Impact of Gleason Subtype on Prostate Cancer Detection Using Multiparametric Magnetic Resonance Imaging: Correlation with Final Histopathology

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Purpose: We determined whether Gleason pattern 4 architecture impacts tumor visibility on multiparametric magnetic resonance imaging and correlates with final histopathology.

Materials and Methods: A total of 83 tumor foci were identified in 22 radical prostatectomy specimens from patients with a prior negative biopsy who underwent magnetic resonance/ultrasound fusion biopsy followed by radical prostatectomy from January 2015 to July 2016. A genitourinary pathologist rereviewed tumor foci for Gleason architectural subtype. Each prostate imaging reporting and data system category 3 to 5 lesion on multiparametric magnetic resonance imaging was paired with its corresponding pathological tumor focus. Univariable and multivariable analyses were performed to determine predictors of tumor visibility.

Results: Of the 83 tumor foci identified 26 (31%) were visible on multiparametric magnetic resonance imaging, 33 (40%) were Gleason score 3 + 3 and 50 (60%) were Gleason score 3 + 4 or greater. Among tumor foci containing Gleason pattern 4, increasing tumor size and noncribriform predominant architecture were the only independent predictors of tumor detection on multivariable analysis (p = 0.002 and p = 0.011, respectively). For tumor foci containing Gleason pattern 4, 0.5 cm or greater, multiparametric magnetic resonance imaging detected 10 of 13 (77%), 5 of 14 (36%) and 9 of 10 (90%) for poorly formed, cribriform and fused architecture, respectively (p = 0.01). The size threshold for the detection of cribriform tumors was higher than that of other architectural patterns. Furthermore, cribriform pattern was identified more frequently on systematic biopsy than on targeted biopsy.

Conclusions: Reduced visibility of cribriform pattern on multiparametric magnetic resonance imaging has significant ramifications for prostate cancer detection, surveillance and focal therapy.

Key Words: magnetic resonance imaging, prostatic neoplasms, biopsy

Abbreviations and Acronyms

ADC = apparent diffusion coefficient
DWI = diffusion weighted imaging
GS = Gleason score
mp = multiparametric
MR = magnetic resonance
MRI = magnetic resonance imaging
PI-RADS™ = Prostate Imaging Reporting and Data System
ROI = region of interest
RP = radical prostatectomy
SB = systematic biopsy
TB = targeted biopsy
US = ultrasound
WI = weighted imaging

MULTIPARAMETRIC MRI of the prostate is increasingly being adopted for prostate cancer detection and surveillance, and as a guide for focal therapy. The advantage of mpMRI is its high sensitivity for the detection of clinically significant prostate cancers which contain Gleason pattern 4. MR/US fusion biopsy technology can aid urologists when targeting specific
lesions and increase the detection rate for clinically significant prostate cancer. An additional advantage of mpMRI is that it more frequently detects GS 3+4 or greater tumors compared to GS 3+3 tumors, since GS 3+3 is increasingly recognized as an indolent cancer with a favorable prognosis.

Several limitations of mpMRI have been previously described. It is well-known that tumor size is one of the strongest predictors of mpMRI detection. Le et al correlated mpMRI findings with tumor characteristics at RP and found that prostate glands with multifocal tumors had more lesions frequently missed compared to glands with solitary tumors. Nevertheless, the missed tumors were typically nonindex tumors, which likely have a less significant role in oncologic outcomes compared to index tumors.

Since mpMRI is rapidly being adopted for use in prostate cancer detection and surveillance, and as a guide for focal therapy, understanding the limits of mpMRI sensitivity for detecting tumors containing Gleason pattern 4 is essential. Gleason pattern 4 is a heterogeneous group that can be further classified into several architectural patterns, including poorly formed, cribriform and fused glands. Recent studies suggest that cribriform architecture may be more aggressive and that further optimization of Gleason scoring may be required.

Another study reported that patients with cribriform pattern had decreased overall survival compared to those with noncribriform pattern 4. Currently, no studies to our knowledge have evaluated the impact of Gleason pattern 4 architectural pattern on the sensitivity of mpMRI for prostate cancer detection.

**METHODS**

In this retrospective study we identified 83 individual tumor foci in 22 RP specimens of patients who consecutively had preoperative MR/US fusion biopsies after at least 1 prior negative systematic biopsy at our institution from January 2015 to July 2016 (table 1). We excluded patients with an existing diagnosis of prostate cancer who underwent fusion biopsy to eliminate any potential bias on mpMRI readers having knowledge of the patient’s prior diagnosis and/or GS. A total of 22 patients met the study inclusion criteria. MR/US fusion biopsy consisted of obtaining at least 3 targeted biopsy cores and a standard 12-core systematic biopsy. This study was approved by the institutional review board.

Prostate specimens were sectioned at 3 to 5 mm intervals from apex to base and were rereviewed by a genitourinary pathologist who was blinded to mpMRI results. Several variables were collected for each tumor focus measuring at least 0.1 cm in greatest dimension, including percent Gleason pattern 4 involvement, overall GS, predominant architectural pattern (poorly formed, cribriform, fused), tumor size, sector (anterior/posterior), regional part (apex/mid/base), laterality (left/right) and presence of extraprostatic extension. The predominant architectural pattern was defined as the pattern occupying more than 50% of regions containing only Gleason pattern 4. GS was assigned in accordance with the most recent International Society of Urological Pathology Consensus Conference in 2014. Gleason Grade Group was also assigned as previously reported.

All prostate mpMRI examinations were performed on 2 3T Siemens Skyra scanners (Erlangen, Germany). All patients underwent scanning without the use of an endorectal coil. Prostate mpMRI examinations consisted of high resolution axial, coronal and sagittal fast spin echo T2-weighted images, axial T1WI of the full pelvis and axial small field of view T1WI. Axial DWI using a high B value of 1,600 (calculated) was obtained. Dynamic post-contrast axial VIBE (volumetric interpolated breath-hold examination) images and full pelvis static post-contrast axial T1 VIBE with fat saturation were obtained. Post-processing of contrast kinetics to assess for rapid wash-in and lesion targeting was performed using Dynacad software (Invivo Corp., Gainesville, Florida).

A suspicion score from 1 to 5 was assigned to each region of interest according to PI-RADS v2 by 2 fellowship trained radiologists with more than 3 years of experience reading mpMRI. Each individual tumor focus on radical prostatectomy and each ROI on mpMRI was assigned a regional part (apex, mid or base), sector (anterior or posterior) and laterality (left or right) in accordance with PI-RADS v2 anatomical designations. Each ROI with a PI-RADS score of 3 to 5 was paired with its corresponding pathological tumor focus by matching anatomical designations. When a tumor focus matched the same regional part, sector and laterality as a ROI, it was classified as “visible.” When a tumor focus lacked a corresponding ROI with the same regional part, sector and laterality, it was classified as “not visible.” For large tumor foci extending across more than 1 anatomical region, if mpMRI was able to detect any portion of the tumor, the tumor was classified as visible. All ROIs were rereviewed by a single mpMRI radiologist to verify that each ROI corresponded to a true pathological tumor focus. No false-positive mpMRI reads were identified.

Univariable analysis was performed using the Mann-Whitney U test for continuous variables and the chi-square test for categorical variables. Tumor size and percent of Gleason pattern 4 involvement were analyzed as continuous variables. Extraprostatic extension, sector,

**Table 1. Patient characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (IQR)</th>
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<tbody>
<tr>
<td>Median age (IQR)</td>
<td>63 (60–69)</td>
</tr>
<tr>
<td>Median ng/ml prostate specific antigen (IQR)</td>
<td>8.5 (5.8–16.3)</td>
</tr>
<tr>
<td>Median ROIs on MRI (range)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Median tumor foci on RP (range)</td>
<td>3 (7)</td>
</tr>
<tr>
<td>No. highest biopsy GS (Grade Group):</td>
<td></td>
</tr>
<tr>
<td>3+3 (1)</td>
<td>2</td>
</tr>
<tr>
<td>3+4 (2)</td>
<td>9</td>
</tr>
<tr>
<td>4+3 (3)</td>
<td>8</td>
</tr>
<tr>
<td>4+4 (4)</td>
<td>3</td>
</tr>
<tr>
<td>No. prostatectomy GS (Grade Group):</td>
<td></td>
</tr>
<tr>
<td>3+4 (2)</td>
<td>10</td>
</tr>
<tr>
<td>4+3 (3)</td>
<td>11</td>
</tr>
<tr>
<td>4+4 (4)</td>
<td>1</td>
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</tbody>
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