MRI in prostate cancer diagnosis

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Introduction
Prostate cancer is the most common male cancer, with 41,736 men in the UK diagnosed with the disease in 2011, and the incidence continues to increase. However, introduction of prostate-specific antigen (PSA) testing has shifted the risk profile of the disease: the majority of men now present with low risk disease, with an overall cancer-specific 10-year survival of 84%. There is debate as to whether low grade Gleason score 6 disease even meets sufficient biological criteria to be labelled as cancer and current practice recommends no treatment for men with such indolent disease because the risks of treatment outweigh the benefits. Conversely, prostate cancer is the second most common cause of cancer death in UK men, and high grade disease requires radical therapy. This dichotomy has led to an urgent need to both diagnose prostate cancer and to accurately risk stratify patients for appropriate management.

Multiparametric MRI
Imaging offers advantages over the traditional random approach of transrectal ultrasound (TRUS) guided prostate biopsy, partly by being non-invasive but primarily by being able to ‘sample’ the whole gland. The supplementation of the sensitive but non-specific anatomical MR images with functional sequences to produce multiparametric (mp) MRI has significantly improved its diagnostic accuracy, with a pooled sensitivity and specificity of 74% and 88%, respectively for detecting tumours. However, the latest National Prostate Cancer Audit in the UK highlights the fact that although 99% of trusts in England have access to on-site MRI, only 75% are providing mpMRI. The functional sequences recommended for mpMRI are diffusion-weighted (DWI) and dynamic contrast-enhanced (DCE) MRI (figure 1). MR spectroscopy is no longer routinely recommended due to the technical input required, cost considerations, and its limited added diagnostic benefit.

Current NICE guidelines in the UK recommend that men with a prior negative biopsy but continuing suspicion of clinically significant disease should undergo MRI to target any repeat biopsy, emphasising the need to accurately identify lesions. There is compelling evidence emerging for this strategy; a recent meta-analysis showed that MRI-guided biopsy in men with a previous negative biopsy increased detection of significant cancers by 54% and limited the so-called “over-diagnosis” of prostate cancer with an 18% reduction in the detection of low grade indolent cancer. Although the benefit in diagnostic yield of significant cancers in biopsy naïve patients is less marked (10% increase), the reduction in diagnosis of indolent disease remains significant (49% reduction), and some centres have started to introduce MRI pre-biopsy in select patient groups.

However, the published studies represent the best results achievable, generally being performed in high-end centres with optimised sequences by sub-specialist reporters, but importantly, also typically on selective, retrospective patient populations. In order to achieve more uniformity in MRI performance, the recently updated Prostate Imaging Reporting and Data System (PI-RADS) criteria have been published aiming to standardise the acquisition, interpretation and reporting of prostate MRI.

Protocol makes perfect
There are a number of technical considerations before even performing a prostate MRI: Patient preparation, choice of endorectal or surface coil, magnet strength, and the use of anti-peristaltic agents. 3.0T offers increased signal-to-noise ratio (SNR) and is considered equivalent to 1.5T with an endorectal coil. However, other factors are relevant including receiver bandwidth, coil design and efficiency, and 1.5T imaging alone is often adequate, particularly if an increased number of phased array coil elements are utilised (≥16). An endorectal coil also has disadvantages including near field flare and gland deformity, as well as being invasive and costly; although not routinely recommended, they may be needed for older generation 1.5T magnets.

Anti-peristaltic agents are not essential given the relatively low position of the prostate in the pelvis and remote location of small bowel, however, in the absence of an endorectal coil they may have a benefit in reducing rectal spasm. The commonest agent used is 20mg hyoscine butylbromide IV which has a rapid onset of action and bowel relaxation effect lasting for 20-30 minutes. It is therefore advisable to do the key sequences and those most motion sensitive (DWI) within this period. Even anti-peristaltic agents may not overcome artefact if significant rectal air is present and consideration can be given to repeat prone imaging or attempted rectal decompression. An appreciation of the key sequences is also needed so that if image quality is suboptimal, measures should be taken to repeat them (table 1). T2-weighted imaging and in particular the axial sequences are key for anatomical detection of tumour. Functional imaging is matched in the axial plane and should be identical in terms of imaging plane angle, location, and slice thickness. The key diagnostic sequences are therefore axial T2WI and the diffusion-weighted imaging. T1-weighted imaging cannot identify tumours, but is useful for assessment of biopsy-related haemorrhage, and can also be used as a sequence from the aortic bifurcation down to evaluate for lymph nodes. Haemorrhage can hinder interpretation of T2-weighted images (figure 2) and most centres would recommend imaging at an interval of four to six weeks post biopsy to mitigate this effect.

For DWI a minimum of two b-values are required to calculate an apparent diffusion co-efficient (ADC) map. The ‘high’ b-value should be 800-1000sec/mm², the ‘low’ b-value should be 50-100sec/mm²: b-0 should be avoided due to pseudo-perfusion effects. A separate ‘high b-value’ sequence is recommended for qualitative assessment and should be ≥b-1400sec/mm² and even up to 2000sec/mm² (if SNR allows). For DCE, a fat-suppressed sequence helps to improve conspicuity, and subtraction imaging can be used for problem solving if haemorrhage is present at baseline.
An injection rate of 2-3ml/s is recommended with a temporal resolution of ≤10s, and imaging for a minimum of two minutes post-injection to assess for washout. There is no evidence for the routine use of DCE pharmacodynamic parameter analysis.

**Contrasting opinions**

There is a difference in opinion regarding the added value of contrast-enhanced sequences. A recent health economic analysis showed that the addition of DCE to anatomical imaging and DWI increases the overall costs from £141.50 to £239.06, allowing for estimates of administration, scanning time, staff, consumable costs and an increased interpretation time.14 The current NICE recommendations are disease specific, rather than radiological guidelines, but do not recommend DCE.15 Conversely PI-RADS and a recent UK consensus document recommend the routine use of DCE.16,17

Apart from cost issues, other arguments against the use of DCE include the limited added value for experienced readers,14 and the fact that when T2W and DWI are of diagnostic quality, PI-RADS guidelines dictate that DCE only plays a minor role in the assessment of peripheral zone (PZ) lesions when DWI is indeterminate. The prostate is unusual because benign conditions such as prostatitis and BPH can demonstrate early contrast wash-in and wash-out, leading to an inability of curve-typeing to accurately differentiate malignancy.15 Conversely, DCE can improve specificity for lesion detection, may detect additional tumours missed by other techniques,16,17 and the sequence becomes essential if there is a technical failure of diffusion weighted-imaging. Furthermore, DCE can play a key role if there is a PI-RADS score 3 area within the PZ, and a recent study suggests this occurs in up to 37% of prostate MRI studies.18 Prospectively it is difficult to identify patients who will have a PI-RADS 3 lesion, or a technical failure of DWI (aside from known presence of pelvic metalwork). This is a more cogent rationale for use of DCE in the absence of on-table decisions being made by a supervising radiologist, which may be impractical depending on working practice.

**Conclusions**

Prostate MRI, aided by the introduction of functional imaging sequences, now provides an accurate means of identifying tumours and directing appropriate management strategies. However, the quality of imaging can be variable and interpretation for the inexperienced radiologist challenging. Following the PI-RADS guidelines and simple protocol tips can help to improve the standard and uniformity of both.

**References**


16. Fucuzawa J, Miura T, Suzuki H. Prostate cancer detection in patients with a PI-RADS score 3 area within the PZ, and a recent study suggests this occurs in up to 37% of prostate MRI studies.18 Prospectively it is difficult to identify patients who will have a PI-RADS 3 lesion, or a technical failure of DWI (aside from known presence of pelvic metalwork). This is a more cogent rationale for use of DCE in the absence of on-table decisions being made by a supervising radiologist, which may be impractical depending on working practice.

**Practical protocol considerations**

- **1.5T provides adequate diagnostic examinations when acquisition parameters are optimised and contemporary technology is employed**
- An endorectal coil is not routinely recommended
- MR spectroscopy is not routinely recommended
- Match DWI and DCE to the axial T2 sequence in terms of imaging angle, location and slice thickness
- Hyoscine butylbromide is effective for 20-30 minutes; perform the key sequences, and in particular DWI, early
- Axial T2WI and DWI are the key diagnostic sequences; if suboptimal measures should be taken to repeat these
- T1 axial imaging is used to demonstrate haemorrhage and can assess nodal stations to the aortic bifurcation. Ideally MRI should be performed 4-6 weeks post-biopsy to mitigate the effects of haemorrhage
- Significant rectal air distorts DWI; consider advising patients to evacuate bowels prior to MRI. Prone imaging may also help
- The ‘low’ b-value for DWI should be 50-10sec/mm² (not b-0)
- Fat-suppressed DCE sequences help improve conspicuity

**TABLE 1**
Figure 1
Multiparametric MRI. 70-year-old patient with PSA 5.3ng/ml and clinical suspicion of prostate cancer; MRI performed pre-biopsy. (A) Axial T2 weighted image shows a focal area of low T2 signal in the lateral aspect of the right mid/apex PZ (arrow). (B) and (C) diffusion-weighted imaging shows corresponding high signal on the b-1400 images (B) and low signal on the ADC maps (C). (D) DCE-MRI shows focal early enhancement compared to background PZ, with subsequent wash-out. Targeted transperineal biopsy showed Gleason 4+3=7 disease in this lesion.

Figure 2
Effect of haemorrhage. 61-year-old patient on active surveillance with Gleason 3+3 disease in 2/6 left sided cores. (A) and (B) Baseline MRI shows haemorrhage in the mid PZ bilaterally on T1WI (arrows in A), with corresponding low T2 signal intensity (arrows in B), which could be confused for appearance of tumour. (C) Follow-up MRI at 12 months, T2WI shows resolution of the low signal confirmed as relating to haemorrhage.