissors, to visualise better the healthy parenchyma surrounding the tumour and to minimise the risk of positive surgical margins. To allow off-clamping dissection, a variety of lasers have been tested for tumour excision, including thulium, $CO_2$, Green Light and diode lasers [16–18]. Although promising, laser excision is not currently regarded as a standard technique; probably due to the lack of the ideal laser.

## 6. RENORRHAPHY

Renorrhaphy is typically performed according to the sliding clip technique, originally described by

Benway *et al.* [19]. Specifically, the inner medullary defect is closed with a running Monocryl 3-0 suture preloaded with a Hem-o-lok clip, taking all retracted calices and vessels in the running suture. The Monocryl suture brought outside through the parenchyma and secured with a Hem-o-lok clip. Through the sliding clip technique, the correct tension is applied to this suture.

Various fibrinogen coagulation enhancers and tissue sealants (e.g., Floseal) can be used on the defect, together with bolsters. However, their usefulness is questionable. Monopolar or bipolar cautery can be applied on the cortex of the resection bed. The borders of the defect are closed with polyfilament 1-0 sutures. According to the surgeon's preference, either interrupted sutures or, more commonly and rapidly, a running suture secured with a Hem-o-lok clip at each passage of the suture can be used and the correct tension is applied to the tissue. Subsequent tension readjustments are possible [19,20]. Notably, some surgeons have advocated avoiding cortical renorrhaphy to reduce the risk of renal function loss. However, there is an absence of significant data on the benefits and risks of this technique (LE 4; GR D).

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# VII. IMPROVING SURGICAL MORBIDITY COMPLICATIONS

## 1. INTRODUCTION

Minimally invasive partial nephrectomy (PN) has evolved to minimise the morbidity of open PN (OPN) while preserving the oncological and functional outcomes. The increase in abdominal imaging has allowed an increased number of renal tumours to benefit from minimally invasive nephron-sparing surgery. A traditional open approach usually involves a loin incision that is painful and may be associated with prolonged pain/discomfort and herniation/wound bulging [1], as well as the cosmetic effects of a larger incision. There are two main types of morbidity and complications that can be improved by a robotic or laparoscopic approach: those to do with the open or minimally invasive surgery itself, that is, postoperative pain, scarring, length of hospital stay, and return to normal activity; and those inherent to the surgical procedure itself, namely, bleeding, margin status, functional outcomes and urine leakage. To be effective, laparoscopic PN (LPN) and robot-assisted PN (RAPN) must be beneficial in both areas. One difficulty in comparing historical open cohorts with current laparoscopic and robotic groups is the absence of Clavien complication scoring [2] and nephrometry scores in earlier studies. Another issue is that length of stay after any surgical procedure depends on the social and cultural features of the healthcare system in which the operation was performed, rather than just the quality of the surgery. This makes comparison between international studies of PN difficult, but despite this, most single-centre studies favour minimally invasive PN over OPN for length of stay and return to full activity.

## 2. OVERALL COMPLICATIONS OF LPN VERSUS OPN

LPN is a challenging and highly demanding procedure with a significant learning curve. Renal failure, postoperative haemorrhage requiring transfusion, urine leakage, and urinary fistula are the most frequently seen complications after open and laparoscopic nephron-sparing surgery (NSS). The re-intervention rate in OPN is ~2.5% [3], with and overall rate of procedure-related complications of 9%. The European Organisation for Research and Treatment of Cancer (EORTC) trial looking at elective, mainly open, NSS found a rate of significant haemorrhage of 3.1%, urinary fistula rate of 4.4%, pleural injury rate of 11.5%, and re-intervention rate of 4.4% [4,5], equivalent to a Clavien IIIa/b complication. A large comparison evaluating OPN (7990) and LPN (523) using the National Inpatient Sample [6] found a transfusion rate of 9.3 versus 3.8% ($P$<0.001), intraoperative complication rate of 2.9 versus 1.5% ($P$=0.06) and a postoperative complication rate of 15.4 versus 11.3% ($P$=0.01). A length of stay ≥5 days occurred in 46.7 versus 20.8% ($P$<0.001) in OPN and LPN, respectively, and in-hospital mortality was identical at 0.4%. Although not including nephrometry scores, after attempts at adjusting for selection bias, the authors concluded that LPN had less morbidity. Another study using nephrometry scores investigating 107 LPN and 82 OPN procedures found higher blood loss and longer hospital stay in the OPN group but significantly more major complications in the LPN group [7]. The urine leakage rate was 3.4% in this study and 3.1% in the largest single-centre comparative study [8]. The results were influenced by the experience of the centre; some centres have found no difference in complication rates between OPN and LPN [9], whereas in highly experienced centres, LPN seems to have less morbidity, including blood loss, and shorter hospital stay [8,10]. Overall complication rate is slightly higher for LPN than OPN in most centres, if adjusted for tumour complexity, as indicated by recent guidelines [11].

## 3. RPN VERSUS OPN

The potential for increased complications seen in some LPN series is potentially minimised by the Da Vinci Surgical System. The relative ease of suturing with robotic technology permits a reduction in warm ischaemia time and improved renorrhaphy closure. This can lead to a reduction in the rates of significant bleeding and urinary leakage/fistula, as well as warm ischaemia time. Although there are few comparisons of LPN and RAPN, data from the National Inpatient Sample found in favour of RPN for complications when compared to LPN [12].

In a single-centre non-randomised study [13], RAPN was superior to OPN in terms of median blood loss (143 vs. 415 ml; $P$<0.001) and length of stay and equivalent in terms of complications. However in a retrospective, multicentre, matched-pair analysis comparing RAPN and OPN [14], postoperative complications were seen in 21.5% of OPN and 14% of RAPN patients ($P$=0.02). Major complications (grade 3/4) were reported in nine (4.5%) patients after both OPN and RAPN.

A recent study has investigated complications during RPN of 44 complex renal tumours with a PADUA score >10 [15]. This group had only two cases of intraoperative bleeding complications, which were managed robotically, and 10 postoperative complications, of which four were Clavien grade IIIb requiring embolisation, ureteric stenting and laparoscopic adhesiolysis. The authors concluded that robotic technology allows safe expansion of RPN to anatomically challenging lesions in tertiary referral centres. Another group has been able to safely excise 65 totally endophytic lesions with no increase in complications, as compared to their exophytic tumour group [16]. In terms of predicting morbidity, significant factors seem to include the experience of

the surgeon, intraoperative blood loss, and whether the collecting system is entered, which is related to the case complexity [17]. Intra-abdominal fat also seems to contribute to the risk of complications [18].

**Overall**, it seems that RPN may have some benefits over LPN in terms of perioperative complications, however, the main difference seems to be reduced WIT rather than morbidity [19,20] (level of evidence 3). RPN does seem to allow surgeons to attempt more difficult cases without increasing complication rates, and RPN has potentially lower rates of conversion to radical nephrectomy (level of evidence 4) [21], while studies from experienced high-volume centres have reported low morbidity [22].

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# VIII. COMPARATIVE OUTCOMES OF LAPAROSCOPIC VERSUS OPEN PARTIAL NEPHRECTOMY

## 1. INTRODUCTION

When comparing laparoscopic partial nephrectomy (LPN) with open PN (OPN), there is a scarcity of randomised studies, and many reports do not account for surgeons' experience or tumour complexity via standardised nephrometry scores. High-quality LPN is usually only delivered by experienced surgeons with excellent laparoscopic suturing skills, enabling them to minimise warm ischaemia time (WIT) while completing a safe and secure renorrhaphy. Delivering a mean WIT of <30 min in initial experience is thought to be challenging and relies on selection of less-complex cases initially.

It has been shown for >10 years that the early morbidity of LPN is reduced when compared with that of OPN [1] in terms of time to resumption of normal diet and hospital stay. LPN generally has a longer renal WIT, more major intraoperative complications, and more postoperative urological complications in comparison to OPN, even in the larger centres [2]. As experience has increased, a matched pair analysis has shown that surgical time, WIT, and hospitalisation time can be reduced with LPN [3]. Compared with OPN, the patients with LPN generally had smaller tumours but formal comparisons of case complexity were not possible. With the advent of the PADUA [4] and RENAL scoring systems, it became clearer which cases were being undertaken by which surgeons/centres and true comparisons could be made.

## 2. EARLY MORBIDITY

One major challenge with LPN was reducing the WIT that was generally 10 min longer than with OPN. This was partially achieved by initiation of early unclamping during renorrhaphy after completion of the parenchymal suturing layer [5]. The largest study to date, with >1800 cases, had a mean WIT of 31 min, which was only significantly reduced with the introduction of early unclamping [6].

In a multicentre analyses, LPN was usually used for smaller tumours, which were less endophytic than for OPN, whereas the LPN group demonstrated similar rates of recurrence-free survival, complications, and postoperative glomerular filtration rate compared with the OPN group [7]. The rate of positive margins was universally low at around 1–2% and equivalent in the larger comparative series [6,7], but again, stratification for tumour complexity was often missing. Some studies have shown higher rates of major complications in the LPN group, which is likely due to renorrhaphy closure technique [8]. If overall results are evaluated in terms of a Trifecta including positive margin rates, complications and WIT, then the Italian 19-centre collaboration RECORd project showed no difference between OPN and LPN [9]. A US comparative study using the Surveillance, Epidemiology, and End Results (SEER) database has shown decreased hospital stay and intensive therapy unit admission for LPN patients but an increased rate of urological complications and postoperative haemorrhage (P<0.001) [10].

## 3. LONG-TERM ONCOLOGICAL AND FUNCTIONAL OUTCOMES

There is no clear evidence to support either OPN or LPN over each other in terms of long-term outcomes. Both have low rates of recurrence and positive margin rates. Both have low levels of deterioration in renal function.

In a recent retrospective case-matched study of 340 patients undergoing OPN versus LPN, WIT was shorter in the LPN group at an impressive 11 min compared to 14 min for OPN. There were no differences in overall and cancer-specific survival at 5 years [11]. Similarly at 7 and 10 years, disease-free survival was excellent in both the LPN and OPN cohorts [12,13].

**In summary** experience with LPN is increasing and results from high-volume centres are promising, with reduced hospital stay and return to full activity. LPN is generally safe and achievable in appropriately trained centres and results in reduced blood loss, hospital stay and return to full activity compared to OPN 9 (level of evidence 3). It remains a highly technically demanding operation with high rates of major complications and increased WIT (level of evidence 3) despite most centres reserving it for smaller and less complex tumours.

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# IX. COMPARATIVE OUTCOMES LPN V OPN

## 1. INTRODUCTION

When comparing LPN with OPN there is a scarcity of randomized studies and many studies do not account for surgeon experience or tumour complexity via standardized nephrometry scores. High quality LPN is usually only delivered by experienced surgeons with excellent laparoscopic suturing skills enabling them to minimize WIT whilst completing a safe and secure renorrhaphy. Delivering a mean WIT under 30 minutes in the initial experience is though to be challenging and relies on case selection of the less complex cases initially.

It has been shown for over 10 years that the early morbidity of LPN is reduced when compared with OPN [1] in terms of time to normal diet and hospital stay. At this point LPN generally had a longer warm renal ischemia time, more major intraoperative complications and more postoperative urological complications in comparison to OPN, even in the larger centres [2]. In the following years with increasing experience others showed that surgical time, WIT, and hospitalisation times could be reduced with LPN [3] in a matched pair analysis. At this stage the series of LPN generally had smaller tumour sizes but formal comparisons of case complexity were not possible. With the advent of the PADUA [4] and RENAL scoring systems it became clearer which cases were being undertaken by which surgeons/centres and true comparisons could be made.

## 2. EARLY MORBIDITY

One major challenge was reducing the WIT that was generally 10 minutes longer than seen in OPN. This issue was partially answered by the initiation of early unclamping during the renorrhaphy after completion of the parenchymal suturing layer [5]. Indeed largest series in the world literature to date with over 1800 cases had a mean warm ischaemic time of 31 minutes overall which was only significantly reduced with the introduction of early unclamping [6].

In a multicenter national analyses LPN was usually used in smaller tumours, which were less endophytic whilst the LPN group demonstrated similar rates of recurrence-free survival, complications, and postoperative GFR change compared with OPN group [7]. The rates of positive margins seem universally low at around 1-2% and equivalent in the larger comparative series [6,7] but again stratification for tumour complexity is often missing. Some series have shown slightly higher rates of major complications in the LPN group, which is likely due to renorrhaphy closure technique [8]. In overall results are evaluated in terms of a Trifecta including positive margin rates, complications and WIT then the Italian 19-centre collaboration RECORd project has shown no difference between OPN and LPN [9]. A US comparative study using the SEER database has shown decreased hospital stay and ITU admission for LPN patients but an increased rate of urological complications and post- operative haemorrhage ($p < 0.001$) [10].

## 3. LONG TERM ONCOLOGICAL AND FUNCTIONAL OUTCOMES

There is no clear evidence to support either OPN or LPN over each other in terms of longer term outcomes. Both have low rates of recurrence and positive margin rates. Both have low levels of deterioration in renal function.

In a recent retrospective case matched study of 340 pts undergoing OPN vs LPN, WIT was less in the LPN group at an impressive 11 minutes compared to 14 minutes for OPN. There were no differences in overall and cancer specific survival at 5 years [11] and similarly at 7 and 10 years disease free survival was excellent in both the LPN and OPN cohorts [12, 13].

**In summary** experience with LPN is increasing and results from certain high volume centres are very promising with reduced hospital stay and return to full activity. LPN is generally safe and achievable in appropriately trained centres and results in a reduced blood loss, reduced hospital stay and reduced return to full activity compared to OPN 9 (LEVEL 3 EVIDENCE). It remains a highly technically demanding operation with higher rates of major complications and increased warm ischaemic times (LEVEL 3 EVIDENCE) despite most centres reserving it for smaller and less complex tumours.

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## X. ROBOTIC PARTIAL NEPHRECTOMY SURPASSING LAPAROSCOPIC PARTIAL NEPHRECTOMY

Laparoscopic partial nephrectomy (LPN) is a challenging procedure with a long learning curve, due to the need to perform delicate extirpative and reconstructive oncological surgery, with negative surgical margins, in one of the most vascularised human organs and in the shortest time possible. In a single-surgeon series of 800 cases performed by one of the pioneers of LPN, who is also one of the surgeons with the most experience in the field, Gill *et al*. demonstrated mean warm ischaemia time (WIT) of ~32 min for the first 500 cases performed, with WIT <20 min in ~15% of the cases only [1]. Complication rates were as high as 24% in the first 275 cases and decreased only to 15% in the subsequent 289 cases [1] [level of evidence (LE) 3; grade of recommendation (GR) C]. Those data suggests that, even with an overwhelming surgical volume, which is impossible to achieve for most laparoscopic surgeons, the procedure is associated with a high risk of complications and long WIT. Consequently, it is not surprising that population-based studies suggest that the adoption of LPN is not really widespread, being adopted in only 9% of all the PN cases performed in the US from 2008 to 2010, as reported in the Nationwide Inpatient Sample dataset [2].

Due to the Da Vinci Surgical System, robot-assisted PN (RAPN) may offer significant advantages over conventional LPN. Two recent systematic reviews and meta-analyses compared the outcome of LPN and RAPN. Froghi *et al*. [3] reported a meta-analysis of six non-randomised comparative studies [4–9] that evaluated RAPN and LPN for treatment of T1a small renal masses. Two hundred and fifty-six patients were included, demonstrating that all the perioperative outcomes, including WIT and complication rates, were similar for LPN and RAPN [3] (LE 3; GR C).

Subsequently, Aboumarzouk *et al*. [10] reported a study with similar methodology, evaluating seven non-randomised observational studies [5,8,9,11–14] that included >300 RAPN and >400 LPN procedures. Finally, RAPN was found to be associated with significantly lower WIT (mean difference 2.7 min; 95% confidence interval 1.1–4.3 min; *P*=0.0008). Conversely, operating times, estimated blood loss, conversion rates, complication rates, and postoperative length of hospital stay were similar in the two groups [10] (LE 3; GR C).

Notably, despite similar inclusion criteria and designs, the two systematic reviews identified different studies, with only three papers [5,8,9] being included in both analyses. That clearly suggests that the systematic searches at the bases of both reviews were not sufficiently sensitive. Regardless of that, virtually all the included studies were of limited methodology, due to lack of randomisation, and small sample size, which does not allow us to draw definitive conclusions.For example, most of the studies included in the meta-analyses included patients treated by surgeons in the initial phase of their RAPN learning curves, as demonstrated by the limited volume of RAPN cases included. Conversely, even for surgeons with previous robotic experience, RAPN outcomes improve after at least the first 50 cases [15]. Consequently, clinically speaking, the only conclusion that can be derived from both reviews is that even during the learning curve, RAPN already resulted in equal perioperative outcomes to LPN performed by more experienced laparoscopic surgeons [16] (LE 3; GR C).

Mature series of RAPN have provided more insights into the huge potential of this surgical approach. For example, in a multicentre series of ~350 cases of RAPN performed in four European and US high-volume referral centres, Ficarra *et al*. demonstrated than WIT <20 min was achieved in 64% of cases (median WIT only 18 min), and overall complication rates as low as 12% (only 3% high-grade complications) [17]. In another multicentre series, including 450 cases from four institutions, Spana *et al*. demonstrated an overall prevalence of complications of 15.8%, with most of the complications being of Clavien grades 1 or 2 and only 3.8% were major complications [18] (LE 3; GR C).

Dulabon *et al*. performed a large multicentre study from four high-volume, US referral centres evaluating the outcome of RAPN in hilar tumours [19]. For complex tumours, with a mean diameter of 3.6 cm, RAPN as performed by experienced surgeons was

associated with mean WIT of 26 min, no risk of conversion to open PN or LPN, no loss of renal unit, low risk of complications (2.4% Clavien grade 2), and low risk of positive surgical margins (2%) [19] (LE 3; GR C).

Two other large multicentre series have demonstrated that RAPN was feasible in cT1b tumours, with acceptable mean WIT (22 and 24 min), low risk of intraoperative complications (4% and 0%) and postoperative high-grade complications (~8%) [20, 21] (LE 3; GR C). Conflicting results have been reported in other studies [22–24] .

Finally, the accuracy of RAPN makes the procedure feasible with good perioperative and functional results also in patients with baseline chronic kidney disease (CKD). In another multi-institutional collaboration, Kumar *et al*. demonstrated that RAPN in patients with baseline CKD was associated with higher risk of complications compared to a matched population of patients with normal renal function undergoing the same procedure [25]. However, patients with pre-existing CKD experienced a more limited decline in glomerular filtration rate [25] (LE 3; GR C).

The results of the available studies indicate that RAPN in the hands of expert surgeons is associated with excellent outcomes in terms of perioperative complications, and functional results. The natural history of the small renal masses typically treated with RAPN, as well as the short-term follow-up available in the published studies, due to the relatively recent development of the procedure, prevent us drawing definitive conclusions on the oncological outcomes. Population-based studies from the US show three greater adoption of RAPN compared to LPN (among 38,000 PNs performed in the US from 2008 to 2010, 24% were RAPN and only 9% LPN) [2], suggesting that RAPN is already the preferred minimally-invasive approach to PN.

## XI. SPECIAL SITUATIONS: HILAR TUMOURS, CENTRAL TUMOURS, MULTIPLE TUMOURS, SOLITARY KIDNEY, AFTER PRIOR FAILED PARTIAL NEPHRECTOMY

Central or hilar renal parenchymal tumours, as well as totally endophytic lesions, are challenging cases regardless of the approach used to perform partial nephrectomy (PN). Other potential special cases are large tumours (≥4 cm), tumours in solitary kidneys, multiple unilateral or bilateral tumours, and local recurrences after previous PN. These special cases deserve a careful evaluation when a minimally-invasive technique is proposed.

### 1. CENTRAL/HILAR AND LARGE TUMOURS

In 1998, Hafez *et al*. defined central tumours as those with extension into the renal sinus [1], however, several definitions of central and hilar tumours have been used in laparoscopic PN (LPN) reports. Some authors have defined central tumours as those directly abutting or approaching the renal sinus fat or the pelvicaliceal system, whereas others have defined them as being completely buried within the renal parenchyma, irrespective of their proximity to the renal sinus [2]. More recently, in a study of robot-assisted partial nephrectomy (RAPN), Dulabon *et al*. defined renal hilar lesions as tumours originating on the medial aspect of the kidney, abutting the renal artery/vein, and/or renal pelvis, with involvement of the renal sinus [3]. As a consequence of such variability in definitions, the prevalence of central tumours in recent surgical series has ranged from 6.5 to 48.5%. Considering the potential limitations related to non-standardised definitions, a systematic review in 2008 concluded that LPN is feasible for central/hilar tumours if performed by experienced laparoscopic surgeons. However, complications rates seem to be higher than those reported after open PN (OPN) [2].

RAPN has been developed and proposed as the natural evolution and simplification of LPN. The advantages offered by the Da Vinci platform (3D vision and patented Endo Wrist technology) can help surgeons to reduce the learning curve and increase the feasibility of a laparoscopic approach for more complex renal tumours [4]. In 2011, Dulabon *et al*. compared 41 patients with hilar renal masses with 405 patients without hilar masses, demonstrating that RAPN is a safe, effective and feasible option for such complex tumours. Only warm ischaemia time (WIT) was significantly longer in hilar than non-hilar tumours (26.3 vs. 19.6 min; *P*=<0.0001), whereas there was no difference in other perioperative and postoperative outcomes and pathological surgical margins. That study was limited by the lack of standard anatomical classification of renal tumours [5].

According to both RENAL or PADUA scores, central/hilar and endophytic tumours suitable for PN were categorised as high risk [6,7]. In an international multicentre study including RAPN performed during the learning curve, 24% of tumours were classified as high risk. Median WIT and console time were 20 and 120 min, respectively. Median estimated blood loss (EBL) was 100 ml. However, 70% of patients required repair of the upper collecting system. Moreover, intraoperative and postoperative complication rates were 6% and 15%, respectively. Specifically, minor and major postoperative complication rates were 10.8 and 4.8%, respectively. Nevertheless, the results can be considered good, although WIT, console time, EBL, and rate of upper collecting system repair in the high-risk group were significantly worse than in the low-risk category and overlapped with the intermediate-risk category. Similarly, intraoperative

and postoperative complications observed in the high- risk group were significantly higher in comparison with the low-risk group and overlapped with the intermediate-risk group [8].

In 2013, Eyraud *et al*. compared 294 non-hilar and 70 hilar tumours treated with RAPN by an expert surgeon. Hilar tumour location in patients undergoing RAPN in a high-volume centre was not associated with an increased risk of transfusion, major complications, or decline in early postoperative renal function. The authors reported longer operating time, longer WIT, and increased EBL in hilar tumours. Conversely, no differences were noted in complications, positive margins, and postoperative estimated glomerular filtration rate (eGFR) at last follow-up. WIT was the only perioperative outcome influenced by hilar location in multivariable analysis [9]. In a recent single-centre study evaluating 44 cases with a PADUA score ≥10 performed by an expert robotic surgeon, the authors confirmed the feasibility of RAPN for complex cases, showing short WIT, acceptable major complication rate, and good long- term renal functional outcomes. Specifically, median operating time, EBL and WIT were 2 h, 150 ml, and 16 min, respectively. Two intraoperative complications occurred (4.5%): one inferior vena cava injury and one bleeding from the renal bed, which were both managed robotically. Postoperative complications were observed in 10 cases (22.7%); four of which (9.1%) were Clavien high grade, including two bleeding episodes that required percutaneous embolisation, one urinoma that resolved with ureteral stenting, and one bowel occlusion managed with laparoscopic adhesiolysis. Two patients (4.5%) had positive surgical margins and were followed expectantly with no radiological recurrence at a follow-up of 23 months. In this study the authors reported no decline in serum creatinine and eGFR at 6 months after surgery [10].

Few studies have compared LPN and RAPN in patients with complex tumours. In 2013, Long *et al*. compared retrospectively 182 consecutive patients who underwent LPN with 199 who received RAPN for tumours with RENAL score ≥7. The authors concluded that RAPN provided functional outcomes comparable to those of LPN for moderately and highly complex tumours, but was associated with significantly lower risk of conversion to radical nephrectomy (RN) (11.5% in LPN vs. 1% in RAPN; $P<0.001$) and a lower decrease in percentage eGFR (16.0% vs. 12.6%, respectively; $P=0.03$) [11]. It has been confirmed that, in experienced hands and referral centres, both LPN and RAPN are feasible for treatment of complex renal tumours. In this scenario, the robotic technology allows safe expansion of the indications of minimally invasive PN to anatomically challenging renal lesions. However, longer follow-up is mandatory to confirm the oncological effectiveness of this procedure at intermediate- and long-term follow-up.

## 2. TUMOUR IN SOLITARY KIDNEYS

LPN in solitary kidneys is feasible but rarely performed, and only in a few experienced centres for selected patients [2]. In a large series of patients treated by LPN performed by a single expert surgeon, only 5.8% of tumours were located in a solitary kidney [12]. In such cases, perioperative outcomes are strongly correlated with the anatomical and topographical characteristics of the treated tumours. In 2006, Gill *et al*. reported an overall complication rate as high as 45.5% for solitary tumours treated with LPN [13].

Similarly, RAPN is rarely used for tumours in solitary kidneys, and is only performed by expert robotic surgeons. In 2013, Hillyer *et al*. reported the results of 26 patients (2.9% of the whole cohort) with a solitary kidney treated at five academic institutions from May 2007 to May 2012. RAPN was a feasible option in this specific population and offered reliable preservation of renal function, low surgical morbidity, and early oncological safety in the hands of experienced robotic surgeons. There was a median WIT of 17 min and only two intraoperative complications. Postoperative complication rate was 11.5% and, at amedian follow-up of 6 months, postoperative eGFR did not decline significantly [14]. In 2013, Panumatrassamee *et al.* [15] compared 52 LPN and 15 RAPN robotic procedures performed in a single institution between June 2000 and April 2012 for tumours in solitary kidneys. The study showed that RAPN offers a significant benefit over LPN in terms of operating time, WIT, and hospital stay. Conversely, no significant differences were found in terms of EBL, transfusion, complications, pathological results, margin status, and postoperative renal function [15].

**In conclusion**, renal tumours in solitary kidneys represent a challenging condition suitable for LPN or RAPN in high-volume referral centres. According to the few available studies, RAPN seems to be slightly better in comparison with pure LPN.

## 3. MULTIPLE TUMOURS

Minimally invasive PN in the setting of multifocal renal masses is challenging but can be performed in experienced hands. Both LPN and RAPN have been described. Although both procedures are feasible, patients must be appropriately informed about the risk of open conversion [16]. For synchronous, bilateral renal tumours that require intervention, the timing of surgery is open to debate. Surgical strategies can be concomitant, bilateral PN, staged PN with the larger/more complex side first, or conversely, staged PN with the smaller/less complex side first. Performing bilateral concomitant LPN or RAPN is difficult due to patient positioning changes and is often not feasible [16]. For staged LPN or RAPN, the strategy to start from the more complex or less complex side is not different from OPN.

In 2009, Boris *et al*. reported their initial experience with RAPN for multiple renal masses, demonstrating the feasibility of this procedure. A total of 24 tumours in nine patients were removed with robotic assistance [17]. In 2013, Abreu *et al*. evaluated perioperative outcomes in a series of patients who underwent minimally invasive PN for multiple renal tumours. Specifically, they performed a matched-pair analysis comparing 33 patients who underwent RAPN for multiple tumours with 33 who received the same treatment for a single tumour. EBL and WIT were similar in both groups. Conversely, median operating time and hospital stay were longer in the patients with multiple tumours. There were two conversions to laparoscopic RN per group. Overall, complications developed in 33% and 21% of the patients treated for multiple and single tumours, respectively. Median eGFR at discharge was similar in the two groups [18].

According to previous data, RAPN/LPN can be safely performed by expert surgeons for multiple tumours with perioperative outcomes similar to those in patients with a solitary tumour.

## 4. REPEAT RAPN FOR NEW OR RECURRENT TUMOUR IN THE SAME KIDNEY

Detecting a new or recurrent tumour in a kidney previously treated with PN is a challenging scenario. Usually, RN should be taken into consideration in most of these cases. However, in selected patients and in referral centres, repeat PN can be planned. If repeat OPN has been shown to be associated with a higher risk of complications, the challenge is significantly higher when a minimally invasive procedure is considered.

Few reports are available in the literature. In 2008, Turna *et al*. reported the first experience with repeat LPN. They included an analysis of 25 cases initially treated with open PN. WIT and EBL were 35.8 min and 215 ml, respectively. No intraoperative complications were reported and postoperative complication rate was 12% [19]. Autorino *et al*. reported the results of the first series of repeat RAPN. They described the perioperative outcomes of nine patients previously treated with OPN, LPN or RAPN. In three cases, the surgeon performed an unclampling technique. In the remaining cases, WIT was 17.5 min, EBL was 150 ml, and no intraoperative complications were reported. Postoperative complications were observed in only two cases [20].

Repeat LPN and RAPN are technically demanding procedures. The literature is limited to a few cases treated in referral centres. Therefore, these procedures must be performed in referral centres by expert surgeons. Although no comparative studies are available, patients should be adequately informed about the potential additional risks of minimally invasive procedures in comparison with open surgery.

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## XII. COMPOSITE OUTCOMES OF PARTIAL NEPHRECTOMY: ACHIEVING THE TRIFECTA

Partial nephrectomy (PN) surgery seeks to achieve three technical goals: negative surgical margins, maximal preservation of renal remnant function, and complication-free recovery. Simultaneous realisation of all three goals in individual patients reflects the best-case scenario of PN surgery. This has been termed the “trifecta” outcome, a concept first proposed by Hung *et al*. [1]. Although used during radical prostatectomy (continence, potency and cancer cure), trifecta outcomes have not been previously ascribed to PN surgery.

In developing the trifecta concept, Hung *et al*. evaluated serial outcomes in 534 patients undergoing robotic/laparoscopic PN for renal tumours over a 12-year period. These patients were retrospectively divided into four chronologic eras: discovery era (139 patients; 1999–2003); conventional hilar clamping era (213 patients; 2004–2006); early unclamping era (104 patients; 2007–2008); and anatomical zero-ischaemia era (78 patients; 2010–2011).

Hung *et al*. used renal function calculations based on the abbreviated MDRD (“modification of diet in renal disease”) -estimated glomerular filtration rate (eGFR) formula, using the latest available serum creatinine value at 1 month post-PN. Percentage kidney saved was documented intraoperatively based on the subjective assessment of the surgeon and two assistants. Predicted postoperative eGFR was calculated by multiplying preoperative eGFR and percentage total kidney saved. Thus, in a patient with two kidneys, if 40% of one kidney was excised during PN, the percentage total kidney tissue preserved was deemed to be 80%, because 60% of one kidney and 100% of the opposite kidney were saved. Thus, if that patient had a preoperative eGFR of 100 ml/min/1.73m$^2$, the predicted postoperative eGFR would be 80 ml/min/1.73m$^2$ (i.e., 100 ´ 80%). Hung *et al*. defined renal functional decrease as >10% reduction in the actual versus volume-predicted postoperative eGFR.

Urological complications were defined as renal haemorrhage (bleeding from the kidney requiring re-operation or radiological embolisation), urine leakage (urine drainage >50 ml/day for >7 days) and kidney loss for whatever reason. Trifecta outcome requires a patient to achieve simultaneously all three key outcomes after PN, that is, minimal (<10%) renal functional decrease, negative cancer margin, and no urological complications.

Hung *et al*. reported the following results. Sequentially over the four eras, tumours trended towards larger size (2.9, 2.8, 3.1 and 3.3 cm; $P$<0.08); nevertheless, the amount of kidney preserved remained similar (89%, 90%, 90% and 88%). Tumour complexity increased during the more recent eras, with more tumors being >4 cm in size (13%, 15%, 23% and 27%; $P$<0.03), centrally located (44%, 57%, 66% and

56%; $P$=0.007) and hilar (1%, 0.5%, 13% and 27%; $P$<0.0001). Notably, PN surgery during recent eras has become more refined, resulting in superior outcomes. Warm ischaemia times decreased (36 min, 32 min, 15 min and 0 min; $P$<0.0001).

As a result, renal functional outcomes improved significantly in recent eras, as reflected by eGFR decreases of 20%, 21%, 11% and 9%, respectively ($P$<0.0001). More patients in the recent eras experienced a <10% decrease of actual versus volume-predicted eGFR (48%, 45%, 64% and 72%, respectively; $P$<0.0001). Uniquely, actual eGFR exceeded volume-predicted eGFR only in the zero-ischaemia cohort when compared to other eras (–9.5%, –11%, –0.9% and 4.2%, respectively; $P$<0.001). Positive cancer margins were routinely low at <1%. Urological complications tended to be lower in recent eras ($P$<0.01). Urological complications decreased (11%, 5%, 4% and 5%, respectively; $P$=0.07), including decreased rates of postoperative haemorrhage (8%, 4%, 2% and 0%, respectively; $P$=0.01).

Overall, trifecta outcomes were achieved more commonly in recent eras (45%, 44%, 62% and 68%, respectively, $P$<0.0002). The authors concluded

that trifecta should be a routine goal during PN surgery. Despite increasing tumour complexity, trifecta outcomes of robotic and laparoscopic PN have improved significantly in recent times.

Following PN surgery, ultimate function is determined primarily by kidney volume and quality. Warm ischaemia time (WIT) is also important, and is the primary surgically modifiable factor [2]. The most important technical evolution in the study of Hung *et al.* was the ongoing reduction in WIT from ~30 min in the initial cases, to 0 min more recently. Renal functional outcomes appeared superior in the more recent eras. Despite similar renal volume preservation, acute kidney injury ($P$<0.05), postoperative eGFR ($P$<0.0001) and actual versus predicted eGFR ($P$<0.0001) improved across the eras. With or without adjusting for remnant volume preservation, eGFR outcomes were superior in the most recent zero-ischaemia cohort. Urological complications tended to decrease across the eras ($P$<0.07) despite two important facts: increasing tumour size/complexity and decreased hilar clamping duration. This provides testimony to the increasing sophistication of minimally invasive PN.

Buffi *et al*. proposed a method for reporting composite post-PN outcomes using a margin, ischaemia and complications (MIC) score [3]. Elements included in the MIC score were negative surgical margins, WIT <20 min, and no major postoperative complications. In a preliminary analysis of 99 patients undergoing robotic PN for clinical T1a–T1b tumors (2008–2012), the overall percentage of positive surgical margins (7%), patients with WIT <20 min (17%) and complications (10%) resulted in a calculated MIC score of 76%. The MIC score gradually increased with surgical experience from 67% to 88% in the most recent tertile of patients. Mean pre- and postoperative eGFR was reported only for the overall cohort and not included in the outcomes calculation of the MIC score.

Khalifeh *et al*. explored a hybrid trifecta definition, which was identical to the MIC score, except for a minor difference of WIT <25 min [4]. They reported outcomes of 500 patients undergoing robotic PN (n=261) or laparoscopic PN (n=231) (2002–2012). Patients in the robotic PN group had more baseline morbidity (Charlson Comorbidity Index 3.8 vs. 1.3; $P$<0.001), more complex tumours (RENAL score 6 vs.7.2; $P$<0.001); shorter operating time (170 vs.192 min, $P$<0.001) and WIT (18 vs. 25 min; $P$<0.001), fewer intraoperative (2.6% vs. 5.6%; $P$<0.001) and postoperative (25% vs. 32%; $P$=0.004) complications, and lower positive margin rate (3% vs. 6%; $P$<0.001). Calculated trifecta rate was higher in patients undergoing robotic PN (58% vs. 32%; $P$<0.001). The authors concluded that trifecta outcomes were better achieved by robotic compared to laparoscopic PN.

Efforts towards defining composite outcomes of PN are necessary and clearly represent a step forward. However, any PN trifecta definition should properly address all three paramount issues of PN surgery – negative surgical margins, preserved renal function, no urological complications – and minimise reliance on surrogate parameters. Renal function is a critical outcome parameter of PN. When assessing post-PN functional outcomes, evaluating only the surrogate of WIT is insufficient. Rather, any reporting of post-PN function must report the actual renal function, after correction for preserved renal volume. Therein lies the fundamental shortcoming of the MIC score and the hybrid trifecta definitions: neither address renal function, *per se*, and instead rely on WIT exclusively, assuming it to be the definitive surrogate for functional outcomes. In contrast, Hung *et al*.'s definition of trifecta incorporates actual volume-adjusted functional outcomes. Relying on WIT to serve as surrogate for functional outcomes (as is done by the MIC score and hybrid trifecta definition) represents an over-simplification that is not supported by the literature. Strictly speaking, WIT is not an end-goal of PN surgery *per se*; rather it is a means to an end, that is, preservation of renal function.

The hallmark difference between trifecta and MIC is that MIC does not reflect post-PN renal function, which is a key outcome measure. Contemporary literature indicates that quantity and quality of preserved parenchyma, not WIT, are the most important factors impacting post-PN function [3]. WIT is only one of the important, not necessarily the most important, surgical determinants of post-PN function. Volume of preserved parenchyma, and quality and vascularity of that preserved parenchyma, matter greatly.

Ideally speaking, the goal of PN should be to achieve trifecta outcomes: complete tumour excision and renal functional preservation without urological complications. Going forward, reporting of post-PN outcomes should include precisely measured renal functional outcomes that reflect the quantity and quality of preserved nephrons.

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# XIII. FUTURE DIRECTIONS OF ROBOTIC PARTIAL NEPHRECTOMY

The field in which improvements in robot-assisted partial nephrectomy (RAPN) seem to be of clinical use is augmented reality. Specifically, intraoperative, or more commonly, preoperative imaging is superimposed onto the surgical field of view to improve the safety and accuracy of the surgical procedure. Specifically, augmented reality could be useful in RAPN to ease rapid and accurate anatomical identification of important structures, including major vessels and the renal vasculature. Tumour resection could be optimised to ensure negative surgical margins and maximise nephron preservation [1,2]. There are some preliminary reports in the literature demonstrating the feasibility and potential benefits of augmented reality in RAPN [3,4]. However, image registration (i.e., alignment in a single coordinate system of radiological and operative field images), organ and camera tracking (i.e., synchronous co-alignment of images with organ and camera movements), and compensation for tumour deformation due to cardiorespiratory pattern, pneumoperitoneum, ischaemia, surgical dissection and resection are major challenges at present [1]. However, the available technology is hopefully sufficient to overtake them, if we consider the current standard of flight simulators, video games, or cinematographic special effects.

A variety of lasers, including holmium, thulium, $CO_2$, Green Light and diode lasers, have been tested for tumour excision during RAPN to ease off-clamp RAPN [5–7]. A significant amount of research is ongoing to identify the characteristics of the ideal laser to be used in RAPN [8].

Finally, although the Da Vinci platform is a powerful tool, there is still room for improvement, especially in reducing the size, increasing the flexibility and accuracy of the surgical instruments, incorporating better haptic feedback for the surgeon, and improving visualisation through superimposed ultrasound images of the patient's anatomy onto the surgeon's real-time view through the endoscope [9]. Although still several years away from clinical practice, several other robotic platforms are in development, including the University of Washington Raven II, Titan Medical Amadeus system, SOFAR Telelap ALF-X, and the ARAKNES project. Future developments of these new platforms, as well as of the current Da Vinci system, could revolutionise the way we currently think about RAPN.

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## Committee 6

# Minimally Invasive Reconstructive Surgery

### Chair

*L. Kavoussi (USA)*

*F. Porpiglia (Italy)*

### Members

*G. Bianchi (Italy)*

*G. Chow (USA)*

*M. Gettman (USA)*

*J. Knoedler (USA)*

*C. Komninos (Greece)*

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*A. Tepeler (USA)*

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### III.REFERENCES

# Minimally Invasive Reconstructive Surgery

*L. Kavoussi, F. Porpiglia*

*G. Bianchi, G. Chow, M. Gettman, J. Knoedler, C. Komninos, S. Micali*

*S. Nakada,A. Rane, M. Rani,P. Rao, K. Rha,L. Sinha, A. Tepeler*

## I. INTRODUCTION

Over the last twenty years minimally invasive surgery has broadened indications to include all aspects of urologic surgery. Initially, the approach was limited to diagnostic and ablative procedures, however, with technical advances; more complex surgeries are now amenable to a minimally invasive approach. Today minimally invasive surgery is the preferred route to accomplish reconstructive surgery.

The goal of reconstructive procedures in urology is to correct anatomical and/or functional (congenital or acquired) abnormalities. For decades this was accomplished with an open approach. With the advent of minimally invasive surgery, specifically laparoscopy, there has been a shift away from traditional open surgery. Currently, pyeloplasty, management of ureteral strictures by uretero-ureterostomy, ureteral reimplantation and vescico- and uretero-vaginal fistulas repair are the most common indications of laparoscopic reconstructive procedures. Laparoscopic approach offers advantages in terms of reduced morbidity and superior cosmetic results if compared to open surgery.

Laparoscopy is continuing to evolve secondary to improvements in instrumentation (e.g. ergonomics), and techniques (e.g. laparo-endoscopic single-site surgery, mini-laparoscopy). Unfortunately laparoscopy requires technical acumen (primarily related to suturing) and is therefore limited to centers with such expertise. An enabling sentinel development in the history of minimally invasive reconstructive urological surgery has been the advent of robotic surgery. Since its introduction in the late 1990s, the applications of robotic technology have permitted dissemination of reconstructive surgery. The advantages to surgeons of three-dimensional vision with stabilization of intraoperative images and the suturing facilitated by increased degrees of movement technology have allowed the diffusion of robotic surgery to many urological centers. Currently, robotic assisted reconstructive surgery is an accepted minimally invasive alternative.

This chapter provides an overview of the current indications and techniques in urologic minimally invasive reconstructive surgery. The most common indications such as pyeloplasty, mid-ureteral strictures treatments, ureteral reimplantation and vesico- and uretero-vaginal fistulas repair are presented. For each of these procedures, minimally invasive reconstructive treatments will be presented in detail, including a comparison of approaches as well as an analysis of the current state of the art.

Francesco Porpiglia MD – Torino, Italy

Louis Kavoussi, MD – New York, USA

## A. MI. PYELOPLASTY

## I. INTRODUCTION

Since Anderson and Hynes first described their approach of dismembered pyeloplasty in 1949, the management of ureteropelvic junction (UPJ) obstruction has undergone radical transformation [1]. While open dismembered pyeloplasty has long represented the gold standard for management of UPJ obstruction, the past two decades have seen the advent of minimally invasive pyeloplasty, beginning with the first report of laparoscopic pyeloplasty in 1993 by Schuessler and colleagues [2]. The dramatic reduction in morbidity associated with minimally invasive pyeloplasty and its increased utilisation have led some to deem this the new gold standard [3]. Subsequently, over the past decade, robotic pyeloplasty has seen a dramatic increase, bringing minimally invasive surgery to a broader range of urological surgeons. However, to justify their increased usage over the past two decades, both laparoscopic and robotic pyeloplasty surgeons must adhere to the same rigorous surgical principles and measures of success defined by the open surgery that predates them. The goals of this chapter are to explore the trends in utilisation of minimally invasive pyeloplasty, as well as its associated outcomes, identify the variations in surgical approach, and define the current comparative

effectiveness of laparoscopic and robot-assisted laparoscopic pyeloplasty.

## II. DIAGNOSIS OF UPJ OBSTRUCTION

UPJ obstruction, while commonly congenital and observed as early as during prenatal ultrasound screening, may occur at any time of life. Although often clinically silent, it may present as intermittent flank pain and is often associated with nausea; the so-called Dietl's crisis. Occasionally, patients may present with urinary tract infections, pyelonephritis, haematuria, or simply incidental hydronephrosis noted on imaging performed for other reasons. Once clinical suspicion is aroused, the primary goal of imaging is to determine whether functional obstruction truly exists. Historically, intravenous pyelography (IVP) was the gold-standard diagnostic imaging method **(Figure 1)**. IVP offers the benefit of both a functional and anatomical study, however, its use has waned with the more detailed imaging available. Computed tomography (CT) offers improved anatomical definition, and is often obtained in the acute care setting where patients initially present. Although CT offers excellent anatomical information, its ability to determine functional obstruction is limited. Therefore, perhaps the most frequent diagnostic procedure to confirm obstruction is diuretic renal scanning, such as Tc99m-MAG3 (mercaptoacetyltriglycine) with Lasix (Furosemide) **(Figure 2a,b)**. Delayed drainage of the radiolabelled isotope that is excreted in the urine, filling the renal pelvis, is diagnostic, with a half-life >20 min typically defined as obstruction.

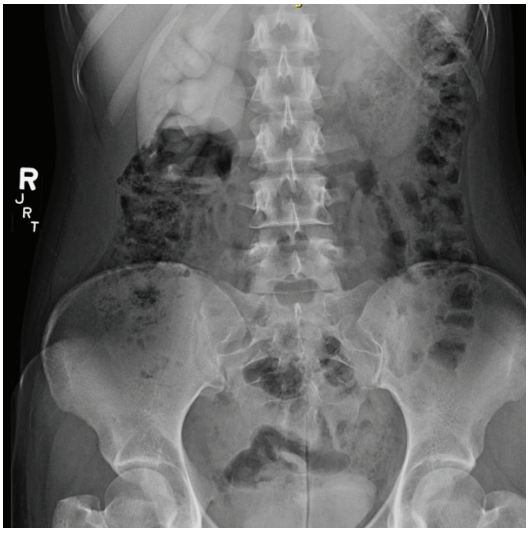


***Figure 1. IVP showing retained contrast on the patient's right and dilation of the renal pelvis with blunting of the calyces.***

The decision to operate for UPJ obstruction may be based on symptomatic obstruction, the presence of renal dysfunction, documentation of obstruction that may lead to renal dysfunction, and the presence of sequelae of obstruction, including infection and stones. The primary goals of surgery include relief of symptoms and preservation of renal function. However, patients should be aware that pain that is present preoperatively may not completely dissipate. Likewise, they should be educated about the risk of continuing renal deterioration, particularly when evidence of dysfunction is present. Finally, they must be informed of the risk of failure of reconstruction, and the possibility of requiring a secondary procedure.

## III. CONTEMPORARY TRENDS OF MINIMALLY INVASIVE PYELOPLASTY

### 1. CONTEMPORARY TRENDS OF PYELOPLASTY IN ADULTS

The past two decades have seen an increasing trend towards minimally invasive surgery, and with it, a dramatic rise in minimally invasive pyeloplasty [4–7]. These shifts in practice have been documented by several studies involving administrative data. Using the Nationwide Inpatient Sample (NIS, USA), Sukumar *et al*. identified a cohort of >29,000 patients and found that the use of minimally invasive pyeloplasty had increased 23-fold, growing from 2.4% in 1998 to 55.3% in 2009, and noted that minimally invasive pyeloplasty was more commonly adopted at urban teaching facilities [7]. Similarly, Jacobs *et al*. found, among a cohort of 3256 patients in the State Inpatient and Ambulatory Surgery Database (Florida, USA) that the rate of minimally invasive pyeloplasty had increased 360% during 2001–2009 [6]. This explosion of minimally invasive surgery has continued as more surgeons recognise the improved morbidity associated with laparoscopy and gain further experience with the procedure. However, within the past decade, this growth has been further hastened by the advent of the Da Vinci Robot (Intuitive Surgical, Sunnyvale, CA, USA). Monn *et al*. found that the number of robot-assisted laparoscopic pyeloplasties had increased since 2008 among the NIS population [4]. Noting that the NIS began recording robotic pyeloplasty as a separate procedure in late 2008, they found a significant increase in the number of pyeloplasties performed, with an increased likelihood of undergoing a robotic procedure at academic centres. Furthermore, they did not find any significant difference in cost compared to that of non-robotic procedures. They identified discrepancies in care, finding that Medicare patients were 46% less likely to undergo a robotic procedure compared to patients with private insurance. Although they did not find any difference in cost among their patients, one may speculate that the expense of robotic pyeloplasty may at least have contributed to this disparity.

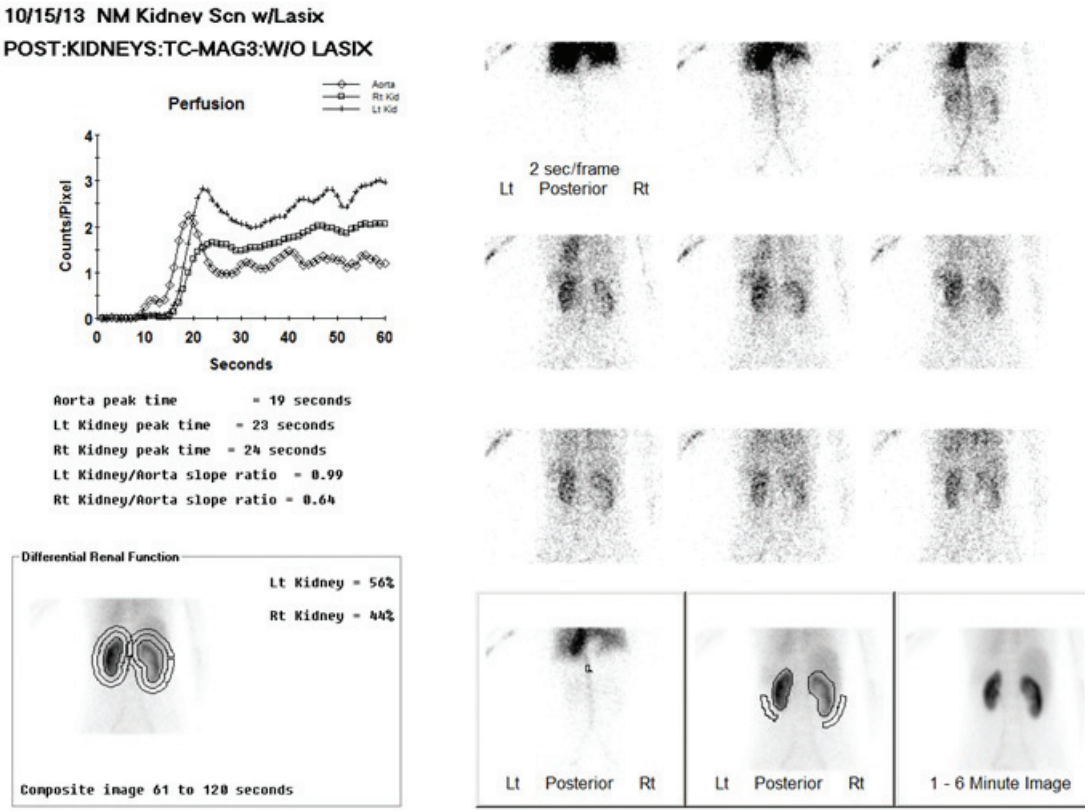


*Figure 2a.*

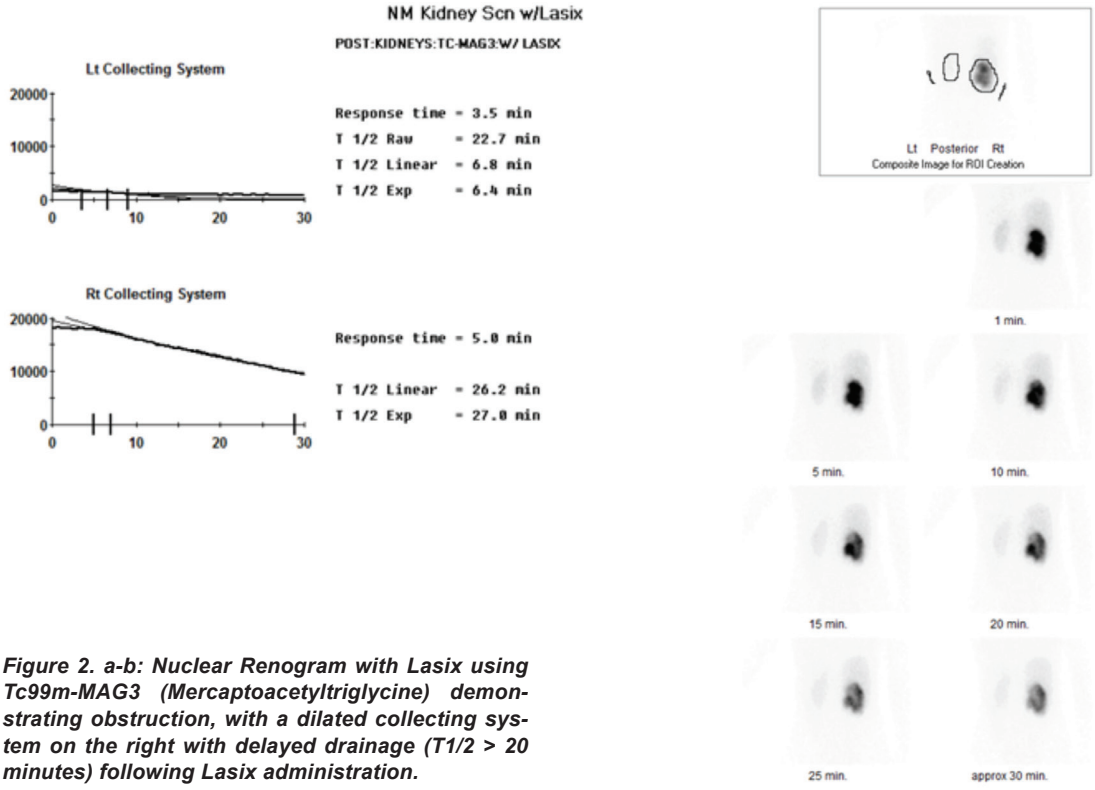


***Figure 2. a-b: Nuclear Renogram with Lasix using Tc99m-MAG3 (Mercaptoacetyltriglycine) demonstrating obstruction, with a dilated collecting system on the right with delayed drainage (T1/2 > 20 minutes) following Lasix administration.***

### 2. CONTEMPORARY TRENDS OF PYELOPLASTY IN THE PAEDIATRIC POPULATION

Over the past two decades the use of laparoscopic pyeloplasty has likewise grown among the paediatric population, although at a more modest pace, and open pyeloplasty still represents a more common procedure within the US [5,8]. Using the Pediatric Health Information Database, Vemulakonda *et al*. identified 2353 paediatric patients undergoing pyeloplasty from 2001 to 2006 [5]. They found that the use of laparoscopic pyeloplasty increased from 2.53% to 9.73%, with the vast majority undergoing open pyeloplasty. Among their population, children undergoing laparoscopic pyeloplasty were significantly older as compared to those undergoing laparoscopic pyeloplasty (8.2 vs. 3.3 years, $P<0.0001$). In comparison, Knoedler *et al*., using the NIS, found a similar age-based utilisation, with older children more likely to undergo laparoscopic pyeloplasty, however, they found a more modest increase in the use of laparoscopic pyeloplasty from 2004 to 2008 of 2.4% to 4.4% ($P=0.22$) [8]. The more modest utilisation of MIP in children may be attributed at least in part to the technical demands of laparoscopic surgery, with the associated steep learning curve, as well as a decrease in the perceived benefit among younger patients. While data are still emerging on the increased use of robotic-assisted laparoscopic pyeloplasty in children, it seems clear that the incidence is rising dramatically, bringing MIP to a broader range of surgeons and patients.

## IV. OUTCOMES FOLLOWING PYELOPLASTY

### 1. OUTCOMES OF PYELOPLASTY IN ADULTS

While laparoscopic pyeloplasty offers the potential for decreased pain and shorter convalescence, it must nonetheless meet the gold standard of success offered by open pyeloplasty. Numerous studies with >100 patients have documented the success of laparoscopic pyeloplasty [9–18]. These series include a combination of transperitoneal and retroperitoneal cases, with reported success rates ranging from 92 to 100%. While these studies seem to document the success of laparoscopic pyeloplasty, leading some to call laparoscopic pyeloplasty the new gold standard [13], the criteria by which successful pyeloplasty is measured are variable.

Successful pyeloplasty may be defined by the resolution of clinical symptoms, improvement of drainage by a variety of imaging techniques, or a combination of the two criteria, and as such, direct comparison of studies can be difficult. Lopez-Pujols *et al*. reviewed a series of 47 cases that defined success according to renal scintigraphy [19]. Defining success as improved drainage on renal scintigraphy, they found an overall objective success rate of 94%, and subjective success rate (improvement of symptoms) of 96%. In comparison, Maynes *et al*. similarly used renal scintigraphy to define success after pyeloplasty and identified a 92% success rate [20]. Alternatively, Pouliot *et al*. categorised success according to strict (half-life <10 min), non-obstructive (half-life <20 min), and technical success (improved half-life) [21]. Among their 111 laparoscopic pyeloplasties, strict success was achieved in only 63%; non-obstructive success and technical success were achieved in 86% and 93%; and clinical success was achieved in 95%. Perhaps most striking, among the patients that were still technically obstructed based on scintigraphic criteria (half-life >20 min), 75% were actually asymptomatic, suggesting that obstruction is often silent in this population, and strongly supporting the need for follow-up imaging.

The duration of follow-up required after laparoscopic pyeloplasty remains controversial. Conventional wisdom has been that pyeloplasty failures occur within 2 years of surgery. However, Madi *et al*. investigated 65 patients who underwent laparoscopic pyeloplasty, and found that among the patients who failed, 30% failed at ≥2 years, reinforcing the need for longer follow-up to avoid late failure [22].

### 2. OUTCOMES OF PAEDIATRIC PYELOPLASTY

Laparoscopic pyeloplasty in paediatric patients has been shown in several case series to be safe and effective, with similar success (92–100%) as in adult series [23–31]. These studies demonstrate that laparoscopic pyeloplasty is feasible, even in children as small as neonates, with appropriate outcomes comparable to their adult counterparts. However, detractors have noted that the perceived benefit of minimally invasive surgery in adults, namely decreased morbidity and associated analgesia, as well as shorter hospital stays, are less significant in children who rebound more rapidly from open surgery. Tanaka *et al*. examined this question in their 2008 study by using data from the Pediatric Health Information System (PHIS) [32]. They found, using multivariate linear regression, that laparoscopy as compared to open surgery decreased analgesia and length of hospitalisation among adolescents (13-19 years) and pre-adolescents (10-12 years), but did not affect children aged <10 years. While the benefits of laparoscopy appear to be most significant among older patients, the perception of benefit among younger patients continues to drive the trend away from open surgery.

### 3. OUTCOMES OF ROBOTIC PYELOPLASTY

The surgical robot has been quickly adopted for minimally invasive pyeloplasty, and brings the challenging skills of laparoscopy to a broader range of surgeons. First described in 2002, it has rapidly gained popularity [33]. Patel *et al*. reported one of the first case-series of significant size, finding 100% success rate at short-term follow-up (11.7 months) [34]. Subsequently, in a series of 92 patients with >39 months

follow-up, Schwentner *et al*. found a success rate of 96.7% [35]. In the largest multi-institutional series to date, Sivaraman and colleagues reported on 168 patients, finding a 97.6% success rate, a 6.6% complication rate, and mean hospital stay of 1.5 days [36]. Therefore, the growing data support robotic pyeloplasty as an effective management for UPJ obstruction, with excellent reported outcomes.

## V. SURGICAL APPROACH – TRANSPERITONEAL, TRANS-MESENTERIC, RETROPERITONEAL, AND ROBOTIC

### 1. TRANSPERITONEAL LAPAROSCOPIC PYELOPLASTY

Transperitoneal laparoscopic pyeloplasty, the original minimally invasive approach to be described [37], represents the gold standard to which all subsequent modifications have been compared. Classically, a stent is placed via cystoscopy prior to laparoscopy, allowing a retrograde pyelogram to assess the ureter. The patient is placed in the lateral decubitus position, access is achieved, and the peritoneum is insufflated with $CO_2$. The ipsilateral colon is reflected along the line of Toldt, and the retroperitoneum entered. The ureter is identified, and followed superiorly to the renal pelvis. With the UPJ identified, the type of repair (e.g., dismembered, or Y-V pyeloplasty) is determined based on patient anatomy, apparent pathology, and surgeon preference. A widely patent reconstruction is performed over an indwelling stent. Based on the foundation of this successful approach, a number of modifications have been made, with the ultimate goals of improving ease of surgery, decreasing surgical time, improving patient convalescence, and preserving outcome.

### 2. TRANSMESENTERIC LAPAROSCOPIC PYELOPLASTY

As an efficient alternative, the transmesenteric approach has been described by Romero *et al*. [9]. Their series included 188 patients undergoing laparoscopic pyeloplasty, with the decision to proceed to transmesenteric pyeloplasty at the surgeon's discretion. Among the selected patients (18/188), surgeons were able to recognise the renal pelvis through the colonic mesentery. This requires a thin mesentery, where a window may be safely created to allow direct access to the UPJ. The authors noted both a shorter operating time as well as faster convalescence for the transmesenteric approach, with 100% success at intermediate follow-up (18–22 months). Due to the required body habitus to visualise the renal pelvis through the mesentery, this approach lends itself to the thin, young patient and may be particularly applicable to paediatric patients.

### 3. RETROPERITONEAL LAPAROSCOPIC PYELOPLASTY

A retroperitoneoscopic approach may also be used, and has both distinct advantages and disadvantages. With the retroperitoneal approach, the surgeon achieves more direct access to the renal pelvis, avoids entering the peritoneal cavity, and potentially minimises pain and shortens recovery. This may be particularly beneficial in patients with prior abdominal surgery, in whom entering the peritoneum may be challenging. However, the approach is foreign to many laparoscopic surgeons, the orientation challenging, and the working space confined. Several studies have reported success ranging from 88 to 100% with a retroperitoneal approach [14,38–48]. Although clearly feasible and safe with reasonable outcomes, the retroperitoneal approach has not become as popular as a traditional anterior approach.

### 4. ROBOT-ASSISTED LAPAROSCOPIC PYELOPLASTY

As first described by Gettman *et al*., robot-assisted laparoscopic pyeloplasty involves three transperitoneal ports (one to allow the robotic camera, and two for robotic instruments), as well as an additional assistant port for retraction, suction, and introduction of sutures [33]. From the basis of this platform, numerous variations have been developed. Similar to laparoscopic pyeloplasty, robot-assisted laparoscopic pyeloplasty may be accomplished through a transperitoneal, transmesenteric or retroperitoneal approach. The degrees of freedom offered from the articulating wrist, as well as the depth perception of the 3D vision associated with the binocular lens, allows a broad range of surgeons to perform minimally invasive pyeloplasty successfully in a safe and effective manner.

### 5. MINI-LAPAROSCOPIC PYELOPLASTY

More recently, publications have advocated mini-laparoscopic pyeloplasty as a means to decrease morbidity and improve cosmesis [49–51]. Porpiglia *et al*. described its application in 2011, using 3-mm instruments and an Anderson–Hynes technique, noting that this approach has typically been restricted to the paediatric population [51]. They noted excellent cosmesis, with barely visible scars postoperatively and 100% success at 12 months after surgery among a small cohort of 10 patients. However, they noted certain limitations, such as impaired visualisation with a 3-mm camera, and the inability to utilise haemostatic clips to control bleeding. Their group subsequently published a retrospective comparison of mini-laparoscopic pyeloplasty and standard laparoscopic pyeloplasty [49]. They found that patients had similar analgesic requirements and functional outcomes, however, the mini-laparoscopic approach resulted in significantly shorter hospital stays and improved patient satisfaction regarding their cosmesis after recovery. Importantly, they noted that one mini-laparoscopic case was converted to standard laparoscopy due to bleeding, highlighting the increased technical difficulty associated with mini-laparoscopic surgery. Nonetheless, mini-laparoscopy represents a viable

approach for pyeloplasty, with potentially improved morbidity and patient satisfaction.

## VI. PLASTY TECHNIQUES

### 1. ANDERSON–HYNES DISMEMBERED PYELOPLASTY

When performing minimally invasive pyeloplasty (whether laparoscopic or robot-assisted laparoscopic), the surgical principles of UPJ reconstruction developed among open surgery continue to apply. Namely, the repair should create a widely patent, watertight, tension-free anastomosis and result in improved functional drainage of the affected renal pelvis. Perhaps the most widely utilised technique for pyeloplasty reported in minimally invasive series is Anderson–Hynes dismembered pyeloplasty, with transection and resection of the diseased segment and widely patent spatulated anastomosis. First described in 1949 for obstruction of a retrocaval ureter, dismembered pyeloplasty represents perhaps the most versatile option for repair, and allows for correction of a wide variety of pathological anatomy, including ureteral transposition in the setting of crossing vessel and renal pelvis reduction for redundant tissue. To perform dismembered pyeloplasty, the ureter and renal pelvis are mobilised, taking care to avoid cautery injury or devascularisation of the tissues. The ureter is spatulated laterally, and the UPJ is spatulated medially after redundant tissue is excised if necessary. If a crossing vessel is found, the ureter may be transposed to correct this, however, the vessel should not be ligated, to avoid devascularisation of a renal segment. A watertight anastomosis is then performed, traditionally over a ureteral stent, and may be accomplished with either interrupted or running absorbable sutures.

### 2. NON-DISMEMBERED PYELOPLASTY: FENGER PLASTY, Y-V PLASTY

In contrast, the non-dismembered pyeloplasty offers a less technically challenging procedure laparoscopically, and so these reconstructions have experienced a resurgence for minimally invasive pyeloplasty. The non-dismembered pyeloplasty offers several advantages to the laparoscopic surgeon. By avoiding complete separation of the ureter, the surgeon is given an extra point to stabilise the ureter for reconstruction. Additionally, the blood flow of the proximal ureter is maintained.

Fenger plasty, originally described in 1900, closes a longitudinal incision of the ureter with a transverse closure, thereby widening the narrowest point, and its use has been described for laparoscopic pyeloplasty among adult and paediatric patients [52–54]. Janetschek *et al*. presented their series of 67 non-dismembered pyeloplasties, with 63 performed as laparoscopic Fenger plasty, with a 98% success rate, noting that a non-dismembered pyeloplasty was preferred at their institution [53]. This is most applicable to short strictures where minimal reconstruction is required, but may not be applicable to longer or more complex repairs.

Y-V plasty has similarly been applied to laparoscopic pyeloplasty as an alternative to dismembered pyeloplasty, and is most applicable to patients with a high insertion into the renal pelvis, absence of long strictures or stenosis, and absence of a crossing vessel. In a retrospective comparison of Anderson–Hynes laparoscopic pyeloplasty versus Y-V pyeloplasty, Szydelko *et al*. found that non-dismembered Y-V plasty resulted in shorter operating times and hospital stays, with similar efficacy [55]. Their group subsequently performed a prospective comparison of the two techniques ($n$=50) and found that there was a trend towards greater success for dismembered pyeloplasty (95% vs. 86%), however, that trend was not significant [56].

With the variety of plasty techniques available, the minimally invasive urologist should be familiar with the varied techniques available to reconstruct the UPJ. While there are strong advocates for dismembered and non-dismembered pyeloplasty, the literature remains divided in terms of the optimal approach. It is notable, however, that with the increased utilisation of robots and the subsequent greater ease of performing the complex manoeuvres required for dismembered pyeloplasty, the impetus to perform non-dismembered pyeloplasty may be lessened.

## VII. MANAGEMENT OF URETERAL STENTING

Minimally invasive pyeloplasty is traditionally performed over a stented anastomosis, with varying techniques used to deploy the stent. The retrograde approach, perhaps most familiar to urologists, involves cystoscopic placement; most commonly immediately preceding the pyeloplasty. This offers the surgeon the opportunity to perform retrograde pyelography and avoids potential difficulty with placing a stent in an antegrade fashion. While familiar and reliable, this requires repositioning of the patient, prolonging operating times, and adding cost. Additionally, the presence of a stent across the UPJ decompresses the renal pelvis, which may make intraoperative identification more challenging, and can interfere with suturing during anastomosis.

As an alternative, antegrade stenting may be performed. A wide variety of techniques have been described to accomplish antegrade stent placement, because placement of an antegrade wire is challenging laparoscopically. Therefore, various authors have created manoeuvres to systematise and simplify the process. For example, Nouira *et al*. described the retrograde placement of a guidewire by cystoscopy

and retrieval of the wire with externalisation through a laparoscopic port and subsequent placement of a stent [57]. Andreoni *et al*. utilised a cholangiography catheter to gain purchase of the ureter [58]. While the wide variety of techniques used to gain access to the ureter and allow antegrade stenting laparoscopically have improved the efficiency of the procedure, perhaps no modification has eased this process as much as the use of robots. With the increased range of motion and control afforded by robot-assisted laparoscopic pyeloplasty, the placement of a guidewire and antegrade stent is fast and reliable. The authors prefer the antegrade placement of a double-J stent over a wire, typically after one half of the anastomosis is completed.

## VIII. MANAGEMENT OF STONES

Patients with UPJ obstruction may additionally present with upper tract stones that mandate concurrent treatment. As the use of laparoscopy has grown, techniques for intraoperative management of stones during pyeloplasty have likewise improved. To date, multiple series have reported success at concurrent pyelolithotomy and pyeloplasty, with reported stone-free success ranging from 75 to 100% [59–66]. Intraoperative pyelolithotomy may be accomplished via direct removal of UPJ stones at the time of pyeloplasty with the assistance of laparoscopic instruments, or intraoperative flexible nephroscopy. Ramakumar *et al*. described their series of intraoperative pyelolithotomy using a flexible cystoscope and a variety of surgical repairs for UPJ obstruction (Anderson–Hynes, Y-V, and Heinecke–Mickulicz) [61]. They removed 1–28 stones in individual patients, and had a resultant stone-free rate of 90% at 3 months, with functional outcomes from pyeloplasty similar to those in the literature. A similar procedure may be accomplished robotically by undocking one arm and guiding the cystoscope into the renal pelvis. However, surgeons should take care to handle the cystoscope gently, because the lack of haptic feedback from the robot makes crush injury to the scope more likely, and results in costly repairs. Additionally, with irrigation of the renal pelvis through the cystoscope at the time of stone removal, the surgeon must take care to avoid spillage of small stones into the retroperitoneum and be diligent in retrieving any stone fragments that escape.

## IX. COMPARATIVE STUDIES IN MINIMALLY INVASIVE PYELOPLASTY

### 1. COMPARISON OF LAPAROSCOPIC VERSUS OPEN PYELOPLASTY

Studies comparing open and laparoscopic pyeloplasty continue to emerge, particularly as increased scrutiny is drawn to surgical cost and outcomes. Although studies have been conducted comparing laparoscopic versus open pyeloplasty in adults and children, most published studies have focused on the paediatric population, where the perceived benefit of minimally invasive surgery may not be as high due to the lower morbidity of open surgery in children [8,67–82]. The majority of these studies were retrospective series, which favoured decreased morbidity and shorter hospital stay for laparoscopic pyeloplasty, with increased operating times.

To date, two randomised controlled trials have compared laparoscopic pyeloplasty with open surgery; one among the adult population and one among paediatric patients [69,82]. Bansal *et al*. prospectively compared 62 patients who underwent pyeloplasty [28 laparoscopic and 34 open) [69]. They found a shorter operating time for laparoscopic compared to open pyeloplasty (mean 122 vs. 244.2 min). However, the laparoscopic group required less analgesia, as measured by diclofenac administration, as well as shorter duration of hospitalisation (mean 3.1 vs. 8.3 days).

While the benefit of laparoscopic surgery is more easily appreciated in the adult population, a debate continues on the value of minimally invasive surgery in children. A recent meta-analysis comparing laparoscopic pyeloplasty to open pyeloplasty in children found that laparoscopy resulted in significantly longer operating times, but shorter hospital stays, with no appreciable difference in outcomes when compared to open surgery [72]. Penn *et al*. have reported the preliminary results of the only published randomised controlled trial among children to date [82]. They compared 20 laparoscopic and 19 open pyeloplasties in children with a mean age 7–8 years. Likewise, they found a trend toward increased operating time for laparoscopic pyeloplasty ($P$=0.09), and shorter hospitalisation that fell short of significance ($P$=0.06), but no perceived difference in analgesia requirement, or overall cost. Perhaps clouding the results thus far may be the difference in benefit among young children (aged <3 years), for whom the benefits of laparoscopy are not as dramatic, and older more muscular children who may derive a benefit more similar to the adult population. In a novel approach, Wang *et al*. evaluated differences in cytokine response following open and laparoscopic pyeloplasty among children, because such a response represents a marker of surgical trauma [83]. They found significantly increased response among patients undergoing open surgery, further substantiating the benefit of laparoscopy.

### 2. COMPARISON OF LAPAROSCOPIC VERSUS ROBOTIC PYLEOPLASTY

The robot has revolutionized the role of minimally invasive pyeloplasty in the treatment of UPJ obstruction. With the degrees of freedom afforded by the surgical arms and the depth perception

offered by 3D visualisation, robotics make the technically challenging procedure of laparoscopic pyeloplasty accessible to a broader range of surgeons. However, the comparative outcomes of robotic versus laparoscopic pyeloplasty continue to emerge. In 2009, Braga *et al*. performed a meta-analysis of studies comparing laparoscopic and robotic pyeloplasty and identified eight appropriate studies [84]. They found that the two procedures offered similar operating times, with no difference in complication rates, however, robotic procedures resulted in significantly shorter hospitalisation. Subsequently, Bird *et al*. reported their comparative series of 98 robotic and 74 laparoscopic pyeloplasties and likewise found similar operating times, complication rates and overall success. In 2012, Lucas *et al*. performed a multi-institutional retrospective comparison of laparoscopic and robotic pyeloplasty that included 759 patients with good follow-up [85]. They found that, on multivariate analysis, previous endopyelotomy or the presence of a crossing vessel increased the risk of needing a secondary procedure, however, there was no difference in the risk associated with undergoing laparoscopic compared to robotic surgery. Cumulatively, the available data support outcomes for robotic pyeloplasty comparable to those of laparoscopic pyeloplasty.

## X. CONCLUSIONS

The past two decades have seen a rapid expansion of minimally invasive surgery for repair of UPJ obstruction. With a large volume of literature available to document the safety and efficacy of laparoscopic and robot-assisted laparoscopic pyeloplasty, a minimally invasive approach may in fact represent a new gold standard. Although minimally invasive pyeloplasty may predominate, its adoption in the paediatric population has been slower. Still, laparoscopic and robotic surgeons have made major inroads, revolutionising pyeloplasty. While adhering to the surgical principles introduced by open pyeloplasty, these procedures offer an improved morbidity to the patient without compromising outcome.

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# B. MANAGEMENT OF MID-URETERAL STRICTURES: ENDOSCOPIC APPROACH AND MINIMALLY INVASIVE SURGICAL TECHNIQUES

## I. INTRODUCTION

Mid-ureteral stricture is defined as a luminal narrowing of the portion of the ureter that extends from the upper to the lower border of the sacrum. If ureteral stricture is left untreated, it results in upper urinary tract obstruction and renal damage [1].

Several factors may contribute to the development of ureteral strictures, including surgical procedures (iatrogenic strictures), stone passage, radiotherapy , penetrating traumatic injuries or idiopathic disorders [2]. Ureteral strictures can be divided into benign or malignant, as well as ischaemic or non-ischaemic. It is of paramount importance to distinguish the cause of ureteral stricture because the management of ureteral strictures varies depending on their aetiology, location and length. Wolf and associates define a stricture as ischaemic when it follows surgery (e.g., hysterectomy) or radiotherapy , whereas the stricture is considered non-ischaemic if it is secondary to stone passage or a congenital abnormality [3]. Ischaemic strictures tend to be associated with fibrosis and scar formation and are thus less likely to respond to endoureterotomy [3]. Malignant strictures are caused by a primary ureteral malignancy or extrinsic mechanical compression by a tumour and are best treated with surgery, indwelling long-term metallic stents, or percutaneous nephrostomy tubes [4].

During recent years, an increasing incidence of iatrogenic strictures has been observed, due to the widespread use of laparoscopy and upper urinary tract endoscopy [5]. Parpala-Sparman *et al*. analysed the data of 72 patients suffering from ureteral injury and reported that most of the injuries were secondary to gynaecological (64%) or general (25%) surgery, while only 11% occurred in association with a urological procedure [5]. Moreover, they announced that ureteral injury was more likely to occur following laparoscopic surgery.

In general, mid-ureteral strictures can be managed by an endoscopic approach **(Table 1)**, or surgical reconstruction, including open or minimally invasive (laparoscopic/robotic) techniques [1] **(Table 2)**. Beiko and Mussari reported the possibility of complete spontaneous self recanalisation in a patient with ureteral injury [6].

Advances in technology have provided new tools to the armamentarium of the endoscopic urological surgeon, while with the spread of laparoscopic training and advancement of robotic technology, minimally invasive surgical ureteral reconstruction is increasing worldwide in popularity and practice [7]. The advantages are negligible scars, less pain, and faster convalescence. In addition, robotic assistance offers some major benefits to urological surgeons when performing this complex procedure, such as instrument flexibility during reconstruction of the ureter, as well as magnified visualisation and tremor elimination.

***Table 1. Main endoscopic approaches***

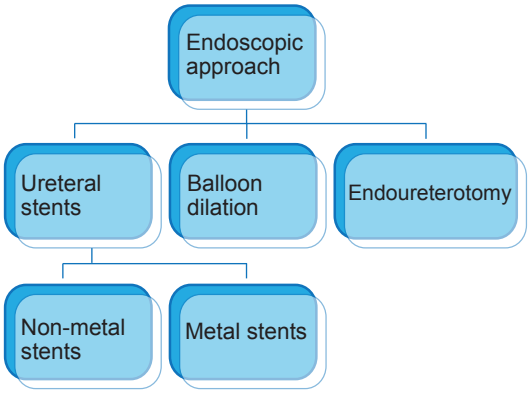
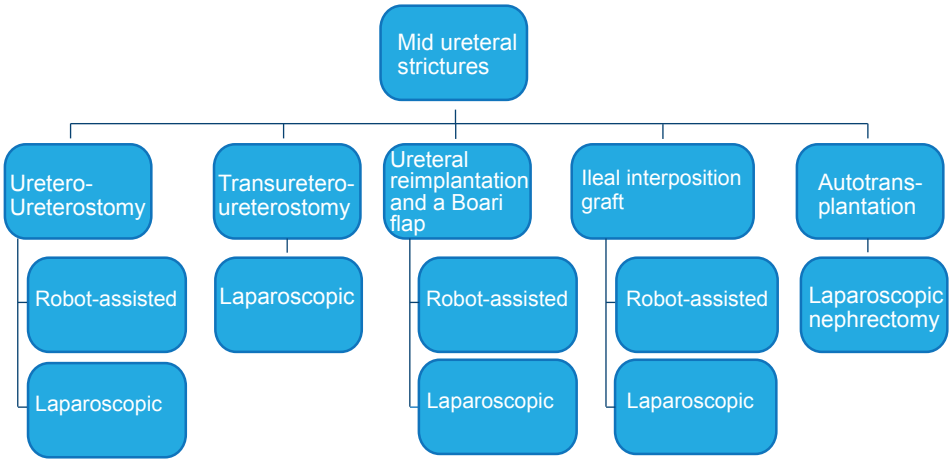



***Table 2. Published minimally invasive reconstruction options for mid-ureteral strictures.***



However, despite the fact that pure laparoscopy and robotics seem to offer important advantages in the treatment of mid-ureteral strictures, only a small number of case series have been published regarding these challenging procedures. Therefore, it is difficult to arrive at a conclusion and produce any recommendations regarding the efficacy and safety of these techniques in the management of mid-ureteral strictures, although all of the studies report comparable results.

A summary of the principal studies on the laparoscopic and robotic management of mid-ureteral strictures is depicted in **Table 3.**

## II. PREOPERATIVE EVALUATION

Patients should be evaluated with urinalysis, urine culture, serum creatinine and electrolytes, renal ultrasound, computed tomography (CT) of the abdomen and pelvis, and diuretic renal scans, in order to determine kidney function and the cause of obstruction. Moreover, a mercaptoacetyltriglycine (MAG3) renal scan provides a baseline for follow-up examinations after surgery. Antegrade pyelography and retrograde pyelography usually provide sufficient information regarding the ureteral anatomy and length of the stricture. Cystoscopy and retrograde pyelography

***Table 3. Published studies on management of mid-ureteral pathological features.***

| Author | Year | No. | Proc | OT (min) | EBL (ml) | LOS (d) | Recur | Follow-up (mo) |
|---|---|---|---|---|---|---|---|---|
| Lee[37] | 2013 | 2 | RUU | 163 | 238 | 3 | 0 | 6 |
| Lee[28] | 2013 | 3 | RUU | 227 | 208 | 2.6 | 1 | 16 |
| Buffi[36] | 2011 | 5 | RUU | 135 | nr | 3 | 0 | 8 |
| Hemal[33] | 2010 | 7 | RUU | 110 | 50 | 3 | 0 | 28 |
| Lee[34] | 2010 | 3 | RUU | 136 | nr | 3 | 0 | 24 |
| Baldie[35] | 2012 | 3 | RUU | 223 | 100 | 1.3 | 0 | 15 |
| | | 1 | RBF | 283 | 300 | 4 | 0 | 2 |
| Simmons[32] | 2007 | 3 | LUU LBF | nr | 86 | 2.6 | 0 | 23 |
| Nezhat[30] | 1998 | 8 | LUU | nr | 100 | nr | 1 | 2-6 |
| Piaggio[39] | 2007 | 3 | LTUU | 263 | 47 | 3 | 0 | 6 |
| Musch[45] | 2013 | 5 | RBF | 287 | nr | 14 | 2 | 14 |
| Castillo[42] | 2013 | 30 | LBF | 161 | 123 | 4.8 | 1 | 32 |
| Yang[46] | 2011 | 2 | RBF | nr | 150 | 5 | 0 | nr |
| | | 1 | RUU | 306 | | 8 | 0 | 20 |
| Schimph[44] | 2008 | 1 | RBF | 172 | 0 | 2 | 0 | 12 |
| Rassweiler[43] | 2007 | 4 | LBF | 253 | 268 | 8 | 0 | nr |
| Wagner[49] | 2008 | 1 | RIIG | 540 | 0 | 5 | 0 | 48 |
| Gill[48] | 2000 | 1 | LIIG | 480 | 200 | 4 | nr | nr |

***LBF, laparoscopic Boari flap; LIIG, laparoscopic ileal interposition graft; nr, not reported; OT, operating time; Proc, procedure; RBF, robot-assisted laparoscopic Boari flap; Recur, recurrence of stricture; RIIG, robot-assisted laparoscopic ileal interposition graft.***

also allow concomitant placement of a ureteral stent, which is preferred by many surgeons. In patients with complete ureteral obstruction that necessitates a nephrostomy tube, antegrade pyelography and retrograde pyelography are simultaneously performed to characterise the ureteral defect. Subsequent ureteroscopy with biopsy and cytology should be carried out in any patient for whom the aetiology of stricture has not been established [2].

## III. ENDOSCOPIC APPROACH

Endourological intervention is considered as the initial management of ureteral strictures because of less invasiveness and shorter operating time, and rapid convalescence, although the general consensus is that endourological techniques do not achieve success rates comparable to those of open or minimally invasive surgery [1]. Available techniques include conventional (non-metal) and metal stent placement, balloon dilatation (retrograde or antegrade), cautery wire balloon incision, and ureteroscopic endoureterotomy [4].

### 1. STENTS

Ureteral stents are inserted when there is a need for temporary or permanent decompression of the upper urinary tract. They are considered as the first option, and convenient to use, especially in cases of ureteral lithiasis. Modifications in design and development of biomaterials have improved the efficacy, durability and patients' tolerability.

#### *a) Conventional (non-metal) stents*

Ureteral stenting is recommended in patients with coexistence of ureteral obstruction and increased comorbidity index. Stent placement can also be performed prior to pelvic radiotherapy or major pelvic surgery. The predictors of renal recoverability show that stenting alone can result in regaining of renal function, as well as in a significant improvement of clinical conditions in such patients [8].

Although retroperitoneal fibrosis, local neoplastic infiltrations, metastatic tumours with simultaneous lymphadenopathy, alteration of the normal position of vessels, gynaecological disorders such as endometriosis can be managed by stent placement, percutaneous drainage may also be considered. However, percutaneous drainage is usually suggested upon impending sepsis, whereas retrograde stenting may be chosen for uncomplicated cases as well as in coagulopathy [9].

Many kinds of ureteral stents are on the market, such as double-pigtal stents, double-J stents, double-coil stents, and stents with different length, loop, diameter, lifetime and purpose. The stents can be placed by retrograde or by antegrade approaches in case of inability to identify the ureteral orifices. Recent advances in guidewire and stent design have led to a significant improvement in success rates [4]. Urgency and urge incontinence, dysuria, lumbar or suprapubic pain, frequency, nocturia, gross haematuria, or a mixture of them seem to be bothersome symptoms affecting quality of life in patients with indwelling stents, while urinary leakage and skin excoriation at the nephrostomy exit site can contribute to poor quality of life after percutaneous nephrostomy placement [4,10]. Significant factors associated with discomfort are a positive urine culture, crossing of the lower end of the stent to the opposite side, caliceal position of the upper coil, and longer stenting duration [11].

#### *b) Metal stents*

Another option in the management of ureteral strictures is the adoption of nitinol alloy metal stents. Metal stents are recommended for long-term use in intrinsic and extrinsic obstruction. Patients with chronic obstructions and previous numerous stent replacements report good tolerability [12].

As an alternative to long-term JJ stenting, Kulkarni and Bellamy reported their experience of 15 patients with ureteric strictures treated with a new nickel–titanium shape-memory alloy stent. This kind of stent has a shaft diameter of 9 Fr and its proximal end expands to 17 Fr by sterile water injection. All patients maintained satisfactory decompression of their upper tracts with no need for re-treatment or stent changes. No stent-related symptoms, for example, pain, sepsis, haematuria or frequency, were noted and no encrustation occurred during follow-up [13]. The same group reported that this stent was better than conventional double-J and other metallic stents in terms of duration and complication-free decompression [14].

Another kind of stent made of nickel–cobalt–chromium–molybdenum alloy is composed of a spiral groove, through which urine flows [4].

Both benign and malignant ureteral obstructions can be treated sufficiently with these metallic stents. In malignant ureteral obstructions, previous radiotherapy constitutes one of the risk factors for stent failure [15].

In case of distal or proximal strictures of the ureter, another option may be adopted. It is a nickel–titanium stent invested with a biocompatible polymer in order to prevent tissue in-growth and encrustation. This kind of stent usually needs a previous balloon dilatation, while replacement may be laboured [4].

A double-layered, coated, self-expandable metallic mesh stent is suggested in patients with malignant ureteral obstructions, and previous polymeric double-J replacements reporting stent malfunctions, polymeric irritations, or severe pain during the changes. This kind of stent has been reported as a

safe and effective option for palliative treatment in this kind of patients [16].

## 2. BALLOON DILATION

Mid-ureteral strictures shorter than 2 cm and with absence of urinary infection can be managed by balloon dilation. This therapeutic option has been proposed as first-choice treatment in patients with short, non-ischaemic ureteral strictures [1,17]. Although balloon dilation is an often-performed procedure in urology, the results are not always definitive, therefore, later dilations or other therapeutic options may be required. The balloon positioning can be performed by an retrograde or antegrade approach. Success rates range from 48 to 88%, with an overall mean of 55%, which is lower than the rate for endoureterotomy [1].

Balloon dilation can be accompanied by cautery wire balloon incision in order to improve the success rate in the treatment of iatrogenic strictures. Seseke and associates reported an overall success rate of 61% in 18 patients with ureteral strictures. Patients with length of stricture <1.5 cm, renal function >25%, and >6 months from the primary surgery to the appearance of the stricture, are suggested as the ideal patients for a successful outcome [18].

### *a) Retrograde approach*

Balloon placement with the retrograde approach is performed if the transureteral approach allows one to reach the stricture area. Usually, retrograde pyelography concomitant with guidewire placement is performed at the beginning. Afterwards, the balloon is inserted and further pyelography is performed in order to check the right positioning. Then, the balloon is inflated and 10 min later the balloon may be deflated and pulled out. Consecutive stent positioning is removed endoscopically after 3–4 weeks.

### *b) Antegrade approach*

Antegrade balloon dilation is more advisable in percutaneous nephrostomy bringer patients or urinary tract infections. Fluoroscopic guidance and stent positioning are used in this procedure.

## 3. ENDOURETEROTOMY

Endoureterotomy is another minimally invasive therapeutic option for the management of mid-ureteral strictures. It can be accomplished by retrograde, antegrade or combined antero-retrograde approach. The retrograde technique is less invasive, thus is more desirable if the set of conditions allows this procedure. The ureteroscope permits direct vision of the stricture, following endoscopic placement of a guidewire. The guidewire positioning across the stricture by fluoroscopic control sometimes is not feasible, so the surgeon should introduce the ureteroscope up to the stricture and afterwards push up the guidewire under direct vision. Cutting modalities for incision of a ureteral stricture include cold knife, cutting electrode knife, and Ho:YAG laser. Direct incision is performed full thickness through the ureter until the retroperitoneal fat is reached. The incision is made posterolaterally for proximal ureteral strictures above the iliac vessels; anteriorly for strictures in the mid-ureter overlying the iliac vessels; or anteromedially for strictures below the iliac vessels to avoid the branches of internal iliac vein and artery, which course lateral to the ureter [1].

Although the site of the stricture has not been shown to influence the results, endoureterotomy performed in mid-ureter for benign strictures seems to be superior in terms of outcome than in distal strictures [4]. Malignant or radiation-induced strictures usually respond poorly to endoureterotomy, due to the ischaemic nature of the stricture.

In 1992, Meretyk *et al*. described endoureterotomy as a safe treatment for ureteral strictures. In 13 patients who were affected by benign ureteral strictures and underwent endoureterotomy followed by balloon dilation, the only single complication was a urinoma, which resolved without surgery [19].

Holmium laser is an efficient procedure for primary treatment in patients affected by ureteral strictures [20]. Gnessin *et al*. reported that 82% of patients who underwent laser endoureterotomy for ureteral strictures were symptom free, and 78.7% were free of radiographic evidence of obstruction after 27 months follow-up. The success rate is higher for non-ischaemic strictures <1 cm long, while stricture length >2 cm is correlated with treatment failure [21,22].

According to Lane *et al*. “Holmium laser is associated with a long-term success rate equivalent to, or better than, other currently available minimally invasive treatment options” [20]. In patients with benign ureteral strictures, YAG-laser endoureterotomy is a recommended procedure, and a safe and minimally invasive therapeutic option [23].

## 4. ENDOMETRIOSIS: ENDOSCOPIC APPROACH

Approximately 15% of premenopausal women are affected by endometriosis. Endometriosis can be located anywhere along the urinary tract including the ureters. It can be a potential problem in terms of renal function if it results in urinary obstruction and impaired renal function. Although surgical resection is the conventional treatment option for intraluminal endometriosis, ureteroscopic management may also be a viable nephron-sparing alternative. Imaging, ureteroscopic and retrograde urography represent the correct follow-up to detect disease recurrence, progression, or both [24].

According to Ting Guo *et al*. “Endoureterotomy with hormonal therapy may not be suitable for ureteral endometriosis due to inadequate cutting and expressional change of estrogen and progesterone receptors” [25].

# IV. MINIMALLY INVASIVE SURGICAL TECHNIQUES

## 1. INDICATIONS FOR LAPAROSCOPIC/ROBOTIC RECONSTRUCTION

The management of iatrogenic ureteral strictures remains challenging, and there is no consensus on optimal strategies. Only small series have adequately reported and detailed this issue. The success of any treatment modality may depend on the length of the ureteral stricture, the cause of the stenosis, and the location of the stricture [2].

Overall, an initial attempt at endoscopic management is indicated in most patients with ureteral strictures, because the potential morbidity and recovery period are generally less with these procedures [3,4]. Additionally, a failed endoscopic procedure does not appear to influence the success of subsequent surgical repair. Although balloon dilation and endoureterotomy for ureteral strictures have high success rates, these do not duplicate the 91–97% rates achieved by surgical repair [18,19].

An indication for the need for ureteral reconstruction is the occurrence of ureteral stricture in a functional kidney. Surgical reconstruction is frequently offered after failed endoscopic management. Repeated endoscopic incisions are more likely to fail, and therefore, surgical repair is recommended. For strictures that develop shortly after external injury or perioperative injury (ischaemic strictures), surgery may be the first choice of treatment. Moreover, strictures >1.5 cm and those associated with radiation or reduced renal function <25% may be managed more appropriately by surgical reconstruction, because of the high failure rate in this group of patients when treated endoscopically [3,26].

Ureteral stricture in a non-functional kidney is an absolute contraindication for ureteral reconstruction. Additionally, history of previous extensive intra-abdominal surgery and morbid obesity are relative contraindications to laparoscopic/robotic ureteral reconstruction, because they may inhibit the ability to establish the operative domain and limit the full range of motion of the instruments [27].

## 2. SURGICAL TECHNIQUES

Various options for surgical reconstruction of mid-ureteral strictures have been reported, including uretero-ureterostomy (UU), transuretero-ureterostomy (TUU) and ureteral reimplantation with a Boari flap [2,27]. The principles of laparoscopic and robotic ureteral reconstruction should not be different from those of open reconstructive urology. Ensuring good vascular supply, complete excision of pathological lesions, good drainage and a wide spatulated, watertight, mucosa-to-mucosa, tension-free anastomosis remain paramount. Defects of 2–3 cm in length may be managed with UU, whereas defects of 12–15 cm may be better managed via TUU or ureteral reimplantation with a Boari flap [27]. Additional length (3–4 cm) can be given by mobilising the ipsilateral kidney and performing a downward nephropexy, with securing the posterior kidney capsule to the psoas fascia, using several absorbable sutures [28]. Care should be taken to avoid injury to the genitofemoral nerve and the femoral nerve in the vicinity when placing the sutures [28].

In case of extensive ureteral strictures, renal autotransplantation or ureteral substitution using the ileum may be required [2].

### *a)* Uretero-ureterostomy

UU is the most common repair performed in the mid-ureter. This approach has been reported in both laparoscopic and robotic studies. The patient is positioned in the dorsal lithotomy and moderate-to-steep Trendelenburg position. The procedural steps consist of mobilisation of the ureter, excision of the diseased segment, spatulation of the ureteral ends, and end-to-end anastomosis by using 4-0 or 5-0 polyglactin sutures, in an interrupted or a running fashion. Spatulation should be carried out at least 5 mm on both the distal and proximal ureteral segment. Particular care should be taken in order to avoid directly grasping or applying monopolar cautery to the ureter, to preserve the periureteric mesentery and blood supply. After completion of the posterior portion of the anastomosis, a double pigtail stent must be introduced through the ureter, across the anastomosis, cephalic into the renal pelvis and caudally into the bladder. A peritoneal or omental flap may be wrapped around the completed anastomosis, so as to maximise the ureteral blood supply and enhance postoperative healing. In case of difficulties in identifying the ureter, it is suggested first to identify a healthy segment of the ureter and then to trace the ureter circumferentially toward the diseased segment. Concomitant downward nephropexy may assist in achieving a tension-free anastomosis [28].

Contraindications to performing UU are long ureteral strictures, which do not allow a tension-free end-to-end anastomosis.

Nezhat *et al*. reported the first successful laparoscopic UU (LUU) for an obstructed ureter due to endometriosis in 1992 [29]. The same group, 6 years later retrospectively analysed the data of eight patients who had undergone LUU and reported that seven were found to have patent anastomosis after short-term follow-up of 6 months [30].

In a review of all published LUU reports from 1990 to 2006, De Cicco and colleagues suggested that recurrence following LUU was comparable to that after the open procedure [31]. However, the authors reported that the published data are scant and heterogeneous and do not permit firm conclusions [31].

In 2007, Simmons *et al*. described their experience with laparoscopic ureteral reconstruction in patients with benign ureteral stricture. The authors retrospectively compared laparoscopic versus open procedures and reported that the open group had greater estimated blood loss (EBL) and longer length of stay (LOS), while there was no difference in the patency success between the two groups (almost 100%). [32]

Hemal and associates, retrospectively analyzed the data of seven patients who had undergone robot-assisted UU (RUU) and reported that the operative success was excellent after an average follow-up of 28 months [33]. The mean operating time was 110 min, mean EBL was 50 ml, mean LOS was 3 days, and there was no surgical complications or recurrence of ureteral strictures. These results were also supported by Lee *et al*. in a case series of three adults with >2 years follow-up [34].

In a large single-institution study, Baldie and associates compared robotic mid-ureteral reconstruction with pure laparoscopic ureteral reconstruction, and reported similar short-term results [35]. Additionally, they observed that patients who had been treated with UU had shorter operating time and LOS compared to those who had undergone ureteral re-implantation. One patient in the robot-assisted group developed a recurrent stricture that was treated by balloon dilatation.

Overall, despite the relatively limited number of patients and studies available, these reports demonstrate that LUU and RUU are safe and have comparable outcomes to the open approach.

In the robotic setting, the intraoperative localisation of ureteral stricture can be particularly difficult, due to the lack of tactile feedback. Thus, various techniques have been described in an effort to overcome this limitation. One such technique is the injection of normal saline through a preoperatively placed ureteral catheter, and subsequent hydronephrosis has been reported to facilitate identification of the stricture location [35].

Buffi *et al*. described a novel technique for the precise definition of the site and extension of the stricture by using a flexible ureterorenoscope [36]. According to this technique, a double surgical approach with robot-assisted laparoscopic access and flexible ureterenoscopy was performed. After the laparoendoscopic identification of the ureter, a flexible ureterorenoscope was inserted into the ureter over a previously placed guidewire. Once they had reached the ureteral stenosis, the laparoendoscopic light was lowered and the ureter was transilluminated to identify the stricture by laparoscopic and endoscopic imaging. The stenotic ureter was excised at the level of the lower edge and the ureter was opened on the upper part to identify all stenotic segments and healthy tissue. The authors reported that this technique was feasible in all five patients who underwent RUU, with no significant complications, acceptable operating time and no ureteral stricture recurrences after 8 months follow-up. The limitation of this method is that only the lower margin of the stricture can be localised during the procedure.

Lee *et al*. presented an interesting technique for intraoperative localisation of ureteral strictures during RUU using indocyanine green visualisation under near-infrared light [37]. The authors inserted preoperatively a 6 Fr ureteral catheter and then intraoperatively they used the catheter to inject 10 ml of diluted indocyanine green above and below the level of the stenosis. The absence or decreased fluorescence of the diseased ureter clearly delineated the upper and lower margins of the ureteral stricture. Postoperatively, all cases were clinically successful after 6 months follow-up.

***b) Transuretero-ureterostomy***

Extensive strictures of the mid-ureter in combination with a low bladder capacity may be treated with TUU. After ligation of the distal ureteral portion, the proximal end (donor ureter) is transposed across the midline through a retroperitoneal tunnel, created with blunt dissection and anastomosed to the contralateral ureter (recipient ureter). Only the portion of the recipient ureter needed for the anastomosis is exposed in order to preserve the periureteral tissue and avoid vascular damage. A longitudinal ureterotomy at the medial aspect of the recipient ureter is performed to match the lumen of the donor ureter. The anastomosis is carried out with running 5-0 or 6-0 absorbable monofilament sutures. A double-J ureteral stent is usually passed from the donor renal pelvis, through the anastomosis, and into the bladder.

Generally, the accepting ureter must be unobstructed and not affected by any disease process that will put both kidneys at risk postoperatively. The insufficient length of the donor ureter (proximal stricture) to reach the contralateral ureter is the only absolute contraindication. TUU is also contraindicated for retroperitoneal fibrosis, upper tract transitional cell carcinoma, and for patients with recurrent nephrolithiasis. The obvious disadvantage of this procedure is the involvement of the contralateral normal kidney and ureter. Reflux to the recipient ureter, if present, should be identified preoperatively with a voiding cystography and corrected simultaneously [2].

The laparoscopic feasibility of the procedure was initially demonstrated in swans with eight out of nine procedures successfully completed and the failure due to an anastomotic stricture in one bird [38].

In 2007, Piaggio and Gonzalez described their initial experience regarding transperitoneal laparoscopic transuretero-ureterostomy (TLUU) in humans [39]. The authors applied this technique in three children. Mean operating time, EBL and LOS

were 263 min, 47 ml, and 3 days, respectively. Postoperative course was uneventful except for immediate postoperative urinary leakage in one case, which was resolved in <24 h. None of the patients developed recurrent stricture after a mean follow-up of 6 months.

***c) Boari flap***

The Boari flap technique is performed in long ureteral obstructed segments with a subsequent large ureteral defect following excision of the stricture. The main principle is to bridge the large gap with a tabularised L-shaped bladder flap. Therefore, the bladder is mobilised, and an anterior bladder flap is created with an apex of ~2 cm and a base of ~4 cm, beginning ~2 cm distal from the bladder neck and extending to the ipsilateral posterior dome [40]. The flap length should be 3–4 cm longer than the estimated ureteral defect if a non-refluxing anastomosis is planned. Additionally, the ratio of flap length to base width should not be greater than 3:1 to avoid flap ischaemia [2]. Afterwards, the apex of the flap is anastomosed to the spatulated ureter using an interrupted 4-0 polyglactin suture.

Typically, the Boari flap is accompanied with fixation of the bladder dome to the ipsilateral psoas tendon to decrease tension and stabilise the bladder. Several absorbable sutures are placed in a direction parallel to the genitofemoral nerve to avoid its entrapment. The superior and mid-vesical arteries on the contralateral side may need to be ligated in order to provide additional mobility.

A small bladder capacity is likely to be associated with inadequate Boari flap creation, warranting consideration in the preoperative surgical planning [2].

The Boari flap was initially described in humans in 1947 [41]. In 2001, Fugita and associates were the first to describe three cases with long ureteral obstruction that underwent laparoscopic Boari flap procedures [40]. The procedures were successfully performed in all patients, without any complications. The mean follow-up time was 11 months and no stricture recurrence was observed.

In 2005, Castillo *et al*. reported the outcomes of 30 patients who were treated with laparoscopic Boari flap in a multi-institutional study [42]. The mean length of ureteral resection was 7 cm (range: 5–20 cm), mean operating time was 161 min, and severe complications occurred in three patients. The overall success rate was 96%, with a mean follow-up of 32 months.

More recently, Rassweiler and colleagues compared the outcomes of four patients who were treated by laparoscopic Boari flap with two patients who underwent open Boari flap reconstruction for similar pathology [43]. The authors reported that although operating time was longer in the laparoscopic group (253 vs. 220 min), EBL was lower (268 vs. 725 ml) and LOS was shorter (8 vs. 17 days). Success rate was 100% after laparoscopy.

Schimpf and Wagner were the first to report robotic Boari flap creation in a 75-year-old woman with an iatrogenic stricture, and additional series have been reported since then [44–46]. The operating time was 172 min and LOS was 2 days, with no recurrence after 12 months follow-up [44].

In general, most of the studies have demonstrated that combined vesico-psoas hitch with Boari flap is safe, with a high success rate, short hospitalisation, and few complications for the treatment of wide ureteral defects in the mid-third of the ureter.

***d) Ileal interposition graft***

Reconstruction of long-segment ureteral strictures is possible using a segment of the intestines, usually the ileum. Incorporation of the ileum in ureteral repair is reserved only for selective cases in which a defect cannot be bridged by other methods, or the bladder is unsuitable for reconstruction. An appropriate segment of the ileum is delivered to the retroperitoneum via a small window in the colonic mesentery. The ileum is anastomosed to the renal pelvis or proximal ureter in an end-to-side, single-layer technique with a running or interrupted Vicryl suture (4-0 or 5-0), in an isoperistaltic orientation between the renal pelvis and bladder, for adequate urine transport. Ileocystostomy is usually performed in a double-layered technique on the posterior bladder wall at 1–2 cm craniolaterally to the native ureteral orifice, to avoid extensive angulation and possible obstruction of the ileum during bladder filling. To avoid metabolic problems, the length of the ileal segment should be as short as possible and ≥15 cm from the ileocecal valve.

Contraindications for ileal ureteral substitution are baseline renal insufficiency with serum creatinine >2 mg/dl, bladder dysfunction, inflammatory bowel disease, or radiation enteritis.

Follow-up should include serum chemistry to diagnose hyperchloraemic metabolic acidosis [47].

Gill *et al*. reported successful laparoscopic ileal ureter replacement in an 87-year-old man with upper tract transitional cell carcinoma. An extracorporeal bowel anastomosis was performed. Total operating time was 8 h, EBL was 200 ml and LOS was 4 days [48].

More recently, Wagner and associates reported their experience in robot-assisted laparoscopic ileal ureter replacement in a patient with recurrent ureteral strictures due to cysteine stones [49]. Total operating time was 9 h, with negligible blood loss. The patient was discharged home on postoperative day 5 and did not experience any complications after 4 years follow-up.

***e) Autotransplantation***

Autotransplantation of the kidney is recommended in patients with extensive ureteral strictures and an absent or poorly functioning contralateral kidney. It can also be considered in cases in which ureteral substitution or repair is not feasible. The kidney is harvested laparoscopically or openly with maximal renal vessel length. Subsequently, the renal vessels are anastomosed to the iliac vessels using open surgical techniques and ureteral re-implantation is carried out. Nephrectomy can be performed laparoscopically, providing reduced postoperative analgesic need and faster recovery compared to the open techniques [2].

## V. POSTOPERATIVE FOLLOW UP

The drain should be removed when its output is low and the drain creatinine level suggests no urine leakage. The urethral catheter should be left in place for 5–7 days in case of bladder incision, while 1–2 days are sufficient if UU has been performed. Some authors suggest performing cystography before catheter removal [36].

The optimal duration for stenting is still undetermined. The rationale for the use of stents after ureteral reconstruction is to promote ureteral healing, prevent extravasation of urine, and avoid re-stricture. However, if left for a long period of time, stents can cause inflammation that may prevent adequate healing or promote formation of hyperplastic muscle or scar tissue. Kerbl *et al*. found no difference in the healing of ureteral strictures regardless of whether a 1-, 3-, or 6-week period of stenting was selected [50]. Most authors recommend removing the ureteral stent at 4–6 weeks after the procedure.

Diuretic renal scintigraphy should be performed ≥3 months postoperatively to assess the patency of the repair [27] The most significant long-term risk associated with the surgical repair of ureteral strictures is recurrent obstruction. Therefore, all patients should undergo evaluation of the upper urinary tract every 6 months after surgery and probably up to 1–2 years. Recurrent strictures can be initially managed by balloon dilation and/or endoureterotomy, before resorting to surgical revision.

## VI. CONCLUSIONS

Endourological techniques have improved our ability to treat ureteral strictures without the need for open or minimally invasive surgery in most patients. However, the success rate cannot reach the rates achieved with surgical techniques. Endoureterotomy may be considered as the first option for intrinsic benign strictures, while malignant and radiation-induced strictures are possibly best treated with long-term metal stents. Although ureteral reconstruction is increasingly being performed through minimally invasive approaches, the clinical experience with laparoscopic and robot-assisted laparoscopic ureteral reconstruction and ileal ureteral substitution is still limited worldwide. Management of ureteral strictures by pure laparoscopy is technically demanding, but robots solve many of the technical complexities that are prohibitive in laparoscopic surgery, especially the intracorporeal suturing and knot tying for reconstruction. Despite the limited data regarding the results of the treatment of mid-ureteral strictures by minimally invasive surgical approaches, most of the studies demonstrate equivalent success rates between laparoscopic, robot-assisted and open techniques. The most important factors responsible for achieving the best outcome include selection of the most appropriate surgical technique, based on the history, location and length of stricture, as well as accomplishment of a tension-free anastomosis using well-vascularised ureteral tissue.

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# C. MI. URETERAL REIMPLANTATION

## I. INTRODUCTION AND AETIOLOGY

The term of ureteral re-implantation describes the re-implantation of ureter in the bladder with bypass of the obstructed distal segment. It is generally performed on patients with benign ureteral diseases, such as distal ureteral obstruction related to radiation, stricture or fibrosis, and iatrogenic reasons such as uro-gynaecological pelvic surgery and malignant conditions such as urothelial cancer. In addition, ureteral re-implantation is performed in the presence of vesicoureteral reflux, leading to recurrent urinary tract infection and renal scarring in paediatric patients.

## II. SURGICAL TREATMENT

The decision about the surgical technique is based on the aetiology, length and location of the stricture, capacity of the bladder, and experience of the surgeon. The procedure may become more complicated as the length of stricture increases.

### 1. SURGICAL TECHNIQUE

Boari flap, transuretero-ureterostomy, ileal ureteral substitution and autotransplantation are considered as treatment alternatives based on the length of the effected segment. While ureteroneocystostomy is generally done for defects <5 cm, larger defects (6–10 cm) are generally treated with psoas hitch and/or Boari flap. Boari flap could be used for longer defects up to 15 cm. However, additional procedures should be done for defects >15 cm. In all of these techniques, the main principles of the surgery are preservation of vascular supply, adequate ureteral mobilisation, generous bladder mobilisation with preservation of blood supply, and to provide a tension-free and watertight anastomosis [1]. Clipping of the proximal and distal ureter to prevent spillage, pelvic lymphadenectomy and frozen sections from distal and proximal parts are critical for patients with urothelial cancer.

### 2. MINIMALLY INVASIVE METHODS

Minimally invasive methods decrease postoperative pain and morbidity, shorten the convalescence period and lead to good cosmetic results. Laparoscopic surgery has been used as an alternative to open surgery for ureteral reconstruction and implantation. In recent years, robotic surgery, which has benefits of improved dexterity, better suturing and knotting skills, and 3D imaging has been used for reconstructive urology.

#### *a) Laparoscopic ureteral re-implantation*

Although laparoscopic surgery has become the standard of care for many ablative procedures, it has not received the same enthusiasm for reconstructive surgery. The requirement of more surgical skill in a limited space is regarded as one of the limitations of laparoscopic ureteral re-implantation.

Laparoscopic ureteral re-implantation was initially reported in 1992 [2,3]. This involved resection of the right distal ureter and re-implantation to the bladder during laparoscopic excision of extensive endometriosis. After demonstrating the feasibility of laparoscopic ureteral re-implantation in animal models, the first series in a paediatric population was reported by Ehrlich *et al*. in 1994 [4,5]. They reported two cases treated with the laparoscopic Lich–Gregior technique, with a mean operating time of 200 min. The patients were discharged after a mean 23 h hospitalisation, with decreased postoperative pain. In the following years, laparoscopic re-implantation has been performed by other experts [6,7]. Janetschek *et al*. concluded that the laparoscopic Lich–Gregoir procedure did not offer any advantage over open surgery [7].

With the refinements in surgical technique and increased experience in laparoscopic surgery, larger studies of laparoscopic re-implantation were published. In 2000, Gill and colleagues succeeded in performing ileal ureteral substitution in a patient with solitary kidney and ureteral tumour [8]. The feasibility of laparoscopic ureteral re-implantation using a Boari flap was initially presented in a porcine model [9]. Subsequently, Fugita *et al*. published three case series with distal ureteral obstruction treated with laparoscopic Boari flap [10]. They did not observe any complications during long-term follow-up.

Simmons and colleagues compared the outcomes of their laparoscopic and open uretero-ureterostomy, uretero-neocystostomy (UNC), and Boari flap procedures performed [1]. They performed open surgery in 34 cases and laparoscopic surgery in 12. The other measures such as ureteral balloon dilation, ureteroscopic holmium laser stricture incision, and prolonged ureteral stenting failed in all patients. The patients with ureteral obstruction related to transitional cell carcinoma and iatrogenic ureteral injuries requiring urgent repair were excluded from the study. Distribution of the procedures and patient demographics were similar in the laparoscopy and open surgery groups. Blood loss and hospital stay were significantly lower in the laparoscopy group. The complication rate was similar (14.7% for open surgery and 8.3% for laparoscopy group). The authors suggested that laparoscopic surgery has the advantage of magnified visualisation of mucosal edges for reliable assessment of tissue quality and viability. However, data about the duration of the operation were not reported.

In another study comparing open and laparoscopic ureteral re-implantation in patients with similar stricture lengths, blood loss, analgesic requirement, hospital stay, and convalescence period were in favour of the laparoscopy group [11]. However, the operating time was significantly shorter in the open surgery group. The authors suggested that the operating time showed a progressive decline with increased experience in laparoscopy.

The largest study of laparoscopic ureteral re-implantation was reported by Seideman *et al*. [12]. Iatrogenic ureteral stricture related to prior gynaecological surgery (23%), pelvic mass (24%), distal ureteral transitional cell carcinoma (11%), stone disease (9%), congenital ureteral strictures (9%), and unknown cause (13%) were the aetiological factors detected in 45 patients. Re-implantation (*n*=22), re-implantation with Boari flap (*n*=16), distal ureterectomy + re-implantation (*n*=2), and distal ureterectomy + re-implantation + Boari flap (*n*=2) were done using a laparoscopic approach. They used a simplified modified Boari flap technique known as the dome advancement technique that allows smaller detrusor incision, less dissection, and shorter operating time [13]. All procedures were completed without open conversion and with a median blood loss of 150 ml. The patients were discharged after mean hospitalisation of 3 days. Postoperative complications were ileus, *Clostridium difficile* colitis, ileus, and respiratory distress. In the follow-up period, two patients with recurrent/persistent stricture were treated with endoureterotomy and ileal interposition. In this series, re-implantation was done in a refluxing manner in all cases. The authors advocate that non-refluxing anastomosis requires longer ureteral length, more surgical skill, and additional operating time. It is reported that refluxing anastomosis does not lead to complications related to reflux [14]. The authors concluded that laparoscopic re-implantation is a safe and effective procedure with high success and low morbidity rates for distal ureteral stricture. The main limitation of the technique is the requirement for advanced surgical skill in suturing and knot tying.

#### 1. Technique in paediatric population

Laparoscopic ureteral re-implantation in paediatric patients with vesicoureteral reflux has been described for both intravesical and extravesical approaches. In 2001, Gill *et al.* described the laparoscopic transvesical ureteral re-implantation technique [15]. The laparoscopic intravesical approach is technically more challenging because of the limited capacity of the bladder. In a study of 32 children treated with laparoscopic transvesical re-implantation, the success rates for vesicoureteral reflux and obstructing mega-ureter were reported as 92.6% and 80%, respectively [16]. The authors emphasised that the procedure is more complicated in patients aged ≤2 years with bladder capacity <130 ml.

With refinement of the extravesical technique, excellent outcomes comparable to those of open surgery were achieved [17]. The main advantages are reduced postoperative discomfort and recovery period. The risk of newly developed voiding dysfunction that can be up to 10% is regarded as the disadvantage of the technique [17].

#### 2. Conclusion

Based primarily on level 3 and 4 evidence, laparoscopic ureteral re-implantation is a feasible and effective minimally invasive technique for benign or malignant conditions of the distal ureter in experienced and specialised centres for laparoscopic surgery. It has the advantages of short hospitalisation and convalescence period and less morbidity compared to open surgery. The steep learning curve and requirement for advanced laparoscopic skill are its main limitations.

### *b) Robotic ureteral re-implantation*

Since the introduction of the Da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) robotics has gained widespread usage for radical prostatectomy. The outcomes of radical prostatectomy have highlighted the advantages of robots especially for the reconstructive part of the procedure.

#### 1. Superiority of the robot

The main advantages of robotic surgery compared to conventional laparoscopic techniques are magnified 3D imaging, image stabilisation, and EndoWrist suturing technology that facilitates reconstructive surgery and the ergonomic set-up of the operation. As a result of this superiority, many reconstructive procedures have been performed robotically by experts. Robotic pyleoplasty, the most common reconstructive surgery, underlines these benefits. Thus robotic surgery has been used for other more sophisticated reconstructive surgery.

#### 2. Robotic ureteral re-implantation in the literature

Yohannes and colleagues reported the first case of robotic UNC for distal ureteral stenosis in 2003 [18]. In the following year, Dinclenc *et al*. published a case in which ureteral injury occurred during robotic radical prostatectomy, which was treated with ureteral re-implantation in the same session [19]. Robot-assisted ureteral re-implantation and the psoas hitch technique have been presented in case reports [20,21].

Do *et al*. presented the outcomes of eight patients with distal ureteral stricture treated with robot-assisted ureteral re-implantation using the Boari flap technique, with the use of four robotic arms and five tocars [22]. They implanted the spatulated ureter to the apex of the Boari flap with the conventional Politano and Leadbetter technique. The mean operating time was 171.9 min and blood loss

was 161.3 ml. They observed anastomotic leakage in one case treated with prolonged catheterisation. Kozinn and colleagues compared the outcomes of robotic ureteral reconstruction (*n*=10) with those in an age-matched control group (*n*=24) treated with open surgery [23]. The aetiology of the stricture was benign, including iatrogenic injury, stone disease, infection, and idiopathic disease in both groups. The demographics of the groups (age, body mass index, and side and stricture length) were similar. Although operating time was shorter in the open surgery arm, blood loss, hospital stay, and postoperative analgesic requirement were lower in the robotic arm. Stricture recurrence was not detected during follow-up in either group.

Schimpf *et al*. reported 11 patients with benign (recurrent stricture, hutch diverticulum, and iatrogenic ureteral stricture) and malignant (ureteral cancer) disease managed with robot-assisted laparoscopic surgery [24]. Mean operating time and hospitalisation were 189 min and 2.4 days, respectively. External iliac vein injury occurred during ureteral dissection and was repaired with no need for open conversion. The other complications were haematuria controlled with fulguration and ileus managed with no intervention. In a study of the outcomes of robot-assisted laparoscopic ureteral re-implantation of 10 cases of ureteral stricture and two of ureterovaginal fistula, mean blood loss was 48 ml [25]. Operating and hospitalisation time were 208 min and 4.3 days, respectively. After a mean 15.5 months follow-up, no recurrence was observed.

Baldie *et al*. retrospectively compared the outcomes of 16 patients who underwent robotic mid-ureteral (3 with uretero-ureterostomy) and distal ureteral repair (13 with ureteral re-implantation) with those of six patients treated with laparoscopic ureteral re-implantation [26]. In the robotic surgery group, 10 patients had a history of open abdominopelvic surgery. Operating time, blood loss, hospitalisation time, and success rate were similar in both groups. In the robotic surgery group, unrecognised enterotomy necessitating surgical treatment occurred in a patient with a history of two laparotomies and failed open stricture repair. In another patient, enterotomy was managed in the same session. In the robotic surgery group, open conversion was required in two cases. In the laparoscopy group, open conversion was required in one patient. The increased operating time, blood loss and complication rate were attributed to dense adhesions related to previous surgery and failed open repair.

Musch *et al*. published the largest single-institution series of 16 patients treated with robotic reconstruction of the distal ureter [27]. The mean operating time was increased in four patients with distal urothelial carcinoma as a result of additional pelvic lymphadenectomy, compared with 12 patients whose distal ureteral stricture was associated with benign conditions (320 vs. 250 min, respectively). The mean hospital stay was 7.5 days. Open conversion was required in a patient with massive peritoneal adhesions related to pancreatectomy. Postoperative complications were observed in 12 patients (10 minor and 2 major). The major complications were silent myocardial infarction and bladder wall insufficiency with urinary leakage and peritonitis. A patient with symptomatic hydronephrosis related to anastomotic stricture was treated with endoscopic laser incision. According the authors, one of the drawbacks of robotic surgery is the use of the transperitoneal route, which has a risk of postoperative ileus and peritoneal urinary leakage. The authors concluded that robotic surgery will replace conventional laparoscopy in reconstructive surgery of the distal ureter.

The largest multi-institutional series reported by Hemal and colleagues included 18 cases of robotic re-implantation of the distal ureter [28]. A total of 44 cases with upper and lower benign and malignant ureteral conditions were enrolled. The mean operating time and hospital stay were 137.9 min and 2.4 days, respectively. The mean blood loss was 98.2 ml. Minor complications were observed in two patients and treated medically. After a mean 13.3 months follow-up, stricture recurrence was not detected in any of the patients.

#### 3. Technique in paediatric population

Robot-assisted ureteral re-implantation for treatment of children with vesicoureteral reflux has been performed using extravesical or intravesical approaches. Although the operating time was longer, robotic surgery was superior to open surgery, with decreased hospitalisation and analgesic requirement [29]. However, other studies have presented similar success rates for open and robotic surgery [29,30]. The magnified 3D technology of robotic procedures provides visualisation of the pelvic plexus, and delicate dissection, with minimal nerve disruption, that is essential for prevention of postoperative *de novo* voiding dysfunction [31]. In a study of the outcomes of 150 patients treated with bilateral extravesical robot-assisted laparoscopic ureteral re-implantation, success was achieved in 99.3 % of patients. The authors did not observe any *de novo* voiding dysfunction in any patients [31].

## III. FOLLOW-UP AND TREATMENT OF COMPLICATIONS

Infectious complications including peritonitis, pyelonephritis and sepsis, and complications related to the anastomosis including urinary leakage, urinoma and anastomotic stricture, and ileus can be seen after surgery. Although infectious complications are treated medically, urinoma and urine leakage are generally treated with additional measures such as drainage or catheter insertion. Postopera-

tive contrast studies are essential for evaluation of renal function and integrity of the anastomosis. The stricture generally occurs within the first year after surgery. Extensive surgery (ureteral re-implantation or ileal interposition) may be required for patients with recurrent anastomosis stricture, despite treatment with minimally invasive methods such as balloon dilation and endoureterotomy.

## IV. CONCLUSION

Level 3 and 4 evidence shows that laparoscopic and robotic ureteral re-implantation is safe and effective in the hands of experienced robotic surgeons. Specifically, there is evidence that operating times and hospital stay are competitive with standard approaches, and analgesic utilisation is decreased in the minimally invasive groups. The numbers of cases reported are low in both groups, and prospective randomised trials are warranted.

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# D. MINIMALLY INVASIVE SURGERY FOR VESICOVAGINAL AND URETEROVAGINAL FISTULAE

## I. VESICOVAGINAL FISTULA

### 1. INTRODUCTION

Vesicovaginal fistula (VVF) is the most common acquired urinary fistula. It is associated with prolonged morbidity and adverse psychological health. The most frequent cause in developed countries is as a complication of gynaecological surgery, and in developing countries, prolonged obstructed labour. Other causes include radiation, malignancies, previous uterine surgery, and infection, although the majority of VVFs occur after routine hysterectomy [1]. There is a 1% risk of developing VVF after radical gynaecological surgery [2]. The first reported repair of VVF was in the classic treatise by Sims [3].

### 2. DIAGNOSIS

The patient usually presents with urine leakage pervaginally after catheter removal or after 7–10 days surgery. Amount of urine leakage depends upon fistula size. Urinary leakage may cause surrounding skin excoriation or bacterial or fungal infection.

Speculum examination must be performed in all patients with VVF. Site, size and number of fistulae should be documented and any sign of inflammation or induration should be assessed. Small fistulae may be diagnosed by instilling methylene blue dye in the bladder and observing bluish fluid emerging pervaginally.

Cystoscopy should be performed in all cases of VVF. In the early period, a fistula may appear as an area of oedematous swelling with or without ostium. A mature fistula appears as an opening with clear well-demarcated margins. Number, site and size of fistulae should be mentioned. The size of the fistula is measured using ureteric catheter markings. In case of malignancy or post-radiotherapy fistulae, biopsy from the margin should be taken to rule out any residual malignancy.

### 3. IMAGING

Cystography with micturating cystogram should be performed. Fistulae are best seen on lateral plates as contrast going posteriorly from the bladder to the vagina. Small fistulae are only seen on voiding films.

Upper tract imaging has to be done because 10–15% of VVFs are associated with ureteric injuries [4]. IVP shows contrast agent leaking from the ureter into the vagina, or dilated ureter and contrast agent not going beyond it. Computed tomography (CT) urography is replacing IVP in many centres. CT can give further information about any urinoma at the site of injury.

### 4. MANAGEMENT

#### *a) Conservative management*

Spontaneous closure of VVF in selected cases can be achieved. In small series, spontaneous closure was seen with an indwelling catheter over a period of 19–54 days [5]. Anticholinergic agents can be added to reduce bladder spasm and encourage healing. Electrocoagulation of fistula edges has been successful in some series with fistulae <3.5 mm [6]. Fibrin glue and other sealants have also been used for fistula healing [7]. Some criteria for success are: (1) fistula detected within 7 days of index surgery; (2) <1 cm; and (3) associated with irradiation or malignancy [8].

#### *b) Surgery*

Surgical repair is necessary in most VVFs. Whichever approach is taken, principles are well vascularised healthy edges, adequate mobilisation of bladder and vagina for tension-free closure, and when required, a vascularised flap in between the bladder and vaginal closure. The bladder and vagina should be closed in opposite directions to each other to avoid overlapping of suture lines. A ureteric catheter should be placed for repair of fistulae close to ureteric orifices. The first repair of fistula has the best chance of success, so it should be well planned.

#### *c) Timing of surgery*

Conventionally, VVFs are repaired at 8–12 weeks after index surgery so that the fistula is matured and oedema and infection are absent. This is a devastating complication for the patient with significant social unacceptability, but nowadays early repair in uncomplicated post-gynaecological surgery fistulae is successful in reducing patient suffering. The presence of oedema and infection should be ruled out before immediate repair [9–14]. In case of post-radiation fistulae, repair should be done after 1 year so that vascularity is well demarcated.

#### *d) Approach*

##### 1. Vaginal

The vaginal approach is best for low uncomplicated fistulae without ureteric injury. Fistulae should be easily reachable from the vagina. Surgeon's preference and expertise are also important in choosing the approach. Postmenopausal atrophic vaginal mucosa can be treated with local oestrogen cream before surgery. Labial fat pad (Martius flap) or peritoneal flap can be used to augment repair.

##### 2. Abdominal

Absolute indications for the abdominal approach include: (1) the need for concomitant abdominal surgery, such as ureteral re-implantation; (2) fistulae cannot be reached pervaginally for repair; (3) a complex fistula involving the ureters, bowel, or other

intra-abdominal structures; and (4) involvement of the VVF with ureteric orifices or close to them.

Abdominal repair is of two types. The classic bivalving repair as described by O' Conor [15,16] in which the bladder is opened vertically, incision extended up to the fistula, the fistula is excised, and the bladder and vagina are closed separately, and if needed, a vascularised omental flap is interposed. The second technique is transvesical repair in which the bladder is opened directly and the entire operation takes place through the bladder. The fistula tract is excised and the vagina and bladder suture lines are perpendicular to each other [17]. Both techniques of abdominal repair of VVF can be done by minimally invasive techniques.

### 5. MINIMALLY INVASIVE APPROACHES

#### *a) Transabdominal laparoscopic repair*

The first cases of laparoscopic repair of VVF were reported by Nezhat and colleagues in 1996 in a retrospective review of 19 cases of bladder injury repair [18]. They concluded that laparoscopic repair is safe and effective in the hands of experienced laparoscopic surgeons.

Sotelo *et al.* described laparoscopic repair of VVF in 15 cases that had clear indications for abdominal repair [19]. All patients had 2 months failed trial of conservative treatment. Their technique involved cystoscopy, catheterisation of the VVF, laparoscopic cystotomy, opening and excision of the fistulous tract, dissection of the bladder from the vagina, cystotomy, and colpotomy closure with interposition of a flap of healthy tissue. They had success in 93% of cases.

The advantage of laparoscopic repair over open repair is magnification, less blood loss, shorter hospital stay, less abdominal pain, and rapid recovery with early return to work [20].

The principle of laparoscopic repair is same as that of open repair. Four or five ports are placed as the peritoneum is reflected from the bladder; the bladder is opened up to the fistula; the fistula is excised and the vagina is separated from the bladder; the bladder and vagina are closed in a tension-free manner; and an omental interposition flap is placed between the bladder and vaginal closure.

#### *b)* LESS transvesical repair

Transvesical laparoscopic surgery in VVF is easily performed using laparoendoscopic single-site surgery (LESS) because bladders with vesicovaginal fistulas tend to be smaller in capacity and have limited space for ports. The ports help to hitch the bladder to the anterior abdominal wall to give an adequate working space. Vaginal packing is placed to prevent leaking of the pneumovesicum. This technique avoids pneumoperitoneum and its sequelae. An extra port can be placed perurethrally and is used for suturing and retraction [21].

We reported three cases of LESS transvesical repair of VVF using the Triport (3 channel, Olympus GmBH) [22]. The fistula tract is excised. Closure of the vagina is achieved pervaginally and the bladder is closed in a single layer perpendicular to the vaginal closure. A barbed unidirectional suture aids suturing through a single port.

#### *c) Robotic repair*

Robotic surgery has the advantage of better magnification, 3D vision, motion scaling, tremor dampening, and articulating instruments, which makes it useful in reconstructive surgery. Most of the described robotic repairs have been by bivalving the bladder using O'Conor's technique.

Patients are placed in an extreme Trendelenberg position. Five ports are placed: one 10-mm supraumblical camera port, three 8-mm robotic arm ports (2 on the left and 1 on the right), and one assistant port for suction or passing of sutures. The technique is similar to open repair [23].

Sundaram *et al.* have described their first series of five patients who underwent robotic repair of VVF [24]. After dissection of the fistula, the bladder and vagina were closed separately; the bladder vertically and the vagina horizontally with omental interposition. Success was 100% with no recurrence at up to 6 months follow-up.

### 6. POSTOPERATIVE CARE

Continuous bladder drainage is maintained by perurethral or suprapubic catheter. Catheter blockage should be avoided. The catheter is maintained in position for 10–14 days. Anticholinergic medication is given to avoid bladder spasm. Oestrogen ointment can be applied to the vagina for atrophic vaginitis. Coitus and tampon use should be avoided for at least 4–6 weeks.

### 7. CONCLUSION

All the described techniques of minimally invasive repair of VVF have high rates of success of 93–100%. This replicates the results of the pioneers of this surgery in the modern era. VVF is one of the most devastating complications of abdominal surgery and life for the patient can be intolerable [14]. Newer techniques such as LESS and robot-assisted surgery seem to replicate the classic techniques of open surgery with equivalent results and the advantage of being minimally invasive. The modern trend towards early surgery as well as minimally invasive surgery for this problem is beneficial to most patients.

## II. URETEROVAGINAL FISTULA

### 1. INTRODUCTION

Ureterovaginal fistula (UVF) is less common than VVF. The most common cause is gynaecological

surgery. Risk factors for UVF are endometriosis, pelvic inflammatory disease, radiation, and malignancy. The incidence of UVF after gynaecological surgery is 0.5–2.5% [25,26]. The mechanisms of iatrogenic ureteral injury are crushing, laceration or transection, thermal injury, suture ligation, or clip application. This type of injury commonly occurs during attempts to stop bleeding. Laparoscopic hysterectomy has the highest incidence of UVF, followed by open abdominal hysterectomy and then vaginal hysterectomy [27].

## 2. DIAGNOSIS

Patients present with urine leakage pervaginally at 1–4 weeks after surgery [28]. Other symptoms may be abdominal pain, fever, nausea, and vomiting due to urinoma in the retroperitoneum. These patients have normal bladder voiding because there is urine from the contralateral kidney.

## 3. IMAGING

All patients with pervaginal urinary leakage postoperatively should be evaluated with Intravenous urography (IVU) and cystography. Cystography is done to rule out concomitant VVF. IVU shows leaking of contrast agent from the ureter into the vagina, collection of contrast agent in the abdominal cavity, and dilatation of the proximal ureter and pelvicalyceal system. CT urography is replacing IVU in many centres. Retrograde pyelography should be done in all case of UVF for documenting the site and extent of ureteric injury.

## 4. MANAGEMENT

### *a) Endoscopic management*

All patients with isolated UVF should be managed endoscopically with stenting if possible. If retrograde pyelography shows some contrast agent going into the ureter proximal to the site of injury, on most occasions, passing a guidewire and then a double-J stent is possible. Stenting decreases urinary leakage and ensures kidney drainage.

In a series of 10 patients with post-gynaecological injury to the ureter, Turner *et al.* successfully treated five patients with double-J stenting for 2–5 months [29]. Among the five patients in whom this was unsuccessful, it was not possible to pass the double-J stent in four patients, and in the other, the ureteric orifice was not seen on cystoscopy. They advocated the initial use of double-J stents in gynaecological ureteric injury. This approach is simple and may cure the fistula. If it is unsuccessful, subsequent reimplantation can be done.

Al-Otaibi had a 64% success rate with internal stenting in 7/11 patients after 6–8 weeks [30]. Four patients had persistent leakage and two of these had leakage after 6 months of stenting. Ureteric stent insertion is a primary management for UVF. When the retrograde approach is impossible, percutaneous nephrostomy and antegrade stent insertion are the second step. At least 6 weeks of stenting is allowed for healing. In the case of failure, surgical repair is necessary.

In cases in which retrograde stenting is not possible, antegrade stenting should be tried. Nephrostomy drainage should be done to stop leakage in cases in which stenting is not possible. In those patients, stenting can be tried after a few days because oedema at the site of injury reduces, and if needed, balloon dilatation can be performed if stricture occurs at the injury site.

### *b) Surgical repair*

In patients in whom stenting is not possible or leakage persists even after stenting, *in situ* surgical repair should be considered.

Timing of surgery is controversial, and most recent studies have suggested early repair has similar results to late repair, with less morbidity [12]. Badenoch and Blandy showed that out of 59 women with post-gynaecological surgery ureteric or bladder injury, 32 were repaired early before 6 weeks and 27 after 6 weeks [10]. Ureteric injuries in 40 patients (43 ureters) were repaired by the Boari–Ockerblad technique. Primary healing was obtained in all cases whether early or late. These results support our recommendation for early intervention in these injuries.

UVF most often occurs due to injury of the distal third of the ureter below the iliac vessels. Due to fibrosis and oedema of the ureter and surrounding tissue, primary repair of the ureter is not possible and uretero-neocystostomy (UNC) is the surgery of choice.

The basic principle of surgery is to dissect the ureter as deep as possible in the pelvis, preserving the periadventitial tissue, transect the ureter just above the injury, and to perform tension-free extravesical UNC. Psoas hitch if needed should be done to avoid tension. Few cases may require Boari flap. Rarely, transuretero-ureterostomy or ileal substitution of the ureter is necessary.

In a study of 17 UVFs in which surgical repair was performed, extravesical modified Lich–Gregoir UNC was done in 82.3% of cases. Psoas hitch or Boari flap was done in 17.6%. The procedure was performed as early as 4 weeks. There were no recurrences in any cases [31].

### *c) Laparoscopic repair*

Laparoscopy as discussed earlier in VVF repair has the advantage of better magnification, early recovery, and shorter hospital stay, with better cosmesis compared with open surgical repair, but it has a steep learning curve in reconstructive surgery.

Ramalingam *et al.* described an initial case of laparoscopic UVF repair with success and stent removal after 6 weeks [32].

Modi *et al*. reported 18 cases of laparoscopic repair of UVF. They were able to reimplant the ureter in 17 cases laparoscopically, and in one patient, they had to do open repair due to development of cardiac arrhythmia because of pneumoperitoneum. They performed the non-refluxing Lich–Gregoir onlay technique. They carried out transperitoneal repair by creating a pneumoperitoneum by Veress needle. A 10-mm camera port was placed at the lower border of the umbilicus. An additional two or three 5–10-mm working ports were placed. The peritoneum was incised over the iliac vessels and the ureter was identified and dissected lower down, up to the stricture. The distal ureter was clipped and proximal healthy ureter was spatulated at the 6 o'clock position. The bladder was filled with saline and after adequate mobilisation, a psoas hitch stitch was made with a polypropyelene suture. The detrussor muscle was incised with electrocautery and the mucosa was opened with scissors. UNC was done using the Lich–Gregoir method with 1:4 tunnel ratios. IVP was done at 3 and 12 months and all 17 patients had no obstruction of the upper urinary tract. The authors do not recommend routine use of ureteric stenting postoperatively. The catheter was kept in place for 7 days post-surgery [33].

Laparoscopic repair has a success rate of 90–100%, without any additional morbidity, as compared to open repair, with a slightly longer operating time.

***d) Robotic repair***

Robot-assisted laparoscopic surgery has the advantage in reconstructive surgery due to its 3D view, better magnification, EndoWrist movement, and motion scaling with dampening of tremor.

Laungani *et al*. reported their initial experience of robotic UVF repair in three cases. They placed a standard six ports. A double-J stent was placed from the left 5-mm port prior to completion of UNC. A Foley catheter was removed after 1–2 days and patients were discharged with the double-J stent *in situ* [34].

## 5. CONCLUSIONS

Endoscopic treatment with a double-J stent is the treatment of choice in all cases of UVF. However, this may be successful in only ~50% of cases. If the ureter has been tied off, or the thermal damage is extensive, endoscopic treatment may fail. In these cases, laparoscopy or robot-assisted laparoscopy for re-implantation of the ureter, with or without a Boari flap or a Psoas hitch, offers similar results as conventional open surgery with the advantages of a minimally invasive approach.

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## Committee 7

# Minimally Invasive Kidney Transplantation

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**Members**

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*M. Bhandari (USA)*

*A. Sood (USA)*

# CONTENTS

# Minimally Invasive Kidney Transplantation: Techniques, Outcomes and Review of the Literature

*M. Menon,*

*R. Ahlawat, M. Bhandari, A. Sood.*

## I. INTRODUCTION

Minimally invasive surgery reduces perioperative morbidity. The benefits of minimally invasive surgery have been demonstrated across multiple surgical subspecialties and have led to its widespread adoption [1–5], including in transplantation [6, 7], such that laparoscopic surgery is currently the preferred modality for live donor nephrectomy.

Kidney transplantation (KT) has traditionally been performed by open surgery, but minimally invasive KT (MIKT) has recently been described by ourselves and others. A pure laparoscopic approach has been described by Rosales *et al.* [8] and Modi *et al.* [9–11], whereas more recently, a laparoscopic approach with robotic assistance has been described by Giulianotti *et al.* [12, 13], Boggi *et al.* [14] and our group [15–18, 25, 26]. There are considerable technical differences among the described approaches. Accordingly, in this chapter, we aim to discuss the technical aspects of these approaches, with an emphasis on robot-assisted laparoscopy, while also reporting on the early outcomes MIKT and how they compare with the outcomes of standard open KT (OKT).

## II. EVIDENCE SYNTHESIS

A literature search of Medline (PubMed) and Embase was performed to retrieve all articles published on MIKT between January 1990 and June 2014. We used the search terms “minimally invasive” OR “laparoscopic” OR “robotic” OR “robot assisted” AND “kidney transplantation”. Papers written in English and concerning technical and/or clinical outcomes following MIKT were selected. Two hundred and twenty-seven articles were retrieved and 12 were relevant: eight on robotic KT (RKT) and four on laparoscopic KT (LKT) **(Figure 1)**. Reference lists of the selected papers were scrutinised for additional relevant articles but yielded none. Our own data comparing outcomes of RKT with regional hypothermia versus OKT were also included.

**Table 1** summarises the studies looking at outcomes following MIKT in patients with end-stage renal disease (ESRD). All studies, except one [19], were published between 2010 and 2014. Seven studies were case reports and/or technical papers [8–10, 12, 14, 15, 19]; three studies reported detailed outcomes following MIKT [11, 13, 17]; and the remaining two studies dealt with safe introduction and adoption of a new technique for RKT [16, 18]. All contemporary RKT studies were from three groups (See **Table 1** legend).

## III. SURGICAL TECHNIQUE

We have previously described our technique of RKT with regional hypothermia in a detailed step-by-step manner (accompanied by a surgical video) [17]. Here, we recapitulate the critical steps of our own technique, and compare it with the RKT techniques described by Giulianotti *et al*. [12] and Boggi *et al.* [14] **(Table 2)**:

### 1. PREPARATION OF GELPOINT:

The GelPOINT device is a hand-access platform and consists of two parts – a GelSeal cap and an access port. It was initially devised for single-site surgery but we use it to deliver ice-slush into the pelvic cavity for regional hypothermia and the graft kidney. A 12-mm camera port and a 5-mm suction port are placed in the GelSeal cap ahead of time **(Figure 2a)**.

### 2. PATIENT POSITION AND PORT PLACEMENT:

Patient positioning and port placement are performed as is typical for the Vattikuti Institute prostatectomy technique of robotic radical prostatectomy [20, 21] **(Figure. 2b)**.

### 3. PREPARATION OF THE VASCULAR BED AND BLADDER:

The dissection begins with the identification of the external iliac vessel bed. Using the 30° down lens, the external iliac vessels are skeletonised (Figure 3a). The camera is changed to the 30° up and the bladder is taken down. After shifting back to the 30° down lens, a transverse incision is made 2–3 cm caudal to the caecum, and peritoneal flaps are raised on both sides over the psoas muscle, to be

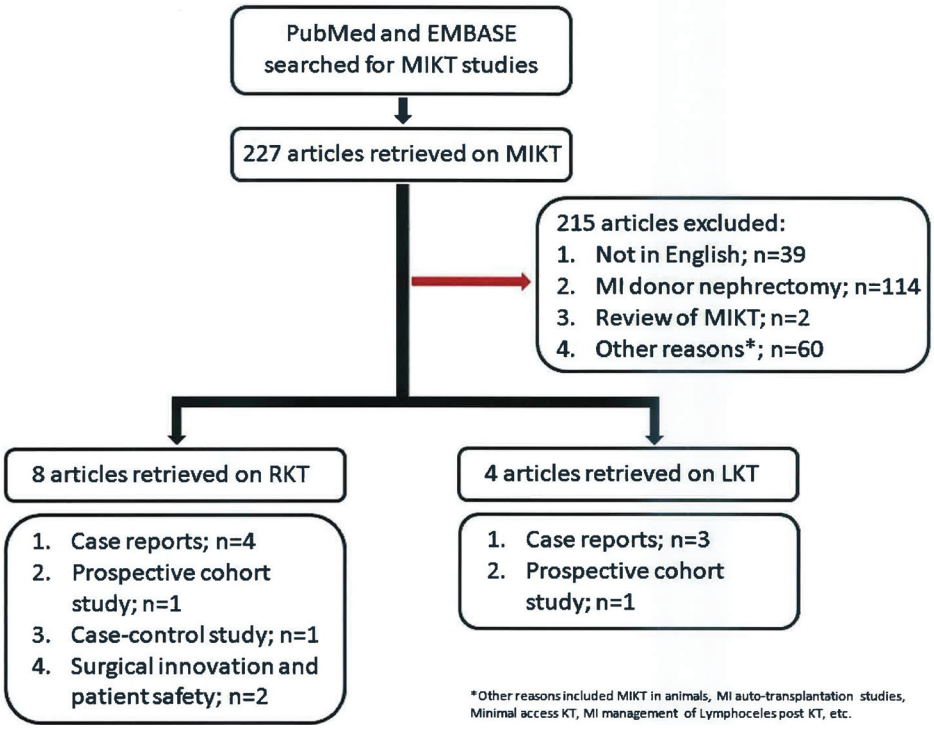


***Figure 1. Flowchart representing the literature search results and inclusion of relevant studies***

***Table 1. Summary of studies of RKT and LKT outcomes in patients with ESRD***

| Study | Publication year | Study period | MIKT approach | Study design | Data collection | Cohort (n) | Level of Evidence |
|---|---|---|---|---|---|---|---|
| Hoznek *et al.* | 2002 | 2001 | RKT[d] | Case report | Prospective | 1 | 4 |
| Giulianotti *et al.*[a] | 2010 | 2009 | RKT | Case report | Prospective | 1 | 4 |
| Boggi *et al.*[b] | 2011 | 2010 | RKT | Case report | Prospective | 1 | 4 |
| Oberholzer *et al.*[a] | 2013 | 2009–2011 | RKT | Case control | Prospective | 56 | 3 |
| Menon *et al.*[c] | 2013 | 2012–2013 | RKT | Surgical safety[e] | Prospective | 7 | 3 |
| Menon *et al.*[c] | 2013 | 2012–2013 | RKT | Cohort study[e] | Prospective | 25 | 3 |
| Abaza *et al.*[c] | 2013 | – | RKT | Technique paper | Prospective | - | – |
| Sood *et al.*[c] | 2014 | 2012-2013 | RKT | Surgical safety[e] | Prospective | 41 | 3 |
| | | | | | | | |
| Rosales *et al.* | 2010 | 2009 | LKT | Case report | Prospective | 1 | 4 |
| Modi *et al.* | 2011 | 2010 | LKT | Case series | Prospective | 4 | 4 |
| Modi *et al.* | 2012 | 2012 | LKT | Case report | Prospective | 1 | 4 |
| Modi *et al.* | 2013 | 2010–2012 | LKT | Cohort study | Prospective | 217 | 3 |

***Currently, only three groups/teams are actively performing RKT who have reported their experience. Only two groups/teams are actively performing LKT: one from India (Modi et al.) and the other from Spain (Rosales et al.)***

***[a]Team from Chicago.***

***[b]Team from Italy.***

***[c]Team from Detroit/India.***

***[d]In this study, the authors used robotic assistance while performing vascular dissection and anastomoses, but access was established in a manner similar to open KT.***

***[e]These studies followed the IDEAL model of safe surgical innovation as proposed by the Balliol Collaboration, Oxford, UK.***

*Table 2. Summary of key steps in RKT*

| Surgical steps | Giulianotti *et al*. | Boggi *et al*. | Menon *et al*. |
|---|---|---|---|
| **Patient position** | Left lateral decubitus | Supine with 25° left lateral tilt and15° Trendelenburg tilt | Lithotomy with 15–20° Trendelenburg tilt |
| **Number of ports** | 5 in total (1 through the LapDisk); two 8-mm robotic ports, one 12-mm camera port, and two 12-mm assistant port (one through the LapDisk) | 4 in total (1 through the LapDisk); two 8-mm robotic ports (left arm port through the LapDisk), one 11-mm camera port, and one 12-mm assistant port | 6 in total (2 through the GelPOINT); three 8-mm robotic ports, one 12-mm camera port (via the GelPOINT), one 12-mm assistant and one 10-mm assistant (via the GelPOINT) |
| **Placement of robotic ports** | Left arm port in the suprapubic region and the right arm port in the right flank | Right arm port placed along the right pararectal line ~5 cm below the costal margin and the left arm port placed through the suprapubic LapDisk | As shown in Fig. 2b |
| **Placement of camera port** | Left lower quadrant, slightly left to midline | Left to the midline below the level of umbilicus | Through the GelPOINT placed at paraumbilical incision |
| **Robot docking** | Right side of patient nearer to the foot end | Right side of patient nearer to the foot end | Between the legs |
| **Incision for graft placement** | 7-cm periumbilical vertical incision | 7-cm suprapubic horizontal incision | 4–6-cm periumbilical vertical incision |
| **Approach** | Transperitoneal | Transperitoneal | Transperitoneal |
| **Use of hand-assisted device** | Yes; hand goes in to deliver and manoeuvre the graft kidney | Yes; hand goes in to perform the ureteroneocystostomy | Yes; hand does not go in. Instead the device is used to deliver ice slush and the graft kidney, and perform circular arteriotomy |
| **Graft placement** | Intraperitoneal | Initially, intraperitoneal shifted to extraperitoneal for final position | Initially, intraperitoneal shifted to extraperitoneal for final position |
| **Use of regional hypothermia** | No | No | Yes; ~300 mL ice slush used and an average graft temperature of 18-20°C achieved |
| **Ureteroneocystostomy** | Re-docking of robot | Open surgery | No re-docking of robot was required |
| **Suture material** | Vascular: 6-0 ePTFE<br>UV anastomosis:6-0 PDS (for mucosal ) and 4-0 PDS (for detrusor) | Vascular: 6-0 ePTFE<br>UV anastomosis:<br>not mentioned | Vascular: 5-0 CV6 ePTFE<br>UV anastomosis: 4-0 PDS (for mucosal ) and 3-0 V-Loc CV23 6" (for detrusor) |
| UV, ureterovesical anastomosis | | | |

***adapted with permission from Wolters Kluwer Health Inc., Minimally invasive kidney transplantaton: perioperative considerations and key 6-month outcomes, Sood et al. Transplantation. 2015 Feb;99(2):316-23)***

used later for extra-peritonealisation of the graft kidney. The bladder is distended with 240 ml normal saline and a detrusor tunnel is prepared for modified Lich–Gregoir ureteroneocystostomy (Figure 3b).

## 4. PREPARATION OF THE DONOR GRAFT:

The graft is harvested laparoscopically, flushed with cold Ringer's lactate (Figure 4a), and wrapped in a gauze jacket filled with ice slush, with an opening to allow egress of the hilar structures (Figure 4b). The upper pole of the kidney is marked with a long silk-tie tail to aid orientation of the graft kidney when it is introduced into the recipient. The ice jacket serves two functions: cooling the kidney, and facilitating atraumatic manoeuvre of the graft.

## 5. INTRODUCTION OF THE GRAFT AND COOLING:

The pelvic bed is cooled to 18–20°C by delivering ~120 ml of ice slush, via modified Toomey syringes, with the nozzle cut off (Figure 4a), immediately before

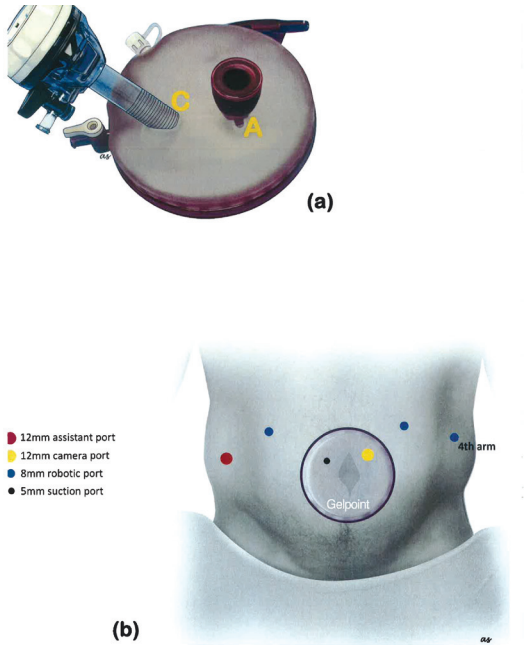


*Figure 2. (a) GelSeal cap with a 12-mm camera port (C) and a 10-mm assistant port, for the 5-mm suction (A). (b) Diagrammatic illustration of port placement for RKT with regional hypothermia (Illustrations reproduced with permission from Elsevier (17)).*

manipulation of the graft once inside the recipient.

**6. VENOUS ANASTOMOSIS:**

The external iliac vein (EIV) is clamped using robotic bulldog clamps **(Figure 5a)** and venotomy is carried out using cold monopolar scissors. The graft renal vein is anastomosed in an end-to-side continuous fashion to the EIV **(Figure 5b)**. Just prior to completing the anastomosis, the lumen is flushed with heparinised saline via a 5 F ureteric catheter introduced through the assistant port. The graft renal vein is occluded using a bulldog clamp and the EIV is unclamped. Additional ice slush is introduced if required (if the anastomosis takes ≥20 min for completion).

**7. ARTERIAL ANASTOMOSIS:**

The external iliac artery (EIA) is clamped. Linear arteriotomy is performed using monopolar scissors, and converted to a circular arteriotomy **(Figure 6a)** using a 3.6-mm aortic punch passed through the GelPOINT. The renal artery is anastomosed in an end-to-side continuous manner to the EIA **(Figure 6b)**. After flushing and testing the integrity of the anastomosis, the graft renal artery is clamped temporarily and the EIA is unclamped. If the anastomosis is secure, all vascular clamps are released and the gauze jacket is cut away and removed. The kidney is extra-peritonealised by approximating the peritoneal flaps prepared previously (this fixes the graft kidney and prevents torsion

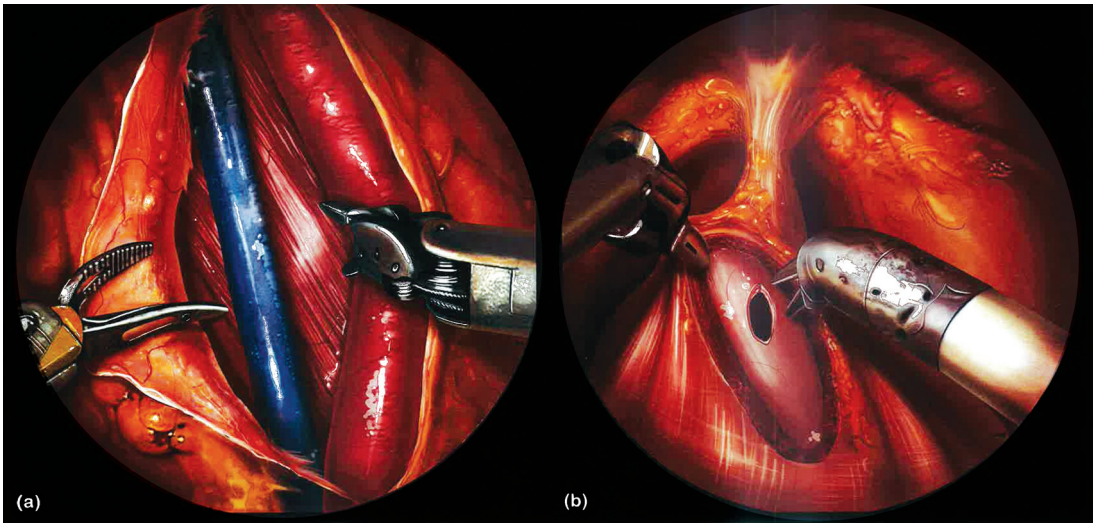


*Figure 3. (a) Skeletonised iliac vessel bed. (b) Bladder preparation: detrusor flaps created for subsequent ureteroneocystostomy (modified Lich–Gregoir technique) (Illustrations reproduced with permission from Elsevier (17)).*

(Figure 4c) and after (Figure 4d) introduction of the graft kidney. For introduction of the graft kidney, the robotic camera arm and GelSeal cap are removed, and the graft in its ice jacket is inserted effortlessly though the access port. It is important to orient the graft properly during introduction, that is, lower pole towards the feet of the recipient and the hilum towards the external iliac vessels, to avoid unnecessary

of the vascular pedicle, and aids graft biopsy if needed). The pneumoperitoneum pressure is dropped to 8–10 mm Hg and an intravenous bolus of 100 mg furosemide is given.

**8. URETERONEOCYSTOSTOMY:**

Using the modified Lich–Gregoir technique, the ureter is approximated to the bladder mucosa in a con-

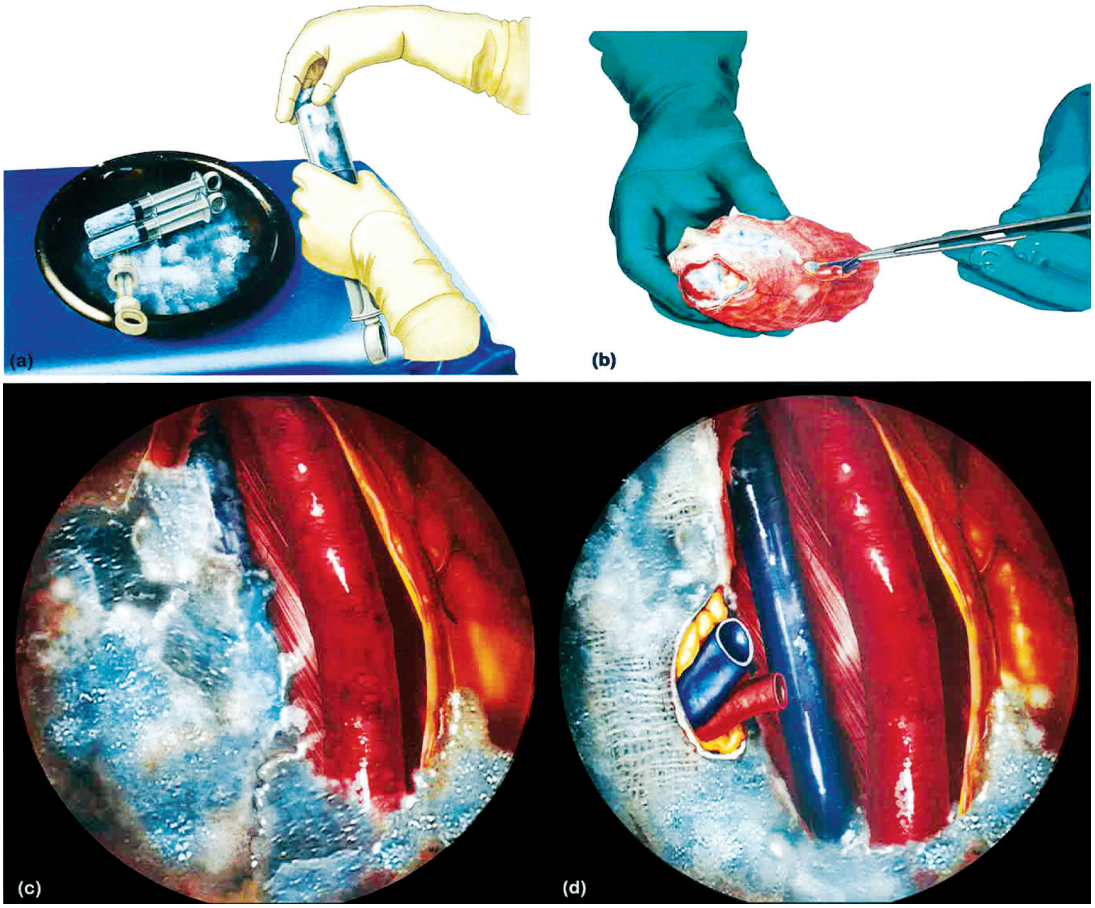


*Figure 4. (a) Multiple modified Toomey syringes (nozzles cut off) being readied for rapid delivery of ice slush. (b) Graft kidney wrapped in a gauze jacket filled with ice slush. (c) Pelvic bed lined with ice slush to achieve cooling before introduction of the graft kidney. (d) Additional ice slush delivered onto the graft kidney immediately after its introduction, to achieve uniform cooling (Illustrations reproduced with permission from Elsevier (17)).*

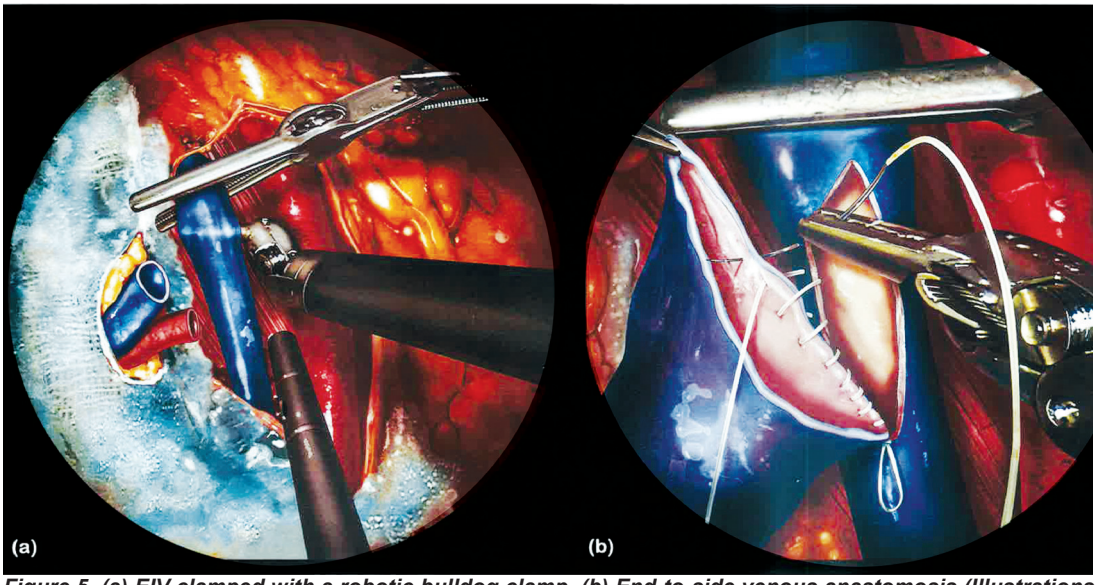


*Figure 5. (a) EIV clamped with a robotic bulldog clamp. (b) End-to-side venous anastomosis (Illustrations reproduced with permission from Elsevier (17)).*

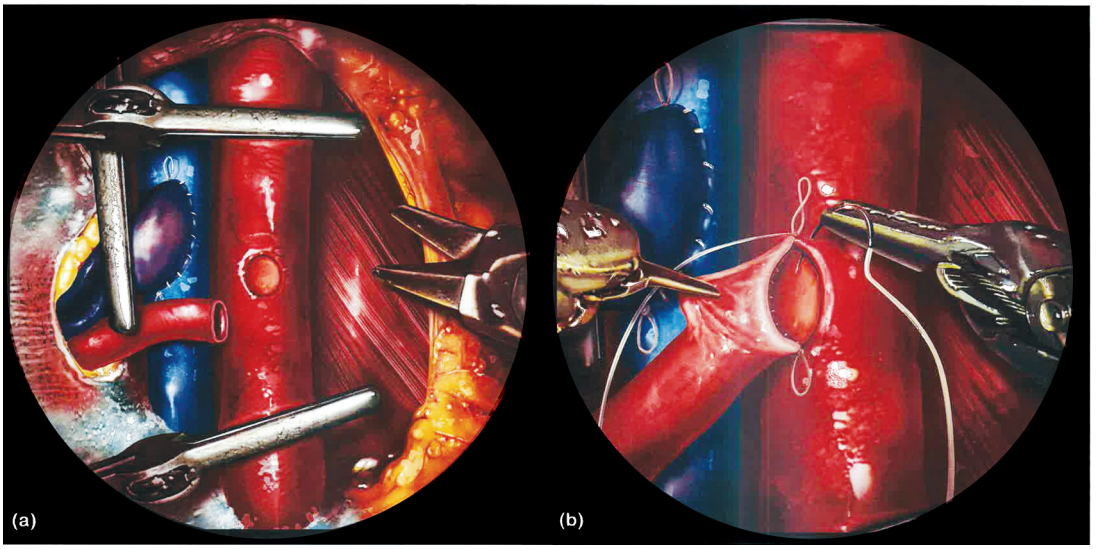


*Figure 6. (a) Linear arteriotomy converted to circular arteriotomy using a 3.6-mm aortic punch. (b) End-to-side arterial anastomosis (Illustrations reproduced with permission from Elsevier (17)).*

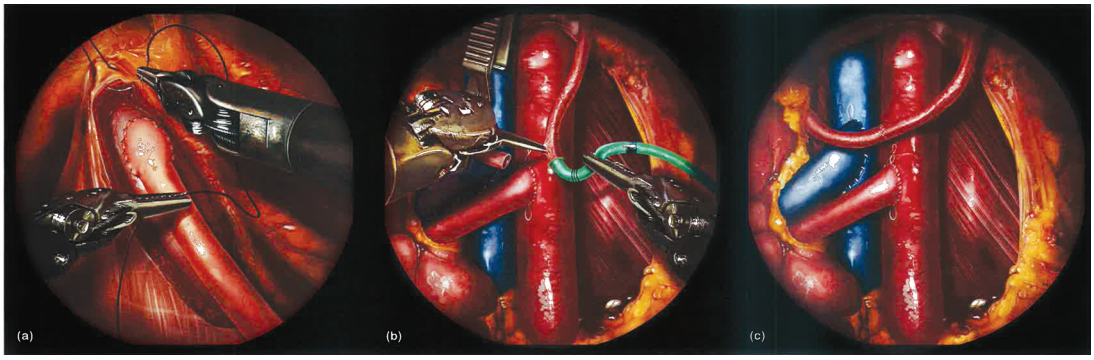


*Figure 7. (a) Ureteroneocystostomy. (b) Inferior epigastric artery being flushed with heparinized saline using a 5 F ureteric catheter. (c) Lower-pole accessory artery anastomosis to the inferior epigastric artery using 6-0 prolene sutures (Illustrations reproduced with permission from Elsevier (17)).*

tinuous fashion. A 6 F, 16-cm double-J stent, introduced through the 12-mm assistant port, is inserted into the ureter after completing the posterior part of the anastomosis. The detrusor muscle is closed atop in a continuous fashion **(Figure 7a)**, creating an anti-reflux mechanism. Extra-peritonealisation should be performed prior to ureteroneocystostomy, because it gives time to observe the graft for any potential vessel kinking or compression that might have occurred during extra-peritonealisation.

## 9. ACCESSORY VESSELS:

In four of 50 cases, the graft kidney had an accessory artery measuring 1.2–1.6 mm in diameter, which perfused >10% of the parenchyma. These arteries were considered unsuitable for bench reconstruction. Thus, we proceeded to anastomose the accessory artery to the recipient inferior epigastric artery (IEA). The recipient IEA is prepared for anastomosis prior to introduction of the kidney. A laparoscopic bulldog clamp is used to occlude the stump, and the distal end is secured **(Figure 7b)**. The lower pole artery is anastomosed to the IEA using 7-0 or 6-0 prolene sutures **(Figure 7c)**.

## 10. INSTRUMENTS:

a. Robotic instruments and ports: 8-mm ports (three required); Maryland Bipolar Grasper (one required); monopolar curved scissors (with cover-tip accessory; one required); Black Diamond Micro Forceps (one required); large needle driver (one required); Hem-o-lok Applier (one required); Pro-Grasp Forceps (on the 4$^{th}$ arm; one required).

b. Laparoscopic instruments: MicroFrance laparoscopic grasper (one required); suture passer (one required); Hem-o-lok applier (5, 10 and 12 mm; one each required); bulldog clamps with appliers (Scanlan International, St Paul, MN, USA); a set of four required.

c. Disposables: GelPOINT platform (one required; Applied Medical Corp., Rancho Santa Margarita, CA, USA); 12-mm camera port (one required) and 12-mm assistant port (one required); 5 F ureteral catheter for flushing (one required).

d. Sutures: 5-0 CV-6 expanded polytetrafluoroethylene (ePTFE; Gore-Tex; Gore & Associates, Flagstaff, AZ, USA); 4-0 PDS / 3-0 V-Loc CV23 6" (Covidien, New Haven, CT, USA).

e. Other equipment: ice slush machine (OR Solutions Model: ORS-1075 H5); Slush Machine drape (OR Solutions Model: ORS-321); Toomey Syringes (modified; 3 or 4 should be readied); 3.6-mm aortic punch (one required; Teleflex Medical Inc, Research Triangle Park, NC, USA).

## IV. REPORTED OUTCOMES AND DISCUSSION

Twelve studies **(Table 1)** have evaluated the role of MIKT and have established the feasibility, safety and reproducibility of the technique, although these studies were performed by surgeons/teams familiar with laparoscopic and/or robotic technology.

Hoznek *et al.* [19] were the first to use robotic assistance during KT. The first case report of a truly robotic KT operation was by Giulianotti *et al.* [12] from Chicago. It took 223 min for the case to be completed with a warm ischaemia time of 50 min. Boggi *et al*. [14] then reported the first RKT case in Europe. Both these studies, although truly robotic, did use hand assistance during at least one phase of the operation **(Table 2)**, whereas, the RKT technique described by Menon *et al.* [17] was completely hand free. Rosales *et al.* [8] and Modi *et al.* [9] described their techniques of LKT in 2010 and 2011, respectively. Warm ischaemia times in these studies were 53 min and 60 min, respectively.

Only three of the 12 studies reported detailed outcomes after MIKT. Two assessed outcomes following RKT and one following LKT. **Table 3** summarises the perioperative outcomes from these studies. The study of RKT by Oberholzer *et al.* [13] and LKT by Modi *et al.* [11] were both performed under warm ischaemia. The mean warm ischaemia times were 48 and 60 min, respectively. The RKT study by Menon *et al*. [17] consistently used regional hypothermia (using ice slush) during vascular anastomosis. We routinely achieved graft surface temperatures of 18–20°C and our mean re-warming time (with ice slush) was 47 min and warm ischaemia time was 2.4 min. Oberholzer *et al*. and Modi *et al.* noted a slower return of graft function in patients undergoing MIKT, which we did not observe, possibly due to the renoprotective effect of hypothermia [22] (**Figure. 8b**; unpublished data). Ourselves and Modi *et al*. have all noted a significant reduction in analgesic requirements in patients undergoing MIKT. On average, OKT patients required 3.2 mg of analgesic medication (morphine equivalent) and LKT patients required 1.4 mg in the study by Modi *et al*.. In our study, patients undergoing RKT used on average less analgesia (unpublished data; 21.1 mg patient controlled analgesia with morphine vs. 29.5 mg), and also reported lower pain scores **(Figure 8a)**. This might be related, at least in part, to the significant reduction in size of the incision. Modi *et al.* reported an average incision size of 5.5 cm in patients undergoing LKT compared to 17.8 cm in OKT patients. Similarly, in our study, RKT patients had an average incision length of 6.1 cm versus 15.6 cm in OKT patients (unpublished data).

**Table 4** summarises the functional outcomes and complication rates in three series of patients

***Table 3. Summary of perioperative outcomes of RKT and LKT outcomes in patients with ESRD[a]***

| Study | MIKT cohort (n) | Donor (living: cadaveric) | Operating time (min) | warm ischemia time (min) | Estimated blood loss (mL) | Conversion to open (%) | LOS (days) |
|---|---|---|---|---|---|---|---|
| Oberholzer et al. | 28 [b] | 26:2 | – | 47.7 | 110 | 0 | 8.2 |
| Menon et al. | 25 | 25:0 | 214 | 2.4 [c] | 151 | 0 | 8.4 |
| | | | | | | | |
| Modi et al. | 72 [b] | 72:0 | 223 | 60.3 | 68 | 4 (5.5) | – |

***[a]For detailed outcomes please refer to individual studies.***
***[b]In these studies, total numbers of patients were 56 (all obese) for the study by Oberholzer et al. and 217 for the study by Modi et al.***
***[c]Warm ischaemia time was the time taken in harvesting the donor kidney; re-warming time (with ice-slush hypothermia) was 47.7 min.***
***LOS, length of stay.***

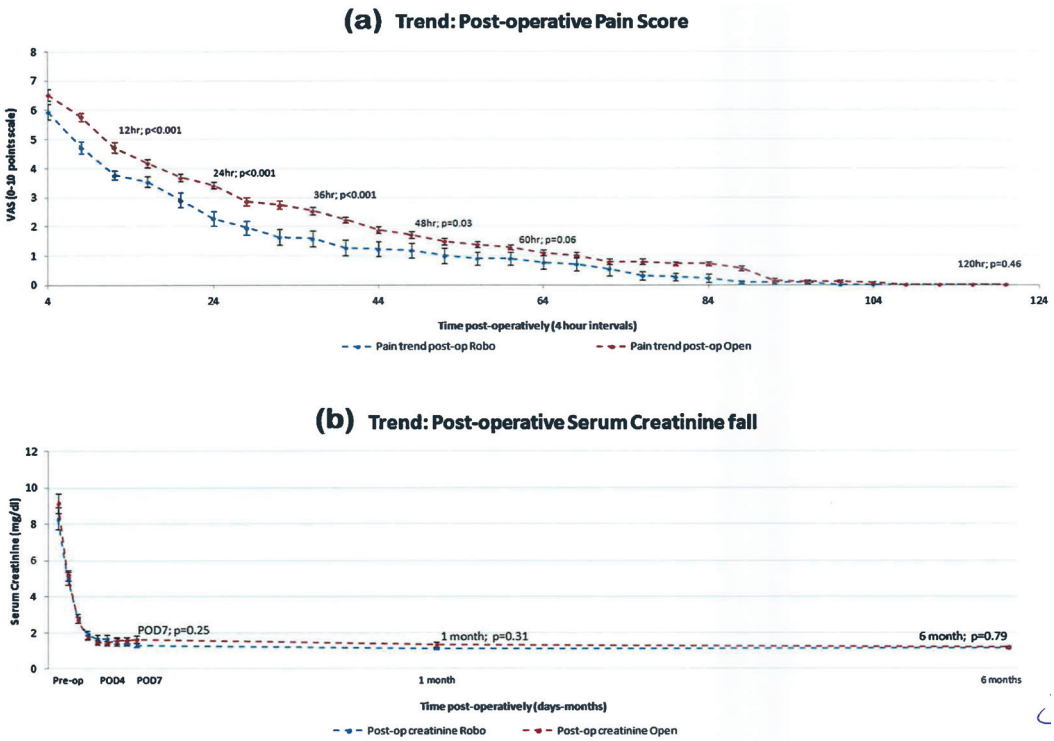


***Figure 8. Trends in (a) postoperative pain; and (b) postoperative decrease in creatinine.***

***Table 4. Summary of functional outcomes of RKT and LKT in patients with ESRD[a]***

| Study | MIKT cohort (n) | Discharge creatinine (mg/dl) | Creatinine 6 months (mg/dl) | DGF (%) | Complications (%) | | Re-explored (%) | Rejection episodes (%) | Graft loss (%) | Patient death (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Vascular | Wound | | | | |
| Oberholzer et al. | 28 [b] | 2 | 1.5 | 1 (4) | 0 | 1 (4) | 0 | 3 (11) | 0 | 0 |
| Menon et al. | 25 | 1.3 | 1.1 | 0 | 0 | 0 | 2 (8) | 1 (4) | 0 | 1 (4) |
| | | | | | | | | | | |
| Modi et al. | 72 [b] | – [c] | – [c] | 6 (8) | 6 (8) | – | – | 11 (15) | 8 (11) | – |

***[a]For detailed outcomes please refer to individual studies.***
***[b]In these studies, the total numbers of patients were 56 (all obese) for the study by Oberholzer et al. and 217 for the study by Modi et al.***
***[c]See Fig. 1 because there are no values listed in the text.***
***DGF, delayed graft function***

undergoing MIKT and OKT. Mean serum creatinine at 6 months in MIKT and OKT patients was equivalent. One (3.6%) patient undergoing RKT had delayed graft function in the study by Oberholzer *et al.* [13], while none of the patients in our cohort had delayed graft function. In both these studies, there were no vascular complications (such as vascular stenosis, leakage or torsion) in patients undergoing RKT, and none of the patients required conversion to open surgery. In contrast, Modi *et al.* [22] needed to convert LKT to open surgery in four (5.5%) patients due to poor graft perfusion or vascular anastomosis leakage. Two more patients who had undergone LKT presented with vascular torsion at 2 and 3 months after KT, and lost their grafts. Following this, Modi *et al.* modified their technique of LKT and started fixing the graft kidney extraperitoneally, rather than leaving it intraperitoneally, and consequently did not notice any torsion following this modification. We routinely extra-peritonealise our graft kidneys, as mentioned previously

in the technique section. Incidence of delayed graft function was higher in patients undergoing LKT, although this did not attain significance [6 (8%) vs. 3 (2%)].

Rejection rates were similar in MIKT and OKT patients **(Table 4)**, across the three series. Oberholzer *et al.* [13] also reported a dramatic reduction in wound complications in patients undergoing RKT (3.6% vs. 28.6%), and there is substantial evidence to support a reduction in wound complications, especially, wound infections leads to improved graft and patient survival in long-term.[23] By decreasing complication rates (such as wound complications and deep vein thrombosis/embolism), RKT might lead to attenuation of disparities with regard to transplant waiting times and access to transplantation in morbidly obese patients, solely due to the fear of having more postoperative complications [24]. We did not note any wound complication in our RKT patients. There was no graft loss in both studies evaluating RKT. One patient died of acute congestive heart failure (1.5 months post-KT) in our study, due to pre-existing cardiac pathology.

## IN CONCLUSION

MIKT appears to be a safe surgical alternative to the standard open approach. MIKT is associated with reduced postoperative pain and analgesic requirement, and better cosmesis. Specifically, the benefits of LKT are more dubious, thus, the use of this technique might only be justified in the hands of an expert. However, RKT, although in its infancy, appears to be associated with lower complication rates when compared to OKT and LKT, and has graft function outcomes that are equivalent to those of OKT.

Grade C recommendation in favour of RKT due to small sample number of studies conducted so far. Grade D recommendation for LKT.

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## Committee 8

# Prolapse Surgery

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*C-H. Rochat (Switzerland)*

# CONTENTS

# Prolapse Surgery

*P.T. Piechaud, M. Kennelly*

*E. Drapier, A. Gozen, D. Kusche, C. Mugnier, A. Nair, M. Odera, C-H. Rochat*

## I. INTRODUCTION

Pelvic Organ Prolapse (POP) can be defined as the prolapse of pelvic organs into the vaginal cavity, further to a weakening in the mechanical resistance of pelvic floor structures and to the stretching of the fixation structures of such organs along with a loosening of vaginal walls.

This mechanical condition often induces an incapacitating physical impairment in female patients. It can also be accompanied by urinary or rectal functional disorders.

The development of POP can be complete as it can affect the three compartments (i.e., anterior compartment leading to a cystocaele, medial compartment leading to uterine prolapse or posterior compartment leading to a rectocele). It can also be partial with the isolated prolapse of one or two pelvic organs.

POP is a common condition and the incidence of prolapse is evaluated to reach approximately 40% in women aged over 50 years in specific epidemiological studies. POP is a common reason for consultation in the fields of urology and gynaecology.

The repair of POP can be performed surgically and several techniques have been described, using either a vaginal route or abdominal access. Sometimes, prosthetic material may be used.

An exhaustive Cochrane comparative review of vaginal or abdominal routes in terms of outcomes and risks of complications has shown favourable results for the use of an abdominal route when the use of mesh is justified in POP treatment

In accordance with such recommendations, the first-line minimally invasive treatment of POP will be envisaged using a transperitoneal laparoscopic approach.

This chapter will first outline the anatomical and pathophysiological principles related to the onset of POP. The different steps involved in the repair technique using a double sacrocolpopexy will then be covered. This technique is considered the gold standard.

All potential technical variations of this procedure will also be detailed. The potential associated manoeuvers, the evolution towards minimalisation of the laparoscopic approach (e.g., single port) and the use of robotic assistance will also be outlined.

## II. ANATOMIC AND PHYSIOLOGIC BASIS OF PELVIC ORGAN PROLAPSE

### 1. INTRODUCTION (**Figures 1,2,3**)

Pelvic organ prolapse (POP) is the downward descent of the pelvic organs which results in protrusion of the vagina, uterus, or both. With anterior compartment prolapse, the bladder or urethra moves downward; prolapse of the central compartment involves descent of the vaginal vault with the uterus or vaginal cuff; and posterior compartment prolapse involves descent of the small intestine or rectum [1]. The lifetime risk of prolapse requiring surgical treatment is approximately 11% [2]. In addition, 29% of those women treated surgically will require reoperation for recurrence [3]. POP rarely results in severe morbidity or mortality; however, it often causes symptoms in the lower genital, urinary, and gastrointestinal tracts which can affect a woman's daily activities and quality of life [4]. It is associated with costs of more than $1 billion annually in the United States alone [5].

Normal pelvic support is provided by an interaction between the pelvic floor muscles, the connective tissue attachments and an intact nerve supply to the pelvis. The primary support of the pelvic floor comes from the pelvic muscles. When the pelvic floor muscles weaken, the endopelvic fascia becomes the primary mode of support. When the endopelvic fascial attachments break down, this eventually leads to POP [6,7].

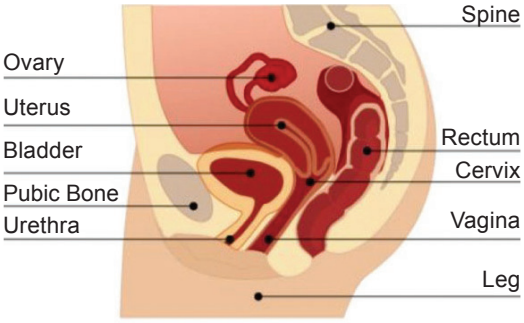


***Figure 1. Lateral Cut-away View of Female Pelvis***

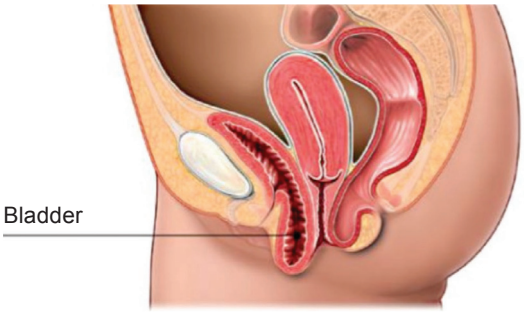


***Figure 2. Cystocele***

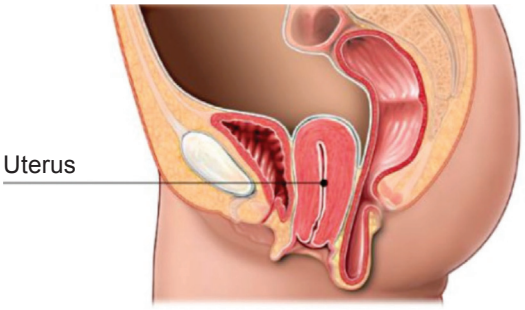


***Figure 3. Procidentia***

## 2. ANATOMY OF THE PELVIC FLOOR

A good understanding of the pelvic anatomy (bony architecture, muscles and fascia) is critical for correct reconstruction. **(Figure 4)**

### *a) Bony Structure of the Pelvis*

The bony pelvis is composed of the two innominate (hip) bones that are connected to one another at the symphysis pubis anteriorly, and fuse to the sacrum posteriorly. Each hip bone has three parts, the ilium, ischium and pubis, which are fused together in the adult **(Figure 5)**. The greater or false pelvis is the part that lies above the pelvic brim and is occupied by abdominal viscera. The narrower lesser or true pelvis lies below the pelvic brim and contains the pelvic viscera. The wider diameter and circular shape of the female pelvis allow for engagement of the fetal head and delivery, while the wider diameter of the outlet predisposes women to pelvic floor weakness [6,7].

The bony architecture of the pelvis serves as sites of attachment for muscles, ligaments and fascia. The ischial spine is an important landmark for the pelvic surgeon. It is the level at which the cervix is located in a woman with normal pelvic support. The ischial spine also serves as the site of attachment of several structures such as the coccygeus muscle, arcus tendineus fascia pelvis, arcus tendineus levator ani and sacrospinous ligament **(Figure 6)**. The ischial spine is also a clinically relevant anatomic landmark for sacrospinous ligament fixation in prolapse repairs. In addition, the pudendal neurovascular bundle lies directly posterior to the ischial spine, while the sciatic nerve lies superolateral to the ischial spine. It is hence palpated when performing pudendal nerve blocks and it is also used as the reference point for fetal presentation during labour [6,7].

The sciatic nerve is a sensory supply to the lower leg through the common peroneal branch, and is the motor nerve for the hamstring and calf muscles. Sciatic nerve injury presents as sensory loss over the calf, dorsum, lateral side and sole of the foot. Patients may have foot drop (weakness of anterior and lateral compartments of the lower leg) or inability to flex the knee (weakness of hamstrings and calf muscles). Although uncommon during pelvic reconstruction, if the sciatic nerve is injured (there are several ways this can occur), sensory deficits may be seen in 0.3% of patients [8]. Pudendal nerve injury presents as paraesthesia or anaesthesia of the perineum or buttock pain. There are no motor deficits with pudendal nerve injury.

The sacrospinous ligament extends towards the lateral margin of the sacrum and coccyx. The anterior surface of the sacrospinous ligament is composed of the coccygeus (or ischiococcygeus) muscle. The sacrospinous ligament is regarded as a degenerated part of the muscle. The sacrotuberous ligament stretches between the lateral margin of the sacrum to the ischial tuberosity and this ligament lies below the sacrospinous ligament [6,7].

## Support to pelvic organs

- **Pelvic ligaments**
  - Uterosacral ligaments
  - Cardinal ligaments
  - Pubocervical ligaments
- **Pelvic muscles**
  - Levator ani muscle
  - Puborectalis muscle
  - Pubococcygeus muscle
  - Iliococcygeus muscle

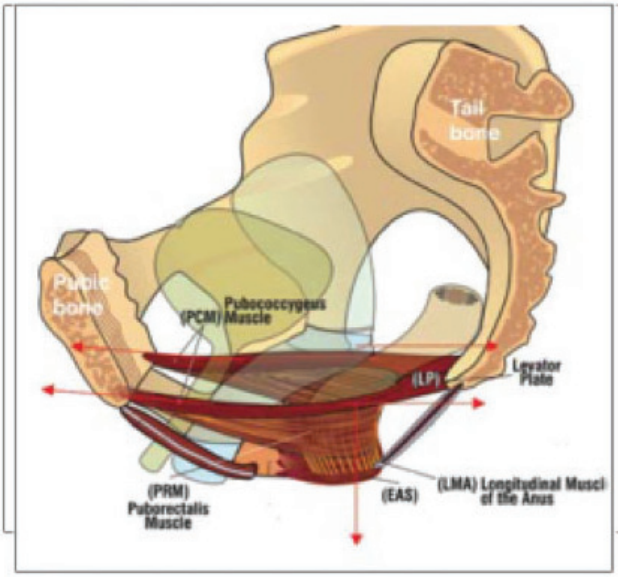


*Figure 4. Support to Pelvis Organs*

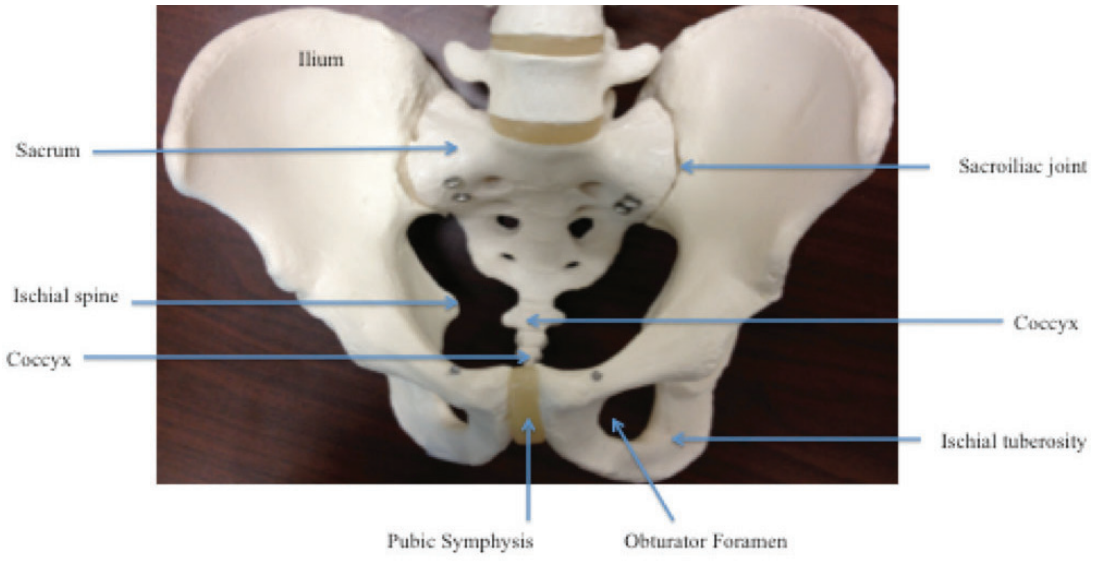


*Figure 5. Bony Architecture of the Pelvis. Head-on view of the pelvis showing the ilium, ischium, pubis, obturator foramen and pubic arch.*

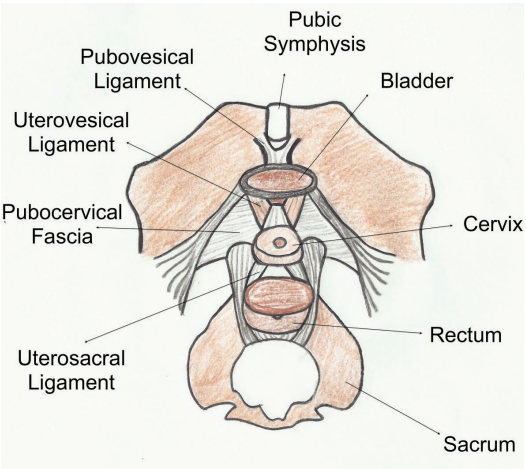


***Figure 6. Ligaments of the pelvis. Illustration of the pelvis showing the uterosacral and cardinal ligaments. The pubovesical ligament and fascia, uterovesical ligament and arcus tendineus fascia pelvis (ATFP) are also shown.***

### *b) Muscular Supports of the Pelvic Floor*

The pelvic floor, made up of muscular and fascial structures, closes the pelvic outlet. The parietal endopelvic fascia covers the skeletal muscles of the pelvis and attaches the muscles to the bony pelvis. The visceral endopelvic fascia exists throughout the pelvis, is not well defined and is seen as a loose meshwork of connective tissue through which the blood vessels, nerves and lymphatics travel from the pelvic side wall to the pelvic organs. The visceral endopelvic fascia may form discrete ligaments in places e.g., the uterosacral and cardinal ligaments.

The pelvic diaphragm is a hammock-like structure created by the levator ani and coccygeus muscles and extends from the pubic bone anteriorly to the coccyx posteriorly. The pelvic diaphragm is attached to the arcus tendineus fascia pelvis (ATFP) along the lateral pelvic walls. The ATFP or white line is a thickened linear band of the obturator internus (parietal) fascia and forms an identifiable line from the ischial spine to the posterior surface of the ipsilateral pubic symphysis.

The levator ani and coccygeus form the muscular part of the pelvic floor **(Figure 7)**. These muscles along with their counterparts from the opposite side form the pelvic diaphragm. The muscles of the pelvic diaphragm have a baseline tone helping to hold and support the pelvic organs in place. During periods of stress (e.g., a rise in intra-abdominal pressure), they actively contract to support the pelvic organs, close the genital hiatus and contribute to fecal and urinary continence mechanisms. Deficiencies in the pelvic floor muscle tone likely contribute to the development of POP.

The levator ani is composed of three muscles, the pubococcygeus, puborectalis, and iliococcygeus **(Figure 7)**. The puborectalis originates from the posterior surface of the inferior pubic ramus, travels posteriorly to create a sling around the vagina and rectum and thus creates the normal anorectal angle. The pubococcygeus has a similar origin, but it inserts into the anterolateral borders of the coccyx and the anococcygeal raphe in the midline. The iliococcygeus originates along the ATFP from the back of the pubis to the ischial spine. It inserts into the anococcygeal raphe.

The coccygeus muscle originates from the ischial spine in front of the sacrospinous ligament and inserts into the lower lateral sacrum and coccyx **(Figure 7)**. The coccygeus forms the posterior part of the pelvic floor. With advancing age, the muscle becomes thin and fibrous and it may often be difficult to distinguish the coccygeus muscle from the sacrospinous ligament. This muscle-ligament complex is often used as the anchoring point in several prolapse repair surgeries such as sacrospinous ligament fixation or iliococcygeus vault suspension. The genital hiatus is the space through which the vagina, rectum and anal canal pass.

The levator ani, coccygeus and obturator internus are striated muscles. The puborectalis and pubococcygeus are often difficult to distinguish separately on imaging techniques and are often grouped together as the pubovisceral muscle.

The levator ani muscle complex is tonically contracted at rest and acts to close the genital hiatus and provide a stable platform for the pelvic viscera. Static and dynamic MRI as well as MR-based diffusion tensor imaging (DTI) have recently been used as a novel potential tool to evaluate and study pelvic floor muscle fibre morphology [9]. Computational models allow accurate anatomical representation and provide information on tissue behaviour. Modelling takes into account the geometry, biomechanical properties (viscoelasticity, anisotropic mechanical response, quasi incompressibility) and fibre direction. Due to limitations in spatial resolution, conventional MRI is not able to provide full insight into muscle anatomy or physiology [10,11,12,13]. DTI overcomes the limitations in spatial resolution and provides detailed information on tissue organisation including the shape, direction, density, pennation, insertion, and internal fibre arrangement of the pelvic floor muscle (PFM). PFM fibre direction obtained using DTI adds information on PFM, fibre orientation and pennation (obliquity between muscle fibres and the main axis of the muscle). Thus, DTI is used as an input for biomechanical simulation models. Finite Element Modelling (FEM) is one of the common approaches used in modelling pelvic structure biomechanical behaviour, and this technology may be useful for simulating the effects of vaginal delivery or in surgical planning [14].

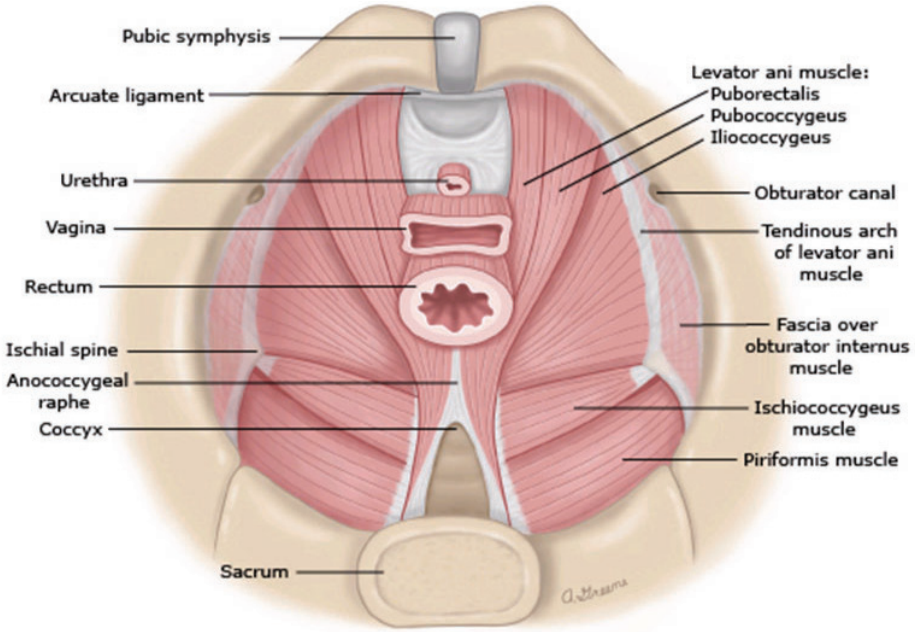


***Figure 7. Pelvic muscles at the level of the pelvic floor. The hammock shaped levator ani, coccygeus and piriformis muscles are seen.***

***(Reproduced with permission from UpToDate)***

### *c) Muscular Supports of the Pelvic Sidewalls*

The obturator internus and piriformis form the muscles of the pelvic sidewalls **(Figure 7)**. The obturator internus muscle originates from the inferior margin of the superior pubic ramus and passes through the lesser sciatic foramen to insert into the greater trochanter of the femur. The obturator membrane is a thin fibrous structure that covers the obturator foramen. The piriformis originates from the anterolateral sacrum, passes through the greater sciatic foramen to insert into the greater trochanter of the femur. It lies dorsolateral to the coccygeus.

### d) Levels of Support of the Pelvic Viscera

DeLancey described 3 levels of support for pelvic viscera **(Figure 8)** [15]**.** Level I support is composed of the uterosacral-cardinal ligament complex, which supports the cervix and upper vagina. This helps to keep the cervix above the ischial spines. Loss of level I support will present as uterine prolapse or post-hysterectomy vaginal vault prolapse. Level II support is provided anteriorly by the ATFP, which supports the paravaginal attachments along the length of the vagina, and posteriorly by the levator ani. It serves to keep the vagina in the midline and creates the lateral fornices. Loss of level II support presents as anterior compartment (midline cystocele, paravaginal defect cystocele, uterine or vault prolapse) or posterior compartment prolapse (rectocele, enterocele). Level III support is provided by the perineal body, which supports the most inferior portions of the vagina and perineum. Defects of this level presents with urethrocele, rectocele or perineal descent. All three levels of support are connected to one another through the endopelvic fascia that is continuous.

## 3. IMPACT OF POP

POP can affect a patient's quality of life in many ways, but predominantly due to bothersome urogenital symptoms. In addition to POP symptoms (vaginal bulge, pressure, pain, bleeding, discharge and low back pain), bladder, bowel and sexual dysfunction symptoms are often attributable to POP. Voiding dysfunction includes urinary-stress, urge, mixed, and coital incontinence, nocturia and recurrent urinary infections): bowel dysfunction includes fecal incontinence, inability to evacuate the bowel spontaneously or completely, the need to splint and/or manually replace the prolapse): and sexual dysfunction includes dyspareunia, both superficial or deep, and vaginal laxity. It should be noted that there is no clear correlation between the extent of the prolapse and the symptoms caused. However, evidence suggests that women with the leading edge of the prolapse beyond the hymenal remnants have increased symptoms [16]. With increasing life expectancy and aging of our population, this is a problem not only for our patients, but also impacts the healthcare system.

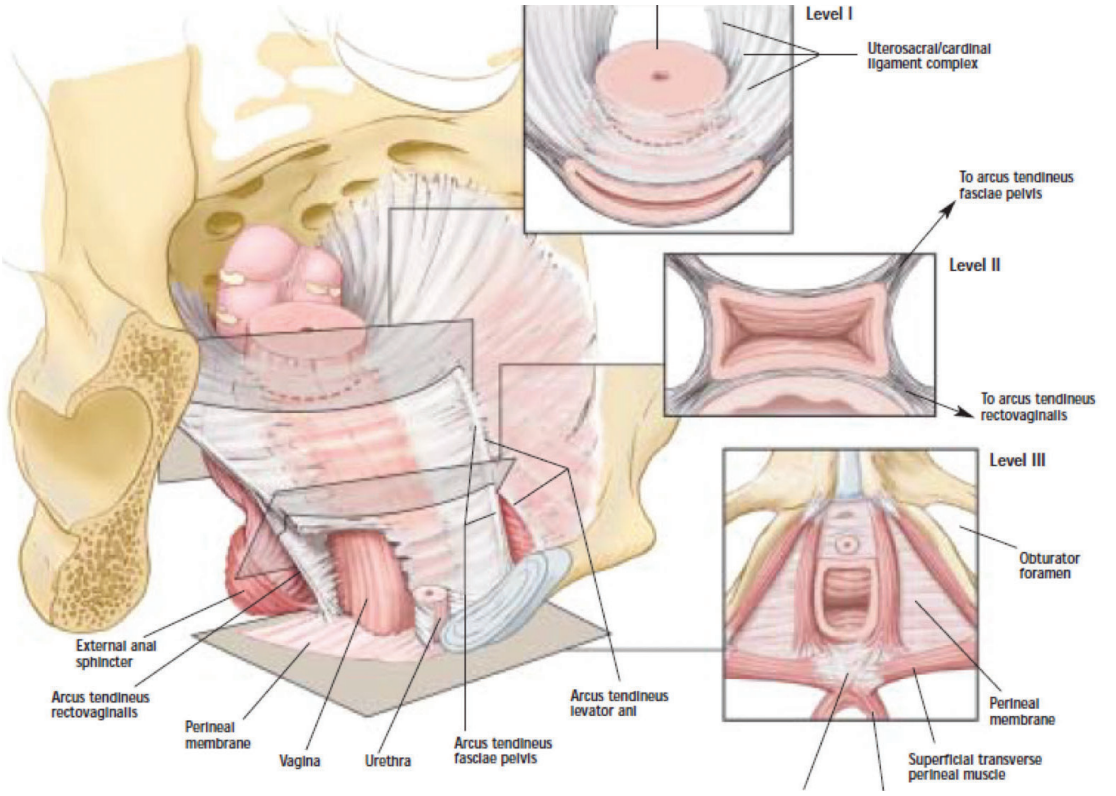


***Figure 8. DeLancey levels of vaginal support. Level I provides apical support. Level II supports the middle portions of the vagina. Level III supports the lower vagina and perineum.***

*(Reproduced with permission from Walters MD, Karram MM. Urogynecology and reconstructive pelvic surgery, 3rd ed, Mosby-Elsevier, 2007).*

### *a) Prevalence*

POP is defined by the International Urogynaecological Association (IUGA) and the International Continence Society (ICS) in their joint report as: the diagnosis by symptoms and clinical examination assisted by any relevant imaging, of descent of one or more of the following structures: the anterior vaginal wall (central, paravaginal or combination), posterior vaginal wall (rectocele), uterus/ cervix or the apex of the vagina (vaginal vault or cuff scar) after hysterectomy [17]. It is generally accepted that 50% of women will develop prolapse but the overall prevalence of POP shows significant variation, depending on the definition used, and ranges from 3% to 50% [18]. When POP is defined and graded on symptoms, the prevalence is 3% to 6%, as compared with 41% to 50% when based on examination, indicating that the majority of women with prolapse are asymptomatic [16,18,19,20]. On examination, anterior compartment prolapse is the most frequently reported site of prolapse, is detected twice as often as posterior compartment defects, and three times more often than apical prolapse [21,22].

In a large demographic study, Luber and associates showed that the peak incidence of symptoms attributed to prolapse is between the ages of 70 and 79 years, whereas POP symptoms are still relatively common in women of younger age [23].

### *b)* Etiopathogenesis of POP

The etiopathologic features of POP are complex, still poorly understood and multifactorial, attributable to a combination of risk factors and vary from patient to patient [24]. No single mechanism adequately explains all the aspects of POP development. Women with several risk factors may have normal pelvic organ support, while others with no risk factors may still develop prolapse.

Bump and Norton hypothesized that a continuum of predisposing, inciting promoting and decompensating factors will result in the development of POP [25]. A reduction in the stability of the pelvic floor muscles and connective tissue through tearing, trauma, and chronically raised intra-abdominal

pressure are likely to be the key mechanisms involved in the development of POP.

Failure of normal levator ani function is an important hallmark of POP. However, the mechanisms by which the levators support the vaginal wall and how these mechanisms fail during the development of prolapse are not well understood. Smooth muscle (SM), an integral part of the vaginal wall and endopelvic structures that support the pelvic viscera, has also been implicated in the pathophysiology of POP [26]. As an example, the SM arising from the vaginal wall attach to the levator ani. Dysfunction of these SM fibres may affect the attachment of the lateral vaginal wall to the pelvic sidewall [27,28]. Studies have described a decrease in the SM content in the ligaments of women with POP [29,30,31].

***c)*** **Risk Factors for POP**

There are many risk factors for the development of POP **(Table 1)**; however, vaginal birth, advancing age, and an increased body mass index (BMI) or obesity are known to be the most consistent risk factors for developing uterovaginal prolapse. Prolapse may occur in young women or nulliparous women who have some of the identifiable risk factors below; but sometimes no obvious risk factor may be evident.

**1. Vaginal Birth**

Based on epidemiologic and cohort studies, vaginal delivery is reported to be the most relevant risk factor for development of pelvic floor dysfunction [20,32,33]. During the **second** stage of labour when the foetal head distends and stretches the pelvic floor, these muscles, their associated connective tissues and nerves sustain mechanical damage. This mechanical damage may be in the form of stretching or rupture of the fibres. In addition, there may be biochemical damage to the soft tissue in this area especially in cases of prolonged second stage of labour.

| |
|---|
| Vaginal childbirth |
| Pregnancy |
| Advancing Age |
| Obesity |
| Genetic factors |
| Race |
| Connective tissue disorders |
| Prior pelvic surgery |
| Chronically elevated intra-abdominal pressure |
| Anatomic/Neurologic abnormalities |

***Table 1. Risk Factors for POP.***

Vaginal delivery leads to tearing, stretching, and dislocation of the pelvic muscles, ligaments, connective tissues and nerves. Irreversible trauma to the pelvic floor during vaginal delivery can lead to pubovisceral muscle avulsions. Avulsions are partial or complete detachments of this muscle complex from its insertion on the pubis [34]. Lammers et al used T2 weighted MRI with a 3D post-processing programme to quantify pubovisceral muscle avulsions and reported that this occurs in >36% of vaginal deliveries [34]. Besides this direct levator muscle injury, it can also be indirectly injured due to denervation causing muscle atrophy or due to ischemia with reperfusion injury. During vaginal delivery, the use of forceps and prolonged second stage of labour are additional factors associated with levator ani muscle avulsions [34].

In general, POP shows an association with parity, but more specifically with vaginal childbirth. Two or four children delivered vaginally results in a relative risk (RR) of developing POP of 8.4 and 10.9, respectively, as compared with nulliparous women. Hendrix and associates showed similar findings, and reported that each additional birth increased the risk of developing POP by 10% to 20% [21]. Forceps delivery, high infant birth weight, prolonged second stage, and young age (under 25 years old) at first pregnancy are considered additional obstetric risk factors for POP, but less than vaginal childbirth and parity [16,35].

Studies conducted in animal models looked at the relationship between childbirth, LOL 1 gene expression and elastin [36]. Elastin fibres undergo degradation before childbirth and show a high turnover after childbirth. This turnover allows tissues to recover postpartum. In addition to differences in LOL 1 expression, it was noted that monocytes were present in the vagina during childbirth. These cells induce elastolysis by chemotaxis. Fibulin is an elastin binding protein that is important for elastinogenesis and cross linking of elastin fibres. Fibulin counteracts elastin degradation and is crucial for its regeneration. Drewes et al demonstrated that mutations in fibulin 5 gene were causative in the progression of POP with age [36].

Cesarean section may be only partially protective for POP. Studies have shown that even though cesarean section may reduce (not totally prevent) incontinence, it helps to considerably lower POP rates [37,38]. The influence of cesarean section after labour (versus no-labour) towards the development of POP was negated in an epidemiologic study that used a validated questionnaire [39]. Lukacz et al reported in their study that elective cesarean section reduces the incidence of POP [40]. For every seven women with elective cesarean section, one woman would be prevented from developing a pelvic organ disorder [40]. Other investigators report that delivery by cesarean section has no effect on the occurrence of prolapse in young women [41,42,43].

### 2. Pregnancy

The question of whether pregnancy is to be considered a risk factor for POP is controversial. While some studies show pregnancy to be a risk factor for the development of POP, others have failed to show such a correlation. Some studies have found stage 2 POP (based on ICS quantitation) in up to 48% of pregnant women [44,45]. The stage of prolapse increased during pregnancy and worsened in the postpartum period if the women were delivered vaginally [46,47]. The anterior vaginal wall was the most frequent site of POP in these studies.

The development of POP during pregnancy is multifactorial including the effect of enzymes and hormones. Progesterone, a hormone that is seen in high levels in pregnancy has smooth muscle relaxing properties and oestrogen antagonistic effects. This leads to a reduction in the tone of ureters, bladder and urethra [48]. Relaxin is another hormone that is elevated in pregnancy and has collagenolytic activities enabling connective tissue remodelling (softening, stretching) in preparation for vaginal childbirth [49]. Investigators have found that during pregnancy, connective tissue can be stretched to a greater extent, contributing to weakness of the fascia during this time. Such changes during pregnancy may cause permanent dysfunction when the fascia or connective tissue is stretched beyond physiologic limits and the changes may be irreversible [50].

However, prolapse can also be seen in nulliparous women; therefore, other factors must be involved in the development of prolapse, which supports the multifactorial model of the genesis of POP.

### 3. Age

Advancing age is strongly associated with POP. Progressive denervation of the pelvic floor muscles with age may contribute to POP [51]. The relative prevalence of POP rises approximately 40% with every decade of life [52]. Even though most epidemiologic studies have determined age to be a big risk factor for POP, the interaction between age and hormonal status/menopause seems to be inseparable [21,22,37,53].

### 4. Obesity

Obesity is defined as a body mass index (BMI) of 30 or more by the World Health Organization. Several investigators have looked at the correlation between BMI and POP. While some studies show obesity to be a risk factor for the development of POP, other studies have failed to show such a correlation. Thus, even though we lack definite evidence of a causal relationship between obesity and POP, no study has found overweight to be protective.

Obesity places excessive strain on the pelvic floor, supporting muscles, connective tissues, and pudendal nerves [16,54]. As a result, women who are overweight or obese are at high risk of developing POP with an OR of 2.51 (95% CI 1.18-5.35) and 2.56, respectively. Increased BMI or increased waist circumference has been shown to increase the risk for POP, rectoceles and cystoceles [22,35,37,52,55].

### 5. Genetics

POP may be attributed to congenital factors as in women with a family history of prolapse or weak connective tissue. Women with prolapse show an association with a strong family history of prolapse, increased prevalence of hernias in patients with POP, racial differences in the prevalence of prolapse, and the increased prevalence in women with a connective tissue disorder (e.g., Marfan syndrome) make it very likely that genetic factors play an important role in the etiology of POP.

Familial incidence of prolapse has been reported to be as high as 30% [56]. Several studies have shown an increased prevalence of POP in family members, especially identical twins [56,57,58]. Gene expression of structural proteins (elastin, collagen etc] may be altered in women with POP. This leads to reduced production of these proteins in areas such as the uterosacral ligaments and other pelvic supportive tissues, thereby contributing to the development of POP [59,60].

Quantitative and qualitative differences in collagen are also likely to contribute to POP. Women with POP have proportionally more type III collagen than other subtypes [61]. Jackson and associates found that in premenopausal women with POP there was a reduction in total collagen and secondary increased collagenolytic activity in samples of vaginal tissue, as compared with those without prolapse [62]. Differences in collagen structure may possibly account for the strong familial links to prolapse development.

POP and hernias share similar pathophysiologic features. Patients with hernias show decreased collagen synthesis and metabolism, a protease-antiprotease imbalance with increased matrix metalloproteinase activity, and a reduced collagen type I/III ratio. Segev and colleagues demonstrated that women with POP have a significantly higher total prevalence of hernias [63].

### 6. Race

Racial or ethnic differences in pelvic floor function have been described. Studies have shown that African-American women have a lower prevalence of POP than Caucasian-American women [23,32,64,65].

In a population-based cohort study of 2270 women, Whitcomb et al reported that Latin and Caucasian women had a 4-5-fold higher risk of symptomatic

prolapse when compared with African-American women [65]. Caucasian women had a 1.4-fold higher risk of objective prolapse with the leading edge of prolapse at or beyond the hymen. The study showed a prevalence ratio of 5.35 (95% CI 1.89 to 15.12) and 4.89 (95% CI 1.64 to 14.58) for symptomatic prolapse in Caucasian and Latin women, respectively, compared to African-American women. This prevalence may be the result of a smaller pelvic outlet, compared with women from European descent.

#### 7. Connective Tissue Disorders

Patients with connective tissue disorders, such as Ehlers-Danlos syndrome and Marfan syndrome with impaired collagen and elastin synthesis and metabolism, have a higher rate of POP. In a small cohort study, 33% of women with Marfan syndrome and 75% with Ehlers-Danlos syndrome developed POP [66]. These findings underline the hypothesis that connective tissue disorders play an important role in the cause of POP. Intrinsic joint hypermobility is another connective tissue disorder that shows an association with POP [67,68,69].

#### 8. Prior Pelvic Surgery

Prior pelvic surgery may also be a risk factor for subsequent POP surgery, depending on the indication [70,71].

Prior pelvic surgery or iatrogenic prolapse is well reported with anterior compartment prolapse observed in up to one third of women after sacrospinous ligament fixation; in addition, posterior compartment defects increased by one third in those who underwent colposuspension as compared to suburethral tape continence surgery or hysterectomy [72,73]. More recently, a single study found that de novo POP greater than the Pelvic Organ Prolapse Quantification (POP-Q) system stage II occurred in 46% after an isolated anterior vaginal mesh repair and in 25% after an isolated posterior vaginal mesh repair [74].

Isolated enteroceles may occur after pelvic surgery, as is seen in over 30% of women after a Burch colposuspension [75,76,77,78].

#### 9. Other Factors

Chronically elevated intra-abdominal pressure (chronic cough, chronic constipation, asthma, chronic obstructive pulmonary disease etc), chronic straining, high impact sports, and regular heavy lifting are other factors that have been implicated in the development of POP [2,24,79,80]. Physically demanding occupations such as nurses, cleaners, or caregivers are twice as likely to develop POP [81]. These occupations place excessive strain on the pelvic floor, supporting muscles, connective tissues, and pudendal nerves [16,54].

Smoking may also be linked to the development of POP [82,83]. Studies have shown that delivery of a higher birth weight infant (>4000 g) may increase risk for POP, as does extensive vaginal tears [32,37,84].

## 4. CONCLUSIONS

POP is a common condition that may require surgical treatment and is prone to recurrence.

The bony, muscular, connective tissues and intact nerve supply provide normal support to pelvic organs.

POP can impact a woman's quality of life in several ways.

POP is multifactorial in origin.

## 5. RECOMMENDATIONS

A clear and thorough understanding of pelvic floor anatomy is crucial for performing pelvic reconstructive surgery.

The dissection and surgical approach should be tailored to allow the patient achieve her goals.

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## III. METHODS OF ACCESS AND TECHNIQUES FOR THE SURGICAL TREATMENT OF POP: CONSENSUS ON COMPARED RESULTS

A few clinical studies have compared the quality of results, safety and rate of complications of different methods of access and techniques for prolapse repair.

### 1. SACROCOLPOPEXY VERSUS VAGINAL SURGERY

A Cochrane review comparing different surgical techniques for the treatment of POP concluded that abdominal sacrocolpopexy (ASC) leads to a lower rate of recurrent vault prolapse (relative risk 0.23) and postoperative dyspareunia (relative risk 0.39) compared with sacrospinous ligament fixation (SSLF), albeit with a longer operative time, recovery period, and greater cost. Abdominal surgery was associated with lower reoperation rates for prolapse, but this association did not reach statistical significance [1]. The incidence of mesh erosions after laparoscopic sacrocolpopexy (LSC) (2.7% on average) was lower than that reported after vaginally placed mesh, which is up to 40% [2]. According to the Cochrane recommendations concerning sacral colpopexy, no mesh should be introduced or sutured by the vaginal route when sacral colpopexy is performed, due to the risk of erosion [1].

A recent randomized trial comparing LSC and total vaginal mesh for vaginal vault prolapse [3], showed that the LSC group had a longer operative time, reduced inpatient days, and quicker return to daily activities as compared with the total vaginal mesh group. At the 2-year review, the total objective success rate at all vaginal sites was 77% for LSC and 43% for total vaginal mesh (P <0.001). Reoperation rate was significantly higher after vaginal mesh surgery (22% vs 5%, P=0.006), and there was a trend for higher mesh erosion rate (9% vs 2%, P=0.11). LSC also resulted in a higher satisfaction rate.

Finally, a prospective study compared changes in urinary symptoms before and after POP surgery only, using either LPS or transvaginal porcine dermis hammock placement with sacrospinous ligament suspension [4]. According to the results, at a follow-up of 32.4 months, most preoperative symptoms decreased after POP surgery with an equivalent proportion of de novo symptoms after the vaginal and laparoscopic approaches.

The main studies addressing a comparison between sacrocolpopexy and vaginal surgeries are reported in T**able 1**.

*Table 1. SC versus VAGINAL SURGERY.*

| Author, year | Surgery, patients | FU, mo | Prolapse recurrence | Success | Complications |
|---|---|---|---|---|---|
| Benson, 1996 **[5]** | Vaginal SSLF (n = 42) | 29 | Reoperations for recurrence 21.4% | Surgical effectiveness 67% | Dyspareunia (35.7%), UTI (21.4%), suture migration into the vagina (0%) |
| | Abdominal SC (n = 38) | | Reoperations for recurrence 13.1% | Surgical effectiveness 84% | Dyspareunia (0%), UTI (0%), suture migration into the vagina (2%) |
| Lo, 1998 **[6]** | Vaginal SSLF (n = 66) | 25 | Surgical effectiveness 80.3% | | Complications that necessitated further surgical correction (10.6%) |
| | Abdominal SC (n = 52) | | Surgical effectiveness 94.2% | | Complications that necessitated further surgical correction (7.6%) |
| Maher, 2004 **[7]** | Vaginal SSLF (n = 48) | 24 | Anterior vaginal wall and vault prolapse 45% | Subjective 91%, objective 69% | Constipation (19%), de novo dyspareunia (6%) |
| | Abdominal SC (n = 47) | 22 | Anterior vaginal wall and vault prolapse 13% | Subjective 94%, objective 76% | Constipation (26%), de novo dyspareunia (4%) |
| Marcickiewicz, 2007 **[8]** | Vaginal sacrospinous colpopexy (n = 51) | 33 | 4 (8%) reoperations for recurrence | Subjective 82% | Urinary (19.6%), bowel (13.7%) symptoms, dyspareunia (25%) |
| | Laparoscopic SC (n = 60) | | 15 (25%) reoperations for recurrence | Subjective 78% | Urinary (25%), bowel (16.4%) symptoms, dyspareunia (28.1%) |
| Maher, 2011 **[3]** | Total vaginal mesh (n = 55) | 24 | 5% reoperations for recurrence | Objective 43% | Vaginal mesh erosions (13%) |
| | Laparoscopic SC (n = 53) | | 0% reoperations for recurrence | Objective 77% | Vaginal mesh erosions (2%) |
| Ramannah, 2012 **[4]** | Vaginal porcine dermis hammock placement with SSL suspension ( n = 64) | 32.4 | 15 (23%) anatomical recurrences | NA | De novo urinary symptoms (45.3%) |
| | Laparoscopic SC (n = 87) | | 2 (2.3%) anatomical recurrences | NA | De novo urinary symptoms (28.7%) |

*Table 2. Laparoscopic SC versus abdominal SC*

| Author, year | Surgery, pts | FU, mo | EBL, ml | OT, min | Recurrence | Success | Complications |
|---|---|---|---|---|---|---|---|
| Hsiao, 2007 **[10]** | LSC: 25 | 6 | 83 | 220 | 100% Baden-Walker stage >0 | | LSC led to shorter hospitalization, better hemostasis and less pain than ASC. |
| | ASC: 22 | 11 | 195 | 185 | 85% Baden-Walker stage >0 | | |
| Klauschie, 2008 **[11]** | LSC: 43 | 7 | 104 | 183 | 9% symptomatic failure | 93% POP-Q point C higher than half vaginal length, 91% subjective improvement | Wound infection (7%), de novo pain (7%), mesh erosion (2 %), bowel complication requiring surgery (2%) |
| | ASC: 41 | 11 | 139 | 168 | 5% symptomatic failure | 88% POP-Q point C higher than half vaginal length, 95% subjective improvement | Wound infection (5%), de novo pain (7%), mesh erosion (2%), bowel complication requiring surgery (2%) |
| Coolen, 2013 **[12]** | LSC: 43 | 2 | 50 | 120 | NA | NA | 7% treated complications no major complications |
| | ASC: 42 | 2 | 200 | 120 | NA | NA | 28.6% treated complications, 7.1% major complications |
| Freeman, 2013 **[13]** | LSC: 23 | 12 | 56 | 144 | -6.67 cm (POP-Q point C), 80% subjective improvement | | NA |
| | ASC: 24 | 12 | 240 | 131 | -6.63 cm (POP-Q point C), 90% subjective improvement | | NA |
| Khan, 2014 **[15]** | LSC: 176 | NA | NA | NA | 3.4% reoperations for anterior vaginal wall prolapse | | 22.7% medical complications, 1.1% febrile morbidity, 26.7% UTIs |
| | ASC: 794 | NA | NA | NA | 0.9% reoperations for anterior vaginal wall prolapse | | 31.5% medical complications, 6% febrile morbidity, 38.8% UTIs |
| Nosti, 2014 **[9]** | LSC: 273 | 8 | 100 | 272 | 6.5% anatomical failure at or beyond the hymen, 11.3% stage 2 or higher | | 18% overall complication rate, 4% mesh erosion, 1.8% ileus/small bowel obstruction |
| | ASC: 589 | 14 | 150 | 222 | 15.1% anatomical failure at or beyond the hymen, 25.3% stage 2 or higher | | 20% overall complication rate, 2.6% mesh erosion, 5% ileus/small bowel obstruction |

## 2. LAPAROSCOPIC VERSUS ABDOMINAL SACROCOLPOPEXY

The outcomes of LSC versus ASC have been compared in several studies [9, 10-13], and the main results are listed in **Table 2**. Only two of these studies are prospective, multicentre studies [11, 12]. According to these studies, the operative times are roughly equivalent between the two approaches, whereas blood loss and hospital stay were reduced following LSC. Surgical outcomes and patient satisfaction are good and comparable in both groups. With regard to morbidity, LSC is associated with a lower rate of complications compared with ASC, which results in high morbidity [14]. This difference in morbidity, however, is not so marked in all the studies, as seen in the retrospective chart review conducted by Klauschie et al [11]. Similarly, Nosti et al [9] detected a higher complication rate following ASC compared with minimally invasive sacrocolpopexy (20% vs 12.7%, $P<0.01$); however, this difference was only slight when comparing ASC with LSC (20% vs 18%).

In relation to surgical morbidity, mesh-related complications were significantly higher when sacrocolpopexy was performed with concomitant hysterectomy [15], as previously demonstrated [16, 17, 18, 19].

## 3. CONCLUSIONS

There are few studies in the literature involving a comparison between sacrocolpopexy and vaginal surgeries. The available studies are quite heterogeneous, as there are several different vaginal approaches. According to a Cochrane review comparing different surgical techniques to treat POP, ASC leads to a lower rate of recurrent vault prolapse and postoperative dyspareunia, compared with sacrospinous ligament fixation. ASC seems to be associated with lower reoperation rates for prolapse when compared to vaginal surgery. No mesh should be introduced or sutured by the vaginal route when a sacral colpopexy is performed, due to the risk of erosion. ASC can be considered the best option for apical and/or multicompartment POP.

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# IV. LAPAROSCOPIC SACROCOLPOPEXY: SURGICAL TECHNIQUE SAINT AUGUSTIN PROTOCOL

For urological surgeons who regularly perform pelvic laparoscopic procedures, LSC is a relatively straightforward procedure, and it may serve as a stepping stone to more complex pelvic laparoscopy such as radical prostatectomy and cystectomy [1]. The surgical technique is described in detail below [1, 2].

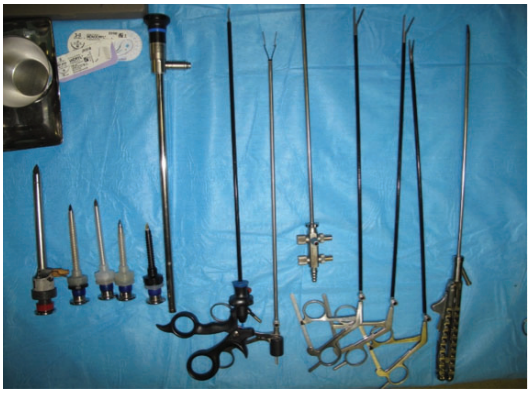

***Figure 1. Instruments***

## 1. INSTRUMENTS

- 10-mm 0° laparoscope and camera port
- Three 5-mm laparoscopic trocars
- 5-mm monopolar diathermy scissors
- 5-mm bipolar diathermy grasper
- Two 5-mm Johann graspers
- 5-mm needle holder
- One Nylon 2/0 ref 2434, straight needle (Ethilon)
- Three Polyester 0 ref 2526, 26-mm needle (Mersuture)
- Two Polypropylene 2/0 ref 8833, 26-mm needle (Prolene)
- One Suction device
- Malleable vaginal valve with blunt end
- Polyglactin 0 ref JV 1037, 32-mm needle (Vycril)

## 2. MESH

If the technique involves total repair of the three prolapse compartments, two meshes will be used **(Figure 2)**, for anterior and posterior vaginal suspension.

For sacrocolpopexy, autologous fascia, allografts such as cadaveric fascia lata or porcine x-linked collagen meshes, and synthetic meshes can be used. The use of synthetic mesh (durable and inert) in ASC has helped achieve its high success. The most commonly used materials for ASC meshes are polypropylene and polyester. A monofilament mesh-like polypropylene has large interstices which allow entry of leukocytes, macrophages, fibroblasts, new blood vessels, and collagen fibres; these features should reduce the risk of infection and erosion. Based on experimental animal studies, the frequency and intensity of prosthetic contraction should be lower with polyester meshes. The erosion rates with polyester are dangerously high only when the vagina is opened. In our daily practice, we knot a suture to the mesh before its insertion in the abdominal cavity, to ease the suturing manoeuvres.

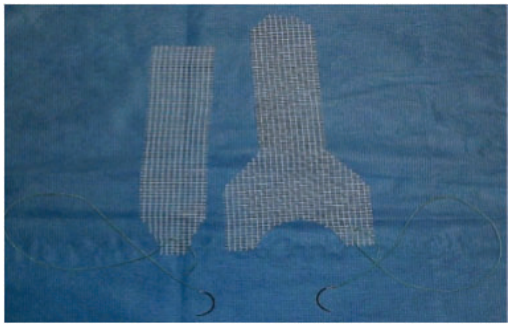

***Figure 2. Example of type of mesh:***

***Parietex: Polyester multi-filament***

## 3. PORT PLACEMENT AND PATIENT PREPARATION (Figure 3)

The patient is placed in a modified lithotomy position, with the legs abducted and parallel to the level of the bed. A 30-degree Trendelenburg position is obtained in order to displace the small bowel from the pelvic area. Pneumoperitoneum is established by 12 mmHg insufflation pressure. A 10-mm camera port is placed at the level of the umbilicus or immediately below, according to the patient's habitus. We commonly use a blind technique with a sharp automatically retracting port, or a Veress needle to create the pneumoperitoneum. Left and right 5-mm working ports are inserted under direct vision at a point 2/3 of the distance between the umbilicus and the anterior superior iliac spine. A third 5-mm port is placed midway between the umbilicus and the symphysis pubis. The surgeon generally works from the patient's left side using the left and midline ports, while the assistant has access to the camera and right port. If needed, another 5-mm trocar can be placed in order to displace the bowel and expose the sacral promontory. The assistant also has access to the vaginal valve in order to correctly show the vaginal vault.

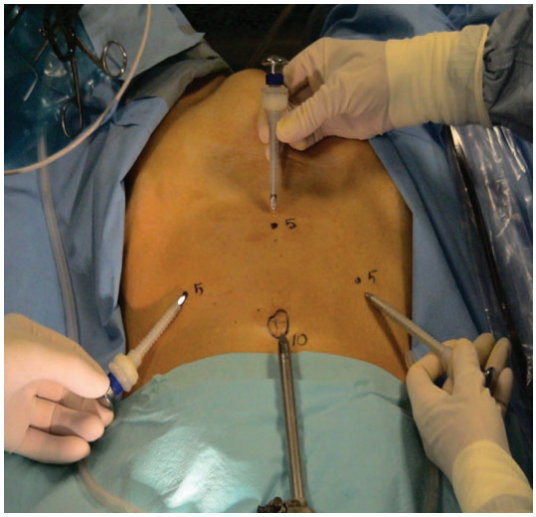

*Figure 3. Port placement.*

## 4. OPERATIVE PROTOCOL: STEP-BY-STEP

### *a) Pelvic Exposure*

The first essential step in achieving adequate exposure of the pelvic organs is to mobilise both the ascending and descending colon as far as the pelvic brim, allowing them to drop back into the abdomen whilst leaving only the bladder, uterus and rectum in the surgical field. To allow access to the posterior compartment, we secure the uterus to the abdominal wall by means of a percutaneous suture on a straight needle, passed suprapubically through the abdominal wall. The suture is passed through the fundus of the uterus.

### *b) Identification of the Sacral Promontory* **(Figure 5)**

With the uterus retracted and the colon mobilised, the sacral promontory is easily identified by the tip of the scissors. The posterior peritoneum is incised over the bony prominence taking care to avoid the ureter as it crosses the pelvic brim. The dissection is gently carried out with the tip of the scissors, allowing the gas to penetrate into the tissues and to open the dissection plane. The pearly white surface of the anterior vertebral ligament and the middle sacral vessels in contact with it are carefully exposed, preparing the surface for the final part of mesh fixation.

### *c) Perirectal Dissection*

The peritoneal incision **(Figure 6)** is continued lateral to the rectum, just beyond the uterosacral ligament ridge. Care is taken to preserve perirectal fat, minimising the risk of iatrogenic bowel injury, ischemia or neurovascular damage. The dissection is carried on laterally until the pelvic floor muscles become visible deep in the pelvis.

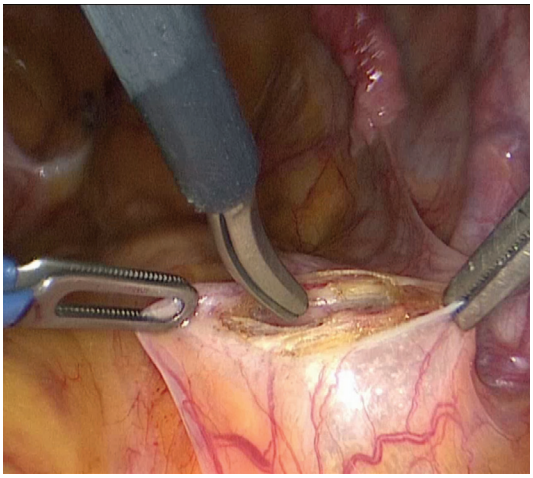

*Figure 5. Sacral promontory exposure.*

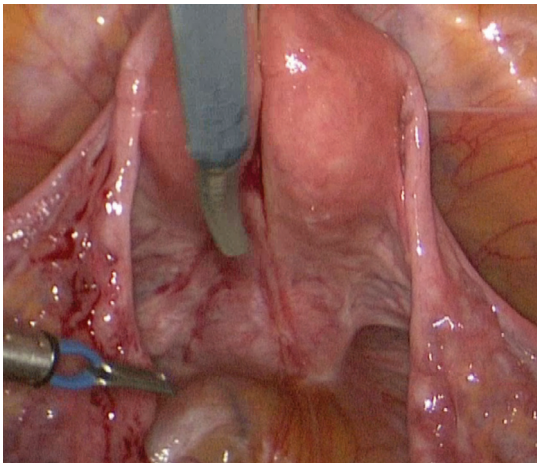

*Figure 4. Pelvic exposure.*

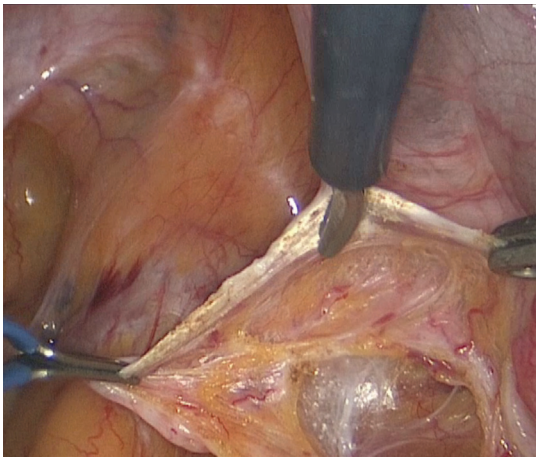

*Figure 6. Peritoneal incision.*

***d) Posterior (Rectovaginal) Dissection***

The peritoneum is also incised on the left side of the rectum. The dissection is facilitated by the insertion of a malleable vaginal valve to show the limits of the vaginal wall. At the end of the dissection, good anchor points on the levator ani muscle **(Figure 7)** should be visible on both sides in preparation for posterior mesh placement.

***e) Posterior Mesh Placement* (Figure 8)**

We use a two-part mesh set with pre-cut anterior and posterior components in polypropylene. The broad end of the posterior mesh is anchored to the levator ani muscle bilaterally as well as to the vaginal vault in the midline, using nonabsorbable sutures. Polyester (Mersutures) is routinely used in this step. Interrupted sutures are applied; the needle is turned from up to down deep into the levator ani, clockwise on the right side and anticlockwise on the left. Care is taken to protect the rectum. The mesh is also anchored to the uterosacral ligament ridge. At the end of this step, the suture placed earlier to retract the uterus can be removed.

***f) Fenestration of the Broad Ligaments* (Figure 9)**

Windows in the broad ligaments are made to allow passage of the anterior mesh, which will later need to be fixed to the sacral promontory. The *pars flaccida* of the broad ligaments is incised, taking care not to damage the uterine arteries and fallopian tubes. This step is obviously omitted in the case of previous hysterectomy.

***g) Anterior (Vesicovaginal) Dissection* (Figure 10)**

A ventral deflection of the malleable vaginal valve shows the anterior limit of the vaginal vault and guides dissection of the bladder from the vagina. The dissection starts in the midline, following the pearly white aspect of the vagina. Diathermy has a very limited role during this dissection, if the correct surgical plane is individuated. Dissection goes up to the retrotrigonal space, until the outline of the bladder catheter balloon can be discerned.

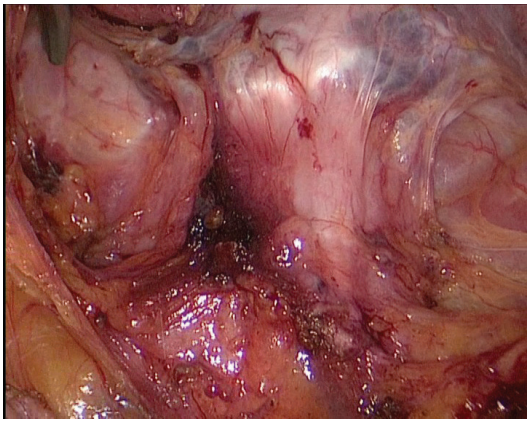

***Figure 7. Anchor points on the levator ani.***

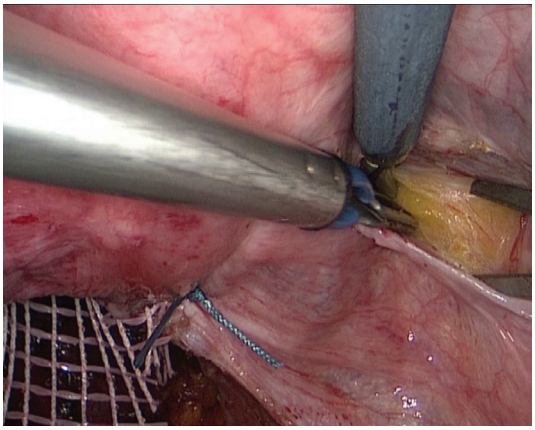

***Figure 9. Fenestration of the broad ligaments.***

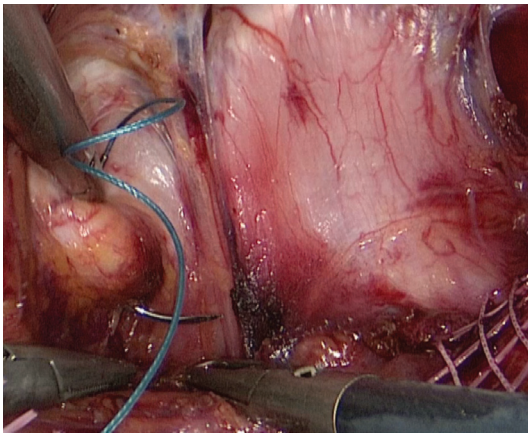

***Figure 8. Suturing the posterior mesh.***

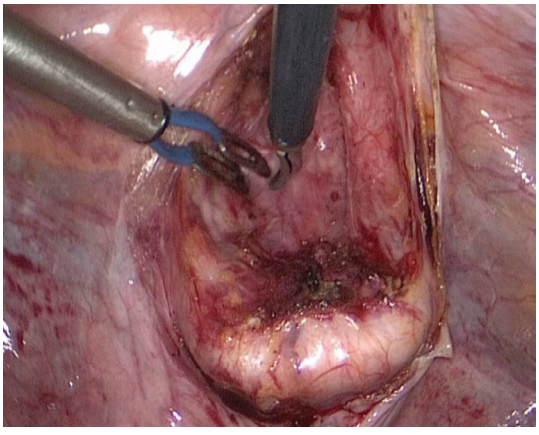

***Figure 10. Anterior dissection.***

***h) Anterior mesh placement* (Figure 11)**

The anterior mesh is then anchored to the vaginal vault with nonabsorbable sutures at the apex and along the lateral aspects, as superficial as possible: either polypropylene (Prolene) or polyester (Mersutures) can be used in this step. Interrupted or running sutures can be applied, avoiding vaginal transfixion at all times. The two tails of the mesh are then pulled through the windows in the broad ligaments and brought together with the posterior mesh.

***i) Mesh fixation to the promontory* (Figure 12)**

The three mesh ends are secured to the sacral promontory with a nonabsorbable suture. The needle passes through the anterior vertebral ligament and the free end of the thread is removed through the 5-mm suprapubic port. An extracorporeal knot is tied while the assistant retracts the three meshes. The meshes are fixed without applying too much tension. Any surplus mesh is cut and removed.

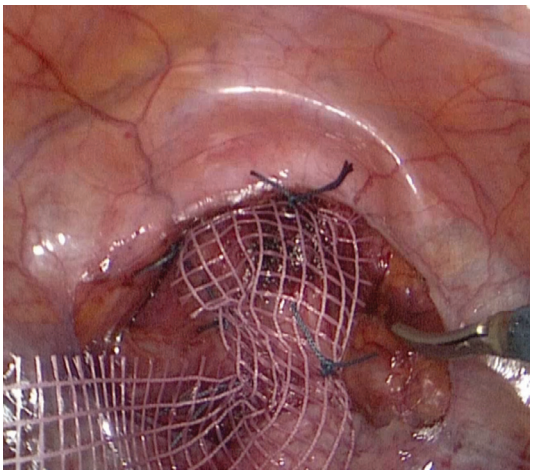

***Figure 11. The anterior mesh.***

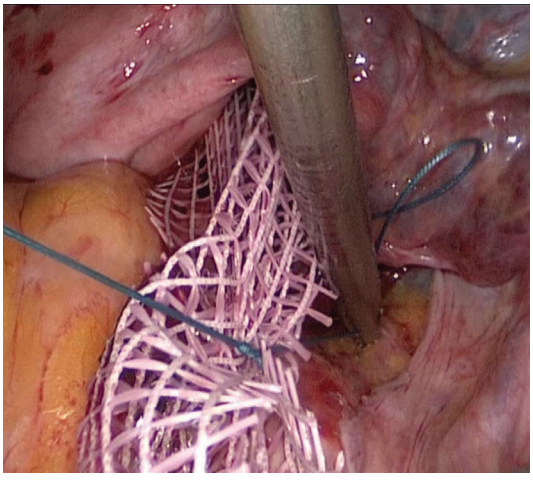

***Figure 12. Mesh fixation to the promontory.***

***j) Reperitionealisation* (Figure 13)**

Reperitonealisation is a very important step which should completely cover the meshes. Attention should be paid to the right ureter, usually fixed to the right part of the posterior peritoneum. We perform a running suture using Polyglactin 2-0 (Vycril). A unique suture can be made for both the anterior and the posterior parts, with translation of the needle through the right window in the broad ligament. In our experience, no drain is needed or advised in the presence of prosthetic material.

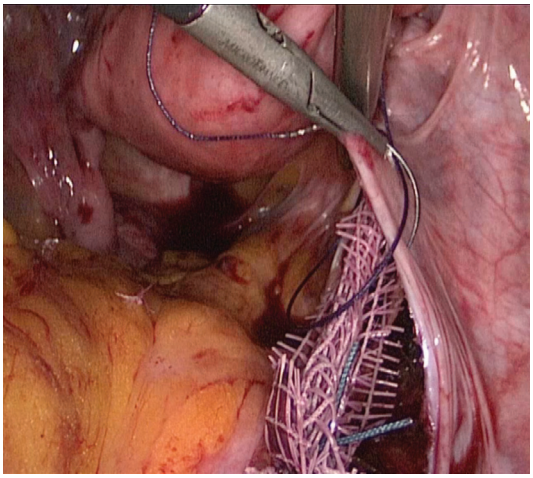

***Figure 13. Reperitonealisation.***

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## 5. LAPAROSCOPIC SACROCOLPOPEXY: TECHNICAL OPTIONS

### *a) Double Mesh Placement*

Double-mesh LSC is designed to simultaneously repair the anterior, apical and posterior compartments via a single surgical approach [1]. Using the laparoscopic approach, it is possible to place the meshes far deeper than with the open procedure, especially the posterior mesh. It is even possible to fix the posterior mesh to the levator ani muscles. A separate mesh is used for the anterior side, where dissection goes up to the retrotrigonal space, until the outline of the bladder catheter balloon can be discerned. Concerning sacral fixation, with laparoscopy it is possible to fix the mesh lower on the sacrum, thereby creating a more physiological vaginal axis [2].

### *b) Single Anterior Mesh*

LSC can be performed with an anterior (vesicovaginal) mesh, a posterior (rectovaginal) mesh, or both [3]. The need for the posterior mesh has been questioned by Antiphon et al [4] in 108 LSC patients. These authors found that although double mesh placement protected against posterior compartment failure (31.3% vs 5.9%, *P*=0.0006), it was complicated by higher rates of posterior vaginal erosion, increased pain, and bothersome postoperative constipation. In addition, the authors found that posterior compartment failure was probably more attributable to the concomitant Burch procedure [4]. Antiphon and colleagues concluded that the systematic placement of the posterior mesh appears unnecessary and must be reserved for the cure of documented rectocele or enterocele, or in the case of associated or previously performed Burch procedure. Several authors, however, questioned the principle of a single anterior mesh, believing that POP arises from a generalized loss of pelvic organ support and suspension system rather than isolated defects. Double-mesh LSC allows the reconstruction of an adequate system of support and suspension of the uterus and vagina, with the repair of multicompartment defects [5].

### *c) Alternatives For Mesh Fixation*

Suture of the meshes to the sacral promontory can be performed using thread/needle or tackers [6]. Tacking devices provide an alternative to traditional laparoscopic suturing, but they have been associated with weaker fixation and higher rates of infection, erosion, and dyspareunia [1, 5]. Boukerrou et al [7] demonstrated that non-absorbable sutures have a stronger biomechanical resistance than staples and that more than one staple is needed to avoid mesh disruption under tension. Moreover, spiral staples would be associated with a higher risk of spondylodiscitis as compared to sutures, because of deeper penetration into the prevertebral ligament (5 mm). On the other hand, the stapler is technically easier to use than suturing and requires less tissue dissection [5]. Few data are available concerning the use of staples for fixation of the mesh to the vaginal walls; nevertheless, due to the high risk of vaginal erosion, the use of these devices for fixation of the meshes to the vaginal walls should be avoided [5]. We were unable to find reliable data in the literature on other methods of mesh fixation, such as bioglues or other techniques.

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# V. COMPLICATIONS

## 1. LONG-TERM OUTCOMES AND COMPLICATIONS OF LAPAROSCOPIC SACROCOLPOPEXY: SAINT AUGUSTIN EXPERIENCE IN 452 CASES

Abdominal sacrocolpopexy (ASC) is regarded as the gold standard procedure for the management of vaginal vault prolapse. Maintaining the good outcomes of ASC with decreased morbidity, laparoscopic sacrocolpopexy (LSC) has the potential to become the best surgical option available for multicompartment POP. Nevertheless, up-to-date long-term data on the outcomes of LSC are lacking, particularly in terms of long-term complications. We report the long-term results in 452 LSC cases consecutively treated at the Clinique Saint Augustin (Bordeaux, France).

### *a) Materials And Methods*

Our retrospective study evaluated a consecutive series of 533 patients who underwent LSC for the treatment of symptomatic POP between 2008 and

2011 at the Clinique Saint Augustin, with at least 2 years of follow-up available. The preoperative work-up involved a detailed urogynaecological history and physical examination, including a Bonney manoeuvre to determine the presence of any preoperative stress urinary incontinence (SUI), which prompted a TOT placement concomitant to LSC. All patients had been diagnosed with POP stage 2 to 4 according to the Pelvic Organ Prolapse Quantification (POP-Q) classification system [11].

The surgical technique has been previously reported in detail [12, 13].

Clinical data on our patients were retrieved from their medical files and were updated through evaluation of an internally developed, self-administered questionnaire investigating urinary continence, constipation, recurrent urinary tract infections (UTIs), complications and satisfaction with the procedure. Complications were reported according to the Clavien classification [14]. All statistical analyses were performed with IBM SPSS Statistics Software version 20.

***b) Results***

Among the 533 patients who underwent LSC, 452 (84.8%) had an updated medical follow-up and completed our questionnaire, while 81 (15.2%) were lost to follow-up. During the follow-up period, eight patients had died of causes unrelated to LSC.

Patient characteristics and main surgical outcomes are detailed in **Table 1**. Mean age was 65 years (range 31-89). Thirty-four patients (7.5%) previously had a Burch or other colposuspension, and 64 (14.1%) had a hysterectomy. All surgeries were successfully completed with no open conversions. Six surgeries were robot-assisted LSC. Mesh placement was only anterior in five cases and only posterior in two. Mean surgery duration was 110 minutes (range 50-180). Intraoperative estimated blood loss was insignificant and no patient needed blood transfusions. Average hospital stay was 4.3 days (range 3-6).

Surgical complications stratified according to Clavien grade are listed in **Table 2**. At a mean follow-up of 51.7 months (range 24-75), LSC-related complications of Clavien grade ≥3 occurred only in 13 (2.9%) cases (3 early, ≤30 days; 10 late, >30 days): 5 vaginal erosions (1.1%), 2 rectal erosions (0.4%), 1 bowel subocclusion (0.2%), 1 bowel occlusion (0.2%), 1 epigastric artery lesion during trocar placement (0.2%), 1 retroperitoneal haematoma (0.2%), 1 mesh infection (0.2%), and 1 breakage of the promontory mesh fixation (0.2%). All these complications required surgical reintervention **(Table 3)**. Overall, minor complications were experienced in 203 (44.9%) cases, including dysuria (n=39, 8.6%), recurrent UTI (n=53, 11.7%) and persistent constipation (n=99, 21.9%). A TOT was placed simultaneously in 294 (65%) patients who had concurrent SUI; among these patients, complications due to TOT placement were experienced by 13 patients (4.4%). The occurrence of dysuria and recurrent UTI was more frequent in the patients who received concomitant TOT placement at the time of LSC; however, the association did not reach statistical significance both in the univariate ($\chi 2$ 2.5, P=0.11) and in the age-adjusted multivariate logistic regression model (exp(B) 1.5, P=0.1).

De novo urinary incontinence was detected in 104 (23%) patients, with clinical characteristics of SUI and urge urinary incontinence (UUI) in 58 (12.8%) and 46 (10.2%), respectively. Serious SUI needing surgical treatment was found only in 35 (7.7%) patients. There was a 3.3% recurrence rate of prolapse (n=15). 97.8% of patients were satisfied with the results of surgery.

***c) Discussion***

As assessed by a recent review of the literature, LSC represents an attractive alternative to ASC, achieving anatomic cure in a mean of 91% of patients, with 92% of satisfied patients [9]. While the outcomes are comparable between LSC and ASC, the real advantage of LSC is reduced patient morbidity, with a lower risk of overall complications compared to ASC [10]. Data on LSC, however, are limited to short- and intermediate-term studies of various sizes [15-22]: the only series with more than 100 patients and a long follow-up (43 months) was reported by Granese et al [23]. To our knowledge, this is the largest, single-centre cohort study reporting on 452 consecutive patients undergoing LSC beyond the learning curve, and one of the few to address the issue of long-term surgical outcomes, with a mean follow-up of 51.7 months.

Our long-term results confirm the high success rate of LSC: our recurrence rate of only 3.3% reflects the efficacy of this highly standardized surgery, and patient satisfaction of 97.8% is in line with other results in the literature [9].

This surgical technique is well established and excellent operative parameters can be achieved after an appropriate learning curve: our mean operative time is one of the shortest when compared to other series [9], and no conversions were reported. There was no need for blood transfusions, due to insignificant intraoperative bleeding. Our average hospital stay was 4.3 days, following French Health Policy.

With regard to long-term complications, LSC has been confirmed to be a safe procedure even in the long-term, with a very low rate of serious complications (2.9%). There are three major risks in this type of surgery: mesh-related problems, bowel complications and mesh infections.

***Table 1. Patient characteristics and main surgical outcomes***

| | |
|---|---|
| Mean age | 65 yrs (31-89) |
| Mean follow-up | 51.7 months (24-75) |
| Deaths due to other causes during follow-up | 8 (1.8%) |
| Previous Burch or other colposuspension | 34 (7.5%) |
| Previous hysterectomy | 64 (14.1%) |
| Surgical technique | |
| - Pure laparoscopic | 446 (98.7%) |
| - Robot-assisted laparoscopic | 6 (1.3%) |
| Mesh fixation | |
| - Double | 445 (98.5%) |
| - Only anterior | 5 (1.1%) |
| - Only posterior | 2 (0.4%) |
| Concomitant hysterectomy | 4 (0.9%) |
| Concomitant TOT placement | 295 (65.3%) |
| Complications due to TOT placement | 13 (4.4%) |
| Mean operative time | 110 minutes (50-180) |
| Mean estimated blood loss | 50 cc (10-300) |
| Mean hospital stay | 4.3 days (3-6) |
| Prolapse recurrences (Baden-Walker stage ≥2) | 15 (3.3%) |
| De novo urinary incontinence | 104 (23%) |
| - Stress urinary incontinence (SUI) | 58 (12.8%) |
| - Urge urinary incontinence (UUI) | 46 (10.2%) |
| De novo SUI which needed surgical treatment | 35 (7.7%) |
| Patient satisfaction | |
| - High | 320 (70.8%) |
| - Acceptable | 122 (27%) |
| - Low | 10 (2.2%) |

***Table 2. Surgical complications according to the Clavien classification***

| | |
|---|---|
| **Grade 1-2 complications** | |
| Recurrent urinary tract infections | 53 (11.7%) |
| Persistent constipation | 99 (21.9%) |
| - Age group <60 yrs | 28/99 (28.3%), *P* >0.05 |
| - Age group 60-69 yrs | 44/99 (44.4%), *P* >0.05 |
| - Age group 70-79 yrs | 25/99 (25.3%), *P* >0.05 |
| - Age group ≥80 yrs | 2/99 (2%), *P* >0.05 |
| Dyspareunia | 7 (1.5%) |
| Pelvic pain | 5 (1.1%) |
| Dysuria | 39 (8.6%) |
| **Grade 3-4 complications** | |
| Post-operative bleeding or haematoma | 2 (0.4%) |
| Mesh erosions | 7 (1.5%) |
| Isolated mesh infections | 1 (0.2%) |
| Mesh-related bowel occlusions | 2 (0.4%) |

*Table 3. Clavien ≥3 complications and their management*

| # | Complication | Months to complication | Management |
|---|---|---|---|
| 1 | Pelvic abscess and sepsis due to mesh infection | 0 | Surgical drainage and mesh ablation |
| 2 | Epigastric artery lesion | 0 | Surgical repair |
| 3 | Bowel subocclusion | 1 | Hospitalisation and medical treatment |
| 4 | Retroperitoneal haematoma | 2 | Surgical drainage |
| 5 | Vaginal pain due to erosion of an anterior mesh stitch | 3 | Surgical resection of the mesh suture |
| 6 | Breakage of promontory suture (prolapse relapse) | 4 | Surgical treatment (new laparoscopic fixation) |
| 7 | Rectal erosion of the posterior mesh | 6 | Open surgical repair and removal of all prosthetic material |
| 8 | Vaginal erosion of an anterior mesh stitch | 11 | Vaginal removal of the anterior mesh |
| 9 | Vaginal bleeding due to vaginal erosion of the anterior mesh | 19 | Vaginal removal of the anterior mesh |
| 10 | Vaginal mesh erosion with vaginal discharge and infection | 20 | Open surgical resection of the visible mesh, in a second time laparoscopic removal of all prosthetic material |
| 11 | Dyspareunia due to vaginal erosion of an anterior mesh suture | 30 | Surgical resection of the mesh suture |
| 12 | Sigmoido-vaginal fistula due to posterior mesh erosion and infection | 41 | Surgical management of the fistula with colon resection and temporary ileostomy |
| 13 | Small bowel occlusion due to incarceration with the mesh (defective reperitonealisation) | 42 | Surgical management of the small bowel occlusion and removal of the anterior mesh |

Mesh erosion inevitably leads to removal of the prosthetic material, exposing the patient to prolapse recurrence. Vaginal and rectal erosions were reported in 1.1% and 0.4% of our patients, respectively, as compared to an average of 2.7% in the literature (0-12%) [8, 9], with a mean of 2.5% with vaginal mesh exposure and 0.5-1% with late visceral exposure [24]. Infection can be a very serious consequence of mesh erosion, especially in cases with rectal erosions. It is well known that the risk of erosion is increased in cases of sacrocolpopexy associated with concomitant hysterectomy [10, 24], thus we tried not to perform the two procedures simultaneously. A careful rectovaginal dissection with good anchorage of the mesh to the levator ani muscles can diminish the risk of visceral exposure. With regard to the anterior mesh, it must be sutured to the pearly surface of the vagina as superficially as possible. Reperitonealisation also has a role in preventing mesh erosion into surrounding tissues, as well as serious bowel complications [9].

Postoperative ileus and small bowel obstruction occur rarely after LSC, with an incidence of 0-6% and 0-5%, respectively [9]. The only case of small bowel obstruction in our series was due to bowel adhesions to the mesh not adequately covered by reperitonealisation. One case of bowel subocclusion was managed with medical therapy: we cannot assess if this was related to LSC.

The risk of mesh bacterial colonisation and subsequent clinical infection, unrelated to mesh erosion, seems negligible, below 1% [23]; however, it must be taken into account as it leads to mesh removal, as seen in one of our patients.

The long follow-up in our study allowed identification of the non-negligible incidence of minor complications such as dysuria (8.6%), recurrent urinary infections (11.7%) and constipation (21.9%). It is difficult to evaluate their pathogenesis, as in some cases these problems may have developed independently of LSC. Postoperative voiding dysfunction remains a major morbidity after POP surgery and may be related to bladder hypocontractility resulting from denervation injury or local dysfunction [9, 15]. Urine retention could then lead to an increased risk of UTI. Constipation may be a consequence of rectal denervation or ischemia: for this reason, we advise preservation of perirectal fat during the posterior dissection. The incidence of postoperative constipation in the literature is up to 20% [18]. Due to the retrospective nature of our study, we could not evaluate whether our patients had already suffered a degree of constipation before LSC. Constipation affects up to 28% of the general population: the risk increases gradually after the age of 50 years, with a steep increase after 70 years [25]. In our series, no statistical differences in constipation incidence were found following age stratification. The risk of dyspareunia is minimised with LSC, ranging from 0 to 3% in the most important LSC series [15, 16, 18, 19, 23]. Only sporadic cases of impaired sexual function were reported in our study.

Urinary incontinence is another important parameter requiring analysis. We followed the policy of performing concomitant SUI surgery in patients with some degree of urodynamically confirmed SUI. According to the recent ICUD evidence [24], anti-incontinence procedures such as Burch colposuspension or sling placement concomitant with sacrocolpopexy can significantly lower the incidence of de novo SUI [26]; this benefit, however, must be balanced against the risk of de novo urinary dysfunction [6]. Indeed, our data highlight a trend toward a higher risk of developing urinary disorders, such as dysuria and recurrent UTI, if a TOT is placed at the same time as LSC. Although interesting, this trend did not reach statistical significance. De novo SUI symptoms have been frequently reported after prolapse surgery, probably because the previously obstructed urethra becomes unkinked. The rate of de novo SUI ranges from 9 to 42% after sacrocolpopexy [6] and up to 55% after LSC [9]. In our series, a degree of postoperative de novo SUI developed in 12.8% of our patients, with a significant majority among those who did not receive a TOT at the time of LSC (21.8% vs 8.1%, P<0.005). Overactive bladder symptoms can either be improved or triggered by prolapse surgery, occurring in 12% of patients [24]. In our series, 10.2% of patients developed symptoms of UUI, irrespective of TOT placement.

Points of strengths in our study are represented by the large cohort of patients and the long follow-up period. However, the study is limited by its retrospective nature, which prevented us collecting more thorough information on our patients. Furthermore, it was not specifically designed to evaluate the relationship between TOT and de novo SUI in LSC patients.

## 2. CONCLUSIONS

Our long-term data demonstrate the safety, feasibility and effectiveness of LSC, which offers excellent results combined with the benefits of minimally invasive surgery. The incidence of persistent constipation after LSC must be kept in mind, as well as the risk of urinary disorders, which can be increased by the placement of a suburethral sling. Late mesh erosion remains a feared complication which, even if rare, inevitably leads to removal of the prosthetic material exposing the patient to prolapse recurrence.

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## 3. COMPLICATIONS AFTER LAPAROSCOPIC SACROCOLPOPEXY: REVIEW OF THE LITERATURE

Several complications can occur following LSC; however, the overall complication rate is lower than that with ASC (12.7% vs 20%) [1]. Similar complication rates have been demonstrated among minimally invasive series [2], even if a greater risk of complications was suggested for LSC compared with robot-assisted sacrocolpopexy (18% vs 7%) [1]. The main complications of LSC are listed below.

1. Bleeding: blood loss with minimally invasive techniques is lower compared to ASC: EBL with LSC or RSC ranges from 22 to 255 cc versus 139 to 240 cc for ASC [2]. Only a few data on transfusion requirements are available in the literature, and transfusions are only exceptionally needed in LSC.

2. Bladder injury: this can occur intraoperatively during the anterior dissection, and ranges from 0 to 7% [2]. It can be managed by immediate repair. Such an injury can jeopardise placement of the mesh, due to the higher risk of mesh infection.

3. Urinary dysfunction: postoperative voiding dysfunction represents a major morbidity after POP surgery. LUTS may develop postoperatively as a consequence of denervation injuries, bladder outlet obstruction, or unmasked detrusor overactivity. The risk is greater if treatment for SUI is performed concomitantly (particularly with placement of retropubic slings as opposed to transobturator slings) [3]. The risk of de novo LUTS after LSC and RSC ranges from 0 to 27% [2].

4. Unmasked urinary incontinence: up to 55% of patients develop a degree of de novo SUI after sacrocolpopexy [2]. Concomitant anti-incontinence procedures, such as Burch colposuspension or sling placement, at the same time as ASC or LSC can significantly lower the incidence of de novo SUI; however, they carry an increased risk of de novo urinary dysfunction. Postoperatively, 11-27% of patients develop detrusor overactivity after suburethral sling placement [4, 5].

5. Dyspareunia: if correctly performed, sacrocolpopexy preserves vaginal length and minimises the risk of dyspareunia. Nevertheless, postoperative sexual dysfunction can occur due to mesh exposure, infection, or misplacement. It has been reported in 0-9% of LSC and RSC patients [2].

6. Bowel injury: this can occur intraoperatively during the posterior dissection and it is usually immediately repaired (2-4%) [2]. Such an injury

prevents placement of the mesh, due to the high risk of infection.

7. Persistent constipation: this can result as a consequence of rectal denervation or ischemia: for this reason, it is advisable to preserve perirectal fat during the posterior dissection. The incidence of postoperative constipation in the literature ranges from 0 to 19% [2, 6].

8. Severe bowel dysfunction: postoperative ileus and small bowel obstruction have both been described, with an incidence of 0-6% and 0-5%, respectively [2, 7]. Reperitonealisation of the mesh is suggested to reduce the risk of bowel injury.

9. Mesh erosions: the average incidence of mesh erosion after LSC is reported to be 2.7% (0-9%), compared to 3-12% in ASC patients [2]. In the literature an increased incidence of mesh erosion was reported when ASC is combined with concomitant total hysterectomy (16%) compared with posthysterectomy patients [2, 6, 8]; this experience has been confirmed in LSC, where mesh erosion rates as high as 32% were reported when concomitant vaginal hysterectomy is performed [9].

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## VI. HYSTERECTOMY ASSOCIATED WITH MINIMALLY-INVASIVE SURGERY FOR PELVIC ORGAN PROLAPSE: WHEN AND HOW?

### 1. INTRODUCTION

Hysterectomy is routinely performed for prolapsed uterus, but a central question has been: is removal of the uterus mandatory during surgical repair of pelvic floor defects? Even with some absolute and relative indications for removing the uterus, should a total or subtotal hysterectomy be performed under these circumstances, and what should happen to the adnexa? If it has to be performed, should hysterectomy occur simultaneously at the time of pelvic floor repair and does a concomitant operation carry an increased risk of erosion if a mesh is used? This chapter examines the minimally invasive surgical management of pelvic organ prolapse (POP) associated with hysterectomy and tries to answer these questions using relevant evidence that currently exists in the field as shown in **Table 1** below:

***Table 1: Key to levels of evidence and grade of recommendations. From Shekelle and all(1)***

**LEVELS OF EVIDENCE:**

- IA Evidence from meta-analysis of randomized controlled trials (RCT)
- IB Evidence from at least one randomized controlled trial
- IIA Evidence from at least one controlled study without randomization
- IIB Evidence from at least one other type of quasi-experimental study
- III Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
- IV Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both

**GRADE OF RECOMMENDATIONS:**

- A Directly based on Level I evidence
- B Directly based on Level II evidence or extrapolated recommendations from Level I evidence
- C Directly based on Level III evidence or extrapolated recommendations from Level I or II evidence
- D Directly based on Level IV evidence or extrapolated recommendations from Level I, II, or III evidence

## 2. ROLE OF HYSTERECTOMY IN PELVIC FLOOR DEFECT REPAIR: CURRENT EVIDENCE

Hysterectomy is one of the most commonly performed operations for benign uterine disease. Some of the indications for hysterectomy include symptomatic leiomyomatous uteri, endometriosis, abnormal uterine bleeding, pelvic inflammatory disease and uterine prolapse.

In POP, it is currently believed that loss of apical support results in both anterior and posterior compartment prolapse and restoration of this support corrects both prolapses. Although hysterectomy is routinely performed for uterine prolapse, the uterus is an organ that defines sexuality and this is particularly important in the premenopausal woman. Its removal therefore would seem to take away a part of this feminine identity and should be approached with caution. However, findings in one cross-sectional study in women seeking care for prolapse symptoms negated these assumptions. In the study, the majority of women believed that the uterus had no important sexual or self-image function and its removal would not affect their femininity or sexuality (III) [2]. In contrast, in another multicentre cross-sectional study evaluating preference for uterus preservation vs hysterectomy in women with POP, 36% of the 213 women studied preferred uterine preservation compared to 20% who would choose hysterectomy if outcomes between the two were assumed to be similar; and the percentage of those preferring uterine preservation if this was superior to hysterectomy rose to almost 50%, compared with 11% who chose hysterectomy if preserving the uterus was associated with superior outcomes, respectively; 21% preferred uterus preservation even if the outcome was inferior to hysterectomy (III) [3]. In a similar assessment of attitudes towards hysterectomy in 100 women undergoing evaluation for uterovaginal prolapse, more than half (60%) would opt for a uterine conserving procedure if this was as efficacious as a hysterectomy (III) [4].

Patient preference alone, however, is not sufficient to answer this question, if long-term consequences are not put into perspective. The difficulty in randomising women to either a uterine-sparing surgery or hysterectomy means that long-term consequences of these approaches cannot be easily analysed. It is currently recommended that patients' preference and wish for uterine preservation be responded to although careful patient selection is crucial (Grade B) [5]. A number of existing studies have shown good results demonstrating that sparing the uterus is a viable procedure in women with POP although the follow-up duration has generally been short and the study participants few in number (III) [6-8].

While one prospective study involving 37 women found no difference in sexual function between the uterine preserving and hysterectomy groups (III) [9], a slightly larger longitudinal follow-up examining the impact of hysterectomy on sexual function using the female sexual function index (FSFI), found that median post-operative scores of desire, arousal, and orgasm domains significantly improved in the uterus-sparing group (n= 32) compared with the hysterectomy group (n=36). Neither recurrence of uterine nor vault prolapse was reported in either group (III) [10].

Well-organised and larger randomised controlled trials are still required, but what seems clear so far is that since the uterus itself does not lead to prolapse, sparing it would be beneficial in women who desire to conceive and has the added advantage of shorter operating time and minimisation of complications related to hysterectomy (Grade C) [11]. A large uterus (>280 g) and benign conditions in which alternative uterine-sparing methods have failed are indications for hysterectomy in the setting of POP.

**IN SUMMARY**

- A good proportion of women would prefer a uterine preserving procedure
- Even with severe prolapse, sparing the uterus is a viable procedure in women with pelvic organ prolapse with the benefits of shorter operating time and minimisation of hysterectomy-related complications
- Patient's preference and careful patient selection are crucial factors to consider when opting for a uterine-sparing procedure

## 3. TOTAL VS SUBTOTAL HYSTERECTOMY IN POP

Whether to perform total or sub-total hysterectomy has been an issue of discussion in uro-gynaecology practice. Arguments that have emerged challenging total hysterectomy include: tendency for urinary tract injury; chronic granulations, reduced room and secretions impairing optimum coital function; and predisposition to vaginal vault prolapse. In contrast, it has been argued that sparing the cervix leaves with it apical supporting structures and hence minimising apical prolapse, cervical secretions and more room for coital function. On the other hand, there is a risk of persistent cervicitis in addition to cervical cancer risk of the cervical stump.

In a Cochrane review comparing short-term and long-term outcomes of total vs subtotal abdominal hysterectomy, the authors concluded that the shorter operative time (mean difference 11 min) and reduced blood loss (57 ml difference) with subtotal hysterectomy would be of insignificant clinical benefit. There were no differences in the rates of other complications intra-operatively, as well as in alleviation of pre-operative symptoms. On-going cyclical vaginal bleeding up to 2 years post-operatively was, however, more likely with subtotal than total hysterectomy. There were no differences between total and subtotal hysterectomy in urinary function (measured by rates of stress incontinence, urgency and incomplete emp-

tying), bowel function (measured by prevalence of constipation and incontinence) and sexual function (sexual satisfaction and dyspareunia) (IA) [12]. The physiologic functioning of the bowel, urinary bladder and sexual function was followed at 2- and 9-years.

While these findings lead us towards the conclusion that there is no benefit in sparing the cervix in view of the quality of life based on the physiologic parameters, which are thought to occur as a result of damage to navicular and supportive structures when the cervix is removed, anatomic consequences of cervix-sparing hysterectomy which would theoretically lead to POP and similar symptomatology in bowel, urinary and sexual function were not directly analysed in the review. A recent prospective multicentre randomised controlled study (median of 11.3 years) of 151 patients seeking to analyse the development of POP after subtotal (SH) and total hysterectomy (TH) in the long-term, and to assess patient-reported symptoms regarding pelvic floor dysfunction (PFD), found no significant differences in the occurrence of stage-2 prolapse or more between the TH and SH group (39% in SH versus 37% in TH) (IB) [13].

## 4. CONCOMITANT SACROPEXY WITH MESH

Sacrocolpopexy with mesh is regarded as a superior approach to other apical prolapse procedures (IA) [14]. Whether a concurrent hysterectomy and mesh repair has benefits over sacrocolpopexy carried out in a second step procedure has been investigated. A major concern is the risk of mesh erosion in a concurrent operation. In a prospective study of 124 women, Brizzolara and colleagues found few and comparable short- and long-term complications including mesh-related complications in women undergoing abdominal sacral colpopexy with concurrent hysterectomy (n=60), compared with women with a prior hysterectomy undergoing sacral colpopexy alone (n=64). In the cohort, with a median follow-up of 35.5 months, only one mesh-erosion was reported and this was in the group with previous hysterectomy (IIA) [15].

In another prospective cohort study, Marinkovic concluded that abdominal hysterectomy if combined with sacrocolpopexy with polypropylene mesh did not increase the occurrence of mesh erosions in the vaginal vault or the anterior or posterior vaginal walls (III) [16]. Between total vaginal hysterectomy (TVH) with uterosacral ligament suspension (USLS) and a robotic hysterectomy (RH) with colpopexy (SCP), in one retrospective cohort study of 84 women, there was good post-operative pelvic floor and sexual function between the two groups, and recurrence of prolapse was similar (13.2% for TVH/USLS vs 6.5% for RH/SCP, P = 0.46). However, a decrease in vaginal length was seen in the TVH/USLS group (III) [17]. Median follow-up duration was 9.5 months. With the robotic approach alone, another retrospective cohort study compared the incidence of mesh erosion after robotic sacrocolpopexy between women undergoing total and those undergoing supracervical hysterectomy and found that mesh erosion occurred in the total hysterectomy group, but not in the supracervical group (14% vs 0%) within 3 months of follow-up. Mesh type was a modifiable factor in the total hysterectomy group, i.e. self-cut polypropylene at site 1 (37% erosion rate) and precut polypropylene at site 2 (3% erosion rate) (III) [18]. Regarding mesh type, synthetic mesh material has been recommended as being superior to biological material for sacrocolpopexy (Grade A) [14].

### IN SUMMARY

- Evidence suggests that there are no significant intraoperative differences between total and subtotal hysterectomy, except reduced operating time and blood loss with subtotal hysterectomy, which may be of no clinical significance.
- Women undergoing subtotal hysterectomy should be informed of the likelihood of on-going cyclical bleeding up to 2 years post-operatively.
- There are no significant post-hysterectomy differences between total and subtotal hysterectomy in terms of urinary, bowel and sexual function
- Subtotal hysterectomy seems to decrease the risk of mesh-related infection/erosion.

## 5. APPROACH TO SURGICAL MANAGEMENT

Clinical history, physical examination and investigations are aimed at helping to decide whether hysterectomy should be performed. As such, malignancy should be ruled out and any other benign conditions that have not been manageable on non-surgical treatment. **(Table 1)**

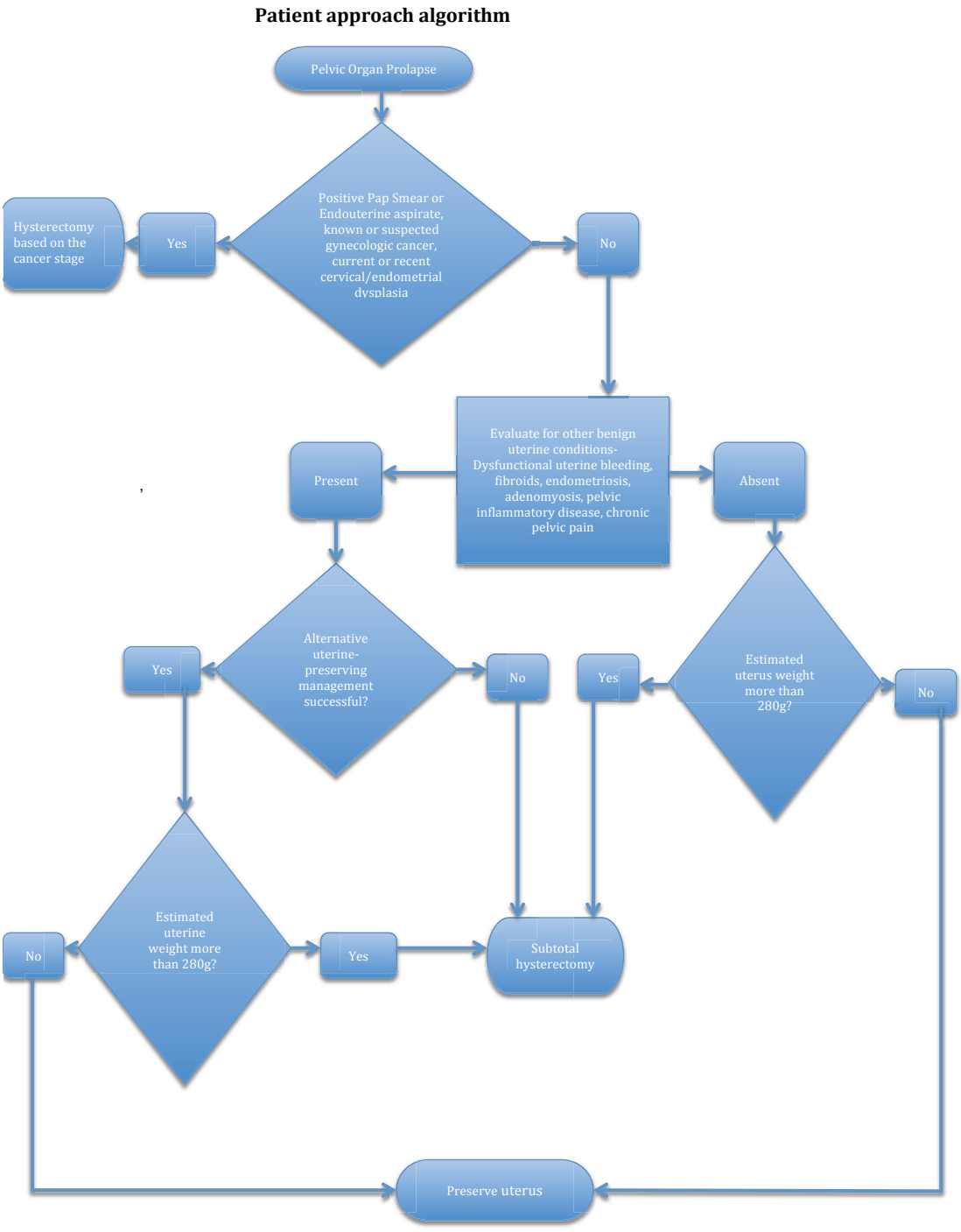
### *a) Clinical history*

A thorough clinical history is crucial in order to optimise the care that the patient with prolapse receives. General well-being is determined in order to rule out co-morbid states that could impact on eventual management or outcome. The obstetric/gynaecologic history should be comprehensive and should include age at first delivery, parity and modes of delivery, abnormal vaginal bleeding, Pap smear and other cancer screening reports as well as history of hormone-replacement therapy and any previous pelvic surgery. Family history of breast, ovarian or endometrial cancer should be identified, and history of previous pelvic surgery noted.

### *b) Physical examination*

Physical examination follows the standard clinical approach of general assessment. Abdominal examination may reveal previous surgery, enlarged uterus or a distended urinary bladder. The examination then proceeds in the lithotomy position, and examination of the perineum may reveal procidentia and a rough estimate of the uterine size. Vaginal examination is important in identifying POP that is not identified on examination of the perineum. A speculum is used to assess

*Table 1. Patient approach algorithm*



apical, anterior and posterior wall defects. Bimanual examination gives an estimate of the uterine size. In a retrospective review of 1238 patients, Barb and colleagues demonstrated that bimanual examination was a more accurate method of preoperative uterine weight estimation compared to ultrasonography [19]. Bimanual assessment also evaluates the adnexa, as well as identifying any pelvic infection or pathology.

### *c) Pap smear*

Pap smear is performed to rule out cervical cancer in women with POP. If cancer is discovered, appropriate staging is then carried out. Hysterectomy is performed if positive and the type is selected depending on the staging.

### *a) Imaging*

#### 1. Ultrasound

Ultrasound is important in a patient with POP in complementing clinical findings, and should not be used to replace the latter. Compared with other forms of imaging, ultrasound provides the combined advantages of accessibility, safety and ease of use. It is useful in identifying concomitant pelvic floor defects in other compartments that are not the primary clinical finding, but does not change ultimate patient management (III) [20]. 3D ultrasonographic imaging of the pelvic floor provides volumetric information as well as observing functional anatomy of the muscles and fascial structures of the pelvic floor (III) [21]. As such, findings may include increased size of the pelvic hiatus, avulsion of the levator ani and spatial derangement of pelvic organs [22]. Hiatal area and levator ani avulsion are also important objective measures of prolapse recurrence after mesh repair both through clinical and ultrasonographic assessment [23]. 4D US enables real-time imaging of the pelvic floor. Doppler ultrasound is equally important in the preoperative evaluation of deep venous thrombosis (DVT) in women with POP and who are also diabetic or obese [24].

#### 2. Magnetic Resonance Imaging (MRI)

MRI offers the benefits of visualising the anterior, apical and posterior compartments concomitantly. Other advantages include lack of ionising radiation, depiction of the soft tissues of the pelvic floor, and multiplanar imaging capability [25]. As such, MRI is important in assessing pubo-visceral muscle avulsions and levator hiatus measurements [26]. Even with this level of detail, it is recommended that imaging findings be interpreted in conjunction with patients' symptoms and findings on clinical examination (Grade C). In a study involving 403 patients, Shiota and colleagues suggested that using MRI, the maximum longitudinal diameter in the sagittal section (a), the maximum lateral diameter (b) and the maximum longitudinal diameter in the transverse section (c) of the uterus can be used jointly in the estimation of uterine weight (y) by applying the formula $y = 0.35x + 107$ ($x = a \times b \times c$), and this can be useful in determining the hysterectomy type (III) [27]. Its application is more crucial in patients with multicompartment prolapse on physical examination or symptoms, posterior compartment abnormalities, severe prolapse, or recurrent pelvic floor symptoms after prior surgical repair [28]. Dynamic MRI with the patient straining enhances visualisation of the prolapse. In cases of uterine prolapse, the cervix is low-lying and therefore appears shortened. In both cystocele and uterine prolapse, the H and M lines are elongated. The M line extends from the pubic symphysis to the posterior anorectal junction, while the H line is drawn rectangular from the M line to the anorectal junction posteriorly **(Figure 1)**.

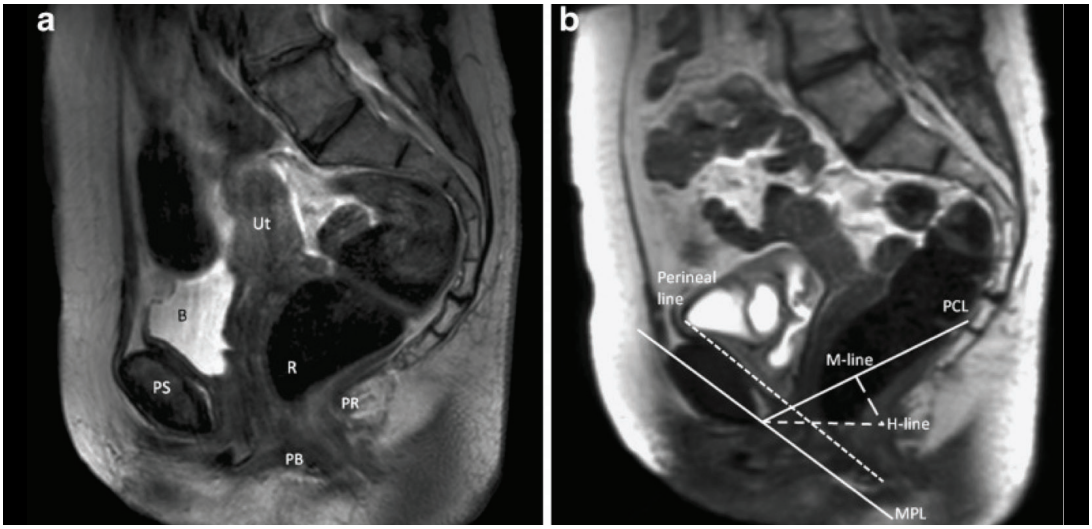



***Figure 1. A static T2-weighted turbo spin echo (TSE) at rest for anatomical reference in the midsagittal plane through the pelvis of a 66-year old woman with pelvic organ prolapse (POP) symptoms. The uterus (Ut), bladder (B), pubic symphysis (PS), rectum (R), and puborectal (PR) are shown. Adapted (pending author permission) from Lakeman et al (29).***

## VII. SURGICAL TECHNIQUES OF ASSOCIATED HYSTERECTOMY

### 1. SUB-TOTAL LAPAROSCOPIC HYSTERECTOMY (SLH)

In sub-total hysterectomy, the cervix is spared as the uterine corpus is amputated. The same procedure as for TLH is followed, but the uterine amputation is performed just below the internal cervical ostium while sparing the utero-sacral ligaments.

#### *a) Preoperative management*

Prior to surgery, adequate patient preparation is crucial. In obtaining informed consent, the procedure is explained to the patient and the risks therein. Some of these complications include intra-operative haemorrhage and the need for blood transfusion, ureteric injury, bowel injury during entry and conversion from laparoscopic to open hysterectomy. Patient counselling is necessary, for the possible psychological consequences of removal of the uterus or adnexa. Post-operative quality of life and sexual function are integral parts of the counselling process.

Appropriate preoperative investigations minimise the chances of missing uterine malignancy in uterine prolapse [30]. It is believed that alternative options to management could have been discussed between the surgeon and patient in the initial encounters. Group and cross-match is an essential aspect of the preoperative work-up. Mechanical bowel preparation has no added advantage in improving surgical field visualisation in laparoscopic hysterectomy (IB) [31]. Subsequently, fasting only without any preoperative diet or bowel preparation is recommended for laparoscopic surgery involving the posterior pelvic compartment (Grade A) [32]. Administration of prophylactic antibiotics is necessary to minimise sepsis. It is currently recommended that all women undergoing surgery for POP and/or stress urinary incontinence should receive a single dose of first-generation cephalosporin 15-60 minutes before incision. Clindamycin, erythromycin, or metronidazole are alternatives in cases of allergy to cephalosporin (IA) [33]. The urinary bladder is catheterised to minimise bladder injury.

#### *b) Intraoperative*

**1. Patient, surgeon and assistant positioning**

Correct positioning offers ergonomic benefits to the team and patient. The patient is placed in a Trendelenburg position with buttocks slightly beyond the edge of the table, and legs supported in stirrups, while the patient's hands are secured by her side. Shoulders are also propped to prevent the patient from sliding. The surgeon, if right-handed, generally stands on the patient's left side when operating on the pelvis unlike the case with operations involving the upper abdomen. For the left-handed surgeon, the opposite is true. The scrub nurse stands on the same side as the surgeon. The first assistant stands on the opposite side, while the third is between the patient's legs [34]. Anaesthetic and video monitors are positioned such that each member of the team can easily access them visually.

**2. Uterine cannulation**

A uterine manipulator is inserted through the vagina and cervix, and is used to raise, lower or move the uterus sideways.

**3. Trocar placement (Figure 2)**

Three ports are used in accessing the pelvis and a fourth may also be necessary. For each of these ports, three 5-12 mm trocars are used, the first, known as the optical trocar, is placed at the umbilicus. The two operating trocars are placed inferolateral to the first through the oblique abdominis muscles, while a fourth is placed below the first, to retract the bowel in obese patients.

After placement of the trocars and insufflation, the abdominal and pelvic cavities are inspected in order to identify any abnormalities such as adhesions in the field of operation, which would then be released first.

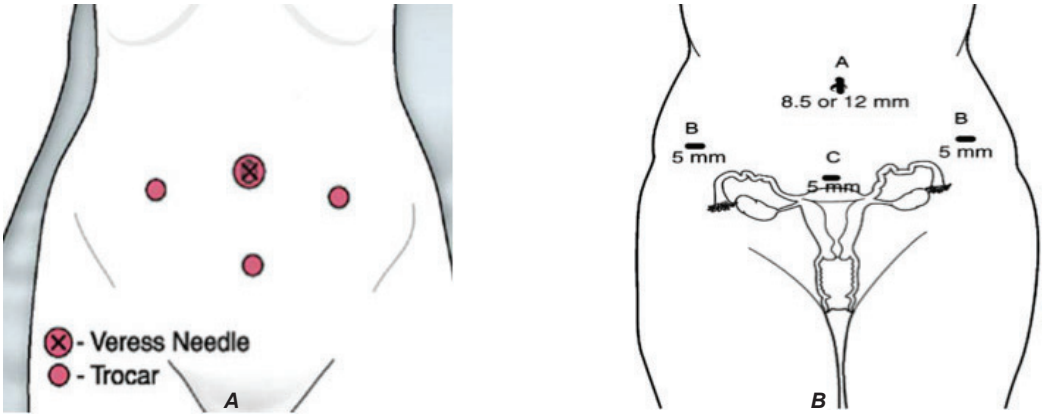



***Figure 2. (A) Position of trocars in gynaecologic operations. Adapted from Daniidilis et al (34). (B) Novel port placement and 5-mm instrumentation for robotic-assisted hysterectomy. From Nezhat et al (35)***

#### 4. Round ligament dissection

With the manipulator pushing the uterus to the left side, the contralateral round ligament is coagulated using bipolar cautery and dissected using a thermal sealing device. The procedure is repeated for the left round ligament.

5. Broad ligament dissection

This step is essential in mobilising the uterus from the urinary bladder. This is achieved by separating the anterior from the posterior leaves of the broad ligament.

#### 6. Utero-ovarian ligament dissection

Simultaneous utero-ovarian ligament and fallopian tube dissection is performed medial to the ovary with care taken not to injure the uterine vein. The posterior leaf of the right broad ligament is incised downward to the level of the insertion of the utero-sacral ligament in the cervix.

#### 7. Separation of adnexa from the uterus

The adnexa are separated from the uterus by creating a window through the avascular portion of the broad ligament and cutting the structures above the window. The ascending branch of the uterine artery is dissected and clipped or coagulated on both sides.

#### 8. Amputation of the uterus

The uterus becomes pale after effective ligation of uterine vessels and amputation is achieved by cutting the uterus from the cervix about 1 cm distal to the utero-cervical junction, starting laterally and proceeding medially. A conical incision minimises residual endometrium. Endocervical ablation is carried out to minimise post-operative bleeding. The peritoneum is closed to cover the cervical stump.

#### 9. Removal of the uterus

The uterus is removed by morcellation. It can also be removed by in-bag morcellation [36, 37].

## 2. TOTAL LAPAROSCOPIC HYSTERECTOMY (TLH)

In TLH, the steps are the same as for subtotal hysterectomy, with differences in amputating the uterus. After the uterine blood supply has been successfully controlled by the preceding steps, the skeletonized uterus is dissected from the vagina along the coloptomy line, and removed through the vagina. Vaginal cuff closure is accomplished by use a running absorbable suture. Horizontal cuff closure results in longer vaginal length than vertical cuff closure in vaginal hysterectomy (IB) [38]. Given that other studies have found no differences in sexual function between total and subtotal hysterectomy, it is doubtful whether the extra length is advantageous. The uterus is removed through the vagina.

## 3. SPECIAL CONSIDERATIONS

### *a) The bulky uterus*

Bimanual palpation preoperatively is important in identifying any concomitant pathology and estimation of uterine size may also be possible. A large uterus, defined as gestation more than 12 weeks or more than 280 g may present some surgical challenges. Many studies have shown that uteri greater than 500 g are associated with increased intra-operative blood loss, operating time, hospital stay and conversion from laparoscopic to laparotomy (III) [39-41].

Estimating uterine size could ensure adequate preparation, guide the choice of hysterectomy based on the surgeon's competence, as well as estimating other parameters such as blood loss and operating time and other risks caused by a large uterus, which should be explained to the patient prior to the operation. In a prospective study of 75 patients undergoing TLH, clinical estimation of uterine size correlated well with histological weight of the uterus, estimated blood loss, and operating time (III) [42]. In another retrospective study (Canadian Task Force II-2) analysing uterine size in TLH, increased uterine size correlated with increasing blood loss and operating time [43].

Although many studies show that laparoscopic hysterectomy is feasible in patients with large uteri, the surgeon's experience remains a crucial factor in minimising intra-operative complications and operating time [39, 43, 44]. To minimise intra-operative haemorrhage, selective coagulation of the uterine artery at its origin during TLH has been recommended (Grade B) [45].

### *b) Removal of the Adnexa*

Even when the decision for hysterectomy has been made, it is not only the removal of the cervix that raises questions, but removal of the adnexa as well. Although bilateral salpingo-oophorectomy has been advocated in view of its protectiveness against the development of ovarian cancer, there are associated health risks such as coronary heart disease and osteoporosis. Although no randomized controlled trials have examined the long-term consequences of oophorectomy [46], two large prospective cohort studies, the Nurses' Health Study which followed 30117 participants for 28 years and the Kaiser Permanente Northern California study which followed 56692 women for 18 years found a protective effect of oophorectomy against ovarian cancer (IIB) [47, 48]. In the Permanente study, the risk of peritoneal cancer was also more than seven times with hysterectomy alone than with hysterectomy and bilateral salpingo-oophorectomy. In the Nurses' Health Study, bilateral salpingo-oophorectomy was also associ-

ated with lower rates of breast cancer in women younger than 47.5 years. However, there was increased mortality from all causes with bilateral salpingo-oophorectomy in women younger than 50 years with no past or current history of oestrogen therapy. For women younger than 50 years who choose to undergo bilateral oophorectomy, these risks should be elaborated in the consenting process as well as the need to use menopausal oestrogen to ameliorate some of the risks (Grade B).

***c) The obese patient***

Obese women tend to have large uteri with antecedent risks already outlined in the section on bulky uterus. One study seeking to identify the influence of body mass index (BMI) on the prevalence of fibroids and uterine weight found that every 1-point increase in BMI resulted in a 4.56 g increase in uterine weight ($P$<0.0001). Of the 873 women studied, almost half were obese and the mean uterine weight in this subset was 349.53 g (III) [49].

In an effort to understand the trends in the route of hysterectomy in relation to BMI, Mikhail and colleagues analysed 18,810 patients who underwent hysterectomy for benign conditions between 2005 and 2011 and found that the rate of TAH increased with BMI increase, whereas the rates of TVH and LAVH decreased. BMI changes with TLH were insignificant (III) [50]. Except for increased operating time with increased BMI, there are mixed findings in the rates of other complications in the obese and morbidly obese patient undergoing hysterectomy for benign uterine conditions including POP. While some studies have found no association between obesity and risk of hysterectomy-related complications (IIA) [51-53], others have found a positive correlation between increased blood loss, operating time and perioperative morbidity (III) [54-57]. However, laparoscopic hysterectomy has generally been shown to be a safe procedure in the obese and morbidly obese patient.

**IN SUMMARY**

- Minimally-invasive hysterectomy is feasible in patients with large uteri (> 280 g)
- Bilateral salpingo-oophorectomy is associated with lower rates of breast and peritoneal cancer in women younger than 50 years. However, there is increased mortality from all other causes with bilateral compared with unilateral salpingo-oophorectomy.
- Laparoscopic hysterectomy has generally been shown to be a safe procedure in the obese and morbidly obese patient.

***d) Conclusion***

Although the incidence of POP is increasing due to the aging population, obesity and vaginal delivery, minimally-invasive surgical approaches should aim to support/correct the underlying condition. Hysterectomy is no longer performed automatically in POP surgery. POP is also prevalent in premenopausal women and a good proportion of women prefer uterine preservation. Sparing the uterus is a viable procedure in women with POP with the advantages of shorter operating time and minimisation of complications related to hysterectomy. Careful patient selection is necessary.

A thorough history of the patient presenting with POP and imaging findings should be correlated with patient complaints and findings on physical examination. Where hysterectomy is indicated such as in women at increased risk for developing endometrial cancer, there are no significant post-hysterectomy differences in urinary, bowel and sexual function when a total or subtotal hysterectomy is performed, although women undergoing supracervical hysterectomy may experience on-going cyclical bleeding for up to 2 years. There is also a risk of developing cancer in the cervical stump and long-term follow-up is necessary. Removal of the adnexa with hysterectomy carries an increased risk of mortality from all causes with bilateral salpingo-oophorectomy compared with unilateral salpingo-oophorectomy, in women younger than 50 years with no past or current history of oestrogen therapy. Such women may benefit from hormone replacement therapy. Sparing the ovaries is considered protective.

Compared with other techniques for apical prolapse repair, sacrocolpopexy is a superior technique and can be safely performed at the time of hysterectomy (if indicated). When a hysterectomy has to be performed, it should be subtotal hysterectomy in order to reduce the risks of mesh erosion and infection in all sacropexy procedures, synthetic mesh is preferred to biologic mesh to minimise erosion complications. Laparoscopic sacrocolpopexy has the advantages of less blood loss, shorter hospital stay and quicker return to normal activity, although operating time is longer. Concomitant laparoscopic total or subtotal hysterectomy is still feasible in patients with large uteri with good surgical experience as well as in obese and morbidly obese patients.

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# VIII. NEW EVOLUTIONS

## 1. PLACE OF ROBOTIC-ASSISTED LAPAROSCOPY IN THE SURGICAL TREATMENT OF POP

### *a) Introduction*

Pelvic organ Prolapse (POP) is quite a common condition in women, especially elderly women, and the incidence of POP is increasing due to obesity, increased age and other risk factors; for minor prolapses, physical therapy and pelvic floor muscle exercises may be a sufficient form of therapy. In women with a greater degree of prolapse, a vaginal pessary can be inserted, and in the case of insufficient non-invasive strategies, surgical repair is advised.

Different surgical repair techniques have been discussed, all of which deal with support of the anterior or posterior vaginal wall. Nevertheless, this support is dependent on the support of the vaginal apex in order to reconstruct the genital axis. This is usually best achieved with sacrocolpopexy in combination with a mesh and was first described in 1958 [1]

Initially performed as an open procedure, this operation was later performed in a conventional laparoscopic manner, combining the very good long-term results of the open procedure with the advantages of minimally invasive surgery. The disadvantages of laparoscopy in complex procedures are the difficult learning curves and the long operation time. To ease the use of minimally invasive surgery, the da Vinci system is used. Robotic surgery can bridge the gap between the advantages of laparoscopy and the difficulties in suturing etc. [2] By doing so this type of robotic surgery can play a key role in prolapse therapy.

### *b) Different methods of sacrocolpopexy*

Sacrocolpopexy can be performed in an open, laproscopic or robotic way. The open technique has been used for a long time and provides excellent long-term results: approximately 4% recurrence for sacrocolpopexy vs. 15% for sacrospinous ligament suspension [3,4].

No significant differences have been recorded between the open approach and conventional laparoscopy. In their analysis of laparoscopic sacrocolpopexy, Ganatra et al. found a reoperation rate of 6.5% and a satisfaction rate of approximately 95% during a mean follow-up period of almost 25 months [5].

Due to the relatively new technology there are few data available on robotic surgery [6].

***c) Techniques of robotic-assisted sacrocolpopexy (single and multiport access, etc.)***

A step-by-step description of the surgical technique Robotic-assisted sacrocolpopexy can be divided into 11 steps [7]:

1. Operation room setup, patient positioning and port placement
2. Preparing the mesh for implantation
3. Anatomical overview and dissection of the anterior vaginal wall
4. Dissection of the posterior vaginal wall
5. Demonstration of the mobilised anterior and posterior vagina
6. Dissection of the sacral promontory
7. Fixation of the ventral part of the mesh
8. Fixation of the dorsal part of the mesh
9. Mesh adjustment and fixation to the promontory
10. Closure of the peritoneum
11. Postoperative care

1. The patient is placed in the supine position on a padded vacuum mattress, both legs slightly spread.

   The ports are placed in a "W"-shaped configuration **(Figure 1)**. The table is placed in a moderate Trendelenburg position. Four robotic arms are used, one for the camera (with a 0° or a 30°down scope), one for Maryland bipolar forceps and a fenestrated Grasper (Pro Grasp), one for robotic scissors (Hot Shears) and one for the large needle driver, respectively. Furthermore, a vaginal retractor is inserted into the vagina simultaneously.

2. It is advisable to have the mesh prepared beforehand **(Figure 2)**. We usually use a semi-absorbable VYPRO ® mesh (Ethicon, Somerville, NJ, USA), 15x10 cm in size. The mesh is cut into two pieces, both 4 cm wide, one of which is again cut to 4 cm in length and is used as the short wing of the Y-shaped form; this short part is attached to the remaining longer part of the mesh with non-absorbable sutures. The anterior wing is usually slightly shorter than the posterior wing (which is 6 cm in size), because the posterior dissection usually reaches more distally. The total length from the base of the "Y" to the tip of the wings should be approximately 15 cm, if there is surplus mesh in the longer portion this is unimportant as it can be cut off later **(Figure 3)**.

3. After port placement and docking of the robot, the abdominal cavity is examined; often peritoneal adhesions from prior surgeries need to be divided first. The iliac vessels, the vaginal stump, the Douglas pouch and the rectum are identified as the most important landmarks.

   The overlying peritoneum is then incised at the line between the bladder and vagina, to mobilise the anterior vaginal wall from the bladder, using careful blunt and sharp dissection. It is important to gain a good length of the freed vaginal wall to be able to attach the mesh to the most distal part of the vagina. The vaginal wall usually has more than one layer of surrounding tissue, for durable fixation it is important to reach a layer with a relatively rough surface.

4. The dorsal vaginal wall is mobilised and dissected off the rectum by opening the recto-vaginal space. An additional rectal retractor can be used, but is not necessary in our experience. The intra-abdominal gas usually creates an emphysematous tissue, reminiscent of spider webs that can be easily pushed away with blunt movements of the robotic instruments.

5. The now freed vaginal walls are moved in all directions with the help of the vaginal retractor, to ensure good mobility of the vaginal stump **(Figure 4)**.

6. The sigmoid colon is retracted using the fourth robotic arm, and the peritoneal overlay of the promontory is incised on the right side of the sigmoid colon. Care is taken not to injure the vessels or the ureter laterally. A switch to a 30° down lens can sometimes be helpful to gain a better view of the presacral area. The anterior longitudinal ligament is identified as a bright and shiny white structure. Care is taken to avoid lesions to the common iliac veins that run in close proximity to the promontory laterally, as well as the presacral vessels, as both could lead to significant haemorrhage.

   The peritoneal incision is then extended towards the primary incision site lateral to the vagina on the right side, always staying medial and a sufficient distance from the ureter and rectum.

7. The pre-fashioned Y-shaped VYPRO II mesh is then inserted, and suture-fixation with 2/0 vicryl sutures using a UR-6 needle is begun at the ventral, most distal part of the mobilised vagina. We recommend 3 rows with at least 2 sutures to avoid torsion of the mesh. The anterior wing is approximately 4 cm long. Care is taken to take good bites, but only penetrate the vaginal wall without perforation of the vaginal lumen, in order to avoid perforation with the consecutive risk of inflammation. The sutures are knotted slightly loose to ensure that the pressure of the net is as low as possible, in order to avoid mesh erosions **(Figure 5)**.

   After ventral fixation, the middle part of the mesh is rolled up and held ventrally, using the fourth arm of the robot, to keep it out of the way for the following steps of the surgery.

In the case of an existing uterus, we typically use the same mesh, but cut it into two single strips of 15/4 cm in length/width, which are not attached to each other.

One mesh is fixed anterior; it is then brought through a tunnelled perforation of the broad ligament on the right side, to bring it to the dorsal side of the uterus in order to reach the promontory. The other mesh is sutured to the posterior vaginal wall, respectively.

8. Fixation of the dorsal vagina and the rear wing of the mesh is then carried out, respectively. In order to avoid future possible enteroceles, a Moschcowitz culdoplasty can be performed, closing the posterior cul-du-sac with a circumferential suture, which in our experience is not necessary.

9. The sigmoid colon is then retracted laterally utilizing the fourth arm of the robot, and the free part of the mesh is unrolled and put under slight tension. The mesh should be anchored to the promontory without tension which can be examined by gentle movements of the vaginal retractor. The mesh is then fixed with interrupted, non-absorbable 0 sutures through the longitudinal ligament of the promontory bone. Excess mesh can be used for better cranial retraction, e.g. by the assistant, then later cut and removed.

10. Finally, the mesh is totally reperitonealised by closing the peritoneal incisions with running sutures using V-loc TM 180 3/0 and a CV 23 needle (Covidien, Mansfield, MA, USA), the braided thread allows for fast closure of the peritoneum. It is very important to have complete peritoneal cover over the mesh in order to avoid future bowel herniation, obstruction, adhesions or inflammatory responses **(Figure 6)**. Once the peritoneum is closed, a drain can be put in place.

11. The patient is mobilised on the day of surgery. For pain, Metamizol is given if needed. The transurethral Foley Catheter can be removed the next morning, followed by voiding and residual urine control. Heavy lifting of more than approximately 7 kg should be avoided for 3 months. A vaginal oestrogen ointment is applied twice weekly starting 6 weeks prior to surgery and can be administered for a further 3 months at least.

After restoring the correct anatomical situation, hidden stress urinary incontinence can occur. In this case, a tension-free tape is implanted after six weeks.

An instructional video for this technique is available from our working group [8].

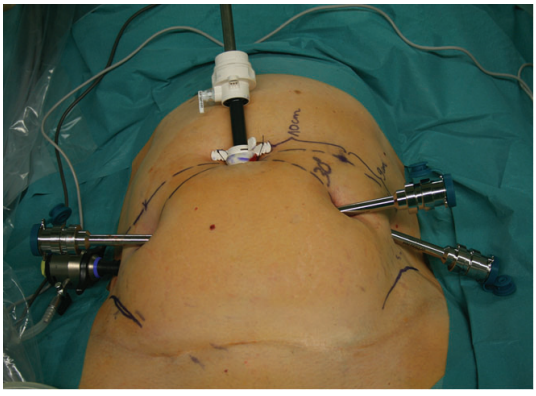

***Figure 1. The ports are placed in a "W- shape configuration".***

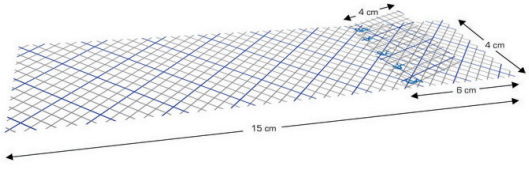


***Figure 2. The mesh is modified preoperatively in a "Y-shape configuration"***

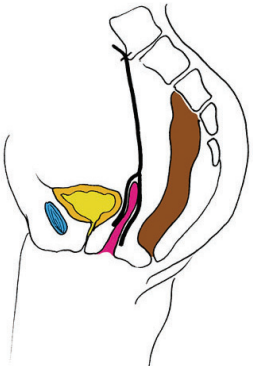

***Figure 3. The mesh is sutured to the anterior and posterior wall of the vagina and the middle part to the promontory***

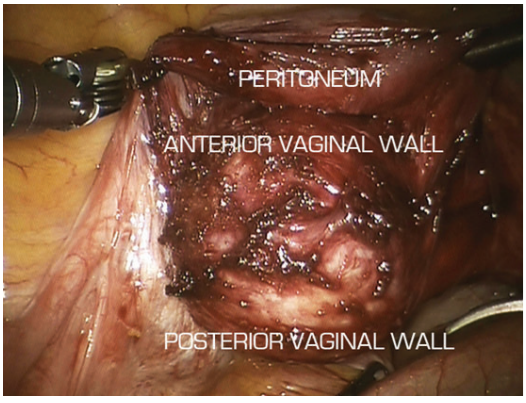


***Figure 4. The vaginal stump is fully mobilised and the mesh can reach the most distal portion of the anterior and posterior vaginal wall***

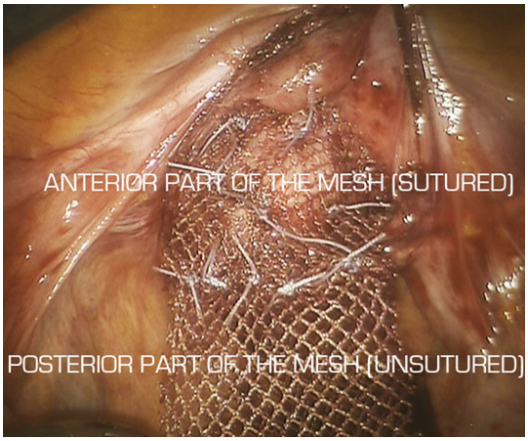


***Figure 5. The anterior wing of the mesh is attached to the anterior vaginal wall***

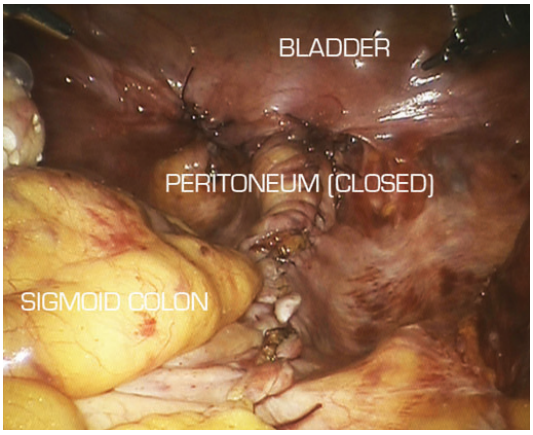


***Figure 6. The peritoneum is entirely closed over the mesh to prevent later complications***

***d) Surgical outcome and complications***

The use of robotic-assisted POP repair is still not very common. The first description of robotic-assisted sacrocolpopexy was in 2004 by Di Marco and coworkers [9].

The literature on robotic sacrocolpopexy is scarce and studies often lack a long follow-up. However, for POP repair the follow-up is crucial to determine whether the quality of life of an individual patient has improved [10].

Remarkably, most authors found a recurrence rate of around 5% [11, 12, 3]. This is promising in comparison to a recurrence rate between 0 and 18% for open procedures, however, in open surgery a longer follow-up is available [13, 4].

This was confirmed by Geller and coworkers, who found similar reconstructive results for the open and robotic procedures, but again a short follow-up period [14].

The same complications such as bowel, bladder and ureter injury, laceration of the vagina, infection, mesh erosion and even osteomyelitis have been reported for open, laparoscopic and robotic procedures. Complications in the literature range from 0 to 8% and are similar for the three different approaches [15].

Other POP operations which can also be carried out using the robot include the lateral repair after Richardson and hysteropexy or anterior rectopexy, of which few data exist.

An interesting new development is the transformation of robotic surgery into a single port approach. This has been performed for pyeloplasty, radical prostatectomy and radical nephrectomy [16,17].

However, as with conventional laparoscopic single port surgery there are some technical problems which need to be overcome. Due to the limited working space, it may be necessary to invent a new robotic design in which the instruments are no longer driven by wires [18].

This is not a frequently used technique, but has great potential and is worth investigating further.

***e) Conclusion and future perspectives***

To repair POP, abdominal sacrocolpopexy is still considered the gold standard. However, due to severe access trauma, other minimally invasive surgical techniques have been introduced to reduce the trauma without increasing recurrences or complications. Laparoscopy as well as robotic operations can reduce trauma, hospital stay and pain. The results are similar or sometimes better than open techniques. The problem of suturing and tissue handling in laparoscopy often found in complex reconstructive procedures can be reduced by use of the robotic device. This combination of minimally invasive surgery with good results and a shorter learning curve has opened a gap for robotic surgery. The biggest disadvantage is the cost of this type of surgery. Being the most expensive way to perform POP repair, further standardization and development of the device may lead to it becoming the future gold standard for POP repair.

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## 2. SINGLE PORT LAPAROSCOPY FOR POP TREATMENT (LESS)

### *a) Introduction*

Laparo-Endoscopic Single-site Surgery (LESS) is a new access option for minimally-invasive surgery and has been developed in many centres. In the literature, most urological procedures have been described using a single port access [1] and case reports are numerous. The series describing more than 50 cases is confidential. In all these articles, LESS appears to be safe and reproducible. But it appears to be a difficult technique. As a consequence, ablative procedures have been preferred.

We have identified the difficulties due to the lack of triangulation and have found solutions to overcome these problems [2]. We have routinely performed sacrocolpopexy with a single port access for five years and have experience of more than 100 cases.

### *b) Material description*

#### 1. The laparoscope

A 30° laparoscope may be useful for the anterior dissection (30° laparoscope looks downwards), but is not useful for the posterior dissection. It is necessary to look upwards to have a good view of the levator, and this may result in conflict between the laparoscope and sigmoid. To look upwards with this laparoscope it is necessary to raise the hand holding the laparoscope and this hand can interfere with other instruments. We recommend the use of a 0° laparoscope.

A flexible laparoscope may be an interesting option, but the extra cost of this type of laparoscope should be considered.

#### 2. The instruments

Articulated and single-use instruments represent an important extra cost and we choose to perform this procedure with reusable instruments.

Articulated and pre-bent instruments have been tried but are difficult to use. These instruments require specific training and are not always well adapted to the patient's morphology.

#### 3. The Single Port

Many different single ports exist and they have all been used. In this procedure, we have used the SILS Port © (Covidien, Mansfield, MA, USA) and Gel Point© (Applied, Santa Margarita, CA, USA) **(Figure 1)**. We found that Gel Point© was easier to use.

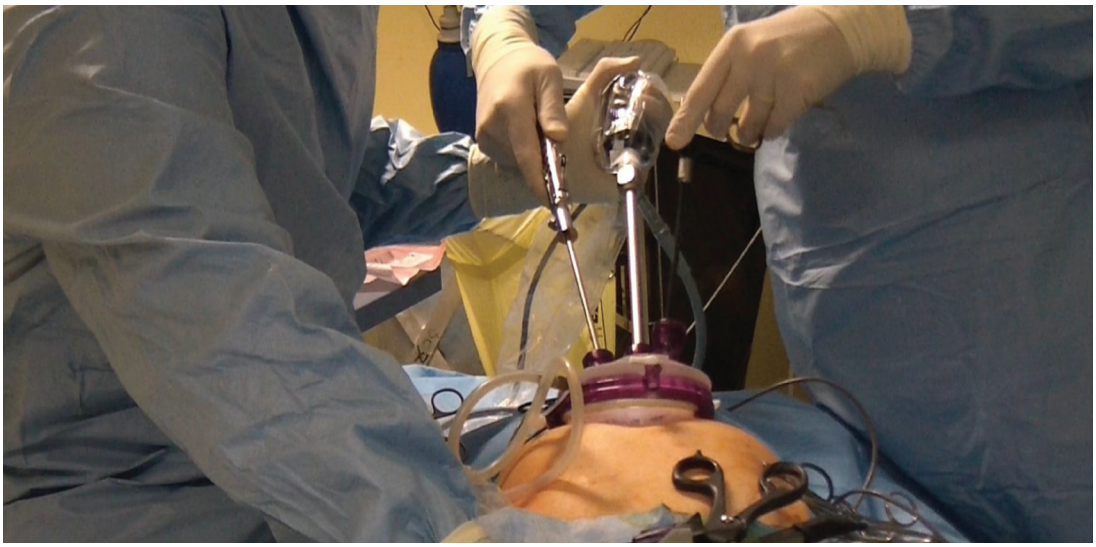

***Figure 1. External operative view***

***c) Procedure description***

Technically, this is a difficult procedure. As the working angles are totally modified, the surgeon's movements must be adapted to this new situation. The working angles that cannot be created from outside (triangulation) must be restored inside to allow proper handling of the needles. For example, using the heel of the needle is a good solution for knot tying. The view may also be different: off-centreing the surgical subject is useful to maintain an excellent view and to free space for the surgeon's hand movements.

A past history of pelvic surgery may sometimes force us to start with adhesiolysis which is feasible with a single port access. The sigmoid and uterus are then placed on the abdominal wall using a straight needle. The promontory is exposed and a tunnel is made under the peritoneum **(Figure 2)**.

A recto-vaginal dissection is performed to expose the levator ani. One hand is used for exposure and the other is used for section and coagulation. The exposing hand is used to grasp tissues away from the dissection zone and to move these tissues in the opposite direction. For example, dissection of the right levator ani requires the left hand to push tissues towards the right. The laparoscope held by the assistant is moved to the left so that the levator ani is off-centre to the right side of the screen. These tricks are very important in providing space for the dissecting hand and will limit conflicts. These tricks are reproduced and adapted to each specific surgical step. The posterior mesh is fixed with wires **(Figure 3)**. The mesh is then placed in the tunnel.

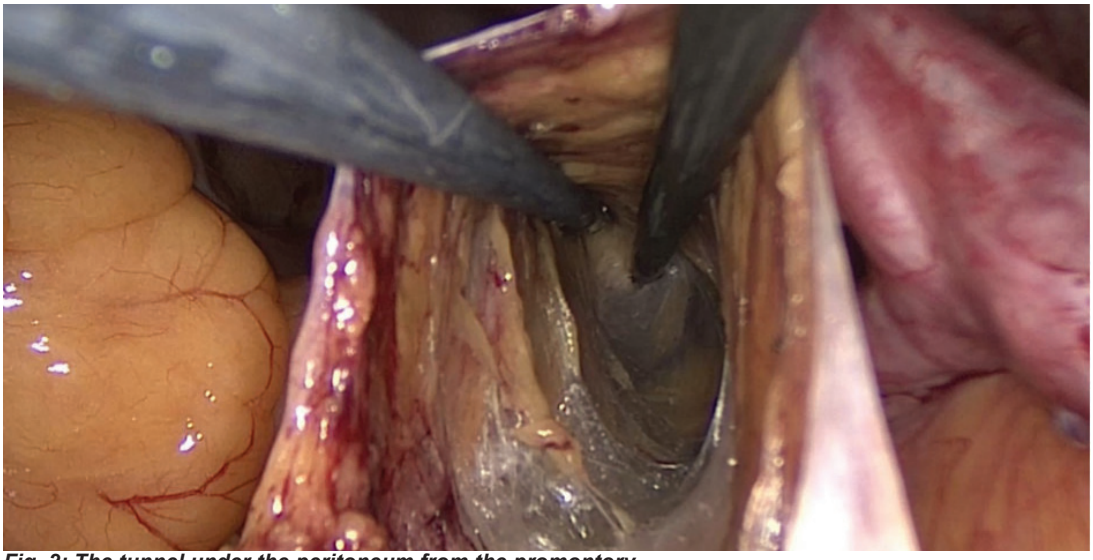

***Fig. 2: The tunnel under the peritoneum from the promontory***

The anterior dissection is less difficult. The exposing hand lifts the bladder up, grasping it away from the dissection zone. The operative view is off-centre to enlarge the space for the dissection hand. The anterior mesh is fixed with wires **(Figure 4)** and intra- or extra-corporeal knots. This mesh is passed under the right adnexa to meet the first posterior mesh in the tunnel.

The two meshes are fixed with wires onto the promontory **(Figure 5)**. All the peritoneal incisions are closed with running sutures and intra-corporeal knots of absorbable wires or absorbable barbed wires.

The abdominal wall is firmly and easily repaired as there is an excellent view due to the 25 mm incision. The umbilicus is sutured and the final scar is small and is subsequently hardly visible **(Figure 6).**

***d) Comments***

To date, only a few cases have been published on the single port surgical treatment of genital prolapse: 10 cases from the Cleveland Clinic group [3], and 4 earlier cases from the same group [4]. These studies concluded that single port sacrocolpopexy is safe with no more complications, same operative time and length of stay as standard laparoscopy or robotic-assisted laparoscopic surgery. We recently published a small series on the day case management of genital prolapse using a single port access [5].

In accordance with our experience and compared to standard laparoscopic series of sacral colpopexy [6] and a recent review of more than 1000 cases [7], operative time seems to be equivalent. In the review, mean operative time was 158 min (96-286 min).

LESS is now generally considered a safe and widely applicable technique [8]. Conversion and complication rates are similar to those obtained with a multiport laparoscopic approach [9]. EAU Guidelines [9] recommend (grade A) that only experienced laparoscopic surgeons should perform this technique and we think that a specific education programme would help.

The immediate cosmetic advantage is considered as evidence of this technique [9,10]

Stolzenburg [11] reported a steep learning curve in the single-port situation due to the lack of triangulation, the crossing of flexible instruments, the crowding of the instruments and the new operative ergonomics. The author showed that a combination of flexible and conventional instruments minimises the impact of the new operative ergonomics. Thus, we chose to use only standard and straight instruments to limit the need for multiple skills. We particularly focused on how to overcome the lack of triangulation [2]. Using standard instruments also plays a part in reducing extra costs.

***e) Conclusion***

LESS is a safe technique and we believe that it is becoming a new surgical standard option. LESS does not require a lot of investment. Performing LESS requires the surgeon to master new hand movements and new ergonomics. A surgeon who is highly skilled at laparoscopic surgery will also have to change habits when beginning LESS and we recommend education and training programmes.

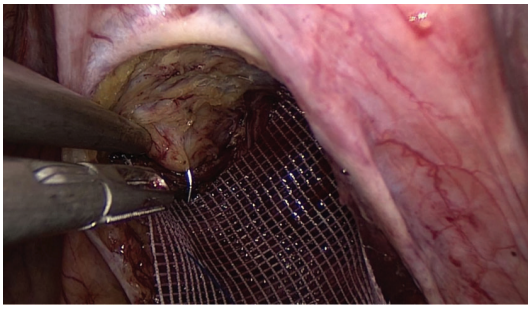

***Figure 3. Posterior mesh being fixed (off-centre view to limit conflict between the instruments and the laparoscope)***

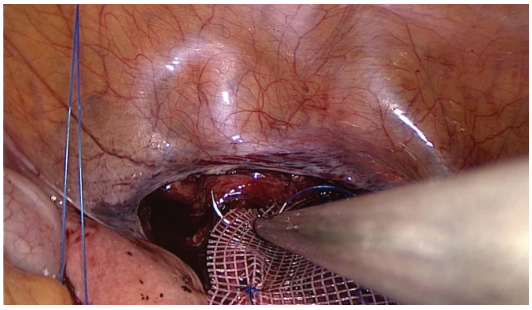

***Figure 4. Anterior mesh being fixed with wire***

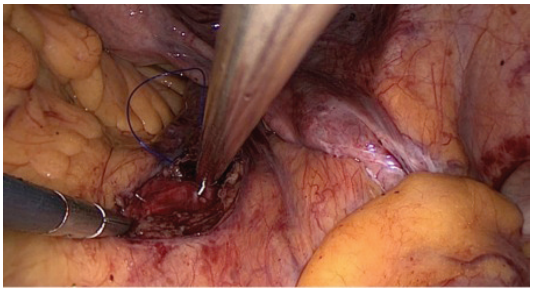

***Figure 5. Meshes being fixed onto the sacral promontory***

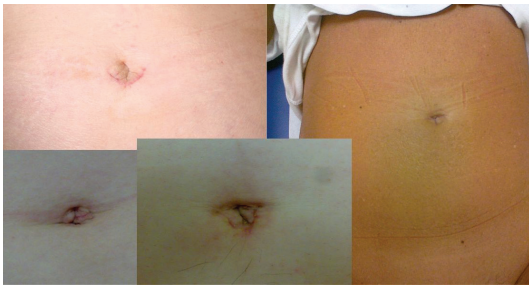

***Figure 6. Umbilical scars after 2 months***

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## Committee 9

# Minimally Invasive Lymphadenectomy

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*J. Porter (USA)*

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*J. L'Esperance (USA)*

*M. Remzi (Austria)*

*M. Santomauro (USA)*

*M. Tyson (USA)*

*R. Van Velthoven (Belgium)*

# CONTENTS

# Minimally Invasive Lymphadenectomy

*G. Janetschek, J. Porter*

*E. Castle, X. Cathelineau, A. Faoud, T. Kunit*
*J. L'Esperance, M. Remzi, M. Santomauro,*
*M. Tyson, R. Van Velthoven*

## A. LYMPHADENECTOMY FOR UPPER TRACT UROTHELIAL CARCINOMA

### I. INTRODUCTION

Upper tract urothelial carcinoma (UTUC) is a relatively rare neoplasm, accounting for only 5% of all urothelial cancers [1]. Approximately 30% of patients have muscle invasive high stage UTUC (>=pT2) at presentation and the incidence of lymph node metastasis ranges from 30% to 40% at surgery [2, 3]. Pathologic stage, determined by the depth of tumour invasion, and tumour grade remain the main predictors of prognosis. Compared with urothelial malignancies of the bladder, upper tract tumours tend to present at a more advanced stage. Kikuchi et al. showed that lymph vascular invasion (LVI) was an independent predictor of recurrence and survival in node positive patients [4]. Nodal involvement is a poor prognostic indicator [2]. However, lymphadenectomy (LA) is not currently performed in all patients treated with radical nephroureterectomy (RNU) for UTUC as it remains controversial whether this procedure improves patient survival. This is in contrast to bladder cancer, where LA has been shown to improve patient outcomes. Several small single institution studies and one multicentre trial showed a survival benefit for patients with locally advanced disease who underwent RNU + LA [5-9]. This review is an evaluation of the current literature on minimally invasive NU and the role of LA in the treatment of patients with UTUC.

### II. DATA ACQUISITION

We performed a systematic review of published original data using the databases MEDLINE and Web of Science. Both Medical Subject Headings (MEDLINE) and free-text protocols (MEDLINE, Web of Science) were employed. The last updated search was performed in April 2014. The search was limited to articles published in the English language.

For Medical Subject Headings [Mesh], we used "lymphadenectomy upper urinary tract carcinoma".

### III. INCIDENCE OF LYMPH NODE INVOLVEMENT IN UPPER URINARY TRACT CARCINOMA (UTUC)

The incidence of lymph node involvement in patients with UTUC is between 30-40% and it is usually associated with high-risk disease. The majority of retrospective studies suggest that LA improves local staging. LA for low stage (<= pT1) during RNU seems to have low impact, because lymph node involvement is rare. In higher stage (>=pT2), a substantial proportion (>15%) of patients will have lymph node involvement [10]. The percentage of patients found to have positive lymph nodes is substantially influenced by the extent of lymph node dissection and the number of lymph nodes removed.

LA also seems to influence survival in patients with high-risk UTUC (clinically infiltrative, high-grade or pathologically muscle-invasive). Thus, LA during RNU should be performed at the time of surgical resection in high risk patients. However, the extent and boundaries of LA needs further investigation and currently there is little agreement on the anatomical regions that should be sampled during LA for UTUC.

In the most recent series of RNU, LA is only performed in around 50% patients, thus lymph node involvement may be underestimated [2, 11]. For laparoscopic RNU (conventional or robot-assisted), oncological outcomes seem to be equivalent to the open approach and have been shown to provide similar outcomes in terms of lymph node yield [12-17].

### IV. ROLE OF LA IN UTUC

The performance of LA has not traditionally been considered to be standard of care for patients undergoing RNU as there has been significant controversy in the literature regarding its therapeutic benefit with several studies suggesting no improvement in survival [7, 8, 18]. In contrast, the advantages of extended LA have been clearly established for bladder cancer, with evidence suggesting improved staging and ac-

curacy, which is important for patient counselling, guiding of further adjuvant therapies, and improved patient survival [19-21]. With respect to urothelial tumours of the bladder, several studies have also demonstrated that increased lymph node removal correlates with improved survival [20, 22]. It would follow that extended lymph node dissection for upper tract urothelial carcinoma should improve prognosis, survival and potentially help determine the need for adjuvant therapies such as chemotherapy or radiation. Although the role of adjuvant therapies for advanced UTUC has not been clearly defined, several studies have demonstrated the importance of LA during RNU for the purpose of prognostication and improving survival [5,6,9].

In the study by Brausi, 40 patients who underwent removal of at least 5 lymph nodes during LA at the time of nephroureterectomy for pT2-pT4 UTUC were compared with 42 patients of similar stage who underwent nephroureterectomy alone [6]. With a median follow-up of 64.7 months, performance of LA, T stage and N stage were significantly related to both time to recurrence and overall survival on univariate analysis. In a Cox proportional hazard model, performance of LA and T stage significantly influenced overall survival, suggesting a possible therapeutic advantage of LA in patients with advanced stage disease. The study by Roscigno et al. confirmed that in patients with muscle invasive UTUC, LA was an independent predictor of disease-free and cancer-specific survival, with survival for pNx patients being significantly worse than that for pN0 patients and comparable to pN+ patients [9]. In addition, for the subgroup of pN0 patients, the number of lymph nodes removed was also an independent predictor of disease-free and cancer-specific survival. The same group evaluated 551 patients from 13 international centres who underwent LA at the time of nephroureterectomy, 140 of whom had positive lymph nodes [3]. They determined that the removal of 13 and 8 lymph nodes resulted in a 90% and 75% probability of detecting at least one positive lymph node, respectively.

Another study confirmed the importance of LA in determining prognosis and consequently, predicting cancer-specific survival. In this study, 412, 578 and 140 patients with pN0, pNx and pN+ disease, respectively, were evaluated for cancer-specific survival [9]. In patients with pT1 disease, there was no difference in survival between patients with pN0 and pNx disease. However, in patients with pT2-pT4 disease, actuarial 5-year cancer-specific survival was lowest in the pN+ group, intermediate in the pNx group and highest in the pN0 group with the differences being statistically significant. Although this study does not necessarily advocate a therapeutic advantage in performing LA, it does reinforce its role in accurate staging and prognostication.

Due to limited data on the therapeutic benefit of lymph node dissection in high-risk UTUC, the performance of LA at RNU is most often surgeon-dependent, and thus a major selection bias has to be considered [23]. Due to this bias, LA in most commonly performed in those with a bulky or infiltrative lymph node pattern, obvious lymph node tumour involvement on preoperative imaging or at the time of surgery.

Pathologic lymph node involvement (N+) compared to negative nodes (N0) have a major impact on disease-specific outcome (RR for tumour-specific death 2-3, **Table 1**). However, the therapeutic effect of removing micrometastasis requires further clarification (N0 compared to Nx, unclear - staging error?)

Roscigno et al. in a large multicentre series reported on staging accuracy based on the number of retrieved lymph nodes. Among 551 patients treated with RNU and regional lymph node dissection in a 15-year period, positive lymph nodes were present in 25% of patients. The removal of 8 nodes resulted in a 75% probability of detecting at least one positive node, while a more extensive lymph node dissection with 13 nodes removed yielded a probability of 90% [3]. Data from the same database (UTUC Collaboration) showed that a cut-off of 8 nodes was the most informative value to predict cancer-specific mortality [24].

Other smaller studies showed that LA during RNU was associated with a lower risk of local recurrence, but did not impact survival [15, 25-27].

In patients with positive lymph nodes (N+), lymph node density <20% decreased recurrence-free survival [27]. Importantly, in patients with clinically node-negative pT1-T4 UTUC a “complete” lymph node dissection, defined in the Kondo boundaries [28], improved cancer-specific survival after adjusting for adjuvant chemotherapy, while the number of removed nodes did not [29]. In another multicentre trial with 1130 patients, LA in stage pT1 disease did not show a significant difference between patients staged pN0 and pNX, whereas in pT2-T4 N0 disease an improved cancer-specific survival compared to pNX was found [9]. This was confirmed by Burger *et al.* [30].

In summary, besides improved nodal staging, the current body of evidence suggests that LA at the time of RNU impacts survival in high-risk UTUC. **(Table 1)**

## V. DOES THE NUMBER OF LYMPH NODES COUNT?

There is mounting evidence that the extent of LA may be important for patient survival. As noted earlier in the study by Roscigno et al, the number of lymph nodes removed predicted disease-free and cancer-specific survival in a subgroup of pN0 patients with muscle-invasive UTUC [3]. Another study examining the impact of the extent of LA on survival evaluated 169 patients who underwent either complete, incomplete or no LA [32]. Complete LA was defined as dissection of all primary sites of nodal metastases as had been previously defined [28]. Al-

***Table 1: Role of LA in RNU***

| Study (number of patients) | Single/Multicentre | Staging impact | Therapeutic impact |
|---|---|---|---|
| Kondo (n=169) [28] | Single | - | LA independent predictor of CSS* |
| Brausi (n=83) [6] | Single | - | LA independent predictor of OS# |
| Roscigno (n=132) [24] | Single | CSS better for pN0 compared to pNX | LA independent predictor of CSS# |
| Roscigno (n=552) [9] | Multi | - | LA independent predictor of CSS# |
| Roscigno (n=1130) [3] | Multi | CSS better for pN0 compared to pNX | - |
| Kondo (n=209) [29] | Single | - | LA independent predictor of CSS# |
| Lughezzani (n=2824) [25] | Multi | CSS better for pN+ compared to pNX | No§ |
| Burger (n=785) [30] | Multi | CSS better for pN+ compared to pNX | No§ |
| Abe (n=293) [31] | Multi | DFS better for pN0 compared to pNX | No, LA independent predictor of recurrence |

***CSS = cancer-specific survival, DFS = disease-free survival *pT3 or higher # pT2 or higher § Outcome of pN0 was equivalent to pNX***

though no difference in survival was seen between the groups, when stratified by tumour stage, patients with stage pT3 disease or higher were more likely to have improved survival with increasing extent of LA. On multivariate analysis, complete LA, T stage and tumour grade were independently associated with cancer-specific survival. The average number of lymph nodes removed was 7.9 and 4.4 for the complete and incomplete LA groups, respectively.

The concept of lymph node density has recently been investigated in 432 RNU patients with lymph node metastases determined by LA [33]. The median lymph node density was reported as 50%, and a threshold of 30% was the most informative in determining the risk of cancer recurrence and mortality.

## VI. BOUNDARIES FOR LA DURING RNU [28, 29, 32]

- Regional lymph nodes are not well defined. Most commonly, hilar, para-aortic (left) and para-caval (right) lymph nodes are mentioned for non-ureter UTUC and intrapelvic (iliacal, obturatoric) for UTUC of the ureter. Kondo et al, included 42 patients in the first mapping study [Kondo] and 75 patients in the confirmation study. [Kondo] regional lymph nodes are as follows:
- Tumours of the renal pelvis (right): hilar, para-caval, retro-caval, interaorto-caval
- Tumours of the renal pelvis (left): hilar, para-aortal
- Lower margin for tumours of the renal pelvis is the inferior mesenteric artery (IMA)
- Tumours of the upper 2/3 ureter (right): hilar, para-caval, retro-calac, interaorto-caval
- Tumours of the upper 2/3 ureter (left): hilar, para-aortal
- Lower margin for tumours of the upper 2/3 of the ureter is the aortic bifurcation
- Tumours of the lower 1/3 ureter: common iliac, presacral, external iliac, obturator, and internal iliac on the tumour side, respectively.

These data may form the basis for future prospective research to better understand the lymphatic spread to the retroperitoneum.

## VII. ROLE OF MINIMALLY INVASIVE SURGERY

Laparoscopic RNU is becoming an established alternative to open RNU [12, 15, 34], due to equivalent oncological results and a simultaneous reduction in morbidity. However, LA during laparoscopic RNU, especially in relatively inexperienced laparoscopic surgeons, or during the learning curve, is often avoided. While laparoscopic RNU has been shown to achieve the same number of lymph nodes, the chance of receiving LA during the laparoscopic approach appears to be lower. In the study by Capitanio et al, lymph node dissection was performed in 42% and 24% of patients treated with open and laparoscopic RNU, respectively [35]. However, the selection bias due to lower stages in laparoscopic RNU was evident. In the only prospective randomised trial by Simone et al. (n=80) [36], no LA was performed during laparoscopic RNU. This might also demonstrate that patients with high stage disease (pT3) showed better disease-free and cancer-specific survival following open RNU compared to laparoscopic RNU.

When comparing open to laparoscopic RNU, the ability to perform an adequate LA during laparoscopic nephroureterectomy has been questioned [37]. In a study by Busby et al [38], there was no difference between open and laparoscopic RNU with respect to the number of lymph nodes retrieved, median number of positive nodes, or median density of positive nodes, proving that LA can be performed in the laparoscopic approach as adequately as in the open approach. Although still a controversial issue, evidence is increasing to suggest that more extended LA at the time of RNU may improve staging and prognostication, while potentially affording a survival advantage for patients with more advanced disease. In addition, LA may be adequately performed by a laparoscopic approach.

LA at RNU is inconsistently used in the open and laparoscopic approach. In a large combined series of 44 institutions, 62% of patients did not undergo any lymph node dissection [Fairey].

## VIII. CONCLUSION

Regardless of the tumour location, radical nephroureterectomy (RNU) with excision of the bladder cuff is the gold standard treatment for UTUC. Lymphadenectomy (LA) performed during RNU allows optimal staging of the disease and some studies suggest a therapeutic benefit. However, the boundaries of LA have not yet been clearly defined. The boundaries depend on the tumour location. The majority of retrospective studies suggest that lymph node dissection improves local staging and influences survival in patients with high-risk UTUC. Therefore, lymph node dissection in patients with high risk (clinically infiltrative, high-grade or pathologically muscle-invasive) UTUC should be recommended at the time of surgical resection, however, the extent of lymph node dissection requires further investigation.

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# B. LYMPHADENECTOMY FOR RENAL CELL CARCINOMA

## I. INTRODUCTION

Lymphadenectomy (LAD) for urologic malignancy has been performed to more accurately define the extent of disease in patients and thereby provide staging information which can better predict the course of the disease. In some cancers, such as testicular and bladder cancer, LAD has been shown to provide a therapeutic benefit beyond removing the primary site of cancer. For renal cell carcinoma (RCC), the role of LAD remains poorly defined due to inconsistent patterns of lymph node involvement, stage migration from more advanced disease to locally confined tumors found incidentally on routine imaging, and failure to prove a therapeutic benefit for LAD in RCC. For many cases of RCC, minimally invasive approaches have provided less patient discomfort and morbidity with similar oncologic outcomes as conventional open surgical techniques. Given the increasing role of minimally invasive surgery (MIS) in the treatment of RCC, we reviewed the current stage of MIS lymphadenectomy for RCC to better define those patients and clinical situations where MIS could provide benefit to the patient.

## II. DATA ACQUISITION

A Medline search was conducted of original articles, review articles and editorials on LAD performed for RCC. Emphasis was placed on publications focused on minimally invasive techniques. Medical Subject Headings (MESH headings) and key words were used to identify publications for review. Key words included renal cell carcinoma, kidney cancer, renal cancer, lymphadenectomy, lymph node dissection, lymph node invasion, and metastatic renal cell carcinoma. For MESH, we used “lymphadenectomy renal cell carcinoma”.

The last updated search was performed in May 2014. The search was limited to the English language.

## III. HISTORY OF LAD IN RCC

Surgical treatment for RCC was first described in 1963 by Robson and included en-bloc excision of the kidney along with the contents within the surrounding Gerota’s fascia, including the ipsilateral adrenal gland, with a complete regional LAD of the para-aortic and paracaval nodes extending from the crus of the diaphragm to the aortic bifurcation [1]. The role of LAD as it pertains to management of RCC has evolved markedly over the last several decades and has become a controversial issue among experts in the field. After the radical template described by Robson, modified templates based on laterality were described based on anatomic study and expected course of lymphatic drainage. Right-sided tumours were managed with a hilar, paracaval, precaval, retrocaval, interaortocaval and preaortic LAD. Left-sided tumours were managed with hilar, preaortic, para-aortic, retroaortic, interaortocaval and precaval LAD [2]. In a subsequent attempt to further reduce the associated morbidity of such extensive LAD, this was further modified to include limited excision of only the hilar, precaval and paracaval nodes on the right and the hilar, para-aortic, and preaortic nodes on the left. This subsequent modification was also facilitated by the advent of MIS and laparoscopy, which made extensive LAD more technically challenging.

## IV. LAPAROSCOPY IN THE SURGICAL MANAGEMENT OF RCC

Clayman et al performed the first laparoscopic radical nephrectomy in 1990. This was carried out without LAD and included morcellation of the specimen for extraction [3]. In the initial experience, laparoscopic nephrectomy was limited to benign disease or low risk malignant disease because the adrenal gland was not removed (which was standard at the time) and due to the inability to accurately stage the morcellated specimen [4]. However, technical expertise grew rapidly and by 2001 Gill et al reported on the largest series of laparoscopic radical nephrectomies for renal masses with regional LAD [5]. Currently laparoscopy is considered the gold standard for management of organ confined renal masses. As technology improves, and as more surgeons are trained in laparoscopy, LAD is no longer considered a relative contradiction to a minimally invasive approach to urologic malignancies and does not compromise nodal yield [6,7]. However, the role of lymph node dissection (LND) in the management of RCC and the indications for LND remain controversial.

## V. INDICATIONS FOR LYMPHADENECTOMY IN RCC

It is worth reiterating that there is no consensus regarding the role of LAD in the management of RCC and given the dearth of randomised research it is a highly debated issue among experts. All the major

associations including the EAU and NCCN have different recommendations ranging from a limited hilar LAD for staging purposes to only resection of clinically suspicious nodes [8, 9].

Several factors contribute to this controversy. First routine LND may result in overtreatment of the vast majority of individuals at low risk for nodal involvement. Since the Robson era there has been a downward stage migration in disease at the time of diagnosis. As more lesions are discovered incidentally and at a lower stage, the proportion of patients with node positive disease has decreased from >30% in the Robson era and is now closer to 3% [10, 11, 12]. Additionally, the likelihood of nodal involvement is directly proportional to clinical stage (with higher incidence in patients with pT3-4 disease) and many argue that the decision to perform LAD should be based on the clinical suspicion of nodal metastasis.

The natural history and pathogenesis of RCC raises concern for the utility of extended LAD, particularly in patients with high-risk features. The incidence of isolated nodal metastasis in RCC is approximately 6% [13] and as RCC has a predilection for haematogenous dissemination, patients with node positive disease also have a high risk of distant metastasis requiring systemic treatment. Furthermore, with more extensive local involvement, lymphatic drainage becomes less predictable and it is less likely that complete nodal debulking is possible.

LAD serves two distinct purposes, either to provide accurate staging information to guide surveillance or adjuvant treatment, or for curative intent by removing potential occult sources of disease thereby decreasing the risk of recurrence and improving survival. It is well established that even in the absence of distant metastasis, lymph node involvement is associated with poor prognosis with 5-year survival rates of 5-35% reported in the literature [14]. Therefore, it is argued that LAD decreases this risk and can be beneficial in patients with clinical evidence of nodal metastasis and in those who appear clinically node negative, but are positive on pathological review. Multiple retrospective series have shown a survival benefit for LAD in patients with positive nodes, and Phillips showed a higher risk of local recurrence in patients not treated with concurrent LAD [15]. However, the rate of node positivity in clinically N0 patients is very low at 3.3% [11] and does not support the use of routine LAD in the absence of clinical suspicion. Furthermore, even in patients with clinically suspicious nodes in the absence of systemic metastasis, less than 50% are positive for metastasis at the time of surgery [16]. It is less clear whether LAD provides any additional benefit beyond staging, as consistent improvement in survival has not been seen in the literature. The EORTC 30881 trial, a large randomised prospective study that evaluated the benefit of routine LAD in clinically N0M0 failed to show a significant survival advantage [11]. Obligatory LAD therefore, given the current overall low incidence of node positive disease at diagnosis, results in overtreatment of >95% of patients. In patients with clinically localised disease, LAD does not appear to significantly improve staging accuracy over conventional imaging methods, nor does it impact disease specific survival and is therefore not recommended. Based on several retrospective series, the current indications for regional LAD include patients with high risk features, clinical suspicion of nodal involvement based on imaging or intra-operative findings, and patients with metastatic disease undergoing cytoreductive nephrectomy.

## VI. LYMPHADENECTOMY TECHNIQUE FOR RENAL CELL CARCINOMA

Minimally invasive surgical techniques for radical nephrectomy are an established approach for treating RCC. However, the role of performing LND during laparoscopic or robotic renal surgery remains undefined. Given that the benefit of open LND during radical nephrectomy remains controversial, few investigators have attempted MIS techniques for LND during radical nephrectomy.

Complicating matters further is the fact that there is significant variability in the lymphatic drainage pattern of the kidney and therefore the ideal dissection template for treating RCC remains undefined. Previously, it was felt that most right-sided renal tumours drained to the paracaval and retrocaval nodes, while left-sided cancers drained to the para-aortic and preaortic landing areas. This was brought into question by Assouad who reported that up to one third of patients with RCC have direct connections to the thoracic duct which bypass normal lymphatic drainage [17]. The supraclavicular and iliac nodes are the only nodes involved in some cases of metastatic RCC further questioning the role of standard LAD. [18] Saitoh reported that the perihilar lymph nodes demonstrated LNI in only 7% of patients with metastatic disease, whereas the para-aortic nodes were involved in 26.8% of cases and the supraclavicular nodes in 20.7% of cases [19]. In an autopsy study of 554 patients found to have kidney cancer at autopsy, 80 were found to have positive nodes, but only 5 (7%) patients had involvement of the paracaval or para-aortic nodes [20]. Finally, RCC is capable of haematogenous spread which may result in metastatic disease without lymphatic involvement [21].

The ability of LAD to accurately predict disease stage and possibly affect survival depends on thorough

removal of the involved lymph nodes. This has led investigators to perform increasingly more extensive LNDs as they gain experience. As would be expected, with enlarging templates of dissection the number of lymph nodes removed and the percentage of patients with positive nodes both increase.

The extent of LND performed concomitant with radical nephrectomy for the treatment of RCC was initially determined by the experience of open surgery. Despite the recognition that LND may provide prognostic information for patients with advanced RCC, there is no agreement as to the scope of dissection. In a survey of urologic oncologists, when performing open radical nephrectomy for localized RCC, 26% reported that they do not perform a formal LND, 41% perform a limited node dissection and 33% perform a full retroperitoneal LND [22]. For metastatic RCC, 21% do not perform a LND, 43% perform a limited LND and 36% perform a full retroperitoneal LND. What constitutes a limited LND during radical nephrectomy varies depending of the study, but in general, includes the paracaval lymph nodes for right-sided tumours and the para-aortic lymph nodes for left-sided tumours. A more extensive dissection may include the retrocaval and interaortocaval nodes for right-sided RCC and the retroaortic lymph nodes for left-sided RCC.

For minimally invasive LAD performed during radical nephrectomy, the extent of dissection mirrors the templates established for open surgical procedures. Chapman described their dissection templates during laparoscopic LND performed during laparoscopic radical nephrectomy for clinically localised RCC [7]. They initially removed the paracaval lymph nodes during right-sided nephrectomy and the para-aortic nodes during left-sided nephrectomy. With increasing experience they expanded the right-sided dissection to include the retrocaval and interaortocaval lymph nodes and the left-sided dissection to include the interaortocaval nodes. When the dissection increased from a limited to an extended template they found the mean lymph node count increased from 4.8 to 8.8 for right-sided cases and 10.5 to 14.3 for left-sided cases. The location of positive lymph nodes was para-aortic in 3, paracaval in one and retrocaval in one, signifying that if the extended dissection was not performed, the positive node in the retrocaval distribution would have been missed.

Abaza reported the first experience with robotic LND during radical nephrectomy for patients with RCC [6]. The robotic approach was performed with the patient in the lateral position using 3 robotic arms. For right-sided cases he removed the paracaval, retrocaval and interaortocaval lymph nodes. For left-sided cases the para-aortic and interaortocaval nodes were removed. Mean lymph node count was 13.6 and there was an increase in nodal yield with experience with the mean node count increasing from 11 to 16.8 comparing the first to the second half of the study.

## VII. OUTCOMES OF LYMPHADENECTOMY FOR RENAL CELL CARCINOMA

There are very few studies evaluating the role of LAD in RCC using minimally invasive techniques, and the available evidence on this topic comes from the open surgical experience. The strongest level of evidence for the role of LND in RCC is the randomised trial of open radical nephrectomy with and without LND [11]. The trial compared 362 patients who received LND and nephrectomy to 370 patients who underwent radical nephrectomy alone. While the final results were published in 2009, the study took place from 1988 to 1991. Patients with evidence of metastases or lymph node enlargement were ineligible for the study. Of the 346 patients who underwent LND, positive lymph nodes were found in 14 (4%). Palpably enlarged lymph nodes were recognized in 51 patients who underwent LND and 10 (20%) of these patients had positive nodes. In the 311 patients without enlarged lymph nodes, 4(1%) were found to have positive nodes on pathologic analysis. With a median follow-up of 12.6 years, there was no difference in overall survival, time to progression of disease, and progression-free survival between the two groups. The complication rate did not differ significantly between the two groups. The authors concluded that the incidence of lymph node involvement is low in patients with RCC and that there is no survival advantage in performing LND with radical nephrectomy.

One of the few reports studying MIS for LND in RCC is that of Chapman et al [7]. They retrospectively reviewed their experience with laparoscopic LND performed during laparoscopic radical nephrectomy and compared them to patients undergoing laparoscopic radical nephrectomy alone. There were 50 patients in each group and the LND group was performed later in their experience than the nephrectomy alone group. All patients had clinically localised disease or metastatic disease, although they used a generous cut-off of 2 cm as the upper limit of normal lymph node size. The dissection template used was paracaval on the right and para-aortic on the left and the template expanded as they gained confidence with laparoscopic LND.

They discovered positive lymph nodes in 5 of 50 (10%) patients undergoing LND and all patients with positive lymph nodes had one or more high risk features including tumour size greater than 7 cm, Fuhrman grade 3 or 4, or T3 or T4 tumours. One of the 5 patients had a positive node in the retrocaval packet which would have been missed with a standard paracaval dissection. Operative time was similar for the LND group vs. the nephrectomy only group (210 vs. 217 min) as was length of stay (1.9 vs. 1.7 days) and estimated blood loss (140 vs. 150 cc). The complication rate was similar for both groups, although in the LND group two patients developed chylous ascites following LND and both cases resolved with conservative management.

The authors concluded that laparoscopic LND during radical nephrectomy is safe and feasible, and staging information from LND has prognostic value and may better select patients for adjuvant therapy. As more and more targeted therapies become available for RCC, accurate staging information will be crucial to properly select patients for clinical trials. There was not enough follow-up on the patients to make any statements regarding the potential therapeutic benefit of LND for RCC.

As previously mentioned, the robotic approach for LND in RCC patients was studied by Abaza et al [6]. This single surgeon, retrospective review of LND during robotic radical nephrectomy evaluated 36 patients with a mean renal mass of 7.3 cm with 16 patients having stage 3 disease and 4 patients with vena caval thrombi. One patient (2.8%) was found to have positive lymph nodes and the mean number of lymph nodes removed was 13.9. The LND added on average an additional 31 minutes to the procedure and on average an additional 74 cc of blood loss. Mean length of stay remained short with the addition of LND with 94% of patients being discharged on POD #1. There were no reported complications. They concluded that robotic LND is safe and feasible with good nodal yield and the robotic approach facilitated lymph node removal.

## VIII. CONCLUSIONS

While the role of LAD in RCC remains controversial, more investigations are providing evidence that a subset of patients with RCC may benefit from LAD. LAD should be considered in patients with lymph node enlargement, patients undergoing cytoreductive nephrectomy and patients with high-risk features such as local invasion and tumour thrombi in the renal vein or vena cava. LAD should also be considered in patients who may receive targeted chemotherapy for RCC. The extent of LAD is not clearly defined due to the significant variability in the pattern of lymphatic drainage associated with RCC. To date, minimally invasive techniques of LAD for RCC appear to provide similar staging information as compared to open LAD and result in less patient morbidity. Patients with clinically localised disease without nodal enlargement should not undergo LAD.

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# C. MI LYMPHADENETOMY FOR BLADDER CANCER DURING RADICAL CYSTECTOMY

## I. INTRODUCTION

The gold standard treatment for non-metastatic muscle-invasive and high-risk superficial bladder cancer is radical cystectomy (RC) with bilateral pelvic lymph node dissection (PLND) [1] [level of evidence: 2a, grade of recommendation B]. Both laparoscopic radical cystectomy (LRC) and robot assisted-radical cystectomy (RARC) have been shown to be safe and reproducible alternatives to the open approach [2]. Regardless of the approach, bilateral standard PLND is an integral part of radical cystectomy. Standard PLND should include all lymphatic tissues around the external iliac, internal iliac and the obturator groups bilaterally [3] [level of evidence: 3, grade of recommendation C]. There is also evidence suggesting that bilateral extended PLND (which includes common iliac nodes) may be associated with an improvement in 5-year progression-free survival [3] [level of evidence: 2b-3, grade of recommendation C]. Thus, LRC and RARC must be able to replicate the standard and extended templates in order to be established as an alternative techniques.

## II. METHODOLOGY AND EVIDENCE ACQUISITION

A detailed online systematic review of the literature was performed to identify articles addressing lymph node dissection in laparoscopic and robotic-assisted radical cystectomy. Original articles, research articles, review articles and meta-analyses published since January 2000 were identified in the Cochrane Library Database, Pubmed and Medline. Articles were reviewed and assigned a level of evidence (LE) according to the criteria by the Centre for Evidence Based Medicine in Oxford, UK [4]. The methodological quality of all studies was assessed using the Newcastle-Ottawa Scale [5]. The checklist of the CONSORT statement was used to evaluate the quality of the randomised controlled trials [6]. Panel recommendations were graded following the system currently used by the EAU guidelines office.

## III. EVIDENCE SYNTHESIS

### 1. THRESHOLD NUMBER OF LYMPH NODES AND EXTENT OF LYMPHADENECTOMY FOR ACCURATE STAGING, REGARDLESS OF APPROACH

Regardless of approach (open versus minimally invasive), the first challenge in developing universally accepted standards for pelvic lymphadenectomy relates to the uncertainty surrounding the minimal number of lymph nodes necessary to impart a survival advantage. In a prospective randomised phase III trial, the extent of lymph node dissection and the individual surgeon's experience have a major impact on surgical outcomes and overall survival [7] [LE: 1b]. Capitanio et al previously demonstrated that the likelihood of finding positive lymph nodes (LNs) varied directly with the total number of LNs removed [8] [LE: 2b]. Their estimates indicate that 15 LNs resulted in an approximately 50% chance of finding at least one positive lymph node in a patient with nodal disease, whereas 25 or more nodes increased this probability to 75%. However, whether this improves survival and the mechanism by which it may improve survival remain unclear. In a separate study addressing this very question, Koppie, et al. studied 1121 patients from MSKCC over a 14-year period and concluded that there was no plateau in the dose-response curve with an increasing number of nodes up to 23 nodes, which lends support to the idea of improved survival with extended lymphadenectomy [9] [LE: 2b]. Leissner et al [10] suggested that a significant survival benefit was maintained if more than 16 lymph nodes were removed [LE: 3], whereas Stein et al [11] reported that survival in patients with positive lymph node disease was better if more than 15 pelvic lymph nodes had been retrieved [LE: 3]. On the other hand, Abdel-Latif and coworkers [12] and Herr [13] could not reproduce the relationship between survival and the number of dissected lymph nodes using multivariable statistics. Taken together, these studies indicate that while the relationship between extent of lymphadenectomy and the detection of positive nodes has been well studied, the relationship with survival is less understood.

***a) Recommendations regarding extent of lymph node dissection:***

1- The extent of lymph node dissection and the individual surgeon's experience has a major impact on the therapeutic outcome and overall survival [LE: 1b, GR: A].

2- The more lymph nodes removed, the higher the probability of detecting at least 1 positive lymph node. However, there is no defined threshold for the number of lymph nodes that need to be removed [LE: 2b, GR: B].

3- There is some evidence from retrospective and prospective analyses that an extended pelvic lymphadenectomy may be associated with an improvement in 5-year progression-free survival [LE 2b-3, GR: B].

4- Standard lymphadenectomy should include all lymphatic tissues around the external iliac, internal iliac and the obturator groups bilaterally and extended lymphadenectomy should include the common iliac groups [LE: 3, GR: B].

## 2. FEASIBILITY AND ADEQUACY OF PLND IN MINIMALLY INVASIVE RADICAL CYSTECTOMY

In this context, the ability to perform an adequate PLND was one of the early criticisms of minimally invasive approaches to radical cystectomy. Mean nodal yields in large series of open radical cystectomy (ORC) from centres that routinely perform extended PLND range from 22-51 with most greater than 30 [14]. In contrast, the mean nodal yields in early reports of PLND in minimally invasive radical cystectomy were less than 20 with none greater than 30 [15]. In a small series of 15 patients, Lavery et al. [16] reported > 25 lymph nodes (LNs) in 13 patients. They demonstrated a nodal yield of 42.5 LNs in an extended PLND similar to an open extended PLND series. Guru et al. [17] demonstrated the feasibility and safety of performing adequate robot-assisted PLND and reported higher yield with increasing case volume [18]. Several authors confirmed these findings in their case series without comparing with the standard ORC [19-24]. Adequate PLND was also reported in large scale population based databases [25]. For example, a collaborative evaluation by the International Robotic Cystectomy Consortium (IRCC) using a multi-institutional international RARC database, found that 82.9% of 527 patients subjected to RARC underwent adequate lymphadenectomy defined as having >10 LNs removed [26]. The authors demonstrated a mean LN yield of 19 with high volume centres (>100 cases per year) having the highest yields. High volume centres and high surgeon volume (>50 cases), two factors suggestive of the learning curve, were predictive of the probability of undergoing an adequate lymphadenectomy with RARC. Recently, several high-quality studies comparing minimally invasive radical cystectomy with ORC were reported with no statistically significant difference in nodal yield between the two approaches [27-31]. A similar LN yield to ORC was achieved in elderly patients > 75 years old treated with LRC [32]. To date, there are two small prospective single centre noninferiority randomised controlled studies comparing open versus minimally invasive approaches to radical cystectomy and PLND. In the first study, Nix et al. [33] demonstrated a mean LN number of 19 in the robotic-assisted group compared to 18 in the open group [LE: 1b]. In the second study, Lin et al [34] demonstrated that the LN yield in the LRC group was not inferior to the ORC group [LE: 1b]. In a recent meta-analysis of nine studies comparing RARC with ORC, higher LN yield was found in the RARC group [35]. Another meta-analysis of eight studies comparing LRC with ORC demonstrated no statistically significant difference in LN yield between the two groups [36]. Furthermore, a second look open PLND by a different experienced open surgeon after previous robotic-assisted extended PLND (median of 43 LNs removed) showed minimal additional LN yield [0-8] [37]. Lastly, the oncologic outcomes of patients with LN-positive bladder cancer treated with RARC compare favourably to previous published studies of ORC at medium-term (mean follow-up of 42 months) [38]. While there is no question that PLND during LRC poses a challenge to the inexperienced laparoscopist, it would seem that expert laparoscopic surgeons are capable of performing an adequate laparoscopic PLND with node counts equivalent to ORC series. The initial concerns that the manoeuvrability of the standard da Vinci system may not permit the same extent and quality of PLND as is possible with ORC have been allayed by technical improvements in the da Vinci S and Si systems as well as by increased surgical expertise and skills.

### 1. Recommendations

1- LRC and RARC can safely yield the same extent of lymph node dissection as ORC [LE: 1b, GR B].

2- The reported number of LNs removed in robotic series may be higher than in open surgical series. [LE: 2a, GR B].

## 3. THE EXTENT OF LYMPH NODE DISSECTION IN MINIMALLY INVASIVE RADICAL CYSTECTOMY

The goal of a meticulous PLND is the removal of all fibro-adipose tissue from the well defined regions. Complete removal of LN-bearing tissue within the boundaries of the standard PLND in minimally invasive approaches is safe and feasible [2]. Dissection up to the aortic bifurcation or inferior mesenteric artery could be more challenging using minimally invasive modalities. However, extended PLND has been demonstrated with minimally invasive approaches with comparable results to the open approach [LE: 1b, GR B]. There are no studies reporting different PLND templates between the groups. However, in pooled data of a meta-analysis reporting early outcomes after RARC compared to ORC, Li et al. [39] found a higher LN yield in level II PLND (around the common iliac artery) in the RARC group. The robot allows for complete skeletonisation and mobilisation of the iliac vessels, and provides perspectives that are difficult to achieve with the open approach, namely the lateral view behind the common iliac artery.

## 4. RECOMMENDATIONS REGARDING THE EXTENT OF LYMPH NODE DISSECTION IN MINIMALLY INVASIVE RADICAL CYSTECTOMY

1- LRC and RARC can achieve similar perioperative templates and oncologic lymph node dissection outcomes as ORC [LE: 1b, GR B].

# IV. CONCLUSION

Regardless of the approach, bilateral standard and extended PLND are an integral part of radical cystectomy. In experienced hands, the minimally invasive approach can safely yield the same extent of LN dissection as the open technique. In the future, long-term oncologic studies will be necessary to confirm the oncologic efficacy of robotic and laparoscopic lymph node dissection in the treatment of bladder cancer.

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# D. MI LYMPHADENECTOMY FOR GERM CELL TUMOR AFTER CHEMOTHERAPY

## I. INTRODUCTION

Laparoscopic retroperitoneal lymphadenectomy (RLA) was first described for clinical stage I testicular cancer, and the results were comparable to the open approach. The first reported case of laparoscopic RLA after chemotherapy (PC-RLA) was performed in 1995 in a patient with a left-sided stage IIb tumour [1]. A first series by the same author including 24 patients, reported good surgical and oncologic results, and there were no conversions [2]. In contrast, another contemporary series of 9 patients reported 7 conversions due to marked desmoplastic reactions [3]. The difference in outcome between these two early series can be explained mainly by patient selection, and the latter series included 7 patients with large tumours not suited for this type of surgery. Initially, only a few groups performed laparoscopic PC-RLA, and this was due to the fact that the combination of a centre caring for patients with testicular cancer and competence in laparoscopic surgery was a rare finding. Now, since laparoscopy has become routine for most laparoscopic surgeons, interest in this important indication is steadily rising.

## II. DATA ACQUISITION

A detailed online systematic review of the literature was performed to identify articles addressing lymph node dissection in laparoscopic (also robotic-assisted) RLA for testicular cancer. Medical Subject Headings (MESH headings) and key words were used to identify publications for review. Key words included testicular carcinoma, testicular cancer, lymph node metastases, chemotherapy, laparoscopy, retroperitoneal lymphadenectomy, and retroperitoneal lymph node dissection. Original articles, research articles, review articles and meta-analyses were identified in the Cochrane Library Database, PubMed and Medline. Articles were reviewed and assigned a level of evidence (LE) according to the criteria by the Centre for Evidence Based Medicine in Oxford, UK. The methodological quality of all studies was assessed using the Newcastle-Ottawa Scale. The checklist of the CONSORT statement was used for evaluating the quality of the randomised controlled trials. The last updated search was performed in July 2014.

## III. PATIENT SELECTION

The indication for PC-RLA was the removal of residual tumour. However, in addition to the residual tumour, all the lymphatic tissue within the template was removed as well. This template was usually bilateral. There is growing evidence that in selected patients, unilateral template resections yield equivalent long-term results compared to bilateral systemic resections [4-9]. When open surgery is replaced by laparoscopy, the indication for PC-RLA should remain unchanged, and the quality and extent of dissection must not be compromised. Patient selection is a crucial factor.

### 1. UNILATERAL RLA

The ideal indication for laparoscopic PC-RLA is a small residual tumour, where dissection can be restricted to a unilateral template. Therefore, we need to exactly define this situation. The primary landing site of lymph node metastases from a testicular tumour is unilateral, and the location is typical for a tumour of the left and right testicle. According to this observation, the extent of a unilateral template has been defined for both sides [4]. In addition, it has been shown that this primary landing site is ventral and never dorsal to the lumbar vessels [5,6]. With growth, further spread may occur to secondary and tertiary landing sites to potentially include tissue behind the vena cava and aorta and at the contralateral site.

Several authors have focused on the selection of patients suitable for unilateral dissection. A limited PC-RLA was performed in 100 patients. In 6 patients the residual tumour was larger than 5 cm. There were 4 relapses, all outside the boundaries of a full bilateral RLA [7]. Another group performed modified unilateral PC-RLAs in 98 patients with a residual mass smaller than 5 cm. Mature teratoma was found in 30.6%, and vital tumour in 14.2%. There were 3 relapses, but all outside the retroperitoneum [8]. Others have confirmed these results in a prospective study [9]. However, it is important not only to focus on the size of the residual tumour, but also to consider the size and extension (laterality) of the tumour prior to chemotherapy, where it also has to be strictly unilateral [8,9]. Some authors even restrict PC-RLA to stage IIb, which only includes tumours up to 5 cm prior to chemotherapy [2,10]. This is a very safe approach, but is obviously too restrictive.

In summary, these criteria allow for a limited unilateral PC-RLA: strictly unilateral tumour prior to chemotherapy, and a unilateral residual tumour up to 5 cm in diameter.

### 2. RLA FOR RESIDUAL TUMOURS < 1 CM

There is consensus that all residual tumours larger than 1 cm must be removed. There is also some argument to remove smaller tumours. Mature teratoma may be found in 13% – 22%, and active tumour in up to 9.4% [2,11, 12]. These figures increased to 41% and 16%, respectively, when the primary tumour contained teratoma [11]. Therefore, PC-RLA may be considered in patients with a residual mass smaller than 1 cm and teratoma in the primary orchiectomy specimen [8]. The group in Innsbruck introduced another approach. They restricted chemotherapy to 2 cycles in stage IIb patients, to replace further chemotherapy by PC-RLA, irrespective of the size of the residual mass [2].

### 3. BILATERAL RLA

Any patient with initial bilateral tumour spread or a residual mass larger than 5 cm requires a full bilateral PC-RLA. A nerve-sparing technique should be attempted. The upper tumour size limit for bilateral PC-RLA cannot be defined exactly and is decided by the surgeon. According to the literature, the largest pre-operative tumour size was 20 cm, and 10 cm after chemotherapy. In this context, attention has to be paid to the fact that complete resection of the residual mass is one of the most important prognostic factors. In a retrospective study, it was shown that approximately 50% of patients who underwent PC-RLA had a local relapse which was obviously due to incomplete resection at initial surgery [13].

## IV. TEMPLATES

The traditional approach to PC-RLA was full bilateral template dissection. However, as previously stated, there are now clear indications where PC-RLA can be restricted to unilateral dissection. The templates for unilateral PC-RLA are the same as for RLA for clinical stage I, and have been best studied and described by Weissbach [4]. On the right side, they include the tissue around the vena cava, the interaortocaval tissue, and the preaortic tissue between renal vessels and the origin of the inferior mesenteric artery. The cranial border is delineated by the renal vessels and the caudal border by the crossing of the ureter with the iliac artery **(Figure 1a)**. On the left side, the template does not include the interaortocaval tissue, but all tissue lateral and dorsal to the aorta as well as the tissue ventral to the aorta between the renal vessels and the origin of the inferior mesenteric artery **(Figure 1b).**

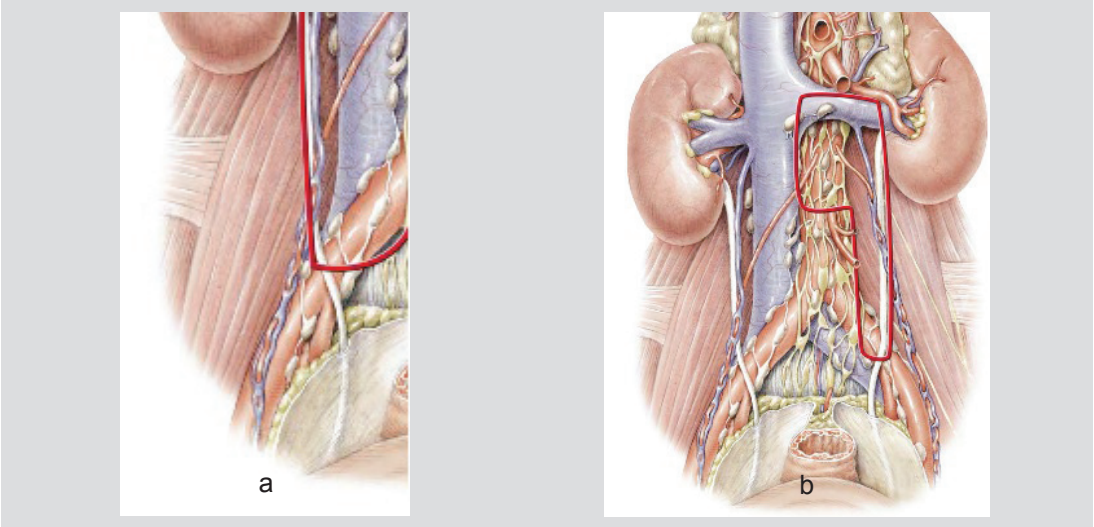


***Figure 1.a,b. Modified unilateral templates according to Weissbach [4]***

***a: template for right tumour, b: template for left tumour With permission from [14]***

## V. SURGICAL TECHNIQUE

### 1. UNILATERAL PC-RLA

#### *a) Transperitoneal approach*

Most authors prefer a transperitoneal approach with the patient in the lateral decubitus position [2,3,15-20,41]. The transperitoneal approach provides exposure comparable to open surgery. An important step is wide dissection and complete displacement of the bowel to gain broad access to the retroperitoneum. The technique of laparoscopic PC-RLA is similar to laparoscopic RLA for clinical stage I. The technical difficulty of dissection mainly depends on the extent of the desmoplastic tissue reaction induced by the precedent chemotherapy. The most severe fibrosis can be observed in seminoma. In addition, pure embryonal carcinoma shows marked fibrosis. In contrast, there is usually little change after chemotherapy for teratoma. The surgeon must be well trained in the handling of large vessels, and he should be prepared to manage vascular injuries by means of laparoscopy.

#### *b) Extraperitonal approach*

LeBlanc initially developed the extraperitoneal approach for laparoscopic RLA in clinical stage I [21]. It is now used for PC-RLA by several groups [10,22-24]. The patient is placed in the supine position. The surgeon stands on the ipsilateral side. Sufficient extraperitoneal space is developed with blunt dissection and carbon dioxide insufflation. As an alternative, a distending balloon may be used [22]. Exposure is very good. There is one main concern with this approach: Instead of harmless chylous ascites frequently observed after transperitoneal PC-RLA, large lymphoceles will develop which are mostly symptomatic and difficult to treat.

### 2. BILATERAL PC-RLA

When analysing the respective publications it is obvious that frequently there was no clear indication for performing bilateral PC-RLA, and the majority of patients could have been treated with unilateral dissection as well **(Tables 1, 2)**. Some groups have even completely replaced unilateral PC-RLA with bilateral dissection for the same indication [18,25]. Busch performed radical bilateral PC-RLA in 26% of his 46 patients, but the largest residual tumour diameter was 3.9 cm only. The tumour size and laterality prior to chemotherapy were not specified. Also he did not describe his technique of bilateral surgery [20]. Small tumours were also predominant in the series by Steiner. 13 of his 29 patients were stage IIb [25]. Aufderklamm compared unilateral (19 patients) with bilateral (20 patients) laparoscopic PC-RLA, but the tumour size was similar in the groups and rather small [18]. In summary, surgery is rarely performed for large tumours.

Nerve-sparing is feasible in bilateral PC-RLA, and results in preservation of antegrade ejaculation in a high percentage of patients [18,25,26].

#### *a) Repositioning*

Complete bilateral laparoscopic PC-RLA by means of a transperitoneal approach obviously requires repositioning of the patient, which substantially increases operative time [18,25,27]. Only one author performed PC-RLA transperitoneally without repositioning the patient, and there was no relapse during the follow-up indicating incomplete dissection [28]. However, in his 4 patients, the size of the residual tumours was between 2-4 cm only, thus bilateral dissection was not indicated. Therefore, the quality of dissection cannot be assessed since even incomplete clearance of the contralateral template would not result in an increased relapse rate.

The exposure provided by the extraperitoneal approach allows for good bilateral exposure and therefore complete bilateral PC-RLA without changing the position of the patient and without the need for additional trocars. Only two authors used this technique in small series of 1 and 4 patients, respectively [10,24]. In addition, these procedures were performed for small tumours only. However, the advantage of the good bilateral exposure has to be weighed against the increased risk of lymphocele formation.

### 3. PRESERVATION OF ANTEGRADE EJACULATION

Loss of antegrade ejaculation is the result of bilateral damage of the sympathetic nerves between L1 –L3 [29]. All ganglia and nerves in this area may be destroyed by full bilateral dissection. Therefore, preservation of these nerves by means of nerve-sparing techniques is mandatory to preserve undisturbed antegrade ejaculation [30]. It has been shown that this nerve-sparing technique is feasible with laparoscopy [26].

Preservation of the sympathetic nerve on one side preserves normal antegrade ejaculation in almost 100%. The sympathetic nerves of the left side run within the left paraaortal lymphatic tissue. They are destroyed with left template dissection, but remain intact with a right template. The situation on the right side is a little more complicated. These nerves run through the interaortocaval space. Therefore, they are removed with a modified right template, but are left intact with the Weissbach template, where the interaortocaval tissue is spared [4] **(Figure 1a,b)**. However, some authors include the interaortocaval space in their left template resulting in loss of ejaculation.

Originally, Donohue who first described the nerve-sparing technique used a large template [30]. When presenting the results of this technique, he had changed to the left template sparing the interaortocaval space, which by itself provides perfect

*Table 1. Reported series on laparoscopic PC-RLA*

| Author | Year of public-ation | Patients | Age (years) | Template | Year enrolled | Median OP Time | Conversion | Blood loss ml | Follow up | Level of Evidence |
|---|---|---|---|---|---|---|---|---|---|---|
| Rassweiler et al. [3] | 1996 | 9 | NR | NR | NR | NR (326-360) | 7 | NR | 29 (NR) | 4 |
| Bales et al. [34] | 1997 | 1 | 42 | Left: 1 | 1997 | NR | 0 | NR | NR | 4 |
| Janetschek et al. [2] | 1999 | 24 | 29.4 (15-48) | Right: 14<br>Left 10 | 1995-1998 | 240 (180-360) | 0 | NR | 24.4 (3-49) | 3 |
| Palese et al. [27] | 2002 | 7 | 36.6 (35-55) | Right: 3<br>Left: 3<br>Bilateral: 1 | 1996-2000 | 400 (188-700) | 2 | 1053 (75-2800) | 24 (12-60) | 3 |
| Hara et al. [22] | 2004 | 3 | 22 (20-27) | Left: 3 | NR | NR (250-310) | 0 | <50ml | NR | 4 |
| Steiner et al. [15] | 2004 | 68 | NR | Unilateral: 68 | 1992-2003 | 243 (120-570) | 0 | 78 (10-1600) | 57.6 (3-121) | 3 |
| Tobias-Machado et al. [35] | 2004 | 2 | 27 (NR) | Left: 2 | NR | 260 (240-280) | 1 | 400 (NR) | 18 (NR) | 4 |
| Albqami et al. [32] | 2005 | 59 | 29.2 (15-56) | Right: 32<br>Left:27 | 1995-2004 | 234 (135-360) | 0 | 165 (20-350) | 53 (10-89) | 3 |
| Corvin et al. [36] | 2005 | 7 | 30 (24-47) | Right: 4<br>Left: 3 | 2002-2003 | 232 (115-365) | 0 | <100ml | 18.6 (NR) | 3 |
| Lima et al. [37] | 2005 | 1 | 23 | Right: 1 | 2005 | 116 | 0 | 100 | 5 | 4 |
| Castillo et al. [38] | 2006 | 1 | 18 | Left: 1 | 2006 | NR | 0 | NR | 60 | 4 |
| Almendos [42] | 2006 | 1 | 33 | Right: 1 | 2006 | NR | 0 | Nr | Nr | 4 |
| Maldonado-Valadez et al. [6] | 2007 | 16 | 31.4 (20-49) | Right: 4<br>Left: 12 | 2002-2006 | 237 (125-370) | 0 | NR | 26 (NR) | 3 |
| Permpongkosol et al. [19] | 2007 | 16 | 34 (16-55) | Right: 7<br>Left: 7<br>Bilateral: 2 | 1996-2005 | 327 (116-700) | 2 | 903 (75 -2800) | 32.7 (5-108) | 3 |
| Skolarus et al. [39] | 2008 | 4 | 31 (NR) | Unilateral: 3<br>Bilateral: 1 | 2003-2007 | 275 (200-369) | 0 | 70 (50-150) | 12.7 (5.8-17.5) | 4 |
| Spermon et al. [40] | 2008 | 1 | 27 | Right: 1 | NR | NR | 0 | NR | 8 | 4 |
| Tanaka et al. [23] | 2008 | 5 | NR | NR | NR | NR | NR | NR | NR | 4 |
| Calestroupat et al. [41] | 2009 | 26 | 31 (26-34) | Right: 9<br>Left 17(2 of them extraperitoneal) | 2000-2006 | 183 (120-260) | 3 (11.5%) | 400 (100-600) | 27 (14-36) | 3 |
| Busch et al. [20] | 2012 | 44 | 32.0 (26.5 – 37.5) | Unilateral: 32<br>Bilateral: 12 | NR | 212.0 (145 – 298) | 3 (6.5%) | >500ml 4/44 | 30.1 (12.1–47.1) | 3 |
| Arai et al. [10] | 2012 | 20 | 27 (18-49) | Right: 7<br>Left: 13 | 2002-2010 | 223 (137-399) | 0 | 20 (10-520) | 24 (11-45) | 3 |
| Aufderklamm et al. [18] | 2013 | 19 | 30.8 (NR) | Right: 5<br>Left: 14 | 2002-2009 | 221 (125-370) | 0 | NR | 24 (4-38) | 3 |
| Kimura et al. [24] | 2013 | 6 | 31 (19-48) | Right: 1<br>Left: 1<br>Bilateral: 4 | 2009-2012 | 394 (212-526) | 0 | 75 (10-238) | 30 (24-36) | 3 |
| Steiner et al. [25] | 2013 | 100 | 29.6 (11.4-52) | Right: 34<br>Left: 37<br>Bilateral:29 | 1993-2010 | Unilateral: 241 (120-480)<br>Bilateral: 343 (300-480) | 1 | 84(10-1600) | 74 (1-222) | 3 |

*Table 2. Bilateral PC-RLA*

| Author | Year of publication | Patients | Age (years) | Year enrolled | Median OP Time | Conversion | Blood loss ml | Follow up | Level of evidence |
|---|---|---|---|---|---|---|---|---|---|
| Basiri et al. [28] | 2010 | 4 | 31.5 (28-35) | 2002-2009 | 330 (240-420) | 0 | NR | 15 (3-66) | 4 |
| Aufderklamm et al.[18] | 2013 | 20 | 31.5 (NR) | 2009-2013 | 270 (186 - 397) | 0 | NR | 13 (3-37) | 3 |

preservation of ejaculation so that additional nerve-sparing was not required. However, he indicated that his good results were exclusively due to the nerve-sparing technique and did not mention the change in template [37].

## VI. RESULTS

### 1. SURGERY

Median operative time varies greatly from 183 – 394 min, with a wide range from 116 - 700 min (**Tables 1, 2)**. Operative time, but also other parameters, are to a great extent influenced by the learning curve. Therefore, small series are not very representative. When considering only series with at least 20 patients, median blood loss is 20 – 500 ml.

With unilateral template resection without additional targeted nerve-sparing, excellent results can be achieved, and ejaculation is preserved in nearly 100% [2, 15, 16, 27,32]. The ejaculation rate after bilateral dissection depends on the quality of nerve sparing and ranges between 83 – 90% [18,25].

### 2. COMPLICATIONS

Since the first reports were published almost 20 years ago, many complications are not classified according to the Clavien system [33]. Therefore, direct comparison of the reported complications is difficult. In addition, most series were investigated retrospectively, which weakens data quality to some extent.

The most frequent adverse event during surgery is injury to a major vessel. This event is reported in up to 50% **(Table 3)**. Therefore, one has to be prepared to solve this type of problem by means of laparoscopy. Intestinal lesions are observed less frequently. As rare events, severe complications have been described such as injury to the renal artery requiring vascular bypass or leading to nephrectomy, transection of the iliac artery, duodenal perforation requiring repair with pyloric excision and hepaticojejunostomy, and intestinal lesion repaired by segmental resection and reanastomosis [19,27,41]. Conversion to open surgery is not a complication per se. Also conversion is not always the result of a complication which cannot be managed laparoscopically any more, but may be due to wrong patient selection. The highest reported conversion rate is 7 out of 9 patients [3]. There are also other small series with conversion rates of 12 – 30% [19,27, 41]. The lowest rates are 0 and 1 in series of 59 and 100 patients, respectively [25,32].

Chylous ascites is a frequent postoperative finding. It can be clinically significant in up to one third of patients. Usually this problem resolves with conservative measures such as a low fat or medium chain triglyceride diet [2]. Such a diet can also be started as a preventive measure prior to surgery. There is only one report of a direct lesion of the cysterna chyli requiring several paracenteses and finally a second-look laparoscopy to perform surgical closure of the leak [38].

The transperitoneal approach does not completely prevent lymphocele formation. For this reason, drainage should be avoided. One author reported on 2 symptomatic lymphoceles requiring marsupialisation due to compression of the vena cava [15].

The risk of lymphocele formation or prolonged lymphorrhea when the operative site is drained is a potential disadvantage of the preperitoneal approach. Arai reported lymphorrhea in 20% and chyle leakage in 45% [10]. The same is true for Hara and Kimura where the incidence of lymphorrhea was 30%, respectively [22,24].

Intra- or postoperative mortality has not been reported in any series.

### 3. ONCOLOGIC RESULTS

The quality of surgery can be best assessed by the rate of relapses within the retroperitoneum, and by the number of relapses within the attempted resection template. However, active tumour is a relatively rare finding. A mature teratoma requires a substantially longer period of time to become evident. Therefore, the problems of incomplete resection may become obvious in the long-term only.

An analysis of larger series including at least 20 patients revealed the following results [2,19,18,20,25,32] **(Table 4)**: The rate of necrosis was 42 – 80%, mature teratoma was found in 10 – 42%, and active tumour was found in 2 – 22%.

*Table 3. Complications of PC-RLA*

| Author | Retrograde ejaculation | Chylous Ascites | Lymphocele | Urinoma | Intra-operative complication | Clavien |
|---|---|---|---|---|---|---|
| Rassweiler et al. [1] | NR | None | 12.5 (1/8) | None | None | NR |
| Bales et al. [2] | NR | NR | NR | NR | None | NR |
| Janetschek et al. [3] | None | 20.83% (5/24) | None | None | None | NR |
| Palese et al. [4] | None | NR | NR | None | 57.1% (4/7)<br>3 vascular injury<br>1 duodenal perforation | NR |
| Hara et al. [5] | NR | 33.33% (1/3) | NR | None | None | NR |
| Steiner et al. [6] | 1.47% (1/68) | 4.4 % (3/68) | 8.8% (3/68) | None | None | NR |
| Tobias Machado et al. [7] | None | None | None | None | None | NR |
| Albqami et al. [8] | NR | 11.86% (7/59) | 6.77% (4/59) | None | 15.25% (9/59), bleeding | NR |
| Corvin et al. [9] | None | None | 4% (1/25) | None | None | NR |
| Lima et al. [10] | None | None | None | None | None | NR |
| Castillo et al. [11] | NR | 100% (1/1) | None | None | None | Clavien III: 1 |
| Maldonado-Valadez et al. [12] | None | None | None | None | None | NR |
| Permpongkosol et al. [13] | None | NR | 6.25% (1/16) | None | 25% (4/16)<br>3 vascular injury<br>1 duodenal perforation | NR |
| Skolarus et al. [14] | NR | None | 25% (1/4) | None | None | NR |
| Spermon et al. [15] | NR | NR | NR | NR | NR | NR |
| Tanaka et al. [16] | NR | NR | NR | NR | NR | NR |
| Calestroupat et al. [17] | NR | NR | None | None | 34.61%(9/44)<br>8 vascular injury<br>1 intestinal Injury | Clavien I: 1<br>Clavien II: 5<br>Clavien III: 2<br>Clavien IV: 1 |
| Busch et al. [18] | NR | NR | NR | NR | 26%(12/44)<br>vascular injury | Clavien II: 1<br>Clavien III: 9 |
| Arai et al. [19] | None | 45% (9/20) | 20% (4/20) | None | None | Clavien I: 13 |
| Aufderklamm et al. [20] | None | None | None | None | None | NR |
| Kimura et al. [21] | None | 33.33% (2/6) | None | None | None | Clavien II: 2 |
| Steiner et al. [22] | 4% (4/100) | 1% (1/100) | 1% (1/100) | None | 1% (1/100)<br>vascular injury | NR |

*Table 4. Complications of bilateral PC-RLA*

| Author | Retrograde ejaculation | Chylous Ascites | Lymphocele | Urinoma | Intra-operative complication | Clavien |
|---|---|---|---|---|---|---|
| Basiri et al [23] | NR | 50% (2/4) | NR | - | - | 2/4 Clavien II |
| Aufderklamm et al [20] | 10% (2/20) | 5% (1/20) | - | - | - | 1/20 Clavien III |

Two authors found no local relapse [2,10], and two others observed 1 relapse each within the retroperitoneum, but outside the surgical template [25,32]. Aufderklamm reported on 2 in-field and one suprahilar relapse [18]. This was the reason for this group completely switching from unilateral to bilateral dissection. A relapse rate of 8.6% - the highest of these large series - was observed by Busch [20]. 3 of the 4 relapses occurred within the template. The location of the fourth relapse was not known. The data from the Busch study allow the conclusion that laparoscopic PC-RLA resulted in incomplete resection in this series. However, this was obviously a problem of the specific group and not the method itself.

Two small series of 3 and 5 patients, respectively, reported relapse rates of 33% and 40% [22,23]. There was also one case report which mentioned both an in-field and a portsite metastasis [40]. This event, which should serve as a warning, can only be explained by an invalid surgical technique and possibly wrong patient selection.

## VII. ROBOT-ASSISTED PC-RLA

No reports on robot-assisted PC-RLA were found in the literature. Only a few reports mentioned use of the daVinci robot for RLA in clinical stage I testicular cancer [32]. The older models of the daVinci robot had a limited operating range, possibly resulting in a problem covering the large template of RLA. However, with the new models, this problem should be solved, and it can be expected that the robotic surgeons will take up this indication.

## VIII. QUALITY OF LIFE

Because excellent results are achieved by RLA, treatment-dependent quality of life has become a major issue. To exclude the bias of the surgeon, a quality-of-life study has been performed in cooperation with psychiatrists [44]. A questionnaire which included 39 questions was distributed to 119 patients and completed in personal interviews by 118 with a compliance rate of 99.2%. The questionnaire included questions regarding the patients' satisfaction, their treatment experience, and side effects. Patients were asked about the period of time needed before they were able to perform gentle physical exercise, return to normal activities, and were free of symptoms. Other questions addressed interest in sexual activity, whether the patient felt "lovable," experienced any problems in his partnership, psyche, or social life, and whether he was anxious about losing his job or had emotional problems associated with the loss of a testicle or the RLA procedure. The open RPLND group included 53 patients (47.3%). The laparoscopic RPLND group comprised 59 patients (52.7%). 70 patients from both groups had also received prior chemotherapy, either as primary therapy or in an adjuvant setting. Surprisingly, both laparoscopic and open RPLND were better tolerated than chemotherapy. Open RPLND impaired quality of life much more than laparoscopic RPLND. The questionnaire did not contain a single item in which open RPLND was superior to laparoscopy. The patients who participated in the study preferred laparoscopic RPLND to all other treatment modalities.

## IX. CONCLUSIONS/RECOMMENDATIONS

The indications for PC-RLA are well defined and include all non-seminoma residual tumours >1 cm after chemotherapy and normalisation of the tumour markers. Standard PC-RLA is bilateral. There is also increasing evidence that a unilateral template dissection is indicated for unilateral tumours not larger than 5 cm after chemotherapy. Several authors reported on unilateral transperitoneal laparoscopic RLA. However, there were no single prospective studies or randomised trials. The highest level of evidence in all of these studies was 3. They all reported that with proper patient selection, appropriate surgical technique and experience, the results were comparable to open surgery with regard to surgical and oncologic outcome. Morbidity was less. The complication rate was low, but there was some risk of severe complications. Therefore, unilateral PC-RLA can be recommended, but only in tertiary centres with experience in both laparoscopy and the management of testicular cancer (Grade C). Very little information on bilateral laparoscopic PC-RLA is documented. Therefore, a recommendation cannot be given.

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# E. MI LYMPHADENECTOMY FOR PENILE CANCER

## I. INTRODUCTION

Lymphadenectomy (LA) is of outstanding importance in the diagnosis and treatment of penile cancer. However, penile cancer is a rare disease in the western civilization with an incidence of 0.1–0.9 new cases per 100 000 males per year [1]. Thus, studies available in the literature are most commonly, case series or single centre retrospective data with a low number of patients. This is especially true for the endoscopic variant of inguinal lymphadenectomy (Endo-iLA). The maximal level of evidence for Endo-iLA is 2; however, most of the studies are case series with a low number of patients and short follow-up [2].

However, LA has a therapeutic role and can be curative in 3 out of 4 patients with minimal tumour burden and only 1-2 positive lymph nodes. The clinical evaluation and even modern imaging do not reliably mirror the lymph-node status in penile cancer [3, 4].

The risk of positive inguinal lymph nodes depends on stage, grade and lymph vascular invasion [5], however, available stratifications have their limits [6]. The standard open LA has a rather high morbidity, thus many attempts have been undertaken to reduce the morbidity, especially by chances of boundaries and the extent of iLA. The indications for limited or extensive LA and their respective benefits remain a matter of controversy [1-7]. Other, not well defined terms used in the literature are radical and modified iLA. Modified LA is described most commonly as not extending lateral to the femoral artery, not caudal to the Fossa ovalis, saving the Saphena magna and does not include Sartorius transpositioning.

In 2007, Sotelo and colleagues as well as Tobias-Machado and colleagues in 2006 introduced an endoscopic technique for inguinal LA in penile cancer and other malignancies (melanoma, vulva carcinoma). This technique has the potential benefits of reducing morbidity, especially cutaneous and infectious complications, which can cause

major morbidity and immobilisation of the patient. Two facts add to the high incidence of infectious and cutaneous morbidity with the standard open approach, even in more recent series [8,9]:

1. The region of the groin is at risk (OR 4.65) for wound infections, especially in patients with adiposity, diabetes mellitus and skin disorders [10].
2. Penile cancer is often associated with super infections and is more commonly found in men with low education and hygienic status [11].

## II. DATA ACQUISITION

This review followed Cochrane standards and the PRISMA guidelines. We performed a systematic review of published original data using the databases MEDLINE and Web of Science. Both Medical Subject Headings (MEDLINE) and free-text protocols (MEDLINE, Web of Science) were employed. The last updated search was performed in April 2014. The search was limited to articles published in the English language.

For Medical Subject Headings [Mesh], we used "lymphadenectomy penile cancer".

## III. ENDOSCOPIC INGUINAL LYMPHADENECTOMY

Inguinal LA for penile cancer can be performed for several reasons:

a) Staging procedure

b) Risk of occult metastases

c) Palpable lymph nodes

d) Imaging positive lymph nodes

The procedure can be diagnostic, therapeutic or even palliative (groin pain, risk of exulceration, morbidity of groin mass) [12, 13].

Even though inguinal LA is widely accepted as being of outstanding importance, it is still feared by many surgeons, because standard open iLA has been reported to have complication rates of 50% to 100% even in experienced centres [14]. Hence, many surgeons as well as their patients try to avoid standard open iLA even if it is beneficial, which is especially true for patients with non-palpable lymph nodes. This fact also leads to the avoidance of surgery on both legs at the same time. After operating on one leg with major complications a significant period of time can pass before the second leg is operated on and sometimes surgery is avoided on the contralateral side. Endo-iLA can be performed on both sides at the same time.

Another potential advantage is that the inhibition threshold is lowered by ENDO-iLA and patients with a potential lower risk for positive lymph nodes undergo ENDO-iLA. Naumann et al. studied a group of men with pT1 moderately differentiated penile cancer, typically eligible for surveillance. They found that metastases were present in 44% during iLA [15]. This was also confirmed by others [14, 16]. Recent data suggest a survival advantage for patients who undergo prophylactic iLA and have positive nodes compared with those treated with surveillance and delayed dissection for positive nodes [17].

Since the introduction of ENDO-LA by Bishoff et al [18] and Sotelo et al [19] in cadavers, Sotelo et al [19] and Tobias-Machado et al [20] presented their first clinical results. Thereafter, several modifications of the technique using different terms (see below) and different energy devices or tools including robot assistance [2] and single site surgery [22] have been described. Very recently, these techniques have also been used for palpable lymph nodes [18-22].

The main purpose of this approach is to reduce skin-related morbidity, while achieving the same oncological results.

### 1. MORBIDITY

The morbidity related to ENDO-iLA varies between studies and ranges from 0 to 40%. This has to be compared to open iLA. Recently, complication rates among men with no palpable lymph nodes have been reported to decrease compared with historical experience with open iLA, however, overall complication rates still range from 10% to 46% [23]. In the study by Schwentner et al. [24], ENDO-LA (28 procedures) was compared to a cohort of open LA (32 procedures) with a mean follow-up of 55.8 months (2–87 months). Both groups were comparable regarding the number of nodes removed, open 7.2, 2–16 vs endoscopic 7.1, 4–13), the number of positive nodes (open 1.8 vs endoscopic 1.6), and local recurrence rates (6.6 vs 7.7%, respectively), however operating time was significantly ($P$<0.01) longer for ENDO-LA compared to open LA, 136.3 [87–186] min vs. 101.7 [38–195] min. Secondary wound healing and leg edema were only seen on one patient (7.1%) . The complication rate for open LA was 55.3%. Reduced morbidity was also seen in the study by Tobias-Machado **(Table 1)** in which 10 open procedures were compared to 20 laparoscopic procedures [20].

Master et al [29] reported on 41 ENDO-iLA in 29 patients with a median follow-up of 604 days (range 177 to 1,172, mean 634). No perioperative mortalities and a total of 11 (27%) minor and 6 (14.6%) major complications were observed. Major complications were readmission for i.v. antibiotics in 3, incision plus drainage in 2 and flap necrosis in 1 patient. According to the Calvien-Dindo classification, there was one Clavien I, ten Clavien II and six Clavien IIIa complications.

*Table 1: Outcome of series with more than 10 ENDO-iLA procedures*

| Reference (Year) | Number of procedures (patients) /patients with penile cancer | Mean number of lymph nodes removed | Complication rate |
|---|---|---|---|
| Sotelo [26] (2007) | 14 | 9 (4-15) | 23% (only lymphocele) |
| Tobias-Machado [20] (2006) | 20 (compared to 10 open) | 10.8 (7-16) | Lymphocele 10% (vs. 20%)<br>Skin 5% (vs. 50%)<br>Haematoma 5% (vs 0%) |
| Schwentner et al [24] (2013) | 28 / 14 (compared to 32 open) | 7.1 +- 2.9 | 1/28 (7.1%) |
| Master et al [28] (2009) | 25 (16) / 6 | 11.8 | 1/6 (16.6%)* |
| Master et al [29] (2012) | 41 (29) / 9 | 11 (3-24) | 1 x Clavien I,<br>10 x Clavien II<br>6 x Clavien IIIa |
| Matin et al [2] (2013) | 20 (10) / 10 | 9 (5-21) | 4/10 (40%)<br>1 x Cellulitis<br>1 abscess drainage<br>1 wound breakdown incision site<br>1 skin necrosis (overlying the dissected field). |
| Romanelli et al [25] (2013) | 33 (20) / 33 | 8 | 33% |
| Pahwa et al [32] (2013) | ? (10) / 10 | 7-12 | 20% 2 x Lymphocele |
| Canter et al [33] (2012) (group of Atlanta / Master et al) | 19 (10) / 10 | 11 (3-26) | 30%<br>1x incision + drainage<br>1 x pneumomediastinum without sequel<br>1 x cellulitis requiring i.v. antibiotics |

For open iLA, Kofiman et al [11], Stuvier et al [30] and Yao et al [31] reported on 340, 237 and 150 patients with removal of a median of 10.9 [6-19], 9 [1-25] and 12.6 lymph nodes with an overall complication rate of 10.3% (4.1% lymphoedema, 1.2% seroma, 0.9% scrotal oedema, 0.9% skin necrosis, 0.9% lymphocele, 0.6% wound infection, 0.6% flap necrosis, 0.6% wound abscess, and 0.6% deep vein thrombosis DVT), 58% (43% wound infection, 24% seromas, 16% skin-flaps) and 14% (13.9% lymphoedema, 4.7% skin necrosis, 2% seroma, 2% lymphocele, 1.4% wound infection, 0.7% DVT), respectively.

## 2. TERMS

The following is a list of terms used in the literature for ENDO-ILA:

Video-endoscopic inguinal lymphadenectomy (VEIL Procedure) [20,22,26]

Leg Endoscopic Groin Lymphadenectomy (LEG Procedure) [27]

Robotic-assisted VEIL (RAVEIL) [2]

Endoscopic inguinal or inguinofemoral lymphadenectomy (ENDO-iLA)

## 3. TECHNIQUES AND LYMPH NODE YIELD

Daseler et al [34] performed anatomical inguinal dissections in 450 lower extremities of cadavers and found that the number of nodes in the superficial field ranged from 4 to 25, with an average of 8.25 per extremity. This number is comparable to those reported in all series **(Table 1)**, thus it is likely that ENDO-iLA reaches the oncological safety.

Yuan et al reported no difference between classic endoscopic or single site and ENDO-iLA complications with a saphena magna sparing technique prospectively [26]. Others used the robot with similar results [2, 35].

Similarly, if a deep inguinal LA or a pelvic dissection is indicated, it should be performed at the same time [2, 36-37].

**Figures 1 to 4** illustrate the technique. The patient is positioned supine with bilateral thigh abduction and a slight out rotation (frog-leg position) **(Figure 1 and 2)**. The first incision is made approximately 2 cm distal to the tip of the femoral triangle **(Figure 3)**. Digital, blunt dissection is used to establish a plane below the Scarpa

fascia on the level of the Fascia lata. Two additional trocars are placed under digital control **(Figure 4, 5)**. Low pressure can be used to maintain the working space (3-8 mmHg CO2). A 30 degree lens is advantageous as the resection field is on the upper site. Different advanced energy tools or clips can be used to seal lymphatic vessels. The landmarks for resection are the same as for open iLA: The sartorius muscle laterally, the inguinal ligament cranially, and the adductor longus muscle medially. Another landmark is the saphenous vein which will lead to the hiatus saphenous. All lymph nodes should be removed.

## 4. CONCLUSION

Endoscopic inguinal lymphadenectomy (ENDO iLA) is a safe and feasible method with the potential to overcome recent problems of LA in penile cancer. It seems to result in lower morbidity for skin- related and infection-related complications and can be performed safely on both sides at the same time. This may reduce the fear of iLA complications associated with the classic open approach and hence will be performed whenever necessary for the patient. Not enough data are available for oncological safety, however, preliminary data show equal lymph node yield and local recurrence rates compared to open iLA. Compared with other endoscopic urological procedures this technique is much easier. Prospective randomised trials are needed to further elucidate this topic.

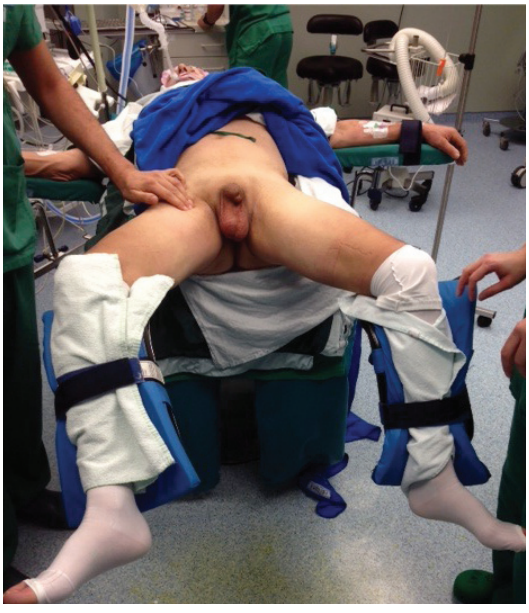

*Figure 1. Position of the patient for ENDO-iLA*

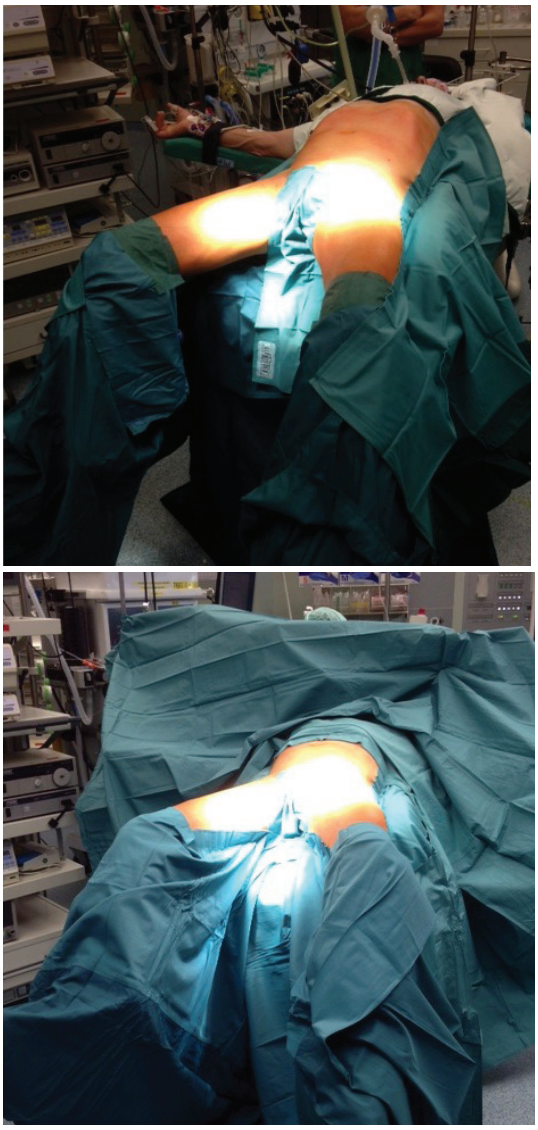

*Figure 2. Coverage of the patient*

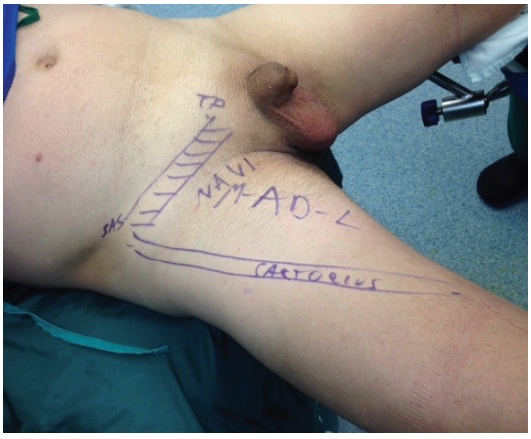


*Figure 3. Femoral triage for planning ENDO-iLA*

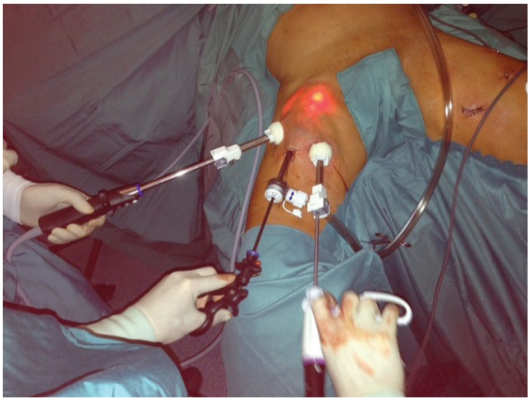

*Figure 4. Trocar positioning*

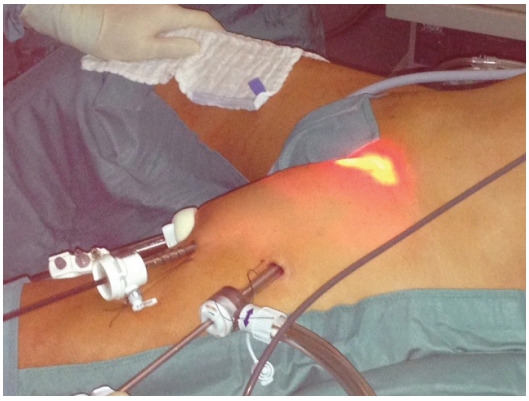

*Figure 5. Trocar positioning*

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## Committee 10

# Minimally Invasive Surgery In Urology Training

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*P. Dasgupta (United Kingdom),*

*H. van der Poel (The Netherlands)*

### Members

*K. Ahmed (United Kingdom),*

*W. Brinkman (The Netherlands),*

*O. Brunckhorst (United Kingdom),*

*M. Do (Germany),*

*P. Dundee (Australia),*

*R. Ganzer (Germany),*

*P. Kallidonis (Greece),*

*M. Khan (United Kingdom),*

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*B. Van Cleynenbreugel (Belgium),*

*S. van Rij (Australia)*

# Content

# Minimally Invasive Surgery In Urology Training

*P. Dasgupta, H. van der Poel*

*K. Ahmed, W. Brinkman, O. Brunckhorst, M. Do, P. Dundee,*
*R. Ganzer, P. Kallidonis, M. Khan,*
*E. Liatsikos, D. Murphy, J-U. Stolzenburg,*
*B. Van Cleynenbreugel, S. van Rij*

## ABSTRACT

Objectives: To describe the progress in training for minimally invasive surgical (MIS) options in urology

Methods: A group of experts in the field provided input to define the recommendations for MIS training. A literature search was carried out on MIS training in general and for urological procedures specifically.

Results: A literature search showed the rapidly developing options for e-learning, box and virtual training and suggested that box training is a relatively cheap and effective means of improving laparoscopic skills. The development of non-technical skills is an integral part of surgical skills training and should be included in training curricula. The application of modular training in surgical procedures showed more rapid acquirement of skills. Training curricula for minimally invasive surgery in urology are being developed in both the US and Europe.

Conclusion: Training in MIS has shifted from "see-one-do-one-teach-one" to structured learning from e-learning to skills lab and modular training settings.

## I. INTRODUCTION

While minimally invasive procedures such as ureterorenoscopy (URS) or transurethral resection of a bladder tumour (TURBT) have been common practice in urology for almost a century, the first laparoscopic procedure in urology was only described in 1976. Laparoscopy (from Ancient Greek λαπάρα (lapara), meaning "flank, side", and σκοπέω (skopeó) [1], meaning "to see") is an operation in the abdomen or pelvis performed through small incisions using long instruments and a camera. The first procedure described in urology was a laparoscopy to aid in the localisation of a cryptorchid testicle [2].

Laparoscopy in urology started to become popular after the first laparoscopic nephrectomy by Ralph Clayman in 1990 [3, 4]. Since then, laparoscopy has been successfully used to remove genitourinary organs, from kidneys and adrenal glands to prostates and bladders. Laparoscopy can also be effectively used for many complex reconstructive procedures, such as pyeloplasty [5]. Potential advantages of laparoscopy are less post-operative pain, earlier recovery and smaller scars. Possible disadvantages, however, are the higher costs of instrumentation and a longer learning curve, due to the indirect view in the operating site, longer instruments, counter-intuitive movements of the instruments and diminished haptic feedback.

Robot-assisted laparoscopy is a possible next step in laparoscopic surgery. Investments from the North American Space Association (NASA) and the US military led to the development of the master–slave system which is commercially available today [6]. Currently, the only commercially available telerobotic system for laparoscopic surgery in humans is the da Vinci® Surgical System (dVSS) (Intuitive Surgical, Mountain View, CA, USA). The dVSS was approved by the Food and Drug Administration (FDA) in 2000, and since then clearance for use of this system in many specialties has been granted. In 2000, urologists started to use the dVSS to perform radical prostatectomy for prostate cancer [7]. Since then, the dVSS has been used successfully for operations on many other organs of the urinary tract, such as the kidney [8] and the bladder [9].

### 1. TRAINING IN LAPAROSCOPIC SURGERY

The classic, but still most common educational strategy for training surgical skills, the master-apprentice model, leads to difficulties when it comes to the introduction of radically new technologies, such

as laparoscopy. The master-apprentice approach is characterised by trainees (postgraduates, novices, apprentices) learning surgical skills by practising directly on patients under the supervision of a 'master' or supervisor. However, being the pioneer of a new technique forces professionals to start applying this technique by operating on patients without the supervision of a master, simply because experienced colleagues are not yet available.

In laparoscopy, the pioneers came to the conclusion that the 'unnatural' counterintuitive psychomotor skills could very well be trained on simulators. To date, simulators have been widely implemented in laparoscopic surgical training programmes to train psychomotor skills associated with this kind of surgery [10]. Various simulators have become available on the market and were validated to facilitate basic laparoscopic skills training [11-15].

A recent systematic review on the effectiveness of training laparoscopic skills showed that training basic laparoscopic skills in a skills lab setting has been proven to improve performance in the operating room [16]. However, the optimal implementation of simulators in training programmes remains a topic of discussion and investigation, as the discussion on training laparoscopy in the skills lab is shifting from: "Is it effective?" to "How can it be most effective?".

## 2. ROBOT-ASSISTED LAPAROSCOPY TRAINING

Compared with laparoscopic surgery, robot-assisted laparoscopic surgery requires other psychomotor skills, such as Endowrist® manipulation and different camera manipulation. In contrast to open and laparoscopic surgery, robot-assisted laparoscopy is characterised by a complete lack of tactile feedback. The marketing of the dVSS focused on its 'intuitive' usability, and indeed some surgeons stated that changing from laparoscopy to robot-assisted laparoscopy only made the procedure easier. However, even for those operators transferring from laparoscopy, slow learning curves were described based on operating time, complication rates and surgical margins [17, 18]. While the basic laparoscopy skills can be learned using relatively simple box trainers, basic robotic skills training requires the whole robotic system to be able to practice. As an alternative, various simulators became available and were validated for their ability to facilitate the development of basic robot-assisted laparoscopy skills [19].

## 3. HOW TO TRAIN AND ASSESS THE OUTCOME OF TRAINING

The literature suggests that the optimal endpoint for simulator training is the attainment of a predefined level, rather than the completion of an arbitrary number of procedures, task repetitions or hours using the simulator [20, 21]. In addition, criterion-based training is thought to boost resident motivation [22]. The development of criterion-based training programmes for laparoscopic and robot-assisted skills fits into the steady evolution towards competency-based postgraduate medical education [23].

The difficulty in criterion-based training is to set proper criteria that comprise the desired components and the appropriate level of skills. However, there is no point in setting criteria, if failure to pass these criteria has no consequence [24]. Therefore, the question 'How to assess' is an important sequel to the question 'How to train'. In 1990, Miller proposed a framework for clinical assessment in the shape of a pyramid **(Figure 1)**. At the bottom of the pyramid there is knowledge (knows). There are many who appear to believe that this is the only thing that should or can be measured. There is, however, more to the practice of medicine, and especially to learning surgery. Therefore, on top of knowledge, Miller's pyramid features 'knows how', 'shows how' and 'does'. If we translate this into laparoscopy training, we could say that 'knows' refers to the knowledge of the indications for and difficulties of laparoscopy. 'Knows how' refers to training laparoscopy skills, 'shows how' refers to the demonstration of these skills for assessment, and 'does' represents the final step of patient-related learning.

In general surgery, the basic laparoscopic skills examination has been in place since 2004, and certification is a requirement for the American Board of Surgery [25, 26]. In urology, however, the qualification and certification of laparoscopic skills performance are still in a preliminary phase. Tjiam et al. developed the programme for laparoscopic urological skills (PLUS) in response to urgent calls from health care authorities and the public for well-defined proficiency standards to safeguard the quality of care [27-29]. For robot-assisted laparoscopy, basic skills programmes have also been described [30], but to

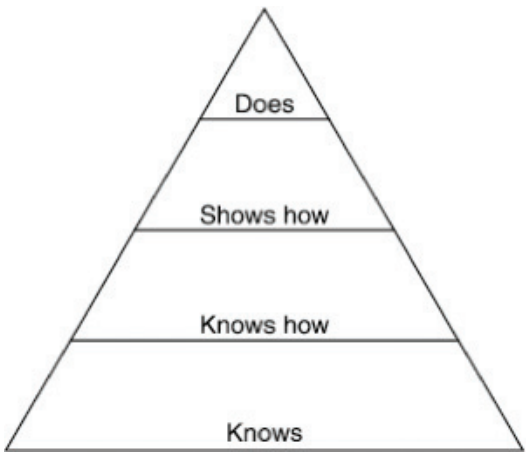


***Figure 1. Miller's pyramid***

date, a widely accepted basic skills programme and examination for this type of surgery do not exist.

## II. E-LEARNING AND SKILLS TRAINING

E-learning can be defined as the use of internet and multimedia technology to deliver instructions and facilitate learning [31]. It is primarily based on cognitivism, an educational framework that sees learning as an active process. In this educational theory, the learners actively construct their own knowledge by assimilating and accommodating new information. This changes and extends their prior knowledge and understanding. In order to motivate the learner, there are 4 steps that need to be followed. These steps are: attention, relevance, confidence and satisfaction. The learner's confidence needs to be built by encouraging and supporting them. Also, the satisfaction of giving them feedback on their performance and allowing them to progress to the next level by successfully completing the previous level, will build up their confidence and motivation.

E-learning has many advantages. The trainee can access learning at their preferred time and place, an important issue in view of the reduction in training hours and training opportunities. However, we must stress that educators often capitalise on the flexible scheduling of e-learning activities without taking into account the cumulative time required to complete all assignments [32, 33].

Another advantage is the possibility to provide individualised learning. Learners can be given greater control over their learning environment, and they can move at their own pace. Another way to individualise lessons, is adaptive instruction in which the computer uses information about the learner to alter and thus optimise the learning experience.

It has been proven that well designed graphics and animations improve learning and narration enhances learning from graphics. E-learning modules can serve in the preparation for performing dexterity training by explanatory videos on the exercises to be performed. Moreover, many manufacturers provide e-learning modules to train personnel and surgeons to become acquainted with the equipment.

There are of course, some disadvantages to e-learning. These disadvantages include poor instructional design: once complete, a website can be viewed and critiqued by all users. A classic example is the "Textbook on the web", which offers little if any advantage over the previous format. The costs are another disadvantage. The development of an effective online tutorial or virtual patient can be very expensive, and each web-based learning course comes at the expense of learner time that might have been devoted to other purposes. The recently introduced TELMA system [34] is a video-based e-learning module for minimally invasive surgery that showed face validity for the training of laparoscopic skills. The EAU developed two basic e-learning modules for laparoscopy (eBasic Laparoscopic Urological Skills) and robotic surgery (eBasic Robotic Urological Skills).

E-learning leads to significant knowledge gains. Compared with traditional teaching methods, however, it is not more effective in improving the learner's knowledge. In conclusion, internet-based instruction is better than no instruction at all, and is as effective as traditional non-internet based instruction methods [33].

## III. HANDS ON TRAINING IN LAPAROSCOPY-BOX TRAINERS

The spatial orientation, the reduced tactile feedback of the instruments, the manipulation of a three-dimensional environment on a two-dimensional screen, the increased tremor of instruments and their paradox movement represent significant problems for any novice surgeon in laparoscopy [35]. The first step for laparoscopic training usually includes hands-on training in mechanical simulators-box trainers which are considered to enhance the acquisition of laparoscopic skills [36].

### 1. BOX TRAINERS (BTS)

BTs are devices which consist of a box, laparoscopic instruments and a digital camera. Objects or organs are placed into the box and can be manipulated by the instruments. A simpler alternative is the exclusion of a digital camera and the use of a box with transparent cover so that the trainee has direct vision of the training field. Another alternative is the use of a tilted mirror at a 45° angle from above. The mirror allows the trainee to work and look in the mirror [37]. Different types of boxes and digital cameras have been used [35, 36]. Low cost boxes consist of clear top or carton boxes which make use of a web-camera connected to a laptop [38]. Commercial BTs are produced by several companies and have different costs depending on the equipment accompanying them. Laparoscopic digital cameras, insufflators and electrocautery units could be a part of the most expensive BTs [36]. In addition, BTs such as the P.O.P trainer (OPTIMIST, Innsbruck, Austria) provide pulsating organ perfusion and more realistic surgical conditions which can replicate an intraoperative incident of haemorrhage [39].

### 2. EVIDENCE ON BOX TRAINERS

A large variety of training instruments and BTs of different properties has been used for training not only in laparoscopic urology, but also in other surgical and endoscopic specialties [40-59]. Although, there are meta-analyses on several aspects of the BTs, the included randomised controlled trials (RCTs) are of variable quality [47]. Large meta-analyses are currently available in simulation training and include evidence for BTs and Virtual Reality trainers (VRTs) [47,

48, 54, 56, 58]. Simulation training in comparison to no intervention seems to be effective regardless of the outcome, level of learner, study design or the laparoscopic task. Outcomes related to knowledge, time, process and product were all statistically and educationally significant in favour of BT training, and simulation training proved to be more efficient in comparison to video-based instructions [47].

## 3. TRAINING OF LAPAROSCOPIC TRAINEES WITH NO OR LIMITED PRIOR EXPERIENCE

When BTs were compared to no training, BTs resulted in a significant reduction in the required training time for laparoscopic tasks. BTs also improved accuracy and performance scores [58]. This evidence was based on 8 RCTs containing some bias and significant heterogeneity [37, 58, 60-66]. The comparison of other methods such as VRTs with BTs showed that differences were present in some of the measured outcomes. Nevertheless, these results were based on small RCTs and no specific conclusions could be drawn in the case of novice trainees [58, 62, 67-71].

Supplementary use of BTs to clinical training improved the technical performance of the trainees in the operative room during the first procedures after box training in comparison to the standard training (no BTs). Nevertheless, the quality of evidence was low (Level 3) [49, 56, 59, 72-76]. No significant differences were observed in terms of surgical morbidity or mortality of the patients for the above groups of trainees [49, 56, 59, 74, 76, 77]. Supplementary box training reduced the operative time by a non-significant 6.5 minutes in the case of laparoscopic hernia repair. The above results represented data from low-risk procedures (laparoscopic hernia repair) and the assessment included only the first case performed by the trainees [49]. Evidence on the efficiency of box training in more complex procedures or the persistence of the above differences beyond the first procedure is not available.

## 4. COMPARATIVE EFFECTIVENESS OF BOX TRAINERS TO OTHER SIMULATORS

A comparison of BTs with VRTs showed that BTs had a favourable outcome in terms of skill time development and trainee satisfaction. No significant difference was observed for any other parameter evaluated [47]. BTs also had favourable training outcomes compared with animal and cadaver models. The BTs were associated with increased physical resemblance and trainee satisfaction [78-80]. Interestingly, no significant difference was observed when laparoscopic training with or without haptic or force feedback were compared [47, 81-84]. Training with haptic feedback in BTs before training in VRTs provided improved performance [81, 82]. A comparison of commercial trainers with simple and less expensive BTs showed no clear benefit for the former. The suturing time was shorter in commercial BTs, while object transfer time was shorter in non-commercial BTs. Nevertheless, none of the above differences were statistically significant. The impact of type of trainer on operative room performance requires further investigation [47, 53].

## 5. THE APPROPRIATE TRAINING SCHEME

The evaluation of trainees during the training process is important for the development of their skills [41, 52, 73, 75, 76, 85-100, 101-109, 110, 111]. The experience of European Basic Laparoscopy Training skills (E-BLUS) showed that high quality of skills may be present, while time-related criteria may not be fulfilled and the need for dedicated laparoscopy training is necessary to reach acceptable time criteria [112]. Increased task complexity resulted in prolonged training time. Nevertheless, the overall skill outcome was improved in the case of complex tasks [113-116]. Training in conditions resembling those of clinical practice such as stress, noise, altered visual dynamics or working against the camera was associated with improved task performance [47, 68, 117-121]. Training focused on mental imagery or cognitive skills demonstrated no significant difference in terms of skills development [47, 117, 122-125]. Extra training including pre-operative training, additional repetitions and post-training reinforcement showed improved training outcomes with faster task completion time, reduced skill decay and cost saving [110, 111].

## 6. FEEDBACK AND MENTORING

Feedback in laparoscopic skills training improves outcome [126, 127]. The timing and the amount of feedback is important [128-131]. Short-term performance was improved by giving feedback during the performance of tasks in comparison to giving feedback at the end of the task and by giving a limited amount of feedback in comparison to extensive feedback [47, 130]. Audiovisual feedback studies showed controversial results [128, 129, 131]. Instructor-regulated and self-regulated learning did not show any significant difference in skills acquisition or time to perform tasks. Nevertheless, there was a tendency towards a more favourable outcome in the case of instructor-regulated learning [132-134]. Distant mentoring was proved to be better than no mentoring and similar to local mentoring regarding the skill process and time outcomes [135, 136].

## 7. EXERCISES AND TIME REQUIREMENTS

Different exercises have been proposed for training in BTs [73, 75, 76, 85-100]. Nevertheless, there is currently no evidence for the recommendation of a specific exercise scheme which could be more efficient in box training.

The time required to achieve the desired level of competence varied among studies and depended on training schemes and endpoints used for competence. The acquisition of laparoscopic suturing skills in BTs varies between 5 and 40 hours [101-103, 106]. Several training schemes for laparoscopic suturing and vesicourethral anastomosis

have been proposed [101-108]. The time required for training of general surgery trainees in BT ranged between 5 and 12 hours depending on the training programme [76, 94]. Mastery learning represents a stringent form of competency-based education [109]. The concept is based on specific complementary features that result in a set of education conditions, a curriculum and an assessment plan that yield high achievement among all learners. Meta-analyses showed that mastery simulation training improved skills and had a moderate effect on patient outcomes [41, 109].

### 8. COST OF BOX TRAINERS

Two studies have evaluated the impact of simulation-based pre-training (BTs) before initiation of a specific laparoscopic training regimen (Fundamentals of Laparoscopic Skills course), and reported that pre-training in BTs decreased the training time and expenses during the above course [52, 110, 111].

### 9. CONCLUSIONS ON BOX-TRAINERS

The BTs are efficient for laparoscopic training of novice and more experienced trainees. The haptic feedback of BTs gives them an advantage over other methods of simulation. The use of simple or more complex commercial BTs is similarly effective. More complex tasks in conditions resembling clinical practice and repetitive use of BTs both improve training outcome. Feedback and mentoring should be considered although not clearly proven by the current evidence. Well-structured training schemes based on the concept of mastery learning should be favoured.

## IV. NON-TECHNICAL SKILLS

Throughout surgical history it has always been believed that the surgeon's technical ability was the primary marker of an effective operator [137]. This view has changed over the years with many believing that non-technical skills are vital and these underpin a surgeon's ability [138]. Without doubt the execution of surgical procedures requires adequate technical competence, and non-technical skills (NTS) are crucial for effective and safer surgical practice. The operating room (OR) environment is highly stressful and requires full team interaction to achieve successful outcomes for the patient [139]. These factors increase the risk of errors most commonly due to suboptimal application of NTS [140, 141] Evidence suggests that deficiency in NTS correlates with poor technical skills [142] and may lead to higher post-operative mortality [143]. This evidence reinforces the fact that NTS is not a peripheral skillset, but a key component that defines surgeons' ability. NTS can be acquired through training [144]. The best modality for acquiring these skills is through simulation-based training [145] as adopted by other high risk industry counterparts such as aviation and nuclear power plants [146]. There is indeed an urgent need to incorporate and integrate non-technical skill training and assessment within current training pathways along with technical skills.

### 1. NON-TECHNICAL SKILLS IN MINIMALLY INVASIVE SURGERY

There are three distinct categories of NTS; cognitive, social and personal resource factors [145]. Cognitive skills include situation awareness, decision-making and planning. Cognitive skills are highly relevant in training for minimally invasive surgery (MIS). For example, situational awareness is important during robotic surgery as the surgeon is placed at a distance from the patient at the console. Higher technical intricacies of minimally invasive procedures demand astute planning and prompt decision-making.

Social skills encompass communication, teamwork and leadership abilities. Effective communication is crucial for the safe performance of any surgical procedure. Considering the additional staff required during a minimally invasive procedure, social skills become even more important for the successful interaction and co-ordination of the numerous staff members in the OR. The final category of NTS is personal resource factors, which implies an individual's ability to cope with stress and fatigue commonly experienced in surgeons. Many of these terms are defined in more detail in **Table 1**. Amongst the various NTS, decision-making is considered to be one of the advanced sets of skills which consolidates exponentially with increasing clinical experience [147].

### 2. TRAINING FOR NON-TECHNICAL SKILLS

There are two principal modalities for the training of NTS; the classroom and the simulation center. Within a classroom didactic teaching highlighting the importance of these skills and their key components can be combined with interactive video analysis of examples of effective and non-effective NTS. Classroom teaching has been demonstrated to be extremely helpful for self-reflection and changing attitudes of trainees [148].

Besides the classroom, simulation-based team training is believed to be one of the best methods for NTS training [149, 150]. High-fidelity team-based simulation training involves the use of a bench or virtual reality-based model placed inside a simulated or real life operative environment. The model is used for technical skills training, but the set up creates a realistic environment [151]. The behaviours observed can be recorded and utilised in a structured debriefing session, vital for non-technical skill acquisition [152]. This feedback should be delivered in a facilitative manner

*Table 1. Non-technical skill components and definitions [196]*

| Term | Definition |
|---|---|
| Situational awareness | Developing and maintaining a dynamic awareness of the situation in theatre based on assembling data from the environment (patient, team, time, displays, equipment); understanding what they mean, and thinking ahead about what may happen next. |
| Decision-making | Skills for diagnosing the situation and reaching a judgment in order to choose an appropriate course of action. |
| Teamwork and communication | Skills for working in a team context to ensure that the team has an acceptable shared picture of the situation and can complete tasks effectively. |
| Leadership | Leading the team and providing direction, demonstrating high standards of clinical practice and care, and being considerate about the needs of individual team members. |

as opposed to an instructional approach to encourage self-reflection and active participation throughout the whole process [145]. A skilled facilitator is vital for effective debriefing [152].

Although training in the OR is very effective [153], logistical difficulties restrict the utilisation of this facility. Hence, a simulated environment offers a more practical and yet high-fidelity option for full immersive simulation. Whilst this can be conducted utilising dedicated rooms within simulation centres, the Distributed Simulation (DS) an exciting new development has made it possible to achieve full immersive training in MIS. The DS **(Figure 2)** is an inflatable "Igloo" used to provide a 360-degree shielded environment acting as a portable OR simulator [154]. Placed within this "Igloo" are simplified representations of common OR components including a scaled-down operating lamp and pull-up photographic banners of the anesthetic machine and equipment trolley. Within this environment procedure-specific equipment for the minimally invasive procedure can be placed. This has already undergone face, content and construct validation [155] with off-site feasibility also demonstrated [156]. DS may therefore provide an effective and yet low cost training modality for NTS within minimally invasive procedures for urology.

Whilst standalone simulation based training is useful, for maximum effectiveness it must be integrated within a comprehensive curriculum [157]. NTS should be integrated into the curriculum with technical skills for minimally invasive procedures within urology. Once validated it should be implemented as part of a standardised training pathway for these procedures. Only then can it be ensured that all trainees are currently acquiring the NTS and technical skills that are essential for safer practice. Although training for NTS can be acquired in the classroom or the simulation centre it can also be consolidated in the workplace via informal methods [151]. After any critical incidents, debriefing can improve these skills further.

## 3. ASSESSING NON-TECHNICAL SKILLS

Several rating scales have been developed that can be utilised for the assessment of training. One example is the Non-technical Skills for Surgeons rating system (NOTSS) [158] **(Figure 3).** Four categories are utilised within the NOTSS, taxonomy including situation awareness, decision-making, communication & teamwork and leadership. Examples of good and bad behaviours are displayed and a rating of up to four is given for the participant's performance in each category. This behaviour rating system has already been investigated for it reliability [159], feasibility and validity [160].

The Observational Teamwork Assessment for Surgery (OTAS) scale [161] is an additional assessment tool **(Figure 4).** Whilst this tool is directed towards a team assessment as opposed to individual performers there is an extensive evidence base behind OTAS including content [162] and construct validation [163] and its applicability within urology

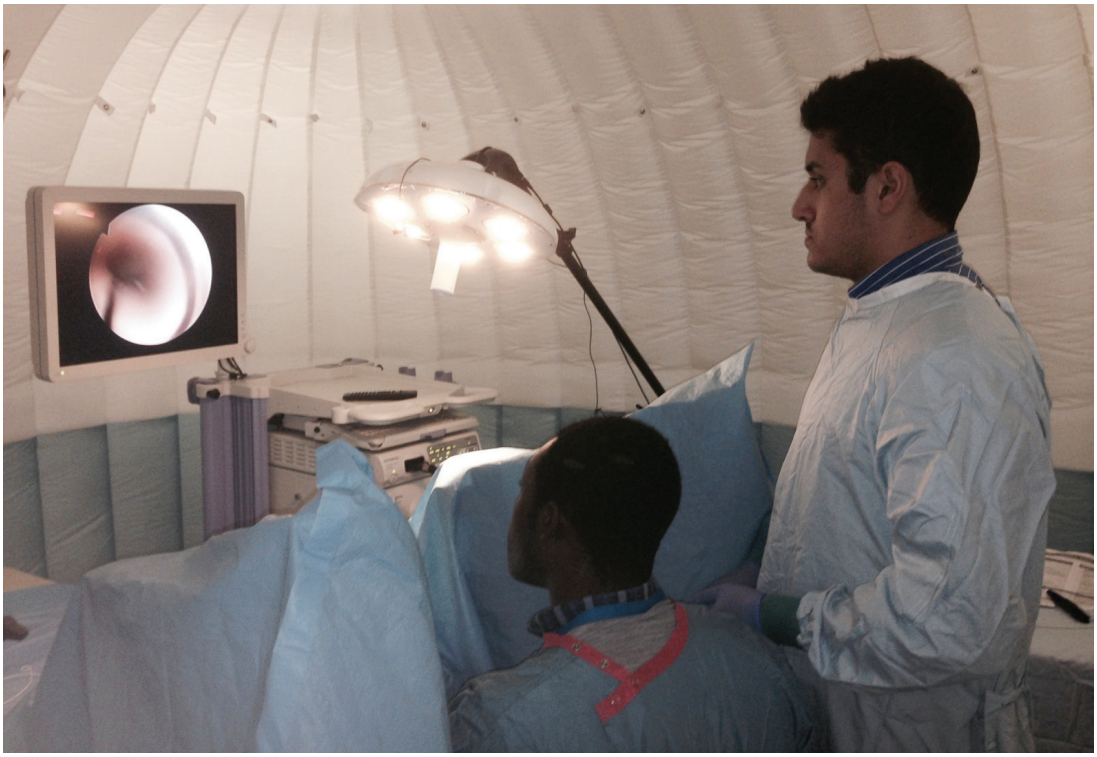

*Figure 2 . Distributed Simulation in an "igloo" being utilised for ureteroscopy training*

has been investigated further [164]. Finally, the non-technical skills (NOTECHS) scale modified from aviation scales [165] has been created with proven reliability in surgery **(Figure 5).**

The rating scales can be utilised for the assessment of an individual or team within a full immersive environment. These should be incorporated within any curriculum to ensure skill acquisition is objectively measured. Furthermore, minimum standards should be set to ensure a proficiency-based curriculum is devised. Through video analysis these rating scales can be utilised not only as assessment tools, but a very valuable source of constructive and unbiased feedback mechanism.

### 4. CONCLUSION ON NON-TECHNICAL SKILLS TRAINING

NTS are of vital importance for the safe execution of minimally invasive procedures performed in surgery in general, and in urology particularly. These skills must be acquired and enhanced as per a standardised curriculum utilising both classroom and simulation-based facilities similar to other high-risk industries. Assessment of non-technical skills can be achieved using various rating scales such as NOTSS, OTAS or NOTECHS and these should be incorporated within the curriculum to assess skill acquisition. Whilst the assessment of technical and NTS is currently seen as separate entities these should ideally be combined within one scenario in full immersive simulation training.

## V. MODULAR TRAINING IN MINIMALLY INVASIVE SURGERY

The growth of laparoscopy (classical laparoscopy and robotic-assisted laparoscopy) during the last decade required significant effort in training due to the different skill requirements for laparoscopy in comparison to open surgery. Laparoscopic procedures are performed with the use of two-dimensional imaging of the operative field, with decreased tactile feedback, paradoxical instrument movements, limited range of motion and augmented instrument tremor. The transfer of skills learned performing open surgery is not appropriate or effective. Consequently, teaching these skills is of paramount importance to urology residents and fellows especially for demanding complex procedures such as laparoscopic radical prostatectomy (LRP). Training in the latter technique requires significant effort by the trainee and the mentor [166]. The robotic-assisted laparoscopic approach also encountered problems with the training of younger surgeons to perform robotic-assisted urologic surgery. Although, complex procedures such as robotic-assisted laparoscopic radical prostatectomy (RALP) have a shorter learning curve in comparison to their respective laparoscopic counterpart [167],

## NON-TECHNICAL SKILLS FOR SURGEONS

Hospital ..... Trainer name ..... Date .....

Trainee name ..... Operation .....

| Category | Category rating* | Element | Element rating* | Feedback on performance and debriefing notes |
|---|---|---|---|---|
| Situation Awareness | | Gathering information | | |
| | | Understanding information | | |
| | | Projecting and anticipating future state | | |
| Decision Making | | Considering options | | |
| | | Selecting and communicating option | | |
| | | Implementing and reviewing decisions | | |
| Communication and Teamwork | | Exchanging information | | |
| | | Establishing a shared understanding | | |
| | | Co-ordinating team activities | | |
| Leadership | | Setting and maintaining standards | | |
| | | Supporting others | | |
| | | Coping with pressure | | |

* **1** Poor; **2** Marginal; **3** Acceptable; **4** Good; **N/A** Not Applicable

**1** Poor — Performance endangered or potentially endangered patient safety, serious remediation is required
**2** Marginal — Performance indicated cause for concern, considerable improvement is needed
**3** Acceptable — Performance was of a satisfactory standard but could be improved
**4** Good — Performance was of a consistently high standard, enhancing patient safety; it could be used as a positive example for others
**N/A** — Not Applicable

***Figure 3. Non-technical Skills for Surgeons rating system (NOTSS).***

| BEHAVIOURAL CONSTRUCT (and definition) | EXEMPLAR BEHAVIOURS | RATING SCALE | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **COMMUNICATION**<br>Quality and quantity of information exchanged among team members | • Asks team if all prepared to begin the operation<br>• Requests and instructions to team communicated clearly and effectively<br>• Provides information to whole team on progress<br>• Surgeon informs the team of technical difficulties and /or changes of plan | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
| **COORDINATION**<br>Management and timing of activities and tasks | • Gives prior notification of requirements to Scrub Nurse to enhance timing of instrument ex change<br>• Surgeons co-ordinate use of equipment, such as camera in minimal access surgery providing adequate view of operating field<br>• Contribute to smooth exchange of instruments and provisions with Scrub Nurse | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
| **COOPERATION/ BACK UP BEHAVIOUR**<br>Assistance provided among members of the team, supporting others, and correcting errors | • Reacts positively to questions and requests from Nursing group<br>• Responds to requests or questions from Anaesthetic group<br>• Helps with smooth instrument exchange with Scrub Nurse<br>• Supports Surgical group assistants and compensates for lack of experience | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
| **LEADERSHIP**<br>Management and timing of activities and tasks | • Instructions and explanations provided to assistants<br>• Advises Anaesthetist if unfamiliar with operative techniques (e.g. tube insertion) to call for senior help<br>• Supervision provided for staff lacking familiarity with tasks or equipment | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
| **MONITORING/ SITUATIONAL AWARENESS**<br>Team observation and awareness of ongoing processes | • Check table positioning and positions of members<br>• Assistants monitor direction of light<br>• Checks team condition<br>• Aware of patient condition including anaesthesia | 0 | 1 | 2 | 3 | 4 | 5 | 6 |

| RATING ANCHORS | BRIEF ANCHOR DEFINITION |
|---|---|
| 6 | Exemplary behaviour; very highly effective in enhancing team function |
| 5 | Behaviour enhances highly team function |
| 4 | Behaviour enhances moderately team function |
| 3 | Team function neither hindered nor enhanced by behaviour |
| 2 | Slight detriment to team function through lack of/inadequate behaviour |
| 1 | Team function compromised through lack of/inadequate behaviour |
| 0 | Problematic behaviour; team function severely hindered |

***Figure 4. OTAS assessment sheet [161]***

Surgeon (initials): Date: _____ Session: _____

Assessor (initials/specialty): Is this a self-rating? Yes/NO

## REVISED NOTECHS SCALE

**Please follow the key below and circle the number corresponding to the Surgeon's performance**

NA-not applicable

| 1 Not done | 2 Not done well | 3 | 4 | 5 | 6 Done very well |
|---|---|---|---|---|---|

| CATEGORY | ELEMENT | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| COMMUNICATION AND INTERACTION | (a) Instructions to assistant clear and polite | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (b) Waited for acknowledgment from the assistant | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (c) Instructions to scrub nurse clear and polite | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (d) Waited for acknowledgement from the scrub nurse | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| VIGILANCE/ SITUATION AWARENESS | (a) Monitored patient's parameters throughout the procedure | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (b) Awareness of anaesthetist | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (c) Actively initiates communication with anaesthetist during crisis periods | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| TEAM SKILLS | (a) Maintains a positive rapport with the whole team | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (b) Open to opinions from other team members | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (c) Acknowledges the contribution made by other team members | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (d) Supportive of other team members | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (e) Conflict handling – eg. concentrates on what is right rather than who is right | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| LEADERSHIP AND MANAGEMENT SKILLS | (a) Adherence to best practise during the procedure – eg. does not permit corner cutting by self or team | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (b) Time management – eg. appropriate time allocation without being too slow or rushing team members | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (c) Resource utilisation – i.e. appropriate task-load distribution and delegation of responsibilities | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (d) Debriefing the team – i.e. provides details and feedback to the entire team about the procedure | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (e) Authority/assertiveness | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| DECISION MAKING- Surgical CRISIS | (a) Prompt identification of the problem | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (b) Informed team members - promptly, clearly and to all team members | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (c) Outlines strategy/ institutes a plan – i.e. asks scrub nurse for suction, instruments, suture material | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (d) Anticipates potential problems and prepares a contingency plan – eg. asks anaesthetist to order blood, calls for help | NA | 1 | 2 | 3 | 4 | 5 | 6 |
| | (e) Option generation - takes the help of the team (seeks team opinion) | NA | 1 | 2 | 3 | 4 | 5 | 6 |

***Figure 5. Revised NOTECHS for surgery assessment sheet [165]***

the need for the surgeon to familiarise themselves with the virtual environment and the new instruments as well as the medico-legal aspects and the quality of the surgical outcomes required the establishment of a structured training programme for robotic-assisted laparoscopy [168]. In an attempt to overcome the above issues, structured stepwise (modular) training schemes for laparoscopic and robotic-assisted laparoscopic urologic procedures have been introduced.

## 1. THE CONCEPT OF MODULAR TRAINING IN LAPAROSCOPY

According to the modular training scheme (MTS) **(Table 2)**, the procedure is divided into individual steps usually based on difficulty level [166, 169, 170]. The trainee initially performs the step (module) of the procedure corresponding to his acquired skill level (usually the easiest step) under the mentoring of an experienced surgeon. The remaining steps are performed by the experienced surgeon. Thus, the efforts of the trainee are focused on mastering a specific step each time. The schedule is repeated during the following procedures until the mentor decides that the trainee can continue to the next module. When the trainee proceeds to the next module, he performs all previous modules and the new module for each case. Eventually, the trainee is able to perform all steps independently. Simulation training (i.e. BTs) usually takes place before initiation of the MTS. Moreover, the trainee observes and assists in a number of cases before performing any of the steps of the procedure.

## 2. CURRENT EVIDENCE

The current literature includes a number of studies proposing and evaluating MTS in laparoscopic and robotic-assisted urologic surgery [166, 168-181]. The majority of the programmes are based on radical prostatectomy training which is considered the most demanding procedure [166, 168-170]. Only one publication describes a MTS for laparoscopic nephrectomy [180]. The MTSs in radical prostatectomy have significant differences in the number of steps in which the procedure is divided, the level and evaluation of the trainees as well as the prior training before initiating the MTS. The peri- operative data presented in the studies are usually difficult to directly compare due to the use of different groups of participants and parameters among them. Moreover, comparative studies among the different MTSs are not available. **Table 3** summarises the training approaches for LRP and RALP.

## 3. LEVELS OF TRAINEES

The LRP MTSs included trainees who were residents and fellows. The number of participants ranged between 2 and 7 for LRP. The experience of the residents included some laparoscopic cases, but usually no prior experience was present. Fellows usually represented experienced surgeons with experience of up to 80 previous laparoscopic procedures [166, 169, 170]. In RALP MTSs, the number of trainees ranged between 2 and 9. Both residents and fellows were included without presenting specific information on prior experience in laparoscopy of the trainees in the majority of the studies [168, 172, 175-179, 181].

## 4. COURSE AND TRAINING PRIOR TO INITIATION OF MODULAR TRAINING

All training programmes for LRP and RALP included the use of some form of simulation prior to initiation of the MTS. The simulation could include either BTs or VRTs [166, 168-181]. The simulation training included either well-defined structured task performance (six pelvitrainer exercises) [170] or just the use of a BT for practice [166, 169]. The use of animal lab training courses has been frequently applied in the RALP MTSs [176, 177]. The majority of RALP MTSs employed courses for basic knowledge of the robotic system [172, 175, 176, 179]. Trainees participated as assistants in a variable number of cases prior to the MTS. The number of cases ranged between 5 and 25 for RALP and 23 to 144 for LRP [166, 168-181].

## 5. MODULES AND EVALUATION METHODS

The LRP procedure was divided into 10-12 segments for the MTSs and the RALP into 3-11 segments [166, 168-181]. In laparoscopic training, the difficulty of each segment was considered and the segments were grouped according to their difficulty to respective modules (modules 1-5) [166, 169, 170]. Evaluation of the trainee for progression in the modules was based on subjective evaluation of the mentor in the case of LRP [166, 169]. Two RALP MTSs made use of scoring systems such as the operative performance form recommended by the Accreditation Council for Graduate Medical Education [168, 177]. Other MTSs used criteria such as the timely completion and superior skill as well as the performance of 10 consecutive cases in the same module before advancement to the next [175, 179]. The clinical performance of the trainees is evaluated by recording and comparing the peri-operative data of the first cases performed by the trainees to their more experienced cases or to cases performed by the mentors [166, 168-181].

## 6. OUTCOMES OF MODULAR TRAINING

An interesting parameter associated with the MTSs was the number of cases required in each module for the trainees to achieve the proficiency level for progression to the next module and the total number of cases required to complete the MTS. LRP trainees required 2-15 mentored cases for each module and in total 32-43 cases to complete the MTS [166, 169]. In RALP MTSs, the required number of cases was reported to be 20-50 cases [172, 177].

***Table 2. The 12 segments of Robotic-assisted Radical Prostatectomy with 5 levels of difficulty based on the modified modular training scheme developed in the University of Leipzig {Stolzenburg, 2006 #162; Stolzenburg, 2005 #165}.***

| No of step | Description of surgical procedure | Module | | | | |
|---|---|---|---|---|---|---|
| | | Lowest level of difficulty | | | | Highest level of difficulty |
| | | I | II | III | IV | V |
| 1a | Trocar placement, Incision of ventral peritoneum and dissection of the Retzius space (transperitoneal access) | X | | | | |
| 1b | Dissection of the preperitoneal space and trocar placement (extraperitoneal access) | | X | | | |
| 2 | Set up of daVinci | X | | | | |
| 3 | Pelvic lymphadenectomy | | | X | | |
| 4 | Incision of the endopelvic fascia and Dissection of the puboprostatic ligaments | X | | | | |
| 5 | Anterior and lateral bladder neck dissection<br>Dorsal bladder neck dissection | | X | <br>X | | |
| 6 | Dissection and division of vasa deferentia | X | | | | |
| 7 | Dissection of the seminal vesicles | | | X | | |
| 8 | Incision/Dissection of the posterior Denonvillier's fascia- mobilisation of the dorsal surface of the prostate fro the rectum | | | X | | |
| 9 | Dissection of the prostatic pedicles and mobilisation of the prostate (wid excision) | | | X | | |
| 10 | Dissection of the prostatic pedicles and nerve sparing procedure | | | | | X |
| 11 | Ligation of Santorini plexus | | X | | | |
| 12 | Apical dissection | | | | X | |
| 12 | Urethrovesical anastomosis (running suture)<br>Rocco stitch<br>Dorsal circumference<br>Lateral circumference<br>Bladder neck closure (if necessary) and ventral stitches | | <br><br>X<br>X | X<br>X | | |
| | | | | | | |

*Table 3. Modular training schemes for laparoscopic and robotic-assisted laparoscopic radical prostatectomy*

| Author | Trainee level | No. Trainees | No. Procedures | Robotic knowledge | Skills training | No. cases Observer | No. cases Assistant | No. Modules | Evaluation method for progression among modules | No. cases for MTS completion | Complication rate |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **LRP** | | | | | | | | | | | |
| Stolzenburg et al. {Stolzenburg 2006 #162} | Residents, fellows | 4 | 150 | N/A | Dry lab course ± animal lab | 4-64 (camera holding) | 15-140 | 12 (5 levels of difficulty) | Subjective evaluation | 32-43 | 0.6% (intra-operatively) |
| Stolzenburg et al. {Stolzenburg 2005 #165} | Residents | 2 | 450 | N/A | Dry lab | 4-62 (camera holding) | 15-140 | 12 (5 levels of difficulty) | Subjective evaluation | 38-43 | 1%-8% |
| Sugiono et al. {Sugiono, 2007 #166} | Experienced Urologists, fellows | 11 | 500 | N/A | Dry lab (structured six steps) | 15-20 (camera holding) | Not reported | 10 (5 levels of difficulty) | Not reported | Not reported | 1.6-23% |
| **RALP** | | | | | | | | | | | |
| Badani et al. {Badani, 2006 #168} | Trainee | Not reported | Not reported | Yes | Dry lab | 10-20 | 15-20 | Calculated steps-not defined | Not reported | 20-30 | Not reported |
| Davis et al. {Davis, 2010 #164} | Resident, Fellow | 7 | 124 | Not reported | Not reported | No reported | Not reported | 12 | Time and quality grading system | 13-37 | 9.6% (overall) |
| Link et al. {Link, 2009 #171} | Fellow | Not reported | 1833 | 2 Intuitive courses | Dry lab | Not reported | 25 | 6 | Subjective evaluation of timely completion and superior technique | Not reported | 0.8-2.3% |

In LRP studies, the trainees required longer operative time in comparison to their mentor [166, 169, 170]. The operative time was reduced with increasing experience [166]. The time required for the accomplishment of tasks in the BT corresponded to the time required for the completion of the same task in the OR [170]. Complication and positive surgical margin rates were similar among the trainees and their mentors [166, 169, 170].

Similar results were observed in the RALP literature, the operative time of the trainees was longer [168, 181] and achieved significance in one study [168]. Other investigators reported similar operative times for the mentor and trainees, while these figures improved with increasing experience of the mentor and the trainees. Nevertheless, the mentor was a fellowship trained laparoscopic surgeon and his experience had probably not overcome the learning curve of the procedure [179].

Positive surgical margin rates were similar among the trainees and mentors in both LRP and RALP MTSs and the rates tended to decrease with increasing experience [166, 168-170, 175-179, 181].

## 7. MODULAR TRAINING SCHEME IN LAPAROSCOPIC NEPHRECTOMY

The only described MTS for laparoscopic transperitoneal nephrectomy included 23 steps which were designated in 5 modules of increasing difficulty [180]. Three trainees with prior laparoscopic

experience and variable experience in open urologic surgery attended the MTS. Before initiation of the training programme, they participated in a dry and wet lab course. A total number of 17-32 cases was necessary for competence in independent practice. Operative time was significantly lower in cases performed by the mentor in comparison to the trainees. Peri-operative parameters such as estimated blood loss, transfusions and complication rate as well as hospital were not related to significant differences among the trainees and mentor.

### 8. CONCLUSIONS ON MODULAR TRAINING

MTSs provided efficient training in laparoscopic and RALP. A number of different training programmes have been proposed without any evidence of superiority of any MTS over the other. The different level of experience of the trainees does not seem to have any significant influence and all trainees achieve a high level of competence after 30-40 cases for LRP and 20-50 for RALP. The perioperative parameters of the cases performed by the trainees are similar to those of their mentors. Operative time seems to be the only parameter in which the mentors have an advantage. Operative time and surgical margin rates are parameters which improve with experience.

## VI. TRAINING AND CERTIFICATION

At present, many urology trainees consider that exposure to formal laparoscopic skills training is deficient with a study of European trainees reporting that only 23% of trainees rated their laparoscopic training as satisfactory [182]. The results of the European Basic Laparoscopic Urological Skills exam also showed that exposure to laparoscopic training was low (only 39% reported access to training), and the skills levels measured were low compared to the expected standard [183]. It should also be considered that while much of the training provided in MIS is directed at surgeons who are in formal training programmes prior to certification as independent specialists, there are a considerable number of established surgeons who have training needs in MIS as they embrace new technologies and interventions in their scope of practice. While much MIS training can be generically applied to both groups, there are challenges in accommodating the training needs of disparate groups.

### 1. WHO SHOULD PROVIDE TRAINING?

For both laparoscopy and robotic surgery, training may be provided by a number of stakeholders including individual institutions, industry, scientific meetings, as well as professional bodies with educational programmes such as the American Urological Association, European School of Urology, Royal College of Surgeons and others around the world. In most circumstances, such training is not coordinated and therefore there may be duplication or omission of certain elements of training. Rather than decree who should provide training, it should be recognised that training may be provided by many stakeholders and that all training adds value. For example, industry-led training allows appropriate technical instruction in advanced technologies such as robotic-assisted surgery. This type of training is important to ensure that complex technologies are understood by operating surgeons and can be safely deployed in clinical situations. Troubleshooting is part of such training and is delivered as part of industry-led training. However, while industry should take the lead in technology training, they should only have a supportive role in clinical training. Clinical training in MIS must be clinician-led and be appropriately supported by industry.

### 2. THE RELATIONSHIP BETWEEN CREDENTIALING AND TRAINING

The credentialing of surgeons to perform surgical procedures is typically determined by the medical board or equivalent of individual institutions. The decision to include MIS procedures within the scope of practice of individual clinicians is influenced by evidence of appropriate training, experience and competency in such procedures. Evidence of training is typically a certificate from the body providing the training activity.

There is therefore considerable responsibility to ensure appropriate certification of MIS training. This is to ensure that training activities are correctly structured with appropriate assessment to guarantee that learning objectives are met. It is not acceptable for a stakeholder to issue a certificate for a training activity unless that activity has been prospectively approved as a professional development activity by a dedicated body such as a surgical training college.

This is especially so as medico-legal concerns exist about such certification due to the relationship between training and credentialing [184-186]. For example, if a surgeon is pursued for a medico-legal claim due to a surgical complication early in his or her MIS experience, the defence will point to evidence of training as proof of competency [187]. Therefore, there is an obligation to ensure that certified training is of an appropriate and consistent standard.

### 3. WHO SHOULD CERTIFY TRAINING?

Individual countries have professional licencing bodies who oversee the rights of doctors to practice. This includes the licencing of specialists such as urologists to practice independently. However, such licencing bodies rely on professional training

bodies such as the Royal College of Surgeons, the American College of Surgeons and others to certify that individual surgeons have attained the competencies to apply for a licence to practice as a specialist. Typically, these professional bodies provide a curriculum including proscribed training and examinations prior to the award of a certificate of training completion.

Similarly, professional bodies such as these oversee continuous professional development (CPD) programmes which recognise educational and training activity and award CPD points for appropriate activity. For training activities to be recognised for CPD points, the overseeing body must prospectively approve the learning objectives, course structure and content, and ensure that feedback is received from course participants. It is entirely appropriate that professional bodies maintain this role in the certification of training.

## 4. CERTIFICATION OF LAPAROSCOPY TRAINING:

The era of MIS has provided both opportunities and challenges in how we train surgeons today. There are challenges as some of the skills required to safely perform complex laparoscopic procedures are different to those required to perform the same procedures using an open surgical approach. Loss of depth perception, decreased tactile sensation, and instrumentation with limited degrees of freedom of movement, mean that certain skills must be acquired to safely and expertly perform surgical procedures with a minimally-invasive approach. However, along with these challenges come excellent opportunities to attain these skills away from the operating room using simulation and dry or wet lab training. While some of these activities have been shown to have good face and construct validity [188] and therefore have a role to play as part of structured training in minimally-invasive urology, there are also reports of such activities not having proven relevance to clinical performance [189]. Conversely, some training activities have been shown to improve performance of clinical activities in vivo such as laparoscopic vesico-urethral anastomosis [190].

There are certain activities such as mini-fellowship training that have been shown to be of value in allowing surgeons to translate their skills into clinical practice [191] and these types of activities are therefore highly appropriate for certification as a high-value training activity. The continuing evolution of laparoscopic surgery with single-port approaches and novel instrumentation mean that this is a dynamic area with evolving training requirements. Certification of training in laparoscopy therefore requires continuous review.

## 5. CERTIFICATION OF ROBOTIC SURGERY TRAINING

As stated previously, training in MIS should be clinician-led. Industry should provide technology training, while clinical training must be clinician-led and supported by industry. The robotic surgery industry has previously provided “clinical training pathways”, but following comments from clinicians [184, 192] and negative publicity regarding inadequate training [193], they have modified their training objectives such that they provide “technology training pathways” [194] rather than aim to provide clinical training. Such technology training pathways are most welcome and it is appropriate that this training is certified by industry itself. Hospital credentialing boards typically require evidence of such training and most consider it mandatory that surgeons seeking privileges to perform robotic-assisted surgery have evidence of formal technology training. This is due to the complexity of the robotic surgery platform, however, technology training is only a small part of the competency required to perform this type of surgery.

However, as most robotic-assisted surgeries are complex procedures such as radical prostatectomy, it is also essential that competencies are achieved in the clinical steps of the procedure and not just in the operation of the device itself. Therefore professional bodies as outlined above should play a proactive role in overseeing training in robotic surgery and provide training activities where appropriate. In many countries, there is limited national experience in the provision of such training and therefore organisations such as the European Association of Urology (EAU) have an important role to play in providing structured training and in certifying training activities. The EAU Robotic Urology Section (ERUS) [195] has provided a robotic surgery curriculum, a pilot fellowship programme, in addition to masterclasses and live surgery demonstrations, all of which are certified by the EAU. This type of approved and structured training in robotic surgery is highly recommended.

## 6. CONCLUSION ON CERTIFICATION

There are excellent training opportunities in MIS in urology, both for conventional laparoscopy and robotic-assisted surgery. Many types of activities are of value and there are multiple stakeholders who may provide training. Certification is necessary to ensure that learning objectives are met and standards are met to fulfill credentialing expectations. Professional bodies are most appropriately positioned to provide such certification.

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## III. ACKNOWLEDGMENTS

Prokar Dasgupta acknowledges support from the NIHR Biomedical Research Centre, MRC Centre for Transplantation, King's Health Partners, Guy's and St. Thomas' Charity, School of Surgery, London Deanery, The Urology Foundation, Olympus, EU-FP7, Prostate Cancer UK, Technology Strategy Board and The Vattikuti Foundation.

As Editor-in-Chief of the BJUI he has no conflicts of interests

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# Future of Minimally Invasive Surgery in Urology

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# Content

# Future of Minimally Invasive Surgery in Urology

*J. Rassweiler*

*T. Bach,E. Liatsikos, A. Rane,L. Richstone, D. Teber, A. Tewari*

## I. INTRODUCTION

Since the end of last century, there has been a significant change from open surgery to minimally invasive or even non-invasive surgery. This has been accomplished by the continuous improvement in video-endoscopic technology, implementation of physical principles and the introduction of robot-assisted surgery. In this chapter, we summarise upcoming technology and speculate on the future patterns of minimally invasive surgery (MIS). In general, this concerns developments in (i) video-endoscopy, (ii) endoscopic armamentarium, (iii) robot-assisted surgery, (iv) imaging, and (v) intraoperative navigation.

## II. DEVELOPMENTS IN VIDEO-ENDOSCOPY

### 1. HD-TECHNOLOGY AND BEYOND

The introduction of *high-definition (HD) video-technology* with significant improvement in image quality (resolution, brightness, depth and magnification) compared to CCD (three-chip)- or even one-chip-technology, has enabled laparoscopic surgeons to safely perform complicated procedures such as radical cystectomy with intraoperative reconstruction of neo-bladders **(Figure 1)**. Recently, Lusch *et al.* [1] demonstrated significantly higher resolution (14.3 vs. 4.0 line pairs/mm), colour representation and depth of field when comparing a HD-digital sensor to a standard fibre-optic cystoscope. Initially, criticism of laparoscopic surgery was focussed on the reduced quality of endoscopic images compared to open surgery resulting in surgical errors due to misinterpretation of the patient`s anatomy. This scenario has now changed completely. The quality of endoscopic images far exceeds the capacity of the human eye and due to the significantly larger eye-object distance compared to a telescope (i.e. in the case of radical prostatectomy 70 vs 5-7 cm), this cannot be compensated completely by the use of magnifying glasses **(Figure 1a)** or microscopic systems [2].

However, information technology is under continuous development and *4K Ultra HD TV* is already available in the consumer entertainment industry. Ultra High Definition is a derivation of 4K digital-cinema standard: while multiplex shows images in 4096 x 2160 4K resolution, the new Ultra HD consumer format has a slightly lower resolution of 3840 x 2160 **(Table 1)**. It delivers four times as much detail as 1080p Full HD (i.e. eight million pixels compared to two million pixels) resulting in more fine detail, greater texture and an almost photographic emulsion of smoothness of the image [3]. Such a quantum leap may help endoscopic surgeons increase the actual image quality, particularly concerning zooming / magnification of the video-signal to almost microscopic dimensions **(Figure 1e).** Thus, it may overcome some of the drawbacks of 3D-HD technology.

### 2. D-VIDEOTECHNOLOGY

One problem of classical laparoscopy is the two-dimensional (2D) view of the telescope. The absence of shadows, stereovision and movement parallax in particular, make it difficult for a surgeon to accurately determine spatial distance and movements [4]. The latter may be compensated by the surgeon's experience, particularly if the working field is small and the camera close to the object.

A number of aids have been described to improve the surgeon's depth perception. Shadows can be introduced using illumination cannula [4]. Stereovision can be accomplished using a stereo-endoscopic system. Earlier systems used two 5 mm-CCD-lenses in one telescope which created a double-image on the video-monitor, which was unified to a 3D picture by the use of *shutter glasses* **(Figure 2a).** The main problem was the fact that only the surgeon had a normal endoscopic picture, whereas the assisting nurses and the anaesthesiologist had to view the double-image on the screen [6].

The next step, was a 3D-system taking two images with one telescope from different angles with digital reconstruction of the image. If the surgeon wears *polarised glasses,* similar to sunglasses, he obtains a 3D image, and without glasses, the picture on the screen is normal **(Figure 2b)**. However, such a system can only be realised for 0°-lenses. Moreover, the image on the screen significantly loses brightness compared to the classical CCD-camera [7].

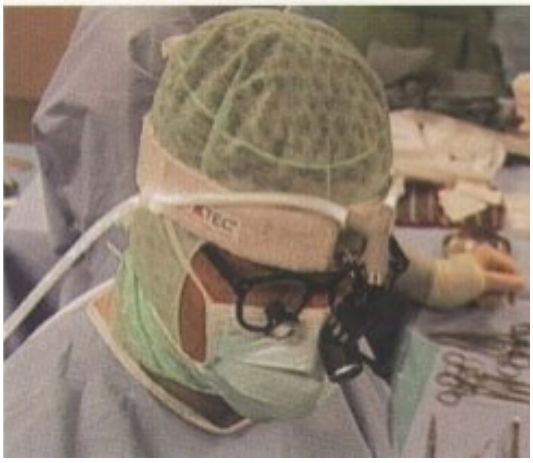

*Figure 1. Actual and future aspects of videotechnology*
*Figure 1a. Operative magnifying glasses for open radical prostatectomy. Excellent resolution of image, but inconvenient for surgeon due to headset with light source and the long distance to working area (70 cm).*

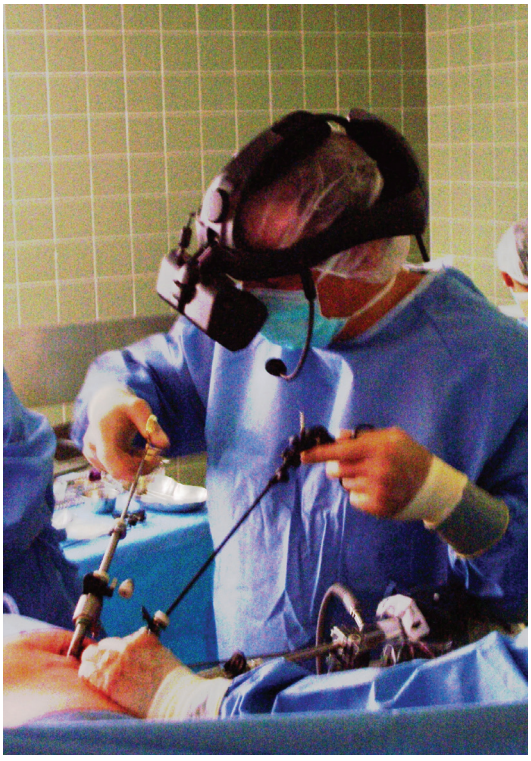

*Figure 1b. Head-set for 3D-CCD-videotechnology (Viking, USA). Quality of 3D-image suboptimal. Inconvenient for surgeon due tot he weight of head-set.*

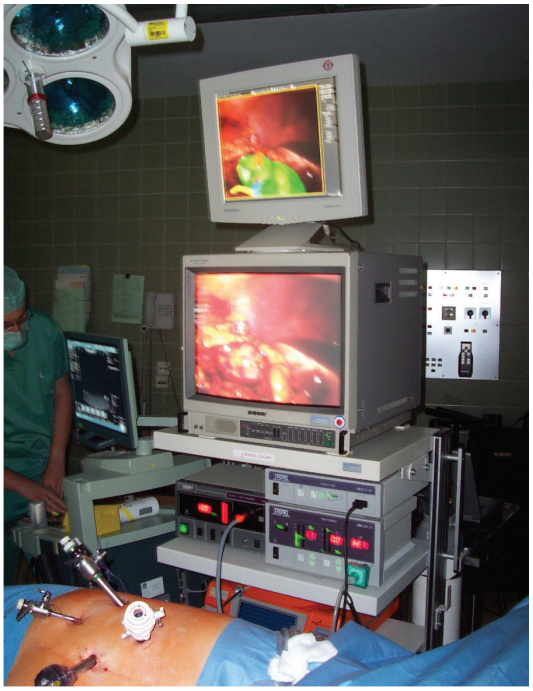

*Figure 1c. CCD-technology during laparoscopic partial nephrectomy (lower monitor). Upper monitor displays augmented reality based on preoperative*

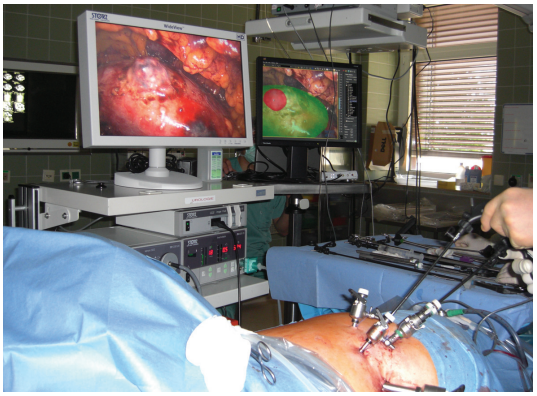

*Figure 1d. HD-technology during laparoscopic partial nephrectomy (left monitor). Right monitor displays augmented reality based preoperative computertomography.*


*Figure 1e. Ultra-HD as next generation of entertainment industry (ie. Samsung, South Korea).*

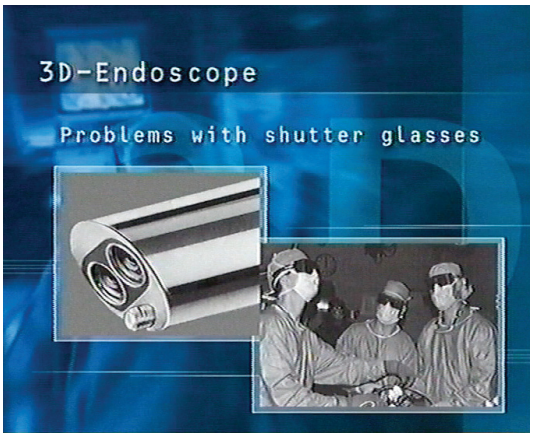


*Figure 2. Past and future modifications of 3D-videotechnology*

*Figure 2a. Stereoscopic system using shutter glasses for creation of 3D-image (Optimed, Karlsruhe, Germany). Inconvenient for surgeon due to shutter mechanism. Operative staff cannot work with shutter glasses and thus has double image on screen (abandoned).*

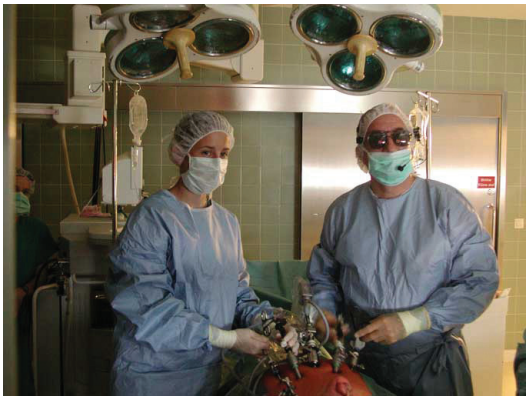

*Figure 2b. 3D-system using polarized glasses to create stereovision (Karl Storz, Tuttlingen, Germany). Parallel working without glasses possible (ie. assistant), but 3D quality not good enough for routine use, only for 0°-lenses (abandoned).*

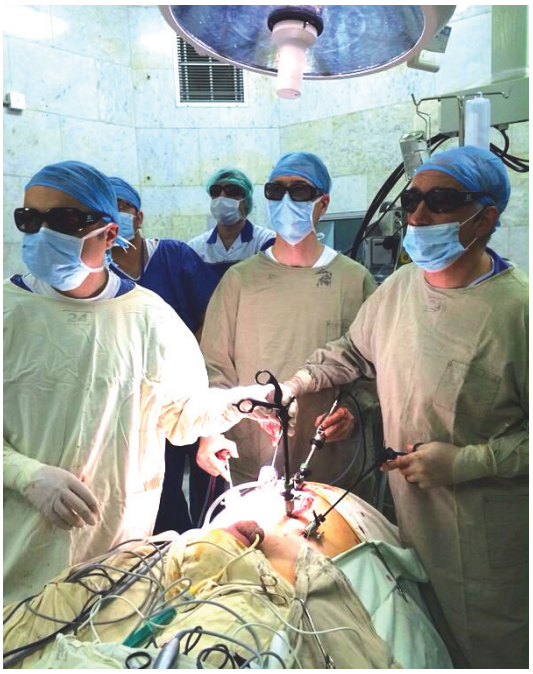

*Figure 2c. HD-3D-system applicable for 0° and 30°-lenses (ie. Karl Storz, Tuttlingen, Germany)*


*Figure 2d. HD-3D-flexible laparoscope (Olympus, Japan), mainly for surgical use (ie colonic surgery) or NOTES-assisted transvaginal nephrectomy.*

*Figure 2e. Console-based 3D-HD-stereovision with two images, which are fused at the console by mirror-technology. (Da Vinci System, Intuitive Surgical, USA) No loss of brightness, no need to wear glasses.*

*Table 1. Review of technical data of present and future videosystems*

| Videosystem | Pixels | Frame Rate (fields/sec) | Picture Aspect Ratio |
|---|---|---|---|
| Standard Definition TV (SDTV) | 640x480 | 60 (NTSC; US/Japan) | 4:3 |
| | 640x576 | 50 (PAL; Europe) | 4:3 |
| High Definition TV (HDTV) | 1920x1080 | 60 (US/Japan) | 16:9 |
| | 1920x1080 | 50 (Europe) | 16:9 |
| Ultra-High Definition TV (Ultra HDTV-4K) | 4096x2160 | 120 | 16:9 |
| (Ultra HDTV-8K) | 7680 × 4320 | 120 | 16:9 |

Another approach is the use of 3D-helmets with two displays, thereby creating the 3D image. However, the image quality on the small monitors showed insufficient resolution and the helmets were inconvenient for the surgeon **(Figure 1b)**. Therefore, such systems are not used.

The current technological generation represent 3D-HD-videotechnology available for 0° and 30° telescopes. There is still the need to use polarised glasses with subsequent reduction of image brightness **(Figure 2c).** HD-technology may compensate partly for this loss. Moreover, the angle of the surgeons to the video-monitor is critical for an optimal 3D image. Other options include flexible 3D/HD-laparoscopes **(Figure 2d).** These are mainly advantageous for laparoscopic sigmoidectomy or natural orifice transluminal endoscopic surgery (NOTES)-assisted transvaginal nephrectomy [8].

There is no doubt, that a console-based system as realised in the da Vinci systems (SI/XI) consisting of *two HD-screens fused by mirror-technology* which is the optimal solution and is even better than an operative microscope **(Figure 2e).**

It remains to be seen, whether Ultra-HD can compensate for the disadvantages of bed-side-based (laparoscopic) systems. There is no doubt, that six degrees of freedom (6-DOF)-instruments require 3D-videotechnology for optimal application. On the other hand, comparisons between mono- and stereo-endoscopes have demonstrated that 3D systems show no advantages for the experienced surgeon. This indicates that the loss of stereovision can be well compensated by the magnification, brightness and sharpness.

## III. ADVANCES IN ARMAMENTARIUM

### 1. DEVICES FOR HAEMOSTASIS (ADVANCED SEALING DEVICES)

Whereas, most instruments for dissection and cutting of tissue are well developed and may not need further improvement, including basic instruments for robot-assisted surgery, there may be a need to improve haemostatic devices. During the last decades, several alternative principles have been tested using ultrasound energy (e.g. harmonic scalpel, Ultracision) and modifying bipolar energy (e.g. Plasma-trisector). Recently, particularly for laparoscopic ablative surgery, new advanced sealing devices enabling easy and quick haemostasis and cutting of the tissue have been introduced by different manufacturers such as (i) ultrasound shears, (ii) radiofrequency-based systems, and (iii) electro-thermal bipolar vessel systems [9].

*Ultrasonic devices* (i.e. Harmonic Ace) combine both sealing and cutting steps into a single process, thus increasing dissection speed. However, it is reported in the literature that ultrasonic devices create temperatures of up to 200°C. This can potentially put adjacent tissue at risk of lateral damage **(Figure 3a).**

*Advanced bipolar devices* (Ligasure, Bicision, and EnSeal) possess active feedback control over the power output. Heat production is kept below 100°C. However, there is no simultaneous tissue division and a cutting blade is required for division, thus increasing operating time **(Figure 3b).** The Enseal (Ethicon, Connecticut, USA) offers articulation of the tip of the device **(Figure 3c).**

The Thunderbeat (Olympus, Japan) has been developed to integrate both ultrasonically generated frictional heat energy and advanced bipolar energy in one instrument. This multifunctional device can interchangeably deliver these energies, thus allowing the laparoscopic surgeon to simultaneously seal and cut vessels up to 7 mm in size with minimal thermal spread. The jaw is designed to provide precise, controlled dissection and continuous bipolar support with grasping capability **(Figure 3c)**. A randomised study showed shorter operating room (OR) time (85 vs 115 min) compared to standard electrosurgery for laparoscopic radical hysterectomy [10].

The Altrus Thermal Tissue Fusion system (ConMed, Centennial, USA) uses electricity to create heat that in turn achieves the desired tissue effect. In contrast to true electrosurgical instruments,

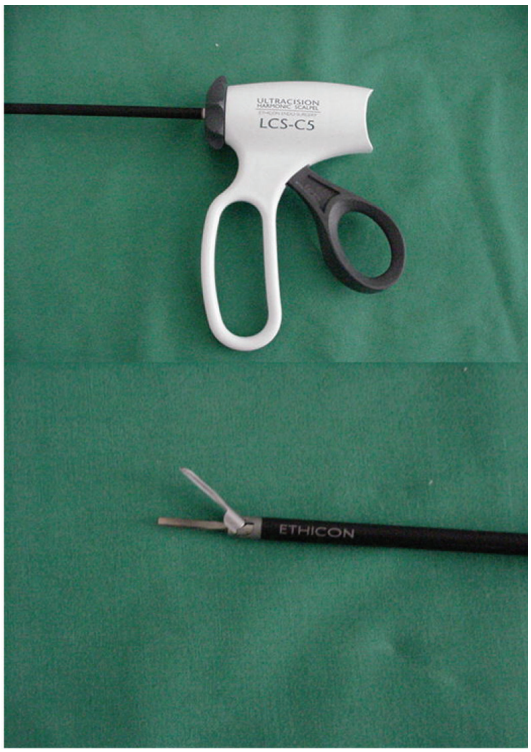


***Figure 3. Standard and advanced sealing devices***

***Figure 3a. Harmonic scalpel (Ultracision, Sonosurge, Harmonic ACE) ultrasonic-based device for hemostasis and cutting of tissue.***


***Figure 3b. Ligasure (Covedien, Boulder, USA) delivering controlled low-voltage energy with minimal lateral spread. A blade can be released to cut the sealed vessel (ie. up to 7 mm).***

***Figure 3c. The EnSeal (Ethicon, Conneticut, USA) offers articulation to apply low-voltage bipolar energy. However, cutting is not possible with this device.***


***Figure 3d. Thunderbeat (Olympus, Japan) combining ultrasonic and bipolar energy in a single device.***

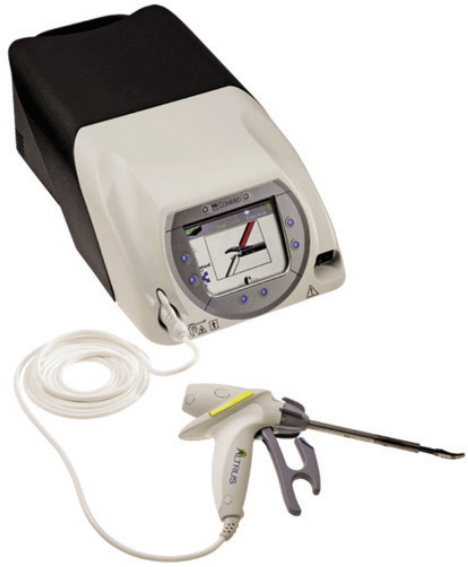

***Figure 3e. Altrus Thermal Tissue Fusion system (ConMed, Centennial, USA) uses electricity to create heat to achieve the desired effect on tissue and thereafter cuts blade-less.***

the Altrus system uses direct current to heat the jaws of the instrument and then passively transfers that heat to the tissue **(Figure 3d)**. No electricity enters the patient through the device. The system monitors the temperature at the jaws and then cuts through the tissue.

Without a doubt, the use of classical monopolar and bipolar technology can be safe and efficient as proven by various comparative studies [11]. However, in some situations (i.e. malignant perinephric fat, control of smaller vessels), such devices may speed up the dissection and help the surgeon to better identify the respective surgical planes [12]. Some of these devices have been modified for use with robot-assisted surgery. These include monopolar and bipolar cautery instruments (electrical energy), the Harmonic™ ACE (mechanical energy), and the PK™ Dissecting Forceps (advanced bipolar). The use of advanced sealing and dissection devices increases procedural costs compared to monopolar or bipolar technology.

## 2. INSTRUMENTS WITH 6 DEGREES OF FREEDOM (DOF)

Laparoscopic surgery is limited by reduced range of motion due to the fixed trocar position determining the angle of the respective instrument to the working field. The incision point acts like a spherical joint that limits the DOF of the instrument from six to only four: jaw, pitch, rotation, insertion plus actuation of the instrument [6,7]. During dissection, this drawback can be overcome by the use of angulated instrument tips (i.e. right angle dissector) and adequate trocar arrangement according to the geometry of laparoscopy [13].

However, such ergonomic disadvantages are critical during the reconstructive section of surgery such as urethra-vesical anastomosis. The Endowrist-technology as used in robot-assisted laparoscopic surgery with all daVinci systems provides the optimal solution.

### *a) Radius Surgical System®*

In 2007, the Radius Surgical System® (Tuebingen Scientific, Germany) was introduced into the clinic. This device enables 6 DOF motions via 10 mm trocars based on movements of the wrist and a wheel for rotation of the instrument (i.e. for suturing). Initially, only two effectors (endo-dissect, needle holder) were available [14]. In addition, bimanual use of the instrument was relatively difficult **(Figure 4a).** The next step represented the introduction of a single-use 5 mm device. However, the stability of the device (i.e. Radius-scissors) was suboptimal as was the grip of the needle holder. On the other hand, the combination of the ETHOS-platform with its armrests significantly improved handling of the instrument **(Figure 4b).** A EUSP-sponsored project examined the efficacy and ergonomics of this setting compared to the gold standard da Vinci system **(Table 4).**

### *b) Cambridge-Endo®*

This instrument applies flexion of the handle to perform 5 and 6 DOF movements. Scissors and dissectors are mainly used to accomplish laparo-endoscopic single site (LESS) surgery [15]. However, the distance from the point of flexion to the end-effector is long compared to other alternatives **(Figure 4c).** This device is not popular in urology.

### *c) Kymerax-System®*

The Kymerax-System® (Terumo, Japan) was carefully designed as a motorised instrument to accomplish 6 DOF movements. Based on an ergonomic handle, the system allows flexion and rotation of the instruments by pressing a button **(Figure 4d)**. The device was tested in vitro and in vivo. However, the simultaneous use of two instruments was difficult to accomplish, whereas clinically the rotation mechanism proved to be helpful. The sterilisation of motorised instruments requires special attention, particularly regarding the cleaning of tissue remnants in the end effectors. Unfortunately, in 2014 Terumo removed the device from the market.

### *d) Dexterité-System®*

This system also uses the combination of an ergonomic handle and motorised instruments **(Figure 4e)** similar to the Kymerax-system®. Early clinical experience with this system is promising for laparoscopic partial nephrectomy and radical prostatectomy (Janetschek G, personal communication).

## 3. ERGONOMIC PLATFORMS

Several factors contribute to the non-ergonomic situation during laparoscopy [16]. Some may be influenced by the surgical platform such as the operating chair. There are only two ergonomic platforms described in the current literature.

Recently, a specially designed ergonomic body support consisting of a platform with a foot pedal, a semi-standing support, a remote control, and a chest support was presented [17]. EMG results showed a 44% reduction in erector spinae activity, 20% reduction in semitendinosus activity and 74% reduction in gastrocnemious muscle activity, when using the chest support. Muscle activity reduction using the semi-standing support was 5%, 12%, and 50%, respectively.

The ETHOS™ chair represents the first platform offering a conceptual solution to the problem [18,19]: The surgeon sits over the patient`s head during pelvic surgery instead of standing or even sitting laterally, thereby avoiding the Torero-position during suturing. Moreover, it creates a quasi-in-line position of the surgeon to the working field with the monitor between the legs of the patient. The surgeon has access to all trocars to help and correct assistants **(Figure 5a)**. The surgeon has

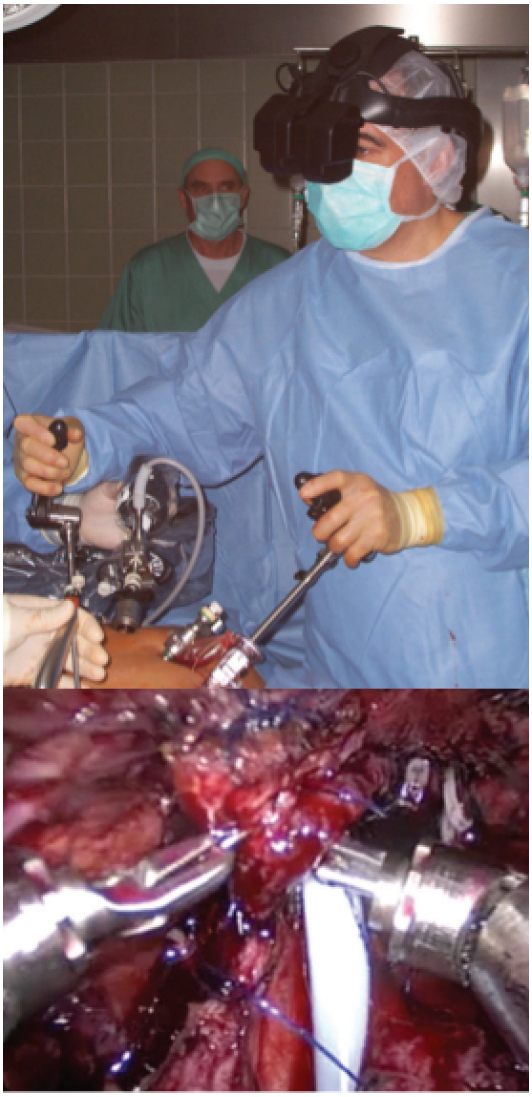

*Figure 4. Instruments providing six degrees of freedom (DOF)*

*Figure 4a. Radius device prototype 10 mm (Tuebingen Scientific, Tuebingen, Germany): Use of two instruments during vesicourethral anastomosis together with 3D-helmet.*

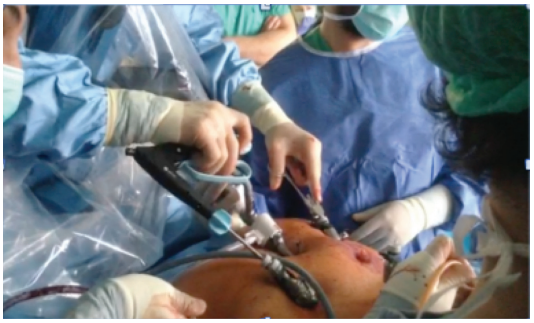

*Figure 4b. Radius device 5mm, disposable. Better use of the instruments in combination with ETHOS-chair*

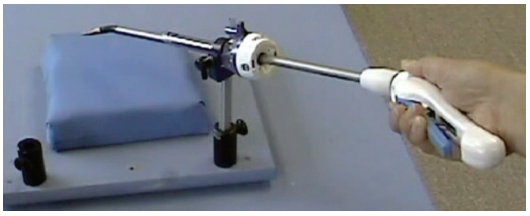

*Figure 4c. Cambridge device using wrist-angulation to bend the tip of the instrument. Mainly used for LESS. For laparoscopy the length of the tip seems to be to long.*

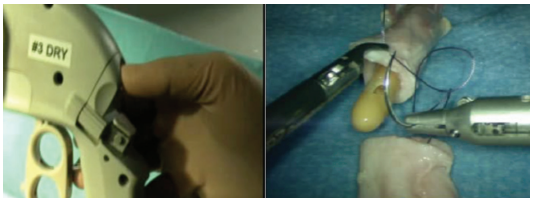


*Figure 4d. Kymerax (Terumo, Japan): Motorized 6-DOF-instrument with specifically designed handle for deflection and rotation of tip of instrument. Removed from market after early clinical experience.*

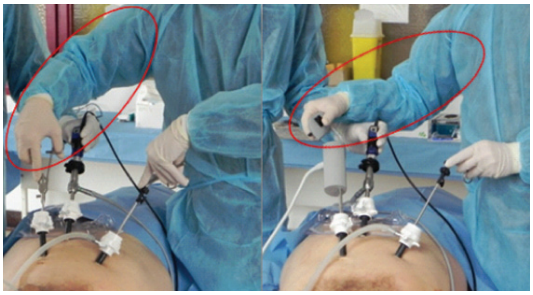

*Figure 4e. Robot Dex (Dextérité Surgical, Annecy, France): Motorized system with ergonomic handle compared to classical suturing. Clinical experience with laparoscopic radical prostatectomy and partial nephrectomy.*

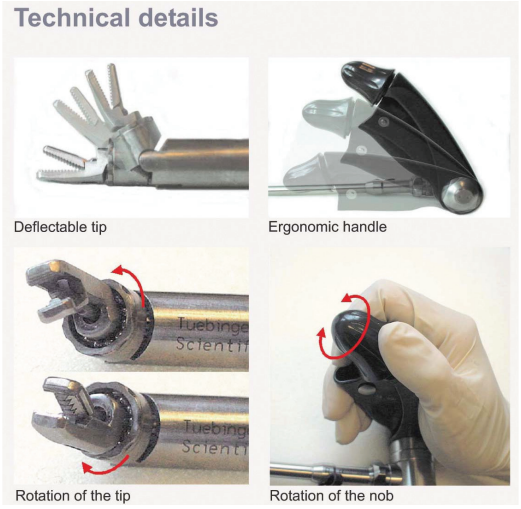


*Figure 4f.*


*Figure 5. ETHOS-platform (ETHOS-Surgical, Portland, USA) to improve ergonomics during laparoscopic surgery. Figure 5a. Surgeons sits over the patient`s head during laparoscopic pelvic surgery.*

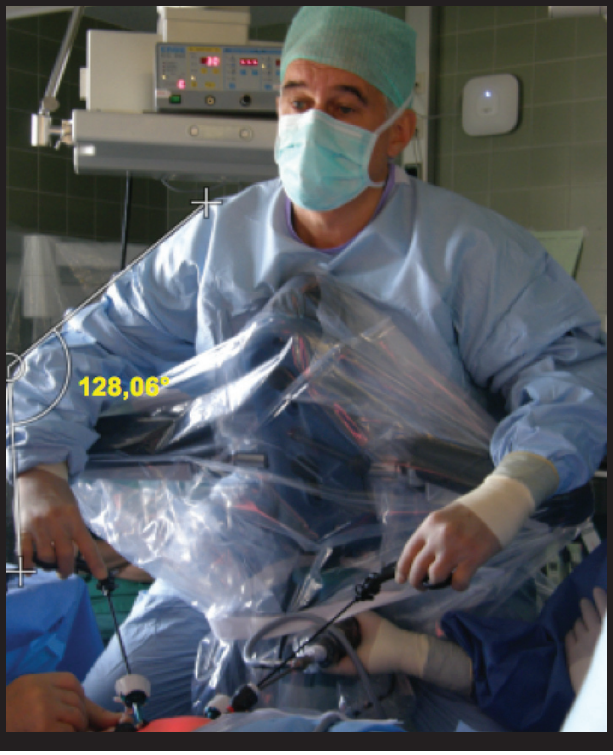


*Figure 5b. Use of ETHOS during retroperitoneoscopic pyeloplasty using 3 and 5 mm-instruments (SMART-technique). The armrest significantly improves ergonomics during suturing.*

two adjustable arm- and footrests with integrated foot switches. This proved to be very helpful during dissection (i.e. no need to search for the foot pedal, ergonomic position of the foot for activation; stabilisation of instrument moves during surgery).

The device can also be used for laparoscopic or retroperitoneoscopic surgery in the upper retroperitoneum, particularly during reconstructive surgery. The sitting position and armrests significantly reduce the fulcrum effect of laparoscopy **(Figure 5b).** The final version offers more features such as electrically motorised movements of the chair.

## 4. PLATFORM FOR SINGLE-PORT SURGERY

The Spider System (Transenterix) is an interesting platform which has been developed to accomplish single-port surgery. The system is based on the manipulation of tubes in which flexible instruments can be manipulated to perform laparoscopic surgery **(Figure 6a).** The initial device used string-based manipulation, whereas future generations may use a vertebra-like technology. The problem with the Spider System is that it was designed for 5 mm instruments only, which made it basically impossible to use in ablative renal surgery without an additional trocar **(Figure 6b)**. Moreover handling of the flexible instruments is difficult, particularly concerning endoscopic suturing. This was reflected in the experimental study by Haber *et al.* [20]. The device was designed mainly to accomplish single-port laparoscopic cholecystecomy. This platform requires better fixation on the OR-Table **(Figure 6c).** For these reasons, Transenterix improved the system considerably providing a robotic arm for the device **(Figure 6d).**

## 5. MANUALLY MANIPULATED ROBOT-LIKE DEVICE

The MIM-system developed by Jaspers et al. at the University of Utrecht [21], is an interesting modification of the bedside-device providing 6 DOF. Based on a parallelogram-design **(Figure 7a)**, the device allows movements of the instruments similar to the da Vinci device. However, the mechanical realisation is still relatively clumsy and has only been tested experimentally **(Figure 7b).**

## 6. ROBOTIC AND MANUALLY MANIPULATED CAMERA-ARMS

### *a) Robotic camera holders*

Principally, there are two basic approaches for camera holder design: (i) a SCARA-type (Selective Compliance Assembly Robot Arm) consisting of three motorised joints in combination with one passive (ball) joint. The three DOF are indirectly translated to the three different DOFs of the scope; (ii) a parallelogram-type, consisting of three motorised joints that directly activate the three DOF of the scope [22,23].

There are a variety of robotic camera holders commercially available. Most clinical experience is with the automated endoscopic system for optimal positioning (AESOP, Intuitive Surgical, Sunnyvale, CA, USA), which enables the surgeon to move the telescope by pre-programmed and individually recorded demands (SCARA-type; **Figure 8a)**. Every surgeon has his own voice-disc which allows him to use any AESOP worldwide [23,24]. The device alone enables solo-surgery (i.e. radical nephrectomy, pyeloplasty) or in the case of radical prostatectomy, the operation can be performed by two surgeons. AESOP was the first robotic device used for transatlantic telementoring [25]. Unfortunately, due to the takeover of Computer Motion by Intuitive Surgical, AESOP is no longer manufactured.

Buess et al. developed a remote-controlled camera (FIPS-endo-arm). Similar to AESOP, the system is driven by speaker-independent voice-control or a finger-ring joy-stick [26].

The EndoAssist / FreeHand (Prosurgics, UK; OR-Productivity, UK), uses the head movements of the surgeon to activate the camera arm **(Figure 8b)**, and the LapMan (Medsys, Gembloux, Belgium) uses control buttons in the surgeon`s hand and recently is connectable to the handle of an endoscopic instrument (LapStick; **Figure 8c)**. The use of head movements proved to be ergonomically inefficient. In clinical trials, no specific advantages of the arm were detected compared to human assistance [24-27].

The Viky-System (Endocontrol, France) uses both a foot pedal and wireless speech recognition to control the motors moving the camera **(Figure 8d)**. According to the procedure, the company offers three models (i.e. a large ring for LESS, a small ring for radical prostatectomy). Recently, the Viky-System was also use to robotically move a transrectal ultrasound (TRUS) probe during robot-assisted laparoscopic radical prostatectomy [28].

Recently, the Soloassist (Actormed, Barbing, Germany) has been developed at the Technical University of Munich. The surgeon uses a small joystick to operate a robotic arm, to determine his own field of vision and thus avoiding such issues. The camera is also held in place mechanically, reducing vibration and stabilising the field of vision. This is particularly important with 3D cameras, which are being used more and more. The Soloassist was compared to conventional laparoscopic cholecystectomy (29). Hospital stay and operation-related complications were not increased in the Soloassist group. The differences in core operation time ($P$ = 0.008) and total operating

*Figure 6. Spider-platform (Transenterix, Durham, USA) developed for LESS*
*Figure 6a. The device consists of two steerable tubes together with a telescope. The tubes can be filled with flexible instruments.*

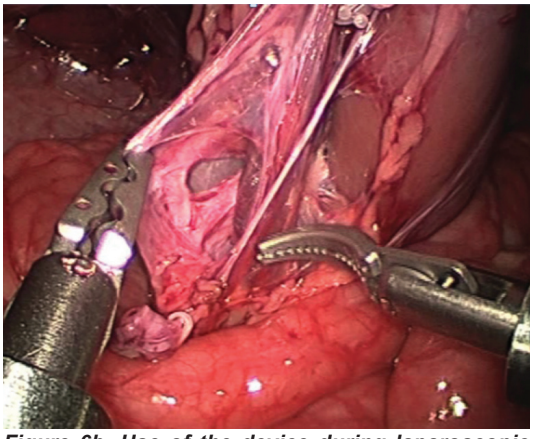

*Figure 6b. Use of the device during laparoscopic nephrectomy in a porcine model.*

*Figure 6c. The device needs to be supported by the assistant during the procedure.*

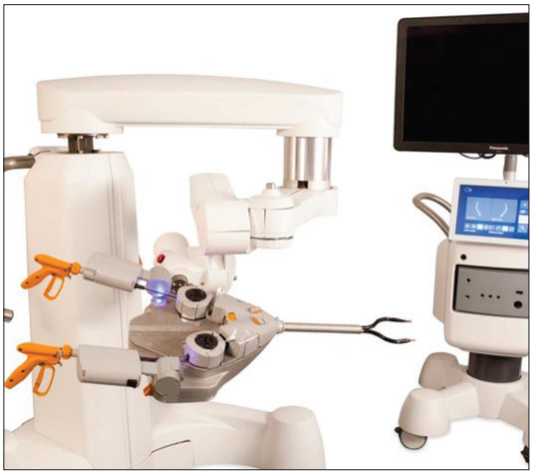

*Figure 6d. Robotic Spider-platform with significant technical improvements.*

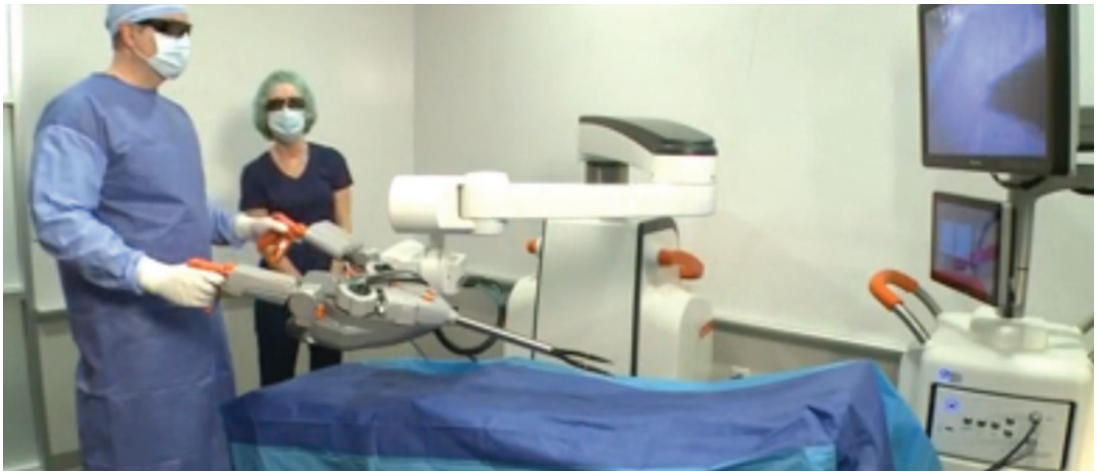

*Figure 6e. Demonstration of system still used at the bedside: Robotic arms may compensate for most of the deficiencies of the initial device, such as optimal fixation, handling of instruments, integration of 3D-telescope, and adjustable motion scaling.*

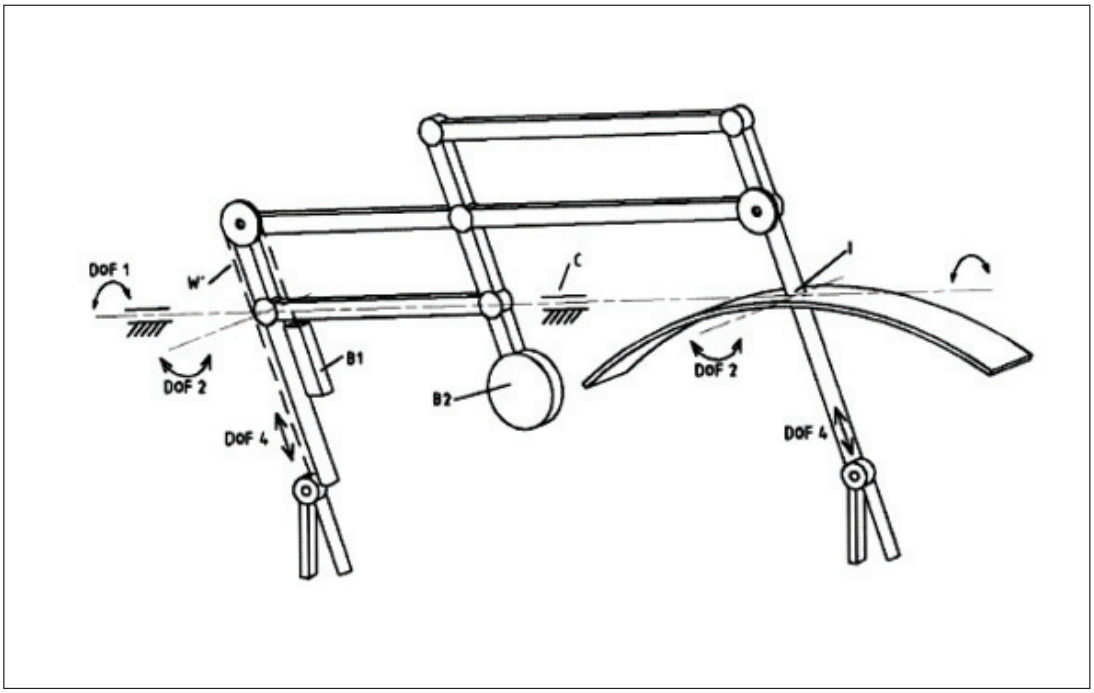


*Figure 7. MIM-system (Minimally invasive manipulator).*
*Figure 7a. Principle of controlling movements by parallelogram.*

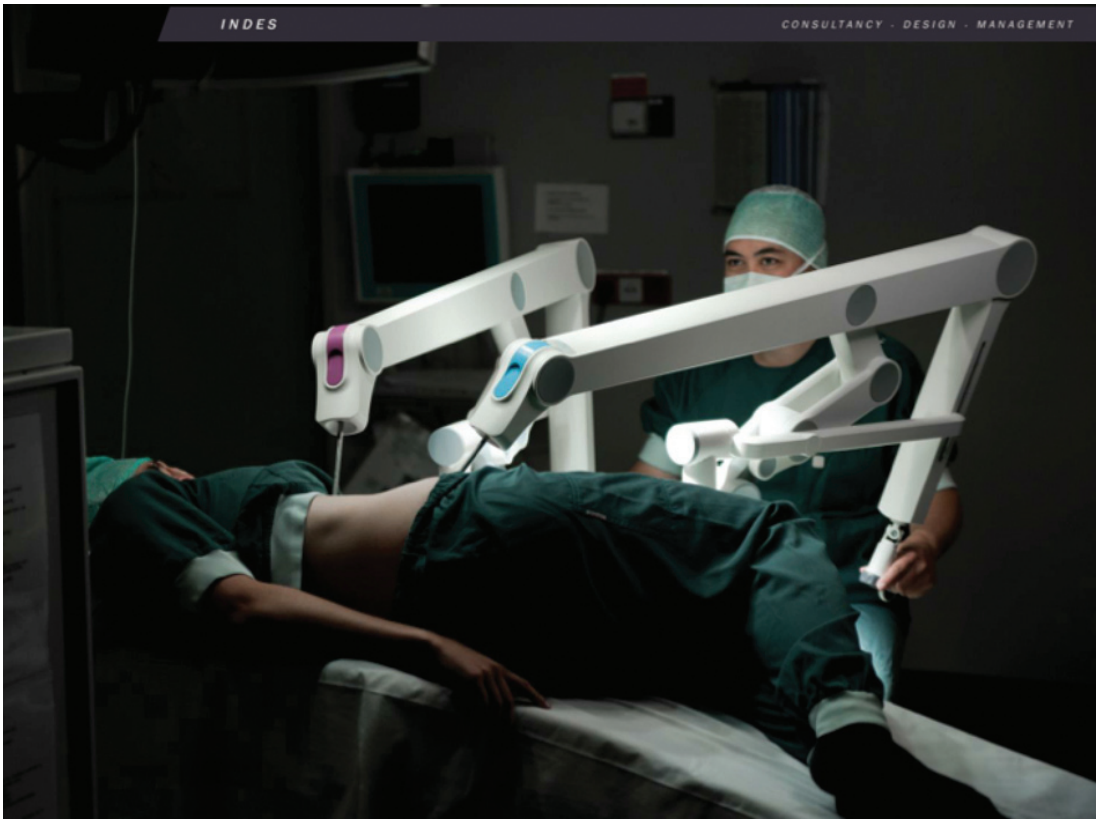


*Figure 7b. Animation of prototype only used in in-vitro experiments.*

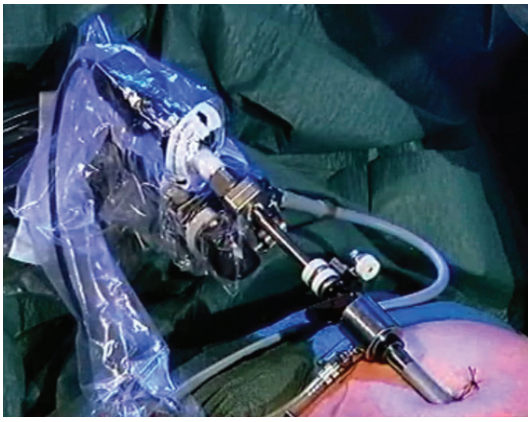

*Figure 8. Robotic camera-holders*

*Figure 8a. AESOP (Intuitive Surgical, USA): Voice-controlled camera-arm requiring no hand for change of position. No more produced.*

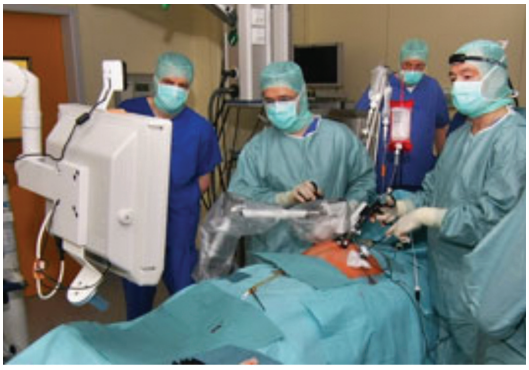

*Figure 8b. Endo-assist / Freehand (Prosurgics, United Kingdom): Camera holder controlled by head movements of the surgeon*

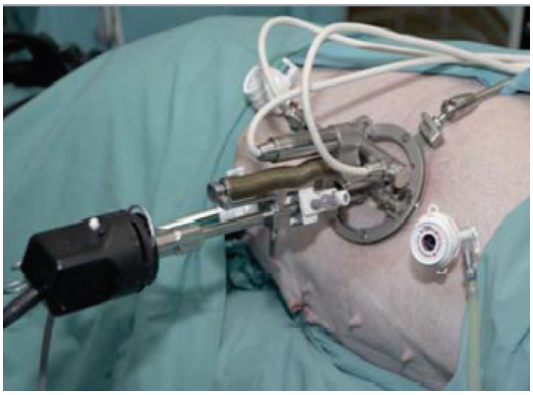

*Figure 8d. Viky-system (Endocontrol, Grenoble, France) uses both a foot peddle and wireless speech recognition to move the motors controlling the endoscope (here in porcine model).*

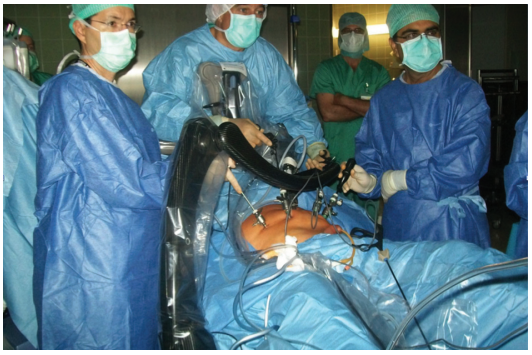

*Figure 8e. Solo-assist (Actormed, Barbing, Germany): The surgeon uses a small joy-stick to move the camera-arm. Here combine use with ETHOS-chair during laparoscopic radical prostatectomy.*

*Figure 8c. LapMan (Medsys, Gembloux, Belgium): Camera arm controlled by a handle (Lapstick) mountable on endoscopic instruments.*

time ($P$ = 0.001) significantly favoured the human assistant. However, the absolute duration of surgery was longer, and the relative operating time (in personnel/minutes/operation) was significantly shorter ($P$ < 0.001). In 4.8% of cases, the operation could not be performed completely with the camera-holding device. We were able to use the device in combination with the ETHOS-chair **(Figure 8e)**, however, use of the joy-stick was not as efficient as using voice-control.

The basic idea behind these active holders is that the surgeon does not need to interrupt the surgical process and it is unnecessary to release an instrument to reposition the camera. Interestingly, with increasing experience, control of the camera holder without hand movements (i.e. by voice) becomes less important. However, the arm should be movable with one hand.

***b) Passive holders for camera and instruments***

In addition, mechanical camera arms powered by high-pressure air (i.e. Unitrack, Aesculap, Tuttlingen, Germany; Endoboy, Endobloc, France; Styrker Scope holder) have been introduced as a cost-effective alternative **(Figure 9a,b)**. Other mechanical holders consisting of a number of bars connected by joints have been initially designed for open surgery (i.e. the Martin arm; **Figure 9c**), and modified for laparoscopy (Karl Storz, Tuttlingen, Germany). These holders can be attached to the operating table and their tips contain a clamp that holds the endoscope or an additional instrument [30,31]. Recently, the University of Utrecht introduced the Movix, a manually controlled camera holder featuring an intuitive one-button control **(Figure 9d).** Such devices do not provide robotic features, such as pre-programmed positioning, voice-controlled movements, or telementoring. According to their design they require one or two hands for manipulation.

**In summary**, camera arms may play a role, particularly in combination with 3D-videotechnology (i.e. to facilitate a stable image with heavy-weight telescopes) in performing solo-surgery. The use of head-sets proved to be ergonomically inefficient, the use of voice-control relatively complicated, and the use of foot pedals or joy-sticks inconvenient for the surgeon. Thus, a motor-controlled movement of the surgeon's or assistant's hand seems to be the most simple and ergonomically most efficient solution.

## IV. NEW ROBOTIC DEVICES FOR LAPAROSCOPY

### 1. HISTORY OF THE DEVELOMENT OF ROBOTIC DEVICES

To understand the development of the long-lasting monopoly of Intuitive Surgical requires analysis of the history of robotic devices for laparoscopy. Various authors have described the concept of intelligent steerable surgical instrument systems **(Table 2a,b).** The first functional master-slave manipulator for surgery was introduced by Green et al. [32,33] in 1991 **(Figure 10a)**. This manipulator was designed for open surgery and only had four DOF on its first release and was the basis for the development of a marketable product providing six (seven) DOF: the da Vinci System.

In Germany, Buess and Schurr et al. [34] developed the ARTEMIS-System and presented the first experimental results in 1994 following successful telesurgery laparoscopic cholecystectomy in swine **(Figure 10b).** ARTEMIS consisted of two parts, the user station (master) and the instruments station (slave). Although this device never made it beyond the experimental stage, other groups designed robotic manipulators for clinical use.

Based on the voice-controlled camera arm, AESOP, the ZEUS-system (Computer Motion Inc., Goleta, CA, USA) was developed and used for cardiac surgery and gynaecological procedures [35]. The ZEUS-system **(Figure 10c)** was based on the combination of a control unit and three tele-manipulators: three separate robot arms were transported on small carts. The arms were mounted by hand on the rails of the operating table. These could be moved freely in the operating field holding the trocar in position, using the so-called "free-pivot" technology. Two arms control 5 mm reusable instruments providing only 4 DOF, the third arm consists of an AESOP camera manipulator. The surgeon is seated in a high-backed chair with armrests, and handles the instrument controllers. The camera is positioned by voice control. Operating field visualisation is provided by a 2D video endoscopic camera. For 3D-vision, the ZEUS-system is combined with a head mounted system (i.e. as provided by VISTA Technologies or Viking). The most impressive demonstration using ZEUS was for transatlantic laparoscopic cholecystectomy (Lindbergh-procedure; **Figure 11**) pioneered by Marescaux [36]. The time delay between Strasbourg and New York was 150 milliseconds.

In urology, the ZEUS-system has been studied experimentally in ablative and reconstructive procedures on kidneys and adrenals [37]. However, mainly because the instruments had only four DOF, urologic surgery has become even more difficult, reflected in longer OR times [38].

The da Vinci system **(Figure 12a)** was the first surgical system to sufficiently address most of the following ergonomic problems: (i) the problem of depth perception (i.e. 3D-vision), (ii) the problem of eye-hand coordination, and (iii) the problem of limited range of motion. For this purpose, a computerised robotic system was designed with a stereo-endoscopic system, a computer-controlled mechanical wrist providing six DOF (plus actuation of the instrument), used from a

*Figure 9. Mechanical passive camera-holders*

*Figure 9a. Unitrack (Aesculap, Tuttlingen, Germany): Pneumatically driven mechanical camera holder.*

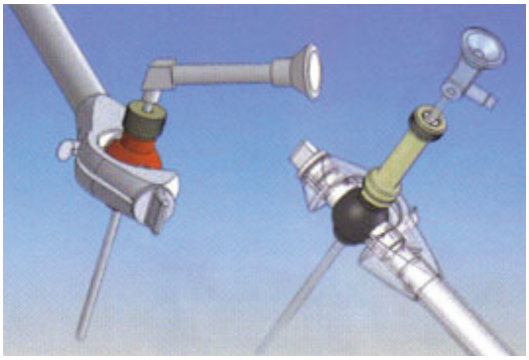

*Figure 9b. Endoboy (Endobloc, France): passive camera holder.*

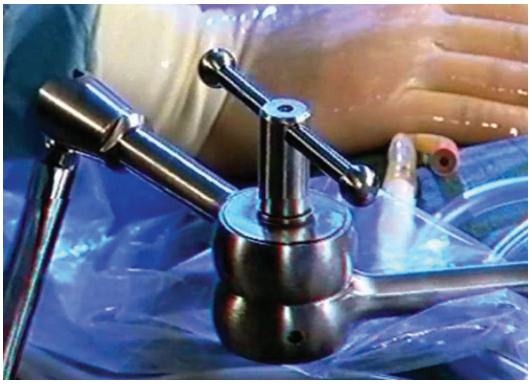

*Figure 9c. Martin-Arm (Martin. Tuttlingen, Germany): Passive instrument holder requiring two hands for change of position.*

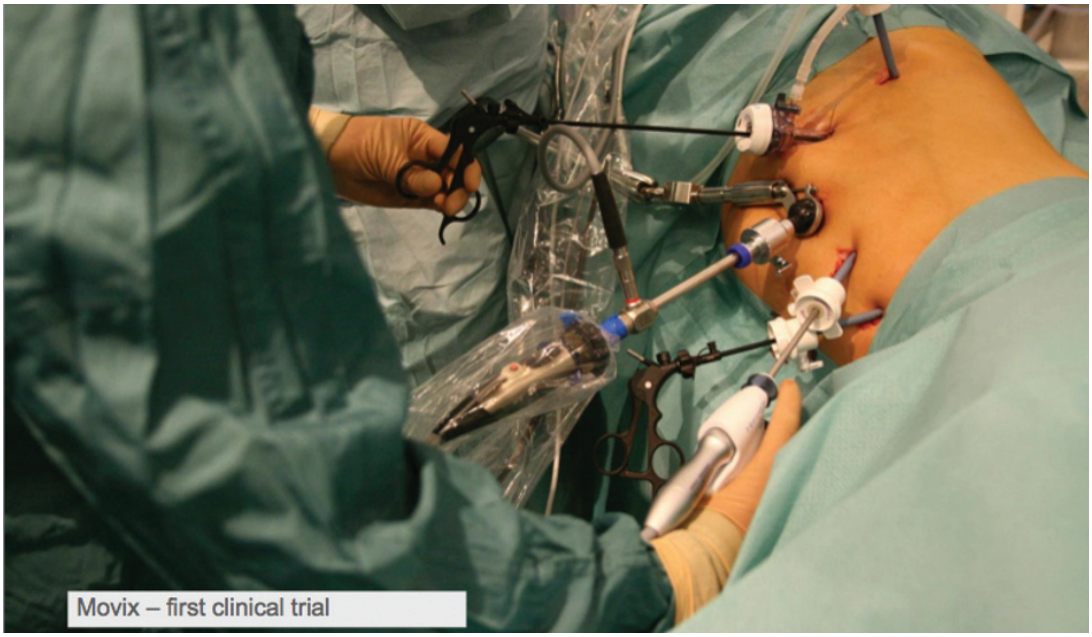


*Figure 9d. Movifix (University of Utrecht, The Netherlands): Manual controlled camera holder featuring an intuitive one button control.*

*Figure 10. Historical robotic devices.*

*Figure 10a. SRS-device as first prototype developed for open telesurgery.*

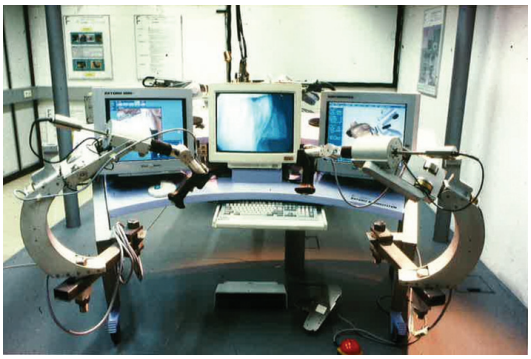

*Figure 10b. ARTEMIS: First experimentally used device for laparoscopic telesurgery (Institute for Nuclear Research Karlsruhe, Germany)*

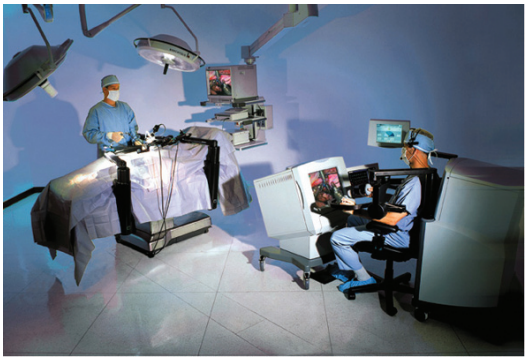

*Figure 10c. ZEUS: First clinically used device for laparoscopic telesurgery consiting of three arms mounted to the operating table and controlled via a console. Instruments provided 4 DOF similar to laparoscopy.*

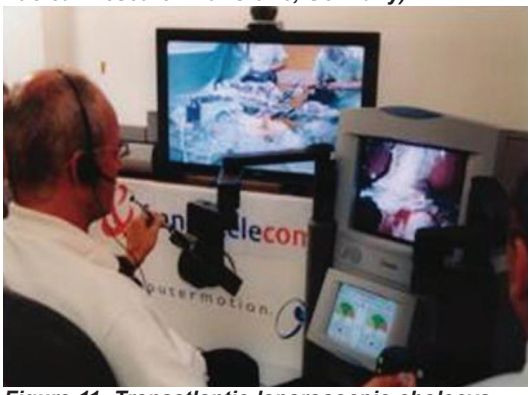

*Figure 11. Transatlantic laparosocpic cholecystectomy using the ZEUS-device in 2001.*

*Figure 11a. Prof. Marescaux at the console in New York.*

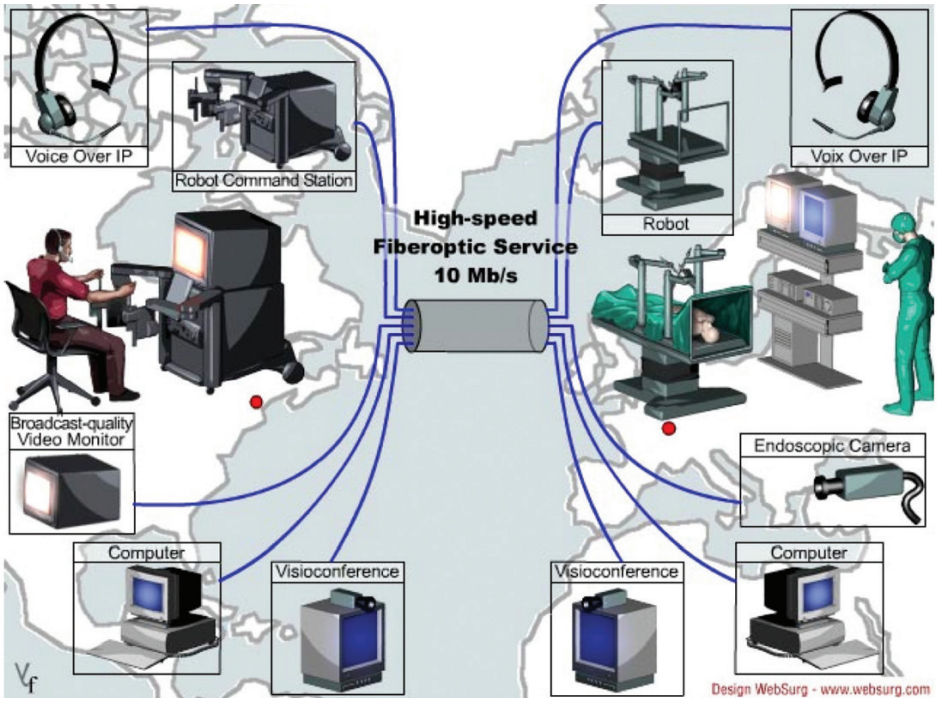


*Figure 11b. Schematic drawing of the design of the project*

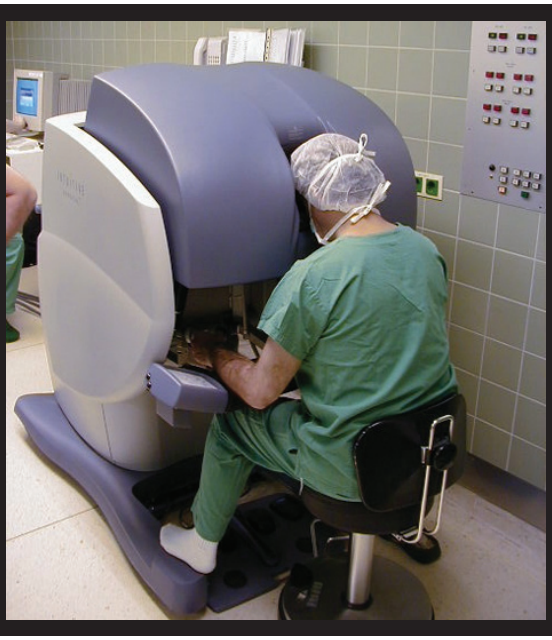

*Figure 12. Da Vinci Robot for laparoscopic surgery.*

*Figure 12a.Console providing armrest and 3D-vision*

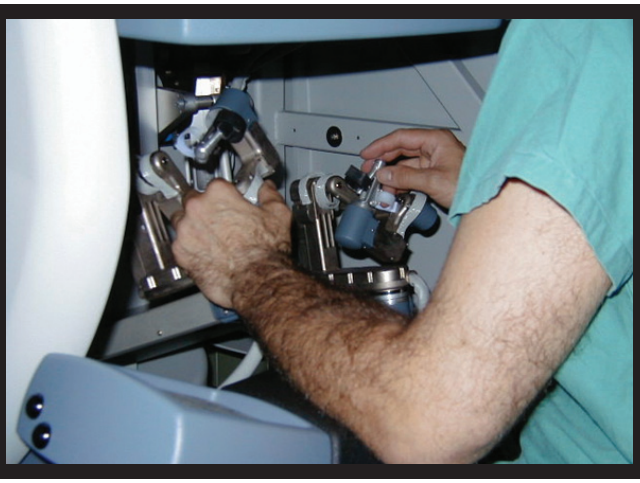

*Figure 12b. Endowrist technology with 7 DOF*

*Figure 12c. Control of camera and clutch mechanism by foot peda*

***Table 2a: Design, advantages and disadvantages of future technical developments improving laparoscopic surgery***

| Criteria | Enhanced Laparoscopy | Single-port robots | Alternate Robo systems | Da Vinci-XI-system | Comment |
|---|---|---|---|---|---|
| Videotech-nology | 2D (Ultra)-HD-camera systems 3D with glasses | 3D HD-camera-systems (small viewing angle) | 3D-HD camera systems with glasses | 3D-HD-camera-system with mirror technology at console | Mirror technology represent best solution<br><br>Single-ports systems provide only small viewing angle<br><br>Laparoscopy may not need 3D-technology |
| Working ergonomy | ETHOS-platform (chest- support, armrest, footrest) with restrictions in lateral working space.<br>MIM-Manipulator with surgeon sitting at bedside | Depending on handle design, no console with integrated arm rest and footpedals<br><br>Standing at bedside using Spider Surgibot | Depending on console and handle design, force-feedback provided | Sitting at console with armrest, Endo-wrist-technology, footpedals, integrated screen functions, motion-scaling, clutch | Da Vinci-console provides all important functions apart from force-feedback<br>Maneuvre of single-port-systems may be limited by small working space at console (ie. no clutch, no armrest)<br>ETHOS-platform improves ergonomy, but does not provide clutch-function<br>MIM has no clutch function and integrated footpedals |
| Instrumentation | 7-DOF- Instruments<br>- mechanical<br>- motorized | Flexible instruments<br>- snake design<br>- tube controlled<br>No retraction possible (need of additional trocars) | 7 DOF<br>-instruments<br>- motorized<br>- cable driven<br>Until now no specific instru-ments shown | 7 DOF<br>- instruments<br>- cable driven<br>- special tools (clip-applyer, stapler, sealing device, succion) | Da Vinci-system with advanced instrument technology using 3 arms<br>Instrumentation of single-port is limited (only small clips, no retraction, …)<br>During enhanced laparoscopy only selective use of 7-DOF-instruments (ie suturing) |

***Table 2b: Summary robotic devices used only experimentally***

| Device | Telescope | Console | Robotic arms | Force - feedback | Degree of freedom of movements (DOF) | Comment |
|---|---|---|---|---|---|---|
| ARTEMIS (Nuclear Research Centre Karlsruhe, Germany) | 2D-CCD-technology controlled by camera-arm (voice, finger-ring) | 2D screens plus 2 joy-sticks with armrest | 2 cable actuated robotic arms | yes | 7 DOF | First robotic device used in experimental surgical models in 1993 |
| MIRO Surge (DLR, Germany) | 2D/3D-CCD-technology | Autostereoscopic Monitor or 3D-glasses Haptic input devices based on finger-tips | 2 light-weighted motorized robotic arm mounted at the operating tabl | Yes (torque-sensors) | 7 DOF | Planning of optimal trocar position Nullspace positioning Actually only 10mm-instruments Only in-vitro studies |
| AMADEUS RSS (Titan Medical, USA) | 3D-CCD-technology | 3D screen with mirror-based technology and loop-handles | 3 cable actuated robotic arms plus telescope arm arranged on 1scart | No | 7 DOF | Development stopped due to patent problems |
| TELELAP ALF-X (Sofar, Italy) | 3D-HD-technology | 3D-glasses and monotor with eye-tracking system special handles providing haptic feedback | 3 cable actuated robotic arms plus telescope arm arranged on 2 carts | yes | 7 DOF | Haptic feedback, eye-tracking system, reusable endoscopic instruments (ie similar to Da Vinci) Supported by the European Commission's Joint Research Centre |
| Kyung Hee SR1 (Samsung, Korea) | 2D-CCD-technology | 2D monitor with two handles | 2 robotic arms (industrial robots; A2) plus camera arm mounted at OR-table | No | 7 DOF | Telepresence surgery in an animal model No technical update published since 2007 |
| RAVEN II/III (CITRIS, USA) | 2D-HD-technology | 2D-monitor | 2 (3) cable arctuated robotic arms plus camera mounted at table | No | 7 DOF | Open platform with the vison to program surgical procedures Mostly used for experiments with remote surgery |
| SOFIE (Medical Robotic Technolo-gies, The Netherlands) | 2D-HD-technology | 2D monitor / direct view with two handles | 2 motorized arms plus camera mounted at table | yes | 7 DOF | Until no in-vivo testing published |

console with handles that can be utilised at the console always in an ergonomic working position due to the clutch-mechanism **(Figure 12b)**.

Primarily, this device was used in cardiac surgery mainly for by-pass surgery [39]. However, initially the device did not allow laparoscopic surgery on the beating heart, which decelerated the diffusion of the device in this speciality. In 2000, Binder [40] performed the first robot-assisted radical prostatectomy followed by Abbou [41], Vallancien [42] and Rassweiler [43]. The break-through, however, has to be attributed to Menon, who established a full-working clinical programme including training of urologists [44]. In 2014, approximately 90% of all radical prostatectomies in the United States were performed using the da Vinci device.

The use of the da Vinci system in urology was initially limited by lack of proper instruments. However, bipolar forceps, Metzenbaum scissors, and special graspers were soon developed. The da Vinci S already provided a better range of motion, longer robotic arms and the option of an HD-videosystem and a fourth arm **(Figure 13a)**. The next generation represented the SI-system **(Figure 13b)** with integrated HD-videotechnology, and a finger-based clutch-mechanism. Moreover, the system could be upgraded to the use of isocyanine green (Fire-Fly) and the 4-DOF-Vespa-system for robot-assisted LESS-procedures **(Figure 13c)**. The idea of a training console was proposed by Autschbach et al [45] in 2000, however, this was finally realised in the SI-system. The da Vinci SI dual console surgical robotic system allows two surgeons to simultaneously collaborate during surgery, thus two sets of eyes, hands and skills are involved in the surgery. Besides possible extension of the indication, this represents an ideal training platform **(Figure 13d)**.

In 2014, Intuitive Surgical launched the da Vinci XI system as the next generation **(Figure 14a)**. In this device, the camera port can be chosen liberally for all four ports. This may be very important for colonic and rectal surgery. The robotic arms have been designed to be much finer to minimize instrument clashing. Also the HD-technology has been further improved. Finally, with this system, the new robotic SP-platform for 7 DOF-robotic LESS-surgery can be used **(Figure 14b**). Kaouk et al [46] have presented preliminary clinical data.

There is no clinically active opponent for Intuitive Surgical, as Intuitive Surgical bought Computer Motion in 2002, and thus all patents concerning single arm devices mounted on the table. In 2009, Intuitive Surgical bought NeoGuide Systems, a company focussed on robot-assisted colonoscopy and NOTES. However, most patents will expire in 2015 and 2016. Which of the numerous existing developments will be successful in the setting of MIS in urology remains to be answered. Alternative developments to the da Vinci systems can be divided into console-based and bedside-based devices.

## 2. CONSOLE-BASED DEVICES FOR ROBOT-ASSISTED LAPAROSCOPY (TABLE 2B)

### *a) MIRO Surge*

Following ARTEMIS, the MIRO Surge from the German Aerospace Centre (DLR) represents one of the most sophisticated devices developed for robotic surgery [47]. Similar to the ZEUS, it consists of three arms mounted on the operating table **(Figure 15a)**. The instruments are driven by micro-motors, which also enable a tactile feedback unlike the da Vinci system based on cable-driven instruments. For this purpose, the device uses potentiometers. The MIRO robot is composed of seven joints with serial kinematics, comparable to the human arm. Moreover, the arms and instruments are light-weight. The surgeon sits in front of an autofocussing monitor **(Figure 15b).** However, to date, the MIRO Surge has only been tested in in vitro models, adequate instruments are missing, and the German Aerospace Centre has not yet found an industrial partner. This may be due to the similarities of the system to those of the ZEUS design.

Nevertheless, the DLR has developed a special instrument (MICA). The *MICA* instrument **(Figure 15c)** consists of a versatile drive train and a detachable task-specific tool with its tool interface, shaft, 2 DOF wrists, 7 DOF-force/torque-sensor and the actuated functional end. With the current cable-driven tool, gripping and manipulation forces of above 10 N are feasible and dynamics are high enough for surgery of the beating heart. The location of motors and electronics for controlling a tool for MIRS is one of the factors differentiating dedicated robotic systems from versatile designs. Dedicated systems connect to a limited set of proprietary instruments; therefore, actuators can be placed within the robotic arm [48]. This results in lighter and less complex instruments at the expense of heavier and more complex robotic arms. In contrast, in the da Vinci surgical system with EndoWrist technology, all actuators and electronics are located in the robotic arms and the driving motion is transmitted mechanically to the instrument interface.

### *b) Amadeus RSS*

The AMADEUS RSS (Titan Medical, Toronto, Canada) has also only reached the experimental level [49]. The device looks very similar to the da Vinci design with a console and 3 robotic arms **(Figure 16a)**. This may be the main reason why, in 2013, Titan Medical stopped the development of AMADEUS RSS and moved to the development of SPORT, a single-port platform [50] **(Figure 16b,c).**

### *c) Telelap Alf X*

Supported by the European Commission's Joint Research Centre of the Institute for the Protection and Safety of the Citizen, the TELELAP Alf-X system

*Figure 13. Next generation Da Vinci Robot versions. Figure 13a. Da Vinci S: With unchanged design of console, but option of HD-videotechnology, longer robotic instruments, and option to fourth arm.*

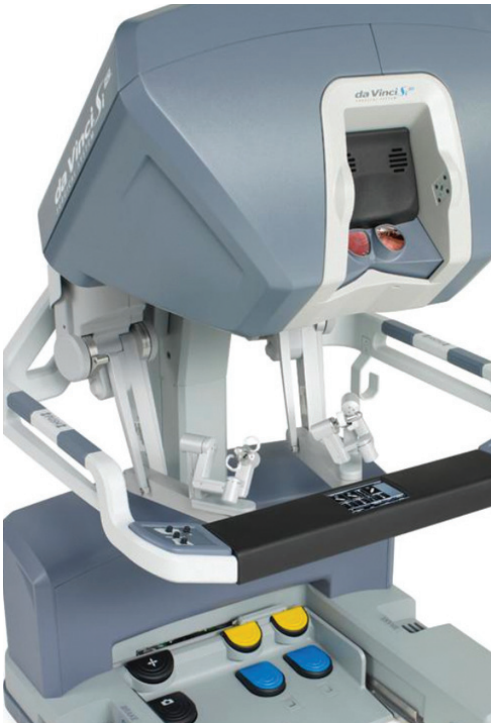

*Figure 13b. Da Vinci SI: With integrated HD-videotechnology, finger-based clutch-mechanism. Moreover, the system allowed to be upgraded to the use of iso-cyanine green (Fire-Fly) and the VESPA-platform.*

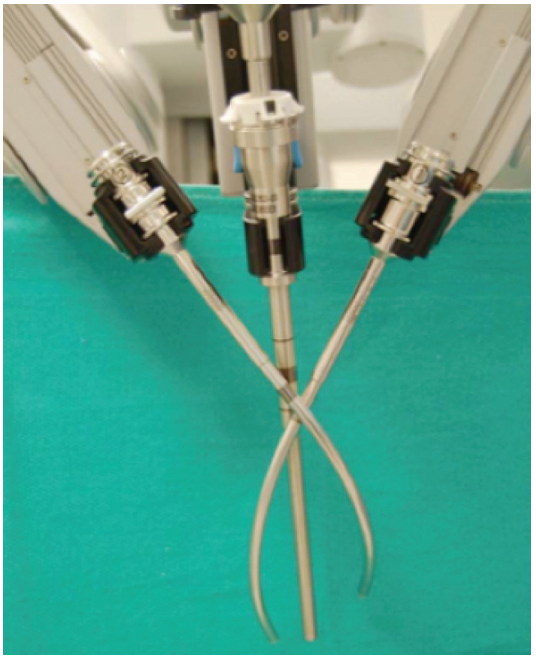

*Figure 13c. VESPA-System: Robotic platform used with the Da Vinci SI for LESS. Two crossing curved instruments with only 4 DOF. Crossed programming of the handles at the console compensates the crossing of the instruments. The surgeon can manoeuvre the right instrument on his 3D-screen with his right hand.*

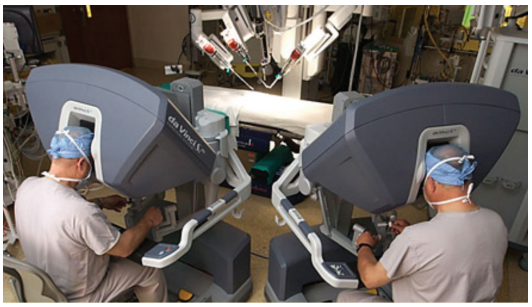

*Figure 13d. Concept of Double console for training and assistance realized with the Da Vinci SI-System.*


***Figure 14. Last generation Da Vinci Robot XI.***

***Figure 14a. Da Vinci XI with finer design of robotic arms to minimize the risk of clashing of instruments. Variable use of robotic arms for the camera. Improved HD-image quality at the console. The XI-system allows the use of the SP-platform.***

***Figure 14b. SP-platform for LESS (single-port surgery) with snake-style wrist at the site of endeffector and an elbow-wrist to allow triangulation.***

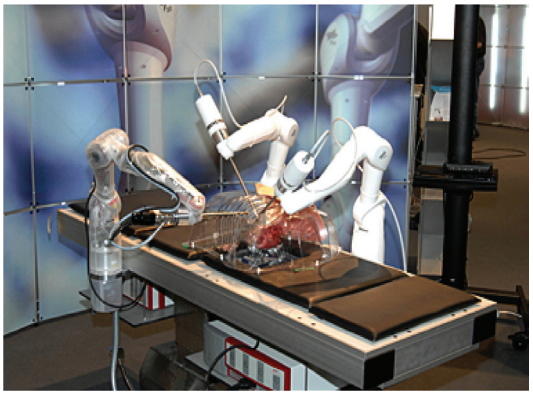

*Figure 15. MIRO Surge-robot for laparoscopic surgery (German Aerospace Centre, Wesseling, Germany). Figure 15a. Three lightweight robotic arms are mounted to the operating table with motorized MICA instruments.*

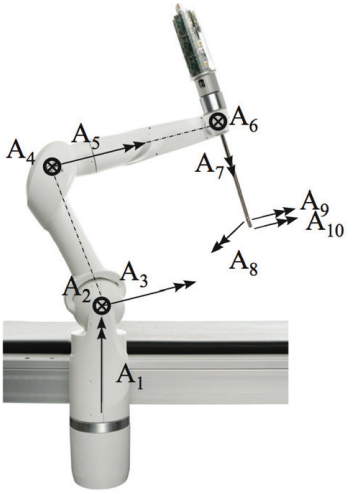


*Figure 15c. The MICA instrument is a self-sufficient 3 degrees of freedom robot, which – in the MiroSurge system – acts as joint 8, 9 and 10 of the telemanipulator.*

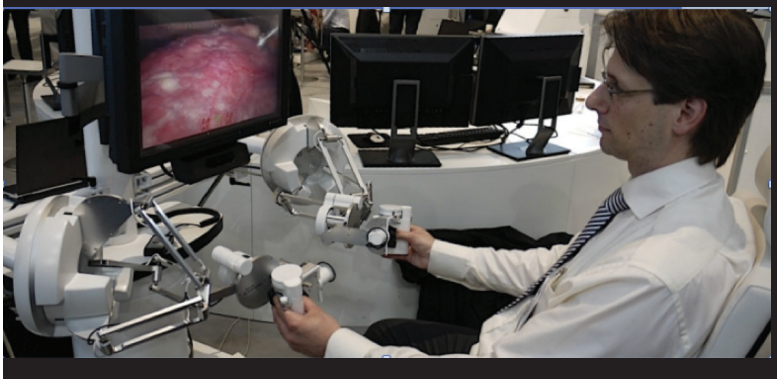

*Figure 15b. Console with autostereoscopic monitor and handles with force-feedback.*

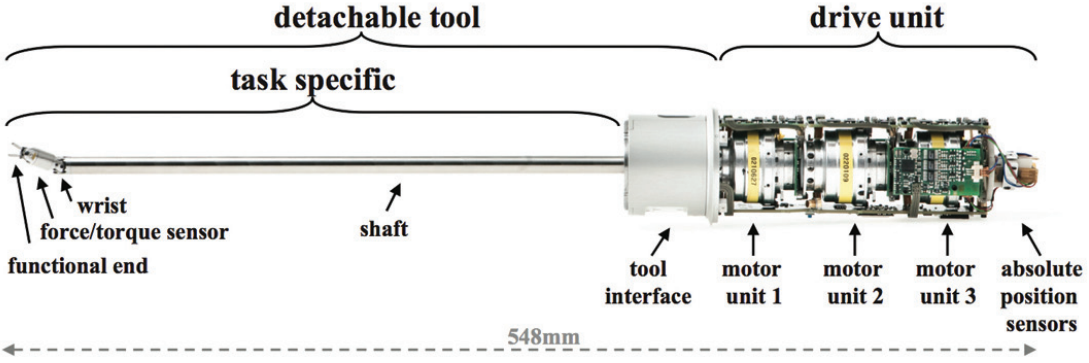


*Figure 15d. The tool consists of drive unit, a tool interface and the task specific tool with its shaft and end effector. In the present configuration the tool is comprised of a 2 DOf wrist, 1 DOF gripper and 7 DOF force/torque sensor. However, tools can range from grippers, scissors, and needle holders.*

*Figure 16. Robotic devices developed by Titan Medical Systems*
*Figure 16a. Amadeus RSS: The design of the device is similar to the Da Vinci system with a console providing 3D-videotechnology and a four-arm robot at the bedside. Development of this device has been stopped.*

*Figure 16b. SPORT: Robotic platform developed for single-port surgery. A console offers 3D-HD-vision and a manipulator at the bedside to perform the procedure.*

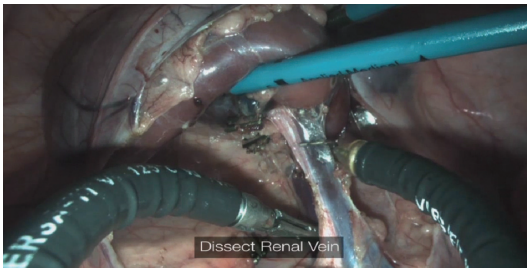


*Figure 16d. Use of SPORT for experimental nephrectomy (dissection of renal vein). Note the use of additional instrument/trocar for retraction of the kidney.*

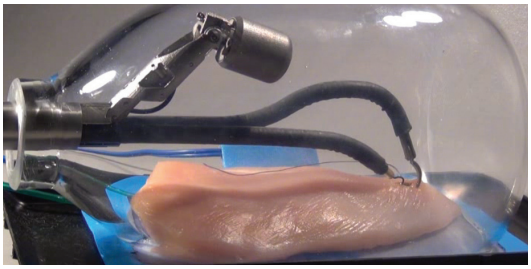

*Figure 16c. SPORT: 3D-flexible telescope with fibre-optic based illumination and two flexible instruments.*

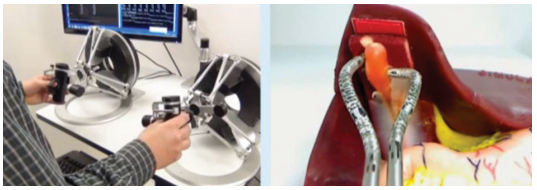

*Figure 16e. Demonstration of the handles for manipulation of SPORT*

(SOFAR, Milano, Italy) was developed. TELELAP is a remotely operated robotic system that utilises a remote control station and robotic arms [51]. Three unique system features include haptic feedback, an eye-tracking system and reusable endoscopic instruments **(Figure 17a).** The eye-tracking system is designed to control the endoscopic view by line of sight **(Figure 17b)**. It also allows the surgeon to activate instruments by looking at an icon located on the screen. The first targets of the TELELAP Alf-X system are gynaecology, urology and thoracic surgery procedures [52]. An experimental study demonstrated the safety of the device, however, handling of TELELAP Alf-X, particularly at the console, did not reach the standard of the da Vinci system [53].

***d) Kyung Hee SR1***

The Kyung Hee SR1 system developed at Seoul Yonsel University College of Medicine in collaboration with Samsung consists of two industrial robots (AS2, Samsung Automation Inc., Korea) providing 6 DOF and force-feedback mounted at the bedside (similar to the ZEUS-system) and a 2D standard laparoscope. The arms are manipulated by two handles using a standard video-screen. Due to the relatively simple design, this system allows the performance of telepresence surgery similar to the ZEUS-system **(Figure 18)**. The observed time delay during *in vitro* testing ranged from 20 to 40 milliseconds. First publications of the experimental set-up of the device date from 2007 and state that the Korean robotic surgical system can be commercialised within three years. However, there are no further available data according to the recent survey by Tuliao et al. [54].

***e) Raven III***

The Raven Project is being developed through the collaborative effort of several universities (Santa Cruz, Berkeley, Davis). The goal is to produce an open source system that would allow two surgeons to operate on a single patient simultaneously [55]. The initial system includes two portable surgical robotic arms, each offering 7 DOF and a portable surgical console **(Figure 19a)**. Similar to the da Vinci system, a lot of research has been dedicated to battlefield and underwater telepresence remote surgery. The Raven II is a two-arm surgical robot designed with a camera and may utilise 3D ultrasound imaging to show internal organs in real time [56]. The Raven III includes four robotic arms and two optional cameras. The system facilitates the collaborative effort of two surgeons interacting with the surgical site using telemedicine **(Figure 19b).**

The Raven platform is one of the most advanced surgical robotics research platforms. The Raven provides higher performance (bandwidth) and is more reliable, the platforms are also more compact, which enables setting them up side-by-side, which is how such robots may be used in practice. However, to date, the device is still experimental. Two primary targets of the Raven projects include endoscopic sinus surgery and cardiovascular surgery.

***f) SOFIE-robot***

SOFIE (Surgeon's Operating Force-feedback Interface Eindhoven) provides a force-feedback interface with less space for the robot [59,60]. The two components (master and slave) are completely separate from each other, however, all communication between the two takes place over data cables arranged in an overhead wiring boom. The three different robotic arms with a maximum of 8 DOF can be fixed to the operating table **(Figure 20a)**. Three arms weigh about 85 kg compared to 544 kg with the da Vinci robot. The frame for the manipulators is of the type used for pick-and-place robots, allowing the manipulators full freedom of motion in space. This means that the surgeon can also choose the optimal direction of approach for any organ, rather than having to move the patient to suit the machine. The manipulators also provide force feedback through the overhead cable boom **(Figure 20b).** The robot was developed at the University of Eindhoven in collaboration with Medical Robotic Technologies (Eindhoven, The Netherlands). To date, no laparoscopic application has been published **(Figure 20c).**

## 3. DEVICES TO ACCOMPLISH ROBOT-ASSISTED SINGLE-PORT SURGERY (TABLE 3B)

Laparo-endoscopic single site surgery (LESS) is viewed as a step to further minimise the access trauma of classical laparoscopic or robot-assisted laparoscopic surgery and as a potential step toward true natural orifice transluminal endoscopic surgery (NOTES). However, the classical LESS technique is significantly impaired by the clashing of working instruments and thus suboptimal ergonomics. Early mechanical multi-tasking platforms **(Table 3a)** including the Octopus-system, Endosamurai (Olympus, Japan; **Figure 21a)**, direct drive endoscopic system (Boston Scientific, Natick, USA), Anubis (Karl Storz, Tuttlingen Germany; **Figure 21b)** or Purdue University devices represent bedside solutions without a console [61,62]. Thus, they have a small operating range, limited flexibility and opposite or retroreflective working is impossible. Robotic technology may overcome most of these problems. Such devices are classified by an insertable robotic end [63].

***a) Sprint robot***

The ARAKNES Project (Array of Robots Augmenting the Kinematics of Endoluminal Surgery) was funded by the European Commission`s Programme [57]. The project hopes to produce a micro-robotic-based smart operating system for advanced endoluminal surgery. The system is based on the common design of a remote console and two robotic arms with rotating grippers on the end (SPRINT robot) introduced via the umbilicus **(Figure 22a)**. The functions of SPRINT are operated via the external manipulator Dionos **(Figure**

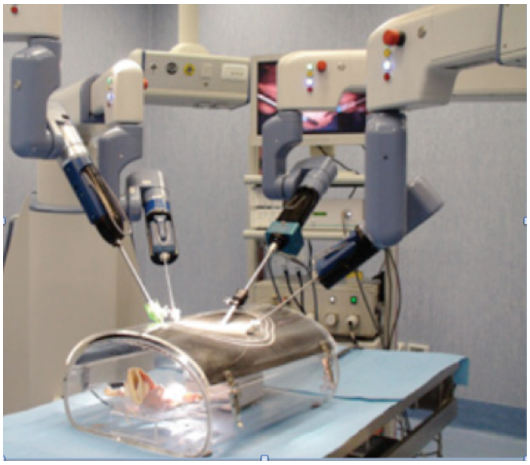

*Figure 17. Telelap ALF X developed by Sofar, Milano, Italy.*
*Figure 17a. Robotic four arm system with instruments mounted on 2 carts*

*Figure 17c. Special handle provides haptic feedback*

*Figure 17b. Console with 3D-Monitor requiring polarizing glasses like for laparoscopy. The endoscopic device includes an eye-tracking system.*

*Figure 18. Kyung Hee SR1 developed at Seoul Yonsel University College of Medicine in collaboration with Samsung consists of two industrial robots (AS2, Samsung Automation Inc, Korea) providing 6 DOF and force-feedback mounted at bedside and a 2D standard laparoscope. Due to the relatively simple design, this system allows to perform telepresence surgery similar as shown on a porcine model. However, there was no update since 2007.*

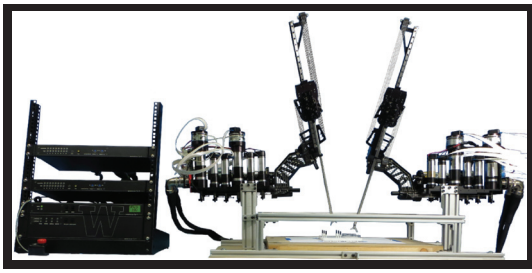

*Figure 19. Raven Surgical Robot*

*Figure 19a. 7-DOF cable-actuated surgical manipulator designed for use in either MIS or open surgery. The software of the robot is compatible with the open source robotics coding platform*

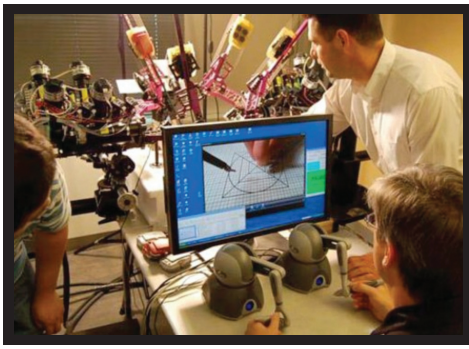

*Figure 19b. The arms are manipulated by two handles plus standard 2D-videoscreen.*

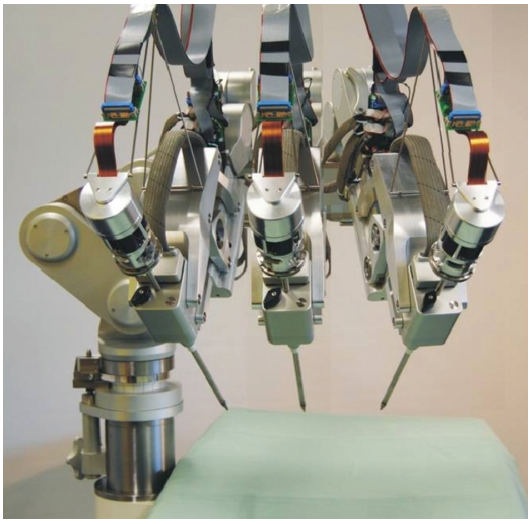

*Figure 20. SOFIE (Surgeon's Operating Force-feedback Interface Eindhoven)*

*Figure 20a. Robotic device providing force-feedback interface with less space. Three different robotic arms with maximally 8DOF can be fixed to the operating table.*

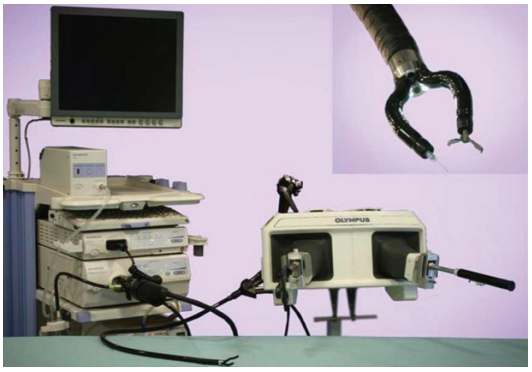


*Figure 21. Mechanical multi-tasking endoscopic platforms*

*Figure 21a. EndoSamurai (Olympus, Japan): Prototype of an advanced platform for NOTES or LESS. The surgeon uses a bi-manual interface to control instruments at bedside (ie mouth) with multiple degrees of freedom.*

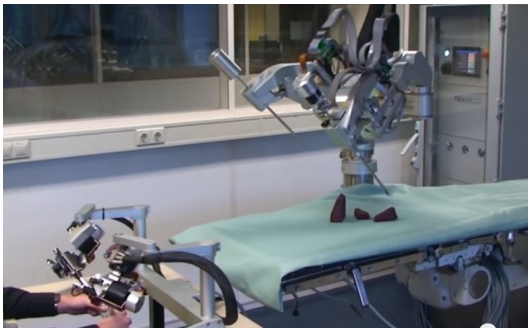

*Figure 20b. The manipulators are controlled at a console with standard 2D-screen showing the operative site.*

*Figure 21b. Anubis (Karl Storz, Tuttlingen, Germany): Platform developed for NOTES with a tip that opens to expose flexible working instruments.*

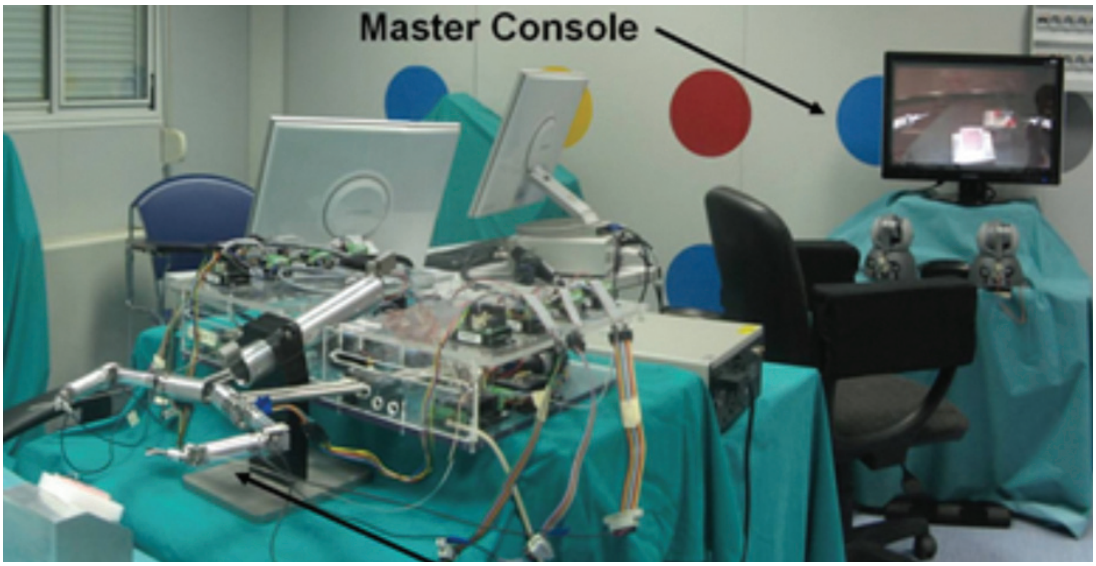


*Figure 22. SPRINT-robot developed in the framework of ARAKNES-project.*

*Figure 22a. The system is based on the design of a remote console and two robotic arms with rotating grippers on the end.*

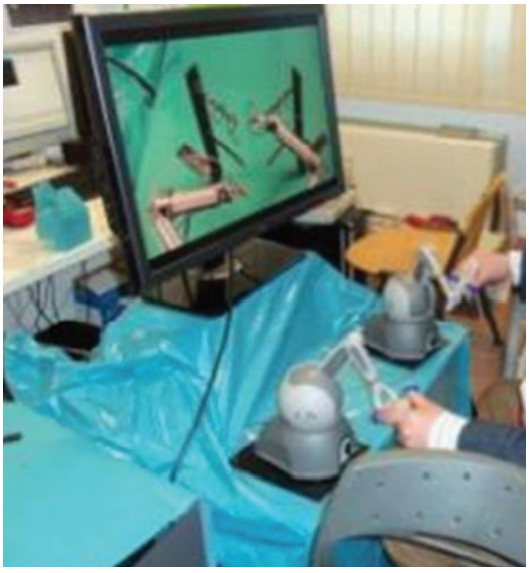

*Figure 22b. External manipulator Dionos with a standard 2D-screen*

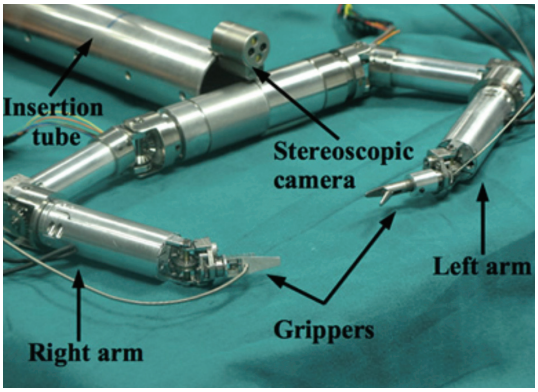


*Figure 22c. The control motors are external thus allowing for a smaller access port for the end-effectors.*

***Table 3a: Summary table of mechanical flexible endoscopic multi-tasking platforms (modified from Yeong BPM and Gourlay T)***

| Device | Outer diameter (mm) | No. of instrument channels | Channel Size (mm) | Length (cm) | Degree of freedom of movements (DOF) | Comment |
|---|---|---|---|---|---|---|
| R-scope (Olympus) | 14.3 | 2 | 2.8 (deflectable) | 133 | Endoscope: 6 DOF* Instrument: 3 DOF+ | Does not allow intuitive bimanual instrument coordination |
| Anubiscope (Karl Storz) | 16 | 3 | 4.2x2 (deflectable) 3.2 (central) | 110 | Endoscope: 6 DOF* Instrument: 7 DOF+ (Tulip-shaped tip) | Instrument insertion does not require an over-tube.<br>Instrument flaps can limit platform manoeuvrability Console under development |
| EndoSamurai (Olympus) | 15 (Endoscope) 18 (Sheath) | 3 | 2.8x3 | 103 | Endoscope: 6 DOF* Instrument: 7 DOF+ | control console with manipulation similar to a laparoscopic system<br>Hollow guide arm concept allows the use of generic endoscopic instrument, |
| Direct Drive Endoscopic System (Boston Scientific) | 15 (Endoscope) 22 (Sheath) | 3 | 4.2 x2 7 | 55 (short!) | Sheath: 6 DOF* Instrument: 7 DOF+ | Platform-based device<br>Limited torque transmission Problem of hysteresis |

** Endoscope Up/Down Left/Right Rotation Translation; + Instrument Up/down Left/Right Open/Close Translation Rotation*

***Table 3b. Summary of robotic flexible endoscopic multi-tasking platforms for single-port surgery***

| Device | Outer diameter (mm) | No. of instrument channels | Robotic arms | Length (cm) | Degree of freedom of movements (DOF) | Comment |
|---|---|---|---|---|---|---|
| MASTER (Nan Yang Tech Uni, Singapore) | 22 | 2-3, depending on attached endoscope | 2 cable actuated robotic arms with fixed endeffectors | 41 | Endoscope: 6 DOF* Instrument: 9 DOF+ due to ellbow joint | It compromises by being a retrofitted device<br><br>Cumbersome external mechanical actuator |
| SPRINT (ARAKNES, Italy) | 25 | None | 2 motor-driven robotic arms with joints for end-effectors (ellbow, wrist) | 30 | Endoscope 4 DOF* Instruments: 7 DOF | Operated by two hand-pieces with haptic interface and a 3D-monitor with glasses actually not comparable to a surgical console.<br>Magnetically controlle endo-camera tested in vivo. No in-vivo tests of the device have been reported yet. Supported by the European Commission's Joint Research Centre |
| Highly versatile single-port system (Tech Uni Munich, Germany) | 33 (single-port) | none | 2 cable actuated robotic arms (12 mm) +semi-flexible telescope (6mm via 10mm tube) | 23 | Endoscope: 6 DOF* Instrument: 7 DOF+ plus 4 DOF of single port trocar | Difficult handling of the system with various DOF and the essential coordination of individual actions of participating physicians. Console under development |
| Insertable Robotic Effectors Platform (Vanderbuilt Uni, USA) | 20 | none | 2 flexible arms with snake segments design + 3D telescope (paralleogram design) | 22 | Endoscope: 2 DOF* Instrument: 9 DOF+ due to snake design | Operated by two hand-pieces and a 2D-monitor actually not comparable to a surgical console.<br>Provides sensory feedback |
| PLATE (DIGIST, Daegu, Korea) | 23 | none | 2 flexible arms with spring mechanism and six joints | 23 | Endoscope: 2DOF* Instrument: 9 DOF+ | Plate-spring mechanism allows transmission of high forces (>14N)<br>Still experimental device |
| SurgiBot (Transenterix, USA) | 21 | 2 working channels tubes (2x5mm) plus 3D/HD flexible laparoscope (5mm) | 2 steerable tubes controlled by endomechanical vertebral arms (adjustable motion scaling) | 30 / 50 | Endoscope: 6 DOF* Instruments: 7 DOF+ | Robotic arm holds the device 3D/HD-vision by polarized glasses Motion of arms like laparoscopic instruments<br>No console, no FDA-approval yet |
| SPORT Surgical System (Titan Medical, USA) | 25 | none | 2 robotic arms with snake- like plus deflectable telescope | 30 | Endoscope: 4 DOF* Instruments: 9 DOF+ Due to snake design | Small console with 3 D monitor<br>For renal surgery additional instruments are necessary |
| SP-Platform (Intuitive Surgical, USA) | 25 | non | 3 robotic arms with snake segments plus flexible 3D telescope | 30 | Endoscope: 6 DOF* Instruments: 9 DOF+ Due to snake design | Controlled by EndoWrist-technology at the Da Vinci-console<br>For prostate surgery additional instruments are necessary |

**22b)**. One primary difference is that the control motors are external thus allowing for a smaller access port **(Figure 22c)**. In addition, this programme has developed a magnetically driven endoscopic camera system [58]. This device is still experimental.

***b) Highly versatile single port system (HVPS)***

To evaluate the potential role of mechatronic platforms for NOTES procedures, the so-called "Highly Versatile Single Port System'' (HVSPS) was developed at the Technical University of Munich. It consists of a two-arm device with two manipulators and a semi-flexible telescope **(Figure 23a).** Both manipulators are partially automated and controlled over a real-time Matlab-Simulik application [64]. In its current state, two joysticks are used as human machine interfaces using Bowden-wires **(Figure 23b).** However, an integration of the system into the ARAMIS platform, which comprises a telemanipulator to guide minimally invasive instruments, is planned for the future [65]. This platform will use two sensible PHANTOMs as input devices and can be used to steer the HVSPS manipulators by Cartesian control. The device is mainly used experimentally for single-port surgery.

***c) Anubis and Stras***

Anubiscope [66] is a flexible endoscope with a diameter of 16 mm and two 4.2 mm working channels **(Figure 21b).** However, clashing of the instruments remains a problem **(Figure 24a).** For this reason the IRCAD-team in Strasbourg are developing a console for the Anubis-system **(Figure 24b)** using motorised movements (STRAS).

Moreover, they are working on interesting features such as visual tracking to compensate for respiratory movement of the target (organ). The endoscope fixes a point at the target and then automatically follows this target. This could also be very helpful for remote-controlled flexible ureteroscopy.

***d) EndoSamurai***

The EndoSamurai (Olympus Medical Systems, Tokyo, Japan) is a manually driven endoscopic system [67]. It has two hollow arms, capable of bending, located at the tip of a flexible endoscope with a diameter of 15 mm with two working channels for flexible instruments **(Table 3)** which can be manoeuvred via a platform at the bedside **(Figure 21a).** In an animal model, transgastric small bowel resection with anastomosis of acceptable quality within a reasonable time was observed [68].

***e) PLAS robot***

The PLAS robot using the PLAte spring mechanism developed by Samsung Advanced Institute of Technology [69] was designed with instruments providing six joints with 9 DOF to guarantee the application of high forces (>14 N force transmission) compared to wire- or link-driven mechanisms and a relatively large working space **(Figure 25).** The main feature is the configuration of the elbow joint which allows insertion of different instruments achieving triangulation. However, the device is still experimental.

***f) Insertable robotic effectors platform***

The IREP (Insertable Robotic Effectors Platform) is currently being developed and tested at Vanderbilt University [70,71] and consists of a 3D-telescope and two flexible arms with a snake segment design providing a passive and active segment **(Figure 26a)**. Enlargement of the working space may be provided based on a parallelogram design of the instrument **(Figure 26b)**. The device is operated by two hand-pieces and a 2-D-monitor not comparable to a surgical console **(Figure 26c).** The small size of this system may overcome the limitations of existing commercial systems, which cannot be mounted on the patient's bed, thus resulting in limitations in surgical set-up time and ability to reorient the patient during surgery.

***g) Waseda-University device***

The WASEDA-University device [72] is a single-port device, which is manipulated at the bedside with the flexible tip of the device **(Figure 27a)**. At this tip, two small flexible instruments can be used **(Figure 27b)**. This device has a very limited working space similar to early instruments designed for NOTES.

***h) University of Nebraska robot system***

The University of Nebraska [73,74] in collaboration with Virtual Incision (Nebraska, USA) presented the prototype of a two-arm dexterous miniature robot system using interchangeable end effectors to provide mono-polar cautery, tissue manipulation, and intra-corporeal suturing capabilities. The device is controlled by two external handles **(Figure 28a).** The modules separate for individual insertion, and the robot is externally supported by a mounting rod assembly **(Figure 28b)**.

***i) Sport-system***

Titan Medical stopped the development of AMADEUS RSS and focussed on the SPORT-system which is used as a platform for robot-assisted single-port surgery. The system consists of a console offering 3D-HD-vision and a manipulator at the bedside to perform the procedure **(Figure 16b).** The basic design of the platform is similar to other solutions and includes a 3D-flexible telescope with fibre-optic based illumination and two flexible instruments **(Figure 16c).** FDA-approval for the system is expected in 2015. The main applications will be robot-assisted LESS-cholecystectomy. Recently, a nephrectomy was performed in an animal model using this system **(Figure 16d).** For more complex procedures, additional trocar(s) are required for retraction, and placement of larger clips.

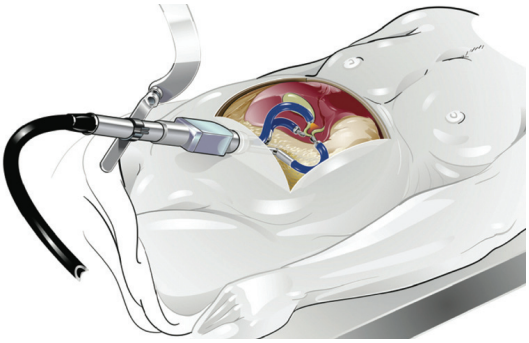

*Figure 23. Highly Versatile Single Port System (Technical University Munich, Germany)*

*Figure 23a. Two-armed device with two manipulators and a semi-flexible telescope.*

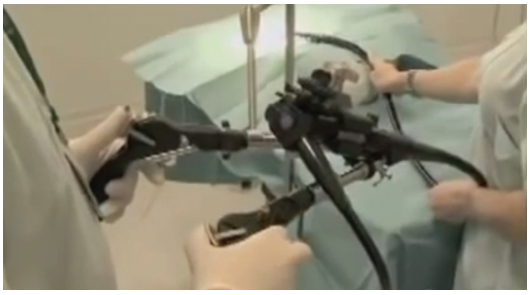

*Figure 24. Anubis (Karl Storz, Tuttlingen, Germany)*
*Figure 24a. Clashing of the instruments remaining a problem with original Anubiscope.*

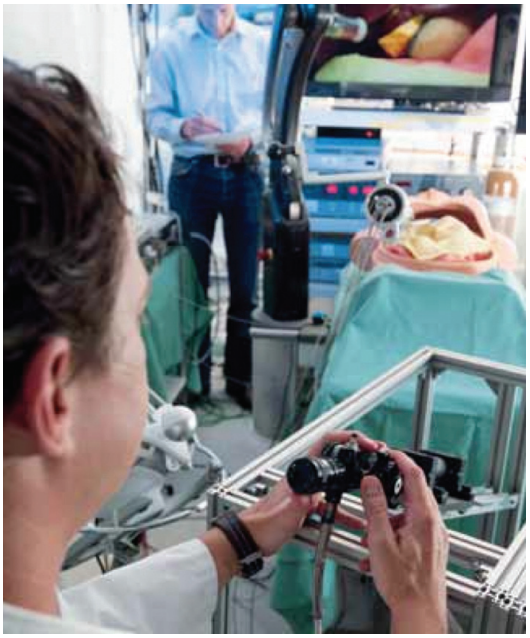

*Figure 23b. Both manipulators are partially automated and controlled over a real-time Matlab-Simulik application: two joysticks are used as human machine interfaces using Bowden-wires.*

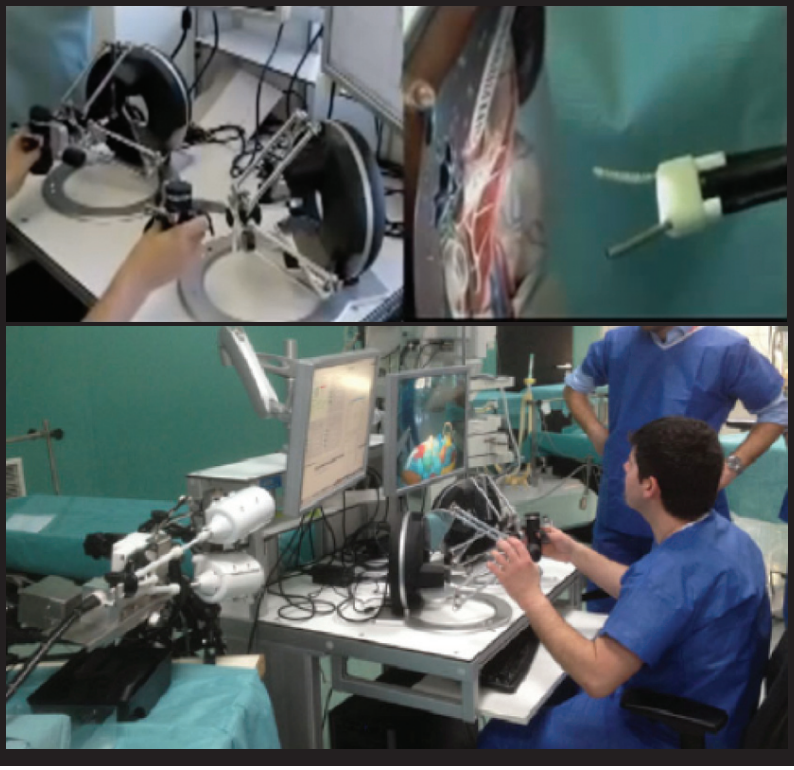

*Figure 24b. Console for the Anubis-System (Ibiscope) using motorized movements (STRAS)..*

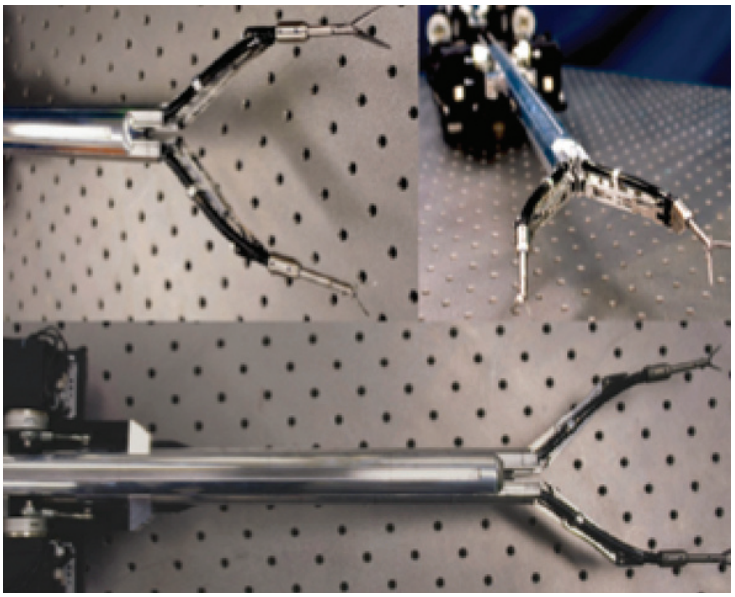

*Figure 25. PLAS robot ( Samsung, South Korea) using PLAte mechanism*

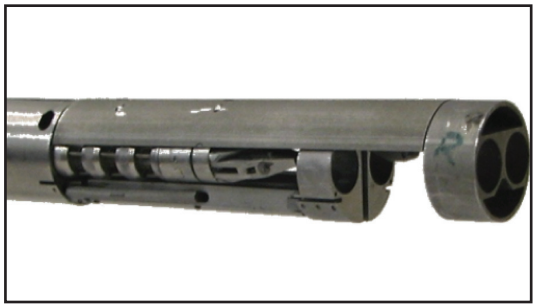

*Figure 26. Insertable robotic effector platform (IREP), Vanderbilt University.*
*Figure 26a. Insertable device consisting of a 3D-telecope and two flexible arms with snake segments design providing a passive and active segment.*

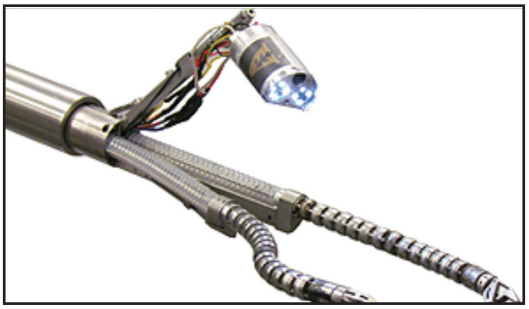

*Figure 26b. Movements of the platform based on parallelogram-design and snake like arms of the endeffectors*


*Figure 26c. The device is operated by two hand-pieces and a 2D-monitor actually not comparable to a surgical console.*

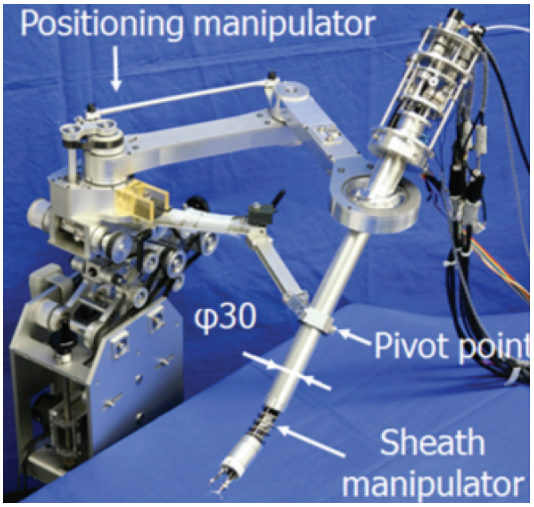


*Figure 27. Waseda University Single Port Device*
*Figure 27a. Single port-device, which is manipulated at bedside with a flexible tip of the device.*

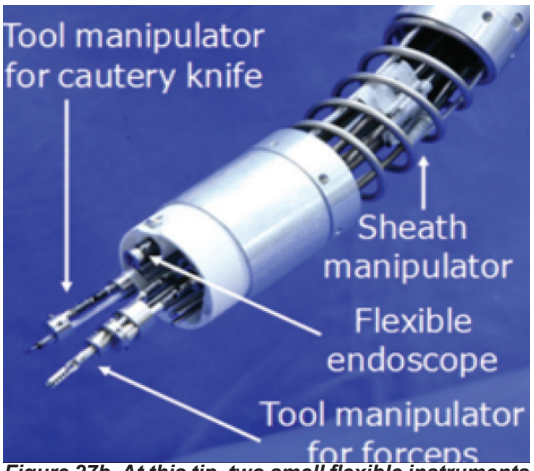


*Figure 27b. At this tip, two small flexible instruments can be used*

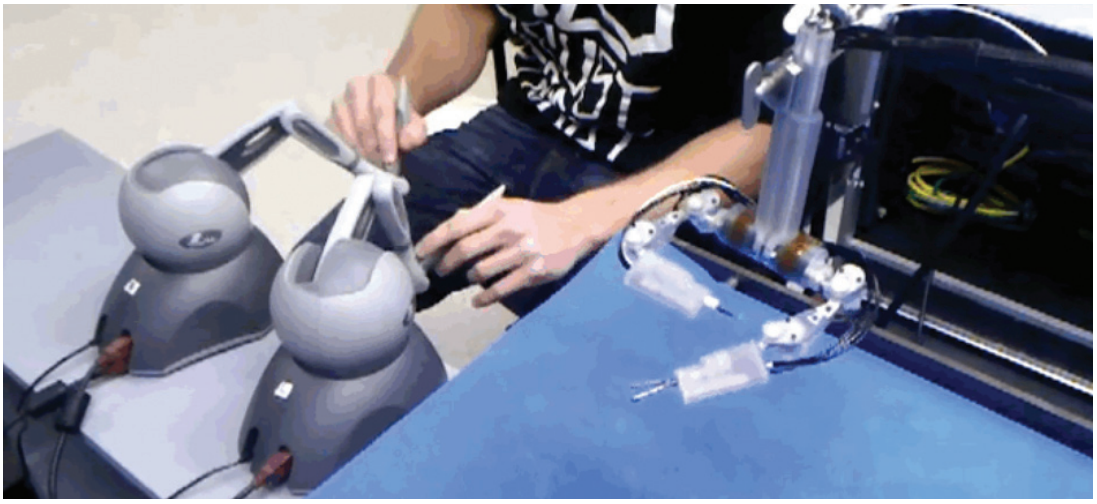

*Figure 28. University of Nebraska Robotic System*
*Figure 28a. Two-armed dexterous miniature robot system using interchangeable end effectors controlled by two external handles.*

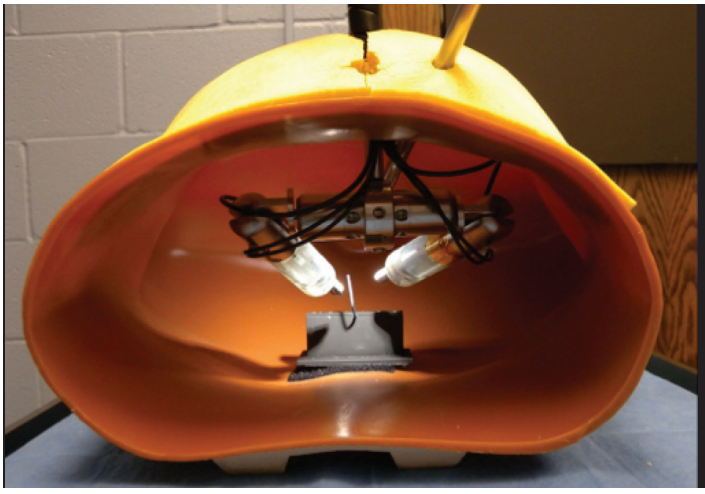

*Figure 28b. The Modules separate for individual insertion and the robot is externally supported by a mounting rod assembly (see phantom model).*

### *j) Spider robotic platform - SurgiBots*

Transenterix has continued to improve the initial Spider-system. A robotic-arm to manipulate and hold the Spider-platform was developed **(Figure 6d)**. The system is still used at the bedside, but the arm may compensate for most of the deficiencies of the initial device, such as optimal fixation of the device and handling of the instruments, integration of a 3D-telescope **(Figure 6e)**, and adjustable motion scaling **(Table 4).** Since, the original Spider-system has already received FDA approval, Transenterix expects FDA approval of the new device in 2015.

### *k) SP-platform*

With the introduction of the da Vinci XI system, Intuitive Surgical has also presented their robotic single-port SP-platform. This represents significant progress over the previously used Vespa-system with crossing instruments which provided only 4-DOF **(Figure 13c).** The design of the SP-platform is similar to the SPORT with a 3D/HD flexible telescope and two flexible instruments **(Figure 14b)**. Once introduced via the umbilical incision, the flexible instruments with a snake style wrist separate to achieve triangulation. However, the device is controlled by use of EndoWrist-technology at the da Vinci console

In contrast to all other devices, the SP-platform has already been used in a clinical pilot study [46]: 19 patients have been treated successfully including 11 radical prostatectomies and 8 renal procedures (4 partial / 4 radical nephrectomies). In four radical prostatectomies, an additional trocar was used (i.e. hybrid LESS). This may change the further development of LESS in urology.

## 4. ROBOTIC DEVICES USED FOR ENDOUROLOGY

Robotic devices for NOTES, but also for classical flexible endoscopy of the upper urinary tract have been developed. Such developments may also be of interest for further laparoscopic applications.

### *a) Sensei-Magelan-System*

In 2011, robotic flexible ureteroscopy was reported using the Sensei-Magelan-system (Hansen Medical, Mountain View, USA) designed for cardiology by Fred Moll, the inventor of the da Vinci system. This device consists of four components: the surgeon's console, a flexible catheter system, a remote catheter manipulation system, and an electronic rack containing computer hardware, power supplies and video distribution units **(Figure 29)**. The robotic flexible catheter system consists of an outer catheter sheath (14/12F) and an inner catheter guide (12/10F). A 7.5F fibre-optic flexible ureteroscope is inserted through the inner catheter guide. Remote manipulation of the catheter system manoeuvres the ureteroscope tip, which is glued in place to the inner guide. The tip of the outer sheath is positioned at the ureteropelvic junction to stabilise navigation of the inner guide inside the collecting system. This means that the ureteroscope is manipulated passively [75].

### *b) Roboflex Avicenna*

The Roboflex™ Avicenna, was specifically developed to perform flexible ureteroscopy **(Figure 30a).** The manipulator directly drives the flexible ureteroscope using its own mechanics. For this purpose the hand-piece of the scope has to be attached directly to the specially designed master plate of the manipulator **(Figure 30b).** Micro-motors move the steering lever of the hand-piece for deflection. In addition, the arm enables bilateral rotation, advancement and retraction of the ureteroscope hand-piece, respectively. Based on this, robotic flexible ureteroscopy FURS can be performed using a standard 10/12F access sheath **(Figure 30c)**. However, several functions can also be integrated such as fine-tuning of the movements, motorised insertion and retraction of a laser fibre, and automatic repositioning for introduction of the fibre **(Figure 30d)**. The central wheel enables finely graduated movement of the steering lever, which cannot be accomplished manually. This is important for control of the laser fibre during ablation / dusting of calculi [76].

## 5. MINIATURISED ROBOTS

A revolutionary idea is the development of modular miniature robots. Modular miniature robots are composed of small subunits (modules), which can be assembled to construct a functional mini-robot. Harada et al. introduced the concept of a reconfigurable self-assembling robot for NOTES [77]. This ARES (Assembling Reconfigurable Endoluminal Surgical system) project is supported by the European Union.

### *a) Modular miniaturised robots*

The ARES system is designed for screening and interventions in the gastrointestinal (GI) tract to overcome the intrinsic limitations of single-capsules or endoscopic devices. In the proposed system, miniaturised robotic modules are ingested and assembled in the stomach cavity. The assembled robot can then change its configuration according to the target location and task **(Figure 31).** However, this concept has yet to be proven.

Controlling modular mini-robots is complicated. Therefore, it is essential to develop appropriate software and hardware technology that will provide the surgeon with all the necessary information and both easy and precise control of his miniature assistants. Zygomalas et al. reported an in silico investigation of a surgical interface for the remote control of modular miniaturised robots in MIS [78]. The development of the conceptual model was based on the idea that the user-surgeon could handle a modular remote controller similar,

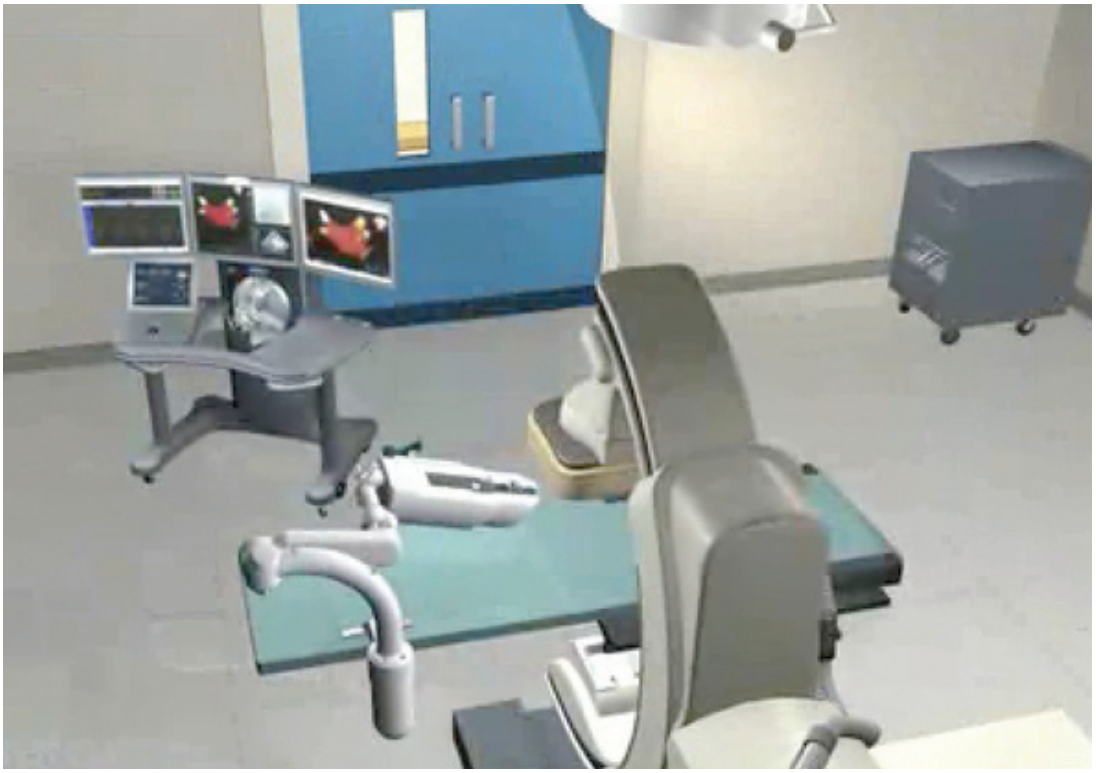

*Figure 29. Sensei-system (Hansed-Medical, USA) for endovascular heart surgery, modified for robotic ureteroscopy.*

*Figure 29a.The device consists of four components: surgeons console, flexible catheter system, remote catheter manipulation system, and electronic rack containing computer hardware, power supplies and video distribution units.*

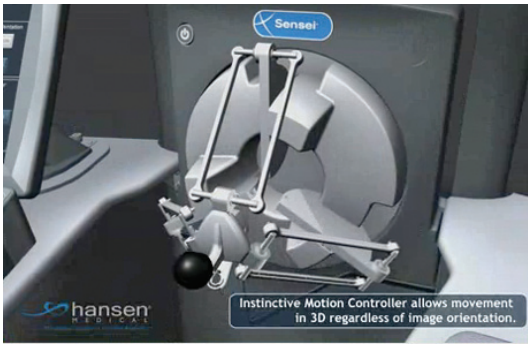


*Figure 29b. Instinctive motion controller at the console.*

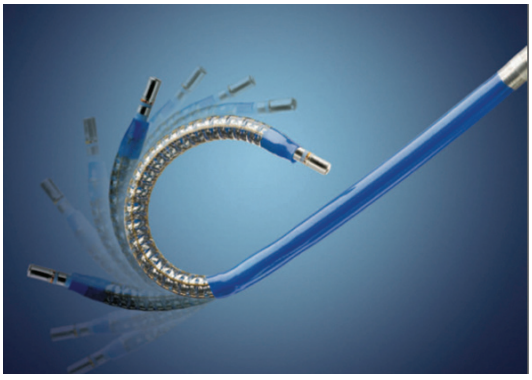

*Figure 29c. Principle of steerable sheath to manipulate indwelling flexible instruments respectively a flexible ureteroscope.*

*Figure 30. Avicenna Roboflex (ELMED, Ankara, Turkey) for flexible ureteroscopy.*
*Figure 30a. Console with seat, adjustable armrest, two joy-sticks, central wheel and touch screen.*

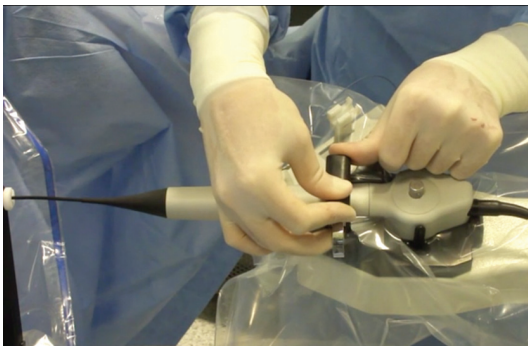

*Figure 30b. Manipulator with exchangable scaffolds fitting for the hand-piece of different flexible ureteroscopes.*

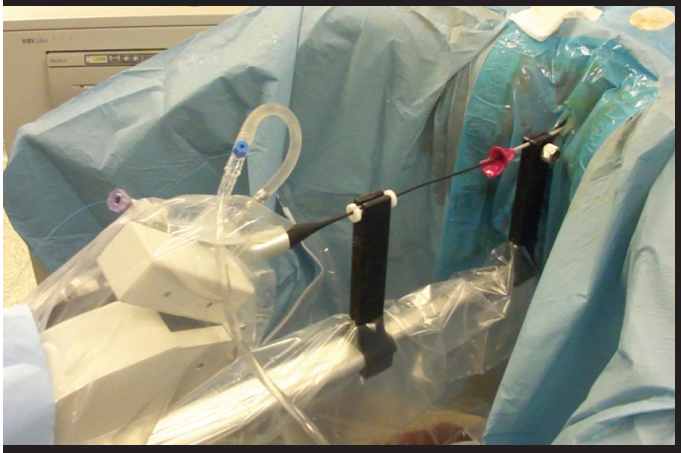

*Figure 30c. The flexible ureteroscope is inserted via an access sheath and supported by two stabilizers*


*Figure 30d. The touch-screen at the console allows monitoring and changes of various functions, such as degree of deflection, insertion and activation of laser fibre, injections speed of irrigation pump.*

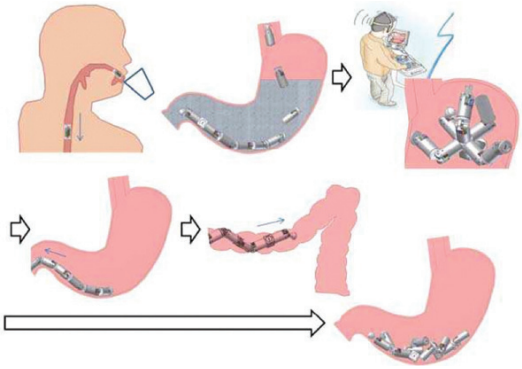

*Figure 31. ARES-project - Assembling Reconfigurable Endoluminal Surgical system.*

*Figure 31a. Concept of the project: Miniaturized robotic modules are ingested and assembled in the stomach cavity. The assembled robot can then change its configuration according to the target location and task.*

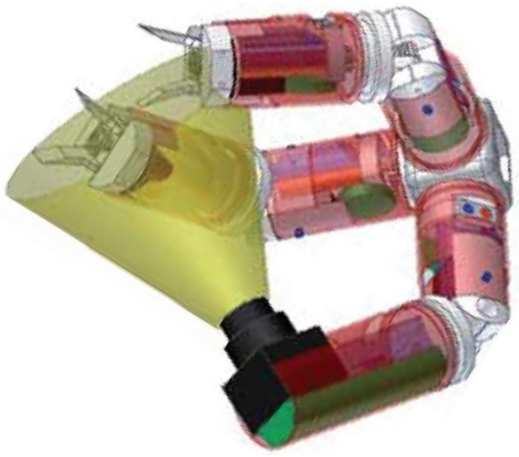

*Figure 31b. Schematic drawing of robotic module with camera and two end-effectors.*

*Figure 31c. Prototype of assembled robot used for experimental studies*

*Figure 31d. Design and prototype of reconfigurable external masterdevice (= manipulator)*

but in large scale, to the intra-abdominal modular mini-robot he wants to control. He then moves the controller's modules as he tries to find a suitable configuration for his miniature assistant. Two different types of modules were designed: a connection module and a camera module **(Figure 32a)**. All modules are symmetrical in the $Z$ axis and are equipped with four active rotational servomotors which provide the assembled mini-robot with motion to provide 360° motion on the $Z$ (or $X$) axis for complete rotation of the module when connected. The intraperitoneal environment was simulated in order to investigate vision and motion of the modular mini-robot in relationship to the controlling capabilities of the modular controlling system (MCS). The MCS allows the user to immediately determine the conformation of the modular mini-robot. Real-time mode allows for standard use of the mini-robot executing pair commands as needed. This is the simplest way to control the miniature robot when it was stationary, for example, while operating on tissues.

***b) Micro-robots controlled by local magnetic actuation***

As demonstrated in experimental trials on animals, dexterous miniature robots with integrated motors [74,77] may allow tissue manipulation and the performance of simple surgical tasks, but they cannot be used to retract an organ or tissue while manipulating it. Accordingly, a retraction task is typically performed through an additional incision to allow triangulation [80]. Several solutions have been proposed and tested on real working scenarios in order to perform retraction tasks by exploiting magnets as previously described [81]. Magnetic coupling is one of the few known natural phenomena that can be harnessed to transmit motions across a physical barrier, and thereby eliminate multiple incisions. This approach enables multiple fully insertable surgical instruments to be deployed through a single tiny incision, which move around inside the abdomen without access-point constraints. However, reliable and precise control of magnetic surgical tools is challenging due to the rapid decay of magnetic field strength with distance (which is particularly significant for obese patients) and in the challenge of modelling the interaction with human tissues.

Although the use of magnets improves the stability of robotic devices and allows the retraction of organs, it is generally difficult to accurately steer the internal robot. Such a robot combines the advantages of magnetic anchoring for positioning and anchoring purposes **(Figure 33a)**; furthermore, it is integrated with motors to enable two active DOF, thus improving the dexterity of the platform.

An external device will change the magnetic field from the patient's skin, thereby causing magnetically coupled surgical tools to move inside the body **(Figure 33b)**. This novel type of robotic actuation, where the source of motion is external to the human body, while the part in motion is inside the abdomen, would allow high dexterity, while minimising access trauma **(Figure 33c).** Magnetic anchoring of surgical tools will also allow repositioning the workspace along the four abdominal quadrants without additional incisions. The first clinical studies [71,82] have proved the feasibility of using magnetic- driven endoscopic cameras **(Figure 33 d,e).**

***c) Concentric tube robots – active cannula***

While many robotic systems have been developed for intravascular interventions, as well as natural orifice surgery through other body orifices or single abdominal ports, comparatively few systems have targeted endonasal surgery. This is likely due to the smaller size of the nostril compared to other natural orifices (e.g. the throat, single abdominal port, etc.). The few endonasal robotic systems that do exist are best considered in terms of their function within the entire surgical workflow [83,84].

A recently invented robot design that matches these characteristics is the concentric tube robot concept **(Figure 34a),** which is also known as the active cannula (mechanics-based models of these robots have been developed over the past several years [71,83,84], and the latest models can describe the shape of the device for the general case of many arbitrarily tubes, with arbitrary pre-curvatures, in the presence of arbitrary external loading. These advanced models lay the foundation for adaptation of concentric tube robots for specific surgical procedures, and progress has been made in applications including cardiac surgery, neurosurgery **(Figure 34b)**, lung interventions, and endonasal surgery [84]. Other options might be 6 DOF micromanipulators as proposed for eye surgery [85].

In urology, these robots offer many potential advantages. Current da Vinci instruments are limited in their size by the underlying wire and pulley architecture. Concentric tube robots have reached a level of maturity that may now enable purpose-specific systems which can be used in the context of biopsies, ablative therapies or micro-laparoscopic robotic platforms [71].

## 6. FUTURE DEVELOPMENT OF ROBOTIC SURGERY IN UROLOGY

Based on the enormous developments in the field of robotic surgery and the clinical monopoly of Intuitive Surgical it is not easy to predict the future course of robotic surgery in urology. Over the years, Intuitive Surgical has built barriers to new entry, including superior product offerings, intellectual property protection, multiple regulatory

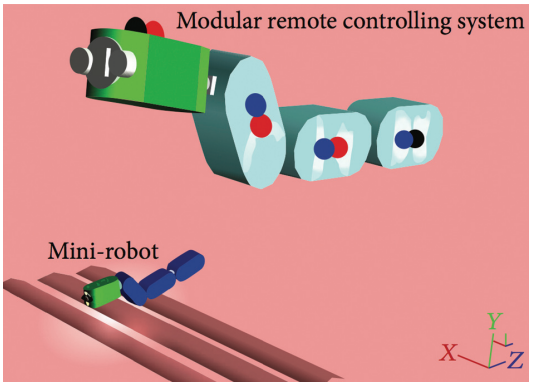


*Figure 32. In silico investigation of a surgical interface for remote control of modular miniaturized robots (according to Zygomalas et al. ) Two different types of modules are designed: a connection module and a camera module. The micro-robots are controlled by external macro-device (remote controlling device). All modules are symmetrical in Z axis and equipped with four active rotational servomotors, which provide the assembled mini-robot with motion even to provide a 360° motion on axis Z (or X) for a complete rotation of the module when connected.*

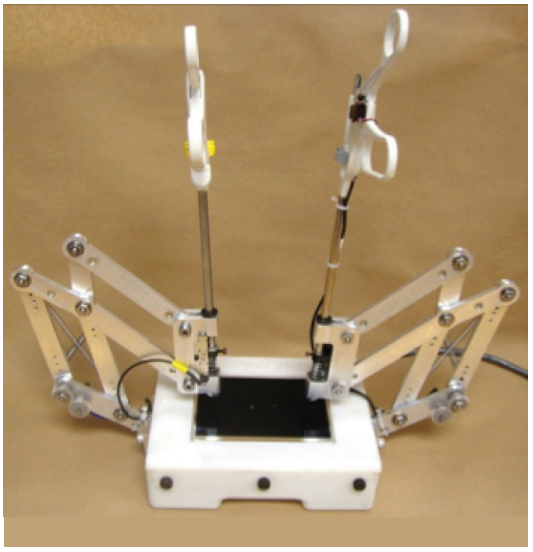

*Figure 33c. Prototype of external manipulator to be anchored to the skin of the patient.*

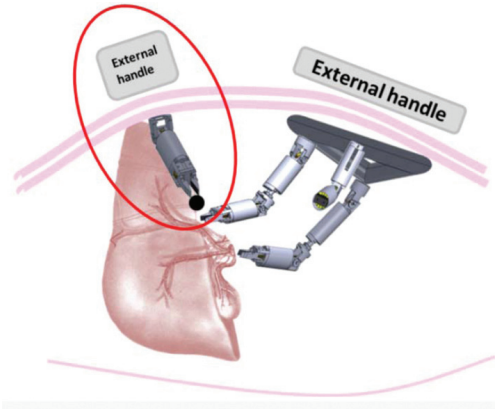


*Figure 33. Microrobots controlled by external magnetic actuation.*
*Figure 33a. Concept of external magnetic actuation*

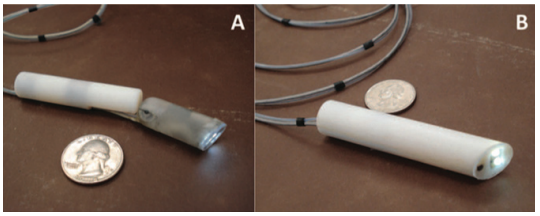


*Figure 33d. Prototype of magnetically controlled endoscopic cameras*

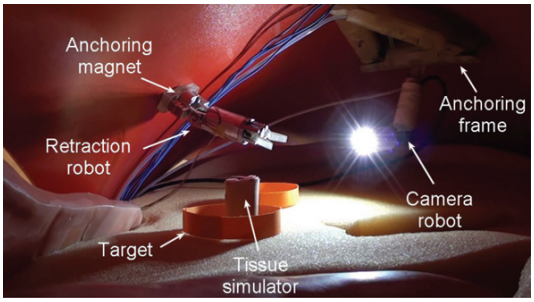


*Figure 33b. Simulation of endoscopic scenario during laparoscopic procedure with external magnetic actuation of retractor and camera*

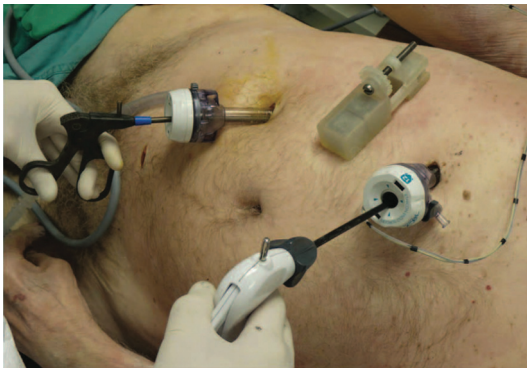

*Figure 33e. First clinical trial with magnetically endoscopic camera (courtesy of D. Herrel).*

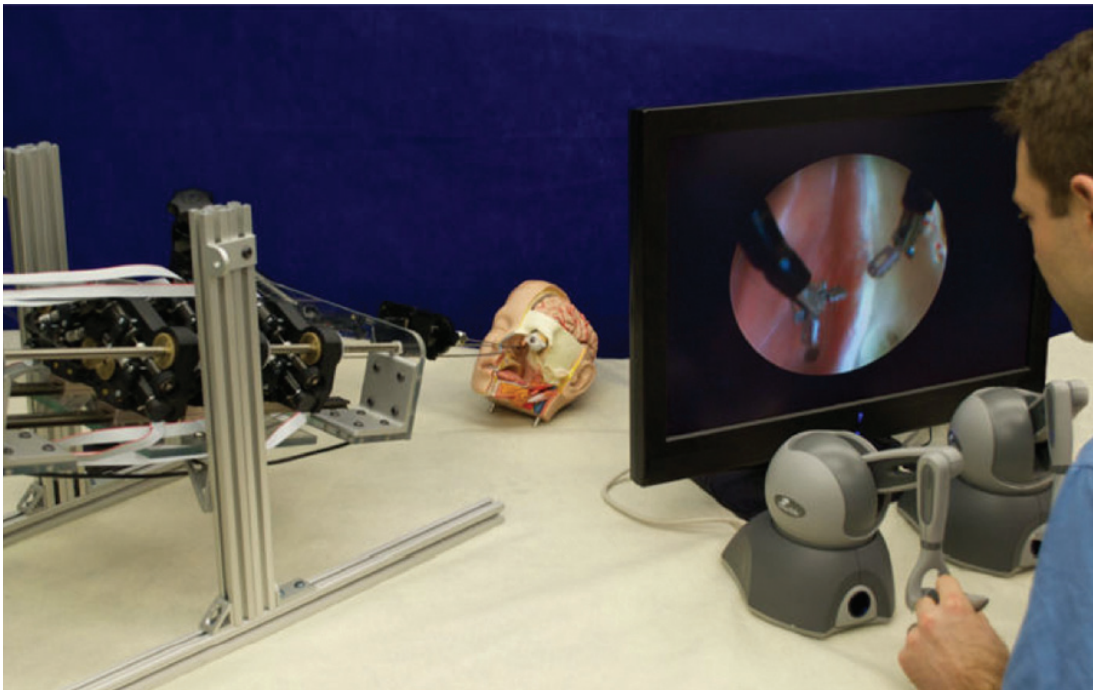

*Figure 34a. Active cannula – concentric tube concept.*

*Experimental setup using active cannula robot for intranasal video-endoscopic micro-surgery (Vanderbilt University)*

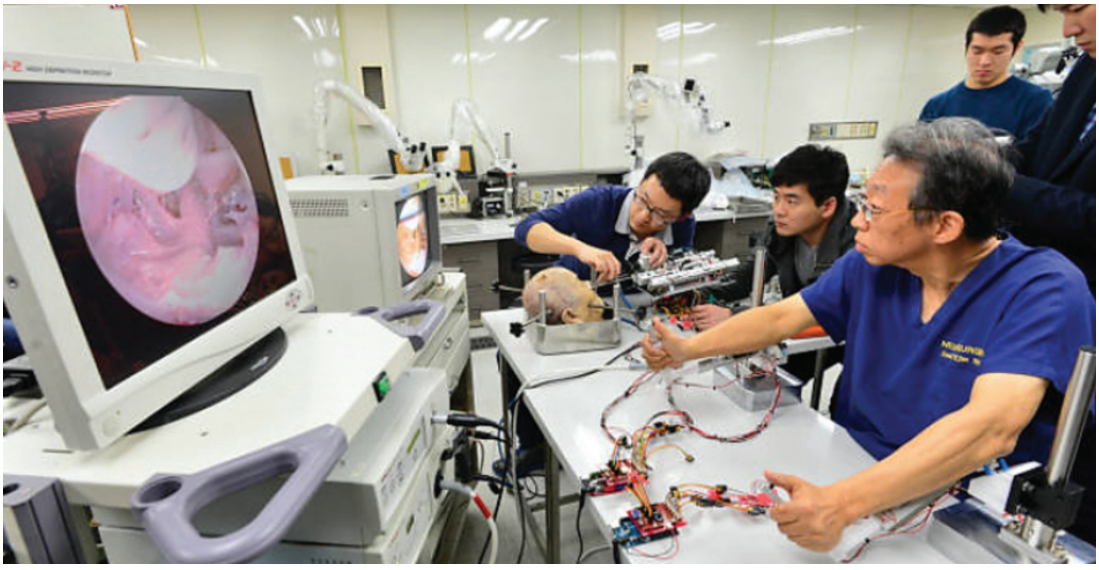

*Figure 34b. Demonstration of video-endoscopic assisted microscopic brain-surgery using active cannula (Severance Hospital, Korean Institute of Science and Technology).*

clearances, a large installation base, worldwide training centres, strong customer relationships, and an excellent balance sheet.

However, expiration of the company`s existing key patents in 2015 and 2016 poses a serious challenge. These include patents acquired from IBM and Computer Motion and others which stemmed from the initial DARPA programme, which spawned Intuitive Surgical. Once these patents expire, competitors can utilise these technologies in the market place, and Intuitive Surgical`s competitive advantage will be lost. In addition, TransEnterix and Titan Medical will be introducing their own robotic surgery platforms.

The costs for the SPORT-system (Titan Medical) are expected to be around 800.000 USD compared to 2.1 USD for the da Vinci XI system [86]. Even though Titan Medical is targeting an expansive market that has not been fully tapped by Intuitive Surgical, it will still face competition from other developmental surgical robot companies. TransEnterix will most likely be Titan Medical's main competitor (besides the da Vinci SI), and because TransEnterix will have a head start in the US market due to its expected timeline of milestone events, Titan Medical will have some ground to make up following the US launch of its system. This will possibly result in new business models: Instead of selling at about $1,000 for the disposable SPIDER device for every surgical procedure, TransEnterix may sell the SurgiBot to the hospital for a one-time fee of $500,000, and then charge $1,000 for the disposable instruments plus an annual service fee of ~$50,000 [87]. At the same time, it should be noted that Titan's SPORT Surgical System offers more sophisticated software and imaging systems than TransEnterix's Surgibot. The costs of both systems will be significantly less than the da Vinci XI system, which allows use of the SP-platform.

The designs of the da Vinci systems proved to be very ergonomic and efficacious. Besides the cost issue, there are no doubts about the use of this advanced technology to achieve similar functional and oncologic results compared to open or laparoscopic surgery with the proven advantages of better ergonomics and a shorter learning curve for the surgeon, less early morbidity for the patient, and thus better long-term outcomes for the health care systems.

Based on this, all other developments will have to stand the test of time. Most of the developments are focussing of single-port surgery **(Table 3b)**, where the ideal indications in urology are not frequent (i.e. pyeloplasty) compared to cholecystectomy. Kaouk *et al.* [46] had to use additional ports (i.e. hybrid-LESS) in 4 of 11 cases of robotic LESS-prostatectomy. Reduced working space will become an issue. It is unlikely that these devices will become our routine approach to radical prostatectomy. Similarly, even the advocates and developers of such devices assume that "mechatronic support tools which solve all of the current existing barriers to NOTES remain closer to vision than to reality" [65].

With regard to the state of alternative console-based robotic devices mimicking classical robot-assisted surgery **(Table 2b)**, there may be several ways to improve the design of robotic arms (i.e. light-weight, smaller size, mounted on the OR-table, tactile-feedback of instruments, motorised arms), however, the da Vinci console is perfectly designed. Thus, all other proposed solutions are critically assessed. It is obvious that Intuitive Surgical has advanced in the last decade **(Table 4)** and includes projects such in space-operations.

On the other hand, all these devices have to be compared with cost-effective bedside solutions using 3D-HD-videotechnology and 6-DOF instruments, respectively, and mechatronically supported systems in combination with surgical seats such as the ETHOS-platform **(Table 4).**

NOTES will not be a real option for frequent urologic indications such as radical prostatectomy or partial nephrectomy. This depends on the individual anatomy and may not change even with the development of highly sophisticated robotic devices. The option of triangulation may facilitate targeted, highly precise surgical actions such as dissection and clipping, when such platforms are brought to the desired position. However, such procedures are currently very time-consuming due to difficulties controlling various DOF of the system, the limited working space (i.e. tunnel view), and the essential coordination of the individual actions of the team members.

On the other hand, endourology may benefit from such developments e.g. when using robot-assisted flexible ureteroscopy [76]. One example is the feature of visual tracking developed for the Anubis-platform [66]. Also micro-robots may be useful for transvesical surgery (i.e. en-bloc removal of bladder tumours) as recently proposed [88].

## V. NAVIGATION, ENHANCED VISUALISATION AND VIRTUAL REALITY FOR SURGERY

Minimally invasive surgical procedures usually require meticulous handling of tissue, involve a narrow working space and limit the surgeon's sense of orientation in the human body. Improvements in tissue handling and working within a narrow working space might be achieved by the use of robotic assistance. Soft tissue navigation may improve orientation by visualising important targets and risk structures intra-operatively, thereby possibly improving patient outcome. Prerequisites

***Table 4a. Features of imaging techniques assisting endoscopic surgery – real-time direct visualization***

| Technique | Principle | Indications | Purpose of imaging | Comment |
|---|---|---|---|---|
| Laparoscopic ultrasound | Real-time B-mode and colour duplex | Laparoscopic / robotic partial nephrectomy | Demonstration of extension and vascularisation of tumour | Recommended by EAU-guide-lines |
| Transrectal ultrasound | Real-time B-mode and colour duplex<br><br>3-D-TRUS | Laparoscopic / robotic radical prostatectomy | Demonstration of course of neuro-vascular bundle and prostate capsule | Clinical pilot studies studies with and without marker-based navigation |
| Digital Fluoroscopy | Real-time fluoroscopy with and without contrast dye | (Robotic) flexible ureteroscopy<br>Percutaneous neph-rolithomy<br><br>Laparoscopic partial nephrectomy | Demonstration of renal collecting system for orientaion<br><br>Demonstration of laparoscopic instruments | Routine during endo-urologic procedures (EAU-guidelines)<br><br>Only used in a pilot study together with Dyna-CT-based navigation |
| Photodynamic diagnosis (PDD) | Intravesical application of hexaminolaevu-linic-acid<br><br>Oral application of 5 aminolaevulinic acid | TUR Bladder<br><br>Laparoscopic partial nephrectomy<br>Laparoscopic radical nephrectomy | Visualization of tumour by induced fluorescence to increase detection<br><br>Visualization of tumour by induced fluorescence to determine complete resectiom | Recommended for Cis in EAU-guideline<br><br>Clinical pilot studies studies<br>Technique frequently used in brain surgery |
| Isocyanine green (ICG) | Intravenous application of ICG<br><br>Intraprostatic application of ICG | Laparoscopic and robotic partial nephrectomy<br><br>Laparoscopic pelvic lymph node dissection | Demonstration of remaining vascular supply of tumour by absence of fluorescence<br><br>Demonstration of course of lymphatic vessels from prostate | Clinical studies are on-going<br><br>Pilot study presented |
| Narrow band imaging (NBI) | Digital restriction of used light spectrum of HD-video-imgae | TUR Bladder<br>Diagnosis of upper tract tumours | Better visualisation of tumours | Clinical studies show advantages for low grade tumours |
| Storz Professional Image Enhancement system (SPIES) | Digital postprocessing of HD-video-image | TUR Bladder<br>Diagnosis of upper tract tumours<br>Laparoscopic partial nephrectomy | Better visualisation of tumours | Clinical studies pending |
| Optical coherence tomography (OCT) | Emission of near-infrared light to create create a cross-sectional image with a high spatial resolution bytransmission, scattering and reflection | TUR Bladder<br>Diagnosis of upper tract tumours<br>Diagnosis of renal biopsies | Creation of microscopic image to analyze architecture of tumours | Time-demanding, best use in combination with PDD<br>Upper tract tumours best suited Only clinical pilot studies |
| Multiphoton microscopy (MPM) | Simultaneous absorption of 2-3 low-energy (near-infrared) photons to cause a non-linear excitation | Robotic radical prostatectomy | Real-time visualization of neuro-vascular bundle or prostatic fascia | First in-vivo test in rat-model |

*Table 4b: Features of imaging-fusion techniques assisting endoscopic surgery – indirect visualization*

| Technique | Principle | Indications | Purpose of imaging | Comment |
|---|---|---|---|---|
| Optical tracking | Placement of optical fiducials on laparoscopic or robotic instruments to identify spatial orientation | Laparoscopic / robotic radical prostatectomy<br>Laparoscopic partial nephrectomy<br>Robotic oesophagectomy | Visualisationof course of neuro-vascular bundle and prostate capsule Orientation of instruments in relationship to tumour (kidney, oesophagus) | Clinical pilot studies studies with laparoscopic and robotic applications |
| Stereoendoscopic visualization | Semi-transparent overlay of augmented reality using a modified 3D-to-3D iterative closest point (ICP) registration | Laparoscopic/ robotic partial nephrectomy | Visualisation of extension of tumour | Pilot-studies<br>published with problems of 3D (virtual reality) to 2D (video-image)<br>First combination of Dyna-CT and Da Vinci system (full 3D-to-3D-overlay) |
| Marker-based navigation | Placement of coloured markers on target organ Segmentation of intraoperatively taken image (ie. TRUS, Dyna-CT) | Laparoscopic / robotic radical nephrecomy<br>Laparoscopic partial nephrectomy | Visualisation of tumour and course of neurovascular bundle by virtual reality | Pilot-studies published<br>First combination of Dyna-CT and Laparoscopy |
| Diffusion tensor magnetic resonance imaging (DTI) | Sensitivity of the water protons measured in the microstructural environmen | Laparoscopic / robotic radical prostatectomy | Assessment of the entire periprostatic nervous plexus and of all bilateral fibers | Pilot-studies published |

for navigation are its integration into the surgical workflow and accurate localisation of both the instruments and patient.

Imaging technologies have undergone significant developments, resulting in their current important role in clinical oncology [89]. The field has expanded greatly and now comprises various modalities including ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT). Because each modality has its specific advantages and disadvantages, combining different techniques such as PET and CT has become the practice for tumour detection, staging, and treatment evaluation. However, when surgery is required, translation of these molecular images to the operative field remains a challenging obstacle.

Advances in molecular imaging (MI) technology enable the non-invasive imaging of specific molecular pathways which are fundamentally involved in disease processes [89]. MI evaluates the molecular signature and changes in cellular physiology and function rather than anatomy. These molecular pathways are likely to be expressed earlier than anatomic deformation, allowing more sensitive representations of the disease process. In addition, detecting tumours via their unique molecular signatures may help to significantly improve the specificity of diagnoses. Ideally this information is put in the hands of the surgeon in real-time imaging that may warrant image-guided surgery (IGS).

### 1. OPTICAL IMAGING (Table 4a)

Intra-operative assessment of the tumour-free margin is critical for prognosis of the patient. Currently the surgeon relies on the visual appearance and digital palpation of the tumour. Optical imaging tech-

niques have the potential to provide real-time visualisation of the tumour during its surgical removal. In optical imaging, properties of light emitted from a light source are exploited to image the anatomic or chemical characteristics of tissue.

For this purpose, either the properties intrinsic to the tissue or analogous to many radiolabelled agents, using ligands conjugated to an optically active antenna to target a recognized disease biomarker are used.

### *a) Fluorescent techniques*

In 2007, Davila et al. [90] evaluated whether fluorescent tracers could consistently label the neurovascular bundles (NVBs) and major pelvic ganglion (MPG) following intra-cavernosal penile injection and thus facilitate nerve-sparing during radical prostatectomy in a rat model using different fluorescent substances such as Fluoro-Gold (FG), Fast-Blue (FB), Fluoro-Ruby (FR) or green fluorescent pseudorabies virus. The authors demonstrated that injecting FG into the rat penis 2–3 days before pelvic surgery may help identify the NVBs under fluorescent light, and suggested that FG acts as a nerve tracer during pelvic surgery in animals.

#### 1. Photodynamic diagnosis

Photodynamic diagnosis (PDD) for cystoscopy represents an optical technique using fluorescence as a contrast mechanism to indicate pathologic tissue. It is based on the phenomenon of concentrations of fluorescent molecules differing in normal and pathologic tissue. Absorption of light of the appropriate wavelength excites the electrovibrational state of fluorophore molecules. When these molecules relax to ground state, a photon is emitted to account for the energy difference. The fluorescent photon has less energy than the excitation photon; since the energy of light is inversely proportional to its wavelength, the emitted light has a longer wavelength than the illuminating light. PDD can be based on either the presence of natural fluorescent molecules (endogenous or autofluorescence) or the administration of agents that increase the production of fluorescent molecules (exogenous fluorescence).

Currently, 5-aminolaevulinic acid (5-ALA), and its ester hexaminolaevulinate (Hexvix) are used most often. Endoscopes with specially developed light sources and yellow filters are used [91,92]. A foot pedal or push-button on the camera enables the switch from white-light cystoscopy (WLC) to PDD-mode. By illuminating the bladder wall with blue light, the malignant tissue appears intensely pink on a blue background **(Figure 35a).**

For cystoscopy, the fluorescent agent can be administered intravesically, whereas for laparoscopy or open surgery oral administration is required. This can only be accomplished with 5-ALA due to oral toxicity of Hexvix. In the microsurgical treatment of glioblastoma, PDD-assisted excision of the tumour is routinely performed **(Figure 35b).** In laparoscopic urological surgery there are only a few published attempts. In 2009, Hoda et al [93] reported their experience with PDD after oral administration of 5-ALA for assessment of tumour type and surgical margins in laparoscopic partial nephrectomy **(Figure 35c).** PDD with 5-ALA was able to predict the type of lesion with an accuracy of 94% and a positive predictive value of 98%. In the same year, Adam *et al.* [94] reported the first prospective study to investigate the feasibility of intra-operative identification of positive surgical margins during open and laparoscopic radical prostatectomy. Thirty-nine patients received 20 mg/kg body weight 5-ALA orally and underwent laparoscopic or open radical prostatectomy. A PDD-suitable laparoscopy optic was used. PDD with 5-ALA–induced fluorescence proved to be a feasible and effective method for reducing the rate of PSM, with a higher sensitivity during laparoscopic radical prostatectomy **(Figure. 35d)**.

#### 2. Isocyanine green application

Conventional fluorescent techniques use probes in the visible light spectrum (~400-750 nm), which is not optimal for intra-operative image-guided surgery. Over the last decade, the development of near-infrared fluorescence (NIRF) cameras which are able to visualise fluorophores and nanomaterials has led to a revolution in optical imaging [95]. This combination provides increasing tissue penetration and allows more precise localisation of cancer. Nevertheless, it should be noted that signal penetration of this technology remains below 1 cm. Thus, the properties of near-infrared (NIR) optical imaging are suited for real-time visualisation of (superficial) lesions during surgery. Ultimately, intra-operative visualisation of tumour margins may improve radical resection without unnecessary damage to healthy tissue [89].

NIRF angiography after isocyanine green (ICG) administration allows for detailed anatomy of the vascular system and has been used to distinguish renal tumours from normal tissue, by highlighting the renal vasculature **(Figure 36a)**, however, the tumour is not fluorescent **(Figure 36b).** This technology has the potential to maximise oncologic control and nephron sparing during robotic and laparoscopic **(Figure 36c)** partial nephrectomy [96,97]; Janetschek, personal communication).

### *b) Optical enhancement techniques*

Based on digital HD-technology, there are optical image enhancement techniques designed for endoscopy to enhance the contrast between mucosal surfaces and microvascular structures without the use of dyes [92].

In narrow band imaging (NBI, Olympus, Japan), the increased vessel density of cancer tissue is used to achieve optical enhancement of the tissue microvasculature differentiating between tumour

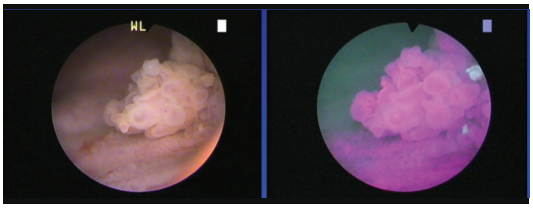


*Figure 35. Photodynamic diagnosis using either 5-aminolevulinic acid (5-ALA) or hexaminolevulinate (Hexvix).*

*Figure 35a. Fluorescence of bladder tumour after intravesical instillation of hexaminolevulinate using a yellow optical filter.*

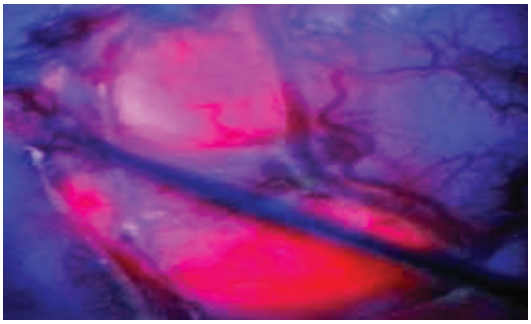

*Figure 35b. Fluorescence-assisted microsurgical excision of glioblastoma after oral application of 5-ALA.*

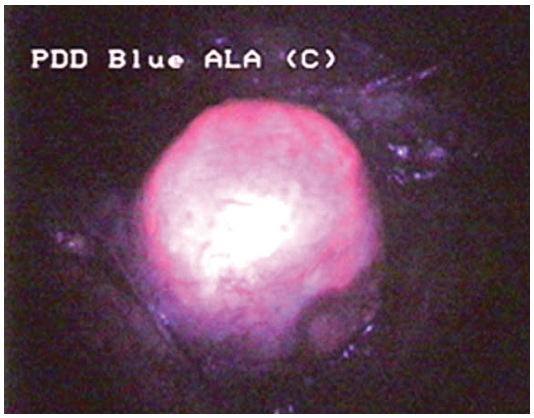


*Figure 35c. Fluorescence-assisted laparoscopic partial nephrectomy after oral application of 5-ALA with fluorescence of tumour.*

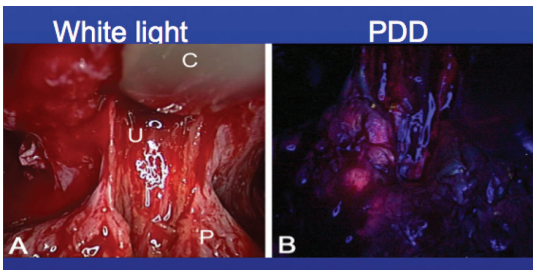


*Figure 35d. Fluorescence-assisted laparoscopic radical prostatectomy with fluorescence of apical tumour after oral application of 5-ALA.*

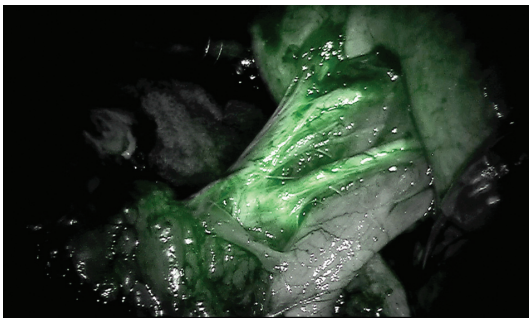

*Figure 36a. Green fluorescence in renal artery 20 seconds after intravenous ICG-administration.*

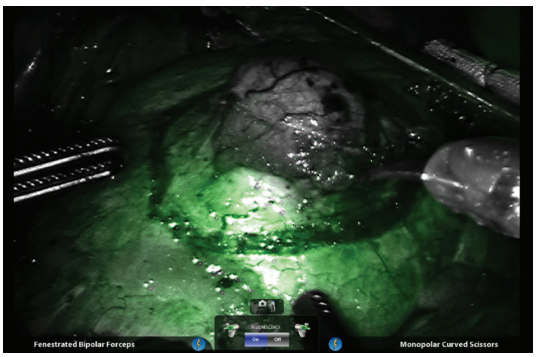


*Figure 36b. Normal renal parenchyma shows green fluorescence in contrast to the renal tumour during robotic partial nephrectomy with Da Vinci SI-system (Fire-fly).*

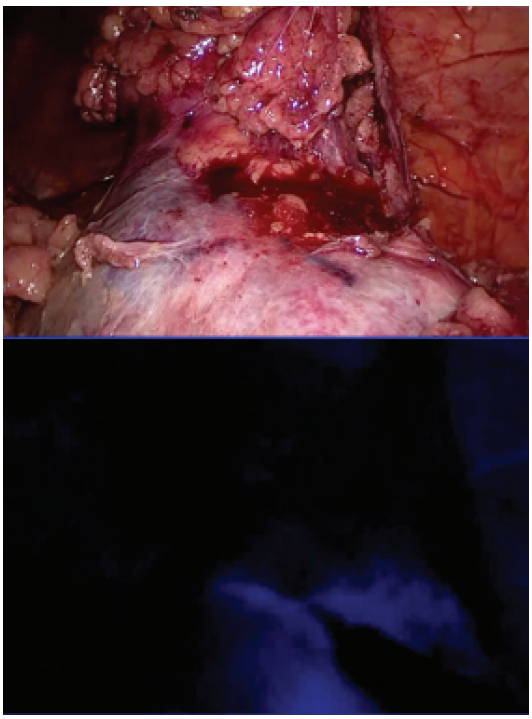

*Figure 36c. ICG-application during laparoscopic partial nephrectomy using Karl Storz System. Normal parenchyma with blue fluorescence (courtesy to G. Janetschek).*

tissue and normal urothelium. To achieve this enhancement, two bands of light (blue at 415 nm and green at 540 nm), which are both absorbed by haemoglobin, are used **(Figure 37a).** While the blue light is absorbed in superficial capillary networks, the green light displays subepithelial vessels **(Figure 37b)**. A combination of both results in a high-contrast image of the tissue surface (98).

As with NBI, the Storz Professional Image Enhancement system (SPIES; Karl Storz, Tuttlingen, Germany) enhances the blue and the green wavelengths of the transmitted image and a three-colour image is built from the components of the spectral input. This effect is achieved by suppression of the red portion of the spectrum using post-imaging processing. By adding different colours to the blue- and green-coloured image (e.g. orange or violet), three types of SPIES images are produced, giving the surgeon three different options for visualisation **(Figure 37c)**. In addition, SPIES CHROMA **(Figure 37d)** intensifies the colour contrast in the image [92]. Clearly visible structure surfaces are given added emphasis, while retaining the natural colour perception in the image. Only preliminary studies are published on the applicability of SPIES-technology during laparoscopic partial nephrectomy (Porpiglia, personal communication).

***c) Optical coherence tomography***

Similar to ultrasonography, optical coherence tomography (OCT) produces a high-resolution image of the tissue structure below the surface. In contrast to ultrasonography, NIR light is emitted, and transmission, scattering and reflection of this light is used to create a cross-sectional image with a high spatial resolution of 10–20 µm. The tissue penetration is only 1.6–2 mm, which is adequate to identify the majority of epithelial cancers. Compatibility of the OCT probes with endoscopes gives the surgeon the ability to perform a quasi-real-time pathological investigation during endoscopy **(Figure 38a)**. Despite promising results, the use of OCT in the bladder still presents a technical challenge. Due to the smaller calibres, OCT seems to be most promising for detection of ureteral tumours **(Figure 38b).** Similarly, OCT may also be used in combination with laparoscopy for detection / classification of renal tumours. To date, only percutaneous application of OCT has been described **(Figure 38c)**. The limitation of OCT is penetration depth. During OCT, the cavernous nerve was distinguished as an intense linear structure separate from the adjacent tissues in *in vivo* experiments on Sprague–Dawley rats; however, the discrimination between adjacent prostatic tissues and nerves was not adequate in *ex vivo* human prostatectomy specimens [99].

***d) Multiphoton microscopy***

Another promising solution in novel non-linear optical imaging technology is multiphoton microscopy (MPM). MPM relies on the simultaneous absorption of two (or three) low-energy (near-infrared) photons to cause non-linear excitation, which greatly reduces the potential for cellular damage. Excitation only occurs where there is sufficient photon density (at the point of laser focus), providing intrinsic optical sectioning with a resolution equivalent to traditional confocal microscopy. Tissue penetration is greater than standard confocal microscopy because absorption and scattering are greatly reduced at NIR wavelengths compared with the visible or ultraviolet spectrum [100,101].

While the miniaturisation of MPM for integration with robotic surgical equipment is currently in progress, Tewari et al. recently carried out a prospective study to assess the feasibility of using MPM/ITE for structure identification in excised prostatic and periprostatic tissue. In all cases, the MPM findings were confirmed by comparison with the gold standard histopathology **(Figure 39a).**

The authors concluded that MPM/ITE could be used to identify pathologies, obtain cancer-grading information and identify sites of inflammation. Most importantly, it provides the ability to discriminate between pathologies and benign inflammation, which can enable more accurate decisions regarding tissue removal. This means that you may be able to use the endoscope as a microscope **(Figure 39b).**

Once technology to translate this imaging modality to the operating room becomes available, it should enable more accurate surgical decision-making. Several technological challenges still remain to make this translation a reality; however, extensive research is continually generating newer solutions for identified problems. Recently, the same working group showed the *in vivo* application of MPM to identify the neurovascular bundle in a rat model **(Figure 39c)**. Furthermore, this technique has been used to study *in vivo* circulation in rat kidneys [102].

## 2. IMAGE-FUSION TECHNOLOGIES (TABLE 4B)

Current interventional MI techniques such as positron emission tomography (PET) are being used to evaluate patients with soft-tissue metastases, particularly prostate, renal, testicular and bladder malignancies in oncology centres and could serve as a guide for ablative therapy [89]. Image fusion technologies and image-augmented navigation have been developed in several other fields and have tremendous potential for use in medical applications. These technologies have the potential to fully integrate preoperative molecular images in the operating room. Previously acquired images, such as CT and MRI scans, can be formatted into 3D image sets and linked to sensors that track the position of surgical instrumentation, in real-time, relative to the image set [103,104].

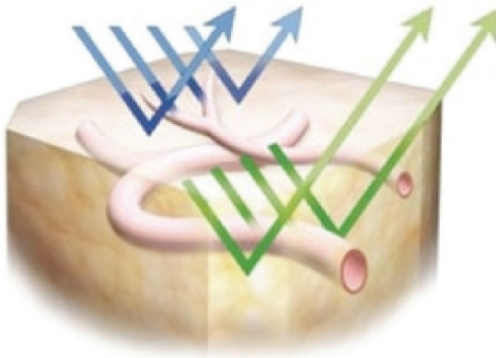

*Figure 37. Optical enhancement techniques.*

*Figure 37a. Narrowband (NBI) imaging: Principle of selective use of green and blue light being absorbed by haemoglobin to improve visibility of superficial bladder tumours.*

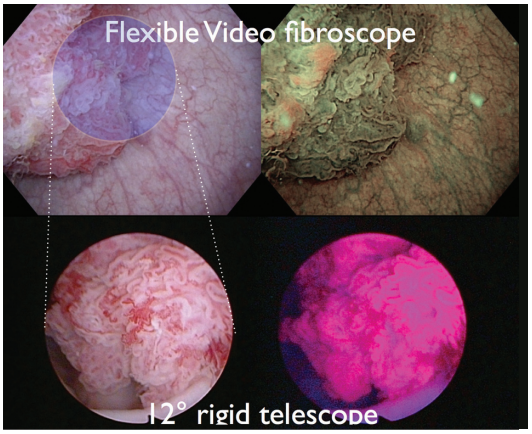


*Figure 37b. NBI-imgage (upper right) via a flexible HD-cystoscope compared with standard HD-white-light imaging (lower right) and PD (lower left).*

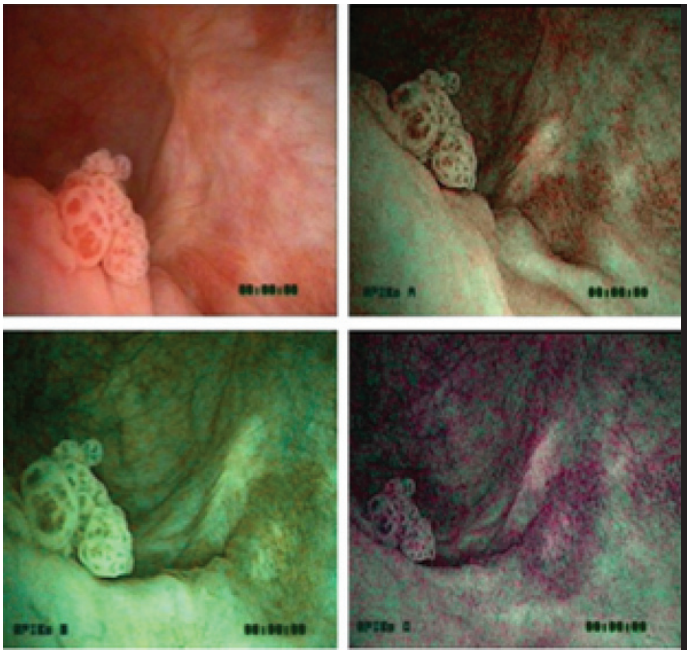

*Figure 37c. Storz Professional Image Enhancement system (SPIES): By adding different colours to the blue- and green-coloured image (e.g. orange or violet), three types of SPIES (A,B,C) images are produced. Here used for endoscopic imaging of a bladder tumour.*

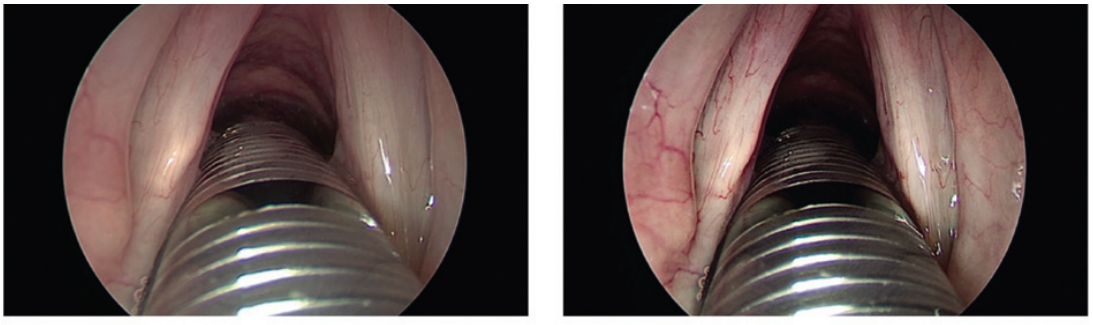


*Figure 37d. SPIES CHROMA intensifies the colour contrast in the image. Clearly visible structure surfaces are given added emphasis while retaining the natural colour perception in the image. Here enhancing the endoscopic view of the glottis.*

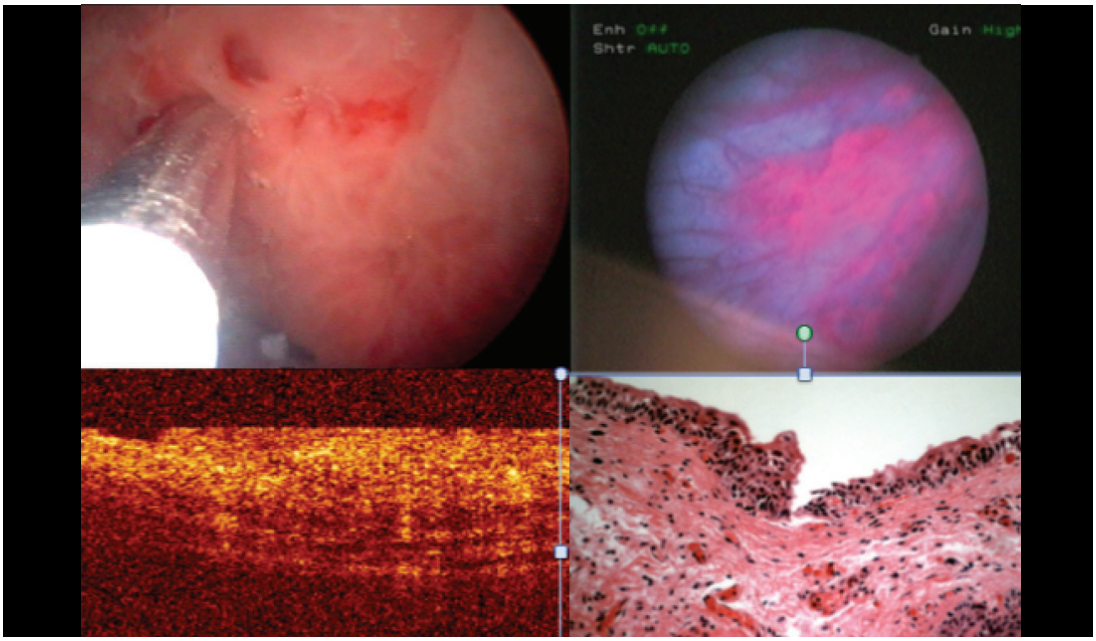


*Figure 38. Optical coherence tomography (OCT)*

*Figure 38a. Compatibility of the OCT probes (upper right) with endoscopes gives the surgeon the ability to perform a quasi real-time pathological investigation during endoscopy. Here identifying carcinoma in situ (lower left) also shown by PDD (Courtesy to H. Schmidbauer).*

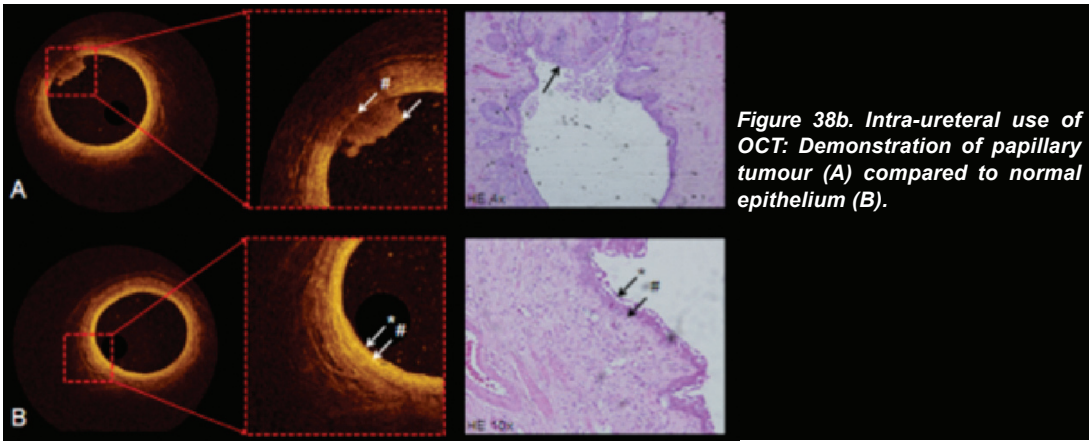


*Figure 38b. Intra-ureteral use of OCT: Demonstration of papillary tumour (A) compared to normal epithelium (B).*

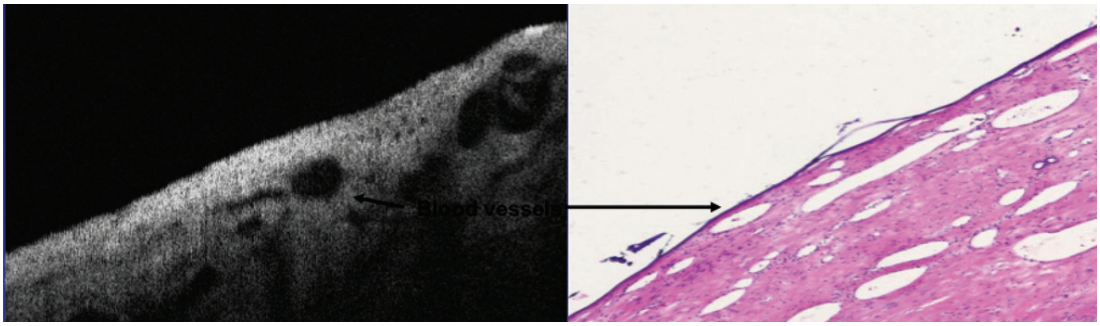


*Figure 38c. Percutaneous application of OCT via biopsy needle identifying a cystic tumour (courtesy to J. De la Rosette)*

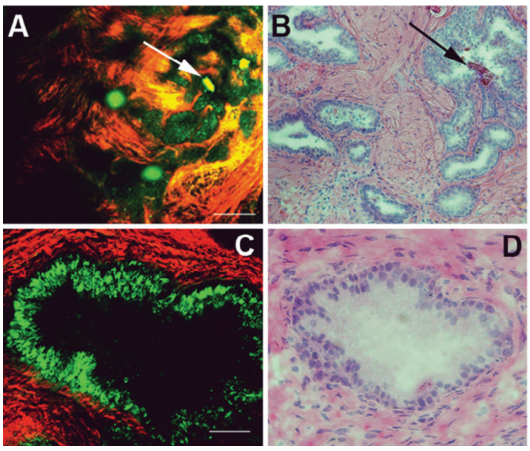


*Figure 39. Multi-photon microscopy (MPM)*

*Figure 39a. MPM image (A) shows acini containing structures that are probably concretions (green; shown by arrows) and collagenous stroma (red). Panel B shows an H&E-stained sample from a corresponding area. (C, D) Higher-magnification view of prostatic glands. The MPM image (C) shows acinar cells (green) and collagenous stroma (red). Panel D shows image of H&E-stained sections from corresponding area.*

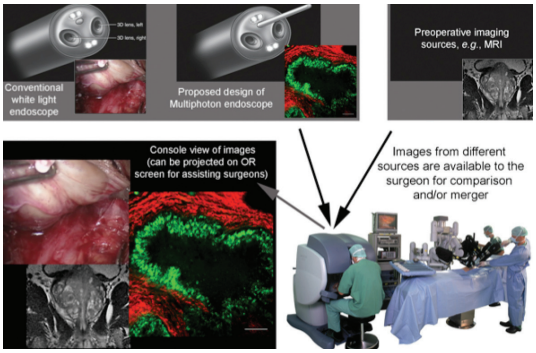


*Figure 39b. Vision of future application of multi-photon microscopy combined with MRI at the Da Vinci-console during robot-assisted radical prostatectomy.*

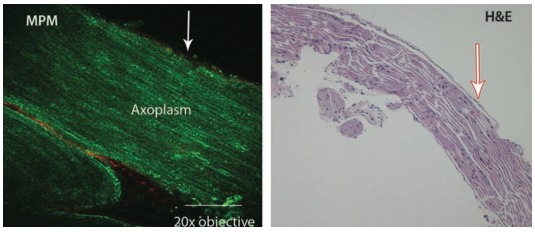


*Figure 39c. Real-time application of MPM in a rat model: Multiphoton microscopy (MPM) images and the corresponding hematoxylin and eosin stained histologic images for validation of the findings. Cavernous nerve at high magnification (20x)—the arrow shows the peri-neural sheath.*

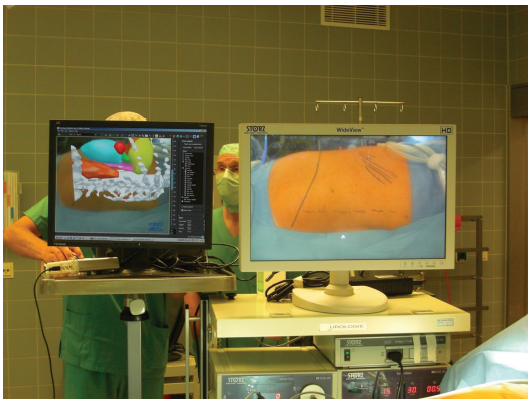

*Figure 40a. Intraoperative navigation during laparoscopic partial nephrectomy using 3D-CT-images as overlay (manual fusion) of segmented anatomical landmarks (ribs, spine, kidney with tumour) for*

*Figure 40a. Trocar placement (using the endoscopic camera)*

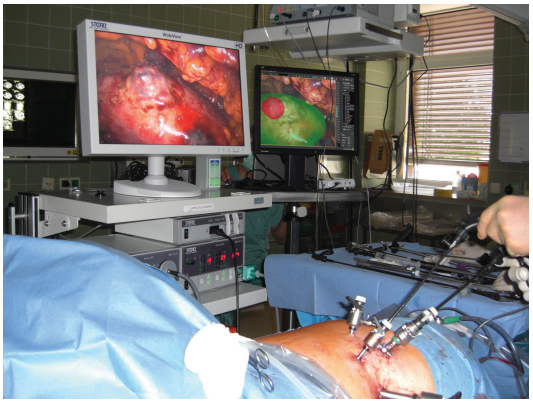

*Figure 40b. Dissection of kidney and tumour*

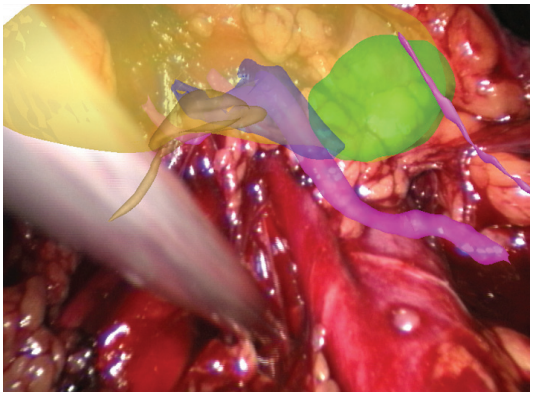

*Figure 40c. Dissection of renal hilar vessels*

By superimposing these images on a video-assisted view of the operative field (i.e. during laparoscopic or robotic procedures), or by co-registering these images with other imaging modalities and fusing them into one augmented compound image, it is possible to improve the surgeon's ability to localise anatomic boundaries. Providing augmented reality (AR) information in the endoscopic view holds great promise for surgeons and represents a great challenge for AR researchers. This helps to improve surgical accuracy. Augmented reality, may for example, enable rigid registration of an abdominal 3D patient model using radio-opaque markers placed on the abdominal skin [106]. The feasibility and benefits of this solution have been shown already in a human application [107]. However, at present, abdominal navigation systems are in experimental use and not yet available for routine daily surgery [108,109].

***a) Intra-operative navigation and renal tumour imaging***

Intraoperative imaging techniques which enhance the view of the operative field might provide better discrimination between tumour tissue and normal renal parenchyma and thus reduce the risk of PSM.

In 2009, Teber et al [108] described a novel soft tissue navigation system developed to enhance the surgeon's perception and to provide decision-making guidance directly before initiation of kidney resection for laparoscopic partial nephrectomy (LPN). During the soft tissue navigation, the navigation aids, a mobile C-Arm capable of cone-beam imaging, and a standard personal computer were used. The navigation procedure was divided into the following main steps: preoperative planning, insertion of navigation aids, planning registration, and real-time inside-out tracking and visualisation. New 3D virtual images of the kidney with neighbouring anatomical structures were created and visualised as an AR overlay of the endoscopic video image. An independent operator manually combined the reconstructed transparent 3D CT images with the real-time video-endoscopic images. Under AR-guidance, the renal vessels and renal tumours were found through the surrounding fat under AR-guidance **(Figure 40)** and in all patients tumour-free margins were obtained.

In a related investigation, Su et al. [110] investigated a marker-less tracking system for real-time stereo-endoscopic visualisation of preoperative CT-imaging as an augmented display during robot-assisted LPN. After generating a 3D surface model of the kidney, tumour and collecting system from the preoperative CT images, the 3D segmented kidney model was then imported onto the endoscopic video segment as an overlay. The tracking system used an automatic registration algorithm, for which several points on the kidney surface surrounding the renal mass were selected as fixed reference points. Triangulation methods were used to calculate the 3D positions of the points on the surface of the kidney and compute the corresponding orientation and position changes of the 3D model overlay. Finally, the system refined the registration using a modified 3D-to-3D iterative closest point (ICP) registration**.** In this way, the authors could track the kidney surface in real time by applying intraoperative video recordings and semi-transparent AR overlays of 3D models of the kidney, the tumour, and the collecting system **(Figure 41).**

***b) Intra-operative navigation during laparoscopic and robotic radical prostatectomy***

Surgical therapy for clinically localised prostate cancer has undergone a significant transition in the past several decades. With wide application of minimally invasive radical prostatectomy, there has been a renewed interest in image-guided navigation techniques that could potentially be used to supplement the tumour resection and visualisation/ preservation of neurovascular bundles (NVBs). Although this area of research is still in its infancy, these imaging techniques hold significant promise in achieving the ultimate goal of radical prostatectomy [111-114].

Several studies have investigated the role of transrectal ultrasound (TRUS) to guide the surgeon during radical prostatectomy and duplex ultrasound has been used to identify the blood flow within the NVBs [89,111-114]. Ukimura *et al.* [112]used real-time power Doppler TRUS to image the NVBs intraoperatively and reported that real-time TRUS helps in identification of the anatomic course of the NVBs, measures the number of visible vessels, and quantifies arterial blood flow resistive index in the NVBs.

In 2008, van der Poel et al [113] found TRUS with duplex ultrasound to be helpful in visualising the NVBs during release of the prostatic apex, identifying hypoechoic prostatic nodules, guiding at areas of suspected extra-capsular extension, and facilitating division of the posterior bladder neck. The authors also reported a lower rate of positive surgical margins with the use of TRUS during LRP and suggested that visualisation with this technology allowed for a more complete dissection and better cancer control as well as improved potency recovery. This approach, while innovative, posed several challenges. For example, operator dependency, variability in probe-positioning and low resolution for defining microscopic structures are the main drawbacks of this technique, resulting in its very limited usage [89].

Recently, an AR navigation system which conveys virtual organ models generated from TRUS onto a real laparoscopic video during radical prostatectomy was described **(Figure 42).** This system uses custom-developed needles with coloured pins inserted into the prostate as soon as the organ surface is uncovered. By tracing the navigation aids in real-time, it allowed registration between the TRUS image and laparoscopic video based on the 2D-3D correspondence points. With this registration, the system cor-

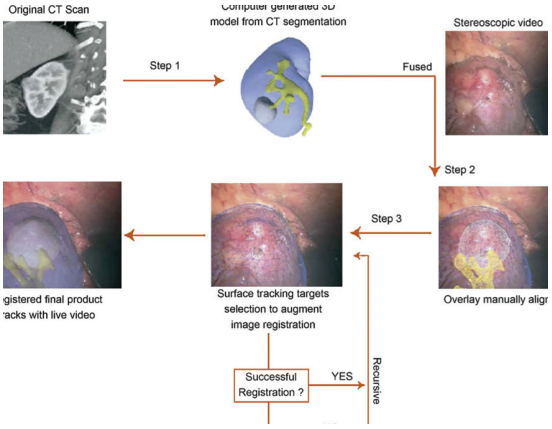


*Figure 41. Flowchart displaying steps needed to achieve successful three-dimensional registration of preoperative computed tomography (CT) image to live stereoscopic video.*
*ICD = iterative closest point.*

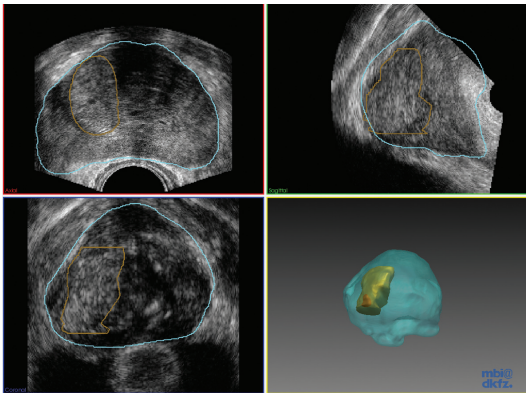

*Figure 42. Marker-based navigation during laparoscopic radical prostatectomy.*
*Figure 42a. Segmentation of intraoperative 3D-TRUS-image identifying suspicious areas and position of inserted needle (navigation aids).*

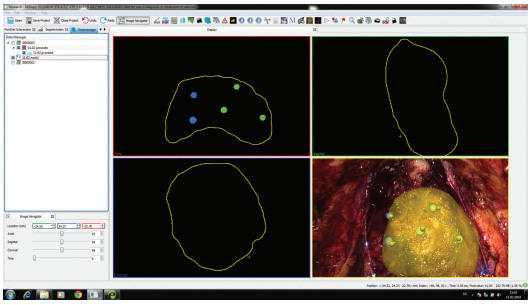

*Figure 42b. Calculation of endoscopic visualized markers and virtual markers as shown in the 3D-TRUS.*

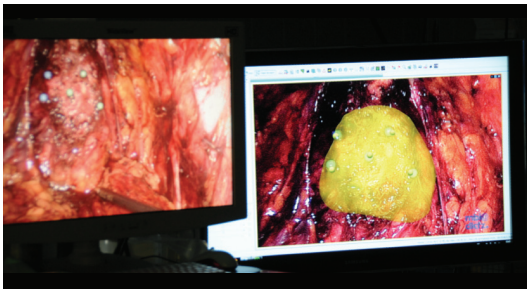

*Figure 42c. Real-time projection of virtual 3D-image on HD-image (right monitor). If the virtual markers and real markers are exactly overlaying, the virtual anatomy fits to the real endoscopic image. For performance of laparoscopic surgery a monitor without overlay is necessary.*

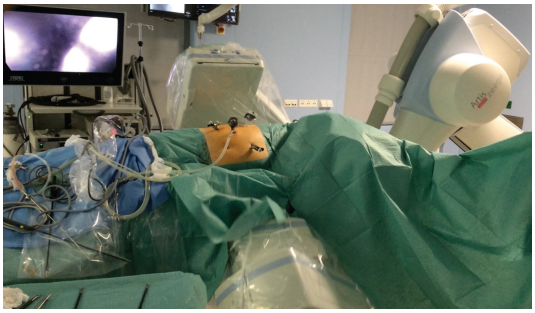

*Figure 43a. Marker based navigation using Dyna-CT for intra-operative imaging for laparosopic renal and adrenal surgery.*

*Figure 43a. Dyna-CT is rotating around the patient after port placement (retroperitoneoscopic adrenalectomy).*

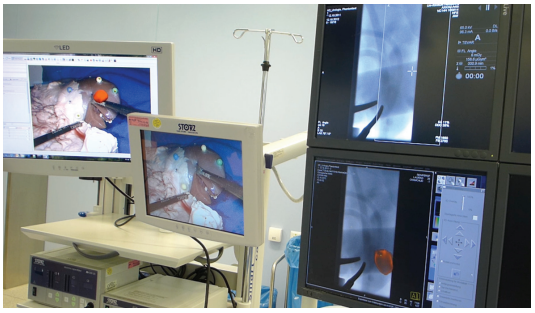

*Figure 43b. Intra-operative navigation in animal model with artificial renal tumour: The virtual image is fused on the endoscopic image based on the correct overlay of virtual and real markers. The virtual image of the tumour can be also displayed on the fluoscopic image of the Dyna-CT. Fluoroscopy allows real-time evaluation of correct angle of the laparoscopic instruments.*

rectly superimposed TRUS-based 3D information on an additional AR monitor placed next to the normal laparoscopic screen **(Figure 42c)**. First initial *in vivo* human application of the surgical navigation system in LRP was successful. No complications occurred, the prostate was removed together with the navigation aids, and the system supported the surgeons as intended with AR-visualisation in real-time (109,114).

Image-guided surgery is likely to be of increasing importance in the near future as treatments for urologic malignancies become more molecularly targeted. Within the field of urology, fluorescence guidance, surgical navigation and AR techniques hold promise for intra-operative identification of sentinel nodes, anatomical structures, and tumour lesions. Moreover, laparoscopic and robotic challenges lie in the further optimisation of targeted and/or activatable (hybrid) imaging agents and the integration between imaging agents and camera systems, thereby enabling more accurate fluorescence image guidance during surgical interventions, thus improving the detection and the therapy of all urologic tumours and enhancing intraoperative genito-urinary oncologic surgery.

***c) Complex intra-operative navigation during robotic and laparoscopic surgery***

The use of modern 3D-fluoroscopic technology originating from angiography and cardiology has enabled the performance of intra-operative computed tomography [115]. Using the Dyna-CT, the source is rotated around the patient creating a quasi-real-time 3D image of the patient **(Figure 43a).** This offers other applications of marker-based navigation, such as during laparoscopic partial nephrectomy. In addition, the fluoroscopic function of the system enables visualisation and control of laparoscopic instruments **(Figure 43b).**

Another high-tech option is the combination of Dyna-CT with the da Vinci device. To date, it was only possible to use electromagnetic and optical tracking of the da Vinci instruments based on pre-operative CT **(Figure 44)**. The combination of Dyna-CT with the da Vinci SI system enables featured tracking-based anatomical landmarks. This resembles the principle stereo-endoscopic visualisation with overlay of pre-operative CT images **(Figure 41).** However, there are two differences: (i) Dyna-CT enables intraoperative imaging, and (ii) the daVinci SI system allows a real 3D-to-3D overlay based on iterative calculation of the closest voxel **(Figure 45).** Of course, the combination of both large devices around the patient is challenging **(Figure 45a).**

***d) Diffusion tensor magnetic resonance imaging (DTI)***

DTI is an emerging technology to facilitate treatment planning (100). It is based on the sensitivity of the water protons measured in the microstructural environment [116, 117]. The main quantitative measurements of DTI include average diffusivity and fractional anisotropy. DTI, currently used for neuroimaging applications, enables tracing of the periprostatic nerves. Its utility in the human prostate was first reported by Sinha in 2004 [117]. In a recent study using DTI along with multi-parametric MRI, the authors demonstrated that of DTI, 2D-T2-weighted MRI and 3D-T2-weighted MRI, only DTI fibre tracking allowed assessment of the entire periprostatic nerve plexus and of all the fibres bilaterally at all levels. The authors concluded that this information could be useful for guiding proper nerve-sparing surgery using an intrafascial or extrafascial robotic approach [117] or even the graded NS approach, thereby ensuring recovery of erectile function after radical prostatectomy **(Figure 46 a,b).** Using OCT, the cavernous nerve could be distinguished as an intense linear structure separate from the adjacent tissues in *in vivo* experiments on Sprague–Dawley rats. However, the discrimination between adjacent prostatic tissues and nerves was not adequate in *ex vivo* human prostatectomy specimens [118].

## 3. OPEN SOURCE CONTROL SOFTWARE FOR SURGICAL ROBOTS

Patients and doctors are surrounded by many medical devices in the operating room as a result of recent advances in medical technology. However, these cutting-edge medical devices are working *independently* and not collaborating with each other, even though the collaborations between these devices such as navigation systems and medical imaging devices are becoming very important for accomplishing complex surgical tasks (such as a tumour removal procedure while checking the tumour location in neurosurgery). On the other hand, several surgical robots have been commercialised, and are becoming common. However, these surgical robots are not open for collaboration with external medical devices. A cutting-edge “intelligent surgical robot” will be possible following the collaboration of surgical robots, various types of sensors, and navigation systems. On the other hand, most of the academic software developments for surgical robots are “home-made” in their research institutions and not open to the public. Therefore, open source control software for surgical robots could be beneficial in this field.

The Open Core Control software was implemented on a surgical master–slave robot and stable operation was observed in a motion test. The tip of the surgical robot was displayed on a navigation system by connecting the surgical robot with a 3D position sensor through the OpenIGTLink. The accessible area was pre-defined before the operation, and the virtual fixture was displayed as a “force guide” on the surgical console. In addition, the system showed stable performance in a duration test with network disturbance. Communisation of the software interface is becoming a major trend in this field. Based on this perspective, the Open Core Control software can be expected to contribute to this field.

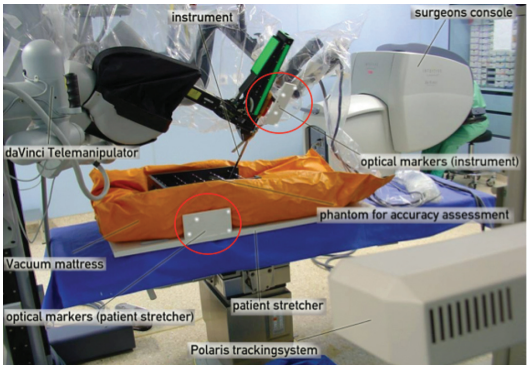


*Figure 44. Experimental evaluation of the use of optical tracking during robot-assisted laparoscopic esophagectomy.*

*Figure 44a. Experimental setup of the in-vitro study with the phantom put in a vacuum mattress, optical markers at stretcher and da Vinci-instrument.*

- mean error: 0.96 mm
- standard deviation: 0.78 mm
- minimum error: 0.02 mm
- maximum error: 3.72 mm

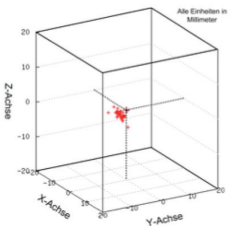


*Figure 44b. Demonstration of in-vitro testing to determine target registration error.*

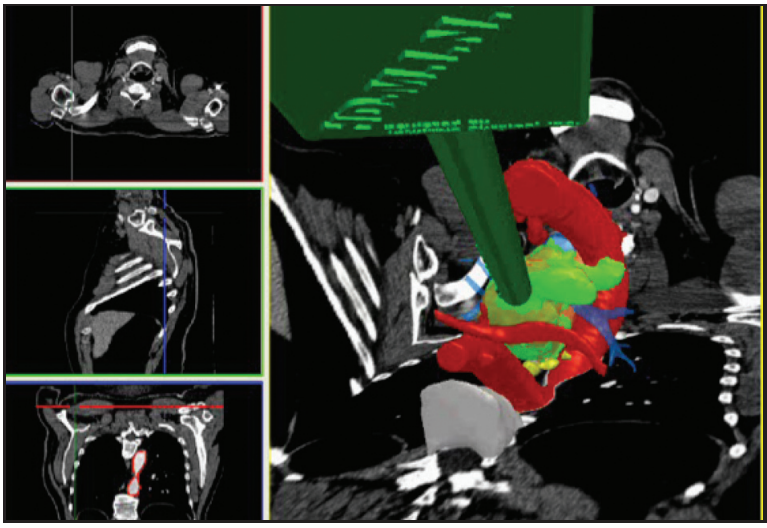

*Figure 44c. Segmentation of computer tomography as basis for navigated esophagectomy.*

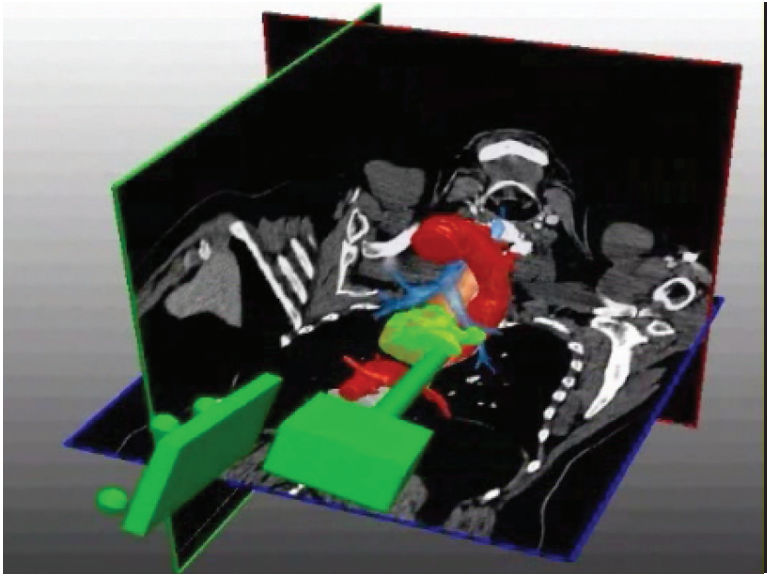

*Figure 44d. Image guided surgery with virtual reality of tracked instruments*

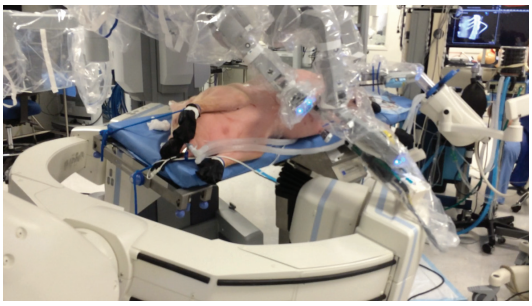

*Figure 45. Experimental evaluation of featured tracking using Dyna-CT during robot-assisted renal surgery. (Courtesy to Jonathan Sorger, Intuitive Surgical).*

*Figure 45a. Dyna-CT is rotating around the patient after port placement and insertion of robotic instruments. Note the narrow space for rotation of Dyna-CT-C-arm.*

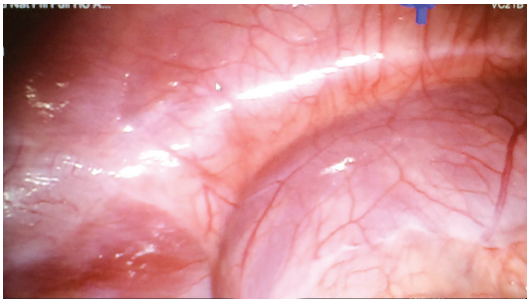

*Figure 45b. 3D-endoscopic view of the porcine kidney.*

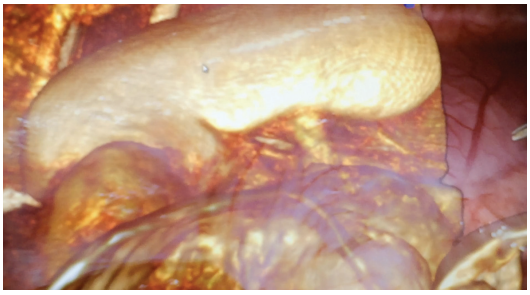

*Figure 45c. 3D-to 3D-overlay of virtual anatomy taken from segmented Dyna-CT images by use of featured tracking based on rigid and radiopaque anatomical landmark (ie ribs.)*

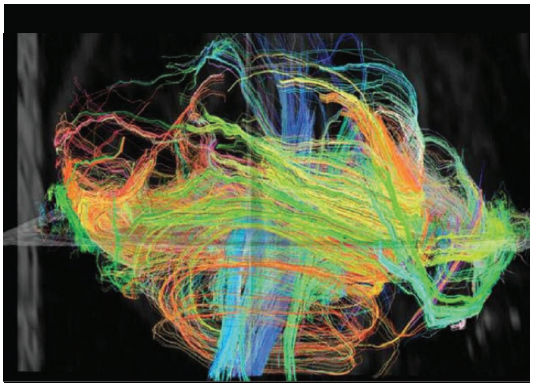

*Figure 46. Ex-vivo robotic radical prostatectomy specimen using high-resolution diffusion tensor magnetic resonance imaging (DTI).*
*Figure 46a. The various colours represent the fibres in and around the prostate.*

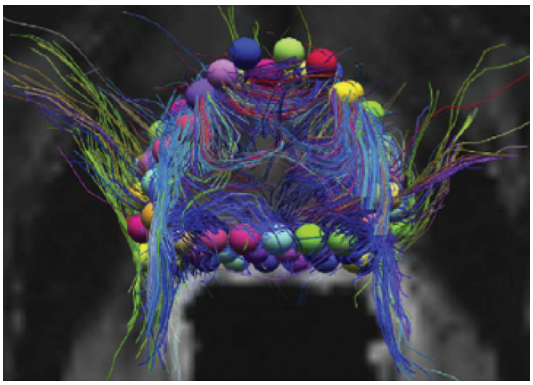

*Figure 46b. Correlation with mp-MRI with special markers for the prostate capsule (coloured dots) show course of neurovascular bundle.*

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