INNOVATIONS IN PROSTATE CANCER SPECIAL FEATURE: FULL PAPER

MRI-directed biopsy for primary detection of prostate cancer in a population of 223 men: MRI In-Bore vs MRI-transrectal ultrasound fusion-targeted techniques

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Objectives: To compare the detection rates of overall prostate cancer (PCa) and clinically significant PCa (csPCa) and the median percentage of cancer per biopsy core between MRI-guided In-bore and MRI-TRUS fusion-targeted biopsy (TBx).

Methods: In this retrospective study, 223 patients who underwent prostate multiparametric MRI (mpMRI) and subsequent MR-directed biopsy were included. For PCa and csPCa detection rate (DR), contingency tables were tested via the Pearson’s chi-squared to explore the variance of the outcome distribution. The percentage of cancer per biopsy core was tested with a two-tailed Mann-Whitney test.

Results: One hundred and seventeen and 106 patients underwent MRI-TRUS fusion or MRI In-bore TBx, respectively. 402 MRI biopsy targets were identified, of which 206 (51.2%) were biopsied with the MRI-TRUS TBx and 196 (48.8%) with the MRI In-bore TBx technique. Per-patient PCa and csPCa detection rates were 140/223 (62.8%) and 97/223 (43.5%), respectively. PCa-DR was 73/117 (62.4%) and 67/106 (63.2%) for MRI-TRUS and MRI In-Bore TBx (p = 0.9), while csPCa detection rate reached 50/117 (42.7%) and 47/106 (44.3%), respectively (p = 0.81). The median per-patient percentage of malignant tissue within biopsy cores was 50% (IQR: 27–65%) for PCa and 60% (IQR: 35–68%) for csPCa, with a statistically significant difference between the techniques.

Conclusion: No statistically significant difference in the detection rate of MRI In-bore and MRI-TRUS fusion TBx was found. MRI In-bore TBx showed higher per-core percentage of malignant cells. Advances in knowledge: MRI In-bore biopsy might impact risk stratification and patient management considering the higher per-core percentage of malignant cells, especially for patients eligible for active surveillance or focal therapy.

INTRODUCTION

Prostate cancer (PCa) is one of the most common solid cancers, with an estimated age-standardized incidence rate of 22% in males, second only to lung cancer. MRI has become the most accurate and cost-effective diagnostic imaging modality for PCa diagnosis, providing a high negative predictive value for the detection of clinically significant PCa (csPCa) ranging from 90.8 to 97.1%. With the emerging technological improvement in biopsy techniques, several investigations evaluated new possible ways to improve early detection of PCa. Four groundbreaking trials represent milestone investigations for the development of the so-called “MRI pathway” and for the validation of MRI-targeted biopsy in naïve males. The Cochrane Review showed a pooled sensitivity and specificity of 0.72 (95% CI: 0.60–0.82) and 0.96 (95% CI: 0.94–0.98), respectively, for the detection of ISUP grading group ≥2 PCa by the MRI pathway. This could lead to important changes in the pre-treatment prognostic models, with less marked survival differences between European Association of Urology (EAU) risk groups, modifying the grade group distribution with an improved detection of high-grade disease.

Several distinct ways for targeted biopsy (TBx) techniques are currently available, including MRI-TRUS fusion TBx, trans-perineal fusion biopsy, MRI In-bore TBx (both
trans-rectal and trans-perineal) and cognitive registration TRUS-TBx. In the MRI-TRUS TBx, information obtained from previously acquired MRI images is fused with real-time TRUS images. The MRI In-bore TBx can accurately target suspicious lesions, but it is more time-consuming, expensive and with somewhat limited access. On the contrary, the MRI-TRUS TBx is less expensive, more readily available, and therefore more commonly performed. Despite there are studies comparing MRI-TRUS fusion TBx and MRI In-bore TBx, there is still no evidence in the literature to strongly support the use of one targeted biopsy technique over the other. Interestingly, Costa et al showed that MRI In-bore TBx offered a lower incidence of Grade Grouping upgrades compared with MRI-TRUS fusion TBx at prostatectomy.

The purpose of this study was to directly compare the performance of two MRI-directed biopsy techniques (MRI In-bore and MRI-TRUS fusion TBx) in a single-center patient population. The primary endpoint of the study was to compare the difference in the detection of overall PCa and csPCa between MRI In-bore and MRI-TRUS fusion TBx performed by the same team interpreting MR images. The secondary endpoint was to compare the two techniques in terms of median percentage of cancer per biopsy core, stratifying the findings according to different clinical variables.

METHODS AND MATERIALS

Patient population and study design

This retrospective study received formal Institutional Review Board and Ethical Committee approval and waiver of informed consent was obtained. The study was conducted in line with the ethical principles laid down by the latest version of the Declaration of Helsinki. A database of 223 biopsy-naïve patients with no prior diagnosis of PCa, who underwent prostate MRI and subsequent MRI targeted biopsy (either MRI In-bore or MRI-TRUS fusion TBx) at our institution between November 2017 and November 2019, was used for this study. Patients underwent prostate MRI for clinical suspicion for PCa (total PSA >4 ng ml⁻¹, or >2.5 ng ml⁻¹ in patients with family history, and/or a positive DRE).

MRI acquisition protocol and image analysis

All exams were performed on a 3.0 or 1.5 Tesla MRI (GE Discovery 750 and PHILIPS Achieva), using a 32-channel surface phased-array body coil (TORSOPA). The exams were performed with a multiparametric protocol, according to PI-RADS v2 recommendations, including high-resolution T2WI on the axial and coronal planes, DWI at b values of 30, 800, 1500 with ADC map computation (based on b values of 50 and 800 to avoid diffusion kurtosis effect), and perfusion (DCE) with the use of GE sequences at a temporal resolution of 6s following a body weight adjusted intravenous bolus of contrast media (gadobutrol, 0.1 mmol/Kg at an injection rate of 3.0 ml/s). Patient preparation consisted in a rectal enema 2–4 h prior to the exam. A detailed list of the acquisition parameters is shown in Supplementary Table 1. Two radiologists with 5 and 15 years of prostate imaging experience at a high volume referral center evaluated all exams adopting the PI-RADS v2 scoring system, blindly with respect to the other reader evaluation, as part of the protocol of data acquisition of a prospectively acquired database. Differences in opinion were resolved by consensus. Reader experience was defined in compliance with the ESUR/ESUI consensus statements on multi-parametric MRI, which is based, among other parameters, on the number of cases reported per year (>800 MRIs for each reader) and participation in multidisciplinary team meetings. Lesion volume was calculated on T2WI using the ellipsoid formula (product of the three diameters × π /6).

MR-directed biopsy

Patients underwent MRI-directed biopsy (MRDB) when a PI-RADS score >3 was reported. Patients assigned a PI-RADS score equal to three and who had a PSA density (PSAd) ≥0.15 were also referred to biopsy. In patients with more than one PI-RADS ≥3 lesion, the index lesion was defined as the one with the highest PI-RADS score, or the most suspicious one when the PI-RADS score was the same (i.e., the most hypointense/hypointense on DWI/ADC for the peripheral zone, the one with the most suspicious pattern on T2WI for the transition zone). Patients were directed to either MRI In-bore or MRI-TRUS fusion TBx according to the patient's and/or operator's preference, the latter mostly depending on lesion size and location, and on prostate size. Specifically, patients with smaller and/or apical lesions and with bigger prostates were preferentially biopsied through MRI In-bore TBx. Both MRI-TRUS and MRI In-bore TBx were performed by the same team that interpreted the MRI images, comprised of two radiologists with 2 and 4 years of experience in the use of both biopsy techniques, respectively. Patient preparation and pre-medication were conducted according to EAU guidelines. Biopsy targets were defined all the suspicious areas identified by the radiologists (PI-RADS score ≥3). The number of biopsy samples per lesion ranged from 2 to 4 according to the volume of the lesion, making sure that specimens of adequate length and integrity were obtained from each lesion. No systematic biopsy samples were obtained with either technique. Once the biopsy cores were sampled and stored in formalin-filled containers, they were reported with a standardized nomenclature, to avoid bias during pathology analysis, by the same pathologist with 15 years of experience in genitourinary pathology. Clinically significant PCa was defined as ≥2Gleason Group 2 PCa. To compare the detection rate (DR) of the two different biopsy techniques, the ratio between positive and total cores was considered.

MRI-TRUS-guided targeted prostate biopsy

MRI-TRUS TBx was performed using a transrectal approach with a dedicated system (UROSTATION KOELIS). During the procedure, an 18-gauge fully automated biopsy needle with a core length of 18 mm was inserted via the rectum attached to the US probe. The software allows to monitor needle orientation during the procedure and to obtain “virtual-biopsy” acquisitions to check the correct aiming of the needle. Once the needle is confirmed to be aligned with the target, the sample is obtained.
and an “actual-biopsy” 3D- US acquisition is performed (Figure 1).

MRI-guided in-bore targeted prostate biopsy
MRI In-bore TBx was performed on a 1.5 T MRI scan (PHILIPS Achieva), with body and spine phased-array coils, with the patient in prone position. An introductory guide filled with a gadolinium-chelate dotted gel was used to guide the 18-gauge fully automated titanium double-shot biopsy gun, with a core length of 18 mm. A portable trans-rectal biopsy device (DynaTRIM) and a dedicated software (DynaCAD) were used for interventional planning, and to align and hold the needle in position. The device arm enables the needle guide to rotate, move forwards and backwards, and to be adjusted in height. Coronal, sagittal and axial T2W images were acquired to visualize MRI targets before and after the biopsy sampling (Figure 2).

Statistical analysis
We stratified the biopsy dataset and our results according to the diagnostic performance achieved by the two biopsy techniques and according to targets’ characteristics including ISUP classification for DR (PCa and csPCa), PI-RADS score (3 vs 4–5), prostate volume (≤ or > than 48 ml), lesion location (transition vs peripheral zone), volume (≤ or > than 0.7 ml) and level (base,
MRI In-bore vs MRI-TRUS targeted biopsy for prostate cancer detection

Figure 2. 66-year-old man with clinical suspicion of prostate cancer (PSA total value of 5.4 ng ml\(^{-1}\)). (a) T2WI acquired on the axial plane showing a hypointense nodule on the mid-left posterior zone, hyperintense on early DCE images (b), with restriction diffusion at b-value 1500 (c) and low ADC value (d), classified as PI-RADS 4. (e) The nodule was biopsied using MRI In-bore TBx, coronal images were acquired during the procedure for needle orientation and after the procedure to document the accurate targeting. (f) Histopathology confirmed the presence of ISUP 2 (GS 3 + 4, in 58% of the core) on the left lobe of the prostate. ISUP, International society of urogenital pathology; GS, Gleason score; PSA, Prostate-specific antigen; T2WI, T\(_2\)-weighted imaging; DCE, Dynamic contrast enhanced; TBx, Targeted biopsy.

mid-gland, apex). Patient demographics and clinical characteristics were analyzed using the Student’s t-test or Mann-Whitney for continuous variables and Pearson’s chi-squared test or Fisher’s exact test when appropriate for categorical variables. For PCa and csPCa DR between the two TBx techniques, 2 × 2 contingency tables were generated and tested via the Pearson’s chi-squared to explore the variance of the outcome distribution. Similarly, the percentage of positive malignant cores detected via the two different TBx were descriptively presented as median (IQR) and tested for detection of difference among the two samples according to two-tailed Mann-Whitney test. ROC analysis was performed for relevant variables of interest (i.e. variables with a statistically significant difference between the two groups in the sample). A multivariable logistic regression model was developed to assess whether the biopsy technique (MRI-TRUS or MRI In-Bore) was an independent predictor for both the outcome of PCa and csPCa diagnosis. All the regression models were adjusted for age (<70 vs. >/=<70 years), PSA (ng/dl), PSA density (<0.15 vs. >/=<0.15), pre-Bx PI-RADS score (3 vs 4–5) as well as lesion volume (ml), location (transitional/anterior vs peripheral) and level (base, mid-gland, apex). According to the available literature and to the cohort quantitative descriptive distribution, after having assumed a relevant threshold of neoplastic median per-core percentage ≥50%, the same regression model was implemented to test the ability of one technique over the other to better characterize the overall sampled tumor tissue within the biopsy cores.\(^{27}\)

A locally weighted scatter plot smoother (LOWESS) function was used to graphically depict the relationship between the predicted probability of csPCa detection vs the quantitative median percentage of malignant sample for the overall length of tissue biopsied. Calculations were performed using Stata v.16.1 (Stata Corporation, College Station, TX, USA) after having assumed a \(p\)-value < .05 as statistically significant.

RESULTS
The 223 patients included in the study had a median age of 68 (IQR: 63–73.5), a median total PSA value of 7.4 ng ml\(^{-1}\) (IQR: 5.2–10.3) and a median PSA density of 0.15 ng/ml ml\(^{-1}\) (IQR: 0.09–0.25), with a statistically significant difference in PSA density between patients without and with PCa (0.11 vs 0.16, \(p\) < 0.0001). The clinical, radiologic and pathologic characteristics of the entire cohort population are summarized in Table 1.
A total of 117 and 106 patients underwent MRI-TRUS fusion or MRI In- bore TBx, respectively. Overall, 402 MRI biopsy targets were identified (168 PI- RADS score 3, 203 PI- RADS score 4, and 31 PI- RADS score 5), of which 206 (51.2%) were biopsied with the MRI- TRUS TBx and 196 (48.8%) with the MRI In- bore technique. A median of two lesions per patient (IQR 1–2) were biopsied in both the MRI- TRUS and the MRI In- Bore group, with no statistically significant difference (\(p > .05\)). A total of 988 cores were obtained (542 vs 446 with MRI- TRUS or In- bore TBx technique, respectively). Median overall number of cores per patient was 4 (IQR: 3–5), with no statistically significant difference between MRI- TRUS and MRI In- Bore TBx (\(p = 0.62\)).

Of note, median lesion volume was different between the two study groups: 0.77 ml (IQR: 0.25–2.27 ml) for MRI- TRUS TBx vs 0.27 ml (IQR 0.27–0.52 ml), for MRI In- Bore, \(p < .0001\) (Table 2).

There was no statistically significant difference in DR between MRI- TRUS fusion and MRI In-Bore TBx for both PCa (73/117, 62.4% vs 67/106, 63.2%, respectively, \(p = 0.9\)) and csPCa (50/117, 42.7% vs 47/106, 44.3%, respectively, \(p = 0.81\)).

The median overall per-patient percentage of malignant tissue within the biopsy cores was higher for MRI In-Bore TBx, with a statistically significantly difference between the two techniques (%-PCa, MRI-TRUS TBx: 33%, IQR: 17–53% vs MRI In-bore TBx: 55%, IQR: 41–65%, \(p < .0001\); %-csPCa MRI-TRUS TBx: 41%, IQR: 20–63% vs MRI In-bore TBx: 60%, IQR: 46–65%, \(p < .0001\)) (Table 2).

When analyzing the whole dataset on a per-lesion basis, the MRI In-Bore TBx was found to be associated with a higher median percentage of tumor tissue within the biopsy core length both for PCa (ORPCa: 3.26, 95% CI: 1.37–7.12, and ORcsPCa: 2.17, 95% CI: 0.82–5.34).
are associated with an increased probability of csPCa detection (Figure 3). In the stratified analysis, the subgroup with inferior median prostate volume (i.e. ≤48 ml) showed a better DR for PCa with MRI-TRUS TBx (64.4% vs 49.6%, p = 0.027), while there was no difference in DR of csPCa (p = 0.15). For larger prostate volumes (i.e. >48 ml), we observed no differences in DR of both PCa and csPCa (p = 0.084 and p = 0.07, respectively). No statistically significant differences in the DR of PCa and csPCa among the two techniques were found, when stratifying according to target location, PI-RADS score, median lesion volume, and lesion level. There was a statistically significant difference in the overall median percentage of tumor tissue detected via MRI In-Bore TBx, which was higher compared to MRI-TRUS when stratified according to radiological parameters (Table 2).

DISCUSSION
Currently, there is controversial data in the literature regarding which type of MRI-directed biopsy technique performs better in terms of csPCa detection rate. Instead, it has been demonstrated in several investigations that MRDB performs better than TRUS-guided biopsy. A few studies directly comparing MRI-TRUS fusion TBx and MRI In-bore have been published.19–22 In this study, we found no statistically significant differences in the DR of both PCa and csPCa between the two biopsy techniques. These results are in line with those reported in the FUTURE trial, where the authors found no difference in terms of PCa detection with three biopsy techniques (fusion vs cognitive vs in-bore), although they found a statistically significant difference in the number of cores, with a median number of cores of four for FUS-TB, three for COG-TB, and two for MRI-TB (p < 0.05).20 In contrast, we did not find differences in terms of number of cores, probably due to the design of our study, in which a single group interpreted MRI images and performed targeted biopsies, minimizing the bias that can occur in a multi step process as PCa diagnosis. Another possible reason for such difference is related

Table 2. Demographic, clinical and pathological characteristics of the MRI biopsy targets (per-lesion cohort, n = 402) stratified according to MRDB technique

| Variable (Per-lesion) | MRI-TRUS TBx (n = 206) | MRI In-Bore TBx (n = 196) | p value* |
|----------------------|------------------------|---------------------------|----------|
| Age, years Median (IQR) | 70 (65–75) | 65 (61–71) | <0.0001 |
| PSA, ng/ml Median (IQR) | 7.7 (5.9–10.3) | 6.7 (5–10.5) | 0.02 |
| PSA density, ng/mL/cc Median (IQR) | 0.15 (0.09–0.26) | 0.15 (0.09–0.27) | 0.78 |
| Prostate Volume, ml Median (IQR) | 48 (36–77) | 44 (34–61) | 0.06 |
| Detection rate PCa n (%) | 101 (49.0) | 94 (48.0) | 0.83 |
| Detection rate csPCa n (%) | 63 (30.6) | 62 (31.6) | 0.82 |
| Ratio of detection rate csPCa/PCa (%) | 63/101 (62.4) | 62/94 (65.9) | _ |
| Lesion location, n (%) | 0.74 |
| Posterior | 184 (89.3) | 173 (88.3) | |
| Transitional/Anterior | 22 (10.7) | 23 (11.7) | |
| Lesion volume, ml Median (IQR) | 0.77 (0.27–2.18) | 0.27 (0.27–0.52) | <0.0001 |
| PI-RADS v2, n (%) | 0.06 |
| 3 | 96 (46.6) | 72 (36.7) | |
| 4 | 92 (44.7) | 111 (56.6) | |
| 5 | 18 (8.7) | 13 (6.6) | |
| ISUP grade (Gleason Score), n (%) | 0.88 |
| negative | 105 (51.0) | 102 (52.0) | |
| 1 (3 + 3) | 39 (18.9) | 32 (16.3) | |
| 2 (3 + 4) | 27 (13.1) | 31 (15.8) | |
| 3 (4 + 3) | 19 (9.2) | 15 (7.7) | |
| 4 (4 + 3 + 5) | 11 (5.3) | 9 (4.6) | |
| 5 (4 + 5 + 4) | 5 (2.4) | 7 (3.6) | |
| % Positive core per-single lesion | |
| PCa - Median (IQR) | 33 (17–60) | 59 (40–65) | <0.0001 |
| csPCa - Median (IQR) | 47 (20–67) | 60 (47–69) | 0.009 |

IQR, Inter quartile range; ISUP, International society of uro-pathology; MRDB, Magnetic resonance-directed biopsy; PCa, Prostate cancer; TBx, Targeted biopsy; csPCa, Clinically significant prostate cancer.

* A p value of < 0.05 was considered for statistical significance
Interestingly, when analyzing the subgroup of patients with inferior median prostate volume (i.e., ≤48 ml), a higher DR in case of PCa detection was found in favor of MRI-TRUS TBx, while there was no difference in csPCa detection (p = 0.15). This is probably linked to the fact that in smaller prostate glands, the errors of TRUS and MRI images fusion are reduced.

We found that MRI In-Bore TBx was associated with a higher per-patient percentage of malignant tissue within the biopsy cores. In the multivariable analysis, the MRI In-bore TBx was strongly associated with the probability of obtaining a percentage of tumor per-biopsy sample superior to 50% (OR = 3.26, p < 0.005). Such data have several clinical implications for patients’ management in terms of both diagnosis and approach to therapy. Several investigations have showed the paramount value of the amount of tumor in prostate needle cores, for correct patient management, in different settings: in the prediction of PSA failure among males undergoing radical prostatectomy; as part of nomograms to predict pathologic stage, extra prostastic extension, seminal vesicle invasion and radiation therapy failure; as survival prognostic factor for patients treated with dose-escalated external beam radiotherapy; and as single best predictor of probability of clinically insignificant PCa detection to enroll patients in active surveillance (AS) protocols. The role of the MRDB should be discussed in-depth for patients enrolled in AS protocols. In a systematic review and meta-analysis on the role of MRDB in addition to systematic confirmatory biopsy in males on AS for low-risk prostate cancer, Schoots et al found that no pathway was more favorable than the other (relative risk [RR] 0.92, 95% CI 0.79–1.06). However, the highest upgrading (Gleason ≥3 +4) was found in 27% (95% CI 22–34%) using a combined approach of MRI-targeted biopsies and confirmatory systematic biopsies. In addition, in two large cohorts, the number of cancer cores and the greatest percentage of cores involved at first biopsy were significant predictors of both PCA reclassification and increased tumor extent at re-biopsy. Such data suggest that MRI In-bore biopsy might provide a crucial clinical impact in the risk stratification and management of patients on AS, for both diagnosis and follow-up. Further studies pointing on this direction are warranted to provide evidence to cover the current need of guidelines based on pathologic parameters from MRDB to stratify patients’ risk and define proper therapeutic planning.

The limitations of this study need to be acknowledged. Firstly, the single-institution retrospective design of the study. Additionally, the statistical analysis lighted out a possible selection bias, showing that patients directed to in-bore biopsies had smaller median lesion volumes. Indeed, smaller foci are preferentially directed to the MRI In-bore technique because a needle-in-target MRI image gives more confidence to the operator. However, multivariable regression analysis and stratified analysis were performed to assess the impact of the different variables on the outcomes, which revealed no statistically significant influence on the biopsy results. Additionally, the ROC analysis performed according to target volume revealed that the AUC was comparable between the two biopsy techniques and showed to be a non-reliable parameter to estimate the lesions’ malignant potential. Of note, the lower median lesion volume in the MRI In-Bore group could have potentially biased results toward a lower DR and/or percentage of malignant tissue within biotic cores. Conversely, MRI In-Bore TBx showed superior percentages of malignant tissue, which bolster confidence in our findings. A further limitation of this study lies in the lack of pathology based on radical prostatectomy specimens. Finally, only transrectal TBx techniques have been evaluated in this study. However, transperineal approach is a valid alternative that is worth investigating in future studies in the context of targeted biopsies. In particular, there is conflicting evidence in the literature regarding post-biopsy complications, with some studies reporting lower rates of infectious complications for transperineal biopsies compared to the transrectal approach. In our experience, however, infectious complications can be nearly completely avoided in...
transrectal TBx by having the patients undergo urine culture to rule out infection or colonization and by administering prophylactic antibiotics prior to the biopsy.

**CONCLUSION**

No statistically significant difference was detected in terms of overall PCA and csPCa detection rate comparing MRI In-bore and MRI-TRUS fusion-targeted prostate biopsy, when performed by the same radiologists’ team as MRI images reader and biopsy operator. However, MRI In-bore TBx showed a higher percentage of malignant cells per-core compared to MR-TRUS TBx, a data that might impact clinical risk stratification and patient management, especially for those eligible for active surveillance protocols and focal therapy.

**REFERENCES**

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68: 394–424. doi: https://doi.org/10.3322/caac.21492
2. Mottet RCN, van den Bergh N, Brier E, Cornford P, De Santis M, Fant S. EAU guidelines: prostate cancer. EAU guidelines. 978th-96th-626715-04-2 ed. 2019.
3. Faria R, Soares MO, Spackman E, Ahmed HU, Brown LC, Kaplan R, et al. Optimising the diagnosis of prostate cancer in the era of multiparametric magnetic resonance imaging: a cost-effectiveness analysis based on the prostate MR imaging study (PROMIS). Eur Urol 2018; 73: 23–30. doi: https://doi.org/10.1016/j.eururo.2017.08.018
4. Panebianco V, Valero MC, Giuliani A, Pecoraro M, Cervello I, Barchetti G, et al. Clinical utility of multiparametric magnetic resonance imaging as the first-line tool for men with high clinical suspicion of prostate cancer. Eur Urol Oncol 2018; 1: 208–14. doi: https://doi.org/10.1016/j.euo.2018.03.008
5. Sanda MG, Cadeddu JA, Kirkby E, Chen RC, Crispino T, Fontanarosa J, et al. Clinically localized prostate cancer: AUA/ASTRO/SUO guideline. Part I: risk stratification, shared decision making, and care options. J Urol 2018; 199: 683–90. doi: https://doi.org/10.1016/j.juro.2017.11.095
6. Türkbey B, Rosenkrantz AB, Haider MA, Padhani AR, Villeirs G, Macura KJ, et al. Prostate imaging reporting and data system version 2.1: 2019 update of prostate imaging reporting and data system version 2. J Urol 2019; 76: 340–51. doi: https://doi.org/10.1016/j.juro.2019.02.033
7. Pavone P, Laghi A, Catalano C, Panebianco V, Fabiano S, Passariello R. MRI of the biliary and pancreatic ducts. Eur Radiol 1999; 9: 1513–22. doi: https://doi.org/10.1007/s003300508877
8. Sathananthan NJ, Omer A, Harris E, Davies L, Kasivisvanathan V, Punwani S, et al. Negative predictive value of multiparametric magnetic resonance imaging in the detection of clinically significant prostate cancer in the prostate imaging reporting and data system era: a systematic review and meta-analysis. Eur Urol 2020; 78: 402–14. doi: https://doi.org/10.1016/j.eururo.2020.03.048
9. Panebianco V, Barchetti G, Simone G, Del Monte M, Ciardi A, Grompone MD, et al. Negative multiparametric magnetic resonance imaging for prostate cancer: what’s next? Eur Urol 2018; 74: 48–54. doi: https://doi.org/10.1016/j.eururo.2018.03.007
10. Kasivisvanathan V, Rannikko AS, Borghi M, Panebianco V, Mynderse LA, Vaarala MH, et al. MRI-Targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med 2018; 378: 1767–77. doi: https://doi.org/10.1056/NEJMoa1801993
11. Rouvière O, Puech P, Renard- Penna R, Claudiun M, Roy C, Mège-Lechevallier F, et al. Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naïve patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study. Lancet Oncol 2019; 20: 100–9. doi: https://doi.org/10.1016/S1470-2045(18)30569-2
12. van der Leest M, Cornel E, Hendriks LC, Gabe R, Hindley RG, Kaplan R, et al. Comparing three different techniques of imaging-guided diagnostic pathway: proposal for a new classification based on MRI-targeted biopsies and early oncologic outcomes after surgery. World J Urol 2020; 38: 2493–500. doi: https://doi.org/10.1007/s00345-019-03053-6
13. Panebianco V, Barchetti F, Manenti G, Aversa T, Catalano C, Simonetti G. Mr imaging-guided prostate biopsy: technical features and preliminary results. Radiol Med 2015; 120: 571–8. doi: https://doi.org/10.1007/s11547-014-0490-0
14. Pokorny MR, de Rooij M, Duncan E, Schröder FH, Parkinson R, Barentsz JO, et al. Prospective study of diagnostic accuracy comparing prostate cancer detection by transrectal ultrasound-guided biopsy versus magnetic resonance (Mr) imaging with subsequent MR-guided biopsy in men without previous prostate biopsies. Eur Urol 2014; 66: 22–9. doi: https://doi.org/10.1016/j.eururo.2014.03.002
15. Venderink W, van der Leest M, van Luijtelaar A, de van WJm, Fütterer JJ, Sedeelaar JPM, et al. Retrospective comparison of direct in-bore magnetic resonance imaging (MRI)-guided biopsy and fusion-guided biopsy in patients with MRI lesions which are likely or highly likely to be clinically significant prostate cancer. World J Urol 2017; 35: 1849–55. doi: https://doi.org/10.1007/s00345-017-2085-6
16. Wegelin O, van Melick HHE, Hooft L, Bosch JLHR, Reitsma HB, Barentsz JO, et al. Comparing three different techniques for magnetic resonance Imaging-targeted prostate biopsies: a systematic review
of In-bore versus magnetic resonance Imaging-transrectal ultrasound fusion versus cognitive registration, is there a preferred technique? Eur Urol 2017; 71: 517–31. doi: https://doi.org/10.1016/j.eururo.2016.07.041

20. Wegelin O, Exterkate L, van der Leest M, Kummer JA, Vreuls W, de Bruin PC, et al. The future trial: a multicenter randomised controlled trial on target biopsy techniques based on magnetic resonance imaging in the diagnosis of prostate cancer in patients with prior negative biopsies. Eur Urol 2019; 75: 582–90. doi: https://doi.org/10.1016/j.eururo.2018.11.040

21. Costa DN, Goldberg K, Leon ADde, Lotan Y, Xi Y, Aziz M, 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. doi: https://doi.org/10.1016/j.euro.2018.08.022

22. Prince M, Foster BR, Kaempf A, Liu J-J, Amling CL, Isharwal S, et al. In-bore versus fusion MRI-Targeted biopsy of PI-RADS category 4 and 5 lesions: a retrospective comparative analysis using propensity score weighting. AJR Am J Roentgenol 2020; 214.20.25207. doi: https://doi.org/10.2214/ajr.20.25207

23. Costa DN, Cai Q, Xi Y, Recchimuzzi DZ, Subramanian N, Bagrodia A, et al. Gleason grade group concordance between preoperative targeted biopsy and radical prostatectomy histopathologic analysis: a comparison between In-Bore MRI-guided and MRI-Transrectal us fusion prostate biopsies. Radiol Imaging Cancer 2021; 3: e200123: e200123. doi: https://doi.org/10.1148/rccan.2021200123

24. Barentsz JO, Weinreb JC, Verma S, Thoeny HC, Tempany CM, Sherten F, et al. Synopsis of the PI-RADS V2 guidelines for multiparametric prostate magnetic resonance imaging and recommendations for use. Eur Urol 2016; 69: 41–9. doi: https://doi.org/10.1016/j.eururo.2015.08.038

25. de Rooij M, Israël B, Timmers M, Ahmed HU, Barrett T, Giganti F, et al. ESUR/ESUI consensus statements on multi-parametric MRI for the detection of clinically significant prostate cancer: quality requirements for image acquisition, interpretation and radiologists’ training. Eur Radiol 2020; 30: 5404–16. doi: https://doi.org/10.1007/s00330-020-06929-z

26. Mottet N, Cornford P, van den Bergh RCN, Briers E, De Santis M, Fant S. EAU guidelines: prostate cancer. EAU Guidel. 978th-94th-92671st-07-3. ed; 2020.

27. Montironi R, Scarpelli M, Mazzucchelli R, Cheng L, Lopez-Beltran A, Montorsi F. Extent of cancer of less than 50% in any prostate needle biopsy core: how many millimeters are there? Eur Urol 2012; 61: 751–6. doi: https://doi.org/10.1016/j.eururo.2011.12.050

28. Freedland SJ, Aronson WJ, Terris MK, Kane CJ, Amling CL, Dorey F, et al. Percent of prostate needle biopsy cores with cancer is significant independent predictor of prostate specific antigen recurrence following radical prostatectomy: results from search database. J Urol 2003; 169: 2136–41. doi: https://doi.org/10.1016/j.juro.2003.06.039.

29. Antonelli A, Vismara Fugini A, Tardanico R, Giovanessi L, Zambolin T, Simeone C. The percentage of core involved by cancer is the best predictor of insignificant prostate cancer, according to an updated definition (tumor volume up to 2.5 cm3): analysis of a cohort of 210 consecutive patients with low-risk disease. Urology 2014; 83: 28–32. doi: https://doi.org/10.1016/j.urology.2013.07.056

30. Vance SM, Stenmark MH, Blas K, Halverson S, Hamstra DA, Feng FY. Percentage of cancer volume in biopsy cores is prognostic for prostate cancer death and overall survival in patients treated with dose-escalated external beam radiotherapy. Int J Radiat Oncol Biol Phys 2012; 83: 940–6. doi: https://doi.org/10.1016/j.ijrobp.2011.09.005

31. Schoots IG, Nieboer D, Giganti F, Moore CM, Bangma CH, Roobol MJ. Is magnetic resonance imaging-targeted biopsy a useful addition to systematic confirmatory biopsy in men on active surveillance for low-risk prostate cancer? A systematic review and meta-analysis. BJU Int 2018; 122: 946–58. doi: https://doi.org/10.1111/biju.14358

32. Tosioian JJ, Mamawala M, Epstein JJ, Landis P, Wolf S, Trock BJ, et al. Intermediate and longer-term outcomes from a prospective active-surveillance program for favorable-risk prostate cancer. JCO 2015; 33: 3379–85. doi: https://doi.org/10.1200/JCO.2015.62.5764

33. Klotz L, Vespri D, Sethukavalan P, Jethava V, Zhang L, Jain S, et al. Long-Term follow-up of a large active surveillance cohort of patients with prostate cancer. JCO 2015; 33: 272–7. doi: https://doi.org/10.1200/JCO.2014.55.1192

34. Xiang J, Yan H, Li J, Wang X, Chen H, Zheng X. Transperineal versus transrectal prostate biopsy in the diagnosis of prostate cancer: a systematic review and meta-analysis. World J Surg Oncol 2019; 17: 31. doi: https://doi.org/10.1186/s12957-019-1573-0

35. Bennett HY, Roberts MJ, D’or S, Gardiner RA. The global burden of major infectious complications following prostate biopsy. Epidemiol Infect 2016; 14: 1784–91. doi: https://doi.org/10.1017/S0950268815002885

36. Mian BM, Kaufman RP, Fisher HAG. Rationale and protocol for randomized study of transrectal and transperineal prostate biopsy efficacy and complications (ProBE-PC study). Prostate Cancer Prostatic Dis 2021; 24: 688–96. doi: https://doi.org/10.1038/s41391-021-00352-1