Clinical Imaging 53 (2019) 1–5

Contents lists available at ScienceDirect

Clinical Imaging

journal homepage: www.elsevier.com/locate/clinimag

Body Imaging

Value of MR-US fusion in guidance of repeated prostate biopsy in men with PSA < 10 ng/mL☆

Sung Il Hwang[a], Hak Jong Lee[b,c,*], Sang Eun Lee[d], Sung Kyu Hong[d], Seok-Soo Byun[d], Sang Chul Lee[d], Gheeyoung Choe[e]

[a] Department of Radiology, Seoul National University Bundang Hospital, Republic of Korea
[b] Department of Radiology, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Republic of Korea
[c] Program in Nano Science and Technology, Department of Transdisciplinary Studies, Seoul National University Graduate School of Convergence Science and Technology, Republic of Korea
[d] Department of Urology, Seoul National University Bundang Hospital, Republic of Korea
[e] Department of Pathology, Seoul National University Bundang Hospital, Republic of Korea

ARTICLE INFO

Keywords:
Prostate cancer
Magnetic resonance imaging
Ultrasonography
Fusion biopsy

ABSTRACT

Purpose: We want to investigate whether MR-US fusion can improve the detection rates of clinically significant prostate cancer in patients with prior negative prostate biopsy with PSA level < 10 ng/mL.
Methods: Thirty nine patients who had previous a history of negative prostate biopsy and PSA levels < 10 ng/mL were included in this study. MR was performed before the biopsy and graded using PIRADS V2. We labeled patients with index lesions with PIRADS scores of 3 or above as the MR-positive group, while patients with PIRADS scores of 1 or 2 were the MR-negative group. Two cores of added biopsy (AB) were performed per each index lesion under MR-US fusion. Twelve cores randomized systematic biopsy (SB) were followed. In MR negative group, two cores of AB were obtained in transition zone, followed by SB. Overall cancer and clinically significant cancer detection rates by patients and by cores were analyzed, and compared between MR-positive and negative group.
Results: The overall cancer detection rates were 51.3% by patient based and 13.8% by core based. While all of AB positive cancer patients were clinically significant cancer patients, five out of seven (71.4%) AB negative cancer patients were clinically insignificant cancer patients. AB results turned another four cancer patients from insignificant to significant cancer. The cancer detection rates between MR-positive and negative group were statistically significant.
Conclusions: Additional biopsy using MR–US fusion showed improved detection of clinically significant prostate cancer.

1. Introduction

Prostate cancer is the most common male cancer in the United States and is the nation's second-leading cause of death [1]. One in six men in the United States will be clinically diagnosed with prostate cancer in his lifetime [2]. Digital rectal exams, prostate-specific antigens (PSA), and transrectal ultrasound (TRUS) of the prostate are used for the detection of prostate cancer. Magnetic resonance (MR) imaging has been used as the main imaging modality for the evaluation of the prostate due to its superiority to other imaging modalities in the detection, localization, and assessment of the disease extent of the prostate. Recent advances in multiparametric MR techniques have helped to increase the diagnostic accuracy of prostate cancer [3]. In addition to the evaluation of prostate cancer, MR can show detailed information for planning prostatectomy and the prediction of postoperative complications.

Although prostate MR is known to be the most accurate imaging method for the detection of prostate cancer, it has usually been performed after confirmation of prostate cancer for staging purposes. Transrectal biopsy of the prostate is usually guided by TRUS. Because

☆ This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (NRF-2013R1A1A2011398).

* Corresponding author at: Department of Radiology, Seoul National University Bundang Hospital, 300 Gumi-dong, Bundang-gu, Seongnam-si, Gyeonggi-do 463-707, Republic of Korea.
E-mail address: hakjlee@snu.ac.kr (H.J. Lee).

https://doi.org/10.1016/j.clinimag.2018.09.012
Received 17 April 2018; Received in revised form 6 September 2018; Accepted 18 September 2018

neither the sensitivity nor specificity of prostate cancer by TRUS are very high [4], performing randomized systematic biopsies of the prostate over twelve cores still remains the gold standard method. Systematic randomized biopsy, however, can yield misleading information. A tumor with a high Gleason score that needs active treatment can be missed by sampling errors, while patients with small, clinically insignificant cancer undergo overtreatment, including radical prostatectomy, despite its high probability of complications; thus, the early detection of clinically significant cancer is essential for the proper treatment of prostate cancer patients [5]. The concept of MR guidance also helps to compensate for the low detection yield of ultrasound for prostate cancer [6].

Researchers have published several promising reports about MR–US fusion biopsy of the prostate [7–9]. Overall detection rates of cancer were increased by targeted biopsy; clinically significant cancer, in particular, is more frequently detected by targeted biopsy, which means that fusion biopsy can reduce the unnecessary numbers of biopsy cores and properly guide the treatment plan. These studies usually have been conducted on mixed populations of patients, however, who had variable prostate cancer risks.

It is well known that the more biopsies are done, the lower the cancer detection rates will be. Djavan et al. reported that cancer detection rates in biopsies 1, 2, 3, and 4 were 22% (231 of 1051), 10% (83 of 820), 5% (36 of 737), and 4% (4 of 94), respectively [10]. In this clinical setting of repeated biopsy, the detection of cancer, especially clinically significant cancer, is crucial, not only to reduce mortality related with cancer, but to reduce morbidity and patients' discomfort and other dangers associated with biopsies. Moreover, it is reported that if the lower PSA level in patients of repeated biopsy, the higher probability of negative follow-up biopsy [11]. Magnetic Resonance (MR) guided prostate biopsy is now regarded as first option in the patient for rebiopsy who had prior negative biopsy results [12,13]. In our study, we focused on the value of MR–US fusion in rebiopsy patients with low risk group, PSA level < 10 ng/mL.

The aim of this study was to investigate whether and how much MR-US fusion can improve the detection rates of clinically significant prostate cancer in rebiopsy patients of low risk group, with control of 14 core biopsy scheme.

2. Materials and methods

2.1. Patient selection

Our institutional review board approved this retrospective study, and waived the written informed consent. From September 2012 to February 2015, MR–US fusion biopsy of the prostate was performed in 137 patients with clinically suspected cancer. Seventy patients with initial prostate biopsy were excluded. The remaining 67 patients had a history of negative prostate biopsy results. In the end, 39 patients with PSA levels of < 10 ng/mL were included in this study. Mean number of previous biopsy session in our patient group was 1.3 (range: 1–5) and mean interval between prior randomized systemic biopsy and fusion biopsy was 712.2 days (range: 21–3581 days).

2.2. MR acquisition and PIRADS scoring

MR was performed before the biopsy in all patients. Antiperistaltic drugs (Buscopan; Boehringer Ingelheim, Germany) were administrated intramuscularly 30 min before each MR examination. MR imaging was conducted using a 3.0 T machine (Achieva Tx and Ingenia; Philips, the Netherlands) with a phased array cardiac 6-channel coil. MR included three orthogonal planes of T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI), and dynamic contrast-enhanced MRI (DCE-MRI). The detailed parameters of the T2 weighted MR were as follows: TR, 2500–3000 ms; TE, 70–90 ms; slice thickness, 3 mm; interslice gap, 1 mm; field of view, 160 mm × 160 mm; matrix, 320 × 320; and number of excitations, 1. Diffusion encoding gradients were applied as a bipolar pair at b-values 0 and 1000 s/mm^2. Apparent diffusion coefficient (ADC) maps were automatically generated on a pixel-by-pixel basis. Although DCE imaging was also performed, we did not use the imaging for the registration.

An experienced uroradiologist, blinded to all clinical information, independently graded the level of suspicion for clinically significant cancer from ADC maps and T2WI using PIRADS V2 from 1 to 5, as follows: grade 1, highly unlikely to be present; grade 2, unlikely to be present; grade 3, equivocal; grade 4, likely to be present; and grade 5, highly likely to be present. A maximum of two index lesions were chosen per each patient. Only ADC maps were used for the selection of image registration, regardless of the location of the index lesion.

2.3. Fusion of MR and US

The fusion imaging technique (Volume Navigation; GE Healthcare, USA) uses an electromagnetic field tracking system; it is composed of an electromagnetic transmitter adjacent to the patient, as well as electromagnetic sensors or trackers attached to the US transducer. A fully integrated position sensor unit installed in the US machine receives the location data from the sensors. Before the examinations in our study, the axial MR images were uploaded from the picture archiving and communication system (PACS) archive to the US machine.

After the upload of the MR images, registration between the MR and US images is necessary in order to fuse both images correctly. Image registration consists of two steps: plane and point registration. All registrations in our study were performed in the axial plane. For plane registration, we used outer contour, location of the seminal vesicle, shape of the transition zone, and apex as landmarks. Once the US image showed similar imaging features with the MR image with the index lesion, we finished the plane registration. The point registration was not done for the further calibration, because constant landmark for registration is sometimes difficult to find in the prostate. When there were two index lesions in the same patient, the registrations were performed again for the next lesion after a biopsy of the first index lesion was performed. Overall estimated time for the registration was < 10 min per lesion.

2.4. Prostate biopsy

TRUS-guided biopsy was performed with a Logiq E9 US machine (GE Healthcare, USA) equipped with a 5–9 MHz multi-frequency endocavitary probe by the same uroradiologist who had conducted the image fusion. Local anesthesia with 10 mL of lidocaine was applied before each biopsy. An 18-gauge, 20 cm automatic cutting needle and an automated biopsy gun (ACECUT, TSK Laboratory, Japan) were used. After the image registration, a side-by-side display of the TRUS and MR images was displayed (Fig. 1).

Under the guidance of the fused MR–US, two cores of needle biopsy per each index lesion were performed. And maximal number of added biopsy was four in a patient. Even when there was no index lesion on the MR (PIRADS 1), we added two cores of the biopsy at each side of the transition zone; controlling the increase in the number of biopsy cores resulted in increased detection rates of cancers by patient.

After biopsies of the index lesion were performed, the routine twelve cores of prostate tissue were taken, including three samples from the peripheral zone and three samples from the inner gland on each side. The biopsy specimens were numbered to match the focal lesions; the pathologic standard was biopsy core–based. The Gleason score for each core was recorded by a genitourinary pathologist who was blinded to the clinical results.

2.5. Outcome interpretation

The overall cancer detection rates by patients and by cores were

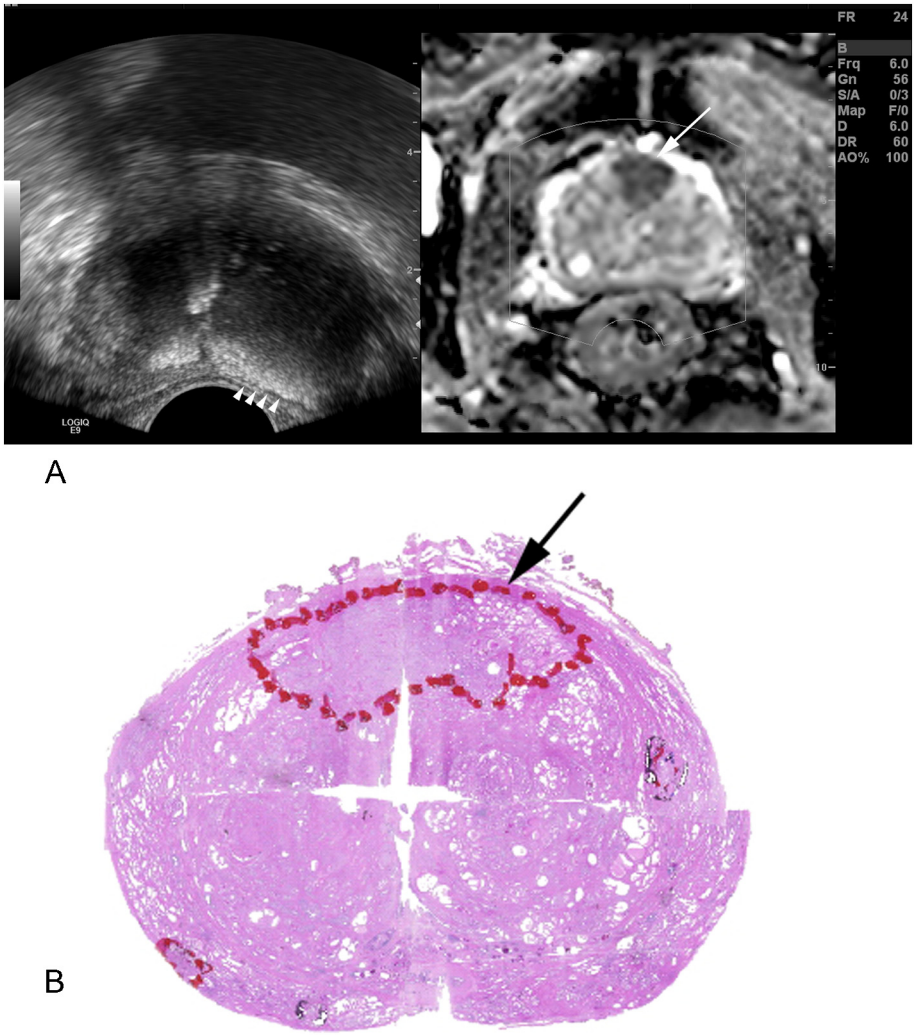

Fig. 1. A side-by side display of US/ADC map of MR (A) and histopathology (B) of the prostate in a 59 year old man with PSA level 4.997 ng/mL. Note decreased ADC area (arrow) at anterior aspect of transition zone. This area is not seen well on US due to dense posterior shadowing of transition zone (arrowheads). The area of prostate cancer on histopathology is well correlated (arrow). Gleason score was seven.

analyzed. The cancer detection rates of added biopsy (AB) were compared with those of systemic biopsy (SB). Clinically significant cancer was defined if any core of biopsy showed Gleason score over 4 + 3 or more than two cores of Gleason score 6 or 3 + 4 were sampled. The mean PIRADS score between the AB-positive and AB-negative patients were compared. We labeled patients with index lesions with PIRADS 3 or above as the MR-positive group, while patients with PIRADS 1 or 2 were the MR-negative group. The cancer detection rates between these two groups were then compared.

2.6. Statistical analysis

Comparisons of the mean PIRADS were performed by the Mann–Whitney *U* test; mean comparisons of frequencies were performed by using the Fisher exact test. All statistical analyses were performed using SPSS 20.0 statistical software (SPSS Inc., Chicago IL, USA).

3. Results

The median age of the patients was 66 years (range: 52–89 years); the mean PSA level was 5.7 ± 2.3 ng/mL (range: 0.607–9.521 ng/mL). The mean time interval between MR and biopsy was 61 ± 122.8 days (range: 0–485 days). Seven patients without any suspicious lesions on MR were scored 1. The remaining 32 patients had a total of 38 separate index lesions on MR: 26 patients (81.3%) had one, and 6 patients (18.7%) had two index lesions (mean 1.19 targets per patient).

The overall cancer detection rates by patient were 51.3% (20/39). Twelve out of 39 patients (30.8%) had cancer positive in both SB and AB. Cancer was detected by SB only in seven out of 39 patients (17.9%). In one out of 39 patients (2.6%), only AB was able to detect the cancer. Clinically significant cancer was detected in 15 out of 20 cancer patients (75.0%). All AB positive patients group ($n = 13$) had clinically significant cancer, while SB positive patients group ($n = 7$) included only two clinically significant cancer (28.6%). Four patients of clinically significant cancer would have been falsely classified as patients with clinically insignificant cancer if AB had not been performed. In 11 out of 13 (84.6%) of the patients, the cores of the highest Gleason score was found by AB. Cancer detection rates by patients to PIRADS score were summarized in Table 1.

The core-based cancer detection rate was 13.8% (77/558). SB detected cancer in 12.5% (56/448) of cores, while AB detected cancer in 23.3% (21/90) of cores. The cancer detection rate of AB increased to 27.6% (21/76) based on cores if the AB of the PIRADS score 1 ($n = 14$) was excluded. The mean PIRADS score between the AB-positive patients (3.92 ± 0.76) and the AB-negative patients (2.31 ± 1.08) were significantly different ($p < 0.000$).

The comparisons between the MR-positive and MR-negative groups

Table 1
Cancer detection rates by patients to PIRADS score.

PIRADS score	Cancer patient	SB positive	AB positive	CSC patient
1 (n = 7)	2 (28.6%)	2 (28.6%)	0 (0%)	0 (0%)
2 (n = 8)	1 (12.5%)	1 (12.5%)	0 (0%)	0 (0%)
3 (n = 12)	6 (50.0%)	6 (50.0%)	4 (33.3%)	5 (41.7%)
4 (n = 8)	7 (87.5%)	7 (87.5%)	6 (75.0%)	6 (75.0%)
5 (n = 4)	4 (100%)	3 (75.0%)	3 (75.0%)	4 (100%)

Abbreviations: PIRADS, prostate imaging reporting and data system; SB, systemic biopsy; AB, added biopsy; CSC, clinically significant cancer.

Table 2
Comparison of detection rate between MR positive and negative.

	MR positive	MR negative	p-Value[a]
By patients	17/24 (70.8%)	3/15 (20.0%)	0.002
By cores	73/342 (21.3%)	4/216 (1.8%)	< 0.001
By clinically significant cancer patients	15/15 (100%)	0/15 (0%)	< 0.001

[a] By Fisher's exact test.

are summarized in Table 2. The overall cancer detection rates between the two groups, by cores and by patients, were statistically significant. The MR-positive group revealed 15 out of 15 (100%) clinically significant cancer patients.

4. Discussion

Our results showed that added biopsies could detect 86.7% (thirteen out of fifteen) clinically significant cancer patients. All of the cancer patients detected by AB were patients with clinically significant cancer. Although SB detected more cancer patients (n = 19), eight of nineteen (42.1%) cancer patients were clinically insignificant cancer patients if AB was not done. This means that SB without MR–US fusion biopsy would miss 26.7% of clinically significant cancer (4 out of 15). If only AB were performed in our population, however, 13.3% of clinically significant cancer patients (2 out of 15) would also be missed. This finding means that SB cannot be omitted in these patients with low-risk cancer (a PSA of < 10 ng/mL) with the rebiopsy setting.

When the patients had MR-positive index lesions, we observed significant differences of cancer detection rates between AB and SB. Only 4 out of 216 cores in the MR-negative group showed cancerous tissue, which implies that 98.2% of the cores in this group were meaningless. Therefore, in this clinical setting of low-risk patients with prior negative biopsy history, MRI is strongly encouraged for triaging patients for the enrollment of repeated biopsy. Considering that cancer detection rates from the repeated biopsies are reported to be low [10], our results of cancer detection rates are much higher (51.3%) than this, even if the study population is patients with a low risk for cancer.

Recent prospective study compared with mpMRI and TRUS biopsy named PROMIS trial have published [14]. MpMRI was more sensitive (93%) than TRUS-biopsy (48%) for detection of clinically significant cancer. They have concluded that up to 18% more cases of clinically significant cancer might be detected using mp-MRI guided biopsy, which findings are in accordance with our results. Sonn et al. reported that targeted biopsy with MR–US fusion was three times more likely to identify cancer than a systematic biopsy (27% vs. 7%) [15]. Of the men with Gleason score 7 or greater cancer, 38% had disease detected only in targeted biopsies. Fusion biopsy can provide improved detection of prostate cancer in men with prior negative biopsies and elevated PSA values. Siddiqui et al. also reported that MR–US fusion-guided biopsy detected 67% more Gleason above-7 tumors than twelve-core biopsy alone, and missed 36% of Gleason under-7 tumors. Fusion biopsy also led to Gleason upgrading in 32% of patients compared with traditional twelve-core biopsy alone [16]. In our study, the upgrade of Gleason score by AB was 15.4%. We compared the results of several studies [17–20] of MR-TRUS fusion biopsy with our results (Table 3). While other studies showed similar or superior detection rate of targeted biopsy over systemic biopsy in cancer detection, our study shows lower (33%) detection rate of TB over SB. This may be mainly attributable to the fact that we included added biopsy without focal lesion on MR (PIRADS 1). Researchers increasingly use both in-bore MR guided biopsy (MRGB) and MR–US fusion biopsies. In-bore MRGB has the advantage of being able to target index lesions precisely in any location of the prostate, and it can reduce the number of biopsy cores that are necessary to perform, although the procedure time is usually longer than with fusion biopsy. MR–US fusion biopsy can be finished within 15 to 20 min (including SB and targeted biopsy) per session, while 45 min to 1 h is required per lesion with MRGB [21]. During MRGB, because patients are required to remain motionless, IV sedation is mandatory. In contrast, only local anesthesia is usually necessary during fusion biopsy, because real-time registration of the fusion technique can compensate for any minor motions by the patient. MRGB requires two separate sessions of MRI, for the detection of cancer and for the procedure, while only detection MRI is needed for fusion biopsy; this makes MRGB expensive compared to fusion biopsy, in addition to the necessity for prolonged procedure times [22].

Table 3
Comparison of MR-TRUS fusion biopsy study results.

Author (year)	Patient group	Detection rate (TB/SB)[a]	Increased CS cancer detection rate by TB
Borkowetz (2015)	First and repeated	44%/35%	44%
Meng (2016)	First and repeated[a]	40%/39%	35%
Salami (2015)	Repeated	52%/49%	56%
Sonn (2014)	Repeated	27%/24%	60%
Our study	Repeated	33%/49%	36%

Abbreviations: TB, targeted biopsy; CS, clinically significant.
[a] This study included both repeated with prior negative and positive cancer patients.

While MRGB can target the suspicious lesion in the prostate directly, fusion biopsy requires image registration between MR and US. The current commercially available machines use a rigid registration and an overlay of two images by rotating, scaling, or translating planes. Introducing the US transducer into the rectum, however, inevitably deforms the prostate gland. When a pelvic phased-array coil is used, the prostate will not be deformed. On the other hand, the prostate will be much compressed anteriorly with the use of an endorectal coil. As a result, elastic deformation of the prostate image, or "nonrigid" registration, appears to be ideal for more precise registration, and for reducing mismatch of these two imaging modalities [22]. Manual correction or point-by-point registration can reduce the errors after plane registration.

4.1. Limitations

The limitations of this study are as follows. First, although the case collection was prospective, this was a retrospective study based on image and histologic review, which means that selection bias may have been present. This study, however, is based on patients who were referred for biopsy consecutively over a certain period of time, to minimize the bias. Second, the study population was relatively small. This may be attributable to the strict inclusion criteria of our study, for repeated biopsy with low risk. Further studies with larger populations would be required to make our study results more generalizable. Third, pathologic confirmation was based on biopsy specimens. Sampling from a needle biopsy of the prostate may not be sufficient for deciding

whether or not a patient had clinically significant cancer. Although TRUS-guided random biopsy is still the gold standard for the detection of cancer, and the patient's management is based on the histological results from the biopsy, our results of increased detection rates of clinically significant cancer by AB will have a clinical impact for patient management. There should be a change from active surveillance to definitive treatment, such as surgery or radiotherapy in this population of repeated biopsy with low risk. Four, although overall cancer detection rates was higher in MR positive group, it is uncertain that either MR or fusion of US played a major role in the guidance of cancer tissue by our results.

5. Conclusion

Additional biopsy using MR–US fusion showed improved detection of clinically significant prostate cancer, especially among patients with suspected cancer in prebiopsy MR. MR can be a useful decision-supporting tool for repeated biopsy for patients under active surveillance.

Ethical standards and conflicts of interest

All human studies have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

The authors declare that they have no conflict of interest

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinimag.2018.09.012.

References

[1] Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012;62(1):10–29.

[2] Stangelberger A, Waldert M, Djavan B. Prostate cancer in elderly men. Rev Urol 2008;10(2):111–9.

[3] Dickinson L, Ahmed HU, Allen C, Barentsz JO, Carey B, Futterer JJ, et al. Magnetic resonance imaging for the detection, localisation, and characterisation of prostate cancer: recommendations from a European consensus meeting. Eur Urol 2011;59(4):477–94.

[4] Halpern EJ, Strup SE. Using gray-scale and color and power Doppler sonography to detect prostatic cancer. AJR Am J Roentgenol 2000;174(3):623–7.

[5] Loeb S, Bjurlin MA, Nicholson J, Tammela TL, Penson DF, Carter HB, et al. Overdiagnosis and overtreatment of prostate cancer. Eur Urol 2014;65(6):1046–55.

[6] Hambrock T, Hoeks C, Hulsbergen-van de Kaa C, Scheenen T, Fütterer J, Bouwense S, et al. Prospective assessment of prostate cancer aggressiveness using 3-T diffusion-weighted magnetic resonance imaging-guided biopsies versus a systematic 10-core transrectal ultrasound prostate biopsy cohort. Eur Urol 2012;61(1):177–84.

[7] Kasivisvanathan V, Dufour R, Moore CM, Ahmed HU, Abd-Alazeez M, Charman SC, et al. Transperineal magnetic resonance image targeted prostate biopsy versus transperineal template prostate biopsy in the detection of clinically significant prostate cancer. J Urol 2013;189(3):860–6.

[8] Puech P, Rouvière O, Renard-Penna R, Villers A, Devos P, Colombel M, et al. Prostate cancer diagnosis: multiparametric MR-targeted biopsy with cognitive and transrectal US-MR fusion guidance versus systematic biopsy–prospective multicenter study. Radiology 2013;268(2):461–9.

[9] Pinto PA, Chung PH, Rastinehad AR, Baccala AA, Kruecker J, Benjamin CJ, et al. Magnetic resonance imaging/ultrasound fusion guided prostate biopsy improves cancer detection following transrectal ultrasound biopsy and correlates with multiparametric magnetic resonance imaging. J Urol 2011;186(4):1281–5.

[10] Djavan B, Ravery V, Zlotta A, Dobronski P, Dobrovits M, Fakhari M, et al. Prospective evaluation of prostate cancer detected on biopsies 1, 2, 3 and 4: when should we stop? J Urol 2001;166(5):1679–83.

[11] Brimo F, Vollmer RT, Corcos J, Humphrey PA, Bismar TA. Outcome for repeated biopsy of the prostate: roles of serum PSA, small atypical glands, and prostatic intraepithelial neoplasia. Am J Clin Pathol 2007;128(4):648–51.

[12] Fulgham PF, Rukstalis DB, Turkbey IB, Rubenstein JN, Taneja S, Carroll PR, et al. AUA policy statement on the use of multiparametric magnetic resonance imaging in the diagnosis, staging and management of prostate cancer. J Urol 2017;198(4):832–8.

[13] Expert Panel on Urologic I, Coakley FV, Oto A, Alexander LF, Allen BC, Davis BJ, et al. ACR appropriateness criteria ((R)) prostate cancer-pretreatment detection, surveillance, and staging. J Am Coll Radiol 2017;14(5S):S245–57.

[14] Ahmed HU, El-Shater Bosaily A, Brown LC, Gabe R, Kaplan R, Parmar MK, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet 2017;389(10071):815–22.

[15] Sonn GA, Natarajan S, Margolis DJA, MacAiran M, Lieu P, Huang J, et al. Targeted biopsy in the detection of prostate cancer using an office based magnetic resonance ultrasound fusion device. J Urol 2013;189(1):86–91.

[16] Siddiqui MM, Rais-Bahrami S, Truong H, Stamatakis L, Vourganti S, Nix J, et al. Magnetic resonance imaging/ultrasound-fusion biopsy significantly upgrades prostate cancer versus systematic 12-core transrectal ultrasound biopsy. Eur Urol 2013;64(5):713–9.

[17] Borkowetz A, Platzek I, Toma M, Laniado M, Baretton G, Froehner M, et al. Comparison of systematic transrectal biopsy to transperineal magnetic resonance imaging/ultrasound-fusion biopsy for the diagnosis of prostate cancer. BJU Int 2015;116(6):873–9.

[18] Meng X, Rosenkrantz AB, Mendhiratta N, Fenstermaker M, Huang R, Wysock JS, et al. Relationship between prebiopsy multiparametric magnetic resonance imaging (MRI), biopsy indication, and MRI-ultrasound fusion-targeted prostate biopsy outcomes. Eur Urol 2016;69(3):512–7.

[19] Salami SS, Ben-Levi E, Yaskiv O, Ryniker L, Turkbey B, Kavoussi LR, et al. In patients with a previous negative prostate biopsy and a suspicious lesion on magnetic resonance imaging, is a 12-core biopsy still necessary in addition to a targeted biopsy? BJU Int 2015;115(4):562–70.

[20] Sonn GA, Chang E, Natarajan S, Margolis DJ, Macairan M, Lieu P, et al. Value of targeted prostate biopsy using magnetic resonance-ultrasound fusion in men with prior negative biopsy and elevated prostate-specific antigen. Eur Urol 2014;65(4):809–15.

[21] Brown AM, Elbuluk O, Mertan F, Sankineni S, Margolis DJ, Wood BJ, et al. Recent advances in image-guided targeted prostate biopsy. Abdom Imaging 2015;40(6):1788–99.

[22] Logan JK, Rais-Bahrami S, Turkbey B, Gomella A, Amalou H, Choyke PL, et al. Current status of magnetic resonance imaging (MRI) and ultrasonography fusion software platforms for guidance of prostate biopsies. BJU Int 2014;114(5):641–52.