Central European Journal of Urology

REVIEW PAPER

UROLOGICAL ONCOLOGY

Prostate-specific membrane antigen radioguided surgery in prostate cancer: A narrative review

Piotr Chuchra[1], Jakub Karwacki[2,3], Akihiro Matsukawa[4,5], Bartłomiej Borek[6], Tomasz Rynkiewicz[7], Omar Tayara[8], Bartosz Małkiewicz[2], Paweł Rajwa[8,9], Andrzej Paradysz[1], Marcin Zyczkowski[10]

[1]*Department of Urology, Medical University of Silesia, Zabrze, Poland*
[2]*Department of Minimally Invasive and Robotic Urology, University Center of Excellence in Urology, Wroclaw Medical University, Poland*
[3]*Department of Pathophysiology, Wroclaw Medical University, Poland*
[4]*Department of Urology, Comprehensive Cancer Center, Medical University of Vienna, Austria*
[5]*Department of Urology, The Jikei University School of Medicine, Tokyo, Japan*
[6]*Department of Urology Sosnowiec City Hospital LLP in restructuring, Poland*
[7]*Polish Center of Advanced Urology, Department of Urology, St. Anne's Hospital EMC, Piaseczno, Poland*
[8]*Second Department of Urology, Centre of Postgraduate Medical Education, Warsaw, Poland*
[9]*Department of Urology, Medical University of Vienna, Austria*
[10]*Clinic of Urology, Institute of Medical Sciences, University of Opole, Poland*

Citation: Chuchra P, Karwacki J, Matsukawa A, et al. Prostate-specific membrane antigen radioguided surgery in prostate cancer: A narrative review. Cent European J Urol. 2025; 78: 470-482.

Article history
Submitted: May 28, 2025
Accepted: Jun. 30, 2025
Published online: Nov. 27, 2025

Corresponding author
Piotr Chuchra
Department of Urology, Medical University of Silesia, Zabrze, Poland
piotr.chuchra456@gmail.com

Introduction Prostate-specific membrane antigen (PSMA) radioguided surgery (RGS) is being tested to personalize lymph node dissection at radical prostatectomy and in the salvage settings.

Material and methods We conducted a narrative review using the MEDLINE database (via PubMed), selecting key publications on the intravenous administration of PSMA to investigate lymph node involvement during surgery.

Results This review provides an overview of the PSMA-RGS methodology and outcomes. The technique demonstrates high specificity, particularly in *ex vivo* settings, with a median ranging from 93.5% to 100%. However, sensitivity varies widely, with a median range of 50% to 100%, often limited by reduced detection of micrometastases. Detailed preoperative, perioperative, and oncological evaluations are summarized in tables.

Conclusions PSMA-RGS is feasible and safe in both primary and salvage settings. In appropriately selected patients, it may contribute to longer therapy-free survival (36 months) and prolonged biochemical recurrence-free survival (19 months).

Key Words: radioguided surgery ‹› prostate-specific membrane antigen ‹› PSMA ‹› pelvic lymph node dissection ‹› lymph node metastases ‹› prostate cancer

INTRODUCTION

The standard local therapies for early-stage prostate cancer (PCa) are radical prostatectomy (RP) or radiotherapy [1]. However, after the treatment, up to 50% of patients experience biochemical recurrence (BCR) caused by local recurrence or distant metastases [2]. Lymph nodes (LNs) are among the first sites for metastasis [3]. One of the possible solutions to remedy this was primary lymph node dissection (LND) during prostatectomy. However, its impact on survival and morbidity remains unclear. One promising advancement is radioguided surgery (RGS), which can improve LN sampling while minimizing side effects of extended LND [4].

When BCR occurs, management options include watchful waiting, salvage radiotherapy (SRT), or androgen deprivation therapy (ADT) [2]. Selecting the appropriate treatment requires balancing

oncologic benefit with physical and mental aspects of patient quality of life [5].

Two key trials, STOMP and ORIOLE, explored whether metastasis-directed therapy (MDT) improves survival. The STOMP trial, a randomized multicenter study in Belgium, included 62 patients with oligometastatic PCa randomized to MDT or surveillance (2012–2015). After three years, ADT was delayed in the MDT group (21 vs 12 months; $p < 0.08$) [6].

The ORIOLE trial (2016–2018, US) enrolled 54 patients with ≤3 asymptomatic metastases. Stereotactic ablative radiation (SABR) was compared to observation in a 2 : 1 ratio. Disease progression was defined as a PSA rise ≥2 ng/dl, radiologic progression, new symptoms, ADT initiation, or death. At 6 months, progression occurred in 19% (SABR) vs 61% (observation) [7]. These trials suggest MDT, including SABR or metastasectomy, may delay progression and improve cancer-specific survival (CSS) [6–8]. However, these are not targeted therapies – except for targeted salvage radiation.

RGS offers intraoperative localization and removal of metastatic lesions. It involves intravenous administration of a radiotracer that binds to prostate-specific membrane antigen (PSMA), a protein overexpressed in PCa cells [9, 10]. The radiotracer emits ionizing radiation (γ or β particles), detected during surgery with a handheld probe, providing visual and auditory cues. This allows for precise excision of metastatic sites, including those otherwise difficult to detect [11–15].

This review summarizes recent developments in RGS using PSMA-targeted tracers. It evaluates the potential of this approach as a therapeutic option for patients with lymph node involvement (LNI) in recurrent PCa.

Search strategy

The review's search strategy and selection criteria were designed to ensure comprehensive coverage of PSMA RGS in recurrent PCa while maintaining methodological precision. The search strategy consisted of Medline database analysis (via PubMed). The papers needed to consider PSMA and RGS applied in *in vivo* settings to be eligible. We did not include papers concerning 11C-choline or conventional imaging to evaluate metastases. The work did not consider papers about sentinel lymph node dissection with or without fluorescence. Only articles written in English or German language were included.

TECHNIQUE CHARACTERISTICS AND THE COURSE OF THE PROCEDURE

RGS is a technique that enables the intraoperative identification of metastatic lesions. A radioactive tracer emitting either β or γ radiation binds to the PSMA, forming a PSMA-ligand. Administered intravenously, this tracer allows for the detection of PCa tissue even at low prostate-specific antigen (PSA) levels. Real-time visual and auditory feedback is provided via a read-out console positioned near the surgical field (Figure 1) [12, 16].

As part of preoperative staging, patients with BCR following primary therapy undergo Gallium-68 (68Ga) PSMA positron emission tomography (PSMA PET) imaging. This is currently considered the most specific modality for assessing LNI [17, 18]. A key advantage of preoperative imaging is the ability to determine the number and anatomical location of metastatic lymph nodes, enabling direct correlation with intraoperative tracer localization.

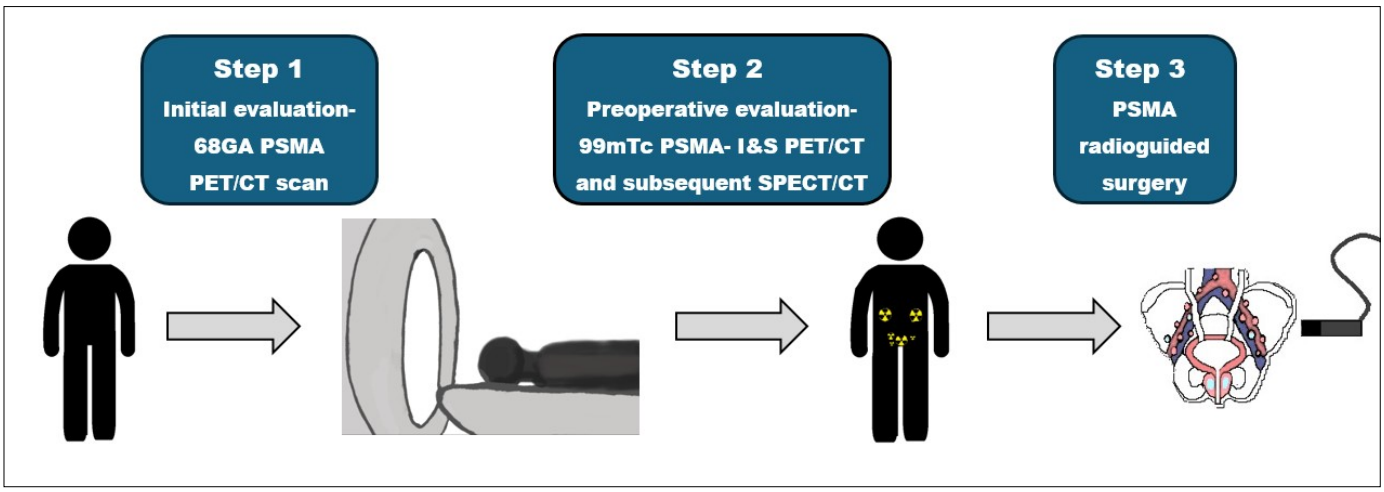

Figure 1. *Graphical representation of the procedure.*

This correlation helps reduce the risk of missing lesions during surgery.

However, it should be noted that despite its high specificity, 68Ga-PSMA PET demonstrates relatively low sensitivity, particularly in low-volume disease. Therefore, it cannot reliably determine the necessity of ePLND in all cases [19].

Approximately one day before surgery, patients receive an intravenous dose of either Indium-111 (111In) PSMA I&T or Technetium-99m (99mTc) PSMA-I&S [11, 19]. This is followed by single photon emission computed tomography/computed tomography (SPECT/CT) imaging, which serves as a quality control measure for radiotracer distribution and helps cross-validate the findings from prior PSMA PET imaging [20].

Preoperative PET imaging presents certain limitations compared to SPECT/CT. One major drawback is the complex process of obtaining 68Ga from the Ge-68/68Ga generator, which significantly restricts the number of patients who can be scanned. Additionally, the short half-life of 68Ga (68 minutes) necessitates on-site synthesis in a nuclear medicine laboratory [21]. In contrast, the 99mTc generator allows for higher radiotracer yield and can serve a substantially larger patient population [22]. Despite these logistical advantages, PSMA PET remains crucial due to the lower sensitivity of SPECT/CT.

For example, Rauscher et al. [23] found that 111In-PSMA I&T SPECT/CT detected only 48.3% of metastatic LNs (14 out of 29), while 68Ga-PSMA HBED-CC PET identified metastases in 59% of patients with early recurrent PCa (13 out of 22). Similarly, Lawal et al. [24] reported that in 14 patients, 68Ga PSMA PET/CT detected 46 lesions with increased PSMA uptake (10 prostate, 24 LNs, 12 bone), whereas 99mTc HYNIC PSMA SPECT/CT visualized only 36 of these 46 lesions (10 prostate, 15 LNs, 11 bone), failing to detect any new ones – even in the presence of high PSA levels (median 45.2 ng/ml).

The next step is the intraoperative detection of metastatic lesions. The previously administered PSMA radiotracer binds to overexpressed PSMA receptors, allowing for detection using a γ-probe during surgery [17]. The γ-probe, functioning as a scintillation counter, can identify small lesions (<10 mm) and locate PCa tissue even in atypical regions, as targeted by tracers like 99mTc-PSMA-I&S. The device provides both visual and auditory signals, with signal intensity proportional to the γ radiation concentration [12].

Schottelius et al. [25] compared the *in vivo* biodistribution of PSMA-I&T labeled with various radionuclides (111In, 68Ga, 177Lu) in LNCaP (human prostate adenocarcinoma cell line) xenograft-bearing mice. They observed that 111In-PSMA-I&T and 177Lu-PSMA-I&T exhibited similar uptake levels, while 68Ga-PSMA-I&T showed significantly lower uptake one hour after radiotracer injection. Despite its effective uptake, 111In-PSMA-I&T has notable limitations, including high cost and limited availability.

99mTc-PSMA-I&S addresses these issues. Robu et al. [26] evaluated the performance of 99mTc-PSMA-I&S in comparison with 68Ga-PSMA-I&T, 177Lu-PSMA-I&T, and 111In-PSMA-I&T. They found comparable internalization rates between 99mTc-PSMA-I&S and 111In-PSMA-I&T (93 ±3% vs 104 ±7% of the reference [125I-BA]KuE) in both *in vitro* LNCaP cell assays and *in vivo* CB17 LNCaP xenograft-bearing mice. Moreover, the study established that the optimal timing for RGS using 99mTc-PSMA-I&S is more than 5 hours post injection, ensuring a high lesion-to-background ratio, specifically referring to the contrast between radiotracer uptake in malignant tissue versus surrounding non-target tissue [26].

Ex vivo scintillation measurements confirm the successful intraoperative removal of malignant tissue [12].

OPEN SURGERY IN OLIGOMETASTATIC PROSTATE CANCER

Maurer et al. [12] conducted the first study utilizing PSMA in RGS, involving five patients (one with primary PCa and four with recurrent disease), all presenting with LNI confirmed by 68Ga-PSMA HBED-CC PET imaging. Building on this, Rauscher et al. performed a prospective study including 31 patients with recurrent PCa, reporting high sensitivity (92.3%), specificity (93.5%), and PPV (88.9%) for RGS using 111In-PSMA. Postoperative PSA levels dropped below 0.2 ng/ml in 20 of the 31 patients, and 13 patients remained free from BCR during a median follow-up of 13.8 months (range: 4.6–18.3 months). Only one patient experienced a complication exceeding grade 1 on the Clavien-Dindo scale (grade 3a), presenting with urosepsis and hydronephrosis [11].

Knipper et al. later published a retrospective study involving 364 patients who underwent PSMA-RGS without concomitant treatments. Metastatic lesions were successfully dissected in 343 of 364 patients (94%). Postoperative complications according to the Clavien-Dindo classification occurred in 24 patients (6.6%) within 3 months. BCR was observed in 225 patients, while 165 achieved complete biochemical response (cBR, PSA <0.2 ng/ml)

within 2–16 weeks after surgery. Median biochemical-free survival (BFS) was 7.8 months (95% CI: 5.4–10.5), and treatment-free survival (TFS) was 35.5 months (95% CI: 25.9–45.9). Independent predictors of BCR following PSMA-RGS included higher preoperative PSA (HR: 1.07; 95% CI: 1.02–1.12), increased number of PSMA-avid lesions (HR: 1.23; CI: 1.08–1.40), multiple lesion localizations (pelvic and retroperitoneal) (HR: 1.90; CI: 1.23–2.95), and retroperitoneal involvement (HR: 2.04; CI: 1.31–3.18) [20].

In a more recent multicenter retrospective study, Knipper et al. analyzed data from 553 patients. Among them, 212 remained BCR-free for a median of 23.7 months (IQR: 10–36). Subgroup analysis revealed superior oncological outcomes for patients with PSA <0.1 ng/ml compared to those with PSA 0.1–<0.2 or ≥0.2 ng/ml, as reflected by TFS at 2-year follow-up: 81.1% vs 56.1% vs 43.1%, respectively (CI: 75.1–87.5% vs 43.6–72.1% vs 35.9–51.7%; p <0.001). Multivariable analysis identified predictors of TFS, including pT stage at RP, time from RP to PSMA-RGS, retroperitoneal metastasis location, number of PSMA PET-visible lesions, and postoperative PSA levels [27].

Details of additional studies are summarized in Tables 1–3 [13, 27–34]. Collectively, these studies suggest that PSMA-RGS is a promising tool for enhancing intraoperative detection of metastatic lesions in PCa, potentially leading to improved oncological outcomes. However, as salvage surgery in oligorecurrent PCa remains an experimental approach and RGS cannot substitute for ePLND or comprehensive histopathological evaluation, careful patient selection is critical.

Multiple studies have demonstrated that both pre- and postoperative PSA levels are significantly associated with longer BFS and treatment-free survival (TFS) [27, 29, 31, 35]. Notably, the most favorable long-term outcomes were observed in patients with PSA levels below 0.1 ng/ml [27]. The interval between RP and PSMA-RGS is another key factor, as are the number of PSMA-avid lesions and the count of histopathologically confirmed positive nodes [27, 31, 35].

Findings on other prognostic indicators, such as the impact of the pathological T stage at RP and the anatomical location of lesions, remain inconsistent across studies [27, 36].

ROBOT-ASSISTED SURGERY IN OLIGOMETASTATIC PROSTATE CANCER

Robot-assisted radioguided surgery (rRGS) has recently emerged as a key area of interest within RGS. Several studies have demonstrated its feasibility. As summarized in Tables 4–6, each study reported outcomes comparable to those of open RGS [36–42]. Ambrosini et al. compared rRGS (n = 24) to open RGS (n = 61), finding similar oncological outcomes between groups (12-month BFS: 41% vs 39%, p = 0.9). rRGS did not significantly reduce estimated blood loss (β = −40 ml; 95% CI: −103 to 22 ml; p = 0.2) and was associated with a significantly longer operative time (β = 28 min; 95% CI: 10–46 min; p = 0.002). No Clavien-Dindo grade III–V complications occurred in the rRGS group, compared to four cases (6%) in the open RGS group. Similar encouraging results were reported regardless of the gamma probe used [42]

Mazzucato et al. identified an intriguing observation: radioactive uptake depends on tumor-occupied tissue. Nodal metastases exhibited higher radioactivity than soft tissue PCa lesions – potentially due to higher tumor cell concentration in lymph nodes. Further studies are needed to validate this finding [42].

Although current data do not show a definitive oncological advantage for rRGS, the technique improves access to local recurrences by enhancing visualization and surgical maneuverability, which may translate into greater precision than open RGS [43].

In a study by Quarta et al. [39], target-to-background (TtB) ratios were evaluated at three thresholds (≥2, ≥3, and ≥4) to assess implications for ePLND in RP settings. A TtB ratio ≥2 yielded the highest sensitivity (78%) but lower specificity (76%), compared to TtB ≥3 (66% sensitivity, 95% specificity) and ≥4 (55% sensitivity, 95% specificity). While a TtB ratio ≥2 could spare 60% of excised LNs and potentially replace ePLND, it risked missing 11% of patients with LNI [39]

Notably, the studies discussed did not report TFS or BFS outcomes. While improving LNI detectability is important, it remains unclear whether removing all metastatic LNs – including micrometastases – leads to improved survival or increased complication rates that may preclude repeat RGS in selected patients. Further well-designed studies are essential to establish robust clinical evidence.

RADIOGUIDED SURGERY VERSUS CONVENTIONAL SURGERY

The previously presented data must be evaluated alongside other therapeutic options to ensure that PCa patients receive the most effective treatment. Knipper et al. [44] compared conventional surgical approaches (CSA), which rely solely on preoperative

Table 1. *Baseline characteristics of prostate cancer patients who underwent open surgery*

Study (number of patients)	Maurer et al. (n = 5)	Rauscher et al. (n = 31)	Horn et al. (n = 63)	Maurer et al. (n = 31)	Horn et al. (n = 121)	Knipper et al. (n = 40)	Mayr et al. (n = 50)	Knipper et al. (n = 364)	Knipper et al. (n = 553)
Hospital	Munich	Munich	Munich	Munich	Munich	Munich, Hamburg	Regensburg	Munich, Hamburg	Hamburg, Munich, Amsterdam
Publishing date	2015	2017	2017	2019	2019	2021	2024	2023	2024
Study type	Prospective	Prospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective
Setting	Recurrent / Primary	Recurrent	Recurrent	Recurrent	Recurrent	Recurrent	Recurrent	Recurrent	Recurrent
Journal	European Urology	BJU international	Der Urologe	European Urology	European Urology	European Urology	World Journal of Urology	European Urology	European Urology Oncology
PSA at primary treatment (ng/ml), median IQR	2.45 (0.46–4.36)	NA	9.7 (NA)	NA	9.5 (6.8–17.9)	7.4 (5.3-10.8)	NA	9 (6,16)	9 (6-15)
pT stage at RP (%)		29 RP	61 RP	31 RP	121 RP	40 RP	50 RP	364 RP	553 RP
pT2	T2c 2 (40)	12 (39)		14 (45)	41 (34)	18 (45)	21 (42)	145 (40)	221 (40)
pT3a	1 (20)	16 (52)		16 (52)	78 (64)	15 (38)	14 (28)	105 (29)	144 (26)
pT3b	1 (20)					7 (17)	13 (26)	107 (29)	155 (28)
pT4	1 (20)	1 (3)				0	0	–	–
NA		2 (6)	63 (100)	1 (3)	2 (2)	0	2 (4)	7 (2)	33 (6)
Gleason grade group (%)									
I	1 (20)	5 (16)		4 (13)	13 (11)	7 (18)	30 (60)	27 (7)	31 (6)
II	1 (20)	15 (49)		8 (26)	58 (48)	12 (30)		96 (26)	135 (24)
III	1 (20)			7 (23)		6 (15)		127 (35)	194 (35)
IV	1 (20)	10 (32)		5 (16)	44 (36)	7 (18)	17 (34)	40 (11)	63 (11)
V	1 (20)			7 (23)		7 (18)		60 (17)	83 (15)
NA		1 (3)	63 (100)		6 (5)	1 (3)	3 (6)	14 (4)	47 (9)
pN stage (%)									
pN0	4 (80)	21 (68)		23 (74)	90 (74)	30 (75)	41 (82)	276 (75)	395 (71)
pN1	1 (20)	6 (19)		5 (16)	25 (21)	6 (15)	7 (14)	60 (17)	98 (18)
pNX		4 (13)		3 (10)	6 (5)	2 (5)	2 (4)	18 (5)	27 (5)
NA			63 (100)			2 (5)	0	10 (3)	33 (6)
Surgical margin status (%)		NA	NA						
R0	3 (60)			22 (71)	78 (65)	27 (68)	35 (70)	266 (73)	386 (70)
R1				5 (16)	22 (18)	11 (28)	9 (18)	72 (20)	112 (20)
RX						2 (5)	4 (8)	11 (3)	15 (3)
NA	2 (40)	31 (100)	63 (100)	4 (13)	21 (17)		2 (4)	15 (4)	40 (7)
Secondary treatment (%)	4 (80)	22 (71)	30 (48)	20 (65)	83 (69)	33 (83)	33 (66)		
RT after RP	2 (40)	20 (65)	23 (37)	18 (58)	77 (64)	33 (83)	3 (6)	224 (62)	310 (56)
No	2 (40)	9 (29)			38 (31)		21 (42)	140 (39)	243 (44)
Salvage LND		4 (13)		3 (10)	8 (7)				-
RT & salvage LND	1 (20)		7 (11)						
ADT		8 (26)		8 (26)	8 (7)		7 (14)		0 (Exclusion criteria)

ADT – androgen deprivation therapy; IQR – interquartile range; LND – lymph node dissection; NA – not applicable; PSA – prostate-specific antigen; pN – pathological regional lymph node; pNX – pathological lymph node impossible to assess; pT – pathological primary tumor; RGS – radioguided surgery; RP – radical prostatectomy; RT – radiotherapy

Table 2. *Preoperative characteristics, pathological results, and complication rates of prostate cancer patients who underwent open surgery*

Study (number of patients)	Maurer et al. (n = 5)	Rauscher et al. (n = 31)	Horn et al. (n = 63)	Maurer et al. (n = 31)	Horn et al. (n = 121)	Knipper et al. (n = 40)	Mayr et al. (n = 50)	Knipper et al. (n = 364)	Knipper et al. (n = 553)
Median age at PSMA-RGS [yr], (IQR)	75 (69–75)	68.2 (52–76)	69 (49–78)	67 (61–74)	70 (63–74)	67 (63–74)	70 (65–73)	67 (62–71)	67 (62–72)
Median time between RP and PSMA-RGS [mo], (IQR)	NA	NA	54 (3–246)	NA	52 (26–113)	102 (72–122)	44 (23–92)	54 (28–93)	49 (25–97)
Median PSA prior to PSMA-RGS [ng/ml], (IQR)	1.46 (0.45–2.93)	1.3 (0.57–2.53)	1.29 (0.65–2.48)	1.13 (0.71–2.35)	1.13 (0.53–2.16)	0.9 (0.5–1.7)	1.2 (0.6–3.0)	1.0 (0.5–1.90)	0.81 (0.42–1,54)
Mean radiotracer activity (range MBq)	146 MBq (110–169)	150 MBq (86–298)	150 MBq (110–190)	571 MBq (221–857)	NA	NA	NA	NA	NA
PSMA PET – avid lesions (%)		Max 5	NA	Max 4	175/171 detected in RGS +9 additional detected		Max. 4		Equivocal findings 63 (11)
0								6 (2)	
1	2 (40)					40 (100)	25 (50)	241 (66)	350 (63)
2	1 (20)						18 (36)	76 (21)	89 (16)
3								24 (7)	≥3 51 (9)
4	1 (20)						7 (14)	12 (3)	
5								4 (1)	
6	1 (20)							1 (<1)	
Lesions localizations (%)	During RGs	During RGS	During RGS	68Ga-PSMA-11 PET			PSMA PET/CT		During RGS
Unilateral pelvic	4	16 (53)	31	17 (54.8) Pelvic (iliaca ext., com., int., obturator)	74 (61)		26 (52)	154 (42)	299 (54)
Bilateral pelvic	6							12 (3)	
Pelvic and presacral or retrovesical					0			32 (9)	
Presacral/pararectal	3	6 (20)	16	9 (29)	31 (26)		7 (14) 3 (6) + Pelvic	48 (13)	
Retrovesical/paravesiacal	2	4 (13)	10	9 (29)	26 (22)	40 (100)	Perivesical: 3 (6)	54 (15)	90 (16)
Retroperitoneal		3 (10)	5	2 (7)	5 (4)		6 (12)	28 (8)	125 (23)
Retroperitoneal and other location							4 (8)	27 (7)	
Intra-abdominal							1 (2)	3 (<1)	
Other			1 Inguinal LN	1 (3) inguinal					8 (1)
None		1 (3)						6 (2)	31 (6)
Number pathologically confirmed lesions (%)		NA	94	58					Unknown 19 (3)
0								21 (6)	31 (6)
1	2 (40)				77 (64)	40 (100)	29 (58)	145 (40)	233 (42)
2	1 (20)				29 (24)		14 (28)	69 (19)	94 (17)
3					15 (12)		7 (14)	34 (9)	≥3 176 (32)
4								24 (7)	
5	1							15 (4)	
≥6	1 (20)							56 (15)	

Table 2. *Continued*

Clavien-Dindo complications (%)	NA	10 (32)	24 (38)	13 (42)	40 (33)	7 (18)	13 (26)	118 (33)	NA
I		6 (19)		12 (39)	29 (24)	4 (10)	4 (8)	81 (22)	
II							1 (2)	13 (4)	
IIIa			6 (10)	1 (3)	11 (9)	3 (8)	0	8 (2)	
IIIb		4 (13)					8 (16)	15 (4)	
IVb								1 (<1)	
V					1 (<1)				

IQR – interquartile range; LN – lymph node; MBq – megabecquerel; mo – months; PET – positron emission tomography; PSA – prostate-specific antigen; PSMA – prostate-specific membrane antigen; RGS – radioguided surgery; RP – radical prostatectomy; yr – years

Table 3. *Outcomes of prostate-specific membrane antigen radioguided surgery in open surgery group*

Study (patients number)	Rauscher et al. (n = 31)	Horn et al. (n = 63)	Maurer et al. (n = 31)	Horn et al. (n = 121)	Knipper et al. (n = 40)	Mayr et al. (n = 50)	Knipper et al. (n = 364)	Knipper et al. (n = 553)
Total number of specimens (total metastatic lesions)	145 (51)	277 (94)	132 (58)	NA	40 (0 – local recurrence)	178	NA	NA
RGS-positive specimens confirmed histologically (All histologically confirmed metastatic lesions)	48 (52)	94 (109)	46 (58)	180 (219)	40 (40 – local recurrence)	(93)	180	NA
RGS-negative specimens confirmed histologically (All histologically non-metastatic lesions)	87 (93)	162 (168)	74 (86)	NA	0	NA	39	NA
Sensitivity (%), 95% CI	92 (83–97)	86.2	83.6 (71–92)	NA	100	NA	NA	NA
Specificity (%), 95% CI	94 (82–98)	96	100	NA	100	NA	NA	NA
PPV (%) 95% CI	89 (73–96)	94	100	NA	100	NA	NA	NA
NPV (%) 95% CI	96 (88–99)	92	89 (78–95)	NA	100	NA	NA	NA
Number of BFS patients (%)	18 (60)	17 (27)	13 (42)	71 (59)	18 (45)	19 (38)	139 (38)	212 (38)
Median BFS months (follow-up range)	NA	12 (7–32)	14 (5–18)	6	24 (12–42)	10 (IQR: 5–21)	8 (5–11)	19 (CI: 7–36)
Number of TFS patients (%)	20 (67)	17 (27)	20 (65)	82 (68)	28 (70)	21 (42)	243 (67)	365 (66)
Median TFS months (follow-up range)	9 (2–19)	12 (7–32)	12 (6–18)	5	46 (12–42)*	13 (6–21)	36 (26–46)	24 (10–36)

*Estimated survival probability based on Kaplan-Meier analyses
BFS – biochemical-free survival; CI – confidence interval; NGV – negative predictive value; PCa – prostate cancer; PPV – positive predictive value; RGS – radioguided surgery; TFS – treatment-free survival

68Ga-PSMA PET imaging to identify affected LNs, with RGS in the context of salvage lymphadenectomy.

This prospective study included 42 patients with PCa recurrence confined to lymph nodes. Of these, 29 underwent CSA and 13 underwent 99mTc-PSMA RGS, using the radiotracer administered one day before surgery. The mean number of LNs removed was 17.8 (range: 1–65) in the CSA group and 19.3 (range: 2–53) in the RGS group. RGS successfully removed all metastatic LNs identified by 68Ga-PSMA PET, whereas CSA failed to confirm histological metastases in 9 patients (31%), despite a mean dissection of 13.6 LNs (range: 5–27). Six-week postoperative PSA levels were significantly lower in the RGS group compared to the CSA group (0.69 ng/ml [<0.01–3.3] vs 2.19 ng/ml [0.01–8.91], p <0.01). Notably, 95% of patients in this study did not receive ADT, allowing for a direct and unbiased comparison between the two surgical methods. These findings suggest the superiority of RGS over CSA. However, the small sample size limits the strength of these conclusions [44].

Furthermore, salvage surgery in oligorecurrent PCa remains an experimental approach, and RGS cannot replace ePLND or detailed histopathological analysis. Larger, well-designed comparative studies are necessary to establish the clinical value of RGS

Table 4. *Baseline characteristics of prostate cancer patients who underwent robot-assisted surgery*

Study (number of patients)	De Barros et al. (n = 20)	Quarta et al. (n = 30)	Gondoputro et al. (n = 12)	Schilham et al. (n = 20)	Gandaglia et al. (n = 12)	Mazzucato et al. (n = 13)	Falkenbach et al. (n = 37)
Hospital	Amsterdam	Milan	Darlinghurst Sydney	Nijmegen	Milan	Hamburg--Eppendorf	Hamburg--Eppendorf
Study type	Prospective	Prospective	Prospective	Prospective	Prospective	Retrospective	Retrospective
Setting	Recurrent	Primary	Primary	Primary	Primary	Recurrent	Repeat salvage surgery
Publishing date	2022	2024	2022	2024	2022	2024	2023
Journal	European Urology	European Journal of Nuclear Medicine and Molecular Imaging	Journal of Nuclear Medicine	Journal of Nuclear Medicine	European Urology	Cancers	World Journal of Urology
PSA at primary treatment (ng/ml), median IQR	NA	8.5 (4.6–16)	9.15 (6.0–21.2)	22.2 (2.9–117)	8.7 (4.8–15.5)	NA	0,64
pT stage at RP (%)	15 RP, 5 RT		Clinical stage	11 RARP + ePLND 9 ePLND + RP		11 RP + ePLND 2 RP	21 sLND 16 RGS
pT1			2 (17)				
pT2		9 (30)	6 (50)				
pT3a		15 (50)	1 (8)		8 (67)		
pT3b		6 (20)	3 (25)		4 (33)		
Gleason grade group (%)	NA			NA	Pathological	NA	NA
II							
III		8 (27)			4 (33)		
IV		12 (40)	3 (25)		2 (17)		
V		10 (33)	9 (75)		6 (50)		
pN stage (%)	NA				Intermediate to high risk cN0 cM0 at conventional imaging		
pN0		21 (70)	3 (25)	4 (20)	8 (67)	9 (69)	26 (70)
pN1		9 (30)	9 (75)	1 (70)	4 (33)	2 (15)	7 (19)
pNX							4 (11)
unknown						2 (15)	
PLND						11 (85)	
Surgical margin status (%)	NA		NA	NA		NA	NA
R0		24 (80)			10 (83)		
R1		6 (20)			2 (17)		
RX							
NA							
Secondary treatment (%)		NA		NA	0		37 (100)
RT after RP	5 (25)					5 (38)	
Salvage Radiotherapy	4 (20) 1 (5)*						
Salvage radical prostatectomy	1 (5)						
No	9 (45)		5 (42)			8 (62)	
Salvage LND	1 (5) 1 (5)*						21 (57)

Table 4. *Continued*

Radioguided surgery						16 (43)
RT & ADT		6 (50)				
ADT		2 (17)			0	
Lutetium PSMA	1 (5)*					

*Tertiary treatment
ADT – androgen deprivation therapy; ePLND – extended pelvic lymph node dissection; IQR – interquartile range; JNM – "The Journal of Nuclear Medicine"; LND – lymph node dissection; NA – not applicable; pN – pathological regional lymph node; pNX – pathological lymph node impossible to assess; PSA – prostate-specific antigen; PSMA – prostate-specific membrane antigen; pT – pathological primary tumor; RARP – robotic-assisted radical prostatectomy; RP – radical prostatectomy; RT – radiotherapy; RGS – radioguided surgery. sLND – salvage lymph node dissection

Table 5. *Preoperative characteristics, pathological results, and complication rates of prostate cancer patients who underwent robot-assisted surgery*

Study (number of patients)	De Barros et al. (n = 20)	Quarta et al. (n = 30)	Gondoputro et al. (n = 12)	Schilham et al. (n = 20)	Gandaglia et al. (n = 18)	Mazzucato et al. (n = 13)	Falkenbach et al. (n = 37)
Median age at PSMA-RGS [yr], (IQR)	68 (66–72)	68 (62–70)	68 (range 57–69)	69 (57–79)	70 (66–71)	71 (66–72)	69
Median time between RP and PSMA-RGS [mo], (IQR)	26 (11–47)*	Simultaneous	Simultaneous	Simultaneous	Simultaneous	49 (25–70)	61
Mean radiotracer activity (range MBq)	541 MBq (526–578)	734 MBq (730-738)	500 MBq	157 MBq (152-164)	735 MBq (731 –738)	NA	NA
PSMA PET/CT- avid lesions (%)	21	NA	11	18F-PSMA PET	11 (PSMA PET/MRI)	13	
0							0
1	18 (90)		6 (55)	3 (15)		13 (100)	22 (60)
2	2 (10)			9 (45)			13 (35)
3				6 (30)	1		2 (5)
4							
5			1 (9)	2 (10)			
> 6					8 lesions 1 (<1)		
Lesions localizations (%)		(during RGs)	PSMA PET/CT	18F-PSMA PET	68Ga- PSMA PET/MRI	PSMA PET/CT	
Unilateral pelvic	12 (60)		2 (17)	46 (94)	1 (8)	12 (92)	30 (81)
Bilateral pelvic					1 (8)		
Pelvic and presacral or retrovesical			1 (8)				
Presacral/ pararectal	2 (10)		4 (33)	3 (6)			
Retrovesical/ paravesiacal	1 (5)						
Retroperitoneal							7 (19)
Other	5 local recurrences					1 extrapelvic	
None					10 (83)		
Number pathologically confirmed lesions (%)	NA	NA	22	NA			
0							2
1					1 (25)	6 (46)	17
2						3 (23)	10
3					2 (50)	≥3 lesions 4 (31)	4
4							≥4 4
5							
≥6					1 (25)		

Table 5. *Continued*

Clavien-Dindo complications (%)	6 (30)	NA	1 (8)	1 (5)	1 (8)	100% <III	3 (8)
I	5 (25)		1 (8)	1 (5)			
II							
IIIa					1 (8)		3 (8)
IIIb							
IVa							
IVb							
V	1 (5)						

*Median time from last treatment to RGS
CT – computed tomography; IQR – interquartile range; mo – months; MRI – magnetic resonance imaging; NA – not applicable; PET – positron emission tomography; PSMA – prostate-specific membrane antigen; RGS – radioguided surgery; RP – radical prostatectomy; yr – years

Table 6. *Outcomes of prostate-specific membrane antigen radioguided surgery in robot-assisted surgery group*

Study (patients number)	De Barros et al. (n = 20)	Quarta et al. (n = 30)	Gondoputro et al. (n = 12)	Schilham et al. (n = 20)	Gandaglia et al. (n = 18)	Mazzucato et al. (n = 13)	Falkenbach et al. (n = 37)
Total number of specimens (total number of metastatic lesions)	75	174 (22)	74 (22)	49523 (45)30	96 (8)	54 (19)	NA
RGS positive specimens confirmed histologically (all histologically confirmed metastatic specimens)	19 (22)	16 (22)	16 (21)	28 (30)	4 (8)	14 (19)	NA
RGS negative specimens confirmed histologically (all histologically non-metastatic specimens)	56 (53)	135 (152)	36 (52)	12 (13)	87 (88)	35 (35)	NA
Sensitivity (%), 95% CI	86 (65–97)	72 (50–89)	76 (53–92)* 76 (53–92)**	67	50	74	NA
Specificity (%), 95% CI	100	88 (83–89)	69 (55–81)* 96 (87–99)**	100	99	100	NA
PPV (%) 95% CI	100	48 (48–93)	50* 89**	97	80	100	NA
NPV (%) 95% CI	95 (86–98)	96 (88–96)	88* 91**	97	96	88	NA
Number of BFS patients (%)	4 (21)	NA	5 (42)	3 (10)	9 (75)	12 (92)	10 (27)
Median BFS months (follow-up range)	Max 15	NA	NA	12	1	4	9 (4–12)
Number of TFS patients (%)	NA	NA	5 (42)	NA	9 (75)	>12 (>92)	19 (51)
Median TFS months (follow-up range)	NA	NA	13 (4–21)	NA	1	4	11 (6–25)

**in vivo*
***ex vivo*
BFS – biochemical-free survival; CI – confidence interval; NA – not applicable; NGV – negative predictive value; PCa – prostate cancer; PPV – positive predictive value; PSA – prostate-specific antigen; RARP – robot-assisted radical prostatectomy; RGS – radioguided surgery; TFS – treatment-free survival

in salvage lymphadenectomy and to define appropriate patient selection criteria.

β RADIATION RADIOGUIDED SURGERY

The previously described RGS technique relies on γ radiation, although PET isotopes undergo both β^+ and γ decay. While γ rays are highly penetrating, their effectiveness depends on low background radiation and minimal uptake by surrounding tissues, limiting the detectability of smaller metastases. To address this limitation, β^+ emission has been explored, allowing for the development of smaller, lighter detectors with reduced collimation requirements [16].

Collamati et al. conducted a feasibility study using 68Ga with a β probe. In a retrospective analysis of 45 patients who underwent PET/CT with 68Ga-PSMA-11, the study demonstrated that β^+ RGS is technically feasible, although it still requires prior PET imaging for accurate localization [16]. In another study involving seven patients, Collamati evalu-

ated the signal-to-background ratio (SBR) during robot-assisted RGS. Lower SBR values (<2.5) indicated tumors located farther from the margin, while higher values correlated with closer proximity to tumor tissue. Of four LNs showing increased tracer uptake, three were histologically confirmed as metastatic [45].
Although further studies are necessary, β^+ detectors show promise for enhancing intraoperative tumor margin assessment and improving the detection of metastatic LNs in PCa.

FUTURE DIRECTIONS

The sensitivity and specificity of PSMA-PET/CT are largely size-dependent; for metastases larger than 4.9 mm, the detection rate exceeds 90% [46]. According to the LN size distribution reported by Falkenbach et al., approximately 75% of metastases are detectable using PSMA-PET/CT [36]. Future research should prioritize technological innovations and the identification of reliable clinical or biological markers to improve patient selection. Emerging biomarkers, such as Cyr61 protein and circulating tumor cells, may enhance the sensitivity of PSMA-RGS, as explored in the BioPoP trial (NCT04324983). Additionally, defining the genetic background of patients could refine prognostic assessment and aid in identifying high-risk PCa patients who may benefit from intensified oncological surveillance or alternative strategies, including repeat RGS aimed at achieving minimal cancer burden [47].
Optimizing the tracer dose and incubation time to reduce background signal could further enhance the sensitivity of PSMA-RGS. Currently, no published data evaluate the impact of PSMA-RGS on ADT. It remains unclear whether short-term systemic ADT after PSMA-RGS can prolong BFS or if continued ADT is necessary until castration resistance develops. Preliminary insights may be available from the ongoing TRACE-II trial, which compares short-term ADT alone with PSMA-RGS combined with short-term ADT (NCT05555017).
Further investigation is also warranted to compare the outcomes of initiating ADT immediately after primary PSMA-RGS versus delaying ADT until BCR. A temporary ADT regimen may extend progression-free survival, as suggested by findings from earlier studies in radiotherapy settings [48].
Although RGS has demonstrated potential in treating recurrent or oligometastatic PCa, current evidence remains limited. One major challenge is the variability in sensitivity across studies, particularly in detecting micrometastases. Additionally, optimal patient selection criteria have yet to be clearly defined.
The role of micrometastatic disease in treatment outcomes is also ambiguous. However, according to Falkenbach et al., biochemical recurrence-free survival (bRFS) appears to correlate with metastasis size. Despite a potentially prolonged time to recurrence, micrometastases continue to present a treatment challenge [49]. Advancements in detection and clearer treatment protocols are needed.
Repeat salvage LND using RGS has shown comparable safety and efficacy to initial salvage LND [36]. Critical questions remain: Can MDT delay the initiation of systemic therapy or castration resistance? Might MDT even cure oligorecurrent PCa? Another avenue of exploration involves comparing oncological outcomes between repeated MDTs (e.g., PSMA-RGS or stereotactic ablative radiotherapy [SABR]) versus early ADT following primary MDT. This question is under investigation in the STORM trial, which compares MDT (surgical or radiotherapeutic) with MDT plus long-term ADT (NCT03569241).
An additional and largely unexplored application of RGS lies in focal therapy. PSMA PET/CT or PET/MR may offer reliable diagnostic capabilities for detecting BCR following focal therapy, potentially allowing precise metastasis-directed surgery to target local or distant recurrences [50].

CONCLUSIONS

PSMA-RGS has proven to be a feasible and safe technique for detecting nodal metastases in salvage surgery. Additionally, rRGS has recently gained attention for its enhanced visualization and maneuverability. While this method consistently demonstrates high specificity, its sensitivity remains variable, particularly in detecting micrometastases. It is important to emphasize that RGS does not replace ePLND based on template lymphadenectomy or thorough histopathological examination. Nevertheless, in carefully selected patients, this approach has the potential to prolong therapy-free intervals and extend biochemical recurrence-free survival. Further large-scale, well-structured studies are required to establish robust evidence and cost-effectiveness.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

FUNDING

This research received no external funding.

ETHICS APPROVAL STATEMENT

The ethical approval was not required.

References

1. Hamdy FC, Donovan JL, Lane JA, et al. 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. N Engl J Med. 2016; 375: 1415-1424.

2. EAU Guidelines Office, Arnhem TN. EAU Guidelines. Edn. presented at the EAU Annual Congress Milan 2023. ISBN 978-94-92671-19-6. n.d. Available at: http://uroweb.org/guidelines/compilations-of-all-guidelines/.

3. James ND, de Bono JS, Spears MR, et al. Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy. N Engl J Med. 2017; 377: 338-351.

4. Małkiewicz B, Kiełb P, Karwacki J, et al. Utility of Lymphadenectomy in Prostate Cancer: Where Do We Stand? J Clin Med. 2022; 11: 2343.

5. Jurys T, Kupilas A, Szczębara M, Changes in the quality of life of a population of Polish men undergoing radical prostatectomy: a 12-month longitudinal observational study. Cent European J Urol. 2024; 77: 375-382.

6. Ost P, Reynders D, Decaestecker K, et al. Surveillance or Metastasis-Directed Therapy for Oligometastatic Prostate Cancer Recurrence: A Prospective, Randomized, Multicenter Phase II Trial. J Clin Oncol. 2018; 36: 446-453.

7. Phillips R, Shi WY, Deek M, et al. Outcomes of Observation vs Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer. JAMA Oncol. 2020; 6: 650-659.

8. Steuber T, Jilg C, Tennstedt P, et al. Standard of Care Versus Metastases-directed Therapy for PET-detected Nodal Oligorecurrent Prostate Cancer Following Multimodality Treatment: A Multi-institutional Case-control Study. Eur Urol Focus. 2019; 5: 1007-1013.

9. Rauscher I, Maurer T, Beer AJ, et al. Value of 68 Ga-PSMA HBED-CC PET for the Assessment of Lymph Node Metastases in Prostate Cancer Patients with Biochemical Recurrence: Comparison with Histopathology After Salvage Lymphadenectomy. J Nucl Med. 2016; 57: 1713-1719.

10. Jilg CA, Drendel V, Rischke HC, et al. Diagnostic Accuracy of Ga-68-HBED-CC-PSMA-Ligand-PET/CT before Salvage Lymph Node Dissection for Recurrent Prostate Cancer. Theranostics. 2017; 7: 1770-1780.

11. Rauscher I, Düwel C, Wirtz M, et al. Value of 111 In-prostate-specific membrane antigen (PSMA)-radioguided surgery for salvage lymphadenectomy in recurrent prostate cancer: correlation with histopathology and clinical follow-up. BJU Int. 2017; 120: 40-47.

12. Maurer T, Weirich G, Schottelius M, et al. Prostate-specific Membrane Antigen–radioguided Surgery for Metastatic Lymph Nodes in Prostate Cancer. Eur Urol. 2015; 68: 530-534.

13. Horn T, Rauscher I, Eiber M, et al. „PSMA-radioguided surgery“ beim lokalisierten Prostatakarzinomrezidiv. Urologe. 2017; 56: 1417-1423.

14. Harke NN, Fuhrmann C, Czerner C, et al. Feasibility of Using a Novel Drop-In Gamma Probe for 99mTc-PSMA-I& S–Guided Lymph Node Detection During Robot-Assisted Radical Prostatectomy for Primary Prostate Cancer. Clin Nucl Med. 2024; 49: 948-952.

15. Collamati F, Morganti S, van Oosterom MN, et al. First-in-human validation of a DROP-IN β-probe for robotic radioguided surgery: defining optimal signal-to-background discrimination algorithm. Eur J Nucl Med Mol Imaging. 2024; 51: 3098-3108.

16. Collamati F, Bocci V, Castellucci P, et al. Radioguided surgery with β radiation: a novel application with Ga68. Sci Rep. 2018; 8: 16171.

17. Silver DA, Pellicer I, Fair WR, Heston WD C-CC. Prostate-specific membrane antigen expression in normal and malignant human tissues. Clin Cancer Res. 1997; 3: 81-5.

18. Pisotskyi O, Petrasz P, Zorga P, et al. The potential of gallium-68 prostate-specific membrane antigen positron emission tomography/ computed tomography as a main diagnostic tool in prostate cancer staging. Cent Eur J Urol. 2025; 78: 52-60.

19. Spena G, Moretti TB, Dávila FS, et al. Ga68-PSMA PET for lymph node staging in intermediate and high-risk prostate cancer patients undergoing robotic assisted radical prostatectomy. Minerva Urol Nephrol. 2024; 76: 467-473.

20. Knipper S, Mehdi Irai M, Simon R, et al. Cohort Study of Oligorecurrent Prostate Cancer Patients: Oncological Outcomes of Patients Treated with Salvage Lymph Node Dissection via Prostate-specific Membrane Antigen–radioguided Surgery. Eur Urol. 2023; 83: 62-69.

21. Hennrich U, Eder M. [68Ga]Ga-PSMA-11: The First FDA-Approved 68Ga-Radiopharmaceutical for PET Imaging of Prostate Cancer. Pharmaceuticals. 2021; 14: 713.

22. Cardinale J, Giesel FL, Wensky C, et al. PSMA-GCK01: A Generator-Based 99m Tc/ 188 Re Theranostic Ligand for the Prostate-Specific Membrane Antigen. J Nucl Med. 2023; 64: 1069-1075.

23. Rauscher I, Maurer T, Souvatzoglou M, et al. Intrapatient Comparison of 111In-PSMA I&T SPECT/CT and Hybrid 68Ga-HBED-CC PSMA PET in Patients With Early Recurrent Prostate Cancer. Clin Nucl Med. 2016; 41: e397-402.

24. Lawal IO, Ankrah AO, Mokgoro NP, et al. Diagnostic sensitivity of Tc-99m HYNIC PSMA SPECT/CT in prostate carcinoma: A comparative analysis with Ga-68 PSMA PET/CT. Prostate. 2017; 77: 1205-1212.

25. Schottelius M, Wirtz M, Eiber M, Maurer T, Wester HJ. [(111)In]PSMA-I&T: expanding the spectrum of PSMA-I&T applications towards SPECT and radioguided surgery. EJNMMI Res. 2015; 5: 68.

26. Robu S, Schottelius M, Eiber M, et al. Preclinical Evaluation and First Patient Application of 99mTc-PSMA-I&S for SPECT Imaging and Radioguided Surgery in Prostate Cancer. J Nucl Med. 2017; 58: 235-242.

27. Knipper S, Lischewski F, Koehler D, et al. Biochemical Response of <0.1 ng/ml Predicts Therapy-free Survival of Prostate Cancer Patients following Prostate-specific Membrane Antigen-targeted Salvage Surgery. Eur Urol Oncol. 2025; 8: 270-277.

28. Maurer T, Robu S, Schottelius M, et al. 99mTechnetium-based Prostate-specific Membrane Antigen–radioguided Surgery in Recurrent Prostate Cancer. Eur Urol. 2019; 75: 659-666.

29. Mayr R, Engelmann SU, Yang Y, et al. Prostate-specific membrane antigen-radioguided surgery salvage lymph node dissection: experience with fifty oligorecurrent prostate cancer patients. World J Urol. 2024; 42: 483.

30. Horn T, Krönke M, Rauscher I, et al. Single Lesion on Prostate-specific Membrane Antigen-ligand Positron Emission Tomography and Low Prostate-specific Antigen Are Prognostic Factors for a Favorable Biochemical Response to Prostate-specific Membrane Antigen-targeted Radioguided Surgery in Rec. Eur Urol. 2019; 76: 517-523.

31. Knipper S, Mehdi Irai M, Simon R, et al. Cohort Study of Oligorecurrent Prostate Cancer Patients: Oncological Outcomes of Patients Treated with Salvage Lymph Node Dissection via Prostate-specific Membrane Antigen–radioguided Surgery. Eur Urol. 2023; 83: 62-69.

32. Rauscher I, Düwel C, Wirtz M, et al. Value of 111 In-prostate-specific membrane antigen (PSMA)-radioguided surgery for salvage lymphadenectomy in recurrent prostate cancer: correlation with histopathology and clinical follow-up. BJU Int. 2017; 120: 40-47.

33. Maurer T, Weirich G, Schottelius M, et al. Prostate-specific membrane antigen-radioguided surgery for metastatic lymph nodes in prostate cancer. Eur Urol. 2015; 68: 530-534.

34. Knipper S, Ascalone L, Ziegler B, et al. Salvage Surgery in Patients with Local Recurrence After Radical Prostatectomy. Eur Urol. 2021; 79: 537-544.

35. Horn T, Krönke M, Rauscher I, et al. Single Lesion on Prostate-specific Membrane Antigen-ligand Positron Emission Tomography and Low Prostate-specific Antigen Are Prognostic Factors for a Favorable Biochemical Response to Prostate-specific Membrane Antigen-targeted Radioguided Surgery in Rec. Eur Urol. 2019; 76: 517-523.

36. Falkenbach F, Knipper S, Koehler D, et al. Safety and efficiency of repeat salvage lymph node dissection for recurrence of prostate cancer using PSMA-radioguided surgery (RGS) after prior salvage lymph node dissection with or without initial RGS support. World J Urol. 2023; 41: 2343-2350.

37. de Barros HA, van Oosterom MN, Donswijk ML, et al. Robot-assisted Prostate-specific Membrane Antigen–radioguided Salvage Surgery in Recurrent Prostate Cancer Using a DROP-IN Gamma Probe: The First Prospective Feasibility Study. Eur Urol. 2022; 82: 97-105.

38. Gondoputro W, Scheltema MJ, Blazevski A, et al. Robot-assisted prostate-specific membrane antigen-radioguided surgery in primary diagnosed prostate cancer. J Nucl Med. 2022; 63: 1659-1664.

39. Quarta L, Mazzone E, Cannoletta D, et al. Defining the optimal target-to-background ratio to identify positive lymph nodes in prostate cancer patients undergoing robot-assisted [99mTc]Tc-PSMA radioguided surgery: updated results and ad interim analyses of a prospective phase II study. Eur J Nucl Med Mol Imaging. 2024; 51: 3789-3798.

40. Schilham MGM, Somford DM, Küsters-Vandevelde HVN, et al. Prostate-Specific Membrane Antigen–Targeted Radioguided Pelvic Lymph Node Dissection in Newly Diagnosed Prostate Cancer Patients with a Suspicion of Locoregional Lymph Node Metastases: The DETECT Trial. J Nucl Med. 2024; 65: 423-429.

41. Gandaglia G, Mazzone E, Stabile A, et al. Prostate-specific membrane antigen Radioguided Surgery to Detect Nodal Metastases in Primary Prostate Cancer Patients Undergoing Robot-assisted Radical Prostatectomy and Extended Pelvic Lymph Node Dissection: Results of a Planned Interim Analysis of a Pro. Eur Urol. 2022; 82: 411-418.

42. Mazzucato G, Falkenbach F, Schmalhofer M-L, et al. Robot-Assisted PSMA-Radioguided Salvage Surgery for Oligorecurrent Prostate Cancer Using the Novel SENSEI® Drop-in Gamma Probe: Correlation of Intraoperative Measurements to Preoperative Imaging and Final Histology. Cancers (Basel). 2024; 17: 93.

43. Ambrosini F, Falkenbach F, Budäus L, et al. Comparative analysis of robot-assisted and open approach for PSMA-radioguided surgery in recurrent prostate cancer. Eur J Nucl Med Mol Imaging. 2024; 51: 3079-3088.

44. Knipper S, Tilki D, Mansholt J, et al. Metastases-yield and Prostate-specific Antigen Kinetics Following Salvage Lymph Node Dissection for Prostate Cancer: A Comparison Between Conventional Surgical Approach and Prostate-specific Membrane Antigen-radioguided Surgery. Eur Urol Focus. 2019; 5: 50-53.

45. Collamati F, van Oosterom MN, De Simoni M, et al. A DROP-IN beta probe for robot-assisted 68Ga-PSMA radioguided surgery: first ex vivo technology evaluation using prostate cancer specimens. EJNMMI Res. 2020; 10: 92.

46. Jilg CA, Drendel V, Rischke HC, et al. Detection Rate of 18F-Choline PET/CT and 68Ga-PSMA-HBED-CC PET/CT for Prostate Cancer Lymph Node Metastases with Direct Link from PET to Histopathology: Dependence on the Size of Tumor Deposits in Lymph Nodes. J Nucl Med. 2019; 60: 971-977.

47. Kazik J. Prostate cancer genetic background. The introduction of genetic testing in the determination of high-risk prostate cancer cases and selection of targeted chemotherapy in advanced prostate cancer patients. Cent Eur J Urol. 2024; 77: 625-636.

48. Cornford P, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part II: Treatment of Relapsing, Metastatic, and Castration-Resistant Prostate Cancer. Eur Urol. 2017; 71: 630-642.

49. Falkenbach F, Kachanov M, Leyh-Bannurah S-R, et al. Size of lymph-node metastases in prostate cancer patients undergoing radical prostatectomy: implication for imaging and oncologic follow-up of 2705 lymph-node positive patients. World J Urol. 2024; 42: 38.

50. Lasorsa F, Biasatti A, Orsini A, et al. Focal Therapy for Prostate Cancer: Recent Advances and Insights. Curr Oncol. 2024; 32: 15. ■