

Detection of Clinically Significant Index Prostate Cancer Using Micro-ultrasound: Correlation With Radical Prostatectomy

Matias F. Callejas, Eric A. Klein, Matthew Truong, Lewis Thomas, Jesse K. McKenney, and Sangeet Ghai

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| OBJECTIVE | To determine the detection of clinically significant prostate cancer (csPCa) index lesion using high resolution transrectal micro-ultrasound (MicroUS) applying PRI-MUS (Prostate Risk Identification using Micro Ultrasound) score v1.0. |
| METHODS | Men who underwent radical prostatectomy following biopsy and MicroUS assessment were included. MicroUS dynamic cine loops of these patients were retrospectively reviewed by an experienced radiologist. The radiologist was aware that patients had undergone radical prostatectomy but was blinded to pathological data. Suspicious sites were assigned a PRI-MUS score. Radical prostatectomy specimens were examined with the quarter mount technique. Detection rate of csPCa index lesion [Grade Group (GG) ≥ 2] by MicroUS was assessed at a patient level. |
| RESULTS | Twenty-five participants were included in the analysis. The median age was 65.5 years (range 56-74). Median PSA was 6.45 ng/dL (range 2-31.72). Two of 25 patients did not have csPCa (GG1 disease) on radical prostatectomy. MicroUS visualized 20/23 (87%) of the csPCa index lesions [median length 9 mm (range 1.5- 28.5)]. All identified lesions were categorized PRIMUS score 4 or 5. The 3 missed index lesions were in the transition zone [median length 10.5 mm (range 4.5-22.5)]. MicroUS missed 11 non index csPCa in 9 participants [median length 1.5 mm (range 1.5-10.5)]. Of these, 8 were GG2, 2 GG3 and 1 GG5. MicroUS identified the csPCa index lesion in all 9 of these men. |
| CONCLUSION | MicroUS showed the high sensitivity (87%) in detecting index lesions in the prostate gland and identified 100% of index lesions in the peripheral zone. UROLOGY 00: 1–6, 2022. © 2022 Elsevier Inc. |

Since its introduction in the 1970s, conventional transrectal ultrasound (TRUS)-guided prostate biopsy has become the standard of care in the diagnosis of prostate cancer.¹ It may be indicated in the setting of suspicious PSA and/or abnormal digital rectal examination. Unfortunately, on conventional (6-9MHz) TRUS, cancerous foci and non-cancerous prostate tissue can have similar appearance thereby limiting the ability of TRUS to be used as a single modality in cancer diagnosis. In fact, if TRUS biopsy was to be performed based only on

suspicious findings, nearly 40% of the tumors could be missed.² This has resulted in ultrasound being used primarily for guidance of systematic biopsy samples that includes non-suspicious areas. There is however the evidence that obtaining targeted samples from TRUS lesions combined with systematic sextant sampling increases prostate cancer (PCa) yield.³

The introduction of multiparametric prostate MRI (mpMRI) into the diagnostic algorithm has improved management of patients with suspected PCa. MpMRI has shown a good performance in detecting clinically significant prostate cancers (csPCa).⁴ Tools that allow co-registering mpMRI data with B-mode TRUS images to guide biopsies are rapidly emerging in clinical settings. There is also an increasing evidence showing non inferiority of mpMRI targeted biopsy compared to systematic sampling in detecting csPCa.^{5,6} Nevertheless, the application of mpMRI to diagnosis or treatment planning still has limitations including limited access to MRI, the high cost and the need of an experienced reader and the fusion biopsy

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From the Toronto Joint Department of Medical Imaging, University Health Network – Mt Sinai Hospital – Women's College Hospital, University of Toronto, Toronto, Ontario, Canada; the Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, OH; and the Robert J. Tomsich Pathology and of Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH

Address correspondence to: Sangeet Ghai, M.D., Department of Medical Imaging, Toronto General Hospital, 585 University Avenue, 1PMB-292, Toronto, Ontario, Canada. E-mail: Sangeet.Ghai@uhn.ca

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expertise.⁷ Also, a small proportion of patients may not be able to undergo MRI for several reasons such as claustrophobia, pelvic hardware or non-compatible pacemakers. This has led to significant efforts being made to develop and test novel ultrasound-based imaging technologies that maintain the current cost-effectiveness of conventional TRUS-guided biopsies but with increased detection of csPCa.

It is well known that prostate cancer is multifocal in many patients. However, there is also an increasing evidence that the prognosis of prostate cancer is mainly driven by the largest lesion (index lesion), which in turn is also the highest grade in over 95%.^{8,9} Consequently, the ability to detect and target the index lesion is of clinical relevance, particularly with the current focus on reducing the number of biopsy cores.¹⁰

Micro-ultrasound (MicroUS) is a promising new ultrasound technology. It operates at 29 MHz (21 MHz center frequency) compared to the 8-12 MHz (6-9 MHz center frequency) for conventional TRUS. Also, its fabrication techniques allow 4-fold higher crystal density along the transducer (512 vs 128 crystals). This provides superior spatial resolution down to 70 microns, which is the diameter of a typical prostatic duct, as opposed to 200 microns or more for conventional TRUS (300% higher resolution compared to conventional frequency TRUS) (Supplementary Figure 1). These improvements enable improved visualization and targeting of suspicious regions as well as the systematic MicroUS guided prostate biopsy.¹¹ The second-generation system was released in 2017 with upgrades in electronics. Recently, there have been few publications investigating the ability of MicroUS in detecting csPCa, the majority of them using needle biopsy as pathologic proof.¹²⁻¹⁴ Although there are a couple of studies using radical prostatectomy as gold standard, their primary objective was to assess the ability of MicroUS in detecting extraprostatic extension.^{15,16} To our knowledge, only one other study has used radical prostatectomy specimens as gold standard¹⁷ to assess the ability of MicroUS in detecting csPCa.

As MicroUS is a new technique, the PRI-MUS score (prostate risk identification using micro-ultrasound)¹¹ risk identification system was developed to help in the interpretation of the images when trying to differentiate between the benign findings and the suspicious lesions. We hypothesized that development of the PRI-MUS risk score and the use of a second generation MicroUS would further improve the identification of csPCa by MicroUS.

The objective of our study was to determine the detection rate of csPCa index lesion using a second-generation MicroUS system and applying PRI-MUS score v1.0.

METHODS

Study design: This study was approved by University Health Network REB (CAPCR-ID 20-6049) and by the IRB at the Cleveland Clinic (IRB EXIM 1819). Written informed consent was obtained from all participants. Twenty-five men who

underwent radical prostatectomy at Cleveland Clinic following MicroUS evaluation and biopsy were included in the study. None of the men were biopsied using MicroUS in this study. Biopsies had been performed using conventional TRUS prior to the MicroUS assessment. MicroUS evaluation was performed prior to radical prostatectomy for the study purpose. The minimum time interval between systematic biopsy and MicroUS evaluation was 6 weeks (range 6-14 weeks). Retrospective analysis of dynamic cine loops obtained with MicroUS for each of these patients was performed.

MicroUS evaluation: MicroUS examinations were performed by 3 urology fellows at a single institution. All patients had examinations performed using a standardized technique in the lithotomy position using ExactVu (Exact Imaging, Markham, Canada) 29 MHz micro-ultrasound system after induction of general anesthesia and prior to the start of the radical prostatectomy. Dynamic cine loops including the entire prostate in 3 depth settings were recorded and available for all patients.

Image analysis: Analysis of all cine loops was performed by a radiologist (SG) experienced in MicroUS who had participated in the development of the PRI-MUS protocol and the initial randomized trial comparing MicroUS to conventional TRUS in detection of csPCa.¹⁸ The radiologist was aware that these men underwent radical prostatectomy but was blinded to any other preoperative imaging, laboratory tests, patient demographics, and pathological data, including cancer location, grade, and stage. Suspicious sites were assigned a prostate cancer risk score using the previously published PRI-MUS v1.0.

Pathologic analysis: All patients had radical prostatectomy and were step-sectioned using quarter mount technique as previously described¹⁹ Location, size and Gleason score/Grade Group (GG) was available for all index lesions in all patients which allowed subsequent correlation with MicroUS findings using Matlab. Grading of prostatic carcinoma was done using the International Society of Urological Pathology (ISUP) Consensus.^{20,21} Lesions with GG ≥ 2 were considered clinically significant. The index lesion was defined as the largest lesion in each patient.

Matlab Analysis: Digital pathology slices were annotated using closed splines for each lesion. Capsule, urethra, ejaculatory ducts, and other anatomical locations were marked manually in preparation for registration to the ultrasound. Slices were then loaded into a 3D model and registered to a 3D model of the ultrasound with the same anatomical locations marked. A rigid-then-elastic model was used to ensure a good fit. The accuracy of this technique has been tested on a similar dataset with an average error of 4 mm. A lesion was considered true positive if at least 20% volume overlap on the 3D model was identified.

Statistical analysis: Sensitivity analysis for the identification of pathologically confirmed index lesion by MicroUS was performed at a patient level. T test was used to compare between the size of the lesions missed and detected by MicroUS.

RESULTS

Patient demographics are listed in Table 1. The median age of participants was 65.5 years (range 56-74) while the median PSA was 6.45 ng/dL (range 2-31.72). Clinical stage was T1c in 24 of 25 patients (non-palpable disease). Needle biopsy results of the highest-grade lesion prior to radical prostatectomy were as follows: Gleason 6 in 5 participants; Gleason 7 in 14 participants; Gleason 8 in 4 participants and Gleason 9 in 4 participants. In 2

Table 1. Demographic, clinical and pathologic data of 25 men with prostate cancer who underwent MicroUS and radical prostatectomy.

| Variable | |
|--------------------------------------|--------------------------------|
| <i>Clinical and demographic data</i> | |
| Age, years | Median (range) 65.5 (56-74) |
| PSA, ng/dL | 7.6 (2-31.72) |
| Prostate volume, cc | 43 (17.5-80) |
| <i>Pathologic data</i> | |
| Pathologic Grade Group score | Participants, n (%) |
| -1 | 2 (8%) |
| -2 | 7 (28%) |
| -3 | 7 (28%) |
| -4 | 5 (20%) |
| -5 | 4 (16%) |
| <i>Pathologic Stage</i> | |
| -T2 | 16 (64%) |
| -T3 | 9 (36%) |

of 25 patients (8%), the radical prostatectomy specimen did not reveal csPCa (both with GG1). In only one of these 2 patients, the lesion was identified by MicroUS and scored a PRI-MUS 3. The lesion was in the peripheral zone (PZ) and measured 4.5 mm on the quarter mount analysis. In the second patient with GG1, the lesion was present in the transition zone (TZ) on radical prostatectomy but was not prospectively identified on the cine loop analysis

Multiple cine loops were obtained for each patient and the overall quality of acquisition was deemed to be adequate by the reader. MicroUS visualized 20/23 (87%) of the clinically significant index lesions. All these lesions were categorized PRI-MUS score 4 (n = 13) (Fig. 1) or 5 (n = 7) (Fig. 2). The mean size of

the index lesions was 11.25 mm [median of 9 mm (range: 1.5-28.5 mm)]. Only one of these lesions was in the TZ.

The 3 missed index lesions were localized in the anterior TZ of the prostate gland. Two were GG2 and 1 was GG3. Their average size was 12.5 mm [median 10.5 mm (range 4.5-22.5 mm)].

Additionally, MicroUS correctly detected 2 non index csPCa: One in the PZ measuring 4.5 mm ISUP2 and other in the TZ measuring 1.5 mm ISUP 2. The average size of all 22 csPCa lesions (20 csPCa index lesions and 2 non index csPCa) identified by MicroUS was 10.5 mm (median 7.5 mm).

MicroUS missed 11 non index csPCa in 9 patients, all in PZ (Table 2). The mean size of these lesions was 2.8 mm [median 1.5 mm (range 1.5 mm-10.5 mm)] compared to 10.5 mm for the 22 csPCa lesions identified on MicroUS ($P \leq .02$). Of these 11 missed csPCa lesions, 8 were GG2, 2 GG3 and 1 lesion was GG5. In all 9 men, MicroUS identified the csPCa index lesion including the participant with 1.5 mm GG5 disease wherein a separate 4.5 mm GG5 index lesion was detected by MicroUS.

MicroUS detected 1 non csPCa (GG1) of more than 5 mm (19.5 mm in the transition zone). It missed 6 non csPCa (GG1). The mean size of these lesions was 8.5 mm [median 7.5 mm (range 7.5 mm-10.5 mm)], 3 of them were in the peripheral zone and the remaining 3 in transition zone. There was 1 patient in our cohort where the largest lesion (7.5 mm, GG2) was not the highest-grade lesion (1.5 mm GG3). In this patient, MicroUS only detected the largest lesion. In 3 other men, there were 2 sites with the same Grade Group disease (GG5 disease in 1 and GG2 disease in the other participant) but MicroUS detected only the larger of the 2 in both men (4.5 mm vs 1.5 mm [GG 5 disease] and 16.5 mm vs 10.5 mm [GG2 disease]). In another patient 2 similar sized (4.5 mm) different grade lesions (GG5 and GG3) were identified in the radical prostatectomy specimen,

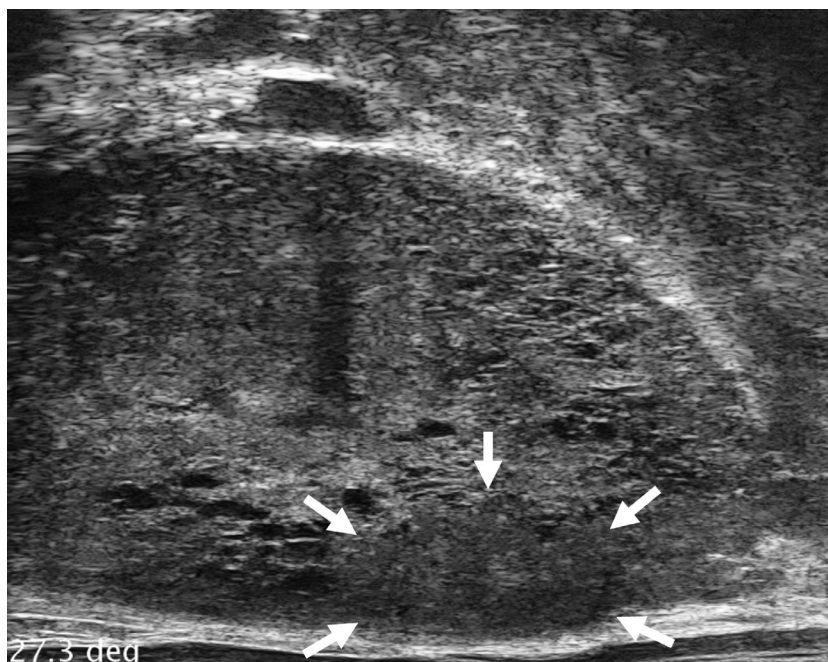


Figure 1. MicroUS image showing a PRI-MUS 4 lesions. High resolution transrectal micro-ultrasound image showing a 1.4 cm peripheral zone lesion centered in the mid-apex of the prostate (arrows). Note the loss of the normal ductal pattern of the gland. This was scored PRI-MUS 4 (“smudgy” appearance. Significant risk of prostate cancer). Pathology showed Grade Group 3 lesion.



Figure 2. MicroUS image showing a PRI-MUS 5 lesions. High resolution transrectal micro-ultrasound image showing a 2.5×1.3 cm peripheral zone lesion centered in the apex (arrows). This was scored PRI-MUS 5. Pathology showed Grade Group 4 lesion. Note the extracapsular extension (arrowheads).

but MicroUS detected only the site of higher-grade disease (GG5).

COMMENT

Our study identified a high (87%) detection of csPCa index lesion using MicroUS, reaching 100% sensitivity in the PZ. These findings highlight the potential of MicroUS in the management of patients with suspected prostate cancer, particularly when considering the additional benefit of MicroUS in allowing the real time guidance for targeted biopsy, as compared to MRI based techniques. Our findings show that all clinically significant index PCa in the PZ were detected by MicroUS.

It should be noted that MicroUS missed 11 non index csPCa. However, these patients had on average smaller

lesions when compared to the ones detected by MicroUS ($P \leq .02$). The one potential implication of missing non index csPCa could be in men being considered for focal therapy, especially if being considered for a targeted focal therapy approach wherein only the imaging visible lesion is treated.

Studies using the radical prostatectomy as the reference test have reported 77.6%-92% sensitivity of MRI for index lesion detection²²⁻²⁴ which is similar to detection of clinically significant index lesions by MicroUS in this study (87%). Additionally, in a large retrospective study comprising of 588 patients with intermediate or the high risk PCa, Johnson et al²⁵ reported that on whole-mount correlation, mpMRI detected 65% of csPCa and that majority (61.1%) of missed csPCa were small and ≤ 1 cm. This is again similar to sensitivity of MicroUS in detection of csPCa in this study (61%). The mean size of missed csPCa in our study was 2.8 mm, while larger and higher-grade tumors where more likely to be detected.

One of the limitations of MicroUS is the tradeoff between resolution and depth, which in turn reduces its ability in detecting anterior zone lesions, particularly in big glands. The advantage of MicroUS over conventional TRUS is lost at a greater depth or height from the rectum. This may have been further exacerbated by the fact that the present version of PRI-MUS only incorporates characterization of PZ lesions. Future iterations of the PRI-MUS protocol are being developed to include characterization of TZ nodules.

Literature on the usefulness of MicroUS are scarce given its recent development. Most studies assessing sensitivity of MicroUS in detection of csPCa have utilized needle biopsy as the reference test.^{26,27} This may lead to

Table 2. Performance of MicroUS in identifying index and non-index clinically significant prostate cancer.

| Variable | Pathologic Lesions | MicroUS Detection |
|---|--------------------|-------------------|
| Total clinically significant lesions | 36 | 22 (61%) |
| Clinically significant index lesion | 23 | 20 (87%) |
| -Peripheral zone | 19 | 19 (100%) |
| -Transition zone | 4 | 1 (25%) |
| Clinically significant non-index lesion | 13 | 2 (15%) |
| -Peripheral zone | 12 | 1 (8%) |
| -Transition zone | 1 | 1 (100%) |

Lesions characterized upon pathologic analysis of radical prostatectomy specimens.

under detection of csPCa with potential of false sense of high sensitivity. A previous pilot study, utilizing radical prostatectomy specimens as the reference test,¹⁷ using the first generation MicroUS and performed prior to the devolvement of the PRI-MUS scoring system revealed csPCa detection rate of 84% (21/25) with 80% (20/25) detection of “index/dominant” lesions, though the authors did not clarify whether all dominant lesions were csPCa. The study also did not differentiate between PZ and TZ “index” PCa. The authors however reported that that MicroUS missed 7 of 8 anterior tumors but apparently, this included all tumors and not just csPCa. In our study, MicroUS missed 3 of 4 anterior index lesions. It is important to note that we did not use prostate size as an exclusion criterion which may have influenced the non-detection of anterior TZ lesions.

Our results highlight the ability of MicroUS in detecting csPCa index lesion, especially in the PZ. Its introduction in the management of patients with suspected PCA could help in improving patient care, particularly in places where there is restricted access to MRI or in men who are unable to undergo MRI for various reasons (claustrophobia, hip prosthesis, pacemaker, etc.). In addition, MicroUS provides the advantage of real time targeting of the visualized lesions.

This study was designed to assess the potential utility of MicroUS in detecting csPCa index lesions. Strengths of the study include expert MicroUS and pathology reviews, standardized image acquisitions, and blinded review of cine loops. Limitations include the sample size; that dynamic cine loops were reviewed after the acquisitions of the images and not in real time, which may have adversely affected interpretation of ultrasound images; and even though the reader was blinded to pathology results, given the retrospective nature of our study, they were aware that patients had undergone radical prostatectomies. This might have led to a bias toward calling csPCa index lesion in every patient. Nevertheless, the reader identified the exact site of disease correctly which validates true visualization of disease on MicroUS.

CONCLUSIONS

MicroUS showed a high sensitivity, particularly in detecting index lesions in the PZ using PRI-MUS v1.0. PRI-MUS v2.0 iterations are required for improvements in the detection of TZ lesions.

DECLARATIONS OF INTEREST

None.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.urology.2022.07.002>.

References

- Rendon RA, Mason RJ, Marzouk K, et al. Canadian Urological Association recommendations on prostate cancer screening and early diagnosis. *Can Urol Assoc J*. 2017;11:298–309.
- Catalona WJ, Richie JP, Ahmann FR, et al. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a Multicenter Clinical Trial of 6,630 Men. *J Urol*. 1994;151:1283–1290.
- Heijmink SWTPJ, van Moerkerk H, Kiemeny LALM, et al. A comparison of the diagnostic performance of systematic versus ultrasound-guided biopsies of prostate cancer. *Eur Radiol*. 2006;16:927–938.
- Fütterer JJ, Briganti A, De Visschere P, et al. Can clinically significant prostate cancer be detected with multiparametric magnetic resonance imaging? A Systematic Review of the Literature. *Eur. Urol*. 2015;68:1045–1053.
- Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. *N Engl J Med*. 2018;378:1767–1777.
- Klotz L, Chin J, Black PC, et al. Comparison of multiparametric magnetic resonance imaging–targeted biopsy with systematic transrectal ultrasonography biopsy for biopsy-naive men at risk for prostate cancer. *JAMA Oncol*. 2021;7:534.
- Manley BJ, Brockman JA, Raup VT, et al. Prostate MRI: a national survey of Urologist’s attitudes and perceptions. *Int Braz J Urol*. 2016;42:464–471.
- Ahmed HU. The index lesion and the origin of prostate cancer. *N Engl J Med*. 2009;361:1704–1706.
- Karavitakis M, Winkler M, Abel P, et al. Histological characteristics of the index lesion in whole-mount radical prostatectomy specimens: implications for focal therapy. *Prostate Cancer Prostatic Dis*. 2011;14:46–52.
- Mottet N, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer—2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. *Eur Urol*. 2021;79:243–262.
- Ghai S, Eure G, Fradet V, et al. Assessing cancer risk on novel 29 MHz micro-ultrasound images of the prostate: creation of the micro-ultrasound protocol for prostate risk identification. *J Urol*. 2016;196:562–569.
- Klotz L, Lughezzani G, Maffei D, et al. Comparison of micro-ultrasound and multiparametric magnetic resonance imaging for prostate cancer: a multicenter, prospective analysis. *Can Urol Assoc J*. 2020;15.
- Wiemer L, Hollenbach M, Heckmann R, et al. Evolution of targeted prostate biopsy by adding micro-ultrasound to the magnetic resonance imaging pathway. *Eur Urol Focus*. 2021;7:1292–1299.
- Lughezzani G, Maffei D, Saita A, et al. Diagnostic accuracy of micro-ultrasound in patients with a suspicion of prostate cancer at magnetic resonance imaging: a single-institutional prospective study. *Eur Urol Focus*. 2021;7:1019–1026.
- Fasulo V, Buffi NM, Regis F, et al. Use of high-resolution micro-ultrasound to predict extraprostatic extension of prostate cancer prior to surgery: a prospective single-institutional study. *World J Urol*. 2022;40(2):435–442.
- Regis F, Casale P, Persico F, et al. Use of 29-MHz micro-ultrasound for local staging of prostate cancer in patients scheduled for radical prostatectomy: a Feasibility Study. *Eur Urol Open Sci*. 2020;19:20–23.
- Pavlovich CP, Cornish TC, Mullins JK, et al. High-resolution transrectal ultrasound: Pilot study of a novel technique for imaging clinically localized prostate cancer. *Urol Oncol Semin Orig Invest*. 2014;32:34.e27–34.e32.
- Pavlovich CP, Hyndman ME, Eure G, et al. A multi-institutional randomized controlled trial comparing first-generation transrectal high-resolution micro-ultrasound with conventional frequency transrectal ultrasound for prostate biopsy. *BJUI Compass*. 2021;2:126–133.

19. Falzarano SM, Nyame YA, McKenney JK, et al. Clinicopathologic features and outcomes of anterior-dominant prostate cancer: implications for diagnosis and treatment. *Prostate Cancer Prostatic Dis.* 2020;23:435–440.
20. Van Leenders GJLH, van der Kwast, TH, Grignon DJ, et al. The 2019 International Society of Urological Pathology (ISUP) Consensus Conference on Grading of Prostatic Carcinoma. *Am J Surg Pathol.* 2020;44:E87–E99.
21. Epstein JI, Egevad L, Amin MB, et al. The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. *Am J Surg Pathol.* 2016;40:244–252.
22. Radtke JP, Schwab C, Wolf MB, et al. Multiparametric Magnetic Resonance Imaging (MRI) and MRI–transrectal ultrasound fusion biopsy for index tumor detection: correlation with radical prostatectomy specimen. *Eur Urol.* 2016;70:846–853.
23. Mirak SA, Shakeri S, Bajgiran AM, et al. Three Tesla Multiparametric Magnetic Resonance Imaging: Comparison of Performance with and without Endorectal Coil for Prostate Cancer Detection, PI-RADS™ version 2 Category and Staging with Whole Mount Histopathology Correlation. *J Urol.* 2019;201:496–502.
24. Le JD, Tan N, Shkolyar E, et al. Multifocality and prostate cancer detection by multiparametric magnetic resonance imaging: correlation with whole-mount histopathology. *Eur Urol.* 2015; 67:569–576.
25. Johnson DC, Raman SS, Mirak SA, et al. Detection of individual prostate cancer foci via multiparametric magnetic resonance imaging. *Eur Urol.* 2019;75:712–720.
26. Lughezzani G, Saita A, Lazzeri M, et al. Comparison of the diagnostic accuracy of micro-ultrasound and magnetic resonance imaging/ultrasound fusion targeted biopsies for the diagnosis of clinically significant prostate cancer. *Eur Urol Oncol.* 2019;2:329–332.
27. Wiemer L, Hollenbach M, Heckmann R, et al. Evolution of targeted prostate biopsy by adding microultrasound to the magnetic resonance imaging pathway. *Eur Urol Focus.* 2021;7:1292–1299.