Is It PRIME Time for Biparametric Magnetic Resonance Imaging in Prostate Cancer Diagnosis?

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Multiparametric magnetic resonance imaging (mpMRI) is now the standard of care in the work-up for patients with suspected prostate cancer (PCa) [1], [2]. However, capacity and resource limitations are a challenge in delivering prebiopsy MRI for all men with suspected PCa. It has been proposed that dynamic contrast-enhanced (DCE) sequences may add little additional value to T2-weighted (T2W) and diffusion-weighted imaging (DWI) sequences, and therefore a shorter biparametric MRI (bpMRI) protocol may be more feasible in delivering MRI to all men who need it [3]. The jury is still out on whether DCE improves the detection of significant cancer or not.

These include a shorter and cheaper scan; a requirement for the presence of fewer health care workers to administer the scan as giving contrast requires a doctor to be present in case of allergic reaction; avoiding the need for cannulation; and avoiding potential basal ganglia accumulation of gadolinium, especially in patients undergoing repeated scans [4]. These all present a cost-effective approach for dealing with the increasing demand for MRI scans, and several studies have investigated the potential of bpMRI as a standard of care for PCa diagnosis or as a population screening test [5], [6]. However, it is important to know what we are missing without the DCE sequence before we recommend bpMRI as the standard of care.

Most of the major studies that validated the use of MRI in PCa diagnosis used mpMRI, and there are some circumstances in which mpMRI may be advantageous over bpMRI [1], [3], [7], [8]. Some lesions may be better seen on DCE (and less visible on other sequences), and this sequence is particularly useful when DWI is degraded by artefacts such as rectal air and hip prostheses. Furthermore, DCE may help with staging decisions and certainty regarding involvement of key structures such as the prostate capsule, seminal vesicles, and bladder neck, which may influence the treatment options a patient is eligible for and how that treatment is administered, for example whether to perform nerve sparing during a radical prostatectomy.

Current evidence provides support that bpMRI can detect a similar amount of clinically significant PCa (csPCa) as mpMRI [9], [10], [11], [12]. However, most of these studies are limited primarily by small sample size, lack of assurance of high-quality MRI scanners, single-site retrospective design, and a lack of blinding of radiologists to the DCE sequence when reporting bpMRI [10]. Previous meta-analyses are limited by the methodological quality of the studies included and by pooling of studies with substantial clinical heterogeneity [12]. In a randomised controlled trial (RCT) by Russo et al [13]mpMRI and bpMRI detected 32.7% and 23.5% of csPCa cases, respectively, which is a wide difference in favour of mpMRI. However, the trial was vastly underpowered for detection of this difference, with only 311 patients, and by our calculations more than 3500 patients would be required to power a noninferiority RCT.

The majority of the existing studies in this area are limited by the scoring system used. Prostate Imaging-Reporting and Data System (PI-RADS) version 2.1 provides significantly more weighting to T2W and DWI sequences and therefore does not upgrade from a score for which a patient does not require a biopsy to a score requiring a biopsy, and only changes score from 3 to 4. Therefore, previous studies using PI-RADS version 2.1 have been unable to assess whether DCE helped to improve cancer detection.

We designed PRIME (PRostate Imaging using Mri +/− contrast Enhancement; NCT04571840), a 500-patient prospective, international, within-patient, multicentre, level 1–evidence clinical trial evaluating whether bpMRI is noninferior to mpMRI in the detection of csPCa. In the PRIME study, radiologists will be strictly blinded to the DCE sequence by an independent person or computer software, and will be asked to submit the bpMRI report first, before they are unblinded to perform the mpMRI reading. This may reduce the impact of incorporation bias. The two MRI reports will influence how biopsies are performed in patients, and the biopsy samples will be labelled appropriately so that the respective contribution to cancer detection can be determined. While an alternative study design such as an RCT may have different benefits (less incorporation bias, allows comparison of completely separate bpMRI vs mpMRI diagnostic pathways) it would require a sevenfold greater sample size, which may not be the most efficient use of public funding. The within-patient design was chosen as it answers the research question in the most efficient way. The international, multicentre, prospective nature of the clinical trial increases the generalisability of the data. The design chosen also allows evaluation of the impact of contrast on staging decisions and treatment eligibility decisions at an individual patient level in a way that an RCT would not.

In addition to the PI-RADS version 2.1 scoring system, PRIME will also use a 5-point Likert radiology reporting scale, allowing evaluation of contrast in a way that does not assume it already does not play a role in deciding whether a patient receives a biopsy [7]. The central quality control process for the PRECISION trial (Prostate Evaluation for Clinically Important Disease: Sampling using image Guidance or Not?) showed that of the three mpMRI sequences, DCE had the greatest room for improvement and the Prostate Imaging Quality (PI-QUAL) version 1 quality control scoring system was devised from this [14]. All MRI scanners will be subject to quality control according to the PI-QUAL scoring system [14] before being used in PRIME. This will allow us to draw conclusions regarding the value of DCE sequences rather than the results being a reflection of the inherent MRI quality.
A total of 60 sites from 22 countries have expressed interest in participating in PRIME. MRI quality control has taken place for 40 sites, with seven, 20, and 13 sites scoring an initial PI-QUAL score of 3, 4, and 5, respectively. Seventeen sites have improved their PI-QUAL score from 4 to 5 with quite simple changes to local scanning protocols, and 30 sites have a PI-QUAL score of 5. PRIME is due to start recruiting in Q1 2022 and end in Q1 2024, with 25 sites already in the set-up stage.

***Conflicts of interest*:** The authors have nothing to disclose.

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References

[1]
V. Kasivisvanathan, A.S. Rannikko, M. Borghi, et al.
MRI-targeted or standard biopsy for prostate-cancer diagnosis
N Engl J Med, 378 (2018), pp. 1767-1777, 10.1056/NEJMoa1801993
View PDFView Record in ScopusGoogle Scholar
[2]
N. Mottet, P. Cornford, R. Van Den Bergh, et al.
EAU guidelines: prostate cancer
European Association of Urology, Arnhem, The Netherlands (2021)
https://uroweb.org/guideline/prostate-cancer/
Google Scholar
[3]
M. van der Leest, E. Cornel, B. Israël, et al.
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 (2019), pp. 570-578, 10.1016/j.eururo.2018.11.023
ArticleDownload PDFView Record in ScopusGoogle Scholar
[4]
M. De Rooij, B. Israël, J.G.R. Bomers, I.G. Schoots, J.O. Barentsz
Can biparametric prostate magnetic resonance imaging fulfill its PROMIS?
Eur Urol, 78 (2020), pp. 512-514, 10.1016/j.eururo.2020.03.002
ArticleDownload PDFView Record in ScopusGoogle Scholar

[5]
D. Eldred-Evans, P. Burak, M.J. Connor, et al.
Population-based prostate cancer screening with magnetic resonance imaging or ultrasonography: the IP1-PROSTAGRAM study
JAMA Oncol, 7 (2021), pp. 395-402, 10.1001/jamaoncol.2020.7456
View PDFView Record in ScopusGoogle Scholar
[6]
L. Boesen, N. Nørgaard, V. Løgager, et al.
Assessment of the diagnostic accuracy of biparametric magnetic resonance imaging for prostate cancer in biopsy-naive men: the Biparametric MRI for Detection of Prostate Cancer (BIDOC) study
JAMA Netw Open, 1 (2018), p. e180219, 10.1001/jamanetworkopen.2018.0219
View PDFView Record in ScopusGoogle Scholar
[7]
H.U. Ahmed, A. El-Shater Bosaily, L.C. Brown, et al.
Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study
Lancet, 389 (2017), pp. 815-822, 10.1016/S0140-6736(16)32401-1
ArticleDownload PDFView Record in ScopusGoogle Scholar
[8]
O. Rouvière, P. Puech, R. Renard-Penna, et al.
Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naive patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study
Lancet Oncol, 20 (2019), pp. 100-109, 10.1016/S1470-2045(18)30569-2
ArticleDownload PDFView Record in ScopusGoogle Scholar
[9]
A. El-Shater Bosaily, E. Frangou, H.U. Ahmed, et al.
Additional value of dynamic contrast-enhanced sequences in multiparametric prostate magnetic resonance imaging: data from the PROMIS Study
Eur Urol, 78 (2020), pp. 503-511, 10.1016/j.eururo.2020.03.002
View PDFGoogle Scholar
[10]
M. Alabousi, J.P. Salameh, K. Gusenbauer, et al.
Biparametric vs multiparametric prostate magnetic resonance imaging for the detection of prostate cancer in treatment-naïve patients: a diagnostic test accuracy systematic review and meta-analysis
BJU Int, 124 (2019), pp. 209-220, 10.1111/bju.14759
View PDFView Record in ScopusGoogle Scholar
[11]
Z. Kang, X. Min, J. Weinreb, Q. Li, Z. Feng, L. Wang
Abbreviated biparametric versus standard multiparametric MRI for diagnosis of prostate cancer: a systematic review and meta-analysis
Am J Roengenol, 212 (2018), pp. 357-365, 10.2214/ajr.18.20103
View PDFView Record in ScopusGoogle Scholar
[12]
S. Woo, C.H. Suh, S.Y. Kim, J.Y. Cho, S.H. Kim, M.H. Moon

Head-to-head comparison between biparametric and multiparametric MRI for the diagnosis of prostate cancer: a systematic review and meta-analysis
Am J Roentgenol, 211 (2018), pp. W226-W241, 10.2214/ajr.18.19880
View PDFView Record in ScopusGoogle Scholar
[13]
F. Russo, S. Mazzetti, D. Regge, et al.
Diagnostic accuracy of single-plane biparametric and multiparametric magnetic resonance imaging in prostate cancer: a randomized noninferiority trial in biopsy-naïve men
Eur Urol Oncol, 4 (2021), pp. 855-862, 10.1016/j.euo.2021.03.007
ArticleDownload PDFView Record in ScopusGoogle Scholar
[14]
F. Giganti, C. Allen, M. Emberton, C.M. Moore, V. Kasivisvanathan
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 (2020), pp. 615-619, 10.1016/j.euo.2020.06.007
ArticleDownload PDFView Record in ScopusGoogle Scholar