A multifaceted approach to quality in the MRI-directed biopsy pathway for prostate cancer diagnosis

Anwar R. Padhani¹ · Ivo G. Schoots^{2,3} · Baris Turkbey⁴ · Gianluca Giannarini⁵ · Jelle O. Barentsz⁶

Received: 22 October 2020 / Accepted: 16 November 2020 / Published online: 25 November 2020
© European Society of Radiology 2020

Key Points

- Identify, assure, and measure major sources of variability affecting the MRI-directed biopsy pathway for prostate cancer diagnosis.
- Develop strategies to control and minimize variations that impair pathway effectiveness including the performance of main players and team working.
- Assure end-to-end quality of the diagnostic chain with robust multidisciplinary team working.

For a urological outpatient population where the prevalence of clinically significant prostate cancer (csPCa) is approximately 20–40% [1], MRI brings the advantages of biopsy avoidance in 37% of men with MRI-negative scans (range, 17–56%) [2–8], and reduced detection of clinically insignificant PCa by 9% [1]. These advantages minimize the harms of unnecessary biopsies, over-diagnoses, and over-treatments [9]. These benefits are related to the consistent high negative predictive value (NPV) and sensitivity of MRI for PCa detection [10, 11] that enable the reliable “ruling-out” of csPCa without needing biopsies [7, 12]. A recent meta-analysis of 36 studies including more than 5000 biopsy-naïve men had an NPV of 91% (95% CI 88–96%), meaning that 1 in 10 men with International Society of Uro pathology (ISUP) Gleason Grade (GG) ≥ 2 remained undiagnosed [10].

We must remember that most of the prospective level 1 evidence studies used for guideline development were performed in high-volume expert centers [2, 5, 6]. However, “real-world” studies show similar NPVs, despite heterogeneities in disease prevalence, MRI scanners, and expertise of radiologists, urologists, and pathologists [1, 3, 8, 10, 11]. These concordant data reinforced the guideline recommendations to use MRI-

negative results for avoiding prostate biopsies, with appropriate clinical caveats and safety-nets protocols [13–15].

The consistent and high NPV is related to fewer confounding factors, mostly related to disease prevalence rates and radiological factors. The latter being image quality, image read-outs, and data processing. Because radiologists have direct control of MRI, they can point to multiple advances including technologies that improve the speed and consistencies of MRI acquisitions, uniform image interpretation criteria [16], certification efforts [17], quality checks scores [18], and recent advances in automated gland contouring and suspicion lesion heat-maps using deep learning techniques [19].

Unfortunately, the “rule-in” ability of MRI is less consistent, with large variances in positive predictive values (PPV) with false-positive rates as high as 50% [20]. This unreliability is seen in the high proportion of PI-RADS 3–4 category patients who have biopsies that are negative for csPCa. On the other hand, patients with PI-RADS 5 category scores have higher csPCa detection rates of 75% (95% CI, 73–78%) [21]. Next to PI-RADS category biopsy thresholds, the variable PPV is related to patient selections, disease prevalence rates, and radiological factors, and whether clinical factors

✉ Anwar R. Padhani
anwar.padhani@stricklandscanner.org.uk

¹ Paul Strickland Scanner Centre, Mount Vernon Cancer Centre, Rickmansworth Road, Northwood, Middlesex HA6 2RN, UK

² Department of Radiology & Nuclear Medicine, Erasmus MC University Medical Center, Rotterdam, The Netherlands

³ Department of Radiology, Netherlands Cancer Institute, Amsterdam, The Netherlands

⁴ Molecular Imaging Branch, NCI, NIH, Bethesda, MD, USA

⁵ Urology Unit, “Santa Maria della Misericordia” Academic Medical Centre, Udine, Italy

⁶ Department of Radiology, Nuclear Medicine & Anatomy, Radboud University Medical Center, Nijmegen, The Netherlands

such as volume-normalized PSA density are used for biopsy decisions [11, 22]. Importantly, urologist expertise, their biopsy equipment, and the methods used including whether systematic biopsy cores in addition to targeted cores are obtained [23] affect csPCa detection rates, as do prostate gland volumes, lesion numbers, their sizes and shapes, and their intraprostatic locations. Finally, pathologic expertise and effective team working also affect the detection rates of csPCa [24] (Fig. 1).

Thus, MRI cannot always deliver binary yes/no answers to “enhanced risk-stratification” expected by urologists [20]. Inherently, biopsy management incorporating MRI information is multi-stepped and multifaceted, which can be confusing for inexperienced urologists [25]. Therefore, going forwards, it is important for radiologists to actively participate in initiatives that aim to deliver consistent biopsy outcomes. Radiologists can do this by integrating into multidisciplinary teams, to aid and help direct MRI-influenced biopsies and treatment decisions [26], explaining and reducing indeterminate MRI cases [26], and to give a fuller understanding to biopsy operators of what the images are showing and the location of suspicious targets [20]. Recent advances in automated gland contouring and suspicion lesion heat-maps using deep learning techniques [19] and unified image transfers that facilitate the integration of diagnosis with biopsy and therapy machines will aid these efforts.

Multidisciplinary team working brings multiple advantages [27, 28] including increased efficiency of the referral pathways, reductions in variations in diagnostic methods used, and therapies offered to patients, which overall can lead to better utilization of healthcare resources. Integrated team working improves adherence to guidelines enabling audits of working of radiologists, urologists, and pathologists. The

demonstration of effective team working will be integral to future accreditations of diagnostic units that will improve the confidence of patients and reimbursement authorities, who can be assured of the quality of the processes deployed. Ultimately, team working will be necessary for promoting the personalization of diagnoses, according to patient preferences and care priorities [29].

To deliver a high-quality prostate cancer diagnosis pathway, several steps must be undertaken (Table 1). Firstly, we must identify the major sources of variability that affect the ability of MRI to reliably detect csPCa (Fig. 1). As pointed out, the most impactful factors affecting the “rule-in” and “rule-out” performances are different. Secondly, measurements, control, and assurance of the sources of variability should be undertaken, such as compliance with technical standards [30], image quality assessment scores [18], inter- and intra-reader/center variability [31], and cancer detection rates (including underdiagnosis cancer rates). Third, we need to develop performance measures for the main individuals participating in the MRI biopsy pathway including radiologists, urologists, and pathologists (and others), ultimately laying down the foundations for the certification of the main players, once tolerances are known [17]. Finally, key performance indices for diagnostic units on their ability to effectively deliver a high-quality service need to be developed, as part of accreditation processes focusing on team working outputs.

In conclusion, to deliver a high-quality prostate cancer MRI-influenced biopsy pathway, we need to identify and more fully understand the major sources of variability regarding the ability of MRI to reliably “rule-in” and “rule-out” clinically significant cancers. Variations that impair the pathway effectiveness must be minimized by standardizing its various components, and the performance of its main players,

Fig. 1 Heterogeneity sources in the MRI-directed biopsy pathway for prostate cancer diagnosis

Table 1 Quality assurance and quality control requirements in the MRI-directed biopsy pathway for prostate cancer diagnosis

Identify and assure sources of variability	Patient selections, risk classification, and disease prevalence Image acquisitions, radiologist, and reading factors Biopsy operators, procedures, and operating factors Histopathology analysis and reading factors Team working
Measure and control variability and assess impacts on pathway outputs	Compliance with technical standards Image quality assessments and their likely diagnostic impacts Cancer detection rates; overdiagnosis and underdiagnosis rates Inter-intra operator variability of diagnostic metrics Inter-intra center variability of diagnostic metrics
Develop performance measures for key individuals for benchmarking (certification)	Radiologist: diagnostic metrics including PI-RADS categories corrected for cancer prevalence; peer review of PI-RADS scores; NPV and PPV variability Urologist: biopsy detection rates corrected for lesion characteristics (size, location, and PI-RADS score) Pathologist: up- and downgrading rates compared to peer review and prostatectomy pathology
Key performance indicators of diagnostic units	Turn-around times Diagnostic metrics for units (biopsy avoidance, biopsy yields, inter- and intra-center variability of PPV and NPV corrected for PI-RADS categories and disease prevalences) Biopsy complications Patient satisfaction

PI-RADS, prostate imaging reporting and data system; NPV, negative predictive value; PPV, positive predictive value

including team coordinators, radiologists, biopsy operators, and pathologists. The end-to-end quality of the diagnostic chain can only be assured with the efficient working of the multidisciplinary teams involved.

Funding The authors state that this work has not received any funding.

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is prof. Anwar R Padhani.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was not required for this study because this is an invited editorial and not the subject of a research article.

Ethical approval Institutional Review Board approval was not required because this is an editorial piece and not subject to a research article.

Methodology

• Editorial opinion—therefore not relevant.

References

1. Drost F-JH, Osses D, Nieboer D et al (2020) Prostate magnetic resonance imaging, with or without magnetic resonance imaging-targeted biopsy, and systematic biopsy for detecting prostate cancer: a Cochrane systematic review and meta-analysis. *Eur Urol* 77:78–94. <https://doi.org/10.1016/j.eururo.2019.06.023>
2. van der Leest M, Cornel E, Israël B et al (2019) Head-to-head comparison of transrectal ultrasound-guided prostate biopsy versus multiparametric prostate resonance imaging with subsequent magnetic resonance-guided biopsy in biopsy-naïve men with elevated prostate-specific antigen: a large prospective multicenter clinical study. *Eur Urol* 75:570–578. <https://doi.org/10.1016/j.eururo.2018.11.023>
3. Sokhi HK, Padhani AR, Patel S, Pope A (2020) Diagnostic yields in patients with suspected prostate cancer undergoing MRI as the first-line investigation in routine practice. *Clin Radiol*. <https://doi.org/10.1016/j.crad.2020.08.011>
4. Boesen L, Nørgaard N, Løgager V et al (2018) Assessment of the diagnostic accuracy of biparametric magnetic resonance imaging for prostate cancer in biopsy-naïve men. *JAMA Netw Open* 1: e180219. <https://doi.org/10.1001/jamanetworkopen.2018.0219>
5. Rouvière O, Puech P, Renard-Penna R et al (2019) Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naïve patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study. *Lancet Oncol* 20:100–109. [https://doi.org/10.1016/S1470-2045\(18\)30569-2](https://doi.org/10.1016/S1470-2045(18)30569-2)
6. Kasivisvanathan V, Rannikko AS, Borghi M et al (2018) MRI-targeted or standard biopsy for prostate-cancer diagnosis. *N Engl J Med* 378:1767–1777. <https://doi.org/10.1056/NEJMoa1801993>
7. Ahmed HU, El-Shater Bosaily A, Brown LC et al (2017) Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *Lancet* 389:815–822. [https://doi.org/10.1016/S0140-6736\(16\)32401-1](https://doi.org/10.1016/S0140-6736(16)32401-1)
8. Zawaideh JP, Sala E, Shaida N et al (2020) Diagnostic accuracy of biparametric versus multiparametric prostate MRI: assessment of contrast benefit in clinical practice. *Eur Radiol*. <https://doi.org/10.1007/s00330-020-06782-0>
9. US Preventive Services Task Force, Grossman DC, Curry SJ et al (2018) Screening for prostate cancer: US Preventive Services Task Force recommendation statement. *JAMA* 319:1901–1913. <https://doi.org/10.1001/jama.2018.3710>
10. Sathianathan NJ, Omer A, Harriss E et al (2020) Negative predictive value of multiparametric magnetic resonance imaging in the

- detection of clinically significant prostate cancer in the prostate imaging reporting and data system era: a systematic review and meta-analysis. *Eur Urol* 78:402–414. <https://doi.org/10.1016/j.eururo.2020.03.048>
11. Stonier T, Simson N, Shah T, et al (2020) The ‘Is mpMRI Enough’ or IMRIE study: a multicentre evaluation of prebiopsy multiparametric magnetic resonance imaging compared with biopsy. *Eur Urol Focus* 1–9. <https://doi.org/10.1016/j.euf.2020.09.012>
 12. Simmons LAM, Kanthabalan A, Arya M et al (2017) The PICTURE study: diagnostic accuracy of multiparametric MRI in men requiring a repeat prostate biopsy. *Br J Cancer* 116:1–7. <https://doi.org/10.1038/bjc.2017.57>
 13. Mottet N, van den Bergh RC, Briers E et al (2019) 2019 EAU - EANM - ESTRO - ESUR - SIOG guidelines on prostate cancer. EAU Guidelines Office, Arnhem
 14. NICE, NATIONAL INSTITUTE FOR HEALTH AND CARE (2019) National Institute for Health and care Excellence. Prostate cancer : diagnosis and management (update) <https://doi.org/10.5094/apr.2010.001>
 15. Padhani AR, Barentsz J, Villeirs G et al (2019) PI-RADS Steering Committee: the PI-RADS multiparametric MRI and MRI-directed biopsy pathway. *Radiology* 292:464–474. <https://doi.org/10.1148/radiol.2019182946>
 16. Turkbey B, Rosenkrantz AB, Haider MA et al (2019) Prostate imaging reporting and data system version 2.1: 2019 update of prostate imaging reporting and data system version 2. *Eur Urol* 76:340–351. <https://doi.org/10.1016/j.eururo.2019.02.033>
 17. de Rooij M, Israël B, Barrett T et al (2020) Focus on the quality of prostate multiparametric magnetic resonance imaging: synopsis of the ESUR/ESUI recommendations on quality assessment and interpretation of images and radiologists’ training. *Eur Urol* 78:483–485. <https://doi.org/10.1016/j.eururo.2020.06.023>
 18. Giganti F, Allen C, Emberton M, Moore CM, Kasivisvanathan V, PRECISION study group (2020) Prostate imaging quality (PI-QUAL): a new quality control scoring system for multiparametric magnetic resonance imaging of the prostate from the PRECISION trial. *Eur Urol Oncol* 3:615–619. <https://doi.org/10.1016/j.euo.2020.06.007>
 19. Schelb P, Kohl S, Radtke JP et al (2019) Classification of cancer at prostate MRI: deep learning versus clinical PI-RADS assessment. *Radiology* 190938. <https://doi.org/10.1148/radiol.2019190938>
 20. Padhani AR, Barentsz JO, Weinreb J, Schoots I, Tempany C (2020) Re: variability of the positive predictive value of PI-RADS for prostate MRI across 26 centers: experience of the Society of Abdominal Radiology Prostate Cancer Disease-focused Panel. *Eur Urol* 296:633–636. <https://doi.org/10.1016/j.eururo.2020.06.015>
 21. Park KJ, Choi SH, Lee JS, Kim JK, Kim MH, Jeong IG (2020) Risk stratification of prostate cancer according to PI-RADS version 2 categories: meta-analysis for prospective studies. *J Urol*. <https://doi.org/10.1097/JU.0000000000001306>
 22. Schoots IG, Padhani AR (2020) Risk-adapted biopsy decision based on prostate MRI and PSA-density for enhanced biopsy avoidance in first prostate cancer diagnostic work-up. *Br J Urol Int*. <https://doi.org/10.1111/bju.15277>
 23. Goldberg H, Ahmad AE, Chandrasekar T et al (2020) Comparison of magnetic resonance imaging and transrectal ultrasound informed prostate biopsy for prostate cancer diagnosis in biopsy naïve men: a systematic review and meta-analysis. *J Urol* 203:1085–1093. <https://doi.org/10.1097/JU.0000000000000595>
 24. Stabile A, Giganti F, Kasivisvanathan V et al (2020) Factors influencing variability in the performance of multiparametric magnetic resonance imaging in detecting clinically significant prostate cancer: a systematic literature review. *Eur Urol Oncol* 3:145–167. <https://doi.org/10.1016/j.euo.2020.02.005>
 25. Venderink W, Bomers JG, Overduin CG et al (2020) Multiparametric magnetic resonance imaging for the detection of clinically significant prostate cancer: what urologists need to know. Part 3: targeted biopsy. *Eur Urol* 77:481–490. <https://doi.org/10.1016/j.eururo.2019.10.009>
 26. Luzzago S, Petralia G, Musi G et al (2019) Multiparametric magnetic resonance imaging second opinion may reduce the number of unnecessary prostate biopsies: time to improve radiologists’ training program? *Clin Genitourin Cancer* 17:88–96. <https://doi.org/10.1016/j.clgc.2018.10.006>
 27. Lamb BW, Jalil RT, Sevdalis N, Vincent C, Green JS (2014) Strategies to improve the efficiency and utility of multidisciplinary team meetings in urology cancer care: a survey study. *BMC Health Serv Res* 14:377. <https://doi.org/10.1186/1472-6963-14-377>
 28. Sciarra A, Gentile V, Panebianco V (2013) Multidisciplinary management of prostate cancer: how and why. *Am J Clin Exp Urol* 1: 12–17
 29. Schoots IG, Padhani AR (2020) Personalizing prostate cancer diagnosis with multivariate risk prediction tools: how should prostate MRI be incorporated? *World J Urol* 38:531–545. <https://doi.org/10.1007/s00345-019-02899-0>
 30. Cuocolo R, Stanzione A, Ponsiglione A et al (2019) Prostate MRI technical parameters standardization: a systematic review on adherence to PI-RADSv2 acquisition protocol. *Eur J Radiol* 120:108662. <https://doi.org/10.1016/j.ejrad.2019.108662>
 31. Park KJ, Choi SH, Lee JS, Kim JK, Kim MH (2020) Interreader agreement with prostate imaging reporting and data system version 2 for prostate cancer detection: a systematic review and meta-analysis. *J Urol* 204:661–670. <https://doi.org/10.1097/JU.0000000000001200>

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.