# REVIEW: EVOLUTION OF MINIMALLY INVASIVE RADICAL PROSTATECTOMY - A CONTINUOUS DEVELOPMENT

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Disclosure: No potential conflict of interest

### ABSTRACT

During the last 15 years, minimally invasive surgery has been introduced gradually in surgical treatment for prostate cancer (CaP). Laparoscopic radical prostatectomy (LRP) was introduced in the late 1990s but never gained widespread acceptance because of the steep learning curve of the technique. However, LRP is still a thriving technique in multiple centres in Europe and in other regions outside the United States. During previous years, LRP has been overshadowed by robot-assisted laparoscopic radical prostatectomy (RALP), which was first reported in 2001. Its use increased dramatically, and in 2008, >75% of all radical surgical procedures for CaP were performed by RALP in the United States. Modifications of the minimally invasive operative technique and gained knowledge of the surgical anatomy have been applied in CaP surgery during the last decade. In addition, technical development of the robotic device with improved vision, and the introduction of new instruments have occurred. Growing concerns about costs in conjunction with surgical treatment for CaP have arisen during recent years. Introduction of LRP and RALP seem to be accompanied by higher costs for healthcare systems. As results regarding oncological and functional outcome have not definitely been proven to be improved with the introduction of new technology, minimal invasive surgery has been questioned, and opposed to traditional (open) retropubic prostatectomy. This review aims at giving a background for the introduction of minimally invasive surgery for CaP treatment.

Keywords: Prostate cancer, laparoscopy, radical prostatectomy, robot-assisted.

### INTRODUCTION

During the last part of the 20<sup>th</sup> century, minimally invasive surgical techniques were introduced. Laparoscopic techniques were also introduced into urology in the 1990s with the intent of reducing the invasiveness of traditional open surgery and improving functional results. The first laparoscopic radical nephrectomy for a renal tumour was performed in June 1990,<sup>1</sup> and today this is considered the gold standard treatment. The aim of this review is to describe the development of minimally invasive surgery in radical prostatectomy (RP) from laparoscopy to robot-assisted laparascopy, and compare these two methods with an emphasis on oncological and functional results, side-effects, and costs.

### LAPAROSCOPIC RADICAL PROSTATECTOMY (LRP)

From 1991-95, Schuessler et al.<sup>2</sup> reported on the first LRP. These pioneers were able to successfully perform nine LRP procedures, but found no benefit over open prostatectomy. The operation was cumbersome and difficult with an unacceptably prolonged operative time averaging 9.4 hours. The authors concluded that the procedure offered no advantage compared with radical retropublic prostatectomy (RRP).<sup>2</sup>

In 1998, Guillonneau et al.<sup>3</sup> presented their stepwise approach to transperitoneal LRP. After developing the techniques at Institut Mutualiste Montsouris in France, Guillonneau and associates<sup>4</sup> showed LRP to be feasible and published their series demonstrating substantial improvements in postoperative convalescence. During 1998 and 1999, these urologists, who were trained in open RRP, performed 260 consecutive LRP operations. The surgery was performed with the assistance of a voice-controlled robot and the laparoscopic transperitoneally, procedure was performed combining anterograde and retrograde approaches in seven standardised steps. Urethrovesical anastomosis was performed with three to zero interrupted sutures tied intracorporeally.<sup>4</sup> Since then, various European teams have contributed to the overall experience with the technique.5-7

At the beginning of the 21<sup>st</sup> century, there was a slow but consistent increase in the popularity of LRP in many countries. Data from the Laparoscopic Working Group of the German Urological Association showed that in 2002, 15% of German and Swiss centres performed LRP. In 2004, 19.2% of German urologic centres offered LRP, and by the year 2006, 50 different surgeons had performed >5,800 LRP procedures.<sup>8</sup>

# ROBOT-ASSISTED LAPAROSCOPIC RADICAL PROSTATECTOMY (RALP)

In the 1950s, robotic arms were initially used in hazardous environments, e.g. the bottom of the ocean, in space, or moving hazardous material. Further key advances in robotics occurred in the 1980s with the development of microelectronics, computing, digital imaging, video electronics, and display technology. The vision of a military remote surgery programme designed for battlefield triage, which was funded by the United States Defense Advanced Research Projects Agency (DARPA), was the stepping-stone for the development of robots suitable for modern surgical practice.<sup>9</sup>

The da Vinci Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) was first introduced in 1999. In 2000, the US FDA approved the da Vinci robot for use in laparoscopic procedures. In the same year, the first reported RALP took place in Paris, France, and in Frankfurt, Germany.<sup>10,11</sup> Initially the robot was intended for cardiothoracic surgery, but did not achieve widespread acceptance in this field. In 2008, less than a decade after its introduction, RALP was used in 75-85% of radical prostatectomies performed in the US.<sup>12</sup> Following a merger in 2003, Intuitive Surgical became the sole producer of robotic surgical devices.<sup>9</sup>

## TECHNICAL ASPECTS: DIFFERENCES BETWEEN LRP AND RALP

Use of LRP never became widespread because of its steep learning curve (LC), and it is now completely overshadowed by RALP. The LRP procedure requires advanced laparoscopic skills to manoeuvre rigid laparoscopic instruments that are fixed at the skin level by trocars, resulting in an overall reduction compared with open surgery in the degrees of freedom (df) for dissection and suturing. The range of motion offered by LRP instruments is only 4 df, and there is only 2D vision, impaired hand-eye coordination (i.e. misorientation between real and visible movements), and a reduced haptic sense (i.e. only minimal tactile feedback).

Robotic systems were introduced in an attempt to reduce the difficulty involved in performing complex laparoscopic urologic procedures. The availability of 3D magnification and tools with 7 df, able to duplicate hand movements with high accuracy and with elimination of surgeon hand tremors, led many urologists to expect that, despite the absence of tactile feedback, the application of robotic surgery in RP might yield real advantages in several aspects of the procedure. One reason for the popularity of RALP seems to be the shallower LC and better ergonomics compared with LRP. However, Sooriakumaran et al.<sup>13</sup> studied 3,794 patients undergoing RALP and demonstrated that positive surgical margin (PSM) rates improved with the surgeon's increasing experience: performance of >1,600 operations was required to achieve a PSM rate <10%, which suggests that the RALP LC is steeper than often cited. Training in robotic surgery has lately been improved by dualconsole capability, which supports training and collaboration during minimally invasive surgery.

The extraperitoneal LRP approach bypasses the possible complications that occur after previous intra-abdominal surgery. However, in our personal experience, previous intra-abdominal surgery is not necessarily a contraindication for transabdominal RALP. A mini-laparotomy can be performed with a midline incision, and after adhesions between the small intestine and the abdominal wall are cut, laparoscopic trocars are inserted. Patients previously operated on for ulcerative colitis or Crohn's disease, or having undergone major large bowel surgery or the creation of an ileo-anal pouch, have been operated on in our department (unpublished data). Patients previously irradiated

for cancers in the pelvic area are also considered for RALP.<sup>14</sup> Even patients irradiated with external beam radiation therapy or high-dose brachytherapy for prostate cancer (CaP), who have a localised cancer relapse, are considered for RALP.<sup>15</sup>

In contrast to LRP, during RALP patients are positioned in an extreme Trendelenburg position at an angle of 35-40°. Such positioning in patients who are extremely obese and have marginal respiratory capacity may be a challenge for the anaesthesiologist.

### PERIOPERATIVE OUTCOMES AND POSTOPERATIVE MORBIDITY

Both robotic and laparoscopic urologic procedures seem to be superior to open surgery with respect to blood loss and length of hospital stay.<sup>8,16</sup> RALP seems to achieve a shorter operation time than LRP,<sup>7,8,16</sup> but times are probably similar to those achieved by RRP.<sup>8</sup>

Salinas et al.<sup>16</sup> found that there were no significant differences between laparoscopic and robotassisted surgeries in any of the peri or postoperative outcomes (operation time, blood loss, transfusion rate, catheter time, days hospitalised, and rate of overall complications). Transition in operative technique from LRP to RALP did not change results in the above-mentioned outcomes either.<sup>17</sup> In a recent review, Tewari et al.<sup>18</sup> found that total intraoperative complication rates were low for both RRP and LRP, but lowest for RALP. Rates for readmission, reoperation, nerve, ureteral, and rectal injury, deep vein thrombosis, pneumonia, haematoma, lymphocele, anastomotic leak. fistula, and wound infection showed significant differences between groups, generally favouring RALP. A review by Ficarra et al.8 concluded that once the LC is complete, LRP and RALP can be performed without a significant risk of major complications and with the same risk for postoperative morbidity as RRP.<sup>8</sup> The critical issue in determining the risk of complications, regardless of the surgical approach, is the level of expertise of the surgeon.

#### **Oncological Outcomes**

A widely acknowledged criterion for the technical quality of RP is the PSM rate, and this rate has been shown to correlate with the risk of biochemical recurrence after surgery.<sup>19-21</sup> Published rates of PSM vary widely (Table 1) and are partly disease-

dependent, with higher rates in higher-stage and higher-grade disease.<sup>22</sup> However, these rates are also surgeon-dependent, and thus can be modified.

In a multinational, multicentre study comparing PSM rates for 22,393 patients undergoing open RP, LRP, or RALP, it was shown that PSM rates may be lower after minimally invasive techniques than after RRP. PSM rates were lowest for RALP (13.8%), intermediate for LRP (16.3%), and highest for open RP (22.8%).19 After adjustment for the effects of age, preoperative prostatespecific antigen, postoperative Gleason score, pathologic stage, and year of surgery, no significant differences in PSM rates were found between LRP and RALP, but both cohorts were better than the RRP group by approximately 25%.<sup>21</sup> Lower-volume centres had increased rates of PSM compared with the highest-volume centre for both LRP and RALP (OR: 1.52, 95% CI 1.14-2.04 for LRP; OR: 6.09, 95% CI 2.74-13.51 for RALP).

The association between surgical volume and PSM status was also corroborated in a Norwegian prospective study comparing the outcome of RP with respect to resection margins.<sup>26</sup> High-volume surgery (>50 operations/surgeon) was performed at hospitals with the capacity for RALP, whereas low-volume surgery was performed by RRP. It was demonstrated that the risk of positive resection margins was 4-times higher in low-volume units. This is consistent with earlier results from a collaborative review by Ficarra et al.<sup>8</sup> who argued that the major factor affecting risk is the surgical volume, not the surgical technique.

With regard to the operative methods and differences in PSM, the study by Sooriakumaran et al.<sup>19</sup> contrasts with a systematic review by Novara et al.,<sup>27</sup> which suggested that PSM rates are similar following RRP, LRP, and RALP. In the RP series evaluated by Novara et al.,<sup>27</sup> 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.

At a conference of 17 world leaders in CaP and RP in Pasadena, California,<sup>28</sup> it was concluded that there exists a consensus on the established role of RALP in the management of patients with clinically localised CaP. Based on the published literature, and in the absence of prospective randomised trials, it appears that RALP allows cancer control equivalent to RRP, although most of the available studies are hampered by relatively short follow-up. Table 1: Positive surgical margins stratified by pT stage.

	LRP n (%)	RALP n (%)	p-value
Asimakopoulos et al. <sup>23</sup>			
pT2	4 (8)	3 (7)	0.7
pT3	2 (25)	5 (56)	
total	6 (10)	8 (15)	
Porpiglia et al. <sup>24</sup>		·	
pT2	6 (16)	5 (14)	0.4
pT3	6 (27)	11 (50)	
total	12 (20)	16 (27)	
Berge et al. <sup>17</sup>		<u>^</u>	
pT2	20 (14)	21 (16)	0.1
pT3	28 (44)	41 (53)	
total	48 (23)	62 (30)	
Willis et al. <sup>25</sup>			
pT2	12 (9)	6 (7)	0.2
pT3	9 (29)	15 (50)	
total	22 (18)	22 (14)	

LRP: laparoscopic radical prostatectomy; RALP: robot-assisted laparoscopic radical prostatectomy.

#### **Functional Outcomes**

Given the overall excellent oncologic control for CaP that RP has been shown to provide, increasing attention has focused on the relative toxicities of surgery in an effort to decrease treatmentrelated morbidity. After the initial studies on the neurovascular bundle (NVB) by Walsh et al.,<sup>29</sup> other research groups studied the anatomic-histologic details of the NVB as well as its function.<sup>30-32</sup> As the 3D camera of the da Vinci robot allows for a greater magnification (up to 12×) during the RALP procedure, even greater emphasis has been focused in recent years on the anatomical dissection of the NVB from the prostate. Thus, surgeons performing RALP have described alternative techniques for dissection of the NVB. Menon et al.<sup>33</sup> described the intrafascial operative technique dissecting between levator and prostatic fascia (see Figure 1). The authors stated that preservation of the NVB with this technique would enhance erectile function after an RP compared to the traditional interfascial technique, where the dissection is between levator fascia and prostatic fascia.

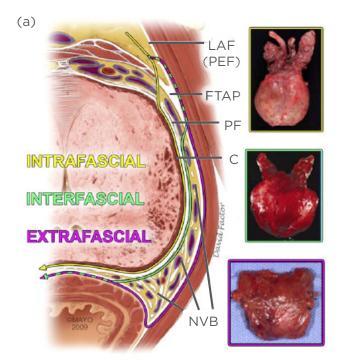


Figure 1: The Intrafascial (yellow line), the Interfascial (green line), and the Extrafascial (purple line) operative approach to preservation of the nerve bundle.

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Unfortunately, as for oncological outcomes, few randomised trial data comparing different surgical methods and other forms of therapy exist that evaluate quality of life (QoL) measures following RP. Willis et al.<sup>25</sup> showed statistically similar 12month postoperative urinary function: 75% and 72% were pad-free in the LRP and RALP group, respectively (p=0.7). RALP patients had an earlier return of sexual function when compared with LRP patients after a bilateral nerve sparing (NS) procedure. Berge et al.<sup>17</sup> reported that in patients operated with bilateral NS, 47% and 49% of LRP and RALP patients, respectively, had regained baseline intercourse frequency 36 months postoperatively (p=0.8). In a meta-analysis, 12-month<sup>8</sup> potency rates for LRP patients varied between 42-62% and for RALP patients, 70-80%.

At the Pasadena Consensus Panel it was stated that although RALP may offer advantages in the postoperative recovery of urinary continence and erectile function, well-controlled comparative studies are lacking, particularly with regard to outcomes of RP surgery performed in accordance with best practice guidelines.<sup>28</sup>

#### COSTS

There are several studies published on the costs of

implementation of minimally invasive CaP surgery. Two kinds of approaches towards reporting of costs are published: reporting direct costs of the procedure, including materials, hospitalisation days, operating room time, and a more holistic approach, including health economic reporting of costs.

In the first scenario - reporting direct costs associated with the RP - it appears that LRP and RALP are significantly more expensive than RRP.<sup>34</sup> It is, however, noteworthy that operating room times reported appear quite long, with a length of 3.5-4 hours for an LRP.<sup>35</sup> Thus, direct costs associated with RRP have been reported to be in the range of \$3,384-4,437, LRP in the range \$5,058-6,760, and RALP in the range \$5,386-11,806. Bolenz et al.<sup>34</sup> concluded that the additional costs for RALP over LRP are \$2,315, and in addition, robot purchase costs amount to \$2,698.

In the other scenario - health economics-related reporting of costs for RP - other costs were included when comparing the different treatment modalities, e.g. the need for adjuvant treatment after an operation, shortening of the sick leave period, which in one study was in favour of minimally invasive procedures,<sup>36</sup> and subsequent costs during the first year from the date of surgery.<sup>37</sup> In addition, costs have been measured assessing QoL issues and successful outcomes, i.e. cancer control or negative resection margins. From the perspective of a smaller country, e.g. Norway, implementation of RALP has led to a centralisation of surgical treatment. Thus, the number of hospitals where RP is performed has dropped from 18 to 13. As addressed in a systematic review by Bolenz et al.<sup>34</sup> the number of procedures plays a role in minimising costs per procedure, as the provider of the robotic system, Intuitive Surgical, has a yearly maintenance fee of approximately \$150,000.

A Canadian study<sup>38</sup> reported that costs for RALP were 25% higher compared to open RP and LRP, with an average lifespan of the robot being 7 years. The extra costs would decrease if volume of operated patients increased and duration of lifespan for the robot increased. However, the extra cost by RALP is far below extra costs resulting from new methods of radiation of CaP. In a recent study by Nguyen et al.<sup>39</sup> they reported the extra cost by minimally invasive RP to be \$4 million compared to \$282 million for intensitymodulated radiation therapy in 2008.

### FUTURE PERSPECTIVE

New instruments are developed continuously, and there are many types of scissors, forceps, and other types of instruments available. Developments in intraoperative sensing at the tips of laparoscopic instruments are likely to occur. LRP procedures are still thriving outside the US due to lower costs. Several companies are developing 3D laparoscopy and it has been introduced in LRP.40 In addition, preoperative staging and imaging with multiparametric magnetic resonance imaging of the CaP gives the surgeon the possibility to form a preoperative plan. Results from several studies show that improved staging of the tumour burden and localisation seems to improve the outcome of RP assessed by achieving free resection margins.<sup>41,42</sup>

#### CONCLUSION

Decreased blood loss during surgery and a shorter duration of convalescence following surgery are definite advantages to minimally invasive approaches. Data from observational studies and systematic reviews have not shown unequivocal of RALP compared with LRP is the shallower LC. superiority of any surgical approach in terms of functional and oncologic outcomes. An advantage

The increased costs with RALP can be minimised with increased surgical volume.

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