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BJU International

Robotics and Laparoscopy

Targeted vs systematic robot-assisted transperineal magnetic resonance imaging-transrectal ultrasonography fusion prostate biopsy

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Objective

To evaluate the performance of transperineal robot-assisted (RA) targeted (TB) and systematic (SB) prostate biopsy in primary and repeat biopsy settings.

Patients and Methods

Patients underwent RA biopsy between 2014 and 2016. Before RA-TB, multiparametric magnetic resonance imaging (mpMRI) was performed. Prostate lesions were scored (Prostate Imaging, Reporting and Data System, version 2) and used for RA-TB planning. In addition, RA-SB was performed. Available, whole-gland pathology was analysed.

Results

In all, 130 patients were biopsy naive and 72 had had a previous negative transrectal ultrasonography-guided biopsy. In total, 202 patients had suspicious mpMRI lesions. Clinically significant prostate cancer was found in 85% of all prostate cancer cases (n = 123). Total and clinically significant prostate cancer detection rates for RA-TB vs RA-SB were not significantly different at 77% vs 84% and 80% vs 82%, respectively. RA-TB demonstrated a better sampling performance compared to RA-SB (26.4% vs 13.9%; $P < 0.001$).

Conclusion

Transperineal RA-TB and -SB showed similar clinically significant prostate cancer detection rates in primary and repeat biopsy settings. However, RA-TB offered a 50% reduction in biopsy cores. Omitting RA-SB is associated with a significant risk of missing clinically significant prostate cancer.

Keywords

robot-assisted transperineal prostate biopsy, mpMRI-TRUS fusion, targeted biopsy, Prostate Imaging Reporting and Data System, #PCSM, #ProstateCancer

Introduction

TRUS-guided prostate biopsy (TRUS-biopsy) frequently fails to detect clinically significant prostate cancer [1]. Recently, the prospective PROstate MRI Imaging Study (PROMIS) assessed the diagnostic accuracy of TRUS-biopsy vs multiparametric MRI (mpMRI). mpMRI outperformed TRUS-biopsy in diagnosis of clinically significant prostate cancer, with a reported sensitivity of 93% vs 48% [2]. Interestingly, several randomised controlled trials found similar detection rates between systematic (SB) and targeted (TB) biopsy in biopsy-naive patients and patients after a previous negative biopsy [3–5]. Today, widespread use of mpMRI in primary diagnosis is mainly limited by availability, costs, and its inter-reader variability [6]. Therefore, current guidelines recommend mpMRI only for men with prior negative biopsies and persistent prostate cancer suspicion [7]. Not only the indication of mpMRI, but also the role of image-guided biopsy is still under discussion. The literature remains difficult to interpret because of heterogeneous patient selection, biopsy systems, and schemes. Nevertheless, different TB methods (in-bore, cognitive or software-based fusion) have been shown to detect more clinically significant and less insignificant prostate cancer compared with SB [8]. Recently, we reported the first use of transperineal robot-assisted (RA) elastic mpMRI-TRUS fusion biopsy [9]. In our experience, RA transperineal biopsy offers the potential of standardising the procedure with reproducible quality independent of individual skillsets. To date, iSR'obot Mona Lisa™ (Biobot

 | doi:10.1111/bju.14089
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Surgical, Singapore) is the only full-robotic system and the only device with RA depth control of the biopsy needle [10]. Furthermore, transperineal RA biopsy decreases invasiveness and risk of infection as there are only two skin punctures irrespective of the number of biopsies taken. In the present series, we evaluated the concept of robot-assistance and mpMRI-guidance in primary and repeat biopsy settings.

Patients and Methods

Between 2014 and 2016 patients with rising or persistently elevated PSA levels who were biopsy naive or had a negative previous TRUS-biopsy underwent 3.0 T or 1.5 T endorectal coil mpMRI referring to the guidelines of the European Society of Urogenital Radiology (ESUR) [11]. Patients without visible or evaluable mpMRI lesion or contraindication to transperineal MRI-TRUS fusion prostate biopsy were excluded. T2-weighted (T2w) images, diffusion-weighted images, and dynamic contrast-enhanced images were included in all mpMRI examinations.

Each lesion was preoperatively assessed and scored by one radiology specialist (S. Kaufmann, 8 years' experience in mpMRI) blinded to clinical outcome using the Prostate Imaging Reporting and Data System (PI-RADS), version 2.0 [12]. Suspicious lesions were sized with a freehand region-of-interest on axial T2w images (in mm^2) by a radiology specialist. Patients with at least one conspicuous lesion in a current mpMRI underwent RA transperineal mpMRI–TRUS fusion prostate biopsy under antibiotic prophylaxis. The study was approved by the Institutional Review Board (397/2012R) and reported in accordance with the Standards of reporting for MRI-targeted biopsy studies (START) protocol [13].

RA mpMRI–TRUS Fusion Prostate Biopsy

mpMRI images were digitally transferred to the image fusion software (Urofusion™, Biobot Surgical, Singapore, Singapore). Organ outline and suspicious lesions were contoured semi-automatically. General anaesthesia of patients guaranteed precise and unimpeded biopsy conditions. In lithotomy, the perineum was cleaned and the ultrasound probe (BK 8848; BK Medical, Peabody, MA, USA) was inserted transrectally together with an ultrasound-compatible sheath to diminish prostate movability. Axial ultrasound images (0.5 mm slice thickness) were three-dimensionally reconstructed. Preoperative mpMRI and intraoperative models were fused by an algorithm (UroBiopsy™; Biobot Surgical) to compensate organ deformity (non-rigid fusion). RA-TBs and -SBs were automatically planned based on lesion or prostate volume. Needle direction, penetration depth and biopsy position were determined by the robotic system. Biopsies were taken manually with a 18-G biopsy needle (3K-CorazorTM; Uromed Ltd., Oststeinbek, Germany). Each biopsy of the right or left prostatic lobe was managed through the same single right or left perineal puncture paramedian to the perineal raphe. Targeted cores were taken first and potted separately. The sampling site of each biopsy was saved as a protocol stating each core position three-dimensionally. The mean (SD) duration of the entire procedure was 43 (6) min; the mean (SD) time from patient positioning to skin dressing was 32 (4) min, and anaesthesia was induced 11 (6) min before RA-fusion biopsy. Specimens were evaluated by experienced uro-pathology specialists. The course of patients with a prostate cancer diagnosis and further treatment was retrospectively assessed. Associated pathology reports after radical prostatectomy (RP) were evaluated and the highest Gleason score from biopsy and corresponding RP specimen were compared. Prostate cancer with a Gleason score ≥7 was classified as significant disease.

Risk stratification was done according to European Association of Urology (EAU) – European Society for Radiotherapy and Oncology (ESTRO) – International Society of Geriatric Oncology (SIOG) risk groups for biochemical recurrence of localised and locally advanced prostate cancer [14]. Complications were reported for 30 days according to the Clavien–Dindo classification [15].

Statistical Analysis

Contingency analyses were used to verify dependence or independence of two or more nominal-scaled variables and chi-squared tests evaluated differences. McNemar's test was used on paired nominal data (detection accuracy of TB vs SB). Dichotomous variables were compared with the two-sided Fisher's exact test and continuous variables with the Mann–Whitney *U*-test. Kaplan–Meier analyses calculated for survival probability within an event history analysis. Uni- and multivariate Cox regressions examined the independent value of one or more contemporaneous relevant influencing factors on the same target variable. A $P < 0.05$ was considered as the level of significant difference. Statistical analysis was performed with JMP 11.2.0 software (SAS Institute Inc., Cary, NC, USA).

Results

During the study period, 232 patients with elevated PSA levels were examined with mpMRI before biopsy. In all, 30 patients (13%) were excluded because of unsuspicious mpMRI, whilst the 202 patients with visible lesions underwent RA-fusion biopsy. In all, 130 (64%) patients were biopsy-naïve, whereas 72 (36%) had a previous negative TRUS-biopsy. Overall, 61% patients were diagnosed with prostate cancer and 85% of cancers were classified as clinically significant. Kaplan–Meier analysis showed no difference in the interval between mpMRI and biopsy

between prostate cancer-positive and -negative patients ($P = 0.07$). There was no significant difference in overall ($P = 0.58$) or clinically significant prostate cancer ($P = 0.67$) detection rates between re-biopsy and biopsy-naive patients. Furthermore, relative risks for re-biopsy and biopsy-naive patients were 0.90 (95% CI 0.61–1.30) and 1.06 (95% CI 0.85–1.31) for overall prostate cancer detection, and 0.92 (95% CI 0.64–1.34) and 1.04 (95% CI 0.85–1.28) for diagnosis of clinically significant prostate cancer, respectively. PI-RADS score was significantly higher in patients with prostate cancer when compared to those with a negative biopsy outcome ($P < 0.001$). A direct correlation between PI-RADS score ≥3 and clinically significant prostate cancer was seen ($P < 0.001$). The probability of clinically significant prostate cancer detection was significantly higher in PI-RADS score 4 ($P < 0.001$) and score 5 ($P < 0.001$) reports, whereas PI-RADS score 2 ($P < 0.001$) and score 3 ($P < 0.001$) were associated with no or insignificant prostate cancer.

Detailed patient and imaging characteristics are shown in Table 1. Overall, 77% of all cancers were detected by RA-TB and 81% by RA-SB. In all, 19% ($n = 23$), 23% ($n = 28$) and 59% ($n = 72$) of the cancers were solely diagnosed by RA-TB, RA-SB, and simultaneously with both techniques, respectively. There was no difference in the detection of clinically significant prostate cancer between RA-TB and RA-SB (80% vs 82%; $P = 0.75$), although the chances of detecting clinically significant prostate cancer by TB with a simultaneous negative SB were higher ($P = 0.02$). In all, 17% ($n = 21$) of clinically significant prostate cancers were missed by RA-TB, whereas 15% ($n = 19$) were not detected by RA-SB. In all, 39% ($n = 7$) of 18 detected low-risk cancers were only diagnosed by RA-SB. Prostate biopsy performance in the overall cohort, RA-TB, and RA-SB subgroup is shown in Table 2. The dominant Gleason score for the final cumulative pathological report was defined in 29% by RA-TB and in 35% by RA-SB. RA-TB and RA-SB showed comparable detection rates for clinically significant prostate cancer (Gleason score ≥7), whereas RA-SB revealed more low-risk cancers (Gleason score ≤6). Sub-analysis of highest Gleason score detected solely in RA-SB or RA-TB in patients with biopsy confirmed prostate cancer is shown in Table 3. Short- and long-term follow-up was available in 70% of all patients with prostate cancer. In this subgroup, surgical treatment was performed in 70% of patients (laparoscopic RA RP: 39% vs open RP: 31%), 12% received radiation therapy, 11% had androgen-deprivation therapy, and 13% patients favoured active surveillance, respectively (Fig. 1). More than two-thirds of clinically significant prostate cancers (68%) were in the peripheral zone and 17% were found in the anterior part of the prostate. RA-TB detected most prostate cancer lesions in the peripheral zone posterolateral on both sides (right 15%, left 9%) of the middle (mid) part and right base (13%) of the prostate. Localisations of detected cancer lesions in correspondence with whole-mount pathology for RA-SB and RA-TB are shown in Fig. 2. In biopsy-naive patients upgrading to high-risk Gleason score after RP was detected in 6% of RA-TB and RA-SB. Details of patients and mpMRI characteristics according to history of prostate biopsy and RP are shown in Table 4. Sensitivity, specificity, negative predictive value, positive predictive value, and accuracy of RA-TB and RA-SB in the detection of clinically significant prostate cancer were: 80%, 89%, 80%, 88%, 84% and 82%, 86%, 81%, 86%, 84%, respectively. The percentage of patients in whom the RP Gleason score grade and risk group was

Table 1 Patient and imaging characteristics.

Patients characteristic	Total cohort	Prostate cancer	Negative biopsy	*P*
Median (SD; IQR)				
Age, years	66 (7.6; 60–73)	69 (7.1; 63–74)	62 (7.6; 58–69)	<0.001
PSA level, ng/mL	8 (5.8; 6–11.9)	8 (6.2; 5.8–12.2)	8.5 (5.0; 6–11.4)	0.86
PSAD, ng/mL/mL	0.21 (0.23; 0.15–0.33)	0.24 (0.26; 0.17–0.44)	0.17 (0.14; 0.11–0.24)	<0.001
Prostate volume, mL	36 (21.8; 26.9-47.8)	31.2 (14.5; 24–40)	46.7 (25.5; 34.7–67.3)	<0.001
Previous prostate biopsy, %	35.6	34.1	38.0	0.58
Imaging characteristic	**Total cohort**	**csProstate cancer**	**Negative biopsy**	***P***
PI-RADS*, score, mean (SD; IQR)	4 (0.9; 3–4)	4 (0.6; 4–4)	3 (0.8; 2–3.2)	<0.001
PI-RADS* score ≥3, %	80.7	97.1	55.7	<0.001
PI-RADS* score <3 (%)	19.3	2.9	44.3	<0.001
N (%)				
PI-RADS* score 5	17 (8.4)	15 (14.3)	1 (1.3)	0.002
PI-RADS* score 4	107 (53)	77 (73.3)	18 (22.8)	<0.001
PI-RADS* score 3	39 (19.3)	10 (9.5)	25 (31.6)	<0.001
PI-RADS* score 2	38 (18.8)	3 (2.9)	34 (43)	<0.001
PI-RADS* score 1	1 (0.5)	–	1 (1.3)	–
Time interval from mpMRI to RA-biopsy, days, median (IQR)	34 (20–56)	32 (18–55)	38 (24–63)	0.02

*cs, clinically significant (Gleason score ≥7 or PSA level ≥10 ng/mL); IQR, interquartile range; PSAD, PSA density. *PI-RADS version 2.*

Table 2 Prostate biopsy performance in the overall cohort and subgroups.

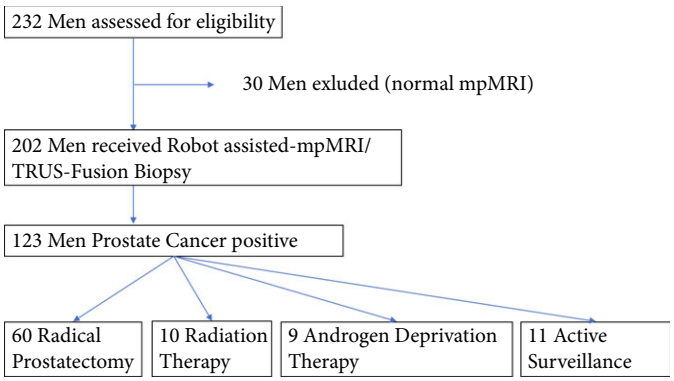
Overall biopsy outcome	*N* (%)
Rate of prostate cancer	123 (61)
Rate of clinically significant prostate cancer (Gleason score ≥7)	105 (85)
Low-risk prostate cancer (Gleason score <7 and PSA level <10 ng/mL)	18 (15)
Intermediate-risk prostate cancer (Gleason score 7 or PSA level 10–20 ng/mL)	61 (50)
High-risk prostate cancer (Gleason score >7 or PSA level >20 ng/mL)	44 (36)
Correct Gleason grading	35 (58)
Gleason score upgrading	10 (17)
Gleason score downgrading	15 (25)
Correct risk stratification (Gleason)	47 (78.3)
Risk stratification upgrading (Gleason)	4 (0.07)
Risk stratification downgrading (Gleason)	9 (15)
RA-SB	
Rate of prostate cancer	100 (81)
Rate of clinically significant prostate cancer	86 (82)
Number of cancer cores	316 (11)
RA-TB	
Rate of prostate cancer	95 (77)
Rate of clinically significant prostate cancer	84 (80)
Number of cancer cores	322 (27)

Table 3 Sub-analysis of highest Gleason score detected solely in RA-SB or RA-TB in patients with biopsy confirmed prostate cancer.

Prostate cancer cohort (*n* = 123)	Highest Gleason score in RA-SB, *n* (%)	Highest Gleason score in RA-TB, *n* (%)
No cancer	23 (18.7)	28 (22.7)
Gleason score 3 + 3	24 (19.5)	19 (15.4)
Gleason score 3 + 4	29 (23.6)	29 (23.6)
Gleason score 4 + 3	18 (14.6)	15 (12.2)
Gleason score 4 + 4	20 (16.3)	22 (17.9)
Gleason score 4 + 5	8 (6.4)	8 (6.4)
Gleason score 5 + 5	1 (0.8)	2 (1.6)
Gleason score ≥7	76 (61.8)	76 (61.8)
Gleason score ≤6	24 (19.5)	19 (15.4)
Dominant Gleason score	43 (34.9)	36 (29.3)

accurately predicted, upgraded or downgraded was 58%, 17% or 25% and 80%, 0.1% or 15%, respectively. RA-TB predicted prostate cancer in 80% of all RP patients, whereas risk stratification was accurately predicted, upgraded or downgraded in 69%, 15% and 17%, respectively.

Fig. 1 Flowchart for study sequence amongst men undergoing RA-TB and RA-SB mpMRI-TRUS fusion biopsy.

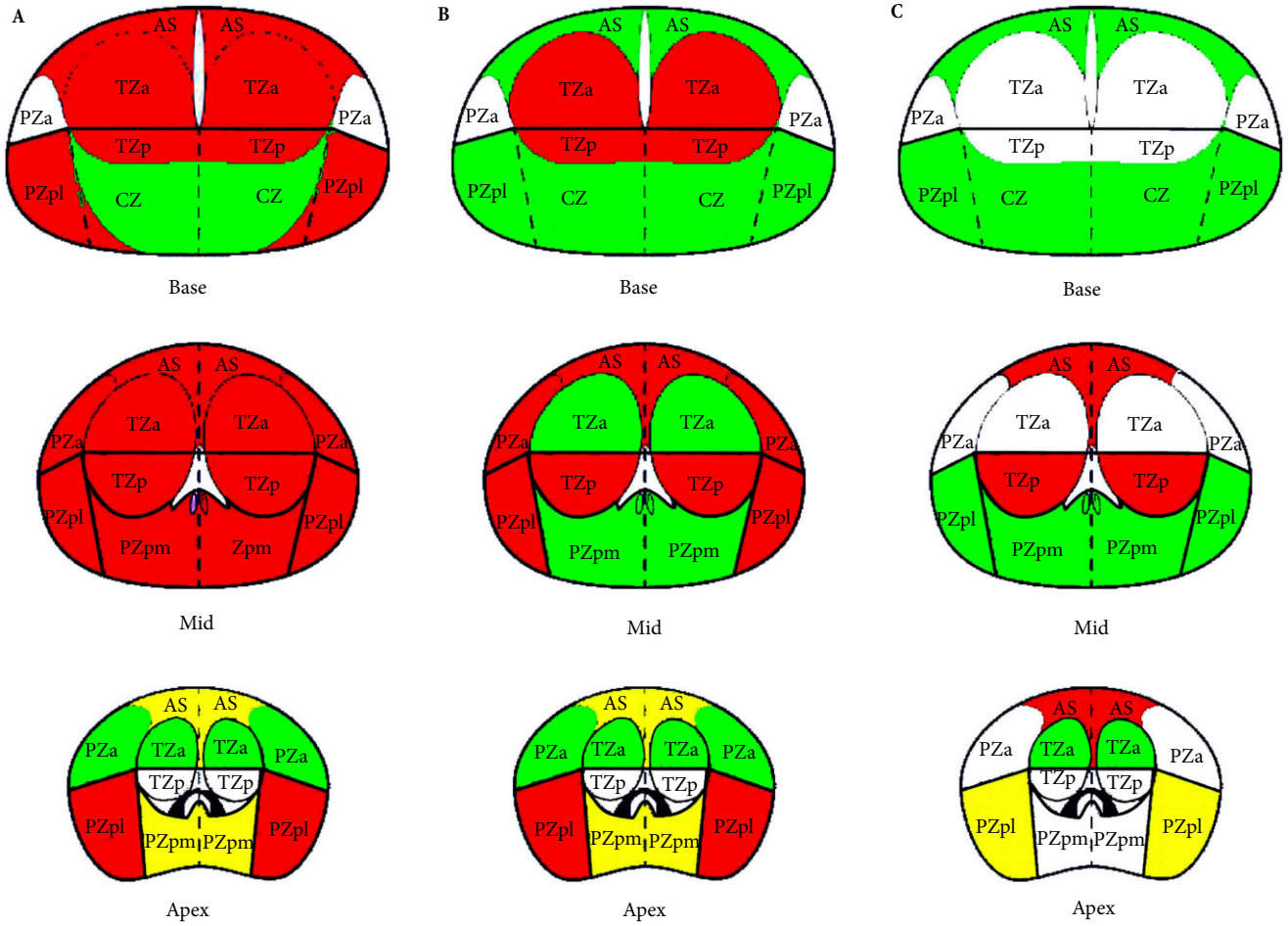


Risk groups according to Gleason score and PSA level for RA-TB, RA-SB, and RP specimens were assessed (Table 5). In total, seven (3%) patients had postoperative complications. There was one (0.005%) iatrogenic rectal injury by the TRUS probe with consecutive peritonitis (Clavien–Dindo ≥III). Minor complications (Clavien–Dindo ≤II) occurred in six patients, whereas three patients needed transurethral catheterisation (Clavien–Dindo I) due to acute urinary retention 10–14 days postoperatively and another three patients presented with subclinical penoscrotal haematoma but no treatment was indicated.

Discussion

Although, prostate biopsy is one of the most commonly performed procedures, many important aspects of prostate biopsy vary amongst urologists, such as route of biopsy, antibiotic prophylaxis, analgesia, prostate biopsy schemes, as well as the use of mpMRI [16]. Considering the results of the recent PROMIS trial the concept of unguided sampling is increasingly questioned, especially in patients with previous

Fig. 2 Detected cancer lesions in correspondence with whole-mount pathology (n = 60). (**A**) Overall prostate cancer (green: more cancers detected in RA-SB; red: more cancers detected in RA-TB; yellow: equivalent; white: no cancer). (**B**) Clinically significant prostate cancer (green: more cancers detected in RA-SB; red: more cancers detected in RA-TB; yellow: equivalent; white: no cancer). (**C**) Cancer only detected by RA-SB (green) or RA-TB (red). CZ, central zone; PZ, peripheral zone; TZ, transitional zone.



untargeted biopsy [2]. Nevertheless, the role of routine mpMRI-guided biopsy is mainly concentrated in specialised centres of excellence. Some of the most important challenges limiting the widespread use of image-guided biopsy involve difficulties with the complex soft- and hardware of available biopsy systems. A possible solution to shorten the learning curve could be the introduction of robotic assistance, such as the iSR'obot Mona Lisa. RA transperineal prostate biopsy was introduced in 2011 by Ho et al. [10]. This first version of iSR'obot was designed for transperineal mapping prostate biopsy under ultrasound guidance. Very recently, we reported the first use of elastic RA-fusion biopsy in 55 patients with negative prior biopsy, inconspicuous DRE but suspicious mpMRI of the prostate. RA-TB enabled reliable detection of all high-risk cancers, whilst off-target cores detected only one additional clinically significant prostate cancer [9]. In the present series, primary and repeat settings confirmed a high rate of prostate cancer (>60%) and clinically significant prostate cancer (>85%). Nevertheless, RA-TB missed 17% of clinically significant prostate cancer detected by RA-SB, which may be attributable to the high rate (68%) of clinically significant prostate cancer in the peripheral zone as a standard biopsy location for RA-SB. However, RA-TB and -SB demonstrated equivalent detection rates for highest Gleason score and almost identical numbers of clinically significant prostate cancer diagnoses.

In this regard, Radtke et al. [17] had no evidence that transperineal 24-core template saturation and transperineal mpMRI-fusion target biopsies lead to different clinically significant prostate cancer detection rates. In accordance with our present results, Kasivisvanathan et al. [18] could also not find a difference in the detection of clinically significant cancer between re-biopsy and biopsy-naive patients. Although, RA-TB mode showed a significantly improved sampling performance, reflected in a 50% reduction of

Table 4 Patients' and mpMRI characteristics according to prostate biopsy and RP.

Patient characteristic	Total biopsy cohort	Biopsy-naive cohort	Pre-biopsy cohort	RP cohort
No. of men (% of total)	202	130 (64)	72 (36)	60 (30)
Age, years, mean (SD)	66 (7.6)	66 (7.4)	66 (8.1)	66 (7.4)
PSA level, ng/mL, median (IQR)	8.1 (6–12)	7.5 (6–10)	9 (7–13)	7.4 (5–11)
Prostate volume, mL, median (IQR)	36 (27–48)	36 (26–48)	35 (28–48)	31 (25–40)
PSAD, ng/mL/mL, median (IQR)	0.21 (0.2–0.3)	0.19 (0.1–0.3)	0.24 (0.2–0.4)	0.22 (0.2–0.4)
Patients with anterior lesions (TZa, PZa, AS), *n* (%)	28 (14)	14 (11)	14 (19)	9 (15)
Targeted cores per patient, *n*, mean (SD)	5.8 (2.8)	6.1 (2.9)	5.3 (2.5)	–
Rate of prostate cancer, %	60.8	62.3	58.3	100
Rate of clinically significant prostate cancer (Gleason score ≥7 or PSA level >10 ng/mL), %	85.4	53.1	50	96.7
Imaging characteristics	**Prostate cancer**	**Biopsy-naive cohort**	**Pre-biopsy cohort**	**RP cohort**
N (%)				
PI-RADS* score 1	–	1 (1)	–	–
PI-RADS* score 2	4 (3.3)	24 (18)	14 (19)	–
PI-RADS* score 3	14 (11.4)	25 (19)	14 (19)	6 (10)
PI-RADS* score 4	89 (72.3)	70 (54)	37 (52)	46 (77)
PI-RADS* score 5	16 (13)	10 (8)	7 (10)	8 (13)

**PI-RADS version 2.*

targeted cores, previous reports of transrectal and transperineal prostate fusion biopsies have shown higher core sampling rates (40–60%) but a similar percentage of positive cores for standard 12-core biopsy [19,20]. Consistent with the literature, RA-SB had more biopsies with insignificant Gleason score (20% vs 15%) and detected 39% more low-risk cancers compared to RA-TB [17,18,21]. Recent biopsy series were mainly focused on patients with PI-RADS score 4/5 lesions and high likelihood of clinically significant prostate cancer [8,22,23]. In contrast, our present patient selection was not restricted to fixed PI-RADS thresholds. Remarkably, only PI-RADS score ≥3 correlated with clinically significant prostate cancer diagnosis. Anterior prostate cancer was only found in 16%, less than previously reported [20,21]. Interestingly, only one-tenth of prostate cancers in the anterior zone [anterior transitional zone (TZa), anterior peripheral zone (PZa), anterior stroma (AS)] were clinically insignificant. Whole-gland pathology after RP as the 'gold standard' was available in 49% (60/123) of all patients with prostate cancer. Compared with previous data [24], our present results showed an accurate Gleason score in 58%, a >50% reduction in upgrading but a higher rate of Gleason score downgrading (25% of all RP patients). As almost one-fifth of clinically significant prostate cancers were missed by RA-TB and one-fifth of RPs were only based on RA-SB findings, we conclude that RA-SB remains an essential step in image-guided biopsy. This may be improvable with further technical progress of MRI efficiency. Drawbacks of RA-TP are narcosis and a more time-consuming procedure when compared to standard prostate biopsy. Therefore, this approach may be less cost-effective than other techniques but this has to be clarified in prospective studies. An advantage of the RA transperineal approach is the use of only two perineal skin punctures, which potentially decreases the risk of infection mainly by reducing tissue trauma irrespective of core number. This is of great interest, as we did not have any patients with infectious complications. In contrast, a recent trial in 34 865 patients showed a high rate of infectious complications after TRUS-biopsy, with a readmission rate of one in 57 biopsies [25], probably caused by worldwide increasing fluoroquinolone resistance. Therefore, some countries routinely perform rectal swab before prostate biopsy and patients with positive cultures receive targeted prophylaxis [26].

Interestingly, Bennet et al. [27] observed that transrectal biopsy was associated with more re-hospitalisation (1.1% vs 0.9%) and sepsis (0.8% vs 0.1%) compared to transperineal biopsy, although this was not statistically significant because of large heterogeneity across countries. The iatrogenic rectal injury by the TRUS-probe in one patient was most probably a result of a long-lasting painful and

Table 5 Number of patients with no-, low-, intermediate- or high-risk prostate cancer according to RA-TB and RA-SB and whole-mount pathology of RP specimens.

	Simultaneous RA-TB + -SB cancer detection/cancer solely in RA-TB, *n*	Simultaneous RA-SB + -TB cancer detection/cancer solely in RA-SB, *n*	Whole-mount pathology RP, *n*
No cancer	107	102	0
Low risk	11/4	14/7	2
Intermediate risk	44/12	49/17	49
High risk	40/7	37/4	9
Total	95/23	100/28	60

therefore probably traumatic endorectal coil mpMRI procedure before biopsy. Some limitations of the present study should be mentioned. Firstly, the retrospective data acquisition, non-randomised study design and relatively small sample size. Secondly, included patients had a higher risk of prostate cancer based on the combination of rising or persistently elevated PSA levels and visible mpMRI lesions, which denotes a potential selection bias. Thirdly, we chose a limited definition of clinically significant prostate cancer by just using Gleason score and PSA level as relevant objective parameters. Lastly, we could not directly compare the RA-transperineal approach to transrectal fusion biopsies.

Acknowledgements

We would like to thank all study participants who were motivated by a strong desire to improve the prostate cancer diagnostic pathway.

Conflict of Interest

The authors declare that they have no conflict of interest.

1 Our institution did not receive payment or services from a third party (government, commercial, private foundation, etc.) at any time for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).
2 No funding or other financial support was received by any entities (regardless of amount of compensation).
3 No patents are planned, pending or issued.
4 No other relationships/conditions/circumstances that present a potential conflict of interest.

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Abbreviations: AS, anterior stroma; IQR, interquartile range; mpMRI, multiparametric MRI; PI-RADS, Prostate Imaging Reporting and Data System; PROMIS, PROstate MRI Imaging Study; PSAD, PSA density; PZa, anterior peripheral zone; RA, robot-assisted; RP, radical prostatectomy; SB, systematic biopsy; T2w, T2-weighted; TB, targeted biopsy; TZa, anterior transitional zone.