Proposed Adjustments to PI-RADS Version 2 Decision Rules: Impact on Prostate Cancer Detection[1]

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Purpose: To test the impact of existing Prostate Imaging Reporting and Data System (PI-RADS) version 2 (V2) decision rules, as well as of proposed adjustments to these decision rules, on detection of Gleason score (GS) 7 or greater (GS ≥7) prostate cancer.

Materials and Methods: Two radiologists independently provided PI-RADS V2 scores for the dominant lesion on 343 prostate magnetic resonance (MR) examinations. Diagnostic performance for GS ≥7 tumor was assessed by using MR imaging-ultrasonography fusion-targeted biopsy as the reference. The impact of existing PI-RADS V2 decision rules, as well as a series of exploratory proposed adjustments, on the frequency of GS ≥7 tumor detection, was evaluated.

Results: A total of 210 lesions were benign, 43 were GS 6, and 90 were GS ≥7. Lesions were GS ≥7 in 0%–4.1% of PI-RADS categories 1 and 2, 11.4%–27.1% of PI-RADS category 3, 44.4%–49.3% of PI-RADS category 4, and 72.1%–73.7% of PI-RADS category 5 lesions. PI-RADS category 4 or greater had sensitivity of 78.9%–87.8% and specificity of 75.5%-79.1 for detecting GS ≥7 tumor. The frequency of GS ≥7 tumor for existing PI-RADS V2 decision rules was 30.0%–33.3% in peripheral zone (PZ) lesions upgraded from category 3 to 4 based on dynamic contrast enhancement (DCE) score of positive; 50.0%–66.7% in transition zone (TZ) lesions upgraded from category 3 to 4 based on diffusion-weighted imaging (DWI) score of 5; and 71.7%–72.7% of lesions in both zones upgraded from category 4 to 5 based on size of 15 mm or greater. The frequency of GS ≥7 tumor for proposed adjustments to the decision rules was 30.0%–60.0% for TZ lesions upgraded from category 3 to 4 based on DWI score of 4; 33.3%–57.1% for TZ lesions upgraded from category 3 to 4 based on DCE score of positive when incorporating new criteria (unencapsulated sheetlike enhancement) for DCE score of positive in TZ; and 56.4%–61.9% for lesions in both zones upgraded from category 4 to 5 based on size of 10–14 mm. Other proposed adjustments yielded GS ≥7 tumor in less than 15% of cases for one or more readers.

Conclusion: Existing PI-RADS V2 decision rules exhibited reasonable performance in detecting GS ≥7 tumor. Several proposed adjustments to the criteria (in TZ, upgrading category 3 to 4 based on DWI score of 4 or modified DCE score of positive; in PZ or TZ, upgrading category 4 to 5 based on size of 10–14 mm) may also have value for this purpose.

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Prostate magnetic resonance (MR) imaging is a valuable and increasingly utilized test for guiding multiple aspects of prostate cancer management (1). However, marked variation in interpretative approaches has historically hindered its clinical application (2). The recently released Prostate Imaging Reporting and Data System (PI-RADS) version 2 (V2) guidelines (2), jointly developed by the American College of Radiology, European Radiology of Uroradiology, and AdMeTech Foundation, represent a key advance in standardizing prostate MR imaging interpretation by providing an explicit system for evaluating individual pulse sequences, as well as for integrating findings across pulse sequences to derive overall risk assessment categories. The system seeks to simplify interpretation through a straightforward framework based on a set of practical criteria that can be readily applied in clinical practice (2). Initial investigations (3,4) have shown moderate interreader reproducibility (eg, κ values of 0.46–0.55 in the peripheral zone [PZ]) with use of PI-RADS V2).

PI-RADS V2 provides assessment categories on a 1–5 scale. These are intended to optimize detection of clinically significant cancer, for which PI-RADS V2 uses a threshold Gleason score (GS) 7 or greater (GS ≥7) (2). Further, PI-RADS V2 states that biopsy should be considered for PI-RADS categories 4 or 5, though biopsy may or may not be appropriate for PI-RADS assessment category 2 or 3, depending on nonimaging factors (2). Given this algorithm, PI-RADS V2 seeks to define the five assessment categories in a way that maintains a balance between achieving high sensitivity for GS ≥7 tumor and avoiding an excessive number of biopsies that are benign or harbor low-grade tumor. In the PZ, the assessment category matches the score assigned for diffusion-weighted imaging (DWI), regardless of the assessment of other pulse sequences, except that dynamic contrast enhancement (DCE) score of positive upgrades the overall category from 3 to 4. In the transition zone (TZ), the assessment category matches the score assigned for T2-weighted imaging, regardless of the assessment of other pulse sequences, except that a DWI score of 5 upgrades the overall category from 3 to 4. Lesion size only influences assessment in that a size of 15 mm or greater increases an individual pulse sequence score on T2-weighted or DWI from 4 to 5. Such criteria for upgrading a lesion's assigned category based on combinations of multiple suspicious findings are intended to help improve the sensitivity of individual PI-RADS assessment categories for clinically significant cancer.

PI-RADS V2 is acknowledged to reflect a combination of available data and consensus opinion (2). In particular, the details of the current decision rules are largely based on the collective experience of the system's authors. While early investigations of PI-RADS V2 have reported the diagnostic accuracy of the various assessment categories (3,5,6), a paucity of studies have provided a more nuanced evaluation of the impact of the existing decision rules. Since PI-RADS V2 is considered

Advances in Knowledge

- In 343 prostate lesions evaluated with PI-RADS version 2 (V2) by two independent readers using MR imaging-US fusion-targeted biopsy as reference, peripheral zone (PZ) lesions upgraded from category 3 to 4 based on dynamic contrast enhancement (DCE) score of positive (focal early enhancement corresponding to suspicious finding at T2-weighted and/or diffusion-weighted imaging [DWI]) were Gleason score 7 or greater (GS ≥7) tumor in 30.0%–33.3%, while transition zone (TZ) lesions upgraded from category of 3 to 4 based on DWI score of 5 were GS ≥7 tumor in 50.0%–66.7%.
- In the two zones combined, lesions upgraded from category 4 to 5 based on a size of 15 mm or greater were GS ≥7 tumors in 71.7% (33 of 46) to 72.7% (24 of 33) of cases.
- Several proposed adjustments to PI-RADS V2 decision rules were associated with GS ≥7 tumor in 20% or more of upgraded cases for both readers: in TZ, upgrading category 3 to 4 based on a DWI score of 4 (30.0%–60.0%); in TZ, upgrading category 3 to 4 based on DCE score of positive (33.3%–57.1%) when incorporating morphologic features of enhancement (encapsulated sheetlike, rather than encapsulated swirled or popcorn-like, enhancement) not currently in PI-RADS V2; and in both zones, upgrading category 4 to 5 based on a size ranging from 10 to 14 mm (56.4%–61.9%).
- A spectrum of additional proposed adjustments to the PI-RADS V2 decision rules were associated with GS ≥7 tumor in less than 15% of cases for at least one reader.

Implication for Patient Care

- Exploratory proposed adjustments to PI-RADS V2 decision criteria may have added value in the use of PI-RADS V2 for detection of GS ≥7 tumor.

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Abbreviations:
DCE = dynamic contrast enhancement
DWI = diffusion-weighted imaging
GS = Gleason score
GS ≥7 = GS 7 or greater
PI-RADS = Prostate Imaging Reporting and Data System
PZ = peripheral zone
TZ = transition zone
V2 = version 2

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Conflicts of interest are listed at the end of this article.

to be a document in evolution, warranting further optimization based on continued experience and objective data (2), scientific investigations are needed to validate the system and help guide potential future revisions. Of note, a number of possible refinements can readily be conjectured based on simple adjustments to the system's current rubric for deriving overall assessment categories. These refinements entail introducing additional criteria for increasing a lesion's final PI-RADS category based on either lesion size or suspicious findings across multiple pulse sequences, with the intent of further improving the sensitivity for GS ≥7 tumor at a given PI-RADS threshold. Although such modifications may lead to a somewhat more nuanced system, these may be warranted if shown to improve the system's clinical performance. Therefore, our aim in this study was to test the impact of existing PI-RADS V2 decision rules, as well as proposed adjustments to these rules, on the detection of GS ≥7 prostate cancer.

Materials and Methods

Patients

This retrospective study was compliant with the Health Insurance Portability and Accountability Act and approved by our institutional review board, which waived the requirement for written informed consent. At our institution (a large academic medical center), prostate MR imaging is routinely performed before all prostate biopsies, in the absence of contraindication to MR imaging, to localize suspicious regions to target at the time of biopsy (7). In addition, during the period of this study (prior to the dissemination of PI-RADS V2), patients were selected for MR imaging-ultrasonography (US) fusion-targeted biopsy based on a combination of factors (patient and physician preference; MR imaging findings; clinical risk factors including family history, prior biopsy results, digital rectum examination findings, prostate-specific antigen level, as well as other serum and urine biomarkers) and not based on any uniform threshold in terms of the level of suspicion at MR imaging. For this investigation, we conducted searches of an institutional database of patients who underwent MR imaging-targeted transrectal US-guided biopsy by using a real-time MR imaging-US fusion system, with MR imaging performed between September 2013 (reflecting the approximate time of incorporation of a new DCE sequence into our institution's prostate MR imaging protocol, as described below) and February 2015 (reflecting the time of the most recent update to the database at the time of the search). MR imaging–targeted lesions were classified into three groups based on the results of the targeted cores: benign, GS 6 tumor (representing the lowest GS assigned at our institution), and GS ≥7 tumor. Given the possibility of misregistration error at the time of fusion targeting (8,9), standardized options within the database were selected at the time of the initial search to filter patients from the search results on the basis of the results of concurrent systematic biopsy; the relative position of the fusion and systematic cores was not explicitly captured in the database as a searchable field and thus not taken into consideration in this process. Specifically, lesions that were benign at targeting were filtered if any concurrent systematic cores were positive for tumor, and lesions that represented GS 6 tumor at targeting were filtered if any concurrent systematic cores were positive for GS ≥7 tumor. Among 413 patients identified with this search process, 70 patients were then excluded as follows: MR imaging performed at outside facility (n = 13), MR imaging performed at 1.5 T (n = 3), intravenous contrast material not administered (n = 3), marked artifact on MR images attributable to hip implant (n = 6), nonstandard MR imaging examination (n = 20), duplicate patient (n = 2), no concurrent systematic biopsy (n = 4), and prior treatment for prostate cancer (n = 19). In patients with multiple lesions, the lesion having the most aggressive pathologic outcome at fusion biopsy was taken into consideration. These exclusions left a final cohort of 343 patients (mean age, 64 years ± 8 [standard deviation]; median, 64 years; mean prostate-specific antigen level, 10.1 μg/mL ± 45.3; median, 5.8 μg/mL) for further analysis. Figure 1 summarizes the process of identifying the patient sample. The indications for MR imaging in these patients were suspicion of prostate cancer without prior prostate biopsy (n = 161), prior negative biopsy findings (n = 107), and prior positive biopsy findings (n = 75). Between two and 195 of the patients were included in earlier unrelated studies from our institution that evaluated the optimization of the acquisition and interpretation of prostate MR imaging (10–13), results from MR imaging-US fusion-targeted prostate biopsy (14–16), or the interobserver reproducibility of PI-RADS V2 (4,17,18); none of these explored the impact of proposed adjustments to the PI-RADS V2 decision rules, as is the subject of the present investigations.

MR Imaging

All MR examinations were performed at 3 T (Magnetom Trio, Skyra, Prisma, or Biograph mMR; Siemens, Erlangen, Germany) by using pelvic phased-array coils (six coil elements for Trio and Biograph mMR imagers; 18 coil elements for Skyra and Prisma imagers). No examinations performed by using the Biograph mMR imager included concurrent positron emission tomographic imaging. Pulse sequences included axial turbo spin-echo T2-weighted imaging (repetition time msec/echo time msec, 4000–4960/105; section thickness, 3 mm; field of view, 180 × 180 mm; matrix, 256 × 256; parallel imaging factor, two; three signals acquired) and single-shot echo-planar DWI (4100/86; section thickness, 3 mm; field of view, 200 × 200; matrix, 100 × 100; parallel imaging factor, two; 10 signals acquired; b values, 50 and 1000 sec/mm^2) with inline reconstruction via a monoexponential fit of the apparent diffusion coefficient map and a calculated high-b-value image set at a b value of 1500 sec/mm^2 (19). In addition, DCE MR imaging was performed per our routine clinical protocol by using a continuously

acquired golden-angle radial acquisition (3192 radial spokes; 4.10/1.89; flip angle, 16°; section thickness, 3 mm; field of view, 240 × 240; matrix, 224 × 224; total acquisition time, 5 minutes 38 seconds); the reconstruction was based on a combination of parallel imaging and compressed sensing at a temporal resolution of 2.3 seconds by using 21 radial spokes for each time point (20). DCE imaging was performed by using 0.1 mmol/kg of gadobutrol (Bayer Healthcare, Leverkusen, Germany) administered at a rate of 3 mL/sec via power injector.

Image Assessment

The biopsy database was queried for the final set of included patients to generate a listing of the location of the targeted lesion in each case, although excluding the actual subsequent biopsy results. A radiologist with 8 years of experience in prostate MR imaging (A.B.R.) initially reviewed the examinations in conjunction with information regarding the lesion location to prepare a digital presentation with a screenshot of the targeted lesion in each case. This presentation contained a single image for each examination that showed the location of the target on a section obtained from the axial T2-weighted pulse sequence. Other pulse sequences were not used to depict the lesion location to avoid influencing the results based on the selected pulse sequence. In addition, an arrow was placed pointing to the approximate center of the target, and a notation was provided assigning the lesion to the PZ or TZ in view of distinct PI-RADS V2 criteria for PZ and TZ lesions. These steps were taken so that the readers would subsequently evaluate the same lesions using the same PI-RADS V2 criteria.

Image Review

Examinations were independently evaluated by two radiologists (A.B.R. and J.M.R., with 3 years of experience in prostate MR imaging) in conjunction with the previously noted presentation of lesion locations. These radiologists had used PI-RADS V2 for clinical prostate MR imaging interpretation for approximately 6 months prior to reviewing examinations for the purposes of this study. In addition, one of the radiologists was a contributor to PI-RADS V2 and provided training to the other radiologist regarding the system's use. All pulse sequences were reviewed in a single session. The readers assigned each lesion a score on a 1–5 scale for both T2-weighted imaging and DWI, as well as a score of positive or negative for DCE. Separate criteria for T2-weighted imaging were used in the PZ and TZ. Given the frequent hypervascularity of benign prostatic hyperplasia nodules (21), we incorporated morphologic criteria for assessing DCE in the TZ that are not a component of PI-RADS V2. Specifically, DCE was not considered positive for TZ lesions exhibiting an encapsulated swirled or popcorn-like enhancement pattern; rather this score was reserved for unencapsulated sheetlike confluent regions of enhancement. In addition, readers measured the size of the lesion based on the measurement approach described in PI-RADS V2. The PI-RADS assessment category was generated on the basis of the readers' interpretations for the individual pulse sequences by using the scheme provided by PI-RADS V2. When the PI-RADS category was 5, the readers noted those cases in which this category was due to the lesion having a size of 15 mm or greater (rather than being on the basis of definitive invasive behavior or extraprostatic extension).

Reference Standard

All MR imaging–identified lesions underwent targeted biopsy performed by a urologist using the Artemis system (Eigen, Grass Valley, Calif). ProFuse software (Eigen) was used to annotate the boundaries of the lesions, as well as to segment the prostate (22). For each lesion, at least two fusion-guided targeted cores were obtained.

Figure 1

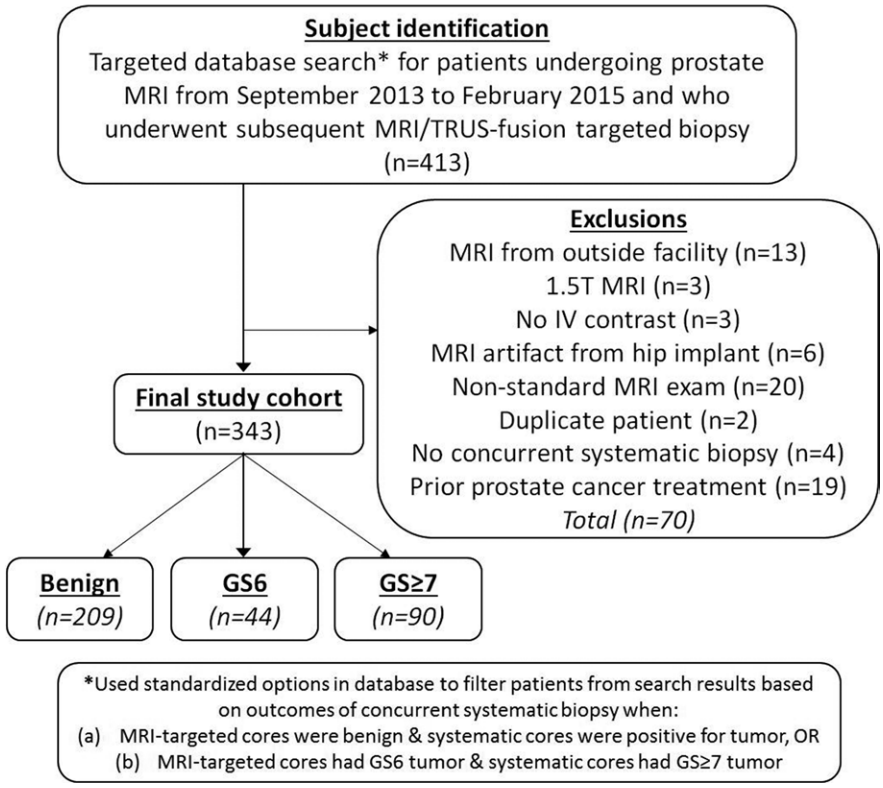

Figure 1: Flowchart depicts the study population. *IV* = intravenous, *TRUS* = transrectal US.

Statistical Assessment

The distribution of the assigned PI-RADS V2 categories was computed, as were the frequency of tumors and of GS ≥7 tumors for each category, overall and separately in the PZ and TZ. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of PI-RADS V2 category 4 or greater (reflecting the threshold at which PI-RADS V2 indicates that targeted biopsy should routinely be considered [2]) tumor and GS ≥7 tumor were computed for the two readers, overall and separately in the PZ and TZ. Interreader agreement for individual pulse sequence scores and for overall PI-RADS category was computed, overall and separately in the PZ and TZ. Agreement was computed by using the simple kappa coefficient for the binary measure of DCE as positive or negative and by using a linear weighted kappa coefficient (weights of 1, 0.75, 0.50, 0.25, and 0 for differences of 0, 1, 2, 3, and 4 categories, respectively) for the remaining five-point ordinal measures. Interreader agreement was classified as follows (4): 0.01–0.20, slight; 0.21–0.40, fair; 0.410–0.60, moderate; 0.61–0.80, substantial, and 0.81–0.99, almost perfect. Then, a series of exploratory assessments were performed to evaluate the impact on tumor detection of the three existing decision rules (hereafter referred to as E1 to E3b) within the PI-RADS V2 guidelines (E1 in PZ, upgrade category 3 to a 4 based on a DCE score of positive; E2 in TZ, upgrade category 3 to a 4 based on a DWI score of 5; E3a in PZ or TZ, upgrade category 4 to a 5 based on a size ≥ 15 mm; E3b in PZ or TZ, upgrade category 4 to a 5 based on a size of 15–19 mm), as well as of eight proposed adjustments (hereafter referred to as P1 to P8) to the decision rules (P1 in PZ, upgrading category 3 to a 4 based on T2-weighted imaging score of 4; P2 in PZ, upgrading category 3 to a 4 based on a T2-weighted imaging score of 5; P3 in TZ, upgrading category 3 to a 4 based on a DWI score of 5; P4 in TZ, upgrading category 3 to a 4 based on a DCE score of positive; P5 in PZ or TZ, upgrading category 3 to a 4 based on a size ≥ 10 mm; P6 in PZ or TZ, upgrading category 3 to a 4 based on a size ≥ 15 mm; P7 in PZ or TZ, upgrading category 3 to a 4 based on a size ≥ 20 mm; P8 in PZ or TZ, upgrading category 4 to a 5 based on a size of 10–14 mm). These decision rules were explicitly framed in terms of either specific pulse sequence–based or size-based criteria for potentially upgrading the overall PI-RADS assessment category. For each existing or proposed adjustment, computations were performed to determine the percentage of examinations that would be eligible for an upgrade in PI-RADS category based on the rule, the percentage of eligible cases in which the PI-RADS category was in fact upgraded by the rule, and the percentage of upgraded cases representing tumor and GS ≥7 tumor. Lesions were only considered to be eligible to be upgraded by the given proposed adjustment when not already being upgraded by the existing decision rules (eg, a PZ lesion being upgraded from category 3 to 4 due to DCE score of positive or a lesion in either zone being upgraded from category 4 to 5 due to definite extra-prostatic extension was not considered to be eligible to be upgraded on the basis of proposed adjustments to the decision rules). The proposed new adjustments largely focused on upgrades from category 3 to 4 given potential application of a threshold category of 4 for selecting patients for targeted biopsy (23). In addition, for purposes of characterizing the size of the lesions within the study cohort, the size measurements of the two readers were averaged and summarized in descriptive fashion. All of these assessments were performed separately for the two readers. Statistical assessment was performed by using SAS software (version 9.3; SAS Institute, Cary, NC).

Table 1

Frequency of Each PI-RADS Category among All Patients, as Well as Frequency of Tumor and GS ≥7 Tumor for Each PI-RADS Category

	Frequency*		Tumor†		GS ≥7 Tumor†	
PI-RADS Category	Reader 1	Reader 2	Reader 1	Reader 2	Reader 1	Reader 2
1	4 (1.2)	14 (4.1)	0 (0/4)	7.1 (1/14)	0 (0/4)	0 (0/14)
2	128 (37.3)	148 (43.2)	8.6 (11/128)	14.2 (21/148)	1.6 (2/128)	4.1 (6/148)
3	79 (23.0)	48 (14.0)	27.8 (22/79)	41.7 (20/48)	11.4 (9/79)	27.1 (13/48)
4	75 (21.9)	90 (26.2)	70.7 (53/75)	63.3 (57/90)	49.3 (37/75)	44.4 (40/90)
5	57 (16.6)	43 (12.5)	84.2 (48/57)	81.4 (35/43)	73.7 (42/57)	72.1 (31/43)

* Data are number patients and data in parentheses are percentages.

† Data are percentages and data in parentheses are numerators and denominators.

Results

Lesion and Tumor Characteristics

Of the 343 lesions, 76.4% (262 of 343) were in the PZ and 23.6% (81 of 343) were in the TZ. At targeted biopsy, 60.9% (209 of 343) of lesions were benign, 12.8% (44 of 343) were GS 6 (3+3), and 26.2% (90 of 343) were GS ≥7 (3+4 [n = 38], 4+3 [n = 21], 4+4 [n = 16], 4+5 [n = 13], 5+4 [n = 2]). Mean lesion size (± standard deviation) at MR imaging was 12 mm ± 6 (median, 11 mm; range, 3–42 mm). At MR imaging, 62.1% (213 of 343), 23.3% (80 of 343), and 9.6% (33 of 343) of lesions were at least 10 mm, 15 mm, and 20 mm, respectively.

Performance of PI-RADS V2

For both readers, the frequency of tumor and of GS 7 or greater tumor showed stepwise increases with increasing PI-RADS category (Table 1, Table E1 [online]). For the two readers, the percentage of lesions positive for GS ≥7 tumor was 0% ([0 of 4] and [0 of 14]) at PI-RADS category 1, 1.6% (two of 128) to 4.1% (six of 148) at PI-RADS category 2, 11.4% (nine of 79) to

Table 2

Diagnostic Accuracy of Detection GS ≥7 Cancer at PI-RADS Category 4 or Greater

	Overall		PZ		TZ	
Statistic	Reader 1	Reader 2	Reader 1	Reader 2	Reader 1	Reader 2
Sensitivity (%)	87.8 (79/90)	78.9 (71/90)	89.6 (60/67)	88.1 (59/67)	82.6 (19/23)	52.2 (12/23)
Specificity (%)	79.1 (200/253)	75.5 (191/253)	79.0 (154/195)	74.9 (146/195)	79.3 (46/58)	77.6 (45/58)
NPV (%)	94.8 (200/211)	91.0 (191/210)	95.7 (154/161)	94.8 (146/154)	92.0 (46/50)	80.4 (45/56)
PPV (%)	59.8 (79/132)	53.4 (71/133)	59.4 (60/101)	54.6 (59/108)	61.3 (19/31)	48.0 (12/25)
Accuracy (%)	81.3 (279/343)	76.4 (262/343)	81.7 (214/262)	78.2 (205/262)	80.2 (65/81)	70.4 (57/81)

Note.—Data in parentheses are numerators and denominators. NPV = negative predictive value, PPV = positive predictive value.

Table 3

Fraction of PI-RADS Assessment Categories Eligible to Be Upgraded and Actually Upgraded Based on Existing and Proposed PI-RADS Decision Rules

	Reader 1		Reader 2	
Decision Rule	Percent Eligible	Percent Upgraded	Percent Eligible	Percent Upgraded
Existing PI-RADS V2				
(E1) In PZ, upgrade 3 to 4 if DCE score of positive	19.8 (68/343)	14.7 (10/68)	14.6 (50/343)	42.0 (21/50)
(E2) In TZ, upgrade 3 to 4 if DWI score of 5	7.0 (24/343)	12.5 (3/24)	7.9 (27/343)	29.6 (8/27)
(E3a) In PZ and TZ, upgrade 4 to 5 if size ≥ 15 mm	31.5 (108/343)	42.6 (46/108)	27.1 (93/343)	35.5 (33/93)
(E3b) Same as above, though only upgrade in 15–19-mm range	31.5 (108/343)	19.4 (21/108)	27.1 (93/343)	20.4(19/93)
Proposed PI-RADS V2				
(P1) In PZ, upgrade 3 to 4 if T2-weighted imaging score of 4	16.9 (58/343)	3.4 (2/58)	8.5 (29/343)	20.7 (6/29)
(P2) In PZ, upgrade 3 to 4 if T2-weighted imaging score of 5	16.9 (58/343)	1.7 (1/58)	8.5 (29/343)	0.0 (0/29)
(P3) In TZ, upgrade 3 to 4 if DWI score of 4	6.1 (21/343)	47.6 (10/21)	5.5 (19/343)	26.3 (5/19)
(P4) In TZ, upgrade 3 to 4 if DCE score of positive	6.1 (21/343)	28.6 (6/21)	5.5 (19/343)	36.8 (7/19)
(P5) In PZ and TZ, upgrade 3 to 4 if size ≥ 10 mm	23.0 (79/343)	62.0 (49/79)	14.0 (48/343)	64.6 (31/48)
(P6) In PZ and TZ, upgrade 3 to 4 if size ≥ 15 mm	23.0 (79/343)	17.7 (14/79)	14.0 (48/343)	12.5 (6/48)
(P7) In PZ and TZ, upgrade 3 to 4 if size ≥ 20 mm	23.0 (79/343)	3.8 (3/79)	14.0 (48/343)	2.1 (1/48)
(P8) In PZ and TZ, upgrade 4 to 5 if size in 10–14-mm range	20.1 (69/343)	60.9 (42/69)	23.3 (80/343)	48.8 (39/80)

Note.—Data are percentages and data in parentheses are numerators and denominators. (E1) to (E3b) = existing decision rules, (P1) to (P8) = proposed decision rules.

27.1% (13 of 48) at PI-RADS category 3, 44.4% (40 of 90) to 49.3% (37 of 75) at PI-RADS category 4, and 72.1% (31 of 43) to 73.7% (42 of 57) at PI-RADS category 5. For overall detection of GS ≥7 tumor, PI-RADS category 4 or greater had sensitivity of 78.9% (71 of 90) to 87.8% (79 of 90), specificity of 75.5% (191 of 253) to 79.1% (200 of 253), negative predictive value of 91.0% (192 of 211) to 94.8% (200 of 211), positive predictive value of 53.4% (71 of 132) to 59.8% (79 of 132), and accuracy of 76.4% (262 of 343) to 81.3% (279 of 343) for the two readers (Table 2). Overall interreader agreement (Table E2 [online]) was moderate for T2-weighted and DCE scores (kappa of 0.48–0.49) and substantial for DWI scores, lesion size, and the overall PI-RADS category (kappa of 0.66–0.70).

Existing PI-RADS V2 Decision Rules

Tables 3 and 4 demonstrate the impact of various existing PI-RADS V2 decision rules. PZ lesions upgraded from category 3 to 4 based on a DCE score of positive (rule E1) were GS ≥7 tumor in 30.0% (three of 10) to 33.3% (seven of 21) of cases. TZ lesions upgraded from category of 3 to 4 based on a DWI score of 5 (rule E2) were GS ≥7 tumor in 50.0% (four of eight) to 66.7% (two of three) of cases. In both zones, lesions upgraded from category of 4 to 5 based on a size of 15 mm or greater (rule E3a) were GS ≥7 tumor in 71.7% (33 of 46) to 72.7% (24 of 33) of cases. Lesions upgraded from category of 4 to 5 based solely on a size ranging 15–19 mm (rule E3b) were GS ≥7 tumor in 63.2% (12 of 19) to 81.0% (17 of 21) of cases.

Proposed Adjustments to PI-RADS V2 Decision Rules

A number of proposed adjustments to the decision rules were associated with GS ≥7 tumor in 20% or more of upgraded cases for both readers (Tables 3, 4): rule P3 in TZ, upgrading category

Table 4

Fraction of Lesions Undergoing an Upgrade in PI-RADS Category Representing Tumor and GS ≥7 or Greater Tumor for Existing and Proposed PI-RADS Decision Rules

	Reader 1		Reader 2	
Decision Rule	Percent Tumor	Percent GS ≥7 Tumor	Percent Tumor	Percent GS ≥7 Tumor
Existing PI-RADS V2				
(E1) In PZ, upgrade 3 to 4 if DCE score of positive	60.0 (6/10)	30.0 (3/10)	47.6 (10/21)	33.3 (7/21)
(E2) In TZ, upgrade 3 to 4 if DWI score of 5	100.0 (3/3)	66.7 (2/3)	75.0 (6/8)	50.0 (4/8)
(E3a) In PZ andTZ, upgrade 4 to 5 if size ≥ 15 mm	84.8 (39/46)	71.7 (33/46)	81.8 (27/33)	72.7 (24/33)
(E3b) Same as above, only upgrade if size in15–19-mm range	85.7 (18/21)	81.0 (17/21)	78.9 (15/19)	63.2 (12/19)
Proposed PI-RADS V2				
(P1) In PZ, upgrade 3 to 4 if T2-weighted imaging score of 4	0 (0/2)	0 (0/2)	33.3 (2/6)	33.3 (2/6)
(P2) In PZ, upgrade 3 to 4 if T2-weighted imaging score of 5	0 (0/1)	0 (0/1)	NA (0/0)	NA (0/0)
(P3) In TZ, upgrade 3 to 4 if DWI score of 4	30.0 (3/10)	30.0 (3/10)	60.0 (3/5)	60.0 (3/5)
(P4) In TZ, upgrade 3 to 4 if DCE score of positive	33.3 (2/6)	33.3 (2/6)	57.1 (4/7)	57.1 (4/7)
(P5) In PZ and TZ, upgrade 3 to 4 if size ≥ 10 mm	26.5 (13/49)	12.2 (6/49)	38.7 (12/31)	25.8 (8/31)
(P6) In PZ and TZ, upgrade 3 to 4 if size ≥ 15 mm	14.3 (2/14)	7.1 (1/14)	50.0 (3/6)	33.3 (2/6)
(P7) In PZ and TZ, upgrade 3 to 4 if size ≥ 20 mm	33.3 (1/3)	0 (0/3)	100 (1/1)	100 (1/1)
(P8) In PZ and TZ, upgrade 4 to 5 if size in 10–14-mm range	78.6 (33/42)	61.9 (26/42)	71.8 (28/39)	56.4 (22/39)

Note.—Data are percentages and data in parentheses are numerators and denominators. (E1) to (E3b) = existing decision rules, (P1) to (P8) = proposed decision rules. NA = not applicable.

3 to 4 based on a DWI score of 4 (30.0% [three of 10] to 60.0% [three of five]); rule P4 in TZ, upgrading category 3 to 4 based on a DCE score of positive (33.3% [two of six] to 57.1% [four of seven); and rule P8 in both zones, upgrading category 4 to 5 based on a size ranging 10–14 mm (56.4% [22 of 39] to 61.9% [26 of 42]). For the first two of these potential adjustments regarding an upgrade of category 3 to 4 in the TZ (rules P3 and P4), only 5.5% (19 of 343) to 6.1% (21 of 343) of patients were eligible for the upgrade for the two two readers. In comparison, for the potential adjustment regarding an upgrade of category 4 to 5 based on a size ranging 10–14 mm (rule P5), 20.1% (69 of 343) to 23.3% (80 of 343) of patients were eligible for the upgrade, of whom 48.8% (39 of 80) to 60.9% (42 of 69) would in fact have undergone this change. Figures 2 and 3 show representative examples of the impact of the proposed adjustments on the PI-RADS category assignment.

A number of other proposed adjustments to the PI-RADS V2 decision rules were associated with GS ≥7 tumor in less than 15% of cases for at least one reader, including in the PZ, upgrading category 3 to 4 based on a T2-weighted imaging score of 4 (rule P1); in the PZ, upgrading category 3 to 4 based on a T2-weighted imaging score of 5 (rule P2); and in both zones, upgrading category 3 to 4 based on size thresholds of 10 mm or greater, 15 mm or greater, or 20 mm or greater (rules P5, P6, and P7).

Discussion

PI-RADS V2 provides a five-point scale for stratifying the likelihood that a focal prostate lesion at MR imaging represents clinically significant prostate cancer (defined in this study as GS ≥7 tumor) in a fashion intended to be useful for guiding the clinical treatment of patients known to have or suspected of having prostate cancer. Ideally, the frequency of GS ≥7 tumor would show a stepwise increase across the five categories; a threshold having a high negative predictive value for GS ≥7 tumor could be identified to guide decisions regarding patient selection for targeted biopsy, and the highest category would confidently be associated with the presence of GS ≥7 tumor.

In our study, PI-RADS V2 showed reasonable performance in these regards for two independent readers. The frequency of GS ≥7 tumor increased with progressive increases in the assigned PI-RADS category, being very low for categories 1–2 and being present in the majority of category 5 lesions. Also, PI-RADS category 4 or greater had high diagnostic accuracy for detection of GS 6 or greater tumor, including particularly high (> 90%) negative predictive value. Interreader agreement was substantial in terms of the overall PI-RADS category. The performance of PI-RADS V2 remained robust in separate assessments of the PZ and TZ.

In addition, individual existing PI-RADS V2 decision rules that are currently routinely applied in clinical practice for upgrading a lesion's overall category performed well. Namely, current criteria calling for upgrading category 3 to 4 in the TZ based on a DWI score of 5, as well as upgrading category 4 to 5 in either zone based on a size of 15 mm or greater, resulted in GS ≥7 tumor in at least half of the upgraded cases for both readers. Upgrading category 3 to a 4 in the PZ based on DCE score of positive resulted in GS ≥7 tumor in approximately a third of patients, a frequency that may be considered sufficient to justify this criterion. Nonetheless, this frequency

Figure 2

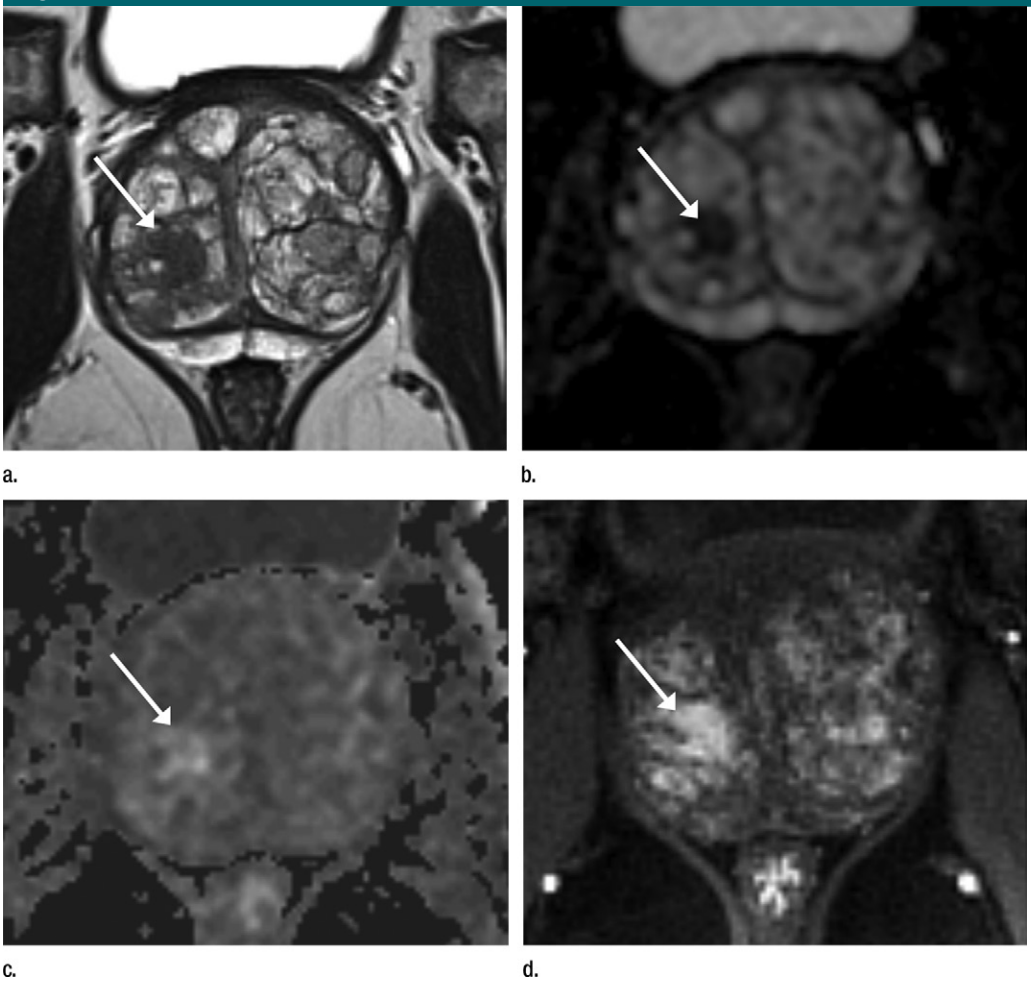

Figure 2: Proposed adjustments upgrading category 3 to 4 in the TZ based on DWI score of 4 or DCE score of positive. Images in a 60-year-old man with prostate-specific antigen level of 5.7 μg/mL and no prior prostate biopsy. **(a)** Axial T2-weighted turbo spin-echo image shows a moderately T2-hypointense lesion in the right TZ (arrow) with a partially circumscribed margin. **(b)** Apparent diffusion coefficient map shows decreased apparent diffusion coefficient (arrow). **(c)** DWI with *b* value of 1500 sec/mm^2 shows increased signal intensity (arrow). **(d)** Early postcontrast T1-weighted image shows unencapsulated sheetlike confluent hypervascularity (arrow). Lesion was assigned T2-weighted imaging score of 3, DWI score of 4, and DCE score of positive. By using existing PI-RADS V2 decision rules, the overall category is 3. By using either of the proposed adjustments (rules P3 or P4), the category is 4. Lesion represented GS 3+4 tumor at MR imaging-US fusion-targeted biopsy.

was lower than that for the other two evaluated decision rules noted above, and this particular aspect of PI-RADS V2 has previously been questioned. A study by Vargas et al reported that DCE added limited additional value to the combination of T2-weighted imaging and DWI, helping to detect only four of 125 PZ tumors with a volume of 0.5 mL or greater (24). In an additional study, among features evaluated in the PZ, those related to DCE had particularly poor interreader reproducibility among expert radiologists (4). Challenges in application of DCE in the PZ relate to technical variability in its acquisition, postprocessing, and interpretation (25). Our findings regarding a moderate frequency of GS 6 or greater tumor in lesions whose score was upgraded by DCE compare favorably with the minimal impact of DCE reported by Vargas et al (24). Nonetheless, continued attention to the standardization and optimization of the pulse sequence are required to optimize its impact when applied for clinical lesion assessment.

A series of proposed adjustments to the PI-RADS V2 decision rules were also evaluated. A number of these, such as those upgrading the category in the PZ based on the T2-weighted imaging score or those upgrading the category from 3 to a 4 based on a size threshold of 10 or 15 mm, were associated with low frequencies of GS ≥7 tumor in the upgraded lesions. On the other hand, some proposed adjustments to the decision rules for assigning a category of 4 or 5 were associated with frequencies of GS ≥7 tumor in the affected lesions comparable to those of existing decision rules, supporting further consideration of these proposed adjustments. Nonetheless, the modifications may not be worthwhile if they actually impact the overall category in exceedingly small fractions of patients, whether due to a very small fraction of cases being eligible for an upgrade or a very small fraction of eligible cases in fact being affected. A key aim of PI-RADS V2 is to simplify interpretation (2). However, any included decision rules increase interpretation complexity and may undermine achieving a straightforward and readily reproducible system. One proposed adjustment that fared well in terms of both impacting the assigned category in a meaningful fraction of

Figure 3

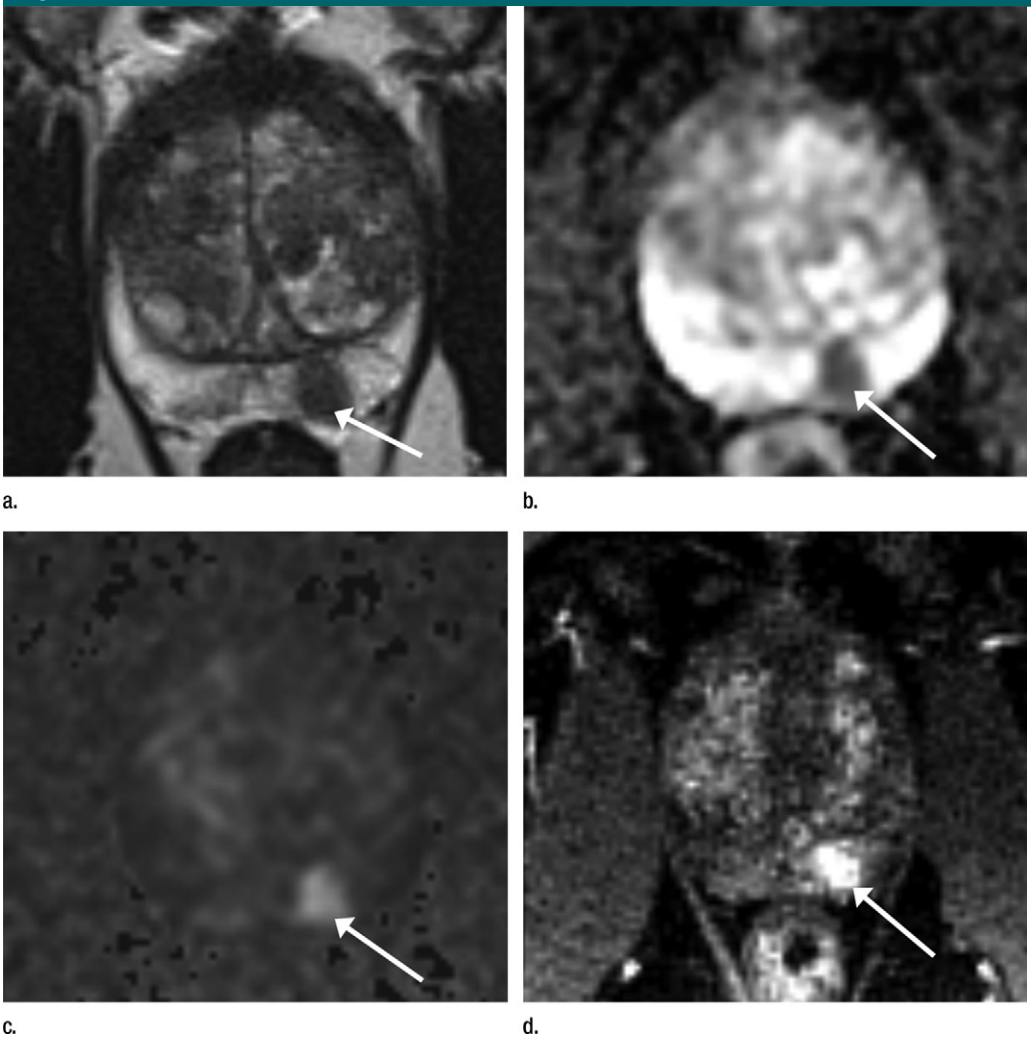

Figure 3: Proposed adjustment upgrading category 4 to 5 based on size of 10–14 mm. Images in a 68-year-old man with prostate-specific antigen level of 3.4 μg/mL and no prior prostate biopsy. **(a)** Axial T2-weighted turbo spin-echo image shows a focal moderately T2-hypointense lesion in the left posterior PZ (arrow). **(b)** Apparent diffusion coefficient map shows decreased apparent diffusion coefficient (arrow). **(c)** DWI with *b* value of 1500 sec/mm^2 shows increased signal intensity (arrow). **(d)** Early postcontrast T1-weighted image shows matching focal early enhancement (arrow). Lesion size was measured on apparent diffusion coefficient map as 10 and 11 mm by two readers. Lesion was assigned T2-weighted imaging score of 4, DWI score of 4, and DCE score of positive. By using existing PI-RADS V2 decision rules, the overall category is 4. By using proposed adjustment rule P8, the category is 5. Lesion represented GS 3+4 tumor at MR imaging-US fusion-targeted biopsy.

cases, as well as resulting in GS ≥7 tumor in the majority of affected cases, entailed upgrading the category from 4 to a 5 at a size threshold of 10 mm, rather than the current threshold of 15 mm. The current size threshold of 15 mm maintains consistency with a size threshold that was empirically used in PI-RADS version 1 from the European Society of Urogenital Radiology (26), although it lacks concrete supporting data. Thus, it remains possible that an alternate size threshold may be preferred. At the same time, while this proposed adjustment yielded GS ≥7 tumor in the majority of affected cases, its adoption would lower the positive predictive value of PI-RADS category 5 for GS ≥7 tumor in our data set, a trade-off to consider if seeking for a PI-RADS category 5 to serve as a highly reliable indicator of GS ≥7 tumor.

Two additional proposed adjustments to the decision rules were associated with GS ≥7 tumor in considerable fractions of affected cases although were eligible adjustments in exceedingly small fractions of cases. Both of these related to potential upgrades from a category 3 to 4 in the TZ. One of these entailed allowing the upgrade for a DWI score of 4, rather than solely a DWI score of 5 as in the present criteria. The role of DWI in assessing TZ lesions is controversial. While it is generally accepted that T2-weighted imaging is the dominant pulse sequence in the TZ (27), the added value of DWI findings is unclear (28,29). Thus, whether it is optimal to apply a DWI threshold of 4 or 5 for upgrading an equivocal TZ lesion is uncertain. The other proposed adjustment that had potential value in upgrading a TZ lesion from category 3 to 4, based on DCE score of positive, may be surprising. DCE is conventionally viewed as having little value in the TZ given substantial overlap between the hypervascularity of benign prostatic hyperplasia nodules and TZ tumors (28). This role that we observed for DCE in the TZ may relate to our incorporation of morphologic criteria for assessing DCE in the TZ lesion that are not a component of PI-RADS

V2. In particular, DCE was considered negative in the TZ in the presence of encapsulated swirled or popcorn-like enhancement (patterns of hypervascularity suggestive of benign prostatic hyperplasia), instead only being deemed positive in this zone in the presence of unencapsulated sheetlike confluent enhancement. Given our findings regarding potential value of DWI and DCE in the TZ, further attention appears warranted for the optimal evaluation of equivocal TZ lesions.

Our findings are, overall, encouraging regarding the clinical impact of PI-RADS V2, as the system generally worked well in our cohort. Nonetheless, future updates of the system are anticipated, similar to serial revisions implemented for Breast Imaging Reporting and Data System BI-RADS (30) and Liver Imaging Reporting and Data System (31). Such updates must reflect the experience of the prostate MR imaging community at large, encompassing a broad range of users of the system across various practice settings, as well as data from multiple independent centers. While a paucity of existing literature formally explores details of PI-RADS V2 decision rules, the present study provides a targeted assessment of such criteria. The reported findings suggest potential refinements to consider, particularly if validated through additional comprehensive evaluations at other centers. The proposed refinements almost exclusively address upgrade from a 3 to a 4 so as to potentially impact clinical decisions regarding patient selection for targeted biopsy. The inclusion of a proposed refinement addressing an upgrade from a 4 to a 5 may also have clinical impact given recommendations that a repeat targeted biopsy be performed following benign results from an initial targeted biopsy of a PI-RADS category 5 lesion (32).

This study has several limitations. First, the proposed adjustments were explored in a retrospective fashion, thereby not assessing their impact when used to guide management in a prospective fashion. In addition, MR imaging–targeted biopsy served as the reference standard. While this is more reliable than standard systematic biopsy (33), it may undersample a fraction of tumors compared with findings from radical prostatectomy (34). To minimize the risk of undersampling even at targeted biopsy, we excluded patients with more aggressive pathologic findings identified in systematic cores. Second, our proposed adjustments to the PI-RADS V2 decision rules were largely focused on the distinction between PI-RADS categories 3 and 4 given that PI-RADS V2 considers a category of 4 as a threshold at which targeted biopsy should routinely be considered (2); we acknowledge that some centers apply a category of 3 as a threshold for this purpose. Nonetheless, even for such centers, improved correspondence between the five PI-RADS categories and biopsy outcomes would be helpful for risk stratification and quality assurance purposes. Third, we identified patients for this study through a search of a database of patients who underwent MR imaging-US fusion-targeted prostate biopsy; thus, the total number of patients who underwent prostate MR imaging but without a subsequent targeted biopsy is unknown. Fourth, the routine prostate MR imaging protocol at our institution uses a DCE methodology based on a continuously acquired radial acquisition with compressed sensing reconstruction. The impact of this approach for prostate DCE on our reported outcomes for decision rules incorporating DCE is unknown from our study. Fifth, we solely evaluated a sample of conjectured alternatives to the PI-RADS V2 decision criteria; further alternatives could be theorized as well. Sixth, the MR imaging examinations were reviewed by two radiologists from the same center, one of whom trained the other in the use of PI-RADS V2. This design may have contributed to an observed interreader reproducibility in our study that is higher than previously reported for PI-RADS V2 (3,4). Finally, the sample sizes for evaluating the individual proposed adjustments to the PI-RADS V2 decision rules were generally small. Given these final two limitations, further investigations by other centers and by using larger sample sizes are required to confirm our preliminary observations.

In conclusion, we showed high performance of PI-RADS V2 for the detection of GS ≥7 prostate cancer by using MR imaging-US fusion-targeted biopsy as reference. Outcomes from existing PI-RADS V2 decision rules for determining the overall PI-RADS category were reasonable in terms of detection of GS ≥7 tumor. A number of exploratory proposed adjustments to the decision rules also appeared to have potential value for detection of GS ≥7 tumor. While the observations may be useful for future PI-RADS updates, further studies from other centers are required for validation.

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References

1. Hoeks CM, Barentsz JO, Hambrock T, et al. Prostate cancer: multiparametric MR imaging for detection, localization, and staging. Radiology 2011;261(1):46–66.
2. Weinreb JC, Barentsz JO, Choyke PL, et al. PI-RADS Prostate Imaging Reporting and Data System: 2015, Version 2. Eur Urol 2016;69(1):16–40.
3. Muller BG, Shih JH, Sankineni S, et al. Prostate cancer: interobserver agreement and accuracy with the revised Prostate Imaging Reporting and Data System at multiparametric MR imaging. Radiology 2015;277(3):741–750.
4. Rosenkrantz AB, Ginocchio LA, Cornfeld D, et al. Interobserver reproducibility of the PI-RADS Version 2 lexicon: a multicenter study of six experienced prostate radiologists. Radiology 2016;280(3):793–804.
5. Baldisserotto M, Neto EJ, Carvalhal G, et al. Validation of PI-RADS v.2 for prostate cancer diagnosis with MRI at 3T using an external phased-array coil. J Magn Reson Imaging 2016 Apr 26. [Epub ahead of print]
6. Greer MD, Brown AM, Shih JH, et al. Accuracy and agreement of PIRADSv2 for pros-

tate cancer mpMRI: a multireader study. J Magn Reson Imaging 2016 Jul 8. [Epub ahead of print]

7. Rosenkrantz AB, Lepor H, Huang WC, Taneja SS. Practical barriers to obtaining pre-biopsy prostate MRI: assessment in over 1500 consecutive men undergoing prostate biopsy in a single urologic practice. Urol Int 2016;97(2):247–248.
8. Xu S, Kruecker J, Turkbey B, et al. Real-time MRI-TRUS fusion for guidance of targeted prostate biopsies. Comput Aided Surg 2008;13(5):255–264.
9. Martin PR, Cool DW, Romagnoli C, Fenster A, Ward AD. Magnetic resonance imaging-targeted, 3D transrectal ultrasound-guided fusion biopsy for prostate cancer: quantifying the impact of needle delivery error on diagnosis. Med Phys 2014;41(7):073504.
10. Rosenkrantz AB, Bennett GL, Doshi A, Deng FM, Babb JS, Taneja SS. T2-weighted imaging of the prostate: impact of the BLADE technique on image quality and tumor assessment. Abdom Imaging 2015;40(3):552–559.
11. Rosenkrantz AB, Khalef V, Xu W, Babb JS, Taneja SS, Doshi AM. Does normalisation improve the diagnostic performance of apparent diffusion coefficient values for prostate cancer assessment? a blinded independent-observer evaluation. Clin Radiol 2015;70(9):1032–1037.
12. Rosenkrantz AB, Shanbhogue AK, Wang A, Kong MX, Babb JS, Taneja SS. Length of capsular contact for diagnosing extraprostatic extension on prostate MRI: assessment at an optimal threshold. J Magn Reson Imaging 2016;43(4):990–997.
13. Rosenkrantz AB, Parikh N, Kierans AS, et al. Prostate cancer detection using computed very high b-value diffusion-weighted imaging: how high should we go? Acad Radiol 2016;23(6):704–711.
14. Mendhiratta N, Meng X, Rosenkrantz AB, et al. Prebiopsy MRI and MRI-ultrasound fusion-targeted prostate biopsy in men with previous negative biopsies: impact on repeat biopsy strategies. Urology 2015;86(6):1192–1128.
15. Mendhiratta N, Rosenkrantz AB, Meng X, et al. Magnetic resonance imaging-ultrasound fusion targeted prostate biopsy in a consecutive cohort of men with no previous biopsy: reduction of over detection through improved risk stratification. J Urol 2015;194(6):1601–1606.
16. Meng X, Rosenkrantz AB, Mendhiratta N, et al. Relationship between prebiopsy multiparametric magnetic resonance imaging (MRI), biopsy indication, and MRI-ultrasound fusion-targeted prostate biopsy outcomes. Eur Urol 2016;69(3):512–517.
17. Rosenkrantz AB, Ayoola A, Hoffman D, et al. The learning curve in prostate MRI interpretation: self-directed learning vs continual reader feedback. AJR Am J Roentgenol (in revision).
18. Ream JM, Doshi AM, Dunst D, et al. Dynamic contrast-enhanced MRI of the prostate: an intraindividual assessment of the effect of temporal resolution on qualitative detection and quantitative analysis of histopathologically proven prostate cancer. J Magn Reson Imaging 2016 Sep 20. [Epub ahead of print]
19. Rosenkrantz AB, Chandarana H, Hindman N, et al. Computed diffusion-weighted imaging of the prostate at 3 T: impact on image quality and tumour detection. Eur Radiol 2013;23(11):3170–3177.
20. Rosenkrantz AB, Geppert C, Grimm R, et al. Dynamic contrast-enhanced MRI of the prostate with high spatiotemporal resolution using compressed sensing, parallel imaging, and continuous golden-angle radial sampling: preliminary experience. J Magn Reson Imaging 2015;41(5):1365–1373.
21. Riches SF, Payne GS, Morgan VA, et al. MRI in the detection of prostate cancer: combined apparent diffusion coefficient, metabolite ratio, and vascular parameters. AJR Am J Roentgenol 2009;193(6):1583–1591.
22. Wysock JS, Rosenkrantz AB, Huang WC, et al. A prospective, blinded comparison of magnetic resonance (MR) imaging-ultrasound fusion and visual estimation in the performance of MR-targeted prostate biopsy: the PROFUS trial. Eur Urol 2014;66(2):343–351.
23. Hoeks CM, Somford DM, van Oort IM, et al. Value of 3-T multiparametric magnetic resonance imaging and magnetic resonance-guided biopsy for early risk restratification in active surveillance of low-risk prostate cancer: a prospective multicenter cohort study. Invest Radiol 2014;49(3):165–172.
24. Vargas HA, Hötker AM, Goldman DA, et al. Updated prostate imaging reporting and data system (PIRADS v2) recommendations for the detection of clinically significant prostate cancer using multiparametric MRI: critical evaluation using whole-mount pathology as standard of reference. Eur Radiol 2016;26(6):1606–1612.
25. Rosenkrantz AB, Oto A, Turkbey B, Westphalen AC. Prostate Imaging Reporting and Data System (PI-RADS), Version 2: a critical look. AJR Am J Roentgenol 2016;206(6):1179–1183.
26. Barentsz JO, Richenberg J, Clements R, et al. ESUR prostate MR guidelines 2012. Eur Radiol 2012;22(4):746–757.
27. Hoeks CM, Hambrock T, Yakar D, et al. Transition zone prostate cancer: detection and localization with 3-T multiparametric MR imaging. Radiology 2013;266(1):207–217.
28. Rosenkrantz AB, Kim S, Campbell N, Gaing B, Deng FM, Taneja SS. Transition zone prostate cancer: revisiting the role of multiparametric MRI at 3 T. AJR Am J Roentgenol 2015;204(3):W266–W272.
29. Elbuluk O, Muradyan N, Shih J, et al. Differentiating transition zone cancers from benign prostatic hyperplasia by quantitative multiparametric magnetic resonance imaging. J Comput Assist Tomogr 2016;40(2):218–224.
30. American College of Radiology. ACR BI-RADS Atlas. http://www.acr.org/Quality-Safety/Resources/BIRADS. Accessed November 1, 2015.
31. American College of Radiology. Liver Imaging Reporting and Data System. http://www.acr.org/quality-safety/resources/LI-RADS. Accessed November 1, 2015.
32. Rosenkrantz AB, Verma S, Choyke P, et al. Prostate magnetic resonance imaging and magnetic resonance imaging targeted biopsy in patients with a prior negative biopsy: a consensus statement of the American Urological Association and the Society of Abdominal Radiology's Prostate Cancer Disease Focused Panel. J Urol 2016 Jun 16. [Epub ahead of print]
33. Siddiqui MM, Rais-Bahrami S, Truong H, et al. Magnetic resonance imaging/ultrasound-fusion biopsy significantly upgrades prostate cancer versus systematic 12-core transrectal ultrasound biopsy. Eur Urol 2013;64(5):713–719.
34. Nassiri N, Natarajan S, Margolis DJ, Marks LS. Targeted prostate biopsy: lessons learned midst the evolution of a disruptive technology. Urology 2015;86(3):432–438.