Three Years of PI-RADS v2: Achievements, Open Questions and Future Perspectives

Bernd Hamm, M.D.

Department of Radiology, Charité University Hospital, Humboldt-Universität zu Berlin and Freie Universität Berlin, Germany

The Prostate Imaging-Reporting and Data System version 2 (PI-RADS v2) was designed to set requirements for multiparametric MR (mpMRI) imaging of the prostate, to optimize image quality and standardize prostate MRI reporting and to reduce variability in image interpretation by proposing assessment categories for detection or exclusion of clinically significant cancer of the prostate. Three years after the introduction of PI-RADS v2, Anwar Padhani and other members of the PI-RADS committee summarize the current state of research and clinical experience with PI-RADS v2, name the strengths and weaknesses and propose directions for future research and improvements of the standard to contribute to value-based health care [1].

Summary

The range of genomic diversity and prognosis of prostate cancer (PCa), the variable prevalence in different populations as well as known limitations of established diagnostic tools, e.g., non-cancer-specific reasons for increased prostate-specific antigen (PSA) levels, and the semi-randomness of transrectal ultrasound (TRUS) biopsies lead to major challenges in the diagnostic management of these patients:

1. Men without clinically significant prostate cancer but elevated PSA levels undergo unnecessary biopsies with attendant morbidity [2].
2. Men with indolent (non-significant) cancers are diagnosed with the disease and undergo therapies which are not positively affecting their overall survival but instead may have severe side effects that significantly impact their quality of life [3].
3. Men having clinically significant cancer are underdiagnosed or the disease may even remain undiagnosed, resulting in suboptimal treatment decisions due to poor tissue sampling.

While there are several diagnostic options besides imaging, including molecular diagnostics, that allow more accurate PCa diagnosis, prostate mpMRI plays an increasingly important role in ruling out or detecting clinically significant cancer in men with elevated PSA levels.

The promotion of PI-RADS v2 as a global standard reduces variation in the acquisition, interpretation and reporting of prostate mpMRI exams and has thus made an important contribution to overcoming the limitations associated with highly variable imaging protocols (and quality of studies), high intra-reader variability and in particular the difficulties in communicating findings to referring urologists. Today, PI-RADS v2 has developed into the universal standard for prostate mpMRI interpretation and reporting, significantly improving communication among radiologists and urologists.

Multiple patient- and lesion-level analyses have shown that PI-RADS v2 assessment categories are effective and improve sensitivity for detection of clinically significant prostate cancer compared to PI-RADS v1. On the lesion level, however, studies indicate that non-index lesions tend to be overlooked (e.g., low-grade and very small prostate cancers). Furthermore, there

is a large body of evidence that both PI-RADS v2 and non-PI-RADS standardized scoring systems (Likert) have a very high "rule out" performance for clinically significant PCa. This has important implications for men with negative MRI findings and may help to significantly reduce the number of patients undergoing random biopsy of the prostate. Two recent prospective studies with excellent study designs – the PROMIS (2017, published in Lancet) and the PRECISION study (2018, published in NEJM) – have shown that mpMRI detects more significant prostate cancers and fewer non-significant cancers compared with random TRUS biopsy [4, 5]. These results will lead to the wider use of mpMRI prior to the first transrectal prostate biopsy in the mid-term.

Beyond summarizing recent studies and developments, the authors also point out limitations of PI-RADS v2, such as the still high intra-reader variability, vaguely defined assessment categories for the transition zone, and the unclear role of dynamic contrast-enhanced (DCE) MRI. While the authors announce some improvements in this regard with the pending update of PI-RADS (version 2.1), general questions and challenges remain and require further investigation.

Accordingly, there is a call to action to address the lack of quantitative metrics in the assessment of diffusion-weighted imaging (DWI) and DCE MRI, to improve the performance of MRI in the transition zone and to work on an expansion of PI-RADS, i.e., for Active Surveillance and recurrent cancer.

Conclusion

PI-RADS v2 was designed to assist in the selection of patients who should undergo prostate biopsy and to establish standards for imaging. It has been shown that the test performance of PI-RADS v2 in research and clinical practice is improved, retaining higher accuracy over systematic TRUS biopsies for PCa diagnosis. Another advantage of PI-RADS is that it markedly improves communication and understanding among radiologists and urologists. Diagnostic strategies that include imaging detect more clinically significant prostate cancers and less low-risk disease. PI-RADS has facilitated the standardization of mpMRI acquisition, interpretation and reporting but open questions and tasks remain.

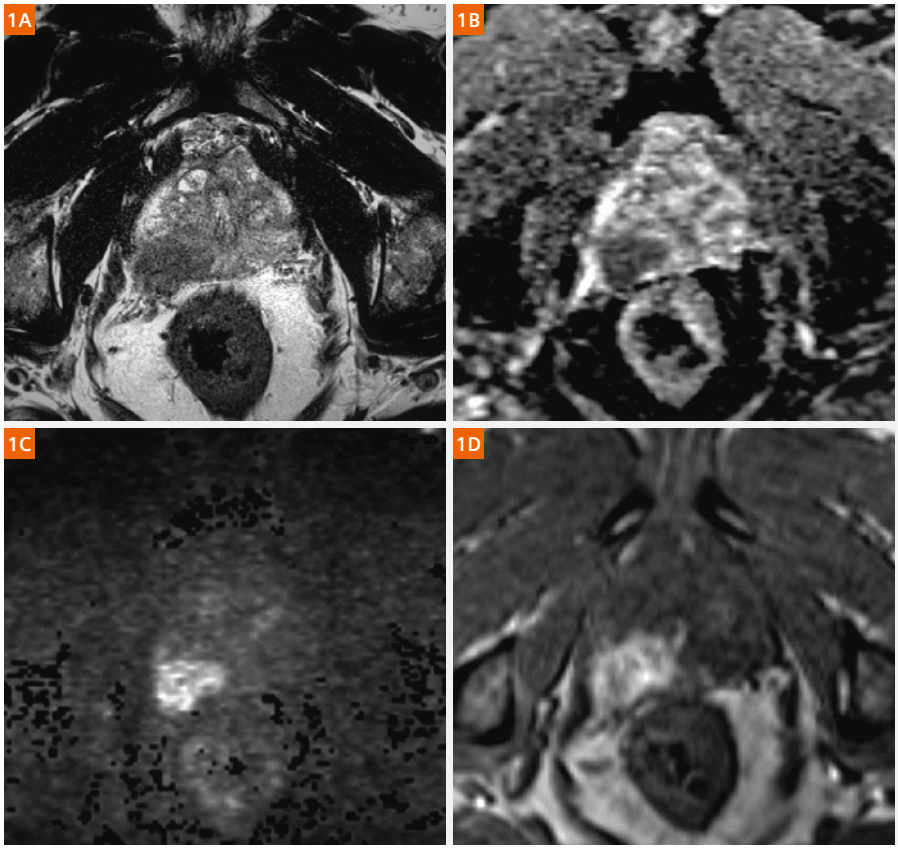

Figure 1:
63-year-old patient with a PSA increase from 5.6 ng/ml to 11.8 ng/ml over a 6-month period. Multiparametric MRI at 3 Tesla (MAGNETOM Skyra). Transverse T2-weighted TSE sequence **(1A)**, diffusion-weighted EPI sequence (ADC map) **(1B)** and calculated b-value of 1400 mm/s^2 **(1C)**, and dynamic contrast-enhanced sequence (TWIST) **(1D)**.

Focal lesion in the posterolateral peripheral zone on the right-hand side with extraprostatic extension and invasion of the neurovascular bundle (1A); there is corresponding marked diffusion restriction (1B, C) and focal early enhancement following contrast agent administration (1D); PI-RADS 5 (histology: Gleason 4+4=8).

Personal comment

Multiparametric prostate MRI is one of the biggest success stories of radiology in the last decade. While we started using MRI as a problem-solving tool in patients with multiple negative biopsies and to assess whether or not patients had extracapsular extension (with sub-optimal results), prostate MRI is clinically used in a much broader scope now. It is no longer questioned whether mpMRI can detect and localize clinically significant PCa and it has been shown that negative MRI findings (in case of high-quality examinations!) allow to safely avoid biopsies and further follow-ups in a significant number of patients. Urologists appreciate the clarity of a PI-RADS report with a standardized prostate pictogram, clearly indicating where to target a biopsy.

On the other hand, however, PI-RADS v2 is reducing our flexibility in imaging interpretation as expert readers, and the recommendations remain vague, for example, with regard to apparent diffusion coefficient (ADC) cutoff values or the assessment of the transition zone. Practical aspects in clinical management of patients such as: "What do we do about mpMRI-negative patients?", "Who should follow up PI-RADS 1-2 patients not undergoing biopsy – what should be the regimen for follow-up?", and "How should we deal with PI-RADS 3 patients?" remain unanswered so far and have to be addressed individually. Hopefully, these issues will be solved in one of the future PI-RADS versions. Therefore, the scientific community is called to action and to address these issues in future studies. Researchers around the globe can contribute and influence the development of future versions of PI-RADS into an even more refined tool in diagnosing and managing prostate cancer.

References

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Contact

Bernd Hamm, M.D.
Professor and Chairman
Department of Radiology
Charité University Hospital
Humboldt-Universität zu Berlin
and Freie Universität Berlin
Charitéplatz 1, 10117 Berlin
Germany
Tel.: +49 30 450 527 082
bernd.hamm@charite.de