Prostate cancer diagnostics is a rapidly evolving field with a plethora of research being undertaken, resulting in changing practice. Most recently, NICE has updated guidelines for the diagnosis and management of prostate cancer, with the full publication released in May 2019.¹ To date, investigation has centred around identification of patients with an abnormally raised serum prostate specific antigen (PSA) undergoing either transrectal or transperineal prostate biopsy. New guidance recommends that men with suspected localised prostate cancer who are suitable for radical therapy should be offered multiparametric MRI (mpMRI) as first-line investigation to stratify those in whom invasive biopsy is indicated and to those on active surveillance who have not had mpMRI previously.¹ This significant change aims to improve care of prostate cancer patients and reduce harms from unnecessary biopsies, with resultant clinical and economic benefits.

**What is mpMRI?**
Multiparametric MRI conventionally combines three imaging parameters to augment the detection and localisation of prostate cancer (see Figure 1). T2-weighted imaging delineates the anatomy of the prostate gland, highlighting areas of greater water concentration with increased signal intensity versus regions of lower concentration.² Diffusion weighted imaging (DWI) evaluates movement of water molecules through interstitial space where signal intensity increases with increasing diffusion gradient. This allows differentiation between regions of greater or lesser cellularity and extracellular space, mapping out tissue architecture. Finally, dynamic contrast enhanced imaging relies on intravenous gadolinium to focus on tissue vascularity and perfusion, again with increased vascularity resulting in higher signal intensity.³ Combination of these techniques facilitates greater prediction of the likelihood of prostate cancer being present and lesions are scored accordingly.

Two main scoring systems exist, both ranging from one to five with increasing probability of cancer. The European Society of Urogenital Radiology formulated the ‘Prostate Imaging and Report and Data System’ (PIRADS) score.⁴ This has been updated since it was initially developed in 2013 and relies on different parameters of mpMRI depending on the zone of the prostate under examination; for example, DWI is the predominant sequence utilised for analysis of the peripheral zone.

The ‘Likert’ scale is the other scoring system employed, and is a visual analogues scale reported according to the radiologist’s overall interpretation of imaging, with studies reporting variable correlation with PIRADS scoring and inter-rater reliability.⁵

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**Figure 1. Components of multiparametric magnetic resonance imaging (mpMRI)**

- **T2-weighted imaging**
  - Low intensity – relatively lower water concentration
  - High intensity – relatively higher water concentration

- **Diffusion-weighted imaging**
  - Low intensity – relatively lower water diffusion coefficient
  - High intensity – relatively higher water diffusion coefficient

- **Dynamic contrast-enhanced imaging**
  - Low intensity – relatively lower vascularity
  - High intensity – relatively higher vascularity
**Why has it changed?**

The ‘PROMIS’ study was a multicentre, paired-cohort, confirmatory study examining the accuracy of mpMRI as a diagnostic triage tool to identify men who could safely avoid biopsy. It aimed to reduce the over-diagnosis of insignificant disease and improve the diagnostic pick-up rate of clinically significant prostate cancer (csPCa), defined as Gleason score ≥4+3, or maximum cancer core length ≥6mm. It surmised that the greater negative predictive value of mpMRI compared with systematic prostate biopsy would enable stratification of patients according to likelihood of harbouring csPCa and help 27% avoid an invasive biopsy, increase diagnosis of csPCa by 18% and reduce the over-diagnosis and thus potential overtreatment of non-significant disease by 5%.

Subsequent research demonstrated that the diagnostic yield of csPCa is likely to be greater when utilising mpMRI to guide biopsy strategy, rather than when undertaking biopsies using a standard template or modified Barzell scheme.

The ‘PRECISION’ multicentre randomised controlled trial sought to determine if mpMRI-guided biopsy (ie targeted biopsy) could negate the need for standard, systematic biopsy. It randomised 500 men to receive standard systematic biopsy or undergo mpMRI and subsequent target biopsy in those with PIRADS of 3–5 lesions. The intervention group showed a greater rate of detection of clinically significant disease (38% versus 26%) and less non-significant prostate cancer (9% versus 22%), concluding that mpMRI prior to targeted prostate biopsy can improve sensitivity in prostate cancer diagnosis.

Porpiglia et al. also randomised 212 men at a single institution to mpMRI pre-targeted biopsy or 12-core standard biopsy to ascertain if this increased the detection rate of csPCa. They too concluded that pre-biopsy mpMRI increased the yield of csPCa (43.9% versus 18.1%, p<0.001), though it also had an higher rate of non-significant disease in the same cohort, contrasting with the findings of Kasivisvanathan et al.

**What are the implications?**

The change in guidance to omit prostate biopsy for patients with...
mpMRI Likert score 1 and 2 is intended to increase the efficiency and cost-effectiveness of prostate cancer diagnosis and reduce physical and psychological morbidity associated with over-investigation and over-treatment.

Evidence demonstrates rates of up to 25% for transient lower urinary tract symptoms after biopsy, and the transrectal route has been associated with infectious complications ranging from 1% to 4% in cases of fluoroquinolone-resistant rectal vault flora. For transperineal template mapping biopsy, adverse events have included 24% of men suffering acute urinary retention, and 41% with perineal pain and significant deterioration in functional domains.

This demonstrates the need for the updated NICE guideline to reduce the invasiveness of the diagnostic pathway for prostate cancer and reduce avoidable complications, with subsequent benefits also reducing the economic burden from biopsy procedures and histological analysis.

However, as seen in the work of Ahmed et al., the sensitivity of mpMRI was 87–93%, and negative predictive value 72–89%, depending on the definition of ‘cancer’ – and Porpiglia et al. did not comment on the number of patients with negative mpMRI who subsequently had a positive biopsy. The potential ‘miss rate’ and variable sensitivity of mpMRI with characteristics such as PSA presents a challenge in potentially missing clinically significant cancers in patients with mpMRI Likert scores of 1–2.

Approximately 20% of primary prostate tumours are ‘invisible’ on mpMRI, though transcriptomic analysis suggests that these have a lower mutational burden and fewer genetic aberrations, resulting in a less aggressive phenotype than mpMRI visible tumours. The prospective ‘MRI-FIRST’ study showed that pre-biopsy mpMRI didn’t negate the need for systematic biopsy in mpMRI negative’ patients. Authors reported 37% detection of clinically significant disease in patients who had mpMRI showing Likert ≤2 lesions. Of these, 14% were detected through standard biopsy alone, 20% by targeted biopsy alone and 66% by the combination of biopsy techniques. Results convey the cumulative benefit of biopsy strategies in conjunction with mpMRI, as well as the potential dangers of over-reliance on imaging within diagnostic pathways. NICE has added the recommendation that for patients with ‘negative mpMRI’ (Likert score ≤2) the discussion of risks and benefits ought to occur prior to shared decision-making (see Figure 2).

The recommendation is that any man with mpMRI Likert score 1–2, or those with Likert score ≥3 and a negative biopsy result, should be evaluated for the presence of risk factors (PSA density greater >0.15ng/ml2, PSA velocity >0.75ng/year, strong family history) and subsequently considered for prostate biopsy in collaboration with the patient and multidisciplinary team (see Figure 2). It remains evident that while mpMRI affords numerous benefits in increasing the efficiency of diagnosing csPCa, it is not a ‘golden bullet’ and the time is ripe for research to further imaging technology.

The logistical implications of mpMRI triage are widespread and noteworthy. Differences afforded to diagnostics by high-standard performance and reporting of mpMRI are evidenced by heterogeneity in the literature; for instance, comparing findings from PRECISION, which utilised both 1.5T and 3.0T machines, with the work by Van der Leest et al. The updated NICE guidance has ‘left this decision with the imaging centres’, though advised minimum appropriate standards of ‘at least 1.5T, diffusion weighted, contrast-enhanced imaging and b value of at least 800’. The consequences of such equipoise must be evaluated through future audit and review. Access to mpMRI has increased, though it remains variable throughout the UK and relies on local funding and radiological expertise. Further investment is needed in training and in standardisation of reporting to reduce inter-rater variability in results and improve inter-rater reliability in reporting for us to fully embrace the benefits that can be conferred by mpMRI triage.

Conclusion

The recent change in guidance within the prostate cancer diagnostic pathway is founded upon the evidence supporting mpMRI as a useful triage tool in biopsy-naive men who are at clinical risk of prostate cancer. With the resultant benefits in reducing the physical, psychological and financial implications of first-line biopsies that have been standard practice to date it is tempting to wholeheartedly rely on radiological triage, but the change does not negate the need for clinical judgement and shared decision-making in at-risk individuals. It promotes holistic consideration of the patient and their biopsychosocial circumstances by primary and secondary care providers alike, and is an incentive to invest in further innovations to provide and advance imaging technology.

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References


