



Universiteit  
Leiden  
The Netherlands

## **Technical refinements in superextended robot-assisted radical prostatectomy for locally advanced prostate cancer patients at multiparametric magnetic resonance imaging**

Mazzone, E.; Dell'Oglio, P.; Rosiello, G.; Puliatti, S.; Brook, N.; Turri, F.; ... ; Mottrie, A.

### **Citation**

Mazzone, E., Dell'Oglio, P., Rosiello, G., Puliatti, S., Brook, N., Turri, F., ... Mottrie, A. (2021). Technical refinements in superextended robot-assisted radical prostatectomy for locally advanced prostate cancer patients at multiparametric magnetic resonance imaging. *European Urology*, 80(1), 104-112. doi:10.1016/j.eururo.2020.09.009

Version: Publisher's Version

License: [Licensed under Article 25fa Copyright Act/Law \(Amendment Taverne\)](#)

Downloaded from: <https://hdl.handle.net/1887/3769443>

**Note:** To cite this publication please use the final published version (if applicable).

## Surgery in Motion

# Technical Refinements in Superextended Robot-assisted Radical Prostatectomy for Locally Advanced Prostate Cancer Patients at Multiparametric Magnetic Resonance Imaging

Elio Mazzone<sup>a,b,c,d,†,\*</sup>, Paolo Dell'Oglio<sup>c,d,e,†</sup>, Giuseppe Rosiello<sup>a,b,c,d</sup>, Stefano Puliatti<sup>c,d,f</sup>, Nicholas Brook<sup>g</sup>, Filippo Turri<sup>f</sup>, Alessandro Larcher<sup>a,b</sup>, Sergi Beato<sup>c</sup>, Iulia Andras<sup>c</sup>, Pawel Wisz<sup>c,d</sup>, Abhishek Pandey<sup>c,h</sup>, Ruben De Groote<sup>c,d</sup>, Peter Schatteman<sup>c,d</sup>, Geert De Naeyer<sup>c,d</sup>, Frederiek D'Hondt<sup>c,d</sup>, Alexandre Mottrie<sup>c,d</sup>

<sup>a</sup> Division of Oncology/Unit of Urology, URI, IRCCS Ospedale San Raffaele, Milan, Italy; <sup>b</sup> Vita-Salute San Raffaele University, Milan, Italy; <sup>c</sup> Department of Urology, Onze Lieve Vrouw Hospital, Aalst, Belgium; <sup>d</sup> ORSI Academy, Melle, Belgium; <sup>e</sup> Department of Urology, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; <sup>f</sup> Department of Urology, University of Modena and Reggio Emilia, Modena, Italy; <sup>g</sup> Department of Urology, Royal Adelaide Hospital, Adelaide, South Australia, Australia; <sup>h</sup> Klinikum Nord, Paracelsus Medical University, Nurnberg, Germany

## Article info

### Article history:

Accepted September 3, 2020

### Associate Editor:

Alexandre Mottrie

### Statistical Editor:

Emily Zambor

### Keywords:

Locally advanced prostate cancer  
Robot-assisted radical prostatectomy  
Preoperative magnetic resonance imaging  
Surgical technique  
Seminal vesicles invasion

## Abstract

**Background:** The feasibility and efficacy of robot-assisted radical prostatectomy (RARP) in locally advanced prostate cancer (PCa) patients with iT3 lesion at magnetic resonance imaging (MRI) are currently not explored.

**Objective:** To describe our revised RARP technique (ie, superextended RARP [SE-RARP]) for PCa patients with posterior iT3a or iT3b at MRI.

**Design, setting, and participants:** Data from 89 patients with posterior iT3a or T3b disease who underwent SE-RARP at a single high-volume centre between 2015 and 2018 were analysed.

**Surgical procedure:** RARP was performed using a DaVinci Xi system. The surgical approach provided an inter- or extrafascial RARP where Denonvilliers' fascia and perirectal fat were dissected free and left on the posterior surface of the seminal vesicles.

**Measurements:** Perioperative outcomes, and intra- and postoperative complications were assessed. Postoperative outcomes were assessed in patients with complete follow-up data ( $n=78$ ). Biochemical recurrence (BCR) was defined as two consecutive prostate-specific antigen values of  $\geq 0.2$  ng/ml. Urinary continence (UC) recovery was defined as the use of zero or one safety pad. Kaplan-Meier and multivariable Cox regression models were used.

**Results and limitations:** The median operative time, blood loss, and length of stay were 204 min, 300 ml, and 5 d, respectively. The median bladder catheterisation time was 5 d. Overall, 28%, 28%, and 27% of patients had pathological grade group (GG) 4–5, pT3b, and positive surgical margins (PSMs), respectively. Three patients (3.4%) experienced intra-operative complications. Among patients with available follow-up data ( $n=78$ ), 14 (18%) experienced 30-d postoperative complications. The median follow-up was 19 mo. Overall, 11 patients received additional treatment. At 2 yr of follow-up, BCR-free and additional treatment-free survival were 55% and 66%, respectively. Pathological GG 4–5

<sup>†</sup> These authors shared first authorship.

On behalf of the ERUS Educational Working Group and the YAU working group on robot-assisted surgery.

\* Corresponding author. Division of Oncology/Unit of Urology URI, IRCCS Ospedale San Raffaele, Via Olgettina 60, Milan 20132, MI, Italy. Tel. +39 02 2643 7286, Fax: +39 02 2643 7298.

E-mail address: [eliomazzone@gmail.com](mailto:eliomazzone@gmail.com) (E. Mazzone).

Please visit

[www.europeanurology.com](http://www.europeanurology.com) and  
[www.urosource.com](http://www.urosource.com) to view the  
 accompanying video.

(hazard ratio [HR] 3.2) and PSM (HR 5.8) were independent predictors of recurrence, as well as of additional treatment use (HR 5.6 for GG 4–5 and 5.2 for PSM). The 1-yr UC recovery was 84%.

**Conclusions:** We presented our revised RARP technique applicable to patients with posterior iT3a or iT3b at preoperative MRI. This technique is associated with good morbidity and continence recovery rates, and might guarantee biochemical control of the disease and postpone the use of additional treatments in patients with low-grade and negative surgical margins.

**Patient summary:** A revised robot-assisted radical prostatectomy technique applicable to prostate cancer patients with posterior iT3a or iT3b lesion at magnetic resonance imaging was described. This novel technique is feasible and safe in expert hands.

© 2020 European Association of Urology. Published by Elsevier B.V. All rights reserved.

## 1. Introduction

Multiparametric magnetic resonance imaging (MRI) has significantly changed the diagnostic pathway of prostate cancer (PCa) patients [1–3]. Moreover, MRI is also a useful tool to assess the clinical relevance and the local extent of disease in PCa patients [4,5] to guide the decision-making process towards the treatment choice [6,7]. Robot-assisted radical prostatectomy (RARP) represents the most common surgical approach performed in patients with localised PCa [8,9]. Moreover, in the setting of locally advanced PCa, the European Association of Urology (EAU) [10] and the National Comprehensive Cancer Network (NCCN) [11] guidelines recommend to perform radical prostatectomy as part of multimodal therapy in highly selected patients who may benefit from this surgical procedure [12]. However, evidence supporting the oncological efficacy of RARP in locally advanced PCa is still sparse. In this regard, Gandaglia et al [13], relying on a multi-institutional database, demonstrated that RARP is a safe and oncologically effective procedure in PCa patients with locally advanced disease. However, the authors [13] included patients with T3 disease, as defined by MRI or rectal examination, in the study cohort. As such, the feasibility and efficacy of RARP exclusively in locally advanced PCa patients with T3 at MRI (iT3), who often are considered inoperable patients, have not been explored so far. Moreover, during the last years, several variations of the original description of RARP have been described [14] and remarkable technological refinements of the robotic platform and its tools have been observed [12].

Based on these premises, relying on a single-institutional database, we described our revised RARP technique for locally advanced PCa patients (ie, superextended RARP [SE-RARP]) applicable exclusively to patients with posterior iT3a or iT3b tumour at multiparametric MRI and reported perioperative, intermediate-term oncological and functional outcomes.

## 2. Patients and methods

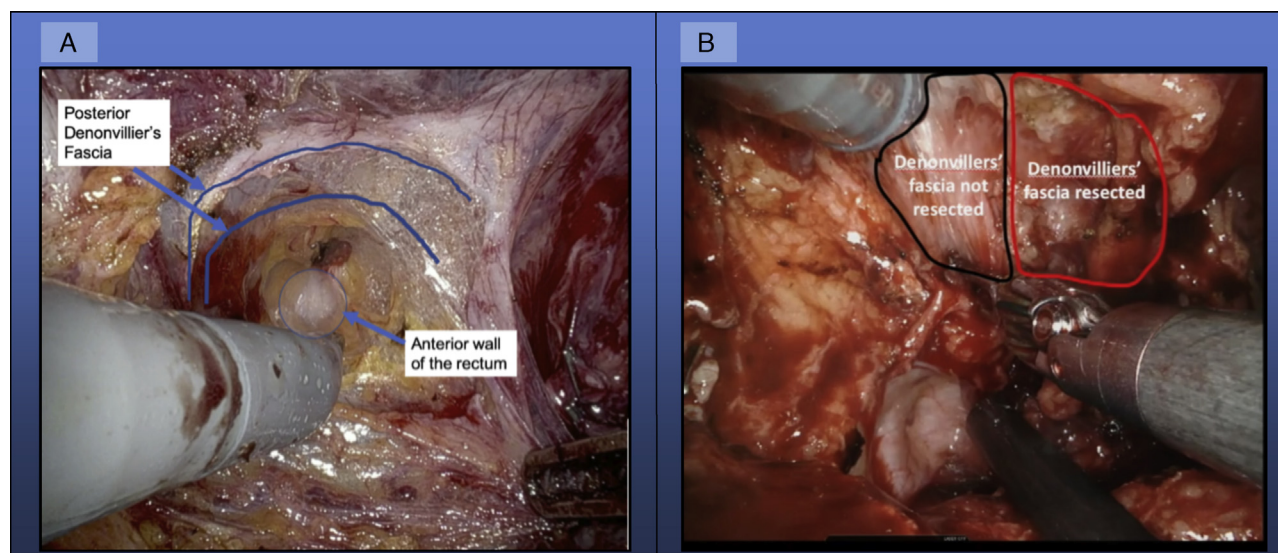
### 2.1. Study population

The current study relied on a prospectively maintained institutional database including PCa patients treated with RARP and pelvic lymph node dissection (PLND) between

2015 and 2018 at a single European high-volume centre (Onze-Lieve-Vrouw Hospital, Aalst, Belgium) by a single expert robotic surgeon (A.M.). For the purpose of the analyses, only patients with available preoperative MRI with either a posterior iT3a or an iT3b lesion who underwent SE-RARP were included. An iT3 lesion was defined as any extracapsular extension (ECE; also including microscopic) at preoperative multiparametric MRI. Notably, this classification differs from the clinical T stage (cT), which is based on digital rectal examination only [10]. All MRI scans were evaluated alternatively by two expert uro-radiologists (F.C. or P.v.H.), who are dedicated radiologists with specific clinical and research interest in prostate MRI imaging and have >5 yr of experience. Overall, 89 assessable patients were included for perioperative outcomes assessment. Thereafter, analyses of postoperative outcomes was performed only in patients with available follow-up data ( $n = 78$ ).

### 2.2. Surgical technique

Before surgery, multiparametric MRI was performed routinely for local staging purpose and surgical planning. All the procedures were performed with a DaVinci (Intuitive Surgical, Sunnyvale, CA, USA) Xi system through a six-port transperitoneal approach. Template definitions for extended or superextended PLND relied on those previously defined by consensus panels [15]. The indications to perform superextended template were as follows: (1) preoperative Briganti risk score for lymph node invasion  $\geq 30\%$  [16] and (2) positive node at external iliac level at frozen pathology [17]. Subsequently, after complete bladder detachment with the median umbilical ligament preservation [18] and the bilateral endopelvic fascia incision, a suspension suture was placed on the prostate to facilitate bladder neck dissection. An initial posterolateral incision of the bladder neck between the bladder and the prostate was performed, and continued towards the midline following the periprostatic fat. After identification of the vas deferens, the peritoneum was incised at the level of the rectovesical pouch. The vas deferens was dissected, the peritoneum was pushed downwards, and the Denonvillier's fascia (DVF) with some perirectal fat were dissected free and pushed upwards with the specimen so that they remain on the posterior surface of the seminal vesicles (Fig. 1A). As a result of the dissection, the seminal vesicle is not visible, as it is



**Fig. 1 – (A)** Posterior Denonvillier's fascia is dissected and pushed upwards with the specimen. **(B)** Monolateral resection of Denonvillier's fascia left on the posterior surface of the seminal vesicles and of the prostate.

completely covered by the DVF and the perirectal fat. The dissection was carried forward to the anterior face of the rectum, pushing the perirectal fat and the DVF upwards with the specimen. Thereafter, an extrafascial dissection with Hem-o-lock clips was subsequently carried out laterally to the levator ani fascia. SE-RARP can be performed with *unilateral* or *bilateral* DVF resection according to the extension of the disease at MRI. If the tumour is unilateral, the seminal vesicle on the side without a tumour burden is released in a standard fashion, leaving the DVF attached to the rectum (Fig. 1B). In this case, an interfascial nerve-sparing (NS) procedure was performed on the side without a tumour burden. Apical dissection of the prostate was performed according to the “collar technique” [19]. Finally, urethrovesical anastomosis was performed, as previously described [20]. In case of unilateral DVF resection, partial monolateral posterior reconstruction is generally performed before urethrovesical anastomosis.

### 2.3. Outcomes and covariates

Intraoperative and 30-d postoperative complications were assessed, according to the Clavien-Dindo classification [21]. The quality criteria for accurate and comprehensive reporting of surgical outcomes recommended by EAU guidelines on reporting and grading of complications were fulfilled (Supplementary Table 1) [22]. During follow-up after surgery, serum prostate-specific antigen (PSA) measurement was tested at 6 wk and at 3, 6, and 12 mo after SE-RARP, every 6 mo thereafter for 3 yr, and then annually. PCa persistence was defined as PSA > 0.1 ng/ml at first dosage (6 wk) after RARP [23]. Biochemical recurrence (BCR) was defined as two consecutive PSA values of  $\geq 0.2$  ng/ml [10]. Additional treatment use was defined as any administration of radiotherapy or hormonal therapy in the adjuvant or salvage setting after RARP according to the clinical

judgement and after discussion with the patient regarding the benefits and possible side effects. Clinical recurrence (CR) was defined as positive imaging during follow-up after the onset of BCR. Early continence was defined as the use of zero or one safety pad within 1 wk after catheter removal [24]. Urinary continence (UC) recovery was defined as the use of zero or one safety pad at the last follow-up. Clinical covariates were defined a priori and consisted of continuously coded preoperative PSA, biopsy grade group (GG; 1–3 vs 4–5), and tumour stage at preoperative MRI imaging (iT3a vs iT3b). Similarly, pathological covariates were also defined a priori and consisted of pathological GG (1–3 vs 4–5), pathological tumour stage ( $\leq$  pT3a vs  $\geq$  pT3b), pathological nodal status (pN0 vs pN1 vs pNx), and positive surgical margins (PSMs; R0 vs R1).

### 2.4. Statistical analyses

Three analytical steps were performed. First, medians and interquartile ranges, as well as frequencies and proportions were reported for continuous and categorical variables, respectively. Second, UC and BCR rates at 1 yr were estimated using Kaplan-Meier analyses. Functional and oncological follow-up analyses were performed only in patients with available follow-up data ( $n = 78$ ). UC recovery rates were tested in the overall population and according to the location of the suspected ECE at preoperative MRI, stratified as apical versus nonapical lesions. Thereafter, Kaplan-Meier plots were used to depict BCR-free, additional treatment-free, and CR-free survival.

Lastly, multivariable Cox regression analyses tested for the predictors of BCR as well as of additional treatment use. Multivariable analyses exploring the predictors of CR were omitted due to the low number of events ( $n = 8$ ) and the consequent risk of model overfitting. In time-to-event analyses, patient without records of events were censored



**Table 1 – Preoperative characteristics of 89 locally advanced PCa patients at MRI treated with SE-RARP between 2015 and 2018 at a single European high-volume centre**

Variables	Overall (N = 89)
Stage at MRI, n (%)	
Posterior iT3a	71 (80)
iT3b	18 (20)
Age at surgery (yr)	
Median	65
IQR	61–69
Body mass index (kg/m <sup>2</sup> )	
Median	26
IQR	25–28
Charlson comorbidity index, n (%)	
0	72 (81)
1	12 (13)
≥2	5 (6)
Neoadjuvant androgen deprivation therapy use, n (%)	2 (2.2)
Preoperative PSA (ng/ml)	
Median	11
IQR	7–14
Positive biopsy cores, n (%)	
Median	6
IQR	4–9
Clinical T stage, n (%)	
T1c	13 (15)
T2a	7 (8)
T2b	9 (10)
T2c	10 (11)
T3a–b	50 (56)
Grade group at biopsy, n (%)	
1–3	70 (79)
4	11 (12)
5	8 (9)
Clinical N stage, n (%)	
Nx	13 (14)
N0	83 (79)
N1	6 (7)

IQR = interquartile range; MRI = magnetic resonance imaging; PCa = prostate cancer; PSA = prostate-specific antigen; SE-RARP = superextended robot-assisted radical prostatectomy.

on the date of the last time the patient was known to be free of BCR or CR, in accordance to the guidelines for reporting statistics [25]. In BCR analysis, adjuvant therapies were censored as an event. As previously specified, two sets of prespecified clinical (PSA at RARP, biopsy GG, and iT stage at MRI) and pathological (pathological GG, pT, pN, and PSM) covariates were used. For all statistical analyses, R software environment for statistical computing and graphics (version 3.6.3) was used. All tests were two sided, with a level of significance set at  $p < 0.05$ .

### 3. Results

#### 3.1. Descriptive characteristics of the study population

Descriptive characteristics of the study cohort are shown in Table 1. Of 89 patients with locally advanced PCa at MRI, 71 (80%) had posterior iT3a and 18 (20%) iT3b disease. The median age was 65 yr (interquartile range [IQR]: 61–69) and the median preoperative PSA was 11 ng/ml (IQR: 7–14). Overall, 17 (19%) patients harboured a Charlson comorbidity index of  $\geq 1$ . At biopsy, GG  $> 3$  was reported in 19 (21%) patients.

#### 3.2. Intra-, peri-, and postoperative outcomes

Table 2 illustrates intra- and perioperative outcomes. Overall, 37 (42%) patients received superextended PLND. The median operative time and blood loss were 204 (IQR:

**Table 2 – Intra- and perioperative characteristics of 89 locally advanced PCa patients at MRI treated with SE-RARP between 2015 and 2018 at a single European high-volume centre**

Variables	Overall (N = 89)
Pelvic lymph node dissection <sup>a</sup> , n (%)	
Extended	52 (58)
Superextended	37 (42)
Nerve-sparing procedure, n (%)	
Not performed	21 (25)
Monolateral	67 (75)
Operative time (min)	
Median	204
IQR	180–272
Blood loss (ml)	
Median	300
IQR	200–400
Length of stay (d)	
Median	5
IQR	4–6
Intraoperative complications, n (%)	3 (3.4)
Catheter removal (d)	
≤2	37 (42)
≥3	52 (58)
Early continence, n (%)	34 (38)

IQR = interquartile range; MRI = magnetic resonance imaging; PCa = prostate cancer; SE-RARP = superextended robot-assisted radical prostatectomy.

<sup>a</sup> Pelvic lymph node dissection templates were defined as follows: extended = obturator, external, and internal iliac lymph nodes; superextended = obturator, presacral, external, internal, and common lymph nodes.

180–272) min and 300 (IQR: 200–400) ml, respectively. A monolateral NS approach was performed in 67 (75%) patients. The median length of stay was 5 (IQR: 4–6) d.

Intraoperative complications were reported in three (3.4%) patients (injury of the bladder below the bladder neck in one, injury of the right iliac vein in one, and injury of the left external iliac vein in one) and 30-d postoperative complications were reported in 14 (18%) patients with complete follow-up data. Of these patients, 10 experienced Clavien-Dindo I–II and four experienced Clavien-Dindo III. Of the four Clavien-Dindo III cases, two had lymphocele treated with percutaneous drainage, one had persistent urethrovesical leakage treated with nephrostomy positioning, and one had abdominal haematoma treated with explorative laparotomy. The 30-d readmission rate was 3.8% ( $n = 3$ ; Supplementary Table 2).

The catheter was removed within 3 d in 37 (42%) patients, and early continence recovery was observed in 34 (38%) patients. At histopathological evaluation, ECE was found in 65 (73%) and seminal vesicle invasion in 25 (28%) specimens. The PSM rate was 27% ( $n = 24$ ; Table 3). Specific PSM locations were classified as follows: 14 apical (58%), four midprostate (17%), six prostatic base (25%), and zero seminal vesicles (0%). Of these, 33% were anterior ( $n = 8$ ), 12% were posterior ( $n = 3$ ), 29% were lateral ( $n = 7$ ), and 25% were multiple sites ( $n = 6$ ).

Considering patients with available follow-up data ( $n = 78$ ), the median follow-up was 19 mo among those who did not experience any event. Overall, 11 patients received additional radiation therapy and 11 received additional hormonal therapy (Table 4). PSA persistence was experienced by 19 (24%) patients. The median 12-mo PSA was 0.03 ng/ml. BCR was observed in 26 patients, and the median time to recurrence was 6 (IQR: 3–9) mo. CR was

**Table 3 – Histopathological features after SE-RARP of 89 locally advanced PCa patients at MRI**

Variables		Overall (N = 89)
Prostate volume (cc)	Median	55
	IQR	39–68
Pathological grade group, n (%)	1–3	64 (72)
	4–5	25 (28)
Pathological T stage, n (%)	≤pT2c	24 (27)
	pT3a	40 (55)
	≥pT3b	25 (28)
Pathological nodal stage, n (%)	pN0	64 (72)
	pN1	25 (28)
Extraprostatic extension, n (%)	Absent	24 (27)
	Focal	24 (27)
	Extended	41 (46)
Seminal vesicle involvement, n (%)	Absent	64 (72)
	Monolateral	4 (4)
	Bilateral	21 (24)
Bladder neck involvement, n (%)	Present	13 (15)
Perineural invasion, n (%)	Present	74 (83)
Surgical margins, n (%)	Positive	24 (27)
Total lymph nodes removed, n (%)	Median	15
	IQR	13–21
Positive lymph nodes removed <sup>a</sup> , n (%)	Median	3
	IQR	1–4

IQR = interquartile range; MRI = magnetic resonance imaging; PCa = prostate cancer; SE-RARP = superextended robot-assisted radical prostatectomy.

<sup>a</sup> Only in 25 patients with positive nodes.

observed in eight patients. No cancer-related death was recorded.

Overall, 84% of patients experienced UC recovery at 12-mo follow-up, and the median time to UC recovery was 3 (IQR: 1–6) mo. After stratification according to the

**Table 4 – Postoperative, oncological, and functional outcomes at follow-up for 78<sup>a</sup> locally advanced PCa patients (61 iT3a and 17 iT3b) at MRI treated with SE-RARP between 2015 and 2018 at a single European high-volume centre**

Variables		Overall (N = 78)
30-d postoperative complications, n (%)	Overall	14 (18)
	CD I	9 (11)
	CD II	1 (1.3)
	CD III	4 (5.1)
	CD IV	0 (0)
	CD V	0 (0)
Additional radiation therapy, n		11
Additional hormonal therapy, n		11
PSA persistence, n (%)		19 (24)
12-mo PSA (ng/ml)	Median	0.03
	IQR	0.01–0.1
Biochemical recurrence, n		26
Time to biochemical recurrence (mo)	Median	6
	IQR	3–9
12-mo biochemical recurrence rate (%)		33
Time to urinary continence recovery (mo)	Median	3
	IQR	1–6
12-mo urinary continence rate (%)		84

CD = Clavien-Dindo; IQR = interquartile range; MRI = magnetic resonance imaging; PCa = prostate cancer; PSA = prostate-specific antigen; SE-RARP = superextended robot-assisted radical prostatectomy.

<sup>a</sup> Only patients with available follow-up data were included.

suspected ECE location at preoperative MRI, no differences in 12-mo UC recovery rates were reported between apical and nonapical lesions (82% and 86%, respectively,  $p = 0.5$ ).

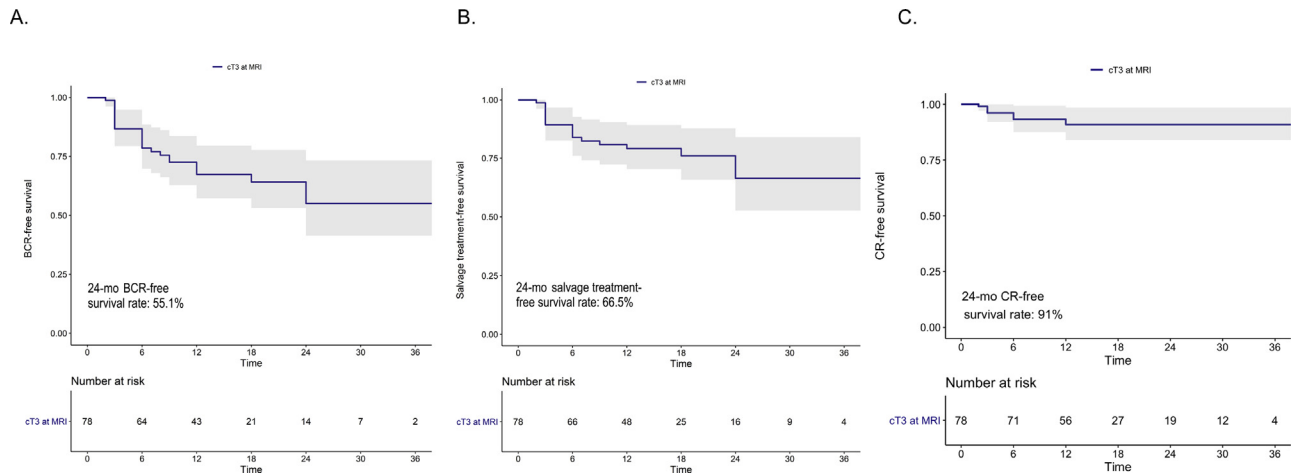
### 3.3. Univariable and multivariable analyses predicting BCR and secondary treatment

At 24 mo of follow-up, Kaplan-Meier plots depicted 55% BCR-free survival (Fig. 2A) and 66% additional treatment-free survival (Fig. 2B) rates. On the contrary, CR-free survival rate at 24 mo was 91% (Fig. 2C). At multivariable Cox regression analyses, pathological GG 4–5 (hazard ratio [HR] 3.17; 95% confidence interval [CI] 1.27–7.83;  $p = 0.01$ ) and PSM (HR: 5.86; 95% CI 2.43–14.1;  $p < 0.001$ ) were independent predictors of BCR after SE-RARP, after adjusting for pathological confounders. Similarly, pathological T stage (HR 3.28; 95% CI 1.65–10.3;  $p = 0.04$ ), pathological GG 4–5 (HR 5.63; 95% CI 1.71–18.5;  $p = 0.004$ ), and PSM (HR 5.23; 95% CI 1.65–16.6;  $p = 0.004$ ) were also independent predictors of additional treatment after SE-RARP. Conversely, stage at MRI was associated neither with BCR nor with additional treatment use after adjusting for clinical covariates (Table 5).

## 4. Discussion

As reported in both EAU and NCCN guidelines [10,11], RP should be part of a multimodal treatment approach for locally advanced PCa. Preoperative staging is essential for optimal planning of radical prostatectomy. In addition to clinical and laboratory analyses, increasingly precise side-specific nomograms and MRI play a leading role in the presurgical study of PCa [1,26]. Taken together, the preoperative use of MRI for identifying extensive posterior PCa involvement combined with technological refinement of the robotic platform and its tools allowed for a revision of our RARP technique for locally advanced PCa and modification of some key steps in order to attempt to optimise cancer control. At the same time, it is also fundamental not to impair patient quality of life by compromising UC. Thus, we aimed to describe our novel RARP technique applicable exclusively to patients with posterior iT3a or iT3b tumour at preoperative MRI (ie, SE-RARP), and to report perioperative and midterm oncological and functional outcomes. Our analyses recorded several noteworthy findings.

First, we described a refined surgical technique based on a series of a single surgeon with previous extensive experience in robotic surgery. Differently from previous analyses [13], improvements in surgical technology, such as the shift towards a DaVinci Xi system and the recent introduction of the Endoscope Plus for the Xi system, allowed for a detailed definition of the anatomical boundaries and a very fine excision of tissue planes with maximum oncological control. For instance, Fig. 1A clearly shows the borders of the DVF that were identified and then excised. Similarly, perirectal fat was identified and left attached to the prostate, while the anterior wall of the rectum represented the caudal limit of the excision plane. Taken together, these technical modifications allowed



**Fig. 2** – Kaplan-Meier plots depicting (A) biochemical recurrence-free, (B) additional treatment use-free, and (C) clinical recurrence-free survival time after SE-RARP in 78 locally advanced PCa patients at MRI treated between 2015 and 2018 at a single European high-volume centre. BCR = biochemical recurrence; CR = clinical recurrence; MRI = magnetic resonance imaging; PCa = prostate cancer; SE-RARP = superextended robot-assisted radical prostatectomy.

optimisation of surgical management of locally advanced PCa cases at MRI, maximising cancer control and reducing the risk of PSM. Indeed, in our cohort, the rate of PSM was 27%, which is remarkably lower than those reported in previous series on cases with pT3a [27] or seminal vesicle invasion at final pathology [12,28]. Additionally, the efficacy of our revised technique on posterior positive margins is also demonstrated by the fact that only three out of 24 PSMs were located at the level of the posterior aspect of the prostate. This rate was also lower than that in the previous analysis on RARP patients with T3 disease, as defined by MRI or digital rectal examination [13]. Thus, as hypothesised in the development of our technique, detailed tissue magnification and recognition of Xi system and its tools resulted into better definition of surgical planes and, in

consequence, in a reduced rate of PSM. This high optical visualisation, in case of monolateral disease, allows performing a meticulous excision of the DVF on one side and DVF preservation on the other (SE-RARP with unilateral DVF resection; Fig. 1B), and an interfascial NS procedure in some patients.

Second, our technique was not associated with an increased rate of postoperative complications after surgery compared with previous RARP series on locally advanced cases [13]. This evidence further supports the feasibility and safety profile of this approach in patients with posterior iT3a or T3b at MRI. Similarly, of the three patients who experienced intraoperative complications, only one (injury of the bladder below the bladder neck) had complications related to the prostatectomy and two had complications

**Table 5** – Multivariable Cox regression models based on clinical or pathological covariates predicting biochemical recurrence and additional treatment use after SE-RARP in 78 locally advanced PCa patients at MRI treated between 2015 and 2018 at a single European high-volume centre

Variable		Biochemical recurrence			Additional treatment use		
		HR	95% CI	p value	HR	95% CI	p value
<i>Clinical covariates</i>							
Tumour stage at preoperative MRI	Posterior iT3a	Ref.			Ref.		
	iT3b	1.80	(0.77–4.18)	0.2	1.67	(0.61–4.55)	0.3
Biopsy grade group	1–3	Ref.			Ref.		
	4–5	2.84	(1.29–6.21)	0.009	6.18	(2.34–16.3)	<0.001
Preoperative PSA (ng/ml)		1.01	(0.98–1.05)	0.5	0.98	(0.93–1.03)	0.5
<i>Pathological covariates</i>							
Pathological tumour stage	≤pT3a	Ref.			Ref.		
	≥T3b	1.76	(0.75–4.11)	0.2	3.28	(1.65–10.3)	0.041
Pathological grade group	1–3	Ref.			Ref.		
	4–5	3.17	(1.27–7.83)	0.01	5.63	(1.71–18.5)	0.004
Pathological nodal stage	pN0	Ref.			Ref.		
	pN1	0.66	(0.26–1.65)	0.4	0.51	(0.15–1.75)	0.3
Surgical margins	R0	Ref.			Ref.		
	R1	5.86	(2.43–14.1)	<0.001	5.23	(1.65–16.6)	0.004

CI = confidence interval; HR = hazard ratio; MRI = magnetic resonance imaging; PCa = prostate cancer; PSA = prostate-specific antigen; Ref. = reference; SE-RARP = superextended robot-assisted radical prostatectomy.

related to the lymph node dissection phase (left and right iliac vein injuries). Notably, the robustness of our results on postoperative complications is supported by the use of standardised methodology provided by the EAU [22]. Indeed, by fulfilling all the suggested criteria, we ensure high reliability of the reported data on postoperative complications.

Third, we demonstrated no major functional impairment after wide excision of the posterior plane, when UC was considered. Notably, the early continence rate was 34%. Overall, the UC rate at 1 yr of follow-up was higher (84%) than those reported for locally advanced PCa in previous mixed [29] or purely RARP [13] series. This might be explained by the fact that, differently from previous series, which relied on multi-institutional data with multiple surgeons involved (with consequent variability of outcomes due to differences in experience and technical skills), we limited the effect of intersurgeon variability [30,31] in RARP performance by reporting the outcomes of 78 patients treated by a single robotic surgeon with previous extensive experience in robotic surgery. However, there is still margin of improvement, suggesting that the learning curve for RARP might be longer than expected also in expert hands [31,32]. Moreover, according to disease extension at MRI, a certain degree of interfascial NS approach was performed, which has been demonstrated to have a protective effect on early continence recovery [29,33,34]. In our series, the overall rate of any interfascial NS was high (75%), and this further supports the recorded differences in UC rate compared with previous analyses [30,31]. Lastly, no significant difference in UC recovery rates was recorded between patients with apical and nonapical lesions (82% vs 86%,  $p = 0.5$ ). These data confirm the efficacy of this revised SE-RARP approach combined with the “collar” technique for apical dissection, which allows for the preservation of the sphincteric structures of the urethral complex even in case with suspected ECE at apical level [19].

Fourth, the rates of BCR at 1- and 2-yr follow-up were 33% and 45%, respectively. These relatively high rates are in line with previous studies on locally advanced PCa [12,28]; however, these might be explained by the low number of adjuvant treatments received by our patients in favour of a strategy based on observation and subsequent salvage treatment.

Fifth, we observed that PSMs [35] and the high grade of the disease were independent predictors of BCR (HR 5.86 and 3.17, respectively) and of additional treatment use (HR 5.23 and 5.63, respectively) in multivariable Cox regression models adjusted for pathological covariates. These findings suggest that patients with negative surgical margins and low-grade disease might be optimal candidates for this surgical treatment without the need for additional therapy at midterm follow-up.

Taken together, we outlined specific technical features of our revised SE-RARP technique for posterior iT3a or iT3b at MRI. Specifically, we described a step-by-step RARP procedure focusing on technical refinements in the DVF dissection for advanced cases, which might play a crucial role in the reduction of PSM risk and in the consequent

optimisation of cancer-related outcomes. This revised RARP technique, combined with the high visual definition of the new DaVinci Xi system features, allows performing a safe procedure with limited impact on the risk of perioperative complications and optimal UC recovery. However, future prospective comparative studies with long-term follow-up are needed to confirm whether SE-RARP allows maximum oncological control without compromising functional outcomes relative to the standard approach.

Despite its strengths, our analysis is not devoid of limitations. Of note, as in case of previous analyses that reported postoperative RARP outcomes, our study is based on a retrospective analysis with all its inherent limitations. Similarly, the small number of patients, the short follow-up, and the small number of events are all potential limitations of the current analysis that need to be acknowledged. Second, our data were derived from a highly experienced surgeon with a high annual caseload. Thus, the generalisability of our findings may be limited to centres with similar caseload and experience. Additionally, it is important to remark that RARP in patients with iT3 disease at MRI represents a procedure with high level of complexity, and in consequence, it should be performed only by expert robotic surgeons in PCa referral centres. Third, due to the low number of events, multivariable Cox models suffer from consistent overfitting, which limits the generalisability of our findings. Thus, our findings need to be necessarily validated in larger cohorts of locally advanced PCa cases. Lastly, due to rapidly evolving recommendations for optimal postoperative management of advanced patients, variability in additional treatment timing and type may have influenced the reported outcomes. However, such a limitation is shared with previous retrospective studies on radical prostatectomy published in highly ranked journals [13,36–38].

## 5. Conclusions

Our revised RARP technique applicable to patients with posterior iT3a or iT3b at preoperative MRI is presented. Considering the locally advanced stage, this technique is associated with good morbidity and UC recovery rates. Moreover, in patients with low-grade and negative surgical margins at final pathology, SE-RARP might guarantee biochemical control of the disease and might postpone the use of additional treatments at midterm follow-up.

**Author contributions:** Elio Mazzone had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Mottrie, Mazzone, Larcher, Dell'Oglio.

**Acquisition of data:** Brook, Puliatti, Turri, Beato, Andras, Pandey, Wisz, De Groote.

**Analysis and interpretation of data:** Mazzone, Mottrie, Dell'Oglio.

**Drafting of the manuscript:** Mazzone, Rosiello, Dell'Oglio, Puliatti.

**Critical revision of the manuscript for important intellectual content:** Mottrie, De Naeyer, D'Hondt, Schattelman.

**Statistical analysis:** Mazzone, Rosiello.

**Obtaining funding:** None.



*Administrative, technical, or material support:* None.

*Supervision:* Motttrie, Schatteman, De Naeyer, D'Hondt.

*Other:* None.

**Financial disclosures:** Elio Mazzone certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

**Funding/Support and role of the sponsor:** None.

## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.eururo.2020.09.009>.

## References

- [1] Dell'Oglio P, Stabile A, Dias BH, et al. Impact of multiparametric MRI and MRI-targeted biopsy on pre-therapeutic risk assessment in prostate cancer patients candidate for radical prostatectomy. *World J Urol* 2019;37:221–34.
- [2] Valerio M, Donaldson I, Emberton M, et al. Detection of clinically significant prostate cancer using magnetic resonance imaging-ultrasound fusion targeted biopsy: a systematic review. *Eur Urol* 2015;68:8–19.
- [3] Fütterer JJ, Briganti A, De Visschere P, et al. Can clinically significant prostate cancer be detected with multiparametric magnetic resonance imaging? A systematic review of the literature. *Eur Urol* 2015;68:1045–53.
- [4] Stabile A, Dell'Oglio M, Soligo M, et al. Assessing the Clinical Value of Positive Multiparametric Magnetic Resonance Imaging in Young Men with a Suspicion of Prostate Cancer. *Eur Urol Oncol* 2019;1–7.
- [5] Costa DN, Goldberg K, de Leon AD, et al. Magnetic resonance imaging-guided in-bore and magnetic resonance imaging-transrectal ultrasound fusion targeted prostate biopsies: an adjusted comparison of clinically significant prostate cancer detection rate. *Eur Urol Oncol* 2019;2:397–404.
- [6] Spahn M, Fehr JL. Multiparametric magnetic resonance imaging for prostate-specific antigen recurrence after radical prostatectomy: are we leaving the “one treatment fits all approach” and moving towards personalized imaging-guided treatment? *Eur Urol* 2018;73:888–9.
- [7] Preisser F, Marchioni M, Nazzani S, et al. Trend of adverse stage migration in patients treated with radical prostatectomy for localized prostate cancer. *Eur Urol Oncol* 2018;1:160–8.
- [8] Gandaglia G, Karakiewicz PI, Sun M, et al. Comparative effectiveness of robot-assisted and open radical prostatectomy in the postdissemination era. *J Clin Oncol* 2014;32:1419–26.
- [9] Mazzone E, Mistretta FA, Knipper S, et al. Contemporary national assessment of robot-assisted surgery rates and total hospital charges for major surgical uro-oncological procedures in the United States. *J Endourol* 2019;33:438–47.
- [10] EAU. Prostate guidelines. Presented at the EAU Annual Congress, Amsterdam. 2020.
- [11] Nelson WG, Carter HB, DeWeese TL, Antonarakis ES, Eisenberger MA. Prostate cancer. In: *Abeloff's clinical oncology*. ed. 5. Elsevier; 2014. p. 1463–96.e9.
- [12] Dell'Oglio P, Stabile A, Gandaglia G, et al. New surgical approaches for clinically high-risk or metastatic prostate cancer. *Expert Rev Anticancer Ther* 2017;17:1013–31.
- [13] Gandaglia G, De Lorenzis E, Novara G, et al. Robot-assisted radical prostatectomy and extended pelvic lymph node dissection in patients with locally-advanced prostate cancer. *Eur Urol* 2017;71:249–56.
- [14] Costello AJ. Considering the role of radical prostatectomy in 21st century prostate cancer care. *Nat Rev Urol* 2020;17:177–88.
- [15] Fossati N, Willemse PPM, Van den Broeck T, et al. The benefits and harms of different extents of lymph node dissection during radical prostatectomy for prostate cancer: a systematic review. *Eur Urol* 2017;72:84–109.
- [16] Gandaglia G, Zaffuto E, Fossati N, et al. Identifying candidates for super-extended staging pelvic lymph node dissection among patients with high-risk prostate cancer. *BJU Int* 2018;121:421–7.
- [17] Briganti A, Suardi N, Capogrosso P, et al. Lymphatic spread of nodal metastases in high-risk prostate cancer: the ascending pathway from the pelvis to the retroperitoneum. *Prostate* 2012;72:186–92.
- [18] Motttrie A, Van Migem P, De Naeyer G, Schatteman P, Carpentier P, Fonteyne E. Robot-assisted laparoscopic radical prostatectomy: oncologic and functional results of 184 cases. *Eur Urol* 2007;52:746–51.
- [19] Bianchi L, Turri FM, Larcher A, et al. A novel approach for apical dissection during robot-assisted radical prostatectomy: the “collar” technique. *Eur Urol Focus* 2018;4:677–85.
- [20] Gratzke C, Dovey Z, Novara G, et al. Early catheter removal after robot-assisted radical prostatectomy: surgical technique and outcomes for the Aalst technique (ECaRemA study). *Eur Urol* 2016;69:917–23.
- [21] Clavien PA, Barkun J, De Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009;250:187–96.
- [22] Mitropoulos D, Artibani W, Graefen M, Remzi M, Rouprêt M, Truss M. Reporting and grading of complications after urologic surgical procedures: an ad hoc EAU G Panel assessment and recommendations. *Eur Urol* 2012;61:341–9.
- [23] Preisser F, Chun FKH, Pompe RS, et al. Persistent prostate-specific antigen after radical prostatectomy and its impact on oncologic outcomes. *Eur Urol* 2019;76:106–14.
- [24] Dalela D, Jeong W, Prasad MA, et al. A pragmatic randomized controlled trial examining the impact of the Retzius-sparing approach on early urinary continence recovery after robot-assisted radical prostatectomy. *Eur Urol* 2017;72:677–85.
- [25] Assel M, Sjöberg D, Elders A, et al. Guidelines for reporting of statistics for clinical research in urology. *Eur Urol* 2019;75:358–67.
- [26] Patel VR, Sandri M, Grasso AAC, et al. A novel tool for predicting extracapsular extension during graded partial nerve sparing in radical prostatectomy. *BJU Int* 2018;121:373–82.
- [27] Lightfoot AJ, Su Y-K, Sehgal SS, et al. Positive surgical margin trends in patients with pathologic t3 prostate cancer treated with robot-assisted radical prostatectomy. *J Endourol* 2015;29:634–9.
- [28] Poelaert F, Joniau S, Roumeguère T, et al. Current management of pT3b prostate cancer after robot-assisted laparoscopic prostatectomy. *Eur Urol Oncol* 2019;2:110–7.
- [29] Suardi N, Moschini M, Gallina A, et al. Nerve-sparing approach during radical prostatectomy is strongly associated with the rate of postoperative urinary continence recovery. *BJU Int* 2013;111:717–22.
- [30] Dell'Oglio P, Mazzone E, Lambert E, et al. The effect of surgical experience on perioperative and oncological outcomes after robot-assisted radical cystectomy with intracorporeal urinary diversion: evidence from a high-volume center. *Eur Urol Suppl* 2019;18:e2637–9.
- [31] Bravi CA, Tin A, Vertosick E, et al. The impact of experience on the risk of surgical margins and biochemical recurrence after robot-assisted radical prostatectomy: a learning curve study. *J Urol* 2019;202:108–13.

- [32] Thompson JE, Egger S, Böhm M, et al. Superior biochemical recurrence and long-term quality-of-life outcomes are achievable with robotic radical prostatectomy after a long learning curve—updated analysis of a prospective single-surgeon cohort of 2206 consecutive cases. *Eur Urol* 2018;73:664–71.
- [33] Srivastava A, Chopra S, Pham A, et al. Effect of a risk-stratified grade of nerve-sparing technique on early return of continence after robot-assisted laparoscopic radical prostatectomy. *Eur Urol* 2013;63:438–44.
- [34] Michl U, Tennstedt P, Feldmeier L, et al. Nerve-sparing surgery technique, not the preservation of the neurovascular bundles, leads to improved long-term continence rates after radical prostatectomy. *Eur Urol* 2016;69:584–9.
- [35] Martini A., Gandaglia G., Fossati N., et al. Defining clinically meaningful positive surgical margins in patients undergoing radical prostatectomy for localised prostate cancer. *Eur Urol Oncol*. In press. <https://doi.org/10.1016/j.euo.2019.03.006>.
- [36] Gandaglia G, Fossati N, Karnes RJ, et al. Use of concomitant androgen deprivation therapy in patients treated with early salvage radiotherapy for biochemical recurrence after radical prostatectomy: long-term results from a large, multi-institutional series. *Eur Urol* 2018;73:512–8.
- [37] Fossati N, Karnes RJ, Colicchia M, et al. Impact of early salvage radiation therapy in patients with persistently elevated or rising prostate-specific antigen after radical prostatectomy. *Eur Urol* 2018;73:436–44.
- [38] Abdollah F, Karnes RJ, Suardi N, et al. Impact of adjuvant radiotherapy on survival of patients with node-positive prostate cancer. *J Clin Oncol* 2014;32:3939–47.



## ESU-ESTU Masterclass on Kidney transplant

28-29 October 2021, Madrid, Spain

[www.esukidneytransplant.org](http://www.esukidneytransplant.org)

**estu** **EAU** **esu** European  
School of  
Urology