ORIGINAL RESEARCH

The Correlation Between PI-RADS Score and the Detection of Prostate Cancer Using MRI-Ultrasound Fusion-Guided Transperineal Prostate Biopsy: The First Philippine Report

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Objective: MRI-Ultrasound fusion guided targeted biopsy has revolutionized the diagnosis of prostate cancer through accurate identification, localization and characterization of prostatic lesions utilizing the prostate imaging reporting and data system (PI-RADS) scoring system by multiparametric MRI (MPMRI). The fusion prostate biopsy system on the other hand, enables accurate targeting and easy access of the tumor. The study objective is to determine the detection rate of clinically-significant prostate cancer using fusion biopsy, and to establish the correlation between PI-RADS score and Gleason's score.

Patients and Methods: A retrospective cohort study was conducted to determine the correlation between PI-RADS score and the presence of prostate cancer using MRI-Ultrasound fusion guided transperineal prostate biopsy. This was carried out from June 2017 to July 2018 in a single institution. One hundred thirty five (135) men were included in this study. They presented with an elevated PSA, abnormal DRE or a previous negative prostate biopsy, but with a persistent rise in PSA. A total of 220 prostate lesions were identified. The following characteristics were measured: patient age; the size, location, the PI-RADS score of each lesion, the maximum PI-RADS score for select patients; and the Gleason score of discovered tumors.

Results: Two hundred twenty PI-RADS 3, 4 and 5 lesions were detected in 135 patients by MPMRI. 131 of the 220 lesions were scored as PI-RADS 3, 61 as PI-RADS 4 and 28 as PI-RADS 5. These lesions were biopsied using the MRI-Ultrasound fusion guided transperineal prostate biopsy system. Thirty-three out of the 131 PI-RADS 3 lesions (25.2%), 44 out of the 61 PI-RADS 4 lesions (72.1%) and 24 out of the 28 PI-RADS 5 lesions (85.7%) respectively were positive for malignancy. Overall, there were 101 (45.9%) lesions classified as PI-RADS 3 to 5 that were positive for prostate carcinoma. Seventy four (74) of the 135 patients (54.8%) were diagnosed with prostate adenocarcinoma. Nineteen out of 65 patients with a maximum score of PI-RADS 3 (29.2%), 33 of 44 with a maximum of PI-RADS 4 (75%) and 22 of 26 with a maximum of PI-RADS 5 (84.6%) harbored malignancy. In terms of location, 45 of the 101 (44.6%) malignancies were in the peripheral sector, 31 (30.7%) in the anterior sector, and 25 (24.8%) in the central sector of the prostate. The mean Gleason grade of PI-RADS 3, 4 and 5 lesions were 6.61, 7.73, and 7.38, respectively. Using Spearman correlation, the rho coefficient was 0.3153 (p-value =.00013) which denotes a significant positive relationship between Gleason and PI-RADS score.

Conclusion: This is the first comprehensive Philippine study on Multiparametric MRI-Ultrasound fusion-guided transperineal prostate biopsy. Present data validate the superiority of MPMRI in the identification, localization and characterization of prostate cancers. The authors also verified the positive correlation between PI-RADS score and Gleason score. Finally, they demonstrated the accuracy of the MRI- ultrasound fusion-guided transperineal prostate biopsy system in targeting prostate lesions.

Keywords: PI-RADS score, transperineal prostate biopsy

Introduction

Since its introduction in the 1980's, transrectal ultrasound (TRUS) guided prostate biopsy has remained as the gold standard in the histopathologic diagnosis of prostate cancer.[1] It is far from the ideal diagnostic procedure. Its low sensitivity and low negative predictive value raise the issues of potentially missing the cancer on biopsy, performing unnecessary biopsy on patients with benign conditions, and tendency for over-sampling or increasing the number of biopsy cores in the hope of increasing the odds of hitting the lesion. The rationale behind TRUS-guided prostate biopsy is the belief that most cancers are located in the peripheral zone. But contemporary evidences state otherwise. Studies on radical prostatectomy specimen concede that as many as 21% of cancers are located in the anterior region, which is relatively inaccessible to transrectal technique.[2-4]

Recent improvement in high resolution magnetic resonance imaging (MRI) technology led to the development of multi-parametric MRI (MPMRI) technique. The procedure employs 3 parameters, namely: T2 weighted image (T2W), diffusion weighted image (DWI) and dynamic contrast enhanced (DCE). T2W is used to delineate prostatic zonal anatomy, assess abnormalities within the gland, and evaluate seminal vesicle invasion. Clinically significant cancers have restricted or impeded diffusion on DWI. Prostate cancer on DCE often demonstrates early enhancement compared to normal tissues.[5] In 2012, the European Society of Urogenital Radiology created a panel of experts and reported a new scheme called Prostate Imaging Reporting and Data System (PI-RADS).[6-7] The PI-RADS assigns a score of 1 to 5 to a 'hot' prostate area. A score of 1 or 2 denotes clinically-insignificant disease, 3 is indeterminate, while 4 and 5 indicate a high likelihood of clinically-significant disease. (See Appendix 1-8).[6,8,9]

The capacity of MPMRI to recognize potentially malignant lesions and the technology to fuse MRI with real-time ultrasound image of the prostate, made targeted needle biopsy easy, simple and extremely accurate. If PI-RADS score correlates with tumor aggressiveness, MPMRI may potentially be used as a screening procedure for prostate cancer.

The authors report on the first Philippine experience utilizing MRI-Ultrasound fusion guided transperineal prostate biopsy in the diagnosis of prostate cancer.

The aim is to determine the detection rate of PI-RADS 3, 4 and 5 using the MRI-Ultrasound fusion biopsy machine in the diagnosis of prostate cancer and to determine if there is a correlation between PI-RADS and Gleason's score or tumor grade.

Patients and Methods

A retrospective cohort study was conducted to determine the correlation between PI-RADS score and the presence of prostate cancer using MRI-Ultrasound fusion-guided transperineal prostate biopsy. This was conducted from June 2017 to July 2018 in a single institution.

A total of 135 patients with 220 prostate lesions detected on MPMRI were included. The patients presented with elevated PSA, abnormal DRE or a previous negative prostate biopsy, but with a persistent rise in PSA.

The following characteristics were measured: patient age; the size, location, the PI-RADS score of each lesion; the maximum PI-RADS score for select patients; and the histopathology and Gleason score of the discovered tumors.

All patients underwent MPMRI of the prostate using the 1.5 Tesla Siemens Avanto. All results were interpreted by a single group of radiologists using the PI-RADS 2 version. All suspicious lesions were marked and assigned a PI-RADS score. An individual patient may have multiple lesions. In this case, the lesions were scored individually, and the highest PI-RADS score recorded was considered the maximum PI-RADS score.

All patients underwent a lesion directed transperineal biopsy under real time fused MRI-Ultrasound imaging. It was performed in a single institution using an MRI-Ultrasound fusion machine with a transrectal ultrasound probe and a transperineal grid template. Under general anesthesia, a minimum of 4 prostate cores were

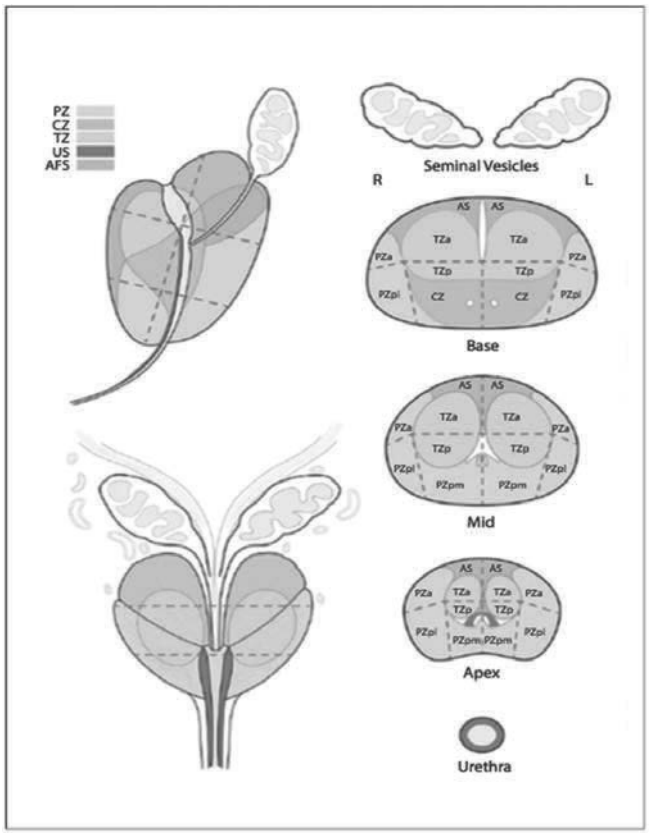


Figure 1. Sector map of PIRADS 2.0 from http://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/Resources/PIRADS/PIRADS%20V2.pdf (accessed on 8/26/2015)

taken per lesion. The PI-RADS score, histopathologic result and Gleason score were tabulated.

Data were encoded in MS Excel. Stata MP version 14 was used for further processing and analysis. Continuous variables were presented as mean/SD or median/IQR depending on data distribution. Categorical variables were presented as frequency or percentage. Pearson correlation coefficient was calculated to determine the relationship between the PI-RADS and Gleason scoring systems. P value ≤0.05 was considered statistically significant.

Results

One hundred thirty five (135) patients underwent MRI-Ultrasound fusion guided transperineal prostate biopsy. The mean age was 66.74 years old (Range: 41-85 years old). The mean prostate size was 44.93 grams (Range: 15-119 grams). A total of 220 lesions were identified in 135 patients. Seventy three (54.4%) patients had only one lesion on MRI. Table 1 summarizes the baseline characteristics.

Table 1. Demographic and clinical profile of patients (N= 135)

Characteristics	n (%)
Mean age (year)	66.74 ± 7.45
Mean prostate size (in grams)	44.93 ± 22.72
Mean number of prostate lesion	1.63 ± 0.78
1	73 (54.1)
2	42 (31.1)
3	17 (12.6)
4	3 (2.2)

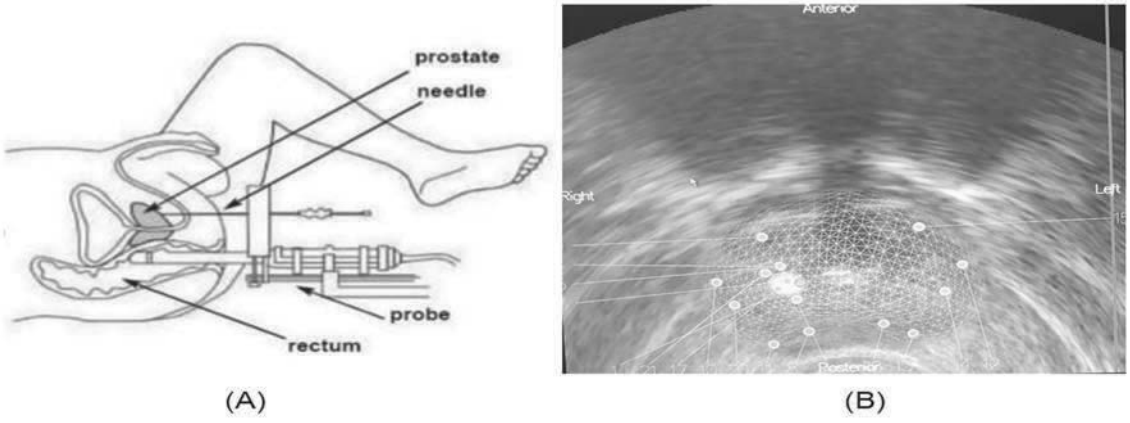


Figure 2. Position of patient with the transrectal probe and transperineal template (Figure A). Image of the prostate lesion with prostate biopsy tracts (Figure B).

The mean lesion size was 1.14cm x 1.13cm x 1.22cm (AP/T/CC). Lesions were found on the right (47.3%) and left (48.2%) half of the prostate. Ninety two (41.8%) lesions were found in the posterior part of the prostate. Seventy eight (35.5%) were anterior and 50 (22.7%) lesions were central. One hundred thirty three (60.5%) lesions were detected in the transition zone, 35% in the peripheral zone, and 4% in the central zone. One hundred nineteen (54%) lesions were found in the mid-prostate. 28% in the apex and 18% in the base. Table 2 summarizes the above data.

Table 2. Prostatic lesion profile (N=220).

	Profile
Mean lesion size (in cm), mean	
AP (n=221)	1.14 ± 0.59
T (n=221)	1.13 ± 0.64
CC (n=165)	1.21 ± 0.95
Laterality	n (%)
Right	104 (47.3)
Left	106 (48.2)
Middle	10 (4.6)
Location	
Anterior	78 (35.5)
Posterior	92 (41.8)
Central	50 (22.7)
Zone	
Transition	133 (60.5)
Peripheral	78 (35.5)
Central	9 (4.1)
Area	
Apex	61 (27.7)
Mid	119 (54.1)
Base	40 (18.2)

Of the 220 lesions, 131 were scored as PI-RADS 3, 61 as PI-RADS 4 and 28 as PI-RADS 5. Thirty-three out of the 131 PI-RADS 3 lesions (25.2%), 44 out of the 61 PI-RADS 4 lesions (72.1%) and 24 out of the 28 PI-RADS 5 lesions (85.7%) respectively yielded malignancy on biopsy. Overall, prostate carcinoma was found in 101 (45.9%) of 220 lesions with a PI-RADS score of 3 to 5. Table 3 summarizes the above findings.

Table 3. Malignancy rate per lesion and PI-RADS score (N=220).

PI-RADS	n	Malignant (n=101) n (%)	Benign (n=119) n (%)
3	131	33 (25.2)	98 (74.8)
4	61	44 (72.1)	17 (27.9)
5	28	24 (85.7)	4 (14.3)

Seventy-four of 135 patients were diagnosed with prostate adenocarcinoma (54.8%). Nineteen out of 65 patients with a maximum score of PI-RADS 3 (29.2%), 33 out of 44 patients with a maximum of PI-RADS 4 (75%) and 22 out of 26 patients with a maximum of PI-RADS 5 (84.6%) respectively, harbored malignancy. (Table 4)

Table 4. Malignancy rate per patient and PI-RADS score (N=135).

PI-RADS	n	Malignant (n=74) n (%)	Benign (n=61) n (%)
3	65	19 (29.2)	46 (70.8)
4	44	33 (75.0)	11 (25.0)
5	26	22 (84.6)	4 (15.4)

In terms of location, 45 out of 101 (44.6%) malignancies were located in the peripheral sector, 31 (30.7%) in the anterior sector and 25 (24.8%) in the central sector of the prostate. (Table 5)

Table 5. Location of PI-RADS 3, 4, 5 lesions with positive cores on histopathology.

Location	(+) malignancy n = 101
Anterior	31 (30.7%)
Central	25 (24.8%)
Peripheral	45 (44.6%)

The mean Gleason grade of PI-RADS 3, 4 and 5 lesion were 6.61, 7.73, and 7.38, respectively. (Table 6). The overall mean PI-RADS 3, 4 and 5 lesions was 3.91, and the mean Gleason grade was

7.28. Using Spearman correlation, the rho coefficient was 0.3153 (p-value = .00013), which indicates a significant positive relationship between Gleason and PI-RADS score. (Figure 3)

Table 6. PI-RADS and Gleason grade

PI-RADS	Gleason Grade (Mean)
3	6.61
4	7.73
5	7.38

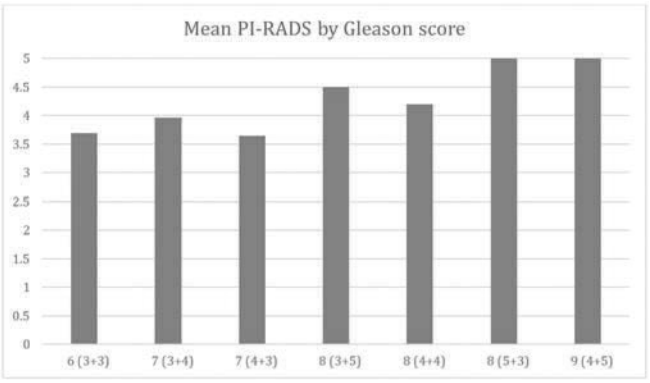


Figure 1. Mean PI-RADS score by Gleason score (n=101)

Discussion

After its introduction in the 1980's, TRUS prostate biopsy has become the gold standard for detection of early prostate cancer.[10] However, the procedure is innately flawed. It has a low detection rate of 33-42% which means that a large number of prostate cancers are missed, or numerous unnecessary biopsies are performed.[11-13] Furthermore, it does not have the ability to differentiate between indolent and significant tumors, which are managed differently. The ideal biopsy procedure must possess better cancer detection rate and provide segregation between indolent and clinically-significant tumor.

MPMRI offers the following improvements over TRUS: A. increased resolution, B. superior imaging of the prostate and the peri-prostatic tissues, C. functional assessment of the prostate, and D. assignment of tumor grades to the suspected lesions using the PI-RADS scoring. MPMRI has a negative predictive value of up to 100% especially when diffusion weighted image (DWI) and T2 weighted image are negative.[14] This technique has a reported positive predictive value of up to 98% for detecting clinically-significant prostate cancer, with better performance in higher grade and larger tumors.[16] Present data indicate that prostate cancer is detectable with MPMRI in the local setting, thus allowing urologists the transition from blind sampling to mapped and targeted biopsies.

MPMRI is superior to the standard transrectal prostate biopsy in the diagnosis of focal prostatic lesions according to Dieffenbacher.[9,6,17] It was also noted by Alpajaro, et al. that multiparametric MRI combined with the use of PI-RADS improves the detection rate and diagnostic accuracy of prostate biopsy in clinically-significant prostate cancers. PI-RADS 3, 4 and 5 had a detection rate of 33.3%, 58.7% and 94.7%, respectively.[18]

Present results indicate a detection rate of 72.1% and 85.7% for PI-RADS 4 and 5 lesions, respectively. Meanwhile, PI-RADS 3 remains an indeterminate score, with a 25.2% probability of malignancy. Therefore, biopsy is still recommended to rule malignancy out. The authors also analyzed the probability of prostate cancer in patients with a maximum PI-RADS of 3, 4 or 5 regardless of the total number of lesions. Their data showed that patients with a maximum PI-RADS score of 4 and 5 had a detection rate of 75% and 84.6% respectively. Patients with a maximum PI-RADS score of 3 had a detection rate of 29.2%. Overall, the 45.9% detection rate per lesion and the 54.8% detection rate per patient using MPMRI and PI-RADS score was significantly better than the historical data with TRUS-guided prostate biopsy of 37.5%.[13]

The utilization of MPMRI to avoid over-diagnosis of indolent tumors is now well-established. Numerous authors state a high negative predictive value of PI-RADS 1 and 2, with a value of 94-100%.[19-21] This indicates that biopsy may be deferred in PI-RADS 1 or 2 lesions since there is a high negative predictive value. By omitting biopsy in these lesions, and the number of unnecessary biopsies is reduced and over-detection of low risk cancers (Gleason ≤6) is avoided.[20]

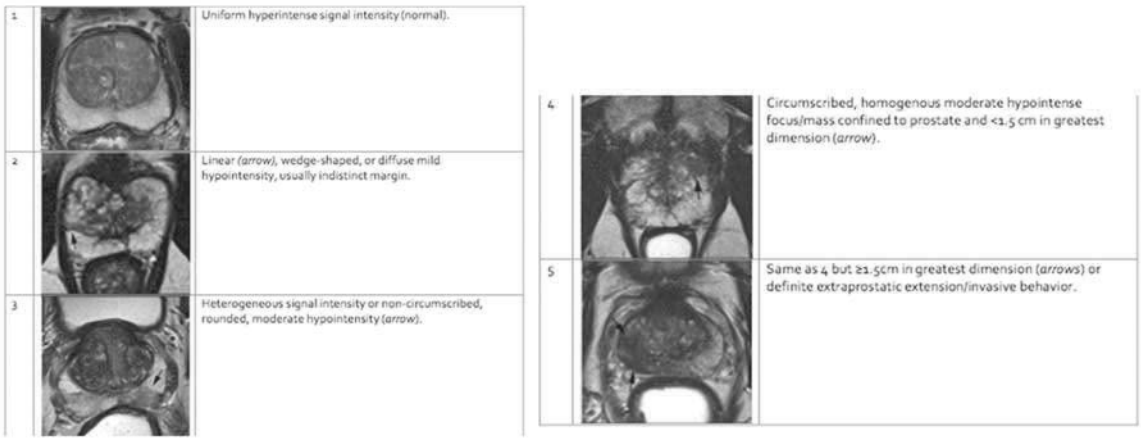
The present study also established the correlation between PI-RADS and Gleason score. It is evident that lower PI-RADS scores indicate tumors with low Gleason score and are therefore probably insignificant. Most malignancies scored as PI-RADS 3 to 5 had a Gleason score of 7 or 8. These cancers are clinically-significant, and warrant more aggressive treatment.

It is of interest that a considerable number of positive biopsy results came from the anterior (30.7%) and central (24.8%) zones. These lesions are usually missed in the standard TRUS biopsy. In contrast, the transperineal approach enables easy and complete sampling in all areas of the prostate.

Conclusion

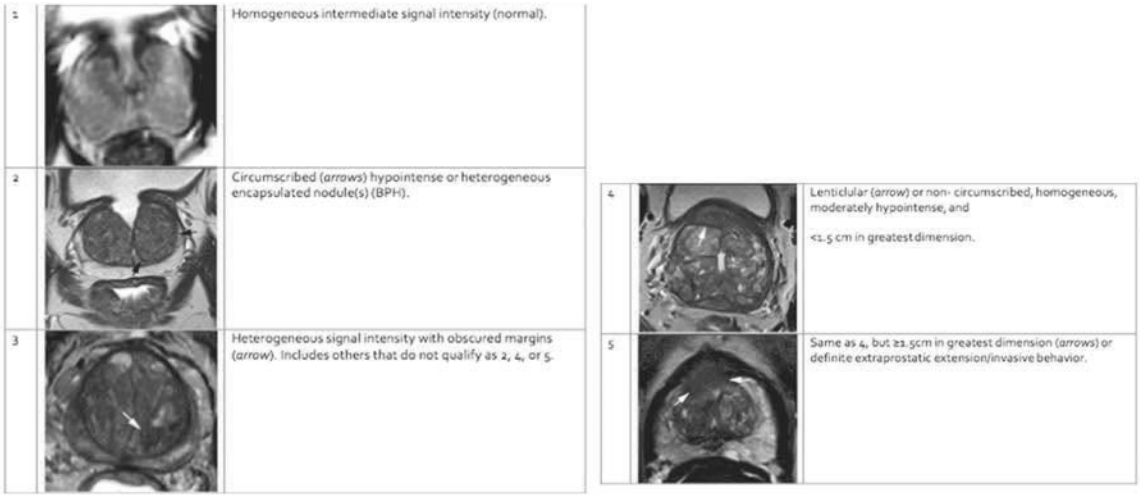
This is the first comprehensive Philippine study on Multiparametric MRI-Ultrasound fusion-guided transperineal prostate biopsy. Present data support the superiority of MPMRI in the identification, localization and characterization of prostate cancers. The authors also verified the positive correlation between PI-RADS score and Gleason score. Finally, they validated the accuracy of the MRI-ultrasound fusion guided transperineal prostate biopsy system in targeting prostate lesions.

Appendix 1: PI-RADS assessment for peripheral zone on T2-weighted image



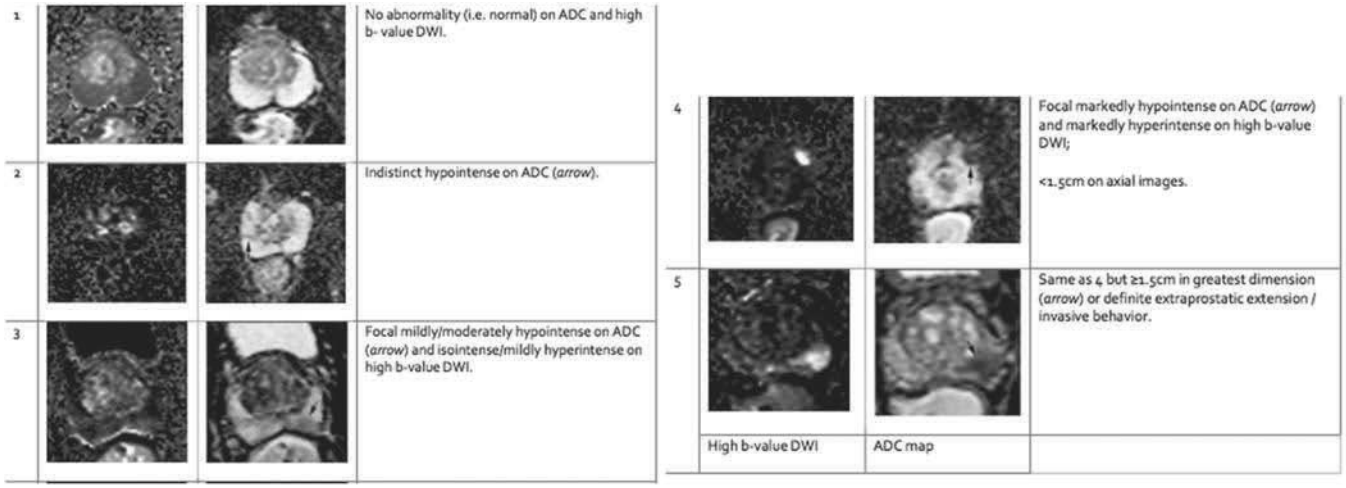
Bonekamp D, Jacobs MA, El-Khouli R, et al. Advancements in MR imaging of the prostate: from diagnosis to interventions. Radiographics 2011;31(3):677.

Appendix 2: PI-RADS assessment for transition zone on T2-weighted image



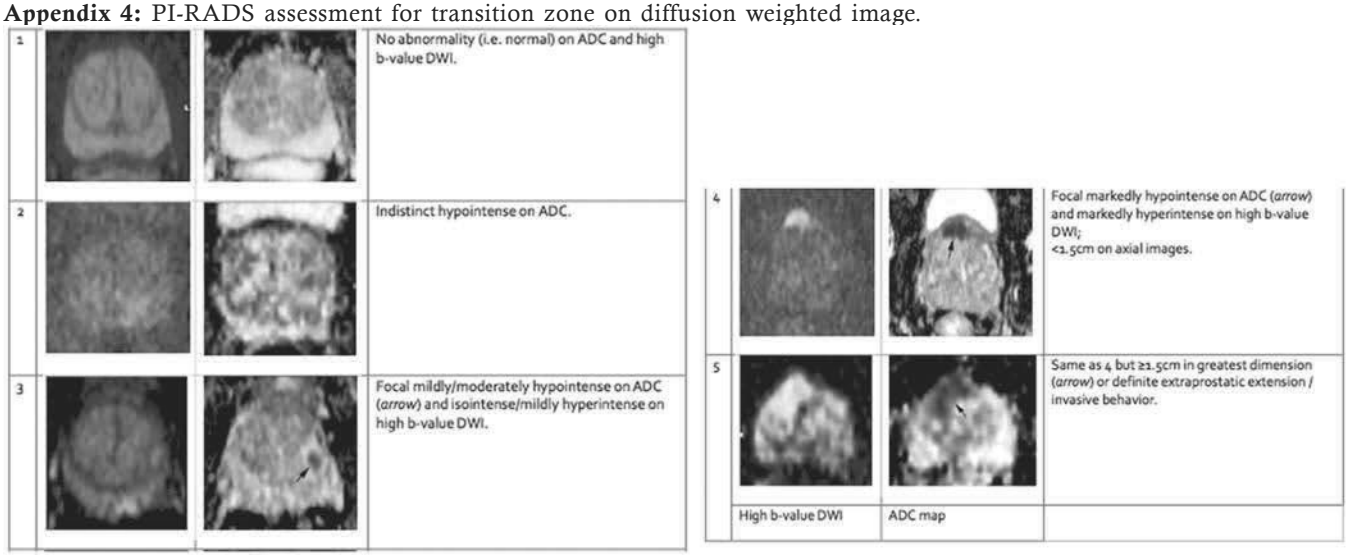
Bonekamp D, Jacobs MA, El-Khouli R, et al. Advancements in MR imaging of the prostate: from diagnosis to interventions. Radiographics 2011;31(3):677.

Appendix 3: PI-RADS assessment for peripheral zone on diffusion weighted image



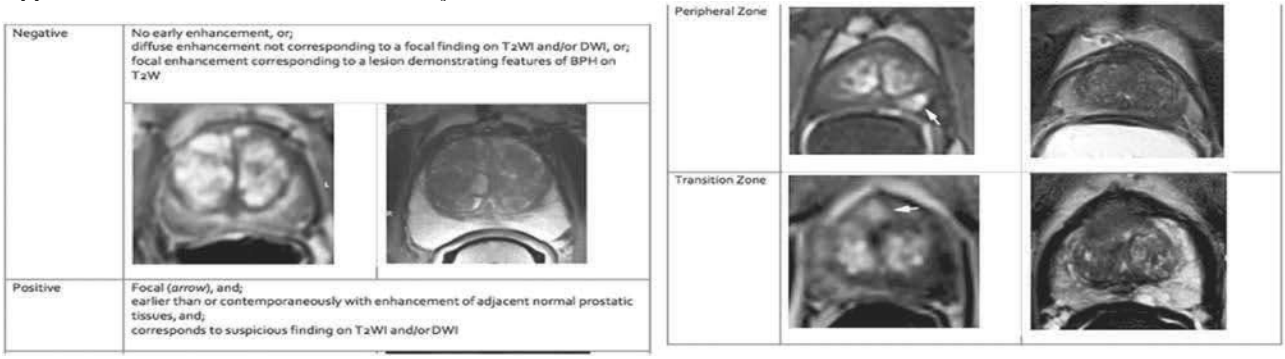
Bonekamp D, Jacobs MA, El-Khouli R, et al. Advancements in MR imaging of the prostate: from diagnosis to interventions. Radiographics 2011;31(3):677.

Appendix 4: PI-RADS assessment for transition zone on diffusion weighted image.



Bonekamp D, Jacobs MA, El-Khouli R, et al. Advancements in MR imaging of the prostate: from diagnosis to interventions. Radiographics 2011;31(3):677.

Appendix 5: PI-RADS assessment for dynamic contrast enhanced MRI



Bonekamp D, Jacobs MA, El-Khouli R, et al. Advancements in MR imaging of the prostate: from diagnosis to interventions. Radiographics 2011;31(3):677.

Appendix 6: PI-RADS Assessment for T2W

Score	Peripheral Zone (PZ)
1	Uniform hyperintense signal intensity (normal)
2	Linear or wedge-shaped hypointensity or diffuse mild hypointensity, usually indistinct margin
3	Heterogeneous signal intensity or non-circumscribed, rounded, moderate hypointensity Includes others that do not qualify as 2, 4, or 5
4	Circumscribed, homogenous moderate hypointense focus/mass confined to prostate and <1.5 cm in greatest dimension
5	Same as 4 but ≥1.5cm in greatest dimension or definite extraprostatic extension/invasive behavior

Score	Transition Zone (TZ)
1	Homogeneous intermediate signal intensity (normal)
2	Circumscribed hypointense or heterogeneous encapsulated nodule(s) (BPH)
3	Heterogeneous signal intensity with obscured margins Includes others that do not qualify as 2, 4, or 5
4	Lenticular or non-circumscribed, homogeneous, moderately hypointense, and <1.5 cm in greatest dimension
5	Same as 4, but ≥1.5cm in greatest dimension or definite extraprostatic extension/invasive behavior

American College of Radiology, PI-RADS version 2, 2015, p. 23

Appendix 7: PI-RADS Assessment of DWI

Score	Peripheral Zone (PZ) or Transition Zone (TZ)
1	No abnormality (i.e., normal) on ADC and high b-value DWI
2	Indistinct hypointense on ADC
3	Focal mildly/moderately hypointense on ADC and isointense/mildly hyperintense on high b-value DWI.
4	Focal markedly hypointense on ADC and markedly hyperintense on high b-value DWI; <1.5cm in greatest dimension
5	Same as 4 but ≥1.5cm in greatest dimension or definite extraprostatic extension/invasive behavior

American College of Radiology, PI-RADS version 2, 2015, p. 25

Appendix 8: PI-RADS Assessment for DCE

Score	Peripheral Zone (PZ) or Transition Zone (TZ)
(–)	no early enhancement, or diffuse enhancement not corresponding to a focal finding on T2W and/or DWI or focal enhancement corresponding to a lesion demonstrating features of BPH on T2WI
(+)	focal, and; earlier than or contemporaneously with enhancement of adjacent normal prostatic tissues, and; correspnds to suspicious finding on T2W and/or DWI

American College of Radiology, PI-RADS version 2, 2015, p. 27

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