

# Commentary regarding a recent collaborative consensus statement addressing prostate MRI and MRI-targeted biopsy in patients with a prior negative prostate biopsy

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Technology and experience in prostate cancer imaging have increased, along with its importance. Additionally, standards for the conduct and reporting of prostate MRI and MRI-targeted biopsy have been developed and refined [1, 2]. Moreover, the emergence of systems for MRI-targeted prostate biopsy has catalyzed greater incorporation of prostate imaging into routine patient care. Although standards from various organizations exist to guide physicians on the use of repeat prostate biopsy after an initial negative prostate biopsy, well-developed guidelines regarding the role of imaging in repeat biopsies are lacking [3]. In the recent joint statement of the American Urological Association (AUA) and the Society of Abdominal Radiology (SAR), *Prostate MRI and MRI-Targeted Biopsy in Patients with Prior Negative Biopsy*, a 12-member expert panel of radiologists and urologists appraised the peer-reviewed literature on the application of prostate MRI and MRI-targeted biopsy in

patients with at least one negative prior biopsy in order to provide guidance on the use of MRI-targeted prostate biopsy in this setting. The full document is publicly available online and provides a series of individual consensus statements to assist clinical decisions for MRI-targeted prostate biopsy [4]. Issues addressed by the consensus statements include the impact of MRI-targeted biopsy on detection of clinically significant cancer, the approach for performing MRI-targeted biopsy, as well as the significance of a negative prostate MRI. This commentary summarizes the recommendations from the consensus statement.

## Existing guidelines

Prior to the consensus document, existing AUA guidelines offered guidance for biopsy-naïve patients, but not for repeat biopsies [4]. However, statements from other organizations have addressed repeat prostate biopsy. The National Comprehensive Cancer Network advises that

several criteria be met before a repeat biopsy is performed [5]. When a repeat biopsy is warranted, the NCCN guidelines suggest that MRI-targeted biopsy be considered. Guidelines from the European Association of Urology also provide several indications for repeat biopsy and acknowledge a role for MRI-targeted biopsy in this setting [6]. In addition, the American College of Radiology Appropriateness Criteria on the topic indicates that prostate MRI may be appropriate for men with a prior negative prostate biopsy [7].

## Recommendations for performance, interpretation, and reporting of prostate MRI

There has been an emerging consensus among radiologists in recent years regarding the optimal conduct and reporting of prostate MRI. This is reflected in the Prostate Imaging and Reporting Data System (PI-RADS) Version 2 (V2), which represents an ongoing effort by the international prostate imaging community to translate growing clinical experience into standards of performance [3]. PI-RADS V2 seeks to decrease the inter-operator variability of prostate imaging by prescribing how prostate images are obtained, interpreted, and reported. PI-RADS V2 provides a system for stratifying MRI detected lesions on a suspicion scale of 1–5. In order for prostate imaging to expand to community settings, a much larger number of radiologists will need to become skilled in the performance and interpretation of prostate MRI; PI-RADS V2 is anticipated to assist in this process. The recommendations for prostate MRI in the repeat biopsy setting, as reached by the present consensus panel [4], rely upon a high-quality MRI that is interpreted by a radiologist with sufficient experience and skill to render a quality interpretation. When high-quality prostate imaging and interpretation are available, including adequate training, adherence to practice standards, and rigorous local quality assurance, MRI should be strongly considered before performing a repeat prostate biopsy.

### *Detection of clinically significant cancer at repeat biopsy using MRI targeting*

Twelve studies from 2001 to 2015 regarding the impact of MRI targeting on the detection of clinically significant cancer on repeat biopsy met the inclusion criteria of the panel's review [5–16]. The detection rate of MRI-targeted biopsy for clinically significant cancer ranged from 11 to 54%. The percentage was higher among studies that defined clinically significant cancer as having a Gleason score greater than or equal to 7. The detection rate of MRI-targeted biopsy exceeded that of standard biopsy in many of the included studies, supporting the role of

MRI-targeted biopsy to improve detection of clinically significant cancer.

### *Patient selection for MRI after a negative biopsy*

Published data support a role for prostate MRI after a prior negative biopsy in patients with a sustained rising PSA compared with earlier values [17–19]. The literature also supports benefit from prostate MRI in the repeat biopsy setting regardless of the number of prior negative standard biopsies [8, 13, 15, 16, 19–24].

### *The need for concurrent systematic sampling when performing MRI targeting*

The evidence indicates that clinically significant cancers are occasionally missed by MRI-targeted biopsy (0–23%), even when the biopsies are performed at expert centers [7, 8, 10, 16, 25, 26]. Thus, the panel advises that a decision to defer concurrent systematic sampling at the time of MRI-targeted biopsy should be carefully evaluated on a case-by-case basis. Moreover, consideration of such deferral should only occur after centers have demonstrated satisfactory local outcomes from MRI-targeted biopsy.

### *Conduct of MRI-targeted biopsy*

Based on the reviewed literature, the panel recommends that patients with PI-RADS V2 category 4–5 lesions routinely warrant a targeted biopsy. In addition, given variable results in the available literature regarding outcomes from targeted biopsy of PI-RADS category 3 lesions, the panel does not support routinely deferring biopsy of such lesions at this time, acknowledging that additional data are needed. While cognitive targeting (i.e., targeting without the use of dedicated technologies to facilitate reliable sampling of the MRI-defined lesion) is a credible approach in experienced hands, TRUS-MRI fusion and in-bore MRI targeting systems can improve targeting accuracy, particularly for MRI lesions that are small or in challenging locations. Each MRI lesion should be sampled by at least two targeted cores. For patients, with PI-RADS V2 category 5 lesions, with an initial negative targeted biopsy, a repeat targeted biopsy may be warranted given the high likelihood of CS disease in such lesions [16.]

### *Deferral of repeat biopsy based on a negative MRI*

Continued clinical surveillance is necessary if deferring a repeat biopsy on the basis of a negative (PI-RADS category (1) or low-suspicion (PI-RADS category (2) prostate MRI [7, 8, 10, 16, 17, 27]. PSA measurements, DRE

evaluations, and possibly repeat MRI examinations should be used for further monitoring of such patients.

### *The role of ancillary markers in MRI-targeted biopsies*

Ancillary markers may help select patients to undergo a repeat biopsy. Such markers include PSA density, PSA velocity, PCA3, prostate health index (PHI), and 4 K score. In numerous multivariate analyses, MRI findings are a significant predictor of biopsy outcomes, independent of these markers. Thus, while targeted biopsy remains warranted in patients with intermediate or high suspicion MRI lesions, the ancillary markers may be most helpful in selecting patients with PI-RADS categories of 1 or 2 for a repeat biopsy.

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### References

- Barentsz JO, Weinreb JC, Verma S, et al. (2016) Synopsis of the PI-RADS v2 guidelines for multiparametric prostate magnetic resonance imaging and recommendations for use. *Eur Urol* 69(1):41–49. doi:10.1016/j.eururo.2015.08.038
- Barentsz JO, Richenberg J, Clements R, et al. (2012) ESUR prostate MR guidelines 2012. *Eur Radiol* 22(4):746–757. doi:10.1007/s00330-011-2377-y
- Vargas HA, Hotker AM, Goldman DA, et al. (2015) Updated prostate imaging reporting and data system (PI-RADS v2) recommendations for the detection of clinically significant prostate cancer using multiparametric MRI: critical evaluation using whole-mount pathology as standard of reference. *Eur Radiol* . doi:10.1007/s00330-015-4015-6
- Joint Consensus Panel of the American Urological Association and Society of Abdominal Radiology. Prostate MRI and MRI-Targeted Biopsy in Patients with Prior Negative Biopsy-Collaborative Initiative of the American Urological Association and the Society of Abdominal Radiology's Prostate Cancer Disease-Focused Panel. Electronically published April 2016. Available at: <https://www.auanet.org/common/pdf/education/clinical-guidance/Consensus-Statement-Prostate-MRI-and-MRI-Targeted-Biopsy.pdf>. Published in April 2016. Accessed 8 Aug 2016
- Mendhiratta N, Meng X, Rosenkrantz AB, et al. (2015) Pre-biopsy MRI and MRI-ultrasound fusion-targeted prostate biopsy in men with previous negative biopsies: impact on repeat biopsy strategies. *Urology* . doi:10.1016/j.urology.2015.07.038
- Arsov C, Rabenalt R, Blondin D, et al. (2015) Prospective randomized trial comparing magnetic resonance imaging (MRI)-guided in-bore biopsy to MRI-ultrasound fusion and transrectal ultrasound-guided prostate biopsy in patients with prior negative biopsies. *Eur Urol* 68(4):713–720. doi:10.1016/j.eururo.2015.06.008
- Abdi H, Pourmalek F, Zargar H, et al. (2015) Multiparametric magnetic resonance imaging enhances detection of significant tumor in patients on active surveillance for prostate cancer. *Urology* 85(2):423–428. doi:10.1016/j.urology.2014.09.060
- Salami SS, Ben-Levi E, Yaskiv O, et al. (2015) 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* 115(4):562–570. doi:10.1111/bju.12938
- Hambrock T, Somford DM, Hoeks C, et al. (2010) Magnetic resonance imaging guided prostate biopsy in men with repeat negative biopsies and increased prostate specific antigen. *J Urol* 183(2):520–527. doi:10.1016/j.juro.2009.10.022
- Sonn GA, Chang E, Natarajan S, et al. (2014) Value of targeted prostate biopsy using magnetic resonance-ultrasound fusion in men with prior negative biopsy and elevated prostate-specific antigen. *Eur Urol* 65(4):809–815. doi:10.1016/j.eururo.2013.03.025
- Kaufmann S, Kruck S, Kramer U, et al. (2015) Direct comparison of targeted MRI-guided biopsy with systematic transrectal ultrasound-guided biopsy in patients with previous negative prostate biopsies. *Urol Int* 94(3):319–325. doi:10.1159/000365397
- Kaufmann S, Bedke J, Gatidis S, et al. (2015) Prostate cancer gene 3 (PCA3) is of additional predictive value in patients with PI-RADS grade III (intermediate) lesions in the MR-guided re-biopsy setting for prostate cancer. *World J Urol* . doi:10.1007/s00345-015-1655-8
- Durmus T, Reichelt U, Huppertz A, et al. (2013) MRI-guided biopsy of the prostate: correlation between the cancer detection rate and the number of previous negative TRUS biopsies. *Diagn Interv Radiol* 19(5):411–417. doi:10.5152/dir.2013.13055
- Hoeks CM, Schouten MG, Bomers JG, et al. (2012) Three-Tesla magnetic resonance-guided prostate biopsy in men with increased prostate-specific antigen and repeated, negative, random, systematic, transrectal ultrasound biopsies: detection of clinically significant prostate cancers. *Eur Urol* 62(5):902–909. doi:10.1016/j.eururo.2012.01.047
- Roethke M, Anastasiadis AG, Lichy M, et al. (2012) MRI-guided prostate biopsy detects clinically significant cancer: analysis of a cohort of 100 patients after previous negative TRUS biopsy. *World J Urol* 30(2):213–218. doi:10.1007/s00345-011-0675-2
- Vourganti S, Rastinehad A, Yerram NK, et al. (2012) Multiparametric magnetic resonance imaging and ultrasound fusion biopsy detect prostate cancer in patients with prior negative transrectal ultrasound biopsies. *J Urol* 188(6):2152–2157. doi:10.1016/j.juro.2012.08.025
- Busetto GM, De Berardinis E, Sciarra A, et al. (2013) Prostate cancer gene 3 and multiparametric magnetic resonance can reduce unnecessary biopsies: decision curve analysis to evaluate predictive models. *Urology* 82(6):1355–1360. doi:10.1016/j.urology.2013.06.078
- Wysock JS, Rosenkrantz AB, Huang WC, et al. (2014) A prospective, blinded comparison of magnetic resonance (MR) imaging-ultrasound fusion and visual estimation in the performance of MR-targeted prostate biopsy: the PROFUS trial. *Eur Urol* 66(2):343–351. doi:10.1016/j.eururo.2013.10.048
- Lee SH, Chung MS, Kim JH, et al. (2012) Magnetic resonance imaging targeted biopsy in men with previously negative prostate biopsy results. *J Endourol* 26(7):787–791. doi:10.1089/end.2011.0393
- Meng X, Rosenkrantz AB, Mendhiratta N, et al. (2015) Relationship between prebiopsy multiparametric magnetic resonance imaging (MRI), biopsy indication, and MRI-ultrasound fusion-targeted prostate biopsy outcomes. *Eur Urol* . doi:10.1016/j.eururo.2015.06.005
- Sonn GA, Margolis DJ, Marks LS (2014) Target detection: magnetic resonance imaging-ultrasound fusion-guided prostate biopsy. *Urol Oncol* 32(6):903–911. doi:10.1016/j.urolonc.2013.08.006
- Schouten MG, Hoeks CM, Bomers JG, et al. (2015) Location of prostate cancers determined by multiparametric and mri-guided biopsy in patients with elevated prostate-specific antigen level and at least one negative transrectal ultrasound-guided biopsy. *AJR Am J Roentgenol* 205(1):57–63. doi:10.2214/ajr.14.12960
- Cash H, Maxeiner A, Stephan C, et al. (2015) The detection of significant prostate cancer is correlated with the Prostate Imaging Reporting and Data System (PI-RADS) in MRI/transrectal ultrasound fusion biopsy. *World J Urol* . doi:10.1007/s00345-015-1671-8
- Kuru TH, Roethke MC, Seidenader J, et al. (2013) Critical evaluation of magnetic resonance imaging targeted, transrectal ultrasound guided transperineal fusion biopsy for detection of prostate cancer. *J Urol* 190(4):1380–1386. doi:10.1016/j.juro.2013.04.043
- Arsov C, Rabenalt R, Blondin D, et al. (2015) Prospective randomized trial comparing magnetic resonance imaging (MRI)-guided in-bore biopsy to MRI-ultrasound fusion and transrectal

- ultrasound-guided prostate biopsy in patients with prior negative biopsies. *Eur Urol* . doi:[10.1016/j.eururo.2015.06.008](https://doi.org/10.1016/j.eururo.2015.06.008)
26. Tewes S, Hueper K, Hartung D, et al. (2015) Targeted MRI/TRUS fusion-guided biopsy in men with previous prostate biopsies using a novel registration software and multiparametric MRI PI-RADS scores: first results. *World J Urol* . doi:[10.1007/s00345-015-1525-4](https://doi.org/10.1007/s00345-015-1525-4)
27. Porpiglia F, Russo F, Manfredi M, et al. (2014) The roles of multiparametric magnetic resonance imaging, PCA3 and prostate health index-which is the best predictor of prostate cancer after a negative biopsy? *J Urol* 192(1):60–66. doi:[10.1016/j.juro.2014.01.030](https://doi.org/10.1016/j.juro.2014.01.030)