The role of Dynamic Contrast Enhancement in prostate MR

Our Position

Until there is trial evidence available that replicates real-world practice to prove the diagnostic accuracy of bi-parametric MRI (bpMRI), we believe that men are more likely to be safely ruled out of an immediate biopsy where practice delivers to the level one evidence provided by the PROMIS Study.[1] This includes the use of dynamic contrast enhancement (DCE) alongside T2-weighted and diffusion weighted imaging (DWI) sequences (with optional T1 sequence).

We recognise that DCE has the potential to be less necessary among radiologists with substantial expertise in prostate MRI. There is some evidence to suggest that 700-800 cases could be a threshold for radiologists to reliably interpret bpMRI,[2] but further prospective research with a larger patient population is needed.

Our aim

We recognise that our position is situated within, and unlikely to resolve, a complex debate about DCE. It has been produced with the aim that all providers deliver prostate MR to the highest possible quality, so that they can confidently triage men and enable some men to safely avoid an invasive and unwarranted biopsy.

Our rationale

Evidence based practice

Several studies have explored the diagnostic accuracy of bpMRI in comparison to mpMRI.[3] These have been limited by their use of different methodologies delivered at single providers with only one or two readers. This makes it likely that bpMRI performance would be degraded in multi-centre clinical trials or regular practice with multiple readers.

A new prospective trial that compares bpMRI to mpMRI in a real-world setting is our means to create a more robust evidence base. Blinded double-reporting to compare MRI protocols could deliver the level of evidence we believe is needed. Calculations suggest that a study to determine non-inferiority would require more than 3,000 men and would be challenging to conduct.[4]

Until this real-world prospective evidence is available, our preference is for providers to adhere to the MRI sequences used in the PROMIS study,[5] which is level one evidence that

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has established mpMRI as the current effective diagnostic triage. This requires the inclusion of DCE.

Image-quality
An audit of MRI image quality across a Cancer Alliance in the South West of England[6] showed that DCE scans were of sufficient quality to contribute to diagnosis in 93% of cases. Scans using the other mpMRI parameters achieved less reliable diagnostic quality. There was also a trend towards lower quality of T2 and diffusion-weighted scans in centres using DCE, though this was not statistically significant. This suggests that the use of DCE is likely to provide added benefit and certainty to diagnosis, especially if the diffusion-weighted scan fails.

We are working to develop a digital means of identifying sub-optimal images that can be accessed by all prostate MR providers. It should enable cost-effective targeted use of medical physicist support that can adjust MRI scanner protocols and ensure these MRI scanners produce the higher-quality images necessary for accurate prostate cancer diagnosis. Until then, we believe that DCE offers a beneficial safety net to ensure that clinically significant cancers are not missed because of poor image quality.

Radiologist expertise
Research has shown that the use of DCE by radiologists new to interpreting and reporting mpMRI scans improves their diagnostic accuracy and increases the agreement of their reporting with that of radiologists expert in mpMRI.[7] DCE is therefore an important part of radiologists' learning curve and necessary for ensuring that, as radiologists develop their reporting skills, clinically significant cancers are not missed.

Equally, this evidence indicates that DCE may be less necessary among expert radiologists. Studies have investigated the diagnostic accuracy between bpMRI and mpMRI among radiologists with varying levels of experience,[8,9] and indicate that there is no difference in sensitivity for those with significant expertise if DCE is absent. However, these have been prospective studies and included limited numbers of patients. Further studies involving larger patient numbers are needed to determine the criteria by which an expert radiologist is defined and diagnostic accuracy not affected.

Wider considerations

There are other factors to consider in relation to the choice between bpMRI and mpMRI.

Resources
The use of DCE can increase scan time. It can require longer slots that have the potential to increase pressure on already stretched MRI services. It also incurs an increased cost. It requires scanning slots with medical coverage in case of a reaction to the contrast agent, meaning they cannot be out-of-hours.

However, without DCE there is potential for re-call and re-referral rates to be higher than in centres providing mpMRI, which can also increase pressure on MRI services. There may also be more equivocal scoring resulting in more men being biopsied, which could lessen the opportunity to reduce the costs associated with this procedure. Leading centres have developed shortened protocols that include DCE, reducing the increase in scan time. There are also centres that use split lists to enable patients contraindicated to DCE to be scanned out-of-hours.

It is therefore not clear that use of DCE has any greater resource impact than not using it, and a health economics study might be needed to draw a conclusion. This study would need to be underpinned by an audit that compares re-call, re-referral and biopsy rates

across bp and mpMRI providers. If done, this could enable an evidence base that determines which imaging technique is most resource effective.

Scoring systems
The PI-RADS scoring system has been recommended by clinical consensus as optimal for radiologists new to interpreting and reporting prostate MR.[10] However, the limited role for DCE in PI-RADS v2 prevented its use in scoring of mpMRI scans and promoted greater reliance on T2 and diffusion-weighted sequences.

In its recent update, PI-RADS v2.1[11] claims that 'DCE in practice has been a safety net or back up sequence, especially when either T2 or DWI is degraded by artifacts or inadequate SNR [signal to noise ratio]'. PI-RADS v2.1 also suggests the potential for an increase in the frequency to miss clinically significant prostate cancers if bpMRI is used across the NHS.

By contrast, the Likert scoring system, which is recommended by NICE Guidelines for prostate cancer diagnosis and management [NG131],[12] requires an equal evaluation of all mpMRI sequences and is considered better able to demonstrate the value of the DCE in the way that PI-RADS v.2.1 describes.[13]

Adverse events
It is known that DCE is contraindicated in patients with poor kidney function, however most referral forms for suspected urological cancer now require an eGFR value to be recorded, meaning there is no uncertainty over which patients can receive contrast. Allergic reactions to gadolinium contrast, while not unknown, are very rare.

It is now accepted that the use of some gadolinium contrast agents results in the deposit of tiny amounts of gadolinium metal in tissues, particularly brain tissues. However, the EU has banned the use of contrast agents with linear chelators that are the major contributing factor to gadolinium deposition, and evidence shows macrocyclic chelators reduce this effect significantly. Some concern has been expressed over gadolinium deposition resulting in cognitive decline and dementia, but there is no evidence in the literature suggesting any association and all studies investigating this hypothesis have found no link.

Conclusion

The use of DCE in prostate MR is the cause of much debate. However, until there is prospective evidence available that can be translated into a real-world setting and demonstrate bpMRI as an imaging technique equal to or better than mpMRI, DCE has an important role to play. Given the variation in image quality and radiologist experience from hospital to hospital and patient to patient, DCE provides the reassurance that every possible effort has been made to achieve an accurate diagnostic MRI scan, and that triaging decisions to omit a prostate biopsy are as safe as can be feasibly achieved.

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