Published in final edited form as:

J Urol. 2017 September ; 198(3): 583–590. doi:10.1016/j.juro.2017.03.131.

Prospective Evaluation of PI-RADS™ Version 2 Using the International Society of Urological Pathology Prostate Cancer Grade Group System

Sherif Mehralivand[*],
Department of Urology and Pediatric Urology, University Medical Center, Mainz, Germany; Urologic Oncology Branch, Molecular Imaging Program, Rockville, Maryland

Sandra Bednarova[*],
Molecular Imaging Program, Center for Interventional Oncology, Radiology and Imaging Sciences, Clinical Center, Rockville, Maryland; Institute of Diagnostic Radiology, Department of Medical and Biological Sciences, University of Udine, Udine, Italy

Joanna. H. Shih,
National Institutes of Health, Bethesda and Biometric Research Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, National Institutes of Health, Rockville, Maryland

Francesca V. Mertan,
Molecular Imaging Program, Rockville, Maryland

Sonia Gaur,
Molecular Imaging Program, Rockville, Maryland

Maria J. Merino,
Laboratory of Pathology, National Cancer Institute, Rockville, Maryland

Bradford J. Wood[†],
Center for Interventional Oncology, Radiology and Imaging Sciences, Clinical Center, Rockville, Maryland

Peter A. Pinto[‡],
Mainz, Germany, Urologic Oncology Branch, Rockville, Maryland

Peter L. Choyke,
Molecular Imaging Program, Rockville, Maryland

Baris Turkbey[§]
Molecular Imaging Program, Rockville, Maryland

Abstract

[§]Correspondence: Molecular Imaging Program, National Cancer Institute, 10 Center Dr., MSC 1182, Building 10, Room B3B85, Bethesda, Maryland 20892 (turkbeyi@mail.nih.gov).
[*]Equal study contribution.
[†]Financial interest and/or other relationship with Philips Invivo.
[‡]Financial interest and/or other relationship with Philips Medical.

Purpose: The PI-RADS™ (Prostate Imaging Reporting and Data System), version 2 scoring system, introduced in 2015, is based on expert consensus. In the same time frame ISUP (International Society of Urological Pathology) introduced a new pathological scoring system for prostate cancer. Our goal was to prospectively evaluate the cancer detection rates for each PI-RADS, version 2 category and compare them to ISUP group scores in patients undergoing systematic biopsy and magnetic resonance imaging-transrectal ultrasound fusion guided biopsy.

Materials and Methods: A total of 339 treatment naïve patients prospectively underwent multiparametric magnetic resonance imaging evaluated with PI-RADS, version 2 with subsequent systematic and fusion guided biopsy from May 2015 to May 2016. ISUP scores were applied to pathological specimens. An ISUP score of 2 or greater (ie Gleason 3 + 4 or greater) was defined as clinically significant prostate cancer. Cancer detection rates were determined for each PI-RADS, version 2 category as well as for the T2 weighted PI-RADS, version 2 categories in the peripheral zone.

Results: The cancer detection rate for PI-RADS, version 2 categories 1, 2, 3, 4 and 5 was 25%, 20.2%, 24.8%, 39.1% and 86.9% for all prostate cancer, and 0%, 9.6%, 12%, 22.1% and 72.4% for clinically significant prostate cancer, respectively. On T2-weighted magnetic resonance imaging the cancer detection rate in the peripheral zone was significantly higher for PI-RADS, version 2 category 4 than for overall PI-RADS, version 2 category 4 in the peripheral zone (all prostate cancer 36.6% vs 48.1%, p = 0.001, and clinically significant prostate cancer 22.9% vs 32.6%, p = 0.002).

Conclusions: The cancer detection rate increases with higher PI-RADS, version 2 categories.

Keywords

prostatic neoplasms; early detection of cancer; reference standards; diagnostic imaging; biopsy

Prostate cancer is the most common cancer type among American men with an estimated 180,890 new diagnoses in 2016.[1] According to current guidelines the standard of care for diagnosing PCa is to obtain transrectal or transperineal 10 to 12 core SB under TRUS guidance.[2] The prostate is sampled using a standardized template of prostate sextants but specific lesions are not necessarily sought out. The CDR with this approach varies between 40% and 45%.[3,4] However, this includes many indolent tumors, which leads to increased medical utilization without benefit to the patient. Meanwhile, CS tumors, defined in this study as those with a Gleason score of 3 + 4 or greater, which lie outside the template, are often missed. Simply increasing the number of biopsy cores slightly increases the CDR of CS tumors but generally at the cost of detecting even more indolent cancers[5,6] while it also increases morbidity.[4,7] Moreover, tumors detected by SB are often under graded or upgraded in the final prostatectomy specimens, which can lead to suboptimal treatment decisions.[8]

mpMRI and mpMRI/TRUS fusion guided TB of the prostate are increasingly used to diagnose patients with suspicion of prostate cancer. The 2 techniques combined show increased detection of CS PCa with decreased detection of clinically indolent cancers and better correlation with final histopathology results.[9,10] However, until recently standardized reporting of mpMRI has not been available.

The PI-RADSv2 system of assessment categories was introduced in 2015 to create a globally accepted standard to detect, score and report suspicious lesions on mpMRI.[11] Compared to version 1 of the document the assessment system was considerably simplified. It also introduced the concept of a zone based dominant sequence, which is used to determine an overall PI-RADSv2 category rather than a summation of categories from each parameter.

While the appearance of a lesion on T2W and DWI still receives a unique 1 to 5 category, DCE positivity is assessed in binary fashion. The overall PI-RADSv2 category is determined by the dominant sequence, which is DWI in the PZ and T2W in the TZ. In the PZ category 3 lesions are upgraded to category 4 if the DCE image is positive in the PZ whereas in the TZ category 3 lesions are upgraded to category 4 if the DWI PI-RADS category is 5. The overall PI-RADSv2 category represents the likelihood that a lesion harbors CS PCa.

While there are merits to developing a single lexicon for mpMRI,[12] the dominant sequence concept as well as the criteria and parameters defining the categories are based on expert consensus opinion rather than on experimental results.[13] Thus, they require validation.

In the same time frame as the development of PI-RADSv2 ISUP introduced a new pathological scoring system based on a 1 to 5 score.[14] The specific goals were to reduce patient anxiety regarding Gleason 3 + 3 tumors, now renamed group 1, and separate Gleason 3 + 4 (group 2) and Gleason 4 + 3 (group 3) cancers, which were formerly characterized together as Gleason 7 tumors. However, PI-RADSv2 was designed to predict clinically significant PCa but not individual Gleason score groups.

The aims of this study were to prospectively evaluate the CDR of each PI-RADSv2 category in patients who underwent SB and TB, and correlate PI-RADSv2 categories with the new ISUP scoring system for PCa.[14]

MATERIALS AND METHODS

Study Population and Design

This prospective, single institution study was approved by the local institutional review board and it was compliant with HIPAA (Health Insurance Portability and Account-ability Act). Informed consent was obtained from each participant. Criteria recommended by the START (Standards of Reporting for MRI-targeted Biopsy Studies) Consortium were followed in this study.[15]

A total of 963 patients were referred for clinical suspicion of PCa and underwent mpMRI between May 2015 and May 2016. Study inclusion criteria were mpMRI with prospective PI-RADSv2 scoring and subsequent SB and/or TB. Exclusion criteria were prior treatment such as radical prostatectomy, radiation therapy, focal ablative therapy, androgen deprivation or intravesical instillation. For patients with multiple biopsy sessions only the first session was considered (fig. 1).

Multiparametric Magnetic Resonance Imaging Acquisition and Interpretation

Prostate mpMRI scans were acquired on a 3 Tesla Achieva 3.0T TX scanner (Philips, Best, The Netherlands) with an endorectal coil and a surface coil in the majority of patients or with only a surface coil. The mpMRI protocol with an endorectal coil was performed with the BPX-30 coil (Medrad®) filled with 45 ml Fluorinert™ and a 16 channel SENSE anterior cardiac coil (Philips). The mpMRI protocol without an endorectal coil was performed with a 32-channel cardiac SENSE coil (Invivo, Gainesville, Florida).

Each imaging protocol used in this study included triplanar T2W turbo spin-echo, DWI, apparent diffusion coefficient maps, high b value DWI (b 1,500 seconds per mm^2 or greater) and DCE MRI sequences. All scans were read by a single highly experienced genitourinary radiologist with at least 5,000 scans read by study commencement. Each detected lesion on mpMRI was assigned a T2W MRI, a DWI MRI and a DCE MRI category, and an overall PI-RADSv2 category.[11]

Biopsy Procedure

Patients with suspicious lesions identified on mpMRI underwent TB using the office based UroNav platform (Invivo) and an 18 × 25 cm spring loaded Bard® Max-Core® core needle biopsy instrument. The decision to biopsy a lesion was made in consensus with the patient.

Besides the overall PI-RADSv2 category, suspicious patterns in other pulse sequences as well as anamnestic and clinical information were regarded. Lesions on T2W MRI were superimposed on the real-time TRUS images. Each lesion was sampled in the axial and sagittal planes. Subsequently SB was obtained with 12 cores from the lateral and medial aspects of the apical, mid and base portion of each side of the prostate. Procedures were performed by an interventional radiologist and/or a urologist. Biopsy specimens were evaluated and assigned Gleason scores by an experienced genitourinary pathologist blinded to MRI findings.

The highest Gleason score per target lesion was assigned to its corresponding ISUP grade group,[14] including ISUP grade 1—Gleason 3 + 3, grade 2—Gleason 3 + 4, grade 3—Gleason 4 + 3, grade 4—Gleason 8 and grade 5—Gleason 9-10. Biopsy specimens scored as ISUP 2 or greater were defined as CS PCa. The SB results were not considered since our analysis was MRI lesion based and it is not possible to accurately associate SB cores with identified lesions after the procedure.

Statistical Analysis

The CDR was defined as the proportion of positive lesions among all detected lesions. The SE and 95% CI of CDRs for each PI-RADSv2 category, for the difference in CDRs between consecutive PI-RADSv2 categories and between each PIRADSv2 and T2W category were calculated from 2,000 bootstrap samples by a random sampling of patients. The 95% CIs were obtained from the 2.5% and 97.5% percentiles of the bootstrap resampling distribution. The significance of the difference in CDRs was tested by the Wald test. To partially account for multiple testing a more conservative significance level of 0.01 was used. The correlation between ISUP scores and PI-RADSv2 categories was determined by the Kendall tau-b.

RESULTS

Our final cohort consisted of 339 patients. Table 1 summarizes demographics. On MRI 737 lesions were detected. Median time between mpMRI and biopsy was 43 days (range 0 to 241). The overall CDRs of all cancers and CS cancers were 47% (346 of 737 cases) and 32% (237 of 737), respectively. Table 2 lists the detection rates of all PCa and CS PCa for PI-RADSv2 categories 1 to 5. In the paired comparison of PI-RADSv2 categories there was a significant difference between the CDR of categories 4 and 5 (all PCa and CS PCa p <0.001). Between categories 3 and 4 the difference was only significant for all PCa but not for CS PCa (p = 0.006 vs 0.012).

On MRI 524 of 737 lesions (71%) were located in the PZ, 207 (28%) were in the TZ and 6 (0.81%) were in the central zone. Table 2 lists cancer detection rates for PI-RADSv2 categories 1 to 5 in the PZ and categories 2 to 5 in the TZ. The CDR was significantly higher for PI-RADSv2 category 5 than for category 4 in the PZ and TZ (p <0.001 and 0.001, respectively). The CDR of category 4 was significantly higher than that of category 3 only in the TZ for all PCa (p = 0.001 vs CS PCa p = 0.19).

Based on the poor sensitivity for overall PI-RADSv2 category 4, which is based primarily on DWI sequences, we evaluated whether the PI-RADSv2 category of the T2W MRI sequence alone could improve the CDR (table 3). This analysis was not done for the TZ since the PI-RADSv2 category there is based on the T2W PI-RADSv2 category. The CDR of T2W MRI categories 1, 2, 3, 4 and 5 in the PZ was 50%, 16.2%, 25.5%, 48.1% and 89.2% for all PCa, and 25%, 7.4%, 13.2%, 32.6% and 77.5%, respectively, for CS PCa. Thus, the CDR of T2W MRI category 4 was significantly higher than that of DWI derived category 4 (all PCa p = 0.001 and CS PCa p = 0.002). However, there was no significant difference in categories 1 to 3 and 5 for the PI-RADSv2 and T2W categories.

On subgroup analysis the lesions were further divided into primary category 4 and upgraded category 4 subgroups, defined as lesions with a category of 3 on DWI but with a positive DCE MRI in the PZ, raising it to category 4, or a category 3 on T2W in the TZ with a category 5 on DWI (table 4). The CDR of the upgraded and the primary category 4 was 26.1% and 46.4% for all PCa, and 16.2% and 25.5%, respectively, for CS PCa. The difference between the upgraded and the primary category 4 was statistically significant for all PCa but not for CS PCa (p = 0.001 vs 0.097). Thus, T2W MRI alone was not contributory in these upgraded category 4 lesions.

Figure 2 shows the distribution of ISUP categories for each PI-RADSv2 category. To correlate PI-RADSv2 and ISUP grade scores PI-RADSv2 categories were grouped into 3 categories corresponding to low risk—PI-RADSv2 categories 1 and 2, intermediate risk—PI-RADSv2 category 3 and high risk—PI-RADSv2 categories 4 and 5. Similarly, ISUP scores were also assigned to 3 risk categories, including low—ISUP 1, moderate—ISUP 2 and high—ISUP 3 to 5. On binary analysis PI-RADSv2 categories were grouped as low—PI-RADSv2 categories 1 to 3 and intermediate to high risk—PI-RADSv2 categories 4 and 5, and ISUP scores were grouped as low risk—ISUP 1 and intermediate to high risk—ISUP 2

to 5. The Kendall tau-b rank correlation was 0.26 and 0.23, and the proportion of concordance was 39.6% and 69.4% for the ternary and binary groups, respectively.

DISCUSSION

The PI-RADSv2 classification was introduced in prior testing in an attempt to standardize the nomenclature. While it achieved its goal of creating a standard lexicon, the performance of PI-RADSv2 has been somewhat disappointing in terms of its ability to predict CS disease.[12,13,16] The almost simultaneous introduction of the new ISUP pathology scoring system further clouds the situation.

Our results are consistent with previous retrospective studies suggesting that higher PI-RADSv2 categories correlate with a higher CDR for all PCa and CS PCa as defined by ISUP criteria.[17-19] The highest CDR was 86.9% for PI-RADSv2 category 5 lesions. However, the CDR of PI-RADSv2 category 4 was lower than expected at only 39.1%. This is surprisingly low for this scoring group since a PI-RADSv2 category 4 is defined as “clinically significant cancer likely to be present.”[11]

Criteria for defining categories 4 and 5 are the same except PI-RADSv2 category 5 requires the lesion to have a diameter of 1.5 cm or greater and/or morphological signs of extraprostatic extension. These more stringent criteria increase the likelihood that a PI-RADSv2 category 5 lesion harbors CS cancer.[20] However, that leaves PI-RADSv2 category 4 with almost no size or feature criteria except abnormal properties on DWI. Thus, a 2 to 3 mm lesion and a 1.4 cm lesion have equal weight in the current PI-RADSv2 system. This study confirms prior observations that category 4 tumors result in a CDR of less than 50%.[12,17] This is clearly a subject that forthcoming versions of PI-RADS should address.

There are several potential corrective measures. The criteria for defining category 4 may not be strict enough, resulting in the inclusion of many false-positive findings. For instance, because there are no size criteria for category 4 lesions, even small lesions are defined as 4, raising the false-positive rate and lowering the CDR. Also, due to smaller size and the known error rate of mpMRI-TRUS fusion guided biopsy (mean ± SD 2.4 ± 1.2 mm), category 4 lesions are more likely to show false-negative results.[21] More precise descriptive criteria and perhaps including size criteria might improve the CDR of category 4 lesions.

Another potential method to improve the CDR of category 4 lesions is to make more use of T2W images, which are essentially ignored in the PZ in PI-RADSv2. We found that T2W categories in the PZ were superior to DWI performance in lesions otherwise characterized as category 4 by PI-RADSv2. T2W MRI has a signal-to-noise ratio superior to that of DWI and DCE MRI, making it easier to differentiate focal lesions from noncircumscribed heterogeneous ones. Related to this is the fact that DWI and DCE images are more subject to susceptibility artifacts than T2W images. Additionally, on T2W MRI the reader only needs to evaluate 1 sequence. This is in contrast to DWI MRI, which requires the reader to evaluate the apparent diffusion coefficient map and high b value images, adding complexity.

Finally, since T2W performed better in the PZ than overall PI-RADSv2 for category 4 cancer detection, it may be useful to more heavily consider the T2W category in the PZ

before finally assigning a category 4 to a lesion. Rosenkrantz et al retrospectively tested alternative criteria to upgrade category 3 lesions to 4.[22] Considering a high T2W category in the PZ instead of DCE positivity did not improve the CDR of CS PCa. However, this study was limited by the small number of such lesions that were evaluated.

We also evaluated whether the so-called upgrading of category 3 lesions to category 4 was influenced by including T2W. Naturally this is only relevant to the PZ because the TZ depends primarily on T2W already. In the current PI-RADSv2 a lesion can be upgraded from category 3 to 4 if the DCE is positive at the same location. We found that the CDR of such upgraded lesions was much lower and closer to that of category 3 lesions than to a primary category 4 lesion for all PCa and for CS disease. This suggests that DCE does not affect the CDR and it may not be as useful a part of mpMRI as previously suggested.[17,23,24] However, the sample size in this subgroup was not large enough to analyze DCE upgraded lesions only. Other definitions of DCE positivity have been proposed and could possibly improve cancer detection[17] but to our knowledge they have not been validated.

Our data suggest only a weak correlation between PI-RADSv2 and ISUP scoring. The purposes of the 2 scoring systems are somewhat different. The former is used to decide which patient should undergo biopsy and the latter is used to determine how aggressive the tumor is biologically. Nevertheless, it is interesting that a weak positive correlation was observed between the 2 scoring systems. ISUP 1 lesions were abundant in all PI-RADSv2 categories. Higher ISUP grades of 2 or greater were more often seen in PI-RADSv2 category 4 or greater lesions. These data raise the possibility that mpMRI may contain data on tumor aggressiveness that could be used prospectively in patient treatment.[17,18]

This study has several limitations. Multireader studies are preferable to test a scoring system since they reveal the interreader variability of a system. However, applying a multireader approach is impossible in a prospective study. The physicians in this study were highly experienced with MRI interpretation and the performance of mpMRI/TRUS fusion guided biopsies, which would tend to optimize the results. Additionally, CDRs were calculated based on targeted biopsy histopathology findings rather than on whole mount pathology results, which remain the gold standard.

Alternatively, studying only a prostatectomy population selects for patients with higher risk disease since those patients must meet surgery criteria. If only patients treated with prostatectomy were included, this would have tended to overstate the performance of mpMRI relative to the general PSA screened population.

We are also aware of selection bias concerning the CDR of PI-RADSv2 category groups 1 and 2 since these lesions are only called and biopsied in certain instances. For example, if there is higher clinical suspicion of prostate cancer, we tend to biopsy lesions that are PI-RADSv2 category less than 3 if no other lesions are detectable. However, in patients with a clear PI-RADSv2 category 4 or 5 lesion, such lesions may not be biopsied. This is also reflected in the low sample size of these 2 scoring groups. Due to this selection bias the observed CDRs are likely to be too high.

Finally, the definition of CS PCa is based on consensus opinion rather than on actual data. For instance, it is likely that many ISUP group 2 lesions, which are now considered CS, will be shown to be indolent using genomic methods. It is hoped in the future that histopathological results will include biomarkers in addition to Gleason scores, which will refine the definitions of indolent and CS PCa.

CONCLUSIONS

PI-RADSv2 category 5 has the highest CDR for all PCa and for CS PCa while PI-RADSv2 category 4 had an unexpectedly low CDR in this study. This implies that there should be stricter criteria for assigning lesions to PI-RADSv2 category 4 than those which currently exist. We found that using T2W PI-RADSv2 categories for category 4 lesions considerably improved the CDR in the PZ, where T2W is not considered a dominant sequence. Perhaps a combination of T2W and stricter size criteria for PI-RADSv2 category 4 lesions may improve the CDR of this category. These findings should inform subsequent versions of the PI-RADS system.

Acknowledgments

Supported by a research grant from the “Dr. Mildred Scheel” foundation, Bonn, Germany (SM).

Abbreviations and Acronyms

CDR	cancer detection rate
CS	clinically significant
DCE	dynamic contrast enhanced
DWI	diffusion-weighted imaging
ISUP	International Society of Urological Pathology
mpMRI	multiparametric MRI
MRI	magnetic resonance imaging
PCa	prostate cancer
PI-RADS	Prostate Imaging Reporting and Data System
PI-RADSv2	PI-RADS version 2
PSA	prostate specific antigen
PZ	peripheral zone
SB	systematic biopsy
T2W	T2-weighted imaging
TB	targeted biopsy

TRUS	transrectal ultrasound
TZ	transition zone

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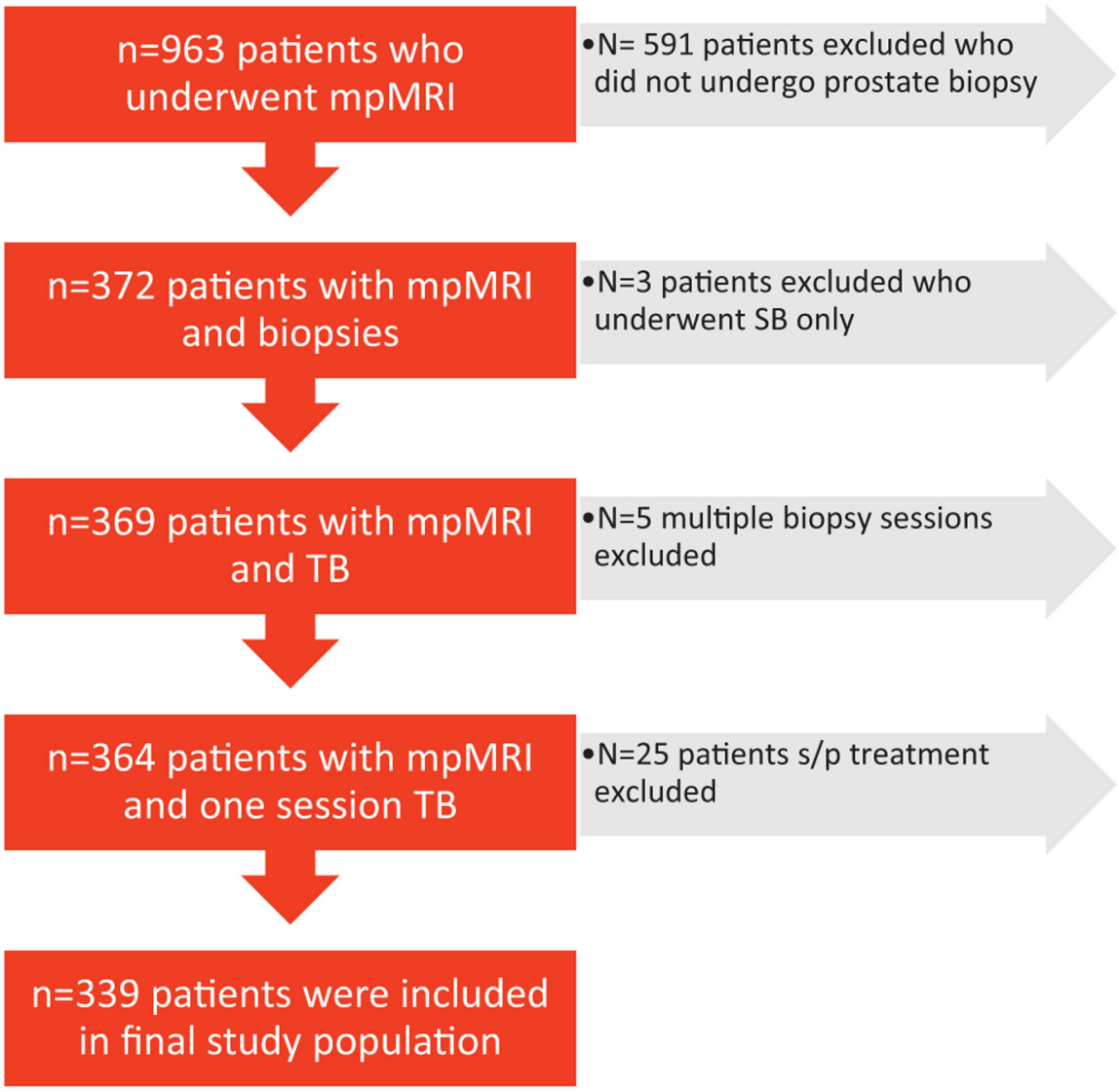
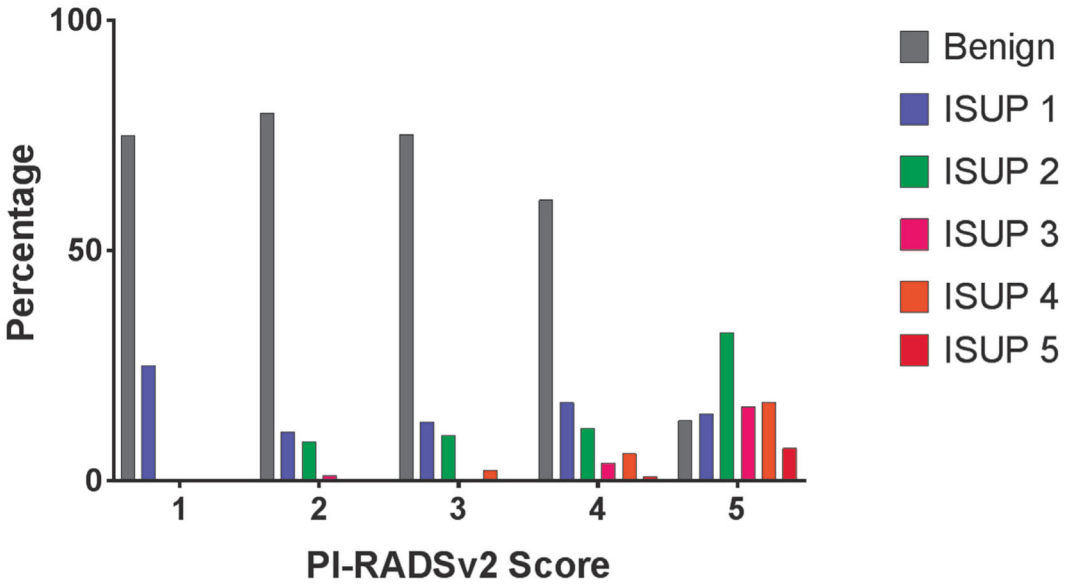


Figure 1.

Study inclusion and exclusion criteria. Previous treatment included radical prostatectomy, external radiation therapy, brachytherapy, focal ablation, vaccine therapy, androgen deprivation and bladder instillation.



PIRADS Score	Benign	ISUP Score				
		1	2	3	4	5
1	3 (75%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2	75 (79.8%)	10 (10.6%)	8 (8.5%)	1 (1.1%)	0 (0%)	0 (0%)
3	100 (75.2%)	17 (12.8%)	13 (9.8%)	0 (0%)	3 (2.3%)	0 (0%)
4	187 (60.9%)	52 (16.9%)	35 (11.4%)	12 (3.9%)	18 (5.9%)	3 (1%)
5	26 (13.1%)	29 (14.6%)	64 (32.2%)	32 (16.1%)	34 (17.1%)	14 (7%)

Figure 2.

Distribution of ISUP scores and benign biopsies among PI-RADS categories. Percentage corresponds to proportion of ISUP scores compared to all cancer positive lesions detected for each category.

Table 1.

Patient demographics

Mean ± SD age	64.1 ± 7
No. ethnicity (%):	
Caucasian	271 (79.94)
African American	48 (14.16)
Asian	12 (3.54)
Hispanic	3 (0.88)
Unknown	5 (1.47)
No. prostate Ca family history (%):	
Yes	83 (24.48)
No	256 (75.52)
No. prior prostate biopsy (%):	
Yes	276 (81.42)
No	63 (18.58)
No. digital rectal examination (%):	
Pos	38 (11.21)
Neg	301 (88.79)
Median ng/dl PSA (IQR)	6.47 (4.59–9.31)
Median ml prostate vol (IQR)	55 (41–79)
Median PSA density (IQR)	0.11 (0.08–0.17)
Mean ± SD No. MRI lesions/pt	2.17 ± 1.2
Mean ± SD No. fusion guided biopsies/pt	4.59 ± 2.54

Table 2.

Lesion based cancer detection rate by PI-RADSv2 category for all prostate cancer and clinically significant prostate cancer

PI-RADSv2 Score	No. Pos	No. False-Pos	% Ca Detection (95% CI)	p Value*
		All PCa		
Overall:				
1	1	3	25 (0–100)	0.85
2	19	75	20.2 (12.9–28.2)	0.4
3	33	100	24.8 (17–33.3)	0.006
4	120	187	39.1 (32.1–45.7)	<0.001
5	173	26	86.9 (81.5–91.5)	–
Peripheral zone:				
1	1	3	25 (0–100)	0.80
2	14	61	18.7 (10.9–27.3)	0.37
3	17	52	24.6 (14.5–36.4)	0.07
4	96	166	36.6 (30–43.9)	<0.001
5	100	14	87.7 (80.5–93.9)	–
Transition zone:†				
2	5	14	26.3 (7.1–50)	0.84
3	15	48	23.8 (13.2–35.5)	0.001
4	23	18	56.1 (38.9–73.3)	0.001
5	72	12	85.7 (76.7–93.1)	–
		Clinically significant PCa		
Overall:				
1	0	4	0 (0–0)	0.002
2	9	85	9.6 (4.1–16.1)	0.57
3	16	117	12 (6.2–18.8)	0.01
4	68	239	22.1 (16.7–27.8)	<0.001
5	144	55	72.4 (64.4–79.8)	–
Peripheral zone:				
1	0	4	0 (0–0)	0.01
2	6	69	8 (2.4–14.5)	0.34
3	9	60	13 (5.6–22.2)	0.05
4	60	202	22.9 (17.1–29.5)	<0.001
5	87	27	76.3 (65.8–85.3)	–
Transition zone:†				
2	3	16	15.8 (0–34.8)	0.52
3	6	57	9.5 (1.9–18.8)	0.19
4	8	33	19.5 (8.3–33.3)	<0.001
5	56	28	66.7 (53.7–79.1)	–

*CDR difference vs next higher PI-RADS category.

† No PI-RADSv2 category 1 lesions.

Table 3.

Lesion based cancer detection rate by overall and T2W PI-RADSv2 categories for all prostate cancer and clinically significant prostate cancer in peripheral zone

	Overall			T2-Weighted			
PI-RADSv2 Score	**No. Pos**	**No. False-Pos**	**% Ca Detection (95% CI)**	**No. Pos**	**No. False-Pos**	**% Ca Detection (95% CI)**	**p Value***
Overall:							
1	1	3	25 (0–100)	2	2	50 (0–100)	0.58
2	14	61	18.7 (10.9–27.3)	11	57	16.2 (7.5–26.7)	0.59
3	17	52	24.6 (14.5–36.4)	54	158	25.5 (19–32.4)	0.87
4	96	166	36.6 (30–43.9)	62	67	48.1 (39.1–57.6)	0.001
5	100	14	87.7 (80.5–93.9)	99	12	89.2 (82.3–94.9)	0.36
Clinically significant:							
1	0	4	0 (0–0)	1	3	25 (0–50)	0.19
2	6	69	8 (2.4–14.5)	5	63	7.4 (1.5–14.3)	0.83
3	9	60	13 (5.6–22.2)	28	184	13.2 (8–19)	0.97
4	60	202	22.9 (17.1–29.5)	42	87	32.6 (23.5–42.3)	0.002
5	87	27	76.3 (65.8–85.3)	86	25	77.5 (67–86.4)	0.42

*Comparing cancer detection rate of each PI-RADS category.

Table 4.

PI-RADSv2 category 4 lesions by upgraded and primary PI-RADSv2 category 4 subgroups

PI-RADSv2 Category 4 PCa Subgroups	No. Pos	No. False-Pos	% Ca Detection (95% CI)
Overall:			
Upgraded	29	82	26.1 (15.8–36.7)
Primary	91	105	46.4 (38.6–54.2)
p Value	–	–	0.001
Clinically significant:			
Upgraded	18	93	16.2 (7.9–25.4)
Primary	50	146	25.5 (19–32.5)
p Value	–	–	0.097

Upgraded refers to PI-RADSv2 category 3 lesions upgraded to PI-RADSv2 category 4 due to DCE positivity in peripheral zone or to DWI PI-RADSv2 category 5 in transition zone.