ORIGINAL RESEARCH

Multi-Parametric Magnetic Resonance Imaging (MpMRI) Based Prostate Imaging and Reporting Archiving Data System (PIRADS): Utility in Improving Cancer Detection, Localization and Characterization

Sigfred Ian R. Alpajaro, MD and Jason L. Letran, MD, FPUA

Section of Urology, Department of Surgery, University of Santo Tomas Hospital

The Prostate Imaging and Reporting Archiving Data System (PI-RADS) uti-lizes multiparametric MRI (mpMRI), allowing for lesion characterization as an aid for prostate cancer detection.
Objectives: This study aimed to determine the sensitivity of PI-RADS in de-tecting clinically significant prostate adenocarcinoma on biopsy, and correlating it with Gleason score.
Materials and Methods: Thirty-two (32) consecutive patients suspected with prostate cancer underwent mpMRI between July 2014 to July 2015. A single radiologist reviewed the mpMRI and assigned PI-RADS scores to lesions detected. Using cognitive technique, prostate biopsy was done via transperineal approach. Regions of interest were initially sampled, followed by areas on systematic sector based on established template. Histopathologic interpretations were done by a single group of pathologists.
Results: The mean age of the study population was 67 years. The mean prostate size was 50.4grams, and the mean PSA was 12.1 ng/dl. Forty-five (45) lesions were detected by mpMRI and assigned a PI-RADS score of 3,4, and 5. Overall, 31/45 (68.8%) lesions described as PI-RADS 3,4, or 5, turned out to be prostate carcinoma. Of those with iden-tified MRI lesions, 3/9 (33.3%) PIRADS 3, 10/17 (58.7%) PIRADS 4, and 18/19 (94.7%) PIRADS 5 were positive for malignancy respectively. The overall mean PI-RADS 3,4 and 5 lesions score was 4.48, and mean Gleason grade was 7.61. Using Kendall rank correlation, the tau coefficient was 0.3266 (p-value = .009), consistent with a positive correlation between PI-RADS score and Gleason grade.
Conclusions: Multiparametric MRI combined with the use of PI-RADS help increase the detection and accuracy in diagnosis of clinically significant prostate cancer. There is cor-relation between PI-RADS and Gleason grade. It's significance lies in potentially pre-venting over diagnosis of indolent, low grade cancers by preventing unnecessary biop-sies while allowing clinically significant cancers to be appropriately managed.

Key words: prostate cancer, multiparametric MRI, Prostate Imaging and Reporting Ar-chiving Data System (PIRADS)

Introduction

Prostate cancer is the most common malignancy in the male population.[1,2] At present, the 12-core transrectal ultrasound guided prostate needle biopsy is the standard for diagnosis of prostate cancer. Review of international data consist-ently revealed a low detection rate, which at best is just a modest 44.4%.[4] In the local setting, the most extensive data review available showed

detection rates of 29.5% for 12-core biopsy and 36.4% for 24-core biopsy.5 Even template mapping biopsy has not reliably increased the diagnosis, with recent reviews yielding only 25-53% detection rates.[3,6-8] The consistently low detection rate has a profound implication of potentially missed cancers in patients needing treatment or performing unnecessary biopsies in patients that indeed do not have malignancy in the first place. Certainly, this diagnostic pathway leaves a lot of room for improvement.

Multiparametric MRI (mpMRI), which combines anatomical and functional data, is now regarded as the most sensitive and specific imaging technique for localizing prostate cancer, allowing for improved detection and lesion characterization.[4,6]

In 2012, the Prostate Imaging and Reporting Archiving Data System (PI-RADS) was introduced by the European Society of Urogenital Radiology (ESUR), with the goal of interpreting and reporting different parametric MR techniques for prostate cancer detection.[10] The PI-RADS is scored as 1-5, with Score 1 meaning that clinically significant disease is highly unlikely and score 5 indicates that clinically significant cancer is highly likely to be present. Score of 3 is indeterminate. (see Appendix 1-5).[3,7]

ESUR has stated MpMRI should at least consist of high-resolution T2-weighted imaging (T2WI) which images the prostate anatomy, and in combination with two functional techniques.[7] Dynamic contrast-enhanced (DCE) MRI detects endothelial permeability and perfusion, diffusion-weighted imaging (DWI) determines cellular density and membrane stability, and proton spectroscopy imaging (MRSI) evaluates tissue metabolism.[3,7-9]

The PI-RADS risk stratification system has shown good reliability in cancer detection based on several series.[10-15] PI-RADS can, likewise, enhance the identification that (PI-RADS≥4) leading to a higher detection rate of significant tumors (i.e. GS≥7).[15,16]

Indeed, a meta-analysis of 14 studies showed PI-RADS to have good diagnostic accuracy in prostate cancer detection. However, there has never been any re-port of its utility in the local setting.

This study aims to report on the first Philippine experience utilizing mpMRI as an aid in the diagnosis of prostate cancer.

The study aimed to determine the sensitivity of PI-RADS in detection of prostate adenocarcinoma in prostate biopsy. It also aimed to correlate PI-RADS score with Gleason scores and determine its ability to detect clinically significant cancers (i.e. Gleason score ≥7)

Materials and Methods

Patient Selection

Thirty-two consecutive patients in whom prostate cancer is suspected underwent 1.5 Tesla mpMRI without endorectal coil between July 2014 to July 2015 and were included in this study. The criteria for performing mpMRI include either: 1. Part of pre-biopsy work-up and imaging, 2. Persistently elevated PSA after a previously negative biopsy to help determine ROIs for possible targeted biopsies. Baseline characteristics of patients including age and PSA levels were gathered.

Data Collection

MRI images were analyzed by a single radiologist with sub specialization on MRI interpretation. Using PI-RADS classification, sector map is provided, which serves as the guide for the sector biopsy. (Figure 1)

The location of individual lesions seen on mpMRI were noted which would form the basis of lesion localization and via cognitive guidance, served as the guide for targeted biopsy utilizing the transperineal approach.

Description of Biopsy Technique: Transperineal Prostate Sector Biopsy

All procedures were done in a single tertiary institution by a single urolo-gist (senior author) using the BK Falcon Ultrasound unit utilizing the 8808 brachytherapy probe. The biopsies were performed under total intravenous sedation anesthesia.

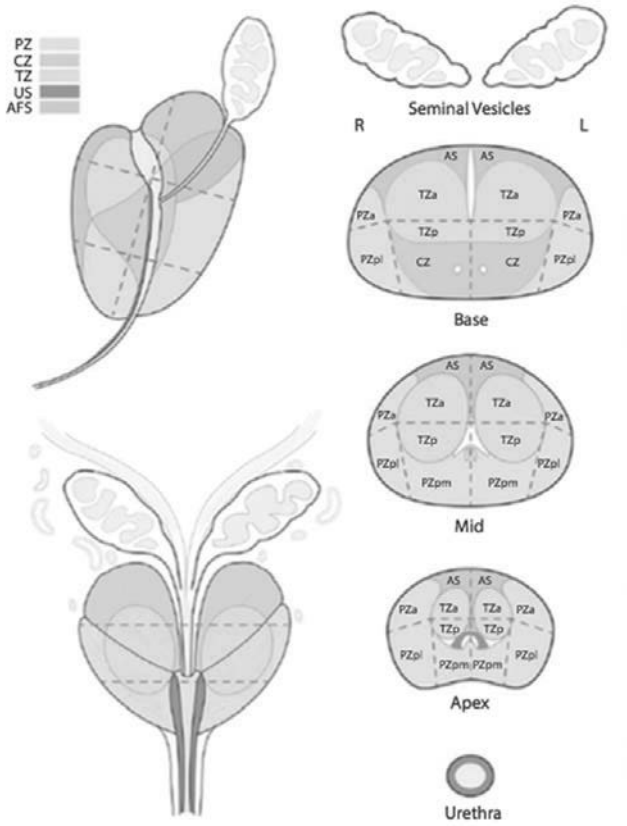

Figure 1. Sector map of PIRADS 2.0 from http://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/Resources/PIRADS/PIRADS%20V2.pdf (accessed on 8/26/2015)

Patients were initially placed in the lithotomy position for the TPSB. A Fr 16 Foley catheter was inserted to facilitate identification of urethra and prostato-vesical junction. (Figure 2)

Targeted biopsy of the regions of interest (ROI) were performed initially based on cognitive method. (Figure 3). This was followed by systematic biopsy of the pros-tate based on universally accepted template introduced by Kuru, et. al to sample the anterior, middle and posterior sectors of both the right and the left side.[19] (Figure 4)

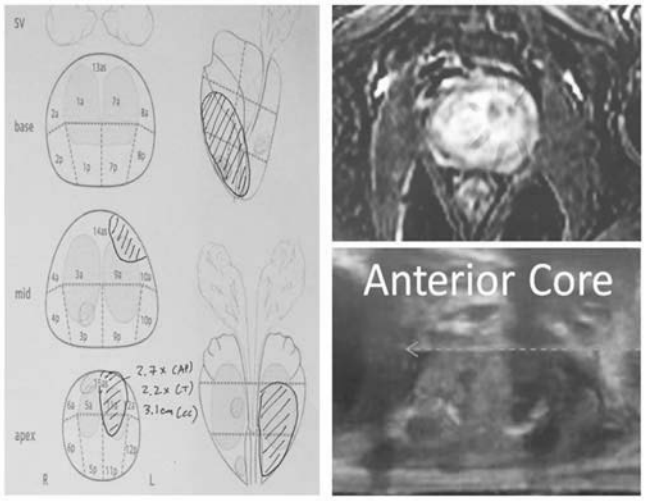

Figure 3. Incorporating data from mpMRI and PI-RADS score, ROIs are identified, and targeted biopsy is done using cognitive method.

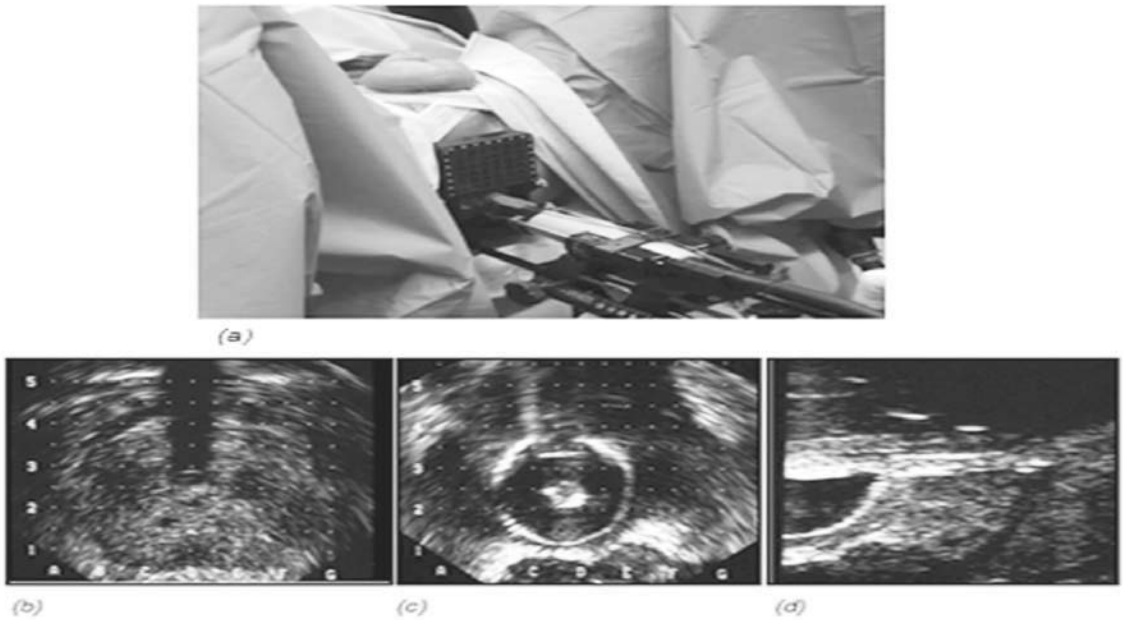

Figure 2. Patient is placed an lithotomy position and draped.(Fig. 2a) Sonographic images showing the urethra at the center of the grid(Fig. 2b) as well as images of the prostato-veiscal junction(Fig. 2c and 2d)

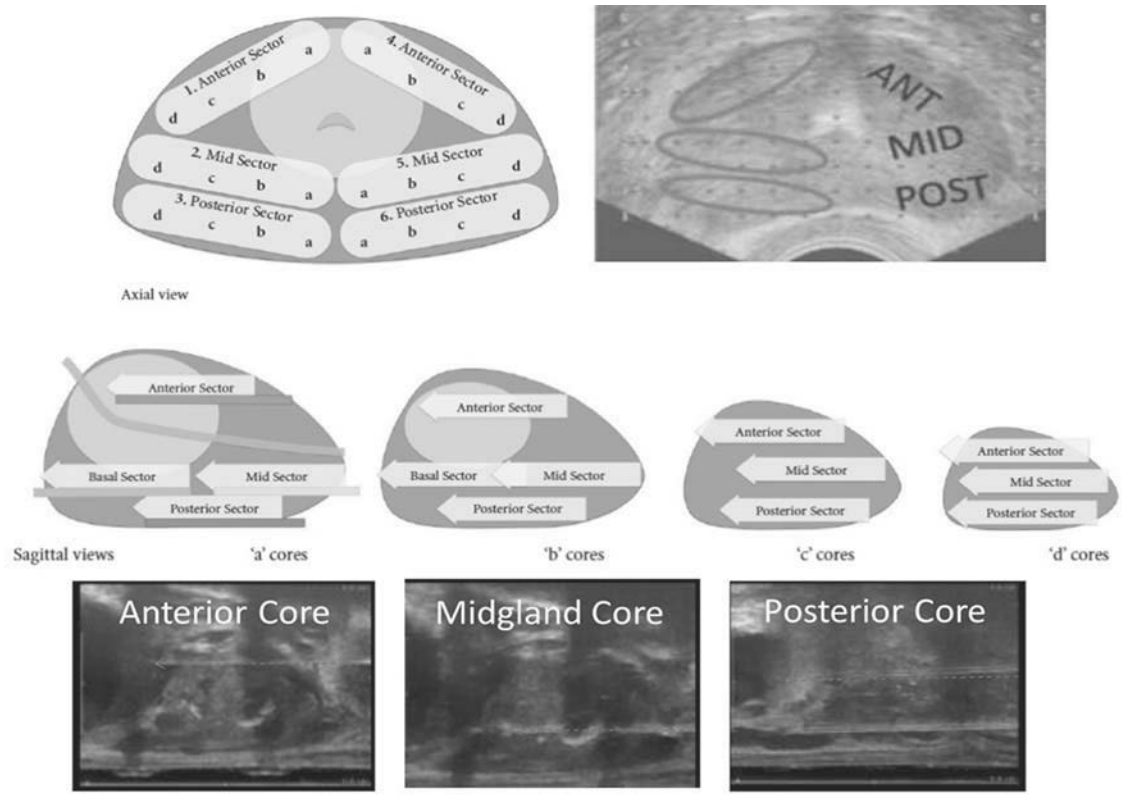

Figure 4. Standard technique of sampling in the Transperineal Prostate Sector Biopsy. Kuru, Timur H, et al. "Definitions of terms, processes and a minimum dataset for transperineal prostate biopsies: a standardization approach of the Ginsburg Study Group for Enhanced Prostate Diagnostics." BJU international 112.5 (2013): 568-577

All specimen were placed in formalin solution, properly labeled, and sent for his-topathologic processing to be interpreted by a single group of pathologists.

Statistics

Mean and standard deviation (SD) will be used to summarize numerical data. Percentages and frequency were used for nominal and ordinal data. The Shapiro-Wilk test was used to assess the normality of distribution. Since the data was not normally distributed, the Kendall rank test was used to evaluate correlation of PI-RADS score and Gleason grade. All the statistical tests were performed using SPSS ver. 20. P-values less than 0.05 are to be considered significant.

Results

A total of 32 patients with suspicious DRE and/or elevated PSA in whom mpMRI with PI-RADS scoring was done were included in the study. The mean age was 67 years. The mean prostate size was 50.4grams, and the mean PSA was 12.1 ng/dl. Table 1 summarizes the baseline characteristics.

Fourteen patients were initial biopsies while 18 were repeat biopsies (previously negative biopsies with continued elevation of PSA and suspicion for malignancy). Overall, 17 out of the total 32 patients (53.1%) turned out positive for

Table 1. Summary of baseline characteristics.

	n = 32 patients
Age (years)	67 (52 - 81)
Prostate size (grams)	50.4 (18 - 141)
PSA (ng/dl)	12.1 (2 - 120.2)

malignancy. Ten out of the 14 (71%) initial biopsies and 7 out of the 18 (38.8%) repeat biopsies were positive for malignancy on histopathology. Table 2 summarizes the above data.

Table 2. Patient biopsy and cancer detection.

	(+) Malignancy	(-) Malignancy	Total
Initial Biopsy	10 (71%)	4 (29%)	14 (100%)
Repeat Biopsy	7 (38.8%)	11 (61.2%)	18 (100%)
Total	17 (53.1%)	15 (46.9%)	32 (100%)

A total of 45 lesions were detected by mpMRI and assigned a PI-RADS score of 3,4, and 5. Of the 9 PI-RADS 3 lesions, 3 (33.3%) were positive for malignancy on histopathology. Of the 17 PI-RADS 4 lesions, 10 (58.7%) were positive for malignancy on histopathology. Finally for PI-RADS 5 lesions, 18 (94.7%) were positive for malignancy. Overall, there were 31 (68.8%) lesions described as PI-RADS 3,4, or 5, that turned out to be prostate carcinoma on final pathology. Of note, 3 biopsy areas turned out positive for malignancy (all Gleason 3+3 = 6) but were not detected or reported by mpMRI. Table 3 summarizes the above findings.

Table 3. PI-RADS and detection of malignancy.

PI-RADS	(+) Malignancy	(-) Malignancy	% detection
3 (n=9)	3	6	33.3
4 (n=17)	10	7	58.7
5 (n=19)	18	1	94.7
Total (45 lesions)	31	14	68.8

*3 biopsy areas (+) for malignancy but not detected by mpMRI/PI-RADS

In terms of location, 16 of the 31 (51.6%) malignancies were peripheral in location. 4 (12.9%) and 11 (35.4%) were located in the anterior and central sectors of the prostate gland. (Table 4)

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

Location	(+) malignancy N=31
Anterior	4 (12.9%)
Central	11 (35.4%)
Peripheral	16 (51.6%)

The mean Gleason grade of PI-RADS 3,4 and 5 lesion were 8.33, 6.77, and 8, respectively. (Table 5). The overall mean PI-RADS 3,4 and 5 lesions was 4.48, and mean Gleason grade was 7.61. Using Kendall rank correlation, the tau coefficient was 0.3266 (p-value = .009), consistent with a positive correlation between PI-RADS score and Gleason grade. (Table 6)

Table 5. PI-RADS and Gleason grade.

PI-RADS	Gleason Grade (Mean)
3	8.33
7	6.77
8	8

Table 6. Correlation of PI-RADS and Gleason grade.

	PI-RADS	Gleason
Overall Mean (+/- SD)	4.48 (+/- 0.68)	7.61 (+/- 1.28)
Range	3 - 5	6 - 10
Mode	5	7
τ	0.33	
p-value	0.009	

Discussion

For the past three decades, digital rectal examination (DRE), serum prostate specific antigen (PSA) and trans-rectal ultrasound (TRUS) guided biopsy have been utilized for cancer screening and detection.[3] However, DRE can miss out many tumors, PSA sensitivity and specificity as the basis for prostate biopsy is less than ideal,

and TRUS guided biopsy focuses on rather invisible targets.[3] Ultrasound also has very limited characterization of suspicious prostatic areas. The classic "hypoechoic" lesion during TRUS imaging, said to be typical of a malignancy, is seen in only 41.5% of prostatic cancers, and up to 31.8% are isoechoic.[8] TRUS approach also does not routinely and easily sample the anterior and even central prostate, potentially missing suspicious sites that require biopsy. It is therefore not surprising that at best, the traditional 12-core biopsy transrectal has a detection rate of 44.4% and while transperineal approach with a modest 48.3%.[4,10]

It can be argued that it is probably only in the prostate gland that image guidance has not been widely utilized as an aid in the performance of a biopsy. In recent years, mpMRI has been continuously gaining ground as an important tool in the diagnosis of prostate cancer. This modality help identifies ROIs and is scored by radiologists using PIRADS or other evaluation system. Using these data for prostate biopsy, and potentially being able to target suspicious areas in the prostate that may not be visible on ultrasound alone, the combination of T2W, DWI and DCE has increased sensitivity, specificity, and accuracy up to 95%, 74%, and 86%, respectively.[7]

Results of this study indicate a detection rate of 58.7% and 94.7% for PI-RADS 4 and 5 lesions, respectively. Meanwhile, PI-RADS 3 remains to be an indeterminate score, with 33.3% being malignant on histopathology. Therefore, it should still be treated as suspicious, and necessitates biopsy to determine the nature of such lesions. Over all, the 53.1% detection rate using mpMRI and PI-RADS is better than the cited biopsy yield rates using ultrasound alone.[4,10] Furthermore, if one would consider just the initial biopsy group from this study, the mrMRI based initial biopsy detection rate is an even higher at 71%.

It is important to differentiate between Gleason score 6 with Geason ≥7, since management decisions rely heavily on risk classification. Low risk cancers (i.e Gleason ≤6) are candidates for active surveillance, while intermediate to high risk cancers (Gleason ≥7) may necessitate more aggressive forms of treatment.[16] The potential discerning characteristics of mpMRI to avoid overdiagnosis of tumors of low aggressiveness while detecting significant and aggressive cancers is only being realized recently.[15] In our series, mpMRI missed 3 Gleason 6 (3+3) lesions. Several authors have already shown the high negative predictive value (i.e. PI-RADS 1-2 have 94-100% NPV) and moderate to high positive predictive value (PIRADS 3,4,5 have PPV of 74, 73, and 100%, respectively).[15,20,21] Translated clinically, one can defer biopsy when only PI-RADS 1-2 is found since there is high NPV and overdetection of low risk cancer (Gleason ≤6) is avoided.[15]

On the other hand, most of the malignancies detected by biopsy of PI-RAD 3,4 and 5 lesions in our series were Gleason 7-8, which are clinically significant cancers. This is consistent with a good number of published data and recently, a metaanalysis that reviewed the ability of mpMRI and yielded rather satisfactory sensitivity and specificity to detect significant and aggressive tumors.[11-13,17-19]

It is worthwhile mentioning that consistent with other published data, our study has further established the correlation between PI-RADS and Gleason score. It seems that lower PI-RADS yield malignancies with low Gleason score (potentially insignificant cancer).[22] If these findings are validated by larger series, a clinician may temper the aggressiveness to performing biopsy and potentially tailor treatment based on PI-RADS.

Also interesting is the improved detection rate of repeat biopsies, which can be attributed to the guidance provided by the mpMRI, and utilization of transperineal biopsy which can target anterior and central lesions which may normally be missed by standard TRUS approach.[23] This fact is emphasized by the findings in the analysis of lesions on mpMRI that turned out positive for malignancy. While majority was in the peripheral zone (51.6%), a considerable number is from the central and anterior sectors of the prostate. If a transrectal approach were done in this series, almost half of the detected malignancies (35.4% from central and 12.9% anterior) would have been missed. Hence, a transperineal approach is highly endorsed by the authors of this study, because it allows biopsy sampling of all sectors of the prostate.

The authors anticipate improving further as both local radiologists and urologists be-come more adept with the use of mpMRI and PI-RADS assignment, and when MRI-US fusion biopsies become available in our country. International series also report higher cancer detection rates using PI-RADS than our reported yield, but the use of 1.5 Tesla (instead of 3T MRI) without endorectal coil may have been a factor for our lower local detection rate. Further fine-tuning and validation of the PI-RADS is important to solidify its role in diagnosis of prostate cancer. The value of mpMRI in identifying often-missed anterior tumors, and PI-RADS characterization can likewise further help classify if anteriorly directed prostate biopsies (i.e transperineal) can be beneficial. Ultimately, the hope is to develop a diagnostic tool or system that is very accurate in detecting significant disease and discerning enough to avoid unnecessary biopsy and overtreatment.

Conclusion

Multiparametric MRI and the use of PI-RADS appear to help in increasing the detection and accuracy in diagnosis of clinically significant prostate cancer. There seems to be a direct correlation between PI-RADS and cancer detection rate as well as the Gleason grade. This can potentially prevent the performance of unnecessary biopsies to patients that indeed do not harbor malignancy as well as overdiagnosis of indolent, low grade cancers while not missing clinically significant cancers. Further refinement of available parameters to increase the clinical reliability, and continuous validation to improve inter-observer variability are still needed.

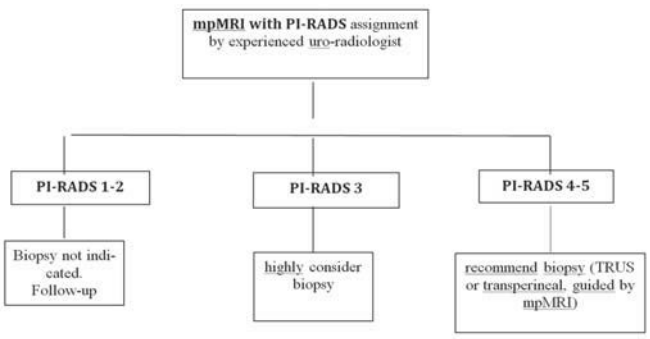

Figure 6. Biopsy Algorithm After mpMRI.

References

1. Bracarda S, de Cobelli O, Greco C, Prayer-Galetti T, Valdagni R, Gatta G, de Braud F, Bartsch G: Cancer of the prostate. Crit Rev Oncol/Hematol 2005; 56: 379-96.

2. Wein A, Kavoussi L, et al. Campbell-Walsh Urology 10th ed. Elsevier Saunders. 2012.

3. Jelle O. Barentsz & Richenberg J, et al. ESUR prostate MR guidelines 2012. Eur Radiol 2012; 22: 746-57.

4. Dickinson L, Ahmed HU, Allen C, Barentsz JO, Carey B, et al. Magnetic resonance imaging for the detection, localisation, and characterisation of prostate cancer: recommendations from a European Consensus Meeting. Eur Urol 2011; 59: 477-94.

5. Fernandez P, Letran J. The superiority of the 24-core transrectal ultrasound-guided biopsy technique in prostate cancer detection and characterization. Unpublished

6. Sciarra A, Barentsz J, Bjartell A, et al. Advances in magnetic resonance imaging: how they are changing the management of prostate cancer. European Urology 2011; 59(6): 962-77.

7. Joyce G, Bomers R and Barentsz JO. Standardization of multiparametric prostate MR imaging using PI-RADS. BioMed Research Int 2014, Article ID 431680, 9 pages http://dx.doi.org/10.1155/2014/431680

8. Girouin N, Me`ge-Lechevallier P, Tonina Senes A, et al. Prostate dynamic contrast-enhanced MRI with simple visual diagnostic criteria: is it reasonable? Eur Radiol 2007; 17(6): 1498-1509.

9. Nagel KN, Schouten MG, Hambrock T, et al. Differentiation of prostatitis and prostate cancer by using diffusion-weighted MR imaging and MR-guided biopsy at 3 T, Radiology 2013; 267(1): 164-72.

10. Hara R, Jo Y, Fujii T, Kondo N, Yokoyoma T, Miyaji Y, Nagai A. Optimal ap-proach for prostate cancer detection as initial biopsy: prospective randomized study comparing transperineal versus transrectal systematic 12-core biopsy. Urology 2008; 71(2):191-5. doi: 10.1016/j.urology.2007.09.029.

11. Junker D, Schäfer G, Edlinger M,Kremser C, Bektic J, Horninger W, Jaschke W, and Aigner F. Evaluation of the PI-RADS Scoring System for classifying mpMRI findings in men with suspicion of prostate cancer. Hindawi Publishing Corporation BioMed Research Int 2013, Article ID 252939, 9 pages http://dx.doi.org/10.1155/2013/252939

12. Baur AD, Maxeiner A, Franiel T, et al. Evaluation of the prostate imaging reporting and data system for the detection of prostate cancer by the results of targeted biopsy of the prostate. Invest Radiol 2014; 49(6): 411-20.

13. Rosenkrantz AB, Kim S, Lim RP, et al. Prostate cancer localization us-ing multiparametric MR imaging: comparison of Prostate Imaging Reporting and Data System (PI-RADS) and Likert scales. Radiology 2013; 269(2): 482-92.

14. Roethke MC, Kuru TH, Schultze S, et al. Evaluation of the ESUR PI-RADS scoring system for multiparametric MRI of the prostate with targeted MR/TRUS fusion-guided biopsy at 3.0 Tesla. Eur Radiol 2014; 24(2): 344-52.

15. Thompson JE, Moses D, Shnier R, et al. Multiparametric magnetic resonance imaging guiding diagnostic biopsy detects significant prostate cancer, and could reduce unnecessary biopsies and over-detection: a prospective study. J Urol 2014; 192: 67-74.

16. Pinthus JH, Witkos M, Fleshner N, et al. Prostate cancers scored as Gleason 6 on prostate biopsy are frequently Gleason 7 tumors at radical prostatectomy: Implication on outcome. JUrol 2006; 176: 979-84.

17. Borkowetz A, Platzek I, Toma M, Zastrow S, Froehner M, Koch R, Wirth M. Evaluation of PIRADS classification in prediction of tumour aggressiveness - comparison to radical prostatectomy specimen. Jof Urol 2015; 193(4): e179-e80.

18. Hamoen E, de Rooij M, Witjes JA, Barentsz JO, Rovers MM. Use of the prostate imaging reporting and data system (PI-RADS) for prostate cancer detection with multiparametric magnetic resonance imaging: A diagnostic meta-analysis. Eur Urol 2015; 67(6): 1.

19. Villers A, Puech P, Mouton D, Leroy X, Ballereau C, Lemaitre L. Dynamic contrast enhanced, pelvic phased array magnetic resonance imaging of localized prostate cancer for predicting tumor volume: correlation with radical prostatectomy findings. J Urol 2006; 176: 2432-7.

20. Chen M, Dang HD, Wang JY, et al. Prostate cancer detection: comparison of T2-weighted imaging, diffusion-weighted imaging, proton magnetic resonance spectroscopic imaging, and the three techniques combined. Acta Radiol 2008; 49: 602.

21. Numao N, Yoshida S, Komai Y et al: Usefulness of pre-biopsy multiparamet-ric magnetic reso- nance imaging and clinical variables to reduce initial prostate biopsy in men with suspected clinically localized prostate cancer. J Urol 2013; 190: 502.

22. Hiester A, Arsov C, Quentin M, Schimmöller L, Blondin D, Antoch G, bers P, Rabenalt R. Correlation of the PI-RADS score and the Gleason grade in prostate cancer lesions after targeted in bore MR-biopsy. Eur Urol Suppl 2014; 13; e1057.

23. Krughoff K, Eid K, Phillips J, Stoimenova D, Smith D, O'Donnell C, Crawford ED, and Barqawi Al. The accuracy of prostate cancer localization diagnosed on transrectal ultrasound-guided biopsy compared to 3-dimensional transperineal approach. Urol 2013, Article ID 249080, 5 pages http://dx.doi.org/10.1155/2013/249080