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Invited Review

Score 3 prostate lesions: a gray zone for PI-RADS v2

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ABSTRACT

Prostate Imaging Reporting and Data System version 2 (PI-RADS v2) does not offer a precise guidance on the clinical management (biopsy or not biopsy) for PI-RADS v2 score 3 lesions. Lesion volume calculated on biparametric MRI (bpMRI) [T2-weighted imaging (T2WI) and diffusion-weighted imaging (DWI)] by introducing a cut-off of 0.5 mL, allows to distinguish the lesions assigned by the multiparametric MRI (mpMRI) to the category PI-RADS v2 score 3 in two subgroups: a) Indolent or low risk lesions with volume <0.5 mL, and b) Significant or high risk lesions with volume ≥0.5 mL. For mpMRI lesions assigned to PI-RADS v2 score 3, we suggest the following management: 1) Subgroup a (low-risk lesion): Clinical surveillance (accurate evaluation of age and clinical informations, periodic monitoring of prostate specific antigen value and repeated bpMRI 1 year later); 2) Subgroup b (high-risk lesion): Targeted biopsy. The proposed management would reduce the use of unnecessary biopsies and increase the diagostic yield of significant prostate cancer of approximately 50% and 30% respectively. These approaches encourage the radiologist to adopt MRI lesion volume to improve PI-RADS v2 and to optimize the management of PI-RADS v2 score 3 lesions.

Keywords: Lesion volume; magnetic resonance imaging; prostate cancer.

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The imaging techniques are the procedure of choice in the detection of early stages of malignacies and in the conclusive determination of equivocal nature of tumors.[1] Today, to obtain a definitive diagnosis in patients suspected of having prostate cancer (PCa), magnetic resonance imaging (MRI) before biopsy may be considered as an additional parameter to the elevation of prostate-specific antigen (PSA).[2-4] Definitive diagnosis of PCa is based on *histologic* examination and the aim of MRI is to detect and localize suspicious lesions for MRI/transrectal ultrasound (MRI/TRUS) fusion guided prostate biopsy by using sector map of the prostate gland.[5-7] The main objective is the improvement of the biopsy yield by targeting suspicious lesions and minimizing the risk of unnecessary diagnosis of insignificant PCa.[8-12]

PI-RADS v2: advantages and limits

Recent Prostate Imaging Reporting and Data System version 2 (PI-RADS v2), is worldwide employed to improve detection, localization, characterization and stratification in patients with suspected PCa and to communicate the conclusive results of the imaging modality to the referring clinician.[13] PI-RADS v2 allows an assessment of categories - ranging from 1 to 5 for each lesion - providing clinical guidelines for multiparametric MRI (mpMRI). Hovewer, PI-RADS v2 shows some potential ambiguities and gaps[14-17] that need to be overcome by introducing and standardizing a simplified PI-RADS v2.

The major limit of PI-RADS v2 is that it does not offer a precise guidance on the clinical management (biopsy or not biopsy) especially for PI-RADS v2 score 3 lesions (equivocal for clinical significant PCa). A proposal is represented by introducing biparametric MRI (bpMRI) [T2-weighted imaging (T2WI) and diffusion-weighted imaging (DWI)] and excluding dynamic contrast-enhanced (DCE) sequences from mpMRI protocol. The advantages of bpMRI are to reduce costs and examination times (approximately 15-20 minutes) and to eliminate the potential risks of nephrogenic

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systemic fibrosis, kidney failure and accumulation of gadolinium-based contrast agents in the brain.[18,19] This encourage its use in clinical practice for PCa detection both in men with and without prior biopsies.[20]

Detection rate of PCa at biopsy for PI-RADS 3 lesions

MRI/TRUS guided fusion prostate biopsy has demonstrated a significant increase in cancer detection rate compared to standard biopsy (64% vs 18-35%).[21,22] The determination of PCa detection rate within PI-RADS v2 category 3 is essential to define its appropriate management. In previous reports, the detection rate of PCa in biopsed PI-RADS 3 lesions has shown a significantly high variability, ranging from 5% to 26%.[23-25] PCa is often a solid lesion with a defined three dimensional shape. Consequently a major diagnostic potential of MRI lesion volume for suspicious PCa might be proposed to identify PI-RADS 3 lesions to be biopsied.[26]

bpMRI protocol and image analysis

In our 5-year experience we used a 3T MR unit, without endorectal coil, which generally produces images with higher signal-to-noise ratio and better spatial resolution as compared to 1.5 T systems. As alternative to mpMRI[19,27], bpMRI protocol excludes the DCE-MRI sequences and includes combined axial fat suppression T1W, T2W and DW MRI series. BpMRI minuscola seems reasonable in the clinical situation where prostate MRI is used as a method for risk stratification of clinically significant PCa in patients with elevated PSA.[28] According to the criteria and lexicon of the PI-RADS v2 guidelines[13], in our experience, the image analysis was based at first on the recognition of lesion pattern on DWI (lesion hyperintense) and apparent diffusion coefficient (ADC) map (lesion moderately/markedly hypointense), and after on the localization of the lesion on T2WI (lesion hypointense) sequences by 39 segmentation model suggested by PI-RADS v2. DWI also with inverted high b values, in addition to ADC images represented the predominant sequence to detect the lesion both in peripheral and transitional zones.

A maximum of 4 lesions can be identified, defining the largest one as the "index lesion". The "index lesion" is condidered as the one with the highest PI-RADS assessment category or, alternatively, the largest lesion (if there are more than one with the same category). The employment of bpMRI in clinical practice is limited by the lack of a standardized scoring system for the risk assessment of suspicious lesions. As consequence, a simplification of PI-RADS v2 scoring system adapted to bpMRI could be standardized, to promote its adoption for an appropriate and more accurate management of PCa.

The volume of lesion on MRI distinguishes two PI-RADS 3 subgroups

Lesion diameter alone, detected by MRI, is not considered adequate to predict tumor aggressiveness.[27] The index lesion volume measurement by bpMRI, could represent a potential improvement for detection, localization and appropriate management of suspected PCa (biopsy or clinical surveillance).

Stamey et al.[29] reported that tumours <0.5 mL are unlikely to become clinically significant within the life span of the patient and need not be treated. Epstein et al.[30,31] validated this threshold, and their definition of insignificant PCa based on radical prostatectomy (RP) specimens is the most widely used definition. Similar criteria were reported by Ohori et al.[32] and to date, represent the most commonly used criteria to define insignificant PCa based on the pathologic assessment of the RP specimen.

Based on previous evidence relating to the strong correlation between lesion volume (measured at MRI) and tumor volume (measured on RP specimen)[22,26,33], the cut-off value of 0.5 mL can be used to identify the suspicious lesions at risk of clinically significant cancer.

Considering both the lesion volume calculated on T2WI and DWI and the cut-off value of 0.5 mL, we suggest the categorization of mp-*MRI* lesions assigned to *PI-RADS 3*, in two subgroups: a) indolent or low-risk lesions with volume <0.5 mL, and b) significant or high-risk lesions with volume ≥0.5 mL.
Consequently the management of PIRADS score 3 lesion should be as follows:

Subgroup 3a (low-risk lesion): Clinical surveillance (accurate evaluation of age and clinical information, periodic monitoring of PSA value and repeated bpMRI 1 year later). This approach is validated by the fact that indolent PCa remains stable over time from diagnosis.[34]
Subgroup 3b (high-risk lesion): Targeted biopsy.
Our proposed management shows that subdivision of PI-RADS 3 lesions into the 2 subcategories would reduce the use of unnecessary biopsies and increase the diagnostic yield of significant PCa of approximately 50% and 30% respectively.

This approach encourages the radiologist to adopt bpMRI lesion volume and to standardize and to simplify the PI-RADS v2 improving the management of PI-RADS 3 lesions.

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References

1. Scialpi M, Cagini L, Pierotti L, De Santis F, Pusiol T, Piscioli I, et al. Detection of small (≤2 cm) pancreatic adenocarcinoma and surrounding parenchyma: correlations between enhancement patterns at triphasic MDCT and histologic features. BMC Gastroenterol 2014;14:16. [CrossRef]
2. Abd-Alazeez M, Kirkham A, Ahmed HU, Arya M, Anastasiadis E, Charman SC, et al. Performance of multiparametric MRI in men at risk of prostate cancer before the first biopsy: a paired validating cohort study using template prostate mapping biopsies as the reference standard. Prostate Cancer Prostatic Dis 2014;17:40-6. [CrossRef]
3. Thompson JE, Moses D, Shnier R, Brenner P, Delprado W, Ponsky L, et al. Multiparametric magnetic resonance imaging guided diagnostic biopsy detects significant prostate cancer and could reduce unnecessary biopsies and over detection: a prospective study. J Urol 2014;192:67-74. [CrossRef]
4. Ahmed HU, Bosaily AES, Brown LC, Gabe, R, Hindley, RG, Kaplan R, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet 2017;389:815-22. [CrossRef]
5. Scialpi M, Falcone G, Scialpi P, D'Andrea A. Biparametric MRI: a further improvement to PIRADS 2.0? Diagn Interv Radiol 2016;22:297-8. [CrossRef]
6. Scialpi M, Martorana E, D'Andrea A. Standardizing biparametric MRI to simplify and improve Prostate Imaging Reporting and Data System, version 2, in prostate cancer management (letter). AJR 2016;207:74-5. [CrossRef]
7. Scialpi M, Martorana E, Scialpi P, D'Andrea A. Re: PI-RADS version 2: what you need to know. Clin Radiol 2016;71:934-5. [CrossRef]
8. Renard-Penna R, Roupret M, Comperat E, Rozet F, Granger B, Barkatzet J, et al. Relationship between non-suspicious MRI and insignificant prostate cancer: results from a monocentric study. World J Urol 2016;34:673-8. [CrossRef]
9. Abd-Alazeez M, Ahmed HU, Arya M, Allen C, Dikaios N, Freeman A, et al. The accuracy of multiparametric MRI in men with negative biopsy and elevated PSA level can it rule out clinically significant prostate cancer? Urol Oncol 2014;32:45.e17-22.
10. Mozer P, Roupret M, Le Cossec C, Granger B, Comperat E, de Gorski A, et al. First round of targeted biopsies using magnetic resonance imaging/ultrasonography fusion compared with conventional transrectal ultrasonography-guided biopsies for the diagnosis of localised prostate cancer. BJU Int 2015;115:50-7. [CrossRef]
11. Arumainayagam N, Ahmed HU, Moore CM, Freeman A, Allen C, Sohaib SA, et al. Multiparametric MR imaging for detection of clinically significant prostate cancer: a validation cohort study with transperineal template prostate mapping as the reference standard. Radiology 2013;268:761-9. [CrossRef]
12. De Visschere PJ, Briganti A, Futterer JJ, Ghadjar P, Isbarn H, Massard C, et al. Role of multiparametric magnetic resonance imaging in early detection of prostate cancer. Insights Imaging 2016;7:205-14. [CrossRef]
13. Prostate Imaging Reporting and Data System (PI-RADS) Reston (VA): American College of Radiology. Available at: http://www.acr.org/Quality-Safety/ Resources/PIRADS/ Accessed March 5, 2015.
14. Rosenkrantz AB, Oto A, Turkbey B, Westphalen AC. Prostate imaging reporting and data system (PI-RADS), version 2: a critical look. AJR 2016;206:1179-83. [CrossRef]
15. Oto A, Kayhan A, Jiang Y, Tretiakova M, Yang C, Antic T, et al. Prostate cancer: differentiation of central gland cancer from benign prostatic hyperplasia by using diffusion weighted and dynamic contrast-enhanced MR imaging. Radiology 2010;257:715-23. [CrossRef]
16. Delongchamps NB, Rouanne M, Flam T, Beuvon F, Liberatore M, Zerbib M, et al. Multiparametric magnetic resonance imaging for the detection and localisation of prostate cancer: combination of T2-weighted, dynamic contrast-enhanced and diffusion weighted imaging. BJU Int 2011;107(9):1411-8. [CrossRef]
17. Rosenkrantz AB, Kim S, Lim RP, Hindman N, Deng FM, Babb JS, et al. Prostate cancer localisation using multiparametric MR imaging: comparison of Prostate Imaging Reporting and Data System (PI-RADS) and Likert scales. Radiology 2013;269:482-92. [CrossRef]
18. Olchowy C, Cebulski K, Łasecki M, Chaber R, Olchowy A, Kałwak K, et al. The presence of the gadolinium-based contrast agent depositions in the brain and symptoms of gadolinium neurotoxicity-A systematic review. PLoS One 2017;12:e0171704.
19. Scialpi M, Rondoni V, Aisa MC, Martorana E, D'Andrea A, Malaspina CM, et al. Is contrast enhancement needed for diagnostic prostate MRI? Transl Androl Urol 2017;6:499-509.
20. Rais-Bahrami S, Siddiqui MM, Vourganti S, Turkbey B, Rastinehad AR, Stamatakis L, et al. Diagnostic value of biparametric magnetic resonance imaging (MRI) as an adjunct to prostate-specific antigen (PSA)-based detection of prostate cancer in men without prior biopsies. BJU Int 2015;115:381-8. [CrossRef]
21. Siddiqui MM, Rais-Bahrami S, Turkbey B, George AK, Rothwax J, Shakir N, et al. Comparison of MR/Ultrasound Fusion–Guided Biopsy With Ultrasound-Guided Biopsy for the Diagnosis of Prostate Cancer. JAMA 2015;313:390-7. [CrossRef]
22. Radtke JP, Schwab C, Wolf MB, Freitag MT, Alt CD, Kesch C, et al. Multiparametric Magnetic Resonance Imaging (MRI) and MRI-Transrectal Ultrasound Fusion Biopsy for Index Tumor Detection: Correlation with Radical Prostatectomy Specimen. Eur Urol 2016;70:846-53. [CrossRef]
23. Pokorny MR, de Rooij M, Duncan E, Schröder FH, Parkinson R, Barentsz JO, et al. Prospective study of diagnostic accuracy comparing prostate cancer detection by transrectal ultrasound-guided biopsy 8 versus magnetic resonance (MR) imaging with subsequent MR-guided biopsy in men without previous prostate biopsies. Eur Urol 2014;66:22-9. [CrossRef]
24. Thompson J, Lawrentschuk N, Frydenberg M, Thompson L, Stricker P. The role of magnetic resonance imaging in the diagnosis and management of prostate cancer. BJU Int 2013;112(Suppl 2):6-20.
25. Liddell H, Jyoti R, Haxhimolla HZ. mp-MRI Prostate Characterised PIRADS 3 Lesions are Associated with a Low Risk of Clinically Significant Prostate Cancer - A Retrospective Review of 92 Biopsied PIRADS 3 Lesions. Curr Urol 2015;8:96-100. [CrossRef]
26. Martorana E, Pirola GM, Scialpi M, Micali S, Iseppi A, Bonetti LR, et al. Lesion volume predicts prostate cancer risk and aggressiveness: validation of its value alone and matched with prostate imaging reporting and data system score. BJU Int 2017;120:92-103. [CrossRef]

Turk J Urol 2017; 43(3): 237-40
DOI:10.5152/tud.2017.01058

27. Scialpi M, Prosperi E, D'Andrea A, Martorana E, Malaspina C, Palumbo B, et al. Biparametric versus Multiparametric MRI with Non-endorectal Coil at 3T in the Detection and Localization of Prostate Cancer. Anticancer Res 2017;37:1263-71. [CrossRef]
28. De Visschere P, Lumen N, Ost P, Decaestecker K, Pattyn E, Villeirs G. Dynamic contrast-enhanced imaging has limited added value over T2- weighted imaging and diffusion-weighted imaging when using PI-RADSv2 for diagnosis of clinically significant prostate cancer in patients with elevated PSA. Clin Radiol 2017;72:23-32. [CrossRef]
29. Stamey TA, Freiha FS, McNeal JE, Redwine EA, Whittemore AS, Schmid HP. Localized prostate cancer. Relationship of tumor volume to clinical significance for treatment of prostate cancer. Cancer 1993;71(Suppl 3):933-8.
30. Epstein JI, Walsh PC, Carmichael M, Brendler CB. Pathologic and clinical findings to predict tumor extent of nonpalpable (stage T1c) prostate cancer. JAMA 1994;271:368-74. [CrossRef]
31. Epstein JI, Chan DW, Sokoll LJ, Walsh PC, Cox JL, Rittenhouse H, et al. Nonpalpable stage T1c prostate cancer: prediction of insignificant disease using free/total prostate specific antigen levels and needle biopsy findings. J Urol 1998;160:2407-11. [CrossRef]
32. Ohori M, Wheeler TM, Dunn JK, Stamey TA, Scardino PT. The pathological features and prognosis of prostate cancer detectable with current diagnostic tests. J Urol 1994;152:1714-20. [CrossRef]
33. Baco E, Ukimura O, Rud E, Vlatkovic L, Svindland A, Aron M, et al. Magnetic resonance imaging-transectal ultrasound image-fusion biopsies accurately characterize the index tumor: correlation with step-sectioned radical prostatectomy specimens in 135 patients. Eur Urol 2015;67:787-94. [CrossRef]
34. Albertsen PC, Hanley JA, Fine J. 20-year outcomes following conservative management of clinically localized prostate cancer. JAMA 2005;293:2095-101. [CrossRef]