

SHORT ABSTRACT

Multiparametric MRI of the Prostate: From Scientific Triumph to Daily Practice

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Multiparametric Magnetic Resonance Imaging (MRI) (mpMRI) of the prostate consists of three parameters: high-resolution T2-weighted anatomical imaging (T2w), diffusion-weighted imaging (DWI), and dynamic contrast-enhanced (DCE) MRI. Minimal technical requirements for the acquisition of dedicated prostate MR-images have been described in the Prostate Imaging Reporting and Data System (PI-RADS), which currently is in its version 2.1 [1]. It also contains a standardized reporting system, which groups imaging findings on T2w, DWI, and DCE and yields a final categorization into a 5-point scale predicting the likelihood of clinically significant prostate cancer.

The diagnostic performance of mpMRI of the prostate using PI-RADS has been amply studied in numerous high-quality studies during the last decade. In 2017, a meta-analysis consisting of 21 studies, including 3857 patients, calculated a pooled sensitivity of 89% (range 73%–100%) and a pooled specificity of 73% (range 7%–100%) [2]. The large ranges can be explained by a number of factors.

- (1) **Technical factors** seem to be of minor importance, as a subgroup analysis did not reveal any significant differences between 1.5T and 3.0T scanners, nor between use or no use of an endorectal coil (ERC) [2]. Nowadays, good results are therefore also possible on state-of-the-art (strong gradients, multiple channels) 1.5T system without ERC, provided that all scan parameters are concordant with the PI-RADS v2.1 minimal technical requirements.
- (2) The **definition of prostate cancer** has an important impact on the diagnostic performance of mpMRI. International Society of Urothology (ISUP) 1 cancers (Gleason 3 + 3) are well-differentiated cancers that are usually indolent and not harmful to the patient. But being well-differentiated, they resemble normal tissue, so they are difficult to visualize on mpMRI. ISUP 3–5 cancers (primary Gleason grades 4 and 5) are poorly differentiated cancers that are readily visible on mpMRI, whereas ISUP 2 cancers (Gleason 3 + 4) are indeterminate. If

a positive mpMRI is defined as a PI-RADS 3–5, then 68% of prostate cancers of any aggressiveness (ISUP 1–5) will be detected, 89% of all clinically significant cancers (ISUP 2–5) and 96% of all highly aggressive cancers (ISUP 3–5) [3]. The latter findings generate the paradigm that a negative mpMRI (PI-RADS 1–2) can spare an unnecessary biopsy and that a positive mpMRI (PI-RADS 3–5) can be used to target a biopsy to the suspicious area. A meta-analysis by Moldovan indeed showed that mpMRI has a negative predictive value of 88% (range 69%–100%) for excluding a clinically significant prostate cancer and another meta-analysis by Fütterer showed a positive predictive value range of 34%–68%, both increasing when highly aggressive cancers (ISUP 3–5) are to be detected [4, 5].

- (3) A chain is of course only as strong as its weakest link. mpMRI can be of excellent quality, both in terms of technique and reporting, but its value remains zero when the **ground truth verification** is ineffective. Each time a mpMRI signals a lesion within the prostate, that lesion should be accurately sampled by a targeted biopsy approach. It has been shown that in-bore prostate biopsy is the optimal choice, followed by ultrasound-MRI fusion techniques and cognitive fusion (i.e. with knowledge of the location on MRI a biopsy is performed in the same area as recognized on ultrasound). However, the sensitivity differences between the three techniques were not statistically significant, suggesting that any technique can suffice when properly executed [6].
- (4) The **clinical scenario** in which mpMRI is performed has a huge impact on its diagnostic performance, mainly because of the varying yields of prostate cancer associated with this clinical scenario. In a patient group with prior negative biopsy, easily detectable prostate cancers have already been filtered away by the prior systematic biopsy, so only cancers that are more difficult to find with systematic biopsy remain, such as small or anteriorly located cancers. These can more easily be found with mpMRI, so it is not surprising that a recent Cochrane review confirmed that the chance of finding a cancer with mpMRI was 44% higher than with standard biopsy

in the prior negative biopsy setting, whereas only 5% higher in the biopsy-naïve scenario [7]. Nevertheless, the European Association of Urology has recently updated its guidelines stating that mpMRI is recommended as a first line test in both the prior negative as in the biopsy-naïve setting. The rationale, however, is different in both settings. In the prior negative biopsy setting, the main advantage is increased cancer detection, whereas in the latter, the main objective is to decrease the total number of biopsies with about 33%, while maintaining the number of clinically significant cancer detections (+2%) and decreasing the number of insignificant cancer detections (−8%) [7]. Similar results are now suggested also with biparametric MRI (bpMRI), consisting of T2w and DWI only, provided that the image quality of DWI is optimal and that this technique is not used for recurrence detection after radical prostatectomy or radiotherapy [8].

- (5) Finally, the impact of **expertise** on the diagnostic results is crucial. The reported ranges in sensitivity, specificity, positive predictive value, and negative predictive value cannot be explained exclusively by the four mentioned reasons above. Multi-reader variability is a well-known and major source of performance variation. The effect of initial training in non-experienced readers (with less than 50 case reads) has been nicely shown by Garcia-Reyes, with accuracies increasing from 74% to 88% following two didactic lectures with interactive case discussions [9]. In a more comprehensive study, Hansen showed that expert readers (>1000 case reads) typically have higher numbers of negative mpMRIs (i.e. less overcalling and less biopsies) than readers with modest experience who turn every uncertainty into a positive read [10]. Experts also have higher positive and negative predictive values, indicating a higher reading confidence and precision.

Quality criteria and subsequent certification are the fastest way to ensure this kind of high-quality reading, similar to what happened in breast cancer screening. The European Society of Urogenital Radiology conducted a Delphi survey among its members to seek consensus about this matter. Preliminary results were that image quality should be optimized through compliance to PI-RADS v2.1 and regular self and peer assessments. Reading quality should equally be compliant to PI-RADS v2.1, with a percentage of PI-RADS 3 results lower than 25% (ideally 15%) and a percentage of PI-RADS 1–2 results higher than 30%. Histopathological feedback is mandatory (e.g. through MDT participation), in order to learn from both successes and mistakes.

In conclusion, mpMRI is a great tool for prostate cancer diagnosis. It results in less (unnecessary) biopsies overall, increases the yield of clinically significant cancers and decreases the number of insignificant cancers. However, the scientific triumphs as reported in the literature do not always translate into daily practice! Urologists who

hear or read about these triumphs expect the same successes in their own hospitals, but if radiologists fail to deliver that quality, they lose credibility and a great tool becomes an unreliable tool... Therefore, technical and reporting standardization of mpMRI is mandatory (as accomplished in PI-RADS v2.1), but there is also a need for training, expanding knowledge and maximizing expertise. Furthermore, quality criteria and certification will pave the way to constant reader quality and referral confidence.

Competing Interests

The authors have no competing interests to declare.

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