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Review

Optimising prostate mpMRI: prepare for success

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Multiparametric magnetic resonance imaging (MRI) now plays an essential role in prostate cancer diagnosis and management. The increasing use of MRI before biopsy makes obtaining images of the highest quality vital. The European Society of Urogenital Radiology (ESUR) 2012 guidelines and subsequent Prostate Imaging –Reporting Data System (PI-RADS) version 2 recommendations in 2015 address the technical considerations for optimising MRI acquisition; however, the quality of the multiparametric sequences employed depends not only on the hardware and software utilised and scanning parameters selected, but also on patient-related factors, for which current guidance is lacking. Patient preparation factors include bowel peristalsis, rectal distension, the presence of total hip replacement (THR), post-biopsy haemorrhage, and abstinence from ejaculation. New evidence has been accrued since the release of PI-RADS v2, and this review aims to explore the key issues of patient preparation and their potential to further optimise the image quality of mpMRI.

Introduction

Prostate cancer (PCa) is the commonest malignancy in Western men and is the second leading cause of cancer-related mortality,[1] with the incidence forecasted to double by 2030.[2] Diagnosis of PCa has traditionally relied on prostate-specific antigen (PSA) levels, digital rectal examination (DRE), and systematic transrectal ultrasound (TRUS)-guided biopsy[3]; however, there is increasing evidence that the pre-biopsy multiparametric (mp) magnetic resonance imaging (MRI) outperforms systematic TRUS-guided biopsy and can lead to an increased detection of clinically significant (cs)PCa whilst at the same time reducing over-diagnosis of clinically insignificant cancer.[4,5] MpMRI in combination with clinical risk assessment can potentially obviate the need for biopsy in 25–30% of men[4,5] due to its high negative predictive value in diagnosing csPCa.[6] As a result, there has been a steady increase in the use of mpMRI, and particularly pre-biopsy mpMRI, which is now being performed in up to 75% of men with suspicion of PCa in the UK.[7]

Given the central role of mpMRI in PCa management pathway, imaging of the highest quality is essential. In order to achieve this, in 2015, the European Society of Urogenital Radiology (ESUR) and American College of Radiology (ACR) published a second, extended version of the Prostate Imaging – Reporting Data System (PI-RADS) recommendation guidelines, which aim to standardise MRI acquisition and interpretation.[8] Detailed guidance is given on technical considerations and diagnostic evaluation; however, no definite recommendation is given regarding patient

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preparation, mainly due to the lack of sufficient evidence available at the time. mpMRI consists of three key sequences: T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI), and dynamic contrast-enhanced (DCE) imaging.[8] The quality of these sequences depends on the hardware and software utilised and scanning parameters selected, but also on several other factors including bowel peristalsis, rectal distension, the presence of total hip replacement (THR), post-biopsy haemorrhage, and abstinence from ejaculation. Since the publication of PI-RADS v2, several new studies exploring these areas have been performed giving us additional insight on how to better overcome these challenges.

The aim of this review is therefore to briefly summarise technical considerations and highlight the key issues of patient preparation in order to further optimise imaging quality of mpMRI.

Technical considerations

Prostate mpMRI at both 1.5 and 3 T can provide satisfactory and reliable diagnostic examinations when appropriate contemporary technology is employed and acquisition parameters are optimised.[8] Three tesla is generally considered superior[8,9] due to increased signal-to-noise ratio (SNR), superior spatial resolution, and decreased acquisition times.[8–10] Performing mpMRI at magnetic field strengths below 1.5 T is not recommended.

The use of an endorectal coil (ERC) provides an increase in SNR, which can lead to improved diagnostic accuracy[9,11–13]; however, the limited number of head-to-head studies comparing 1.5 T ERC to 3 T pelvic phased-array coil (PPAC) have demonstrated no significant difference in either cancer detection rate or local staging accuracy.[14–16] Additionally, there are several drawbacks to ERC use, including distortion of the prostate contour, near-field coil flare, increased time and cost of examination, and an important increase in patient discomfort during the examination when compared to the PPAC (Figs 1 and 2).[8,9] Routine use is not currently recommended, however, an ERC should be employed to improve SNR on some older 1.5 T scanners or in larger patients where SNR in the gland may be reduced with the use of PPAC alone.[8] In case of ERC use, perfluorocarbon fluid or barium sulfate suspensions are advised to fill the balloon in order to minimise the susceptibility artefacts, which can affect DWI.[8]

Sequences

PI-RADS v2 recommends that T2WI, T1WI, DWI, and DCE pulse sequences are included for all prostate MRI examinations.[8] A full review of the PI-RADS guidelines for technical parameters is beyond the scope of this article; however, a summary of key recommendations is outlined in Table 1.

Orientation of the axial plane

It is mandatory for DWI and DCE sequences to match the location and section thickness of axial T2W, thereby allowing synchronous scrolling and comparison between the sequences. All sequences are acquired without breath-holding. PI-RADS v1 recommends obtaining an oblique axial plane, i.e., orthogonal to the rectum[17]; however, the updated version of the guidelines make no recommendation on the orientation of the axial plane. Some authors obtain an axial plane perpendicular to the long axis of prostate,[18] which could minimise partial volume effects at the posterior border (Fig 3). There is no evidence of potential superiority of one approach over another, but a recent UK consensus paper recommends obtaining a true axial plane to the patient, which is easier to set for radiographers and is more reproducible, especially for active surveillance and measuring lesion size.[19]

A potential downside of the true axial approach is compromising the correlation with prostatectomy specimens, but this issue will typically only affect research studies.[20] Theoretical mismatches in apex, mid, and base may occur when performing cognitive fusion with true axial

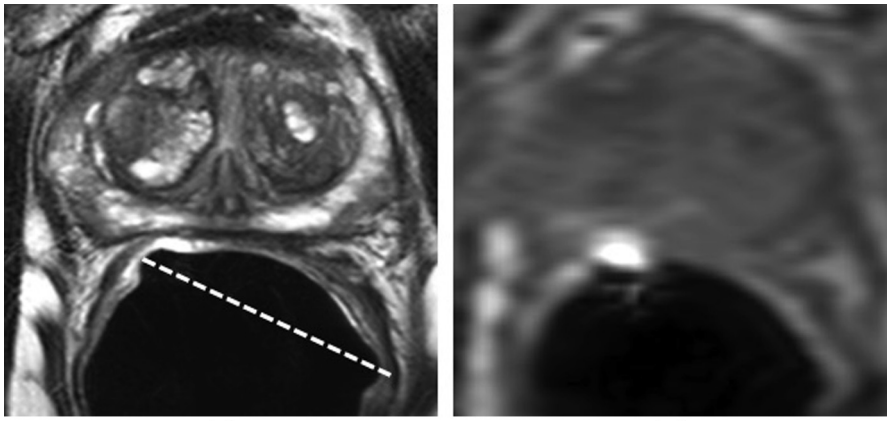

Figure 1 ERC incorrectly sited. (a) T2 axial image with ER coil sites; dotted line highlights coil plane. (b) Flare from the coil elements in the right mid PZ on T1-weighted imaging pre-contrast may mask enhancement or be mistaken for early enhancement if not appreciated.

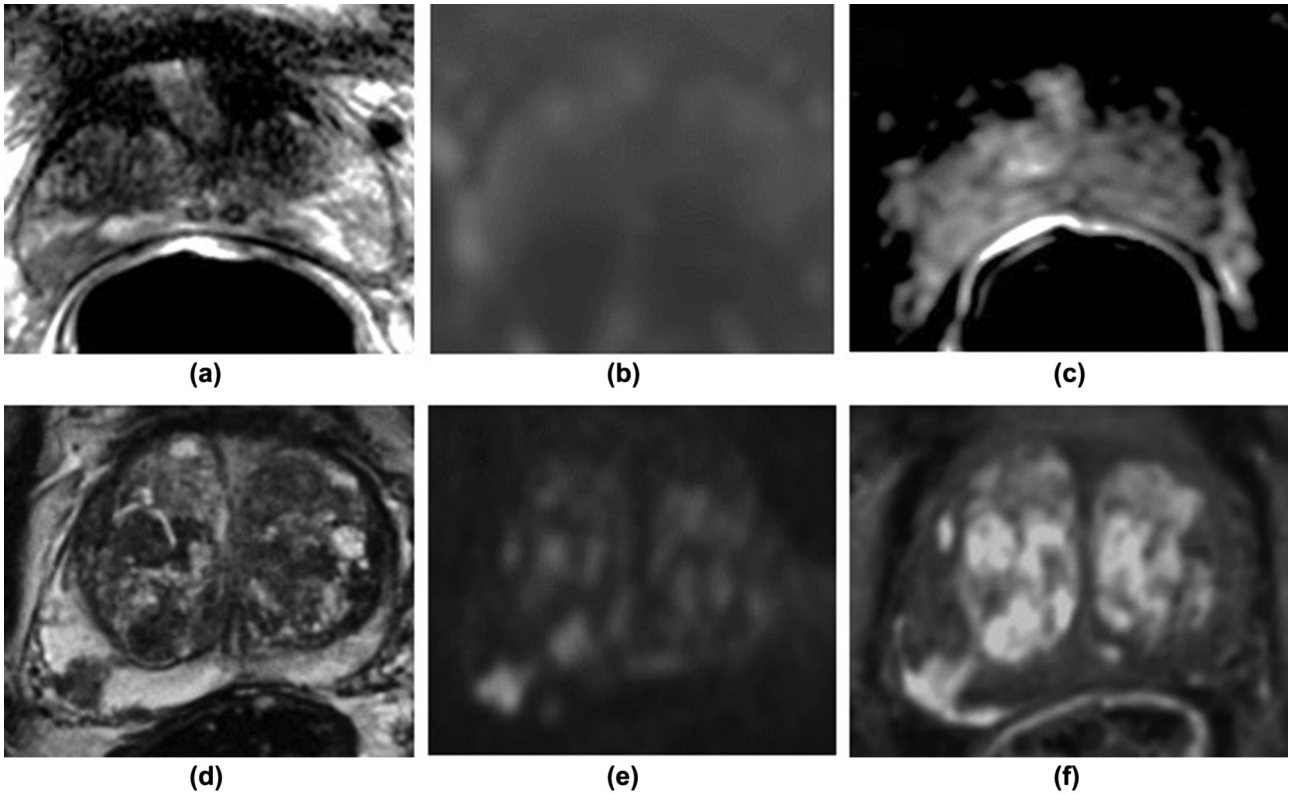

Figure 2 ERC distortion effect. Top Row: 1.5 T ERC imaging. (a) T2WI shows a focal area of low T2 signal in the right mid PZ. (b,c) No restricted diffusion on b-value imaging (b) or ADC maps (c), the dominant PZ sequences. Bottom row: same patient with repeat imaging at 3 T with a pelvic phased-array coil. Right mid-gland PZ lesion is well demonstrated on T2WI (d) and with marked restricted diffusion on b-value DWI (e) and additional early enhancement at DCE (f). Lesion confirmed as Gleason grade 4+3 on targeted biopsy. Image courtesy of Dr Clare Allen, UCL, London.

MRI images being compared TRUS probe images in the plane axial to the prostate[21]; however, any errors may be less significant than inter-reader variability between radiologists when defining sector location within the gland.[22] Similar mismatches may occur if rigid fusion software is used for biopsy procedures, which use a transrectal probe regardless of a transrectal or transperineal approach; however, any quantification of mismatch and/or error rates are yet to be defined (Fig 4).

Time interval after biopsy

In addition to lesion detection prior to biopsy, indications for mpMRI include local staging of TRUS-guided biopsy-proven carcinoma or previous negative systematic biopsy.[23,24] Standard systematic TRUS-guided biopsy acquires 10–12 biopsy cores, which induce haemorrhage and inflammation of the gland,[25,26] which may remain for many weeks and even months.[27] Recent biopsy can induce capsular irregularity and be mistaken for extracapsular extension (ECE). Persistence of haemorrhage is not easily predicted and may relate to variation in citrate levels in the peripheral zone (PZ) epithelial cells[28]; citrate primarily functions as a semen preservative,[28] but additionally exhibits anticoagulant properties.[29] The PZ is thus generally the more affected, with areas of haemorrhage exhibiting T1 hyperintensity and intermediate-to-low T2 signal.[30] The packed cells within tumours act as a barrier to the spread of haemorrhage and the concentration of citrate is additionally reduced in PCa; thus blood products within cancerous tissue resolve more rapidly than in the normal PZ.[30,31] This can be exploited in cases of post-biopsy haemorrhage for detection, with lesions demonstrating the "haemorrhage exclusion sign" (i.e., no T1 hyperintensity) in combination with homogeneously low T2, which is highly predictive for malignancy with PPV at 96%[32] (Fig 5); however, the presence of haemorrhage more typically causes a diagnostic challenge as it can either mask the tumour, or potentially lead to a false-positive call. The T1W images therefore warrant assessment prior to assessment of the other sequences. It should be noted that haemorrhage-induced T2 changes can persist even after resolution of T1 hyperintensity, and therefore, knowledge of any previous biopsy also has to be considered, with DWI and ADC key to differentiate tumour.[33,34] Haemorrhage may also be present in the seminal vesicles (SVs) due to either direct trauma from biopsy or by retrograde spread via ejaculatory ducts.[35] The same evaluation approach as for lesion detection is required, in order to avoid overcalling T3b disease[27,36,37] (Fig 6).

Overall, post-biopsy haemorrhage can compromise imaging interpretation and there is no clear optimal time window prior to MRI, with persistence in an individual patient hard to predict. Studies have reported conflicting results with suggested time intervals ranging from 0 to 6

Table 1
Prostate Imaging – Reporting Data System (PI-RADS) version 2 recommended magnetic resonance imaging (MRI) protocols.

Imaging sequence	Technical parameters
T2-weighted imaging	Fast-spin-echo (FSE) or turbo-spin-echo (TSE) imaging
	Multiplanar imaging (axial, coronal and sagittal)
	FOV: 12–20 cm to encompass the entire prostate gland and seminal vesicles
	Section thickens, gap: 3 mm, 0 mm
	In-plane resolution: ≤0.7 mm (phase) × ≤0.4 mm (frequency)
Diffusion- weighted imaging	Axial plane (same locations as for T2WI)
	Free-breathing spin echo EPI sequence combined with spectral fat saturation is recommended
	Section thickness: 3 mm, 0 mm
	TE: ≤90 ms; TR: >3,000 ms
	FOV: 16–22 cm
	In plane dimension: ≤2.5 mm phase and frequency
	At least two b-values should be acquired in three orthogonal directions ADC map calculation: low b-value should be set at 50–100 s/mm^2, high b-value should be >800 s/mm^2, up to a maximum of 1,000 s/mm^2. Additional b-values may provide more accurate calculations.
	"High b-value": if adequate SNR permits, b-values of 1,400–2,000 s/mm^2 or higher are preferred; it can be acquired by scanning or calculated.
Dynamic contrast-enhanced imaging	Axial plane (same locations as for T2WI)
	Fat suppression and/or subtraction is recommended
	2D or preferably 3D T1 gradient echo (GRE) sequence
	Section thickness, gap: 3 mm, 0 mm
	Dose: 0.1 mmol/kg
	Injection rate: 2–3 ml/s
	TR/TE: <100 ms/<5 ms
	In-plane dimension: ≤2×≤2 mm
	Temporal resolution: <10 s (<7 s is preferred)
	Total observation: >2 min

FOV, field of view; EPI, echo planar imaging; ADC, apparent diffusion coefficient; 2D, two-dimensional; 3D, three-dimensional; TR, repetition time, TE, echo time; T2WI, T2-weighted imaging; GRE, gradient echo.

weeks, likely due to significant differences in methodology.[27,38,39] PI-RADS v2 recommends a minimum delay of 6 weeks for the purpose of local staging[8]; however, even at this time-point around half of the patients still exhibit some haemorrhage[37]; this needs to be balanced against any delay in cancer treatment pathways.

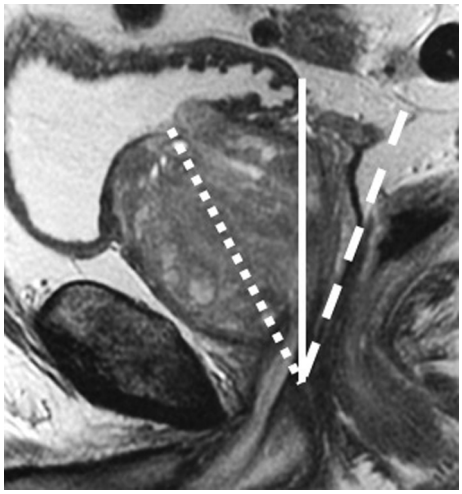

Figure 3 Representation of potential axial imaging planes. Lines represent the orthogonal plane from which images will be acquired. Solid line indicates the true axial plane to the patient as recommended in current UK consensus documentation.[19] Dashed line is oriented orthogonal to the rectum and posterior aspect of the prostate. Dotted line indicates a plane axial to the long axis of the prostate.

Abstinence from ejaculation

PI-RADS v2[8] makes no recommendation on abstinence from ejaculation prior to prostate MRI, given the limited available evidence at the time; however, some institutions instruct the patients to refrain from ejaculation for 3 days prior to MRI examination in order to achieve maximal distension.[40,41] Several recent studies support this practice, demonstrating a significant decrease in SV volume after ejaculation, which could theoretically hinder interpretation of SV invasion (T3b disease; Fig 7).[42–45] The average reported decreases in SV volume are 41% immediately after one ejaculation,[42] and 57% immediately after two consecutive ejaculations.[43] The average volume reduction of 25.6% after 24 h and recovery to baseline at day 3 is likely to be of more clinical relevance.[44] It should be noted that this latter study involved relatively young volunteers (mean 35.9 years) and that the process of seminal fluid replenishment may take longer in older individuals[45]; hence an abstinence of 3 days was therefore proposed as a minimum.[44,45]

Beside SV volume, ejaculation has also been shown to have effect on ADC and T2 values by dehydrating the gland, i.e., decreasing the bulk water content. Medved *et al.* and Shin *et al.* reported significantly decreased ADC values of the PZ by 14.5% and 18.6%, respectively, whilst the difference in the central gland (combined transition and central zone) was non-significant.[42,43] Barrett *et al.* also demonstrated significantly lower ADC values post-ejaculation, but with a lower difference at 4%,[44] possibly reflecting the whole-gland ADC measurement employed. T2 values have also been shown to be significantly lower post-ejaculation

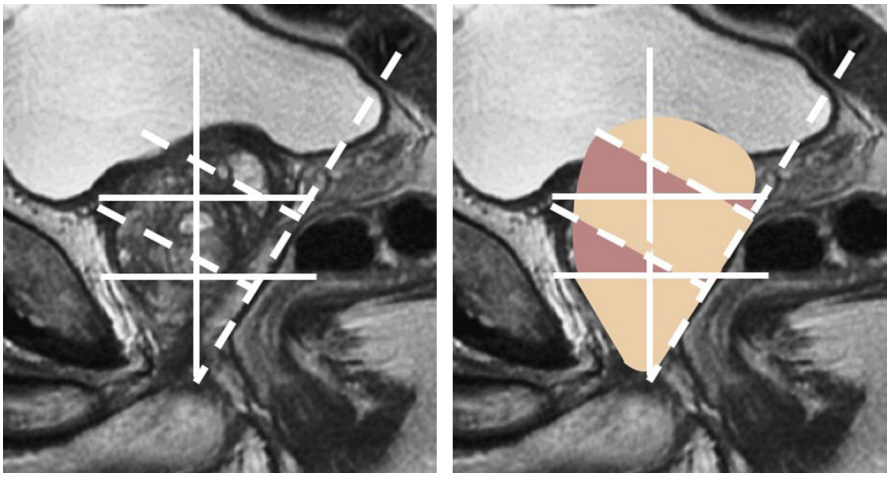

Figure 4 Potential mismatch between true axial and axial-to-prostate acquisitions.Prostate base, mid, and apex sectors as defined by true axial plane (solid lines) and the plane orthogonal to the rectum and posterior prostate (dashed lines). The difference in angle will determine the degree of mismatch (highlighted pink) compared to matching areas (orange).

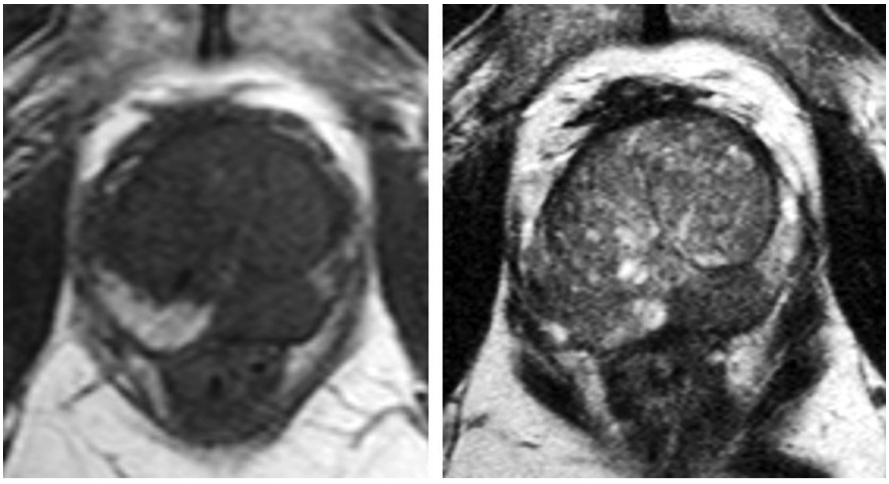

Figure 5 Haemorrhage exclusion sign. TRUS biopsy demonstrates a Gleason 4+4 lesion in left mid PZ. MRI performed post-biopsy shows haemorrhage in the right PZ on T1WI (a) with ill-defined matching low T2 signal (b). Tumour in the left mid PZ demonstrates more focal low T2 signal (a) and "excludes" haemorrhage, which surrounds and outlines the lesion on T1WI (a).

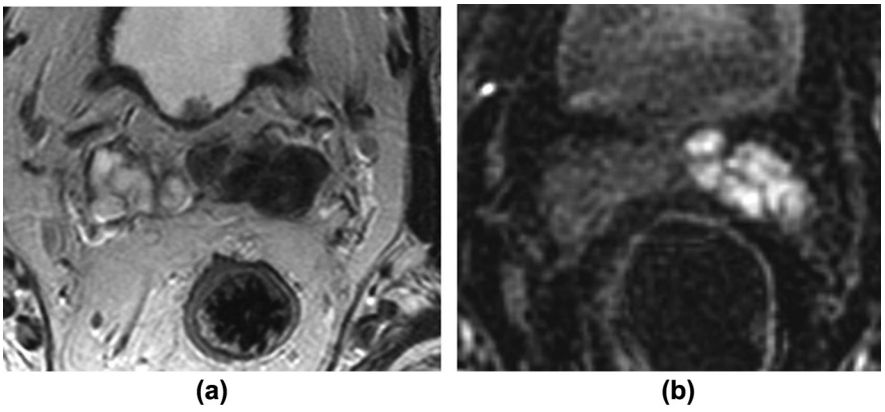

Figure 6 Haemorrhage in the SVs. Haemorrhage in the left SV mimicking T3b disease with low T2 signal (a), but high signal on T1WI with fat suppression (b).

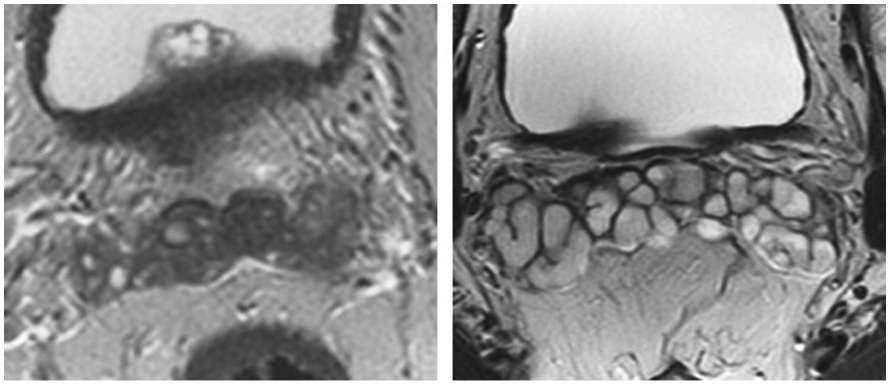

Figure 7 Effect of abstinence from ejaculation. (a) A patient with collapsed SV (volume 3.8 ml) imaged within 1 day of ejaculation. (b) A patient with over-distended SV (volume = 34.9 ml) imaged with a minimum of 3 days abstinence from ejaculation.

with the reported differences in the PZ between 13–18%.[42,43] The effect of post-ejaculatory status ADC and T2WI is potentially more clinically significant as this may affect lesion conspicuity and detection, whilst SV invasion can be assessed by other secondary signs such as asymmetry or bulging and focal areas of enhancement and/or restricted diffusion.

The current evidence suggests that 3 days of ejaculatory abstinence prior to prostate MRI may be beneficial for SV and PZ evaluation but further longitudinal studies including patients with PCa would help to establish the effect on lesion detection.

Anti-Spasmodic agents

Bowel peristalsis is known to cause motion artefact at MRI; however, it has been suggested that the low pelvic location of the gland, remote from the small bowel, may limit the benefit of anti-speristaltic agents in prostate MRI.[46,47] All studies to date have investigated the use of hyoscine butylbromide (HBB); however, this could be substituted by glucagon (1 mg) depending on local preference, or if HBB is contraindicated. HBB administration does carry a risk of side-effects, mainly related to its anti-cholinergic activity,[48,49] and its use will add to the time and the cost of the MRI appointment. Nevertheless, recent studies, which are the largest to date,[50,51] are in agreement with earlier work[52,53] and highlight a significant improvement in image quality of T2WI after intravenous administration of HBB. Caglic *et al.* reported significantly better T2W image quality with less blurring and motion in 173 patients administered 20 mg HBB intravenously,[50] and Ullrich *et al.* showed significantly improved visualisation of anatomical details and decreased motion artefacts on T2W in 70% of 103 patients assessed using 40 mg HBB intravenously, thereby reducing non-diagnostic MRI to <1%.[51] Of the two negative studies, it should be noted that Roethke *et al.* reported reduced artefact in all the assessed categories, but not reaching significance, and recommended the use of HBB in patients with hyper-motile intestine and flatulence.[46] The second study used an ECR, which is not reflective of current UK practice, and may have served as a mechanical barrier to movement of the rectum and prostate, thus minimising the effects of HBB.[47] Only one of these studies assessed the mpMRI functional sequences in addition to T2WI.[50] Although the results showed a trend towards improved quality of DWI and DCE, this did not reach significance. This may reflect reduced effect over time or inherent differences in acquisition of these functional sequences, making them less sensitive to motion artefact. HBB anti-peristaltic effect lasts 20–40 minutes[54,55] suggesting that either a second bolus of HBB prior to DCE[56] or a combination of HBB with longer-acting intramuscular glucagon[54] may be beneficial in the setting of longer imaging protocols; however, this requires further evaluation.

In conclusion, the current evidence suggests routine use of anti-peristaltic agents (recommended dose 20 mg HBB intravenously) prior to prostate mpMRI is necessary to optimise T2WI image quality, a key sequence of mpMRI, in particular for transition zone assessment and local staging.

Bowel preparation

Increased rectal loading has been shown to significantly correlate with increased DWI distortion and reduced DWI image quality by inducing susceptibility artefacts[57] (Fig 8). These especially affect echo planar imaging (EPI) sequences, which are currently the most commonly used DWI sequence in abdominal and pelvic imaging, and these effects are further magnified at higher 3 T field strengths.[58–60] Susceptibility artefacts occur in areas around the air–tissue interfaces,[58–60] such as the rectum and posterior part of the gland, which is where the majority of prostate carcinomas arise.[61] Although no study to date has prospectively evaluated the potential effect of compromised DWI on lesion detection and staging, there is a tendency towards taking biopsies in a higher number of patients as the rectal distension increases and with a higher percentage of these being false positive, suggesting decreased reader confidence.[57] In addition to compromising DWI, increased rectal distension has also been

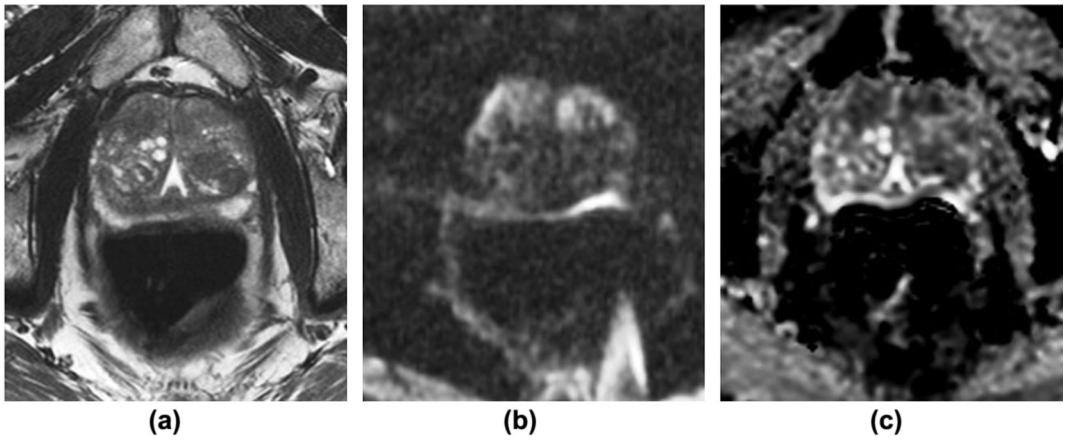

Figure 8 Effect of increased rectal loading. A 64-year-old man with a of PSA 4.11 ng/ml, undergoing MRI pre-biopsy. (a) T2 axial image shows marked rectal loading. (b,c) DWI shows warping on b=1,400 images (b) and ADC map (c), particularly effecting the posterior gland.

shown to significantly increase motion artefact on T2WI[57] by inducing rectal contractions.[62]

A variety of approaches have therefore been proposed in order to overcome these issues, including simple advice for patients to empty their bowel prior to the examination. Another solution may be switching to a prone position to allow air to move to a non-dependent location away from the prostate. More invasive steps involve either actively removing the air from the rectum with a small catheter,[8] or administration of a micro-enema.[63,64] Griethuysen *et al.* evaluated 335 MRI studies at 1.5 T, including patients who self-administered a micro-enema shortly before acquisition, and reported significantly decreased incidence and severity of gas-induced artefacts.[63] A smaller study at 3 T showed no improvement in DWI or T2WI image quality with the use of a pre-MRI enema[64]; however, only a minority of patients in the control, non-enema group (16%) had a moderate or severely distended rectum and use of the enema itself may introduced have rectal air. Another factor to consider is the potential for an enema to irritate the bowel and propagate peristalsis.

Overall, there is currently no technique that has been shown to reduce rectal loading consistently, and thus correlation with DCE, which is less prone to susceptibility artefacts,[57] is recommended or recalling patients in specific non-diagnostic studies may be considered. This mirrors the difficulties faced in radiotherapy planning where several strategies have been investigated, but with no clear evidence to suggest the use of one over another.[65,66] Thus, non-patient-related approaches, including post-processing techniques or changing acquisition parameters, warrant attention. Among these techniques, reduced field-of-view (FOV) DWI,[67,68] read-out segmented EPI sequences,[69] parallel imaging,[68] and acquisition of opposite phase-encoding polarities to correct magnetic field inhomogeneity,[70] or post-processing techniques including correcting for B_0 distortion effects,[71] all of which have shown promise for improving image quality.

Implanted devices and THR

Although it is often safe to image at 3 T, THR patients should be imaged a 1.5 T due to significant distortion artefact, which compromises image quality and will likely render the study non-diagnostic[58,59,72] (Fig 9). THR is an established standard treatment for end-stage hip disease,[73]

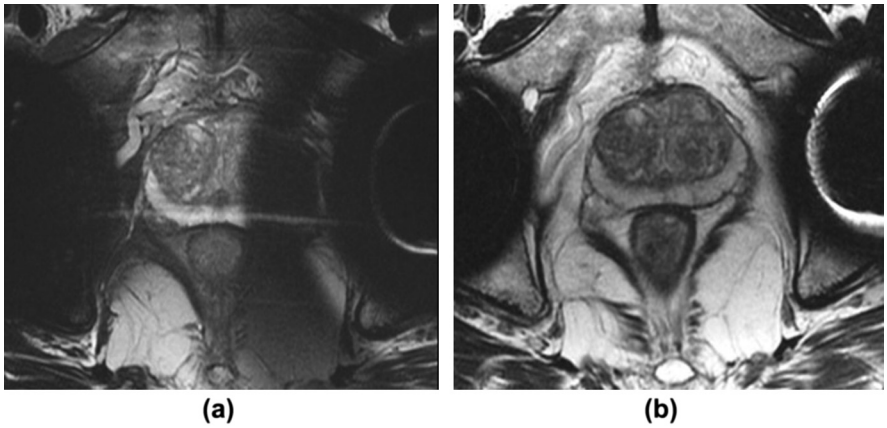

Figure 9 THR artefact on T2WI. Same patient scanned in the same session at 3 T (a) then moved to 1.5 T (b). There was no clinical detail stating the patient had bilateral THRs prior to scheduling.

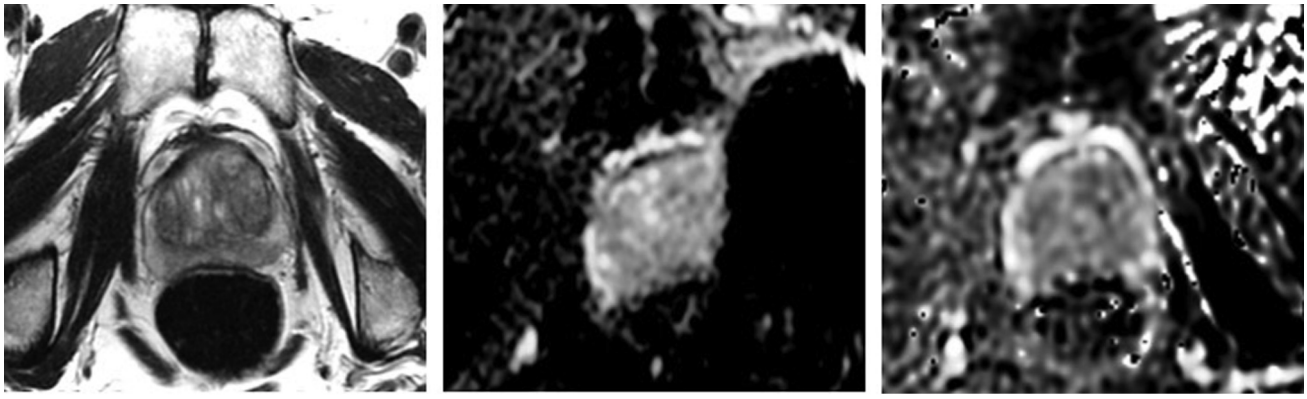

Figure 10 THR artefact on DWI improved with PROPELLER 71-year-old patient with left THR imaged at 1.5 T. (a) T2 WI. (b) ADC map from EPI-DWI shows warping and distortion. (c) ADC map from PROPELLER-DWI has little artefact or distortion (note streak artefact from THR in the top right-hand side of the image).

the typical patient age group overlaps with that of PCa, and the number of procedures is expected to double by 2030,[74] making this more of an issue. DWI is the dominant sequence for PZ assessment[8]; however, it is the most prone to THR artefact, with the echo planar readouts being susceptible to the local B_0 magnetic field inhomogeneities induced, with resultant signal dropout and geometric distortions.[58–60]

Current evidence for reducing THR distortion is limited. Techniques used to reduce rectal gas distortion[67–71] could theoretically also limit THR-induced susceptibility. Rosenkrantz *et al.* reported improved image quality at 3 T MRI by using reduced-field of view (FOV) DWI with parallel imaging in two patients with THR.[75] In a larger 1.5 T study by Czarniecki *et al.*, the use of periodically rotated overlapping parallel lines with enhanced reconstruction (PROPELLER) DWI significantly reduced distortion and improved image quality compared to the standard EPI DWI[76] (Fig 10). Although the latter work showed promising results, additional studies are clearly needed in order to establish a standardised imaging protocol, which would provide adequate diagnostic performance for the increasing cohort of patients with THR and suspicion of PCa.

Conclusion

MpMRI has become established for the detection, local staging, and treatment planning of PCa, emphasising the need for high-quality studies. Image quality depends on the acquisition parameters employed, but also other factors including bowel peristalsis, rectal distension, post-biopsy haemorrhage, post-ejaculatory status, and presence of metalwork. Increasing evidence exploring aspects of patient preparation has been accrued since the release of the PI-RADS v2 guidelines in 2015; however, further prospective studies that include PCa patients are needed in order to inform decision-making and standardisation of these aspects for mpMRI protocols.

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