



Platinum Priority – Editorial

Referring to the article published on pp. 385–396 of this issue

What Needs To Be Done Before Prostate Magnetic Resonance Imaging Can Safely Be Applied in the General Population

Jochen Walz *

Department of Urology, Institut Paoli-Calmettes Cancer Centre, Marseille, France

There is no doubt that multiparametric magnetic resonance imaging (mpMRI) is about to change paradigms in the diagnosis and management of prostate cancer. However, there are also drawbacks and limitations. In this issue of *European Urology*, Padhani et al. [1] provide a review of the Prostate Imaging-Reporting and Data System v2 (PI-RADS v2) and associated clinical experience. The authors nicely and critically highlight the current achievements and limitations of prostate mpMRI. The review allows identification of several points that need to be improved before mpMRI can be extended safely to the general population.

Even after more than 10 yr of “prostate mpMRI”, the data reviewed by Padhani et al demonstrate that there still is significant variability in results [1,2]. For example, despite the fact that PI-RADS 3–5 lesions are well defined by PI-RADS v2, prostate cancer detection rates vary widely from 12% to 33% for PI-RADS 3 lesions, from 22% to 71% for PI-RADS 4 lesions, and from 67% to 91% for PI-RADS 5 lesions [1]. The detection rates are certainly influenced by the global risk of finding prostate cancer in the study cohorts, but at least PI-RADS 4 or 5 lesions are well defined and should be associated with a reproducible risk of finding prostate cancer. This wide variability was also recently addressed by Sonn et al. [3]. The authors explored the variability of detection rates for significant prostate cancer according to PI-RADS score and to the reader who assigned the PI-RADS score. A PI-RADS 2 lesion read by one radiologist was associated with almost the same risk of finding significant prostate cancer (34%) as a PI-RADS 5 lesion read by another radiologist (40%) [3]. In view of this wide variability, it is clear that further work needs to be done to obtain reproducible results.

The first “standards” for prostate MRI were set in 2011 in a consensus article by Dickinson et al. [4] with the aim of improving the wide variability in diagnostic performance. Later the first version of PI-RADS was published, with recommendations on how prostate mpMRI should be performed and reported [5]. Today it is clear that reproducible standards and stable levels of high-quality imaging and interpretation for prostate mpMRI represent the cornerstone for the general use of this imaging technique. To achieve these goals, we will need systematic and robust training for radiologists, clear quality criteria for image acquisition and reporting, and effective quality assurance structures. This is also of relevance for urologists, who need to handle the information generated by mpMRI and who will need to consider this mpMRI information in the clinical context for each individual patient. Initiatives to develop standards and certification or accreditation are urgently needed. Without these standards, the necessary quality will not be available outside of reference and expert centers and more harm than benefit could be done with poorly acquired and poorly read prostate mpMRI scans.

In view of the limited quality of prostate mpMRI performed by less experienced radiologists, it is likely that many cases will be scored as PI-RADS 3. This will happen because inexperienced radiologists will not “dare” to score a clear suspicion for significant cancer or to clearly rule out significant disease. As a result, they will tend to give equivocal scores, which will leave the urologist back facing the dilemma of uncertainty about the need for further diagnostics. Hopefully, better training, standardization, and maybe new technology will keep the rate of this diagnostic PI-RADS 3 entity low. Alternatively, this entity might be the

DOI of original article: <https://doi.org/10.1016/j.eururo.2018.05.035>.

* Department of Urology, Institut Paoli-Calmettes Cancer Centre, 232, Boulevard Ste. Marguerite, 1327 Marseille, France. Tel. +33 4 91223532; Fax: +33 4 91223613.

E-mail address: walzj@ipc.unicancer.fr.

<https://doi.org/10.1016/j.eururo.2018.10.020>

0302-2838/© 2018 European Association of Urology. Published by Elsevier B.V. All rights reserved.



ideal field for molecular tests that could help to better stratify these men [6]. Specifically, in the case of PI-RADS 3 scores, the clinical expertise of the urologist will be essential to identify men who can be left alone because of a low risk of finding prostate cancer and those men who need further diagnostic workup.

Finally, the review concludes that the best way to use mpMRI currently is to “rule out” a lesion. The authors argue in favor of this approach because they consider that mpMRI provides high sensitivity and a high negative predictive value (NPV). It is obvious that systematic use of mpMRI increases the detection rate over random biopsies and thus obviously the sensitivity. However, to truly “rule out” a lesion and with this the need for biopsy, the NPV counts. The only study so far that provides a reliable NPV using template mapping biopsy as a reference, the PROMIS trial, showed NPV of 76% for Gleason pattern $\geq 3+4$ prostate cancer [7]. This means that one in four patients with negative mpMRI will have such a cancer missed. These numbers are close to the data we observed in the random biopsy era, when prostate cancer detection rates after a first negative biopsy were somewhere between 20% and 30% [8]. Moreover, it is known that cribriform prostate cancer is at risk of being missed by mpMRI [9]. Cribriform prostate cancer can account for up to 40% of all Gleason pattern 4 cancers and is associated with a less favorable prognosis [10]. I remain cautious about the true clinical value of a normal mpMRI in ruling out the need for further diagnostic workup. When deciding on what further steps to take, it is necessary to analyze information not only from imaging in isolation but also from the patient, clinical examinations, and biomarkers. Only such a “global” approach will allow improvement in the management of men at risk of prostate cancer. Contrary to the opinion of the authors, for me the best way to use MRI in the current situation is to “rule in” a lesion for targeted biopsy in a patient for whom biopsy seems necessary and not to “rule out” a lesion and with this the need for biopsy. The limited NPV for Gleason 3 + 4 and

cribriform prostate cancer and the lack of reliable quality in the general population make this approach the safer strategy.

Conflicts of interest: The author has nothing to disclose.

References

- [1] Padhani AR, Weinreb J, Rosenkrantz AB, Villeirs G, Turkbey B, Barentsz J. Prostate Imaging-Reporting and Data System Steering Committee: PI-RADS v2 status update and future directions. *Eur Urol* 2019;75:385–96.
- [2] 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.
- [3] Sonn GA, Fan RE, Ghanouni P, et al. Prostate magnetic resonance imaging interpretation varies substantially across radiologists. *Eur Urol Focus* 2017. <http://dx.doi.org/10.1016/j.euf.2017.11.010>, In press.
- [4] Dickinson L, Ahmed HU, Allen C, 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] Barentsz JO, Richenberg J, Clements R, et al. ESUR prostate MR guidelines 2012. *Eur Radiol* 2012;22:746–57.
- [6] Cucchiara V, Cooperberg MR, Dall’Era M, et al. Genomic markers in prostate cancer decision making. *Eur Urol* 2018;73:572–82.
- [7] Ahmed HU, El-Shater Bosaily A, Brown LC, 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.
- [8] Walz J, Graefen M, Chun FK, et al. High incidence of prostate cancer detected by saturation biopsy after previous negative biopsy series. *Eur Urol* 2006;50:498–505.
- [9] Truong M, Hollenberg G, Weinberg E, Messing EM, Miyamoto H, Frye TP. Impact of Gleason subtype on prostate cancer detection using multiparametric magnetic resonance imaging: correlation with final histopathology. *J Urol* 2017;198:316–21.
- [10] Kweldam CF, Kummerlin IP, Nieboer D, et al. Disease-specific survival of patients with invasive cribriform and intraductal prostate cancer at diagnostic biopsy. *Mod Pathol* 2016;29:630–6.