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Validation of Prostate Imaging-Reporting and Data System Version 2: A Retrospective Analysis

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Purpose: Use of magnetic resonance imaging (MRI)/transrectal ultrasound fusion biopsies to determine the accuracy of multiparametric MRI (mpMRI), using Prostate Imaging-Reporting and Data System version 2 (PI-RADSv2), for detecting clinically significant prostate cancer in the overall gland and specifically the peripheral zone (PZ) and transitional zone (TZ).

Methods: A retrospective analysis of patients who underwent fusion biopsy identified 137 men with 231 prostate lesions was approved by the Institutional Review Board. Subjects initially classified under PI-RADSv1 criteria were regraded using PI-RADSv2 by a radiologist blinded to PI-RADSv1 score and biopsy results. Spearman correlation, chi-squared, and logistic regression analysis were performed.

Results: There was positive correlation between PI-RADSv2 and Gleason scores ($P < 0.001$). In the PZ, mpMRI demonstrated 100% sensitivity, 100% negative predictive value, and 35.9% positive predictive value, compared to 100%, 100%, and 27.1%, respectively, for TZ lesions. When predicting clinically significant prostate cancer, the PI-RADSv2 area under the curve for TZ lesions was 0.844 (95% CI: 0.753-0.935, $P < 0.001$) and 0.769 (95% CI: 0.684-0.854, $P < 0.001$) for PZ lesions. Combining PI-RADSv2 with additional risk factors (body mass index, prostate-specific antigen density, digital rectal examination) improved the area under curve.

Conclusions: PI-RADSv2 achieves excellent sensitivity and negative predictive value for both PZ and TZ lesions.

Introduction

Prostate cancer (PCa) is the second most common cancer among men worldwide.[1] In the USA, Canada, and Europe, current expert opinion and guidelines recommend a 10-12 core transrectal ultrasound (TRUS) guided biopsy for men with elevated prostate-specific antigen (PSA) or abnormal digital rectal examination (DRE).[2-4] However, the false-negative rate of 12-core biopsies can exceed 30%,[5] and saturation prostate biopsy as an initial screening strategy does not significantly improve cancer detection.[6] Multiparametric magnetic resonance imaging (mpMRI) of the prostate coupled with MRI/TRUS fusion biopsy has been proposed to improve PCa detection rates.[7]

MpMRI combines T2-weighted, diffusion-weighted (DWI), apparent diffusion coefficient mapping, dynamic contrast enhancement, or spectroscopy to evaluate the prostate gland. Prostate mpMRI is a useful tool for tumor detection,[8,9] particularly in patients with higher-grade PCa,[10] and for identifying potential active surveillance patients.[11,12] Compared to TRUS alone, fusing mpMRI and TRUS data during prostate biopsy can increase cancer detection rates.[13,14]

Given the lack of uniform mpMRI protocols and prostate reporting, the European Society of Urogenital Radiology (ESUR) produced a set of standardized guidelines in 2012.[15] These guidelines, Prostate Imaging-Reporting and Data System version 1 (PI-RADSv1), have previously been validated as a risk stratification model with high PCa detection accuracy.[16-20] When used to guide biopsies, mpMRI using PI-RADSv1 can help detect a larger proportion of clinically significant PCa (csPCa) than standard TRUS-biopsy.[7,12] However, mpMRI-guided biopsy alone has been shown to miss some PCa that would be detected by random TRUS-biopsy; and authors have found best results with combined guided and random TRUS-biopsy.[7,21]

Nonetheless, as discussed by Barentsz et al,[22] PI-RADSv1 has its shortcomings. In 2014 the American College of Radiology (ACR) and the ESUR steering committee introduced a revised scoring system, PI-RADS version 2 (PI-RADSv2).[23] PI-RADSv2 was developed to improve standardization and efficacy of the PI-RADS scoring system, focusing on csPCa by addressing the evaluation of PI-RADS score 3 lesions and the establishment of a global PI-RADS score.[17,24,25] Significant changes from PI-RADS version 1 to version 2 involved the establishment of DWI as the primary sequence determining scores in the peripheral zone, (PZ) with dynamic contrast enhancement serving to influence PI-RADSv2 scores of 3; and T2 as the primary sequence for the transitional zone, (TZ) with DWI influencing PI-RADSv2 scores of 3. PI-RADSv2 eliminated the use of MR spectroscopy in the paradigm.[26,27]

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Although prior studies have contributed to validating PI-RADSv2 as an accurate method to detect PCa,[7,26,27] few studies, such as Cash et al,[7] have used the added benefit of MRI/TRUS fusion biopsy for radiologic-pathologic correlation, or further stratified accuracy and risk into PZ or TZ lesions.[19,20,28]

We hypothesize that PI-RADSv2 scores have a high diagnostic accuracy for csPCa and a positive correlation with Gleason score. Thus, the purpose of our study is to use a combination biopsy method (12-core plus MRI/TRUS fusion biopsies) to determine and compare the accuracy of mpMRI, using PI-RADSv2, for detecting csPCa in the PZ and TZ.

Materials and Methods

A retrospective study protocol with strict adherence to the United States Health Insurance Portability and Accountability Act (HIPAA) policies was reviewed and approved by the Institutional Review Board. The informed consent requirement was waived by the Institutional Review Board.

In this single center retrospective study, we reviewed the records of 206 consecutive patients who underwent prostate mpMRI, owing to elevated PSA, abnormal DRE, or other concerning clinical findings at the discretion of our urologists from September 2014 through November 2015. Subject inclusion criteria for this study were: males having undergone mpMRI with subsequent 12-core Artemis 3D TRUS (Eigen, Grass Valley, CA) and MRI/TRUS fusion biopsy using Artemis and ProFuse software (Eigen, Grass Valley, CA) at our institution. Subjects were excluded from the analysis if they did not undergo both 12-core and MRI/TRUS fusion biopsy, or if complete follow-up data was unavailable. Subjects younger than 40 years old were considered outliers from the clinically encountered presentation of PCa and excluded from the analysis.

A total of 137 men (Table 1), having a mean age of 65.2 years (age range: 41-96 y) with a total of 231 identified prostate lesions on mpMRI, were included in this study.

PI-RADSv2 Evaluation

All mpMRI data were reviewed and scored under PI-RADS v2 criteria by a fellowship-trained, board-certified radiologist (R.H.), with 5+ years of experience with prostate MRI. The radiologist was given access to prebiopsy clinical data, per usual routine, but blinded to biopsy results to prevent bias. The reader was blinded to prior mpMRI reports, including any previously reported lesions.

Definition of Terms Used in Analysis

A DRE was considered abnormal if there was any palpable nodule. A positive 12-core or fusion biopsy was defined as Gleason score ≥6 lesion within the same sector as a corresponding lesion identified on mpMRI. A positive concordant 12-core biopsy was a Gleason score ≥6 lesion that lateralized to the corresponding lesion identified on mpMRI. A positive combination biopsy was defined as any identified mpMRI lesion having a corresponding positive 12-core or fusion biopsy.

Our study defined csPCa as biopsies with a Gleason score ≥7.

A negative mpMRI study for csPCa of the prostate was defined as an overall PI-RADSv2 score 1-2, whereas a positive study was defined as a PI-RADSv2 score 3-5. Our initial experience with PI-RADSv2 score 1-2 lesions demonstrated only negative biopsies and as such we defined those lesions as low suspicion or negative for csPCa with no clinical indication for fusion biopsy. A subset of lesions ($n = 39$) was given a PI-RADSv2 score of 1 or 2, but were still biopsied owing to clinical factors at the discretion of the performing urologist.

TABLE 1
Baseline characteristics of patient cohort

Median age in years (IQR)	65.0 (60-71)
Median BMI in kg/m^2 (IQR)	27.0 (24.6-29.7)
Median PSA in ng/mL (IQR)	6.8 (4.6-9.4)
Median prostate volume in mm^3 (IQR)	50 (36-75)
Median PSA density in ng/mL*mm^3 (IQR)	0.12 (0.08-0.19)
% Abnormal DRE	13.0 (17/137)

The baseline clinical characteristics of the patient cohort of this study ($n = 136$). PSA density was calculated using the following formula: PSA density = PSA/prostate volume on MRI.
IQR = interquartile range.

Statistical Tests

Statistical analysis was performed with SPSS version 22.0 (IBM, Armonk, New York). PI-RADSv2 score was redefined into binary values for chi-squared analysis. Given that Gleason score is the major basis of our definition of csPCa, the Spearman rank-order correlation test was used to evaluate the association between Gleason score and overall PI-RADSv2 score. The higher Gleason score of the two biopsy methods (12-core or MRI/TRUS fusion biopsy) was ued for Spearman correlation. Logistic regression models with receiver operating characteristic curve and area under the curve (AUC) analysis were used to assess the relationship between csPCa and overall PI-RADSv2 score, adjusting for variables such as patient age, PSA, body mass index (BMI), PSA density, and DRE findings. Statistical significance was defined as $P < 0.05$.

Results

The baseline clinical characteristics of the study cohort are presented in Table 1.

mpMRI, TRUS-Guided 12-Core Biopsy, and MRI/TRUS Fusion Biopsy Results

The mean PI-RADSv2 scores of PZ, TZ, and all lesions on mpMRI were 3.4 ($n = 142$), 3.2 ($n = 89$), and 3.3 ($n = 231$), respectively. A total of 192/231 (83.1%) identified lesions were considered positive on mpMRI. The median number of days between the subject's mpMRI and prostate biopsy was 35 days (interquartile range: 14.0-64.5 d).

No patient had a history of prior positive prostate biopsy. For all TRUS-guided 12-core biopsies, 82/231 (35.5%) lesions were positive, and 42/231 (18.2%) lesions were found to be csPCa. In the PZ, 59/142 (41.5%) lesions were positive on 12-core biopsy, and 31/142 (21.8%) were found to be csPCa. In the TZ, 23/89 (25.8%) lesions were positive on 12-core biopsy, and 11/89 (12.4%) were found to be csPCa.

When assessing the MRI/TRUS fusion biopsy results, a total of 77/231 (33.3%) lesions were positive, and 50/231 (21.6%) were found to be csPCa. Of the biopsied PZ lesions, 55/142 (38.7%) were positive on MRI/TRUS fusion biopsy, and 36/142 (25.3%) were found to be csPCa. Of the biopsied TZ lesions, 22/89 (24.7%) were positive on MRI/TRUS fusion biopsy, and 14/89 (15.7%) lesions were found to be csPCa.

When considering the dual TRUS-guided 12-core and MRI/TRUS fusion biopsies as a single combination biopsy method, 98/231 (42.4%) lesions were positive, and 58/231 (25.1%) were found to be csPCa. For PZ, 68/142 (47.9%) lesions were positive on combination biopsy, and 42/142 (29.6%) were found to be csPCa. Of the biopsied