Prebiopsy MRI and MRI-ultrasound Fusion—targeted Prostate Biopsy in Men With Previous Negative Biopsies: Impact on Repeat Biopsy Strategies

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OBJECTIVE To report outcomes of magnetic resonance imaging (MRI)-ultrasound fusion—targeted biopsy (MRF-TB) and 12-core systematic biopsy (SB) over a 26-month period in men with prior negative prostate biopsy.

MATERIALS AND METHODS Between June 2012 and August 2014, 210 men presenting to our institution for prostate biopsy with ≥1 prior negative biopsy underwent multiparametric MRI followed by MRF-TB and SB and were entered into a prospective database. Clinical characteristics, maximum mpMRI suspicion scores (mSS), and biopsy results were queried from the database, and the detection rates of Gleason ≥7 prostate cancer (PCa) and overall PCa were compared between biopsy techniques using McNemar's test.

RESULTS Forty seven (29%) of 161 men meeting inclusion criteria (mean age, 65 ± 8 years; mean prostate-specific antigen, 8.9 ± 8.9) were found to have PCa. MRF-TB and SB had overall cancer detection rates (CDRs) of 21.7% and 18.6% ($P = .36$), respectively, and CDR for Gleason score (GS) ≥7 disease of 14.9% and 9.3% ($P = .02$), respectively. Of 26 men with GS ≥7 disease, MRF-TB detected 24 (92.3%) whereas SB detected 15 (57.7%; $P < .01$). Using UCSF-CAPRA criteria, only 1 man was restratified from low risk to higher risk based on SB results compared to MRF-TB alone. Among men with mSS <4, 72% of detected cancers were low risk by UCSF-CAPRA criteria.

CONCLUSION In men with previous negative biopsies and persistent suspicion of PCa, SB contributes little to the detection of GS ≥7 disease by MRF-TB, and avoidance of SB bears consideration. Based on the low likelihood of detecting GS ≥7 cancer and overall low-risk features of PCa in men with mSS <4, limiting biopsy to men with mSS ≥4 warrants further investigation. UROLOGY 86: 1192—1199, 2015. © 2015 Published by Elsevier Inc.

Approximately 1 in 5 men treated surgically for prostate cancer (PCa) undergoes multiple prostate biopsies before being diagnosed with cancer.[1,2] Recent evidence demonstrates that men with negative primary prostate biopsy often undergo repeat biopsy, with up to 25% cancer detection even after the fourth repeat biopsy.[3,4] Multiple repeat biopsies increase cost, delay diagnosis, and risk unnecessary morbidity, all of which would improve with more accurate biopsy.

Recent investigations into image-guided prostate biopsy using multiparametric magnetic resonance imaging (mpMRI) have demonstrated the superior ability of MRI-targeted biopsy to detect clinically significant cancers missed by systematic biopsy (SB).[5,6] However, the performance of targeted biopsy in improving high-risk cancer detection, as well as reducing overdetection of low-risk disease, is influenced by the prevalence of cancer in the tested population, which varies widely with the clinical indication for biopsy and prebiopsy characteristics.[7] Men with prior negative biopsies and persistent suspicion of PCa represent a population with a relatively low prevalence of disease because of prior sampling. As such, prebiopsy MRI may enhance detection of occult cancers by localization of disease in areas of the prostate undersampled by SB. Additionally, prebiopsy mpMRI may not only predict the likelihood and severity of occult disease, as previously reported,[8,9]

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but also provide further discriminating information so as to identify candidates who are least likely to benefit from prostate biopsy.

In this study, we report the overall cancer detection rates (CDRs) and high-grade CDRs of MRI-ultrasound (US) fusion—targeted biopsy (MRF-TB) and 12-core SB in men with previous negative biopsies and persistently elevated prostate-specific antigen. In an effort to define an optimal biopsy approach for these men, we further investigate the clinical impact of prebiopsy characteristics, including mpMRI, in the ability to identify men who may derive maximal benefit from MRF-TB, minimal benefit from SB, and minimal benefit from prostate biopsy overall with respect to high-grade cancer detection.

MATERIALS AND METHODS

Study Design and Population

Between June 2012 and August 2014, all men presenting to our institution for prostate biopsy were offered prebiopsy mpMRI to identify areas within the prostate suspicious for cancer. A total of 199 men with prior negative biopsies and areas of suspicion identified on mpMRI underwent MRF-TB and SB (193 simultaneous MRF-TB/SB and 6 SB $\leq$ 18 months prior to MRF-TB), and outcomes were recorded in an institutional review board—approved database. We retrospectively analyzed clinical characteristics, maximum mpMRI suspicion scores (mSS), and biopsy results from men with at least 1 previous negative biopsy. Men were excluded if they had a history of MRF-TB (n = 4), had undergone MRI at an outside institution or using nonstandard protocol (n = 12), or had an incomplete record in our database (n = 22). Clinical datapoints, such as biopsy indication, prostate-specific antigen, mSS, and biopsy outcomes, were queried from the database.

Multiparametric MRI

mpMRI was performed using a 3T whole-body system and a pelvic phased-array coil and included multiplanar turbo spin-echo T2-weighted images, axial single-shot echo-planar imaging diffusion-weighted imaging with b-values of 50 and 1000 sec/mm^2, and dynamic contrast-enhanced MRI following intravenous administration of gadolinium-chelate. Before biopsy, MRI studies were reviewed by a single fellowship-trained radiologist with 5-6 years of experience in prostate MRI at the time of this study, who identified suspicious foci within the prostate. The probability for tumor was scored on a 5-point Likert scale, as previously reported[7,10,11]: mSS 2 (low probability), 3 (equivocal), 4 (high probability), or 5 (very high probability). Studies with no identified suspicious region received a score of 1 and were not candidates for MRI-targeted biopsy.

MRI-US Fusion—targeted Biopsy

MRF-TB was performed using the Artemis/Pro-fuse (Eigen, Grass Valley, CA) prostate biopsy system, as described in our previous work.[7] In brief, T2 sequences with delineated tumor boundaries were transferred to the Artemis system before biopsy. Computer-assisted coregistration of segmented MRI and US images of the prostate was performed using manual rigid translation followed by elastic deformation. Transrectal biopsies were obtained with the patient in left lateral decubitus position, beginning with 3-4 cores targeted to each suspicious lesion followed by 12 systematically distributed cores. The locations of the 12 systematic cores were automatically generated by the Artemis system and not by the urologist. The procedure used the Pro Focus (BK Medical, Peabody, MA) or Noblus ultrasound system (Hitachi Aloka Medical America, Wallingford, CT), endfire probe, 18G needles, and local anesthesia with 1% lidocaine infiltration.

For each patient, systematic and targeted biopsies were performed by 1 of 4 faculty urologic oncologists, experienced in prostate biopsy. All biopsy cores were analyzed by 1 of 3 subspecialized genitourinary pathologists at our institution. Biopsy results were compared using the highest Gleason score (GS) obtained by each technique. Analysis of clinically significant cancer detection was done based on 2 definitions for clinical significance: GS $\geq$7 and primary Gleason grade 4 or higher (pGG $\geq$4). Analysis of clinically insignificant cancer detection was done based on Epstein[12] and UCSF-CAPRA[13] (score $\leq$2) criteria.

Statistical Analysis

Categorical variables, including a history of high-grade prostatic intraepithelial neoplasia (HGPIN) and/or atypical small acinar proliferation (ASAP), median time since last biopsy, and percentage of positive biopsy cores, were compared using the chi-square test. Normally distributed continuous variables were evaluated with the Student *t* test. Comparison of CDRs between SB and MRF-TB was assessed by McNemar's test. All analyses were carried out in SPSS version 21.0 software (IBM Corp., Armonk, NY).

RESULTS

A total of 199 men with prior negative biopsies who underwent mpMRI followed by biopsy were identified, of whom 161 men met inclusion criteria, as described previously. Clinical characteristics are described in Table 1. The mean number of lesions and biopsy cores taken per prostate were 1.5 and 18.2, respectively.

Cancer Detection: MRF-TB vs SB

Overall, cancer was identified in 47 (29%) men. Although CDRs were higher for MRF-TB than SB, this difference was not clinically significant (21.7% vs 18.6%, respectively; P = .36; Table 2). Compared to SB, MRF-TB detected more GS $\geq$7 disease (92% vs 58%, P = .02) and more pGG $\geq$4 disease (88% vs 63%, P = .28). MRF-TB demonstrated improved sampling efficiency compared to SB, as a total of 113 of 966 (11.7%) targeted cores and 67 of 1860 (3.6%) systematic cores identified PCa, and the mean number of cores required per diagnosis of GS $\geq$7 cancer was 40 and 124 on targeted and systematic biopsy, respectively.

Whereas no men with GS $\geq$7 cancer detected by SB had negative MRF-TB, 2 GS (3+4) cancers identified by SB were mischaracterized as GS 6 by MRF-TB. One case demonstrated <10% pattern 4 disease in only 1 SB core. In the second case, GS 7 cancer was detected on the SB core adjacent to the area of the prostate with the targeted MRI lesion.

Compared to men with negative biopsies, men with positive MRF-TB or SB had no significant difference in

Table 1. Patient characteristics

		Results of MRF-TB and SB			Results of MRF-TB and SB		
	Total N = 161	Cancer n = 47 (29.2%)	No Cancer n = 114 (70.8%)	*P* Value	GS ≥7 Cancer n = 26 (16.1%)	GS 6 or no Cancer n = 135 (83.9%)	*P* Value
Age (mean, y)	64.9 ± 7.5	65.9 ± 7.7	64.4 ± 7.4	.243*	65.1 ± 8.2	64.8 ± 7.4	.873*
PSA (mean [SEM], ng/mL)	8.9 [0.7]	11.6 [1.4]	7.7 [0.7]	**.008***	14.9 [2.1]	7.6 [0.6]	**<.001***
Number of previous biopsies (mean)	2.23	2.16	2.26	.781*	2.51	2.18	.433*
MRI Prostate volume (mean [SEM], cc)	72.5 [3.22]	69.1 [6.6]	74.0 [3.7]	.643*	70.8 [9.3]	76.7 [3.3]	.628*
Time since last biopsy (median, mo)	31.2	30.8	31.4	.881†	25.1	32.4	.603†
Previous HGPIN/ASAP							
HGPIN or ASAP	52 (32.3%)	16 (34.0%)	37 (32.5%)	.846†	8 (30.8%)	44 (32.6%)	.855†
HGPIN	43 (26.7%)	11 (23.4%)	32 (28.1%)	.543†	4 (15.4%)	39 (28.8%)	.154†
ASAP	25 (15.5%)	11 (23.4%)	14 (12.3%)	.076†	8 (30.8%)	17 (12.6%)	**.019**†
HGPIN and ASAP	16 (9.9%)	7 (14.8%)	9 (7.9%)	.177†	4 (15.4%)	12 (8.9%)	.311†
mSS distribution				**<.001**‡			**<.001**‡
mSS 2	53 (32.9%)	9 (19.1%)	44 (38.6%)		2 (7.7%)	51 (37.8%)	
mSS 3	55 (34.2%)	9 (19.1%)	46 (40.4%)		2 (7.7%)	53 (39.3%)	
mSS 4	39 (24.2%)	17 (36.2%)	22 (19.3%)		10 (38.5%)	29 (21.5%)	
mSS 5	14 (8.7%)	12 (25.5%)	2 (1.8%)		12 (46.2%)	2 (1.5%)	

ASAP, atypical small acinar proliferation; GS, Gleason score; HGPIN, high-grade prostatic intraepithelial neoplasia; MRF-TB, MRI-ultrasound fusion–targeted biopsy; MRI, magnetic resonance imaging; mSS, maximum mpMRI suspicion score; PSA, prostate-specific antigen; SB, systematic biopsy; SEM, standard error of mean.

Values in bold indicate $P < .05$.

* Student *t* test.

† Chi-square test for independence.

‡ Wilcoxon rank-sum analysis.

Table 2. Cancer detection rates: MRF-TB vs SB

	MRI-targeted Biopsy, n (%)			
	Gleason ≥7	Gleason 6	No Cancer	Total
Systematic biopsy, n (%)				
Gleason ≥7	13 (8)	2 (1)	0 (0)	15 (9)*
Gleason 6	1 (1)	2 (1)	12 (7)	15 (9)
No cancer	10 (6)	7 (4)	114 (71)	131 (81)
Total	24 (15)*	11 (7)	126 (78)	161 (100)

Abbreviations as in Table 1.
* $P = .027$.

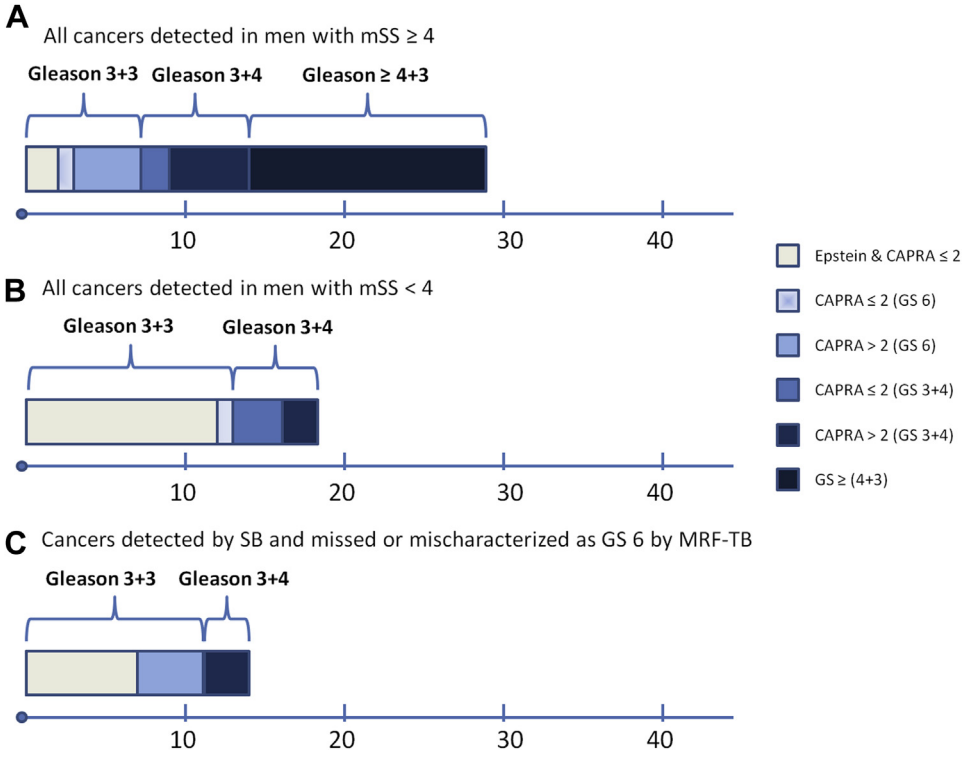

Figure 1. Grade distribution of detected prostate cancers showing the number of men (x-axis) with the indicated prostate cancer grade among **(A)** men with mSS ≥4, **(B)** men with mSS <4, and **(C)** men with cancer on SB which was missed or mischaracterized as Gleason 6 by MRF-TB. GS, Gleason score; MRF-TB, MRI-ultrasound fusion–targeted biopsy; MRI, magnetic resonance imaging; mSS, maximum MRI suspicion score; SB, systematic biopsy. (Color version available online.)

the time elapsed since last standard transrectal biopsy ($P = .88$) or number of previous biopsies ($P = .78$). There was additionally no association between the number of previous biopsies and the probability of cancer detection by SB ($P = .38$) or MRF-TB ($P = .59$). Among 35 men with PCa detected by MRF-TB, 16 (46%) had PCa identified in the anterior prostate only, among whom SB yielded no cancer in 9 of 16 (56%).

Maximum mpMRI Suspicion Scores

mSS 2-5 were reported in 53 (32.9%), 55 (34.2%), 39 (24.2%), and 14 (8.7%) men, respectively. Men with mSS ≥4 lesions harbored the majority of GS ≥7 and pGG ≥4 cancers detected (22/26 [84.6%] and 16/16 [100%], respectively). In men with mSS ≥4 lesions, MRF-TB detected all 22 GS ≥7 cancers, whereas SB missed 9 of 22 (41%, $P = .008$; Fig. 1).

mSS <4 had a negative predictive value (NPV) of 96% and 100% for GS ≥7 and pGG ≥4 disease, respectively. Of all cancers detected in men with mSS <4 lesions, most were clinically insignificant by Epstein (67%) and UCSF-CAPRA (72%) criteria, respectively. Of all GS ≥7 cancers found in men with mSS <4, 75% demonstrated GS 7 (3+4) cancer in only 1 core with ≤10% Gleason pattern 4, and 50% demonstrated UCSF-CAPRA score ≤2 (Table 3). Only 1 of 108 (0.9%) men with mSS <4 was found to have GS 7 (3+4) in multiple cores, and none were found to have pGG ≥4 PCa.

COMMENT

The management of men with previous negative biopsy, and persistent clinical suspicion of PCa, remains a challenging task for the practicing urologist. In addition to

Table 3. Characteristics of detected PCa

All PCa	Men with mSS ≥4 (n = 29)	Men with mSS <4 (n = 18)	SB Positive, MRF-TB Negative or GS 6 (n = 14)
Maximum GS			
6 (3+3)	7 (24%)	14 (78%)	12 (86%)
7 (3+4)	6 (21%)	4 (22%)	2 (14%)
≥7 (4+3)	16 (55%)	0 (0%)	0 (0%)
Clinically insignificant cancers			
Epstein[10] criteria	2 (7%)	12 (67%)	7 (50%)
UCSF-CAPRA[11] score ≤2	4 (14%)	13 (72%)	7 (50%)
Gleason ≥7 PCa	(n = 22)	(n = 4)	(n = 2)
Number of cores with pattern 4 disease			
1	6 (27%)	3 (75%)	1 (50%)
2	2 (9%)	0 (0%)	0 (0%)
≥3	14 (64%)	1 (25%)	1 (50%)
Involvement of pattern 4 disease (max)			
≤10%	4 (18%)	4 (100%)	1 (50%)
10%-50%	1 (5%)	0 (0%)	1 (50%)
≥50%	16 (73%)	0 (0%)	0 (0%)
Not reported	1 (5%)	0 (0%)	0 (0%)
Maximum cancer core length			
≤2 mm	3 (14%)	3 (75%)	1 (50%)
2 mm to 4 mm	2 (9%)	0 (0%)	0 (0%)
≥4 mm	16 (73%)	0 (0%)	1 (50%)
Fragmented	1 (5%)	1 (0%)	0 (0%)
Clinically insignificant cancers			
UCSF-CAPRA[11] score ≤2	1 (5%)	2 (50%)	0* (0%)

PCa, prostate cancer; other abbreviations as in Table 1.
* All 3 GS 7 cancers detected by SB also demonstrated UCSF-CAPRA score >2 based on MRF-TB alone.

the absence of consensus guidelines regarding the indication of repeat biopsy, the optimal approach to such patients when biopsy is indicated is unclear. We have previously shown that men with persistent suspicion of cancer often undergo repetitive cycles of biopsy before diagnosis.[4] Prior studies have explored the potential for MRI-targeted biopsy to better detect cancers than SB among men with prior negative biopsies and, in doing so, reducing the need for multiple subsequent biopsies and delays in diagnosis.[14-16] In this study, we aimed to expand on these findings and provide data to shape a clinical paradigm for this population, specifically by evaluating the characteristics of cancers missed by targeted biopsy and by exploring the relationship between prebiopsy MRI and the likelihood of cancer on biopsy. Our data suggest not only that avoidance of SB, which has minimal contribution to the detection of high-grade cancer, may be considered, but also that prebiopsy MRI may allow identification of men with prior negative biopsies who have a low likelihood of high-grade disease and who may not benefit from repeat biopsy at all. Until a time when the implementation of MRI-targeted biopsy in clinical practice is clearly defined and accepted, we feel there is a tremendous need for data supportive of, or refuting, the paradigm.

In a recent report of 1003 men undergoing MRF-TB by Siddiqui et al,[17] among whom 43% had prior negative biopsies, the investigators demonstrated a 30% improvement in high-grade cancer detection with MRF-TB compared to SB; however, 15% of men demonstrated a higher risk category with SB compared to MRF-TB. In our study, the overall contribution of SB to MRF-TB results was limited. Among the few men with GS ≥7 disease detected by SB and missed or mischaracterized by MRF-TB, most had low-volume disease, and only 1 was classified as higher risk by SB compared to MRF-TB using UCSF-CAPRA criteria. Additionally, SB made no contribution to the detection of GS ≥7 cancer in men with MRI abnormalities of mSS ≥4. Collectively, as suggested in prior series,[16] these findings indicate that SB has minimal impact on the detection of high-grade cancer and risk stratification among men with prior negative sampling, and thus may be of little value in combination with MRF-TB.

One potential reason why MRF-TB was superior to SB in detecting PCa may be that over 40% cancers identified by MRF-TB were found in the anterior prostate. Although it has been proposed that transperineal template biopsy may be an option for men with previous negative biopsies due to improved access to the anterior prostate, current evidence suggests that MRI-targeted biopsy has a comparable detection rate of clinically significant cancers while reducing overdetection of clinically insignificant disease as compared to transperineal template biopsy.[18-20]

Ultimately, the likelihood of high-grade cancer detection was strongly predicted by mSS. Previous studies have similarly demonstrated a strong association between suspicion of cancer based on mpMRI and cancer detection.[16,21,22] Salami et al[16] recently reported outcomes of a

prospective trial comparing MRF-TB to SB in 140 men with prior negative biopsies. They demonstrated a strong association between increasing mSS and CDR of both MRF-TB and SB. Their reported overall CDR of 65.0% is higher than that found in our series, although this is likely due in part to a lower proportion of their cohort with low suspicion lesions (mSS 2 in 6% vs 31%). Sonn et al[23] reported a series of 105 men with previous negative biopsy who underwent MRF-TB and SB and demonstrated that lesions with suspicion scores of 2, 3, 4, and 5 corresponding to 6%, 4%, 21%, and 75% detection of clinically significant PCa, respectively.

Our results specifically suggest that abnormalities of mSS 2 and 3 predict a very low likelihood of cancer overall, and an even lower likelihood of high-grade disease. Electing to forego any biopsy in the 108 men with low probability or equivocal lesions would have avoided detection of clinically indolent cancers in 12 to 13 men (depending on the definition used), while missing GS 7 (3+4) cancers in 4 (4%) men and GS 7 (4+3) or higher grade cancers in no men. Two of the 4 GS 7 cancers may have been considered low risk based upon further analysis as previously discussed. These findings suggest that cancers identified in men with previous negative biopsies and low to equivocal mSS are largely low risk. As such, prebiopsy mpMRI may have the potential to identify men within this population who may be able to safely avoid repeat biopsy due to a low likelihood of significant disease.

Strengths of this study protocol include the fact that all men presenting to our center for consideration of repeat biopsy were recommended prebiopsy mpMRI, MRI suspicion grading was carried out by a single radiologist, and our biopsy approach with software coregistration was standardized among a few experienced operators. Limitations of our study include the potential for selection bias given its retrospective nature and the referral pattern of our practice. As a result, indications for biopsy in the population of men receiving MRI were not ascertained. Additionally, not all men with normal MRI (mSS 1) were recommended biopsy because they had undergone one or more recent SB before presentation. Another potential limitation is the use of Epstein and UCSF-CAPRA criteria for the assessment of clinically insignificant cancers, which, although conservative and not yet validated in targeted biopsy, may be the best available measure to estimate the proportion of indolent disease. Finally, as many men underwent previous biopsies outside of our institution, the technique of previous biopsy and the pathologic interpretation of such biopsies were not standardized. Nonetheless, we believe the study provides important insight into the conduct of biopsy in men with previous negative sampling and provides additional supportive data for the use of prebiopsy mpMRI in this group of men.

CONCLUSION

In men with one or more previous negative biopsies, and persistent suspicion of PCa, the use of prebiopsy mpMRI followed by MRF-TB provides greater overall and clinically significant cancer detection than SB alone. The marginal contribution of SB to the detection of clinically significant cancer suggests that MRF-TB alone may be a sufficient biopsy strategy in this cohort, especially in men with mSS $\geq$4. Among men with mSS <4, the low rate of GS $\geq$7 PCa detection as well as overall low-risk features of all detected PCa may warrant consideration of avoiding biopsy in these men. Further prospective studies comparing MRF-TB and SB in men with previous negative biopsy, along with community-based standardization of prostate mpMRI acquisition and interpretation, are needed before widespread implementation of the approach.

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APPENDIX

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.urology.2015.07.038.

EDITORIAL COMMENT

In this retrospective single-center study, Mendhiratta et al examine cancer detection rates (number of men with cancer per 100 men biopsied) of magnetic resonance imaging-ultrasound fusion–targeted biopsy (MRF-TB) vs systematic biopsy among 161 men who underwent a repeat biopsy after a previously negative prostate biopsy.[1] Twenty-four of 26 men diagnosed with high-grade cancer were identified via MRF-TB (sensitivity of 92%). Systematic biopsy contributed minimally beyond MRF-TB to the detection of high-grade cancer—just 2 of the 26 men (8%) would have been missed had systematic biopsy been omitted. Concluding that their findings support omission of systematic biopsy in this circumstance, the authors propose that MRF-TB alone may well be sufficient—adding to the literature supporting the use of this promising new technology in the repeat biopsy setting.[1]

In addition, the authors propose that performing a prostate MRI could allow a subset of men to completely avoid repeat prostate biopsy.[1] Men with low suspicion scores on prebiopsy MRI have a low likelihood of harboring clinically significant disease: prostate cancer with a UCSF-CAPRA score >2 was detected in just 4 of 108 (4%) with an MRI suspicion score <4. These data add to the growing literature supporting the use of MRI for selecting men for a repeat prostate biopsy.[2,3]

What the authors do not mention is that the most considerable advantage of performing MRF-TB and omitting a systematic biopsy may be a reduction in overdiagnosis of low-risk prostate cancer. Replacing systematic biopsy with MRF-TB reduces detection of low-risk cancers while improving detection of higher grade disease, as recently shown by investigators from the National Cancer Institute who evaluated 1003 men undergoing MRF-TB (43% of whom had undergone a prior negative biopsy).[4] The present study confirms these findings, albeit in a much smaller cohort. Performing MRF-TB alone would have avoided a diagnosis of Gleason 6 cancer in 12 men—over half of the 21 men diagnosed with Gleason 6 cancer in this study.[1]

We believe, however, that a broader rollout of this promising new MRF-TB technology will be challenging—and that real-world effectiveness may not match the efficacy seen in this and other studies. Accurately performing and reading these prostate MRIs is difficult, and the importance of dedicated training in prostate MRI has been well documented in the radiologic literature.[5] As with other imaging studies,[6,7] the complexity of performing and reading prostate MRIs means that accuracy and quality is far from assured when performed outside of centers of excellence by radiologists not specifically trained, or interested, in reading prostate MRI.

In summary, the study by Mendhiratta et al, although single center and small in size, contributes substantively to the literature supporting the use of prostate MRI for selection of men for repeat biopsy as well as the use of MRF-TB while performing the biopsy.[1] Before advocating more widespread implementation of this new and costly technology, however, we recommend careful evaluation of its performance when used outside of centers of excellence.

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