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The impact of prostate MR/ultrasound fusion-guided biopsy on radiation treatment recommendations

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Abstract

Background—Targeted magnetic resonance (MR)/ultrasound fusion prostate biopsy (MRI-Bx) has recently been compared to standard of care extended sextant ultrasound-guided prostate biopsy (SOC-Bx) and was associated with an increased rate of detection of clinically significant prostate cancer. This study sought to determine the influence of MRI-Bx on radiation and androgen deprivation therapy (ADT) treatment recommendations.

Methods/Materials—All patients treated with radiotherapy that underwent SOC-Bx and MRI-Bx at our institution were included. Using clinical T stage, pretreatment PSA, and Gleason score, patients were categorized into NCCN risk groups and radiation/ADT treatment recommendations were assigned. Intensification of recommended treatment after multiparametric MRI, SOC-Bx, and MRI-Bx was evaluated.

Results—From January 2008 to January 2016, 73 patients received radiation therapy at our institution after undergoing a simultaneous SOC-Bx and MRI-Bx (n=47 with prior SOC-Bx). Repeat SOC-Bx and MRI-Bx resulted in frequent upgrading compared to prior SOC-Bx (Gleason 7: 6.7% vs. 44.6%, $p<0.001$; Gleason 8–10: 2.1% vs. 38%, $p<0.001$). MRI-Bx increased the proportion of patients classified as very-high risk from 24.7% to 41.1% ($p=0.027$). Compared to SOC-Bx alone, including MRI-Bx findings resulted in a higher percentage of pathologically positive cores (mean 37% vs. 44%). Incorporation of multiparametric MRI and MRI-Bx results increased the recommended use and duration of ADT (duration increased in 28/73 patients, addition in 8/73 patients).

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Conclusion—In patients referred for radiotherapy, MRI-Bx resulted in an increase in the percentage of positive cores, Gleason Score, and risk grouping. The benefit of treatment intensification based on MRI-Bx findings is unknown.

SUMMARY

Prostate MR/ultrasound fusion-guided biopsy has recently been shown to identify clinically significant prostate cancer at rates higher than standard extended sextant ultrasound guided biopsy. Targeted biopsy often results in an increase in tumor grade. As fusion biopsy becomes more prevalent, an understanding of how it may alter radiation recommendations as a result of risk group migration is important. This study demonstrates a general pattern of increasing risk group and treatment intensification when results of fusion biopsy are incorporated.

Keywords

Fusion biopsy; MRI; radiation; prostate

INTRODUCTION

Magnetic resonance imaging (MRI) screening enhances detection of occult prostate cancers [1–6]. Multi-parametric MRI (mpMRI), including T2-weighted imaging (T2W), diffusion-weighted imaging (DWI), and dynamic contrast enhancement (DCE), has further advanced the detection of clinically relevant cancers [1]. Recently, targeted MRI/ultrasound fusion-guided prostate biopsy (MRI-Bx) has been found to increase the detection of high risk prostate cancer when compared to standard-extended sextant ultrasound-guided prostate biopsy (SOC-Bx) [2, 3]. We hypothesized that MRI-Bx results would intensify androgen deprivation therapy (ADT) and radiotherapy (RT) recommendations.

METHODS AND MATERIALS

All patients treated with intact prostate radiotherapy (January 2008 to February 2016) at our institution who underwent SOC-Bx and mpMRI with MRI-Bx were included. All patients provided informed consent for participation in IRB approved protocols. Pretreatment T2W images, DWI with ADC mapping, high b value DWI ($b = 2000 \text{ s/mm}^2$) images were obtained on a 3Tesla MRI scanner with an endorectal coil (BPX-30, Medrad, Pittsburgh, PA) filled with 45 ml fluorinert (3M, Maplewood, MN) using previously defined sequence parameters [2, 7]. Images were interpreted prospectively by two prostate-dedicated radiologists using an in-house classification system [2, 8].

mpMRI-identified lesions were superimposed on real time TRUS images using the UroNav platform (in vivo, Gainesville, Florida). At least two targeted biopsies from each suspicious lesion were obtained. Repeat SOC-Bx was usually obtained at the time of MRI-Bx. All specimens, including outside biopsies, were reviewed by a senior genitourinary pathologist.

Patients were re-stratified utilizing NCCN criteria (Version 3.2016). The highest Gleason Score was utilized for classification. MRI evidence of T3 disease was only considered for staging if prospectively defined as “probable”, “highly suspicious”, or “definite.” Treatment

recommendations were re-defined to account for changes in standard of care over time: low risk: RT alone, high risk: RT with long-course ADT. Intermediate risk patients were stratified into favorable or unfavorable [9] with short-course ADT recommended only for unfavorable-intermediate risk patients.

Statistical computations were performed in “R” [10] using a 2-sided significance level ($p = 0.05$). Wilcoxon rank sum test was used to compare quantitative variables with SOC-Bx and MRI-Bx. Fisher test was used to compare proportions of patients in a category (risk group, Gleason score) before and after a modality (outside SOC-Bx, repeat SOC-Bx and MRI-Bx).

RESULTS

Characteristics of the 73 patients are described in Table 1. After repeat SOC-Bx ($n=47$), the proportion of patients with benign pathology decreased from 49% to 6.5% ($p<0.001$, Figure 1) and more patients had Gleason score 7 (14.9% vs. 38.3%, $p<0.001$) or Gleason score 8–10 (2.1% vs. 38.3%, $p<0.001$) disease. When including mpMRI findings, only two of 73 patients escalated risk group (Figure 2).

MRI-Bx resulted in an increase in Gleason 8–10 histology compared to SOC-Bx (41 vs 34 patients, Table 2, Figure 3A), with primary Gleason pattern 4 or 5 increasing from 41 to 51 patients (Table 2, Figure 3B). The number of involved cores and percent positive cores increased with MRI-Bx compared to SOC-Bx (Table 2). After MRI-Bx, the proportion of high or very-high risk patients increased from 50.7% to 63.0% (Figure 3C), with the very-high risk group increasing from 24.7% to 41.1% ($p=0.027$). Despite identical numbers of unfavorable-intermediate risk patients before and after MRI-Bx, patients moved among categories: unfavorable-intermediate to very-high risk ($n=4$), favorable to unfavorable-intermediate risk IR ($n=2$), very-low risk to unfavorable-intermediate ($n=1$), and benign to unfavorable-intermediate risk ($n=1$). The mpMRI for a patient upgraded by MRI-Bx findings is shown in Figure 3D. Following MRI-Bx, ADT recommendations were intensified in 16% ($n=12$) of patients (Figure 4) and PNI was added in 11% ($n=8$).

DISCUSSION

This study provides evidence that MRI-Bx intensifies ADT recommendations when compared to SOC-Bx. Several series have demonstrated that mpMRI improves diagnostic accuracy for high grade prostate cancer [1, 2, 11–13]. Similarly, MRI-Bx is known to enhance detection of clinically significant prostate cancer [2, 14, 15]. Despite a lack of guidelines for integrating the results of these studies, they are increasingly utilized in clinical decision making.

Integrating mpMRI and MRI-Bx results can result in increased T stage or Gleason score, and subsequent treatment intensification. The need for therapeutic intensification using MRI-Bx findings remains unclear. Prospective evaluation is required to determine if, and when MRI-Bx findings warrant intensification. Care should be exercised when considering both percent positive cores and the percent of each core involved if MRI-Bx findings are integrated.

In contrast to prior studies, mpMRI findings in isolation did little to change risk grouping and treatment recommendations. Other studies typically altered recommendations based on any level of suspicion for T3 disease [16, 17], while in this study, only lesions with high suspicion of T3 status were used for risk grouping.

Consistent with prior reports [18, 19], Gleason score often increased with repeat SOC-Bx, possibly due to rigorous adherence to clinical protocols at our facility, knowledge of MRI findings, progression between biopsy attempts, or sampling error.

Limitations of this study relate to the inclusion of patients with MRI-visible prostate lesions, and their referral for radiotherapy, both possibly selecting for more aggressive disease. In addition, treatment recommendations may not always correlate with treatment received.

This small retrospective study demonstrates that MRI-Bx can alter treatment recommendations for radiotherapy and ADT. Further studies are needed to evaluate whether treatment intensification is beneficial and justifies the associated increased toxicity and costs of treatment.

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Figure 1. Pathologic upgrading after repeat SOC-Bx

Comparison of highest Gleason score in the subset (n=47) that underwent outside SOC-Bx and repeat SOC-Bx at our institution.

Figure 2. Changes in risk grouping based on MRI
Two patients changed risk groups as a result of mpMRI findings.

Figure 3. Impact of MRI-Bx on pathologic grading

Highest Gleason score (A) and primary Gleason pattern (B) were compared between SOC-Bx and MRI-Bx. (C) Risk group categorization before (left) and after (right) MRI-Bx. (D) A patient with known Gleason 3+3=6 disease underwent mpMRI. MRI-Bx of the mpMRI-identified midline apical anterior transition zone lesion (arrows) revealed Gleason 4+4=8 disease.

Initial Recommendation No ADT**Initial Recommendation Short Course ADT**

Figure 4. Impact of MRI-Bx on treatment recommendations

Final ADT recommendations after MRI-Bx for patients in whom no ADT (left panel) or short-course ADT (right panel) were initially recommended.

Table 1

Patient characteristics

	Number of Patients (%)
PSA (ng/ml)	
<10	32 (43.8)
10–>20	19 (26.0)
>20	22 (30.1)
Highest Gleason Score	
Benign	5 (6.9)
Gleason 6	8 (11.0)
Gleason 7	26 (35.6)
Gleason 8–10	34 (46.6)
Clinical T Stage (No MRI)	
T1c–T2a	67 (91.8)
T2b–T2c	3 (4.1)
T3a–T3b	3 (4.1)
Initial NCCN Risk Group	
No Malignancy Identified	5 (6.8)
Very-Low Risk	1 (1.4)
Low Risk	3 (4.1)
Intermediate Risk	27 (37.0)
High Risk	19 (26.0)
Very-High Risk	18 (24.7)

*
of the 73 total patients included in the study

Table 2

Comparison of Pathologic findings from SOC-Bx and MRI-Bx

		SOC-Bx	MRI-Bx	Combined
Total Number of Cores				
	Range	12–25	2–12	14–35
	Mean	15.5	6.11	21.65
	Median	12	6	20
Percent Positive Cores				
	Range	0–100%	0–100%	6.75–100%
	Mean	36.74%	70.90%	45.66%
	Median	33%	75%	44.01%
Primary Gleason Pattern		Number of Patients (%)	Number of Patients (%)	Combined (%)
	Benign	5 (6.8)	3 (4.1)	0
	3	27 (37.0)	19 (26.0)	18 (24.7)
	4	39 (53.4)	50 (68.5)	53 (72.6)
	5	2 (2.7)	1 (1.4)	2 (2.7)
Total Gleason Score		Number of Patients (%)	Number of Patients (%)	Combined (%)
	Benign	5 (6.8)	3 (4.1)	0
6	3+3	8 (11.0)	4 (5.5)	2 (2.7)
7	3+4	19 (26.0)	15 (20.5)	16 (21.9)
	4+3	7 (9.6)	10 (13.7)	10 (13.7)
8–10	4+4	20 (27.4)	22 (30.1)	24 (32.9)
	4+5	12 (16.4)	18 (24.7)	19 (26.0)
	5+4	2 (2.7)	1 (1.4)	2 (2.7)
	5+5	0	0	0