The Role of Ipsilateral and Contralateral Transrectal Ultrasound-guided Systematic Prostate Biopsy in Men With Unilateral Magnetic Resonance Imaging Lesion Undergoing Magnetic Resonance Imaging-ultrasound Fusion-targeted Prostate Biopsy

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OBJECTIVE To determine how ipsilateral (ipsi) and contralateral (contra) systematic biopsies (SB) impact detection of clinically significant vs insignificant prostate cancer (PCa) in men with unilateral magnetic resonance imaging (MRI) lesion undergoing MRI-ultrasound fusion-targeted biopsy (MRF-TB).

MATERIALS AND METHODS A total of 211 cases with 1 unilateral MRI lesion were subjected to SB and MRF-TB. Biopsy tissue cores from the MRF-TB, ipsi-SB, and contra-SB were analyzed separately.

RESULTS A direct relationship was observed between MRI suspicion score and (1) detection of any cancer, (2) Gleason 6 PCa, and (3) Gleason >6 PCa. MRF-TB alone, MRF-TB + ipsi-SB, and MRF-TB + contra-SB detected 64.1%, 89.1%, and 76.1% of all PCa, respectively; 53.5%, 81.4%, and 69.8% of Gleason 6 PCa, respectively; and 73.5%, 96.0%, and 81.6% of Gleason >6 PCa, respectively. MRF-TB + ipsi-SB detected 96% of clinically significant PCa and avoided detection of 18.6% of clinically insignificant PCa. MRF-TB + contra-SB detected 81.6% of clinically significant PCa and avoided detection of 30.2% of clinically insignificant PCa.

CONCLUSION Our study suggests that ipsi-SB should be added to MRF-TB, as detection of clinically significant PCa increases with only a modest increase in clinically insignificant PCa detection. Contra-SB in this setting may be deferred because it primarily detects clinically insignificant PCa. UROLOGY 102: 178–182, 2017. © 2016 Published by Elsevier Inc.

Systematic biopsy (SB) of the prostate is typically performed by random systematic tissue sampling of the peripheral zone under transrectal ultrasound (US) guidance. The primary limitations of SB are its high detection rate of clinically insignificant disease, which has implications related to cost, morbidity of unnecessary treatment, and anxiety associated with active surveillance (AS). Another limitation of SB is underdetection of clinically significant disease.[1,2]

Increasing evidence shows that the addition of magnetic resonance imaging (MRI)-US fusion-targeted prostate biopsy (MRF-TB) to SB increases the cancer detection rate (CDR) of clinically significant disease.[2-9] However, the combination of MRF-TB and SB also exacerbates overdetection of clinically insignificant disease. Ideally, prostate biopsy strategies must find a balance between detection of clinically significant and clinically insignificant disease. The present study independently evaluated the SB obtained ipsilateral (ipsi-SB) and contralateral (contra-SB) to a unilateral MRI lesion subjected to MRF-TB to determine the relative contribution of these biopsy sites to the detection of clinically significant vs clinically insignificant disease. The hypothesis being tested was that contra-SB disproportionately increases the detection of insignificant prostate cancer (PCa) and therefore should not be routinely performed. This hypothesis is based on the very

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high negative predictive value of multiparametric MRI (mpMRI) for clinically significant PCa.[10-12] Cases with a unilateral MRI lesion were selected because this would be the ideal cohort to question the utility of contra-SB.

MATERIALS AND METHODS

Beginning in June 2012, only uro-oncologists perform prostate biopsy at our institution. The overwhelming majority (>95%) of candidates for prostate biopsy presenting to our institution since 2012 underwent prebiopsy mpMRI on a 3T clinical instrument using a previously described technique.[3,13,14] The axial T2-weighted images, dynamic contrast enhancement images, and diffusion-weighted images (acquired b-values of 50 and 1000 seconds per mm^2; calculated b-value of 1500 seconds per mm^2; reconstructed apparent diffusion coefficient map) were reviewed and, using a 5-point suspicion scale, the MRI lesions were assigned a suspicion score (ss) of 2 (clinically significant disease is unlikely to be present), 3 (clinically significant disease is equivocal), 4 (clinically significant disease is likely to be present), or 5 (clinically significant disease is highly likely to be present).[15,16] All men assigned a suspicious score on prebiopsy mpMRI underwent an MRF-TB. MRF-TB was performed using an Artemis prostate biopsy system and ProFuse (Eigen, Grass Valley, CA) software for MRI segmentation, co-registration of MRI and US images, and 3-dimensional biopsy planning, as previously described.[3,13,14] A single uro-radiologist performed or directly supervised the MRI segmentation. Prostate US was performed using the Pro Focus (BK Medical, Peabody, MA) or Noblus US system (Hitachi Aloka Medical America, Wallingford, CT). After targeting 4 biopsies into each MRI lesion, SB was performed by sampling 12 software-populated spatially distributed sites selected by the Artemis Device.

Data and Statistical Analysis

A total of 211 consecutive cases with a single unilateral MRI lesion subjected to both MRF-TB and SB were identified from 679 biopsy cases performed by 2 experienced users of the ProFuse and Artemis systems (HL or WCH). None of the cases had biopsy-proven cancer. Demographics, serum prostate-specific antigen (PSA) levels at time of mpMRI, mpMRI interpretations, and prostate biopsy pathology reports were reviewed. The linear lengths of the individual biopsy cores and the linear lengths of all Gleason pattern disease were recorded. The percentages of Gleason patterns in the individual biopsy cores were calculated. Clinically significant and clinically insignificant disease were defined as Gleason >6 PCa and Gleason 6, respectively. The MRF-TB, ipsi-SB, and contra-SB were analyzed separately.

The sensitivities for detection of any cancer, clinically significant cancer, and clinically insignificant cancer were determined for various combinations of MRF-TB, ipsi-SB, and contra-SB. Intergroup differences between sensitivities were considered statistically significant if the mean of 1 group did not overlap with the 95% confidence interval of another group.

RESULTS

A total of 211 consecutive men with an elevated PSA or prostate nodule, or both, and a single unilateral MRI lesion on mpMRI underwent MRF-TB and SB. Table 1 shows characteristics of the study population, as well as the relationship between ss of the MRI lesions and CDR. Fifty-nine cancers were detected by MRF-TB. Both overall CDRs and the detection rates of Gleason >6 PCa increased with increasing ss.

Table 1. Baseline characteristics (n = 211)

Median age (IQR)	61.0 (56-66)
Median PSA before MRI (IQR)	5.3 (3.8-6.9)
Positive DRE (n, %)	44 (20.9)
Prior prostate biopsy (n, %)	87 (41.2)

	MRF-TB		
mpMRI ss (n)	Any Cancer (n, %)	Gleason 6 (n, %)	Gleason >6 (n, %)
2 (77)	6 (7.8)	4 (5.2)	2 (2.6)
3 (73)	14 (19.2)	6 (8.2)	8 (11.0)
4 (45)	23 (51.1)	11 (24.4)	12 (26.7)
5 (16)	16 (100)	2 (12.5)	14 (87.5)
Total (211)	59 (28.0)	23 (10.9)	36 (17.1)

DRE, digital rectal examination; IQR, interquartile range; mpMRI ss, multiparametric magnetic resonance imaging suspicion score; MRF-TB, MRI-US fusion targeted biopsy; PSA, prostate-specific antigen; ss, suspicion score.

As shown in Table 2, a strategy to perform only MRF-TB + ipsi-SB would detect 96% of clinically significant PCa and avoid detection of 18.6% of clinically insignificant PCa. The ratio of additional clinically significant PCa vs additional clinically insignificant PCa detected by adding ipsi-SB to MRF-TB was 0.92:1. Additionally, as shown in Table 2, a strategy to perform only MRF-TB + contra-SB would detect 81.6% of clinically significant PCa and avoid detection of 30.2% of clinically insignificant PCa. The ratio of additional clinically significant PCa to additional clinically insignificant PCa detected by adding contra-SB to MRF-TB is 0.57:1.

The 2 cases of Gleason >6 disease identified exclusively by contra-SB had linear volumes of Gleason pattern 4 of 0.2 mm and 1.2 mm.

DISCUSSION

The widespread acceptance of PSA screening, SB, and aggressive treatment of PCa beginning in the 1990s are major factors contributing to the profound decline in PCa mortality rates.[17,18] This widely accepted paradigm for screening, detection, and treatment of PCa has substantial limitations. Because of the low specificity of PSA screening, approximately 70% of men undergoing prostate biopsies are exposed to the morbidity of unnecessary biopsies.[19] Approximately half of cancers detected by SB are Gleason 6 PCa.[20] According to National Comprehensive Cancer Network guidelines, many Gleason 6 PCa should be managed with AS to limit overtreatment of the disease.[21] A limitation of AS strategies is that about half of the prostate glands with Gleason 6 PCa detected by SB harbor unrecognized aggressive disease.[22] The challenge for the urology community is to develop clinical pathways that preferentially detect clinically significant disease.

There is compelling and consistent evidence that adding MRF-TB to SB increases the detection of both clinically