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## Review Article

# Magnetic resonance imaging for prostate cancer: Comparative studies including radical prostatectomy specimens and template transperineal biopsy

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## ABSTRACT

**Purpose:** Multiparametric magnetic resonance imaging (mpMRI) is an emerging technique aiming to improve upon the diagnostic sensitivity of prostate biopsy. Because of variance in interpretation and application of techniques, results may vary. There is likely a learning curve to establish consistent reporting of mpMRI. This study aims to review current literature supporting the diagnostic utility of mpMRI when compared with radical prostatectomy (RP) and template transperineal biopsy (TTPB) specimens.

**Methods:** MEDLINE and PubMed database searches were conducted identifying relevant literature related to comparison of mpMRI with RP or TTPB histology.

**Results:** Data suggest that compared with RP and TTPB specimens, the sensitivity of mpMRI for prostate cancer (PCa) detection is 80–90% and the specificity for suspicious lesions is between 50% and 90%.

**Conclusions:** mpMRI has an increasing role for PCa diagnosis, staging, and directing management toward improving patient outcomes. Its sensitivity and specificity when compared with RP and TTPB specimens are less than what some expect, possibly reflecting a learning curve for the technique of mpMRI.

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## 1. Introduction

Prostate cancer (PCa) is the second most common cause of cancer death in Australian men and is the most commonly diagnosed internal malignancy with one in seven Australian men being diagnosed with PCa by the age of 75.<sup>1</sup> PCa may first present with elevated prostate-specific antigen (PSA) on screening or symptomatically with lower urinary tract symptoms, bony pain from metastases or uncommonly with hematuria, urinary retention, or renal failure.<sup>2</sup> The definitive diagnosis of PCa is generally made by a biopsy, typically transrectal ultrasound (TRUS)-guided biopsy. Staging is typically by a nuclear medicine bone scan or computed tomography–positron emission tomography.<sup>3</sup>

An influential work by McNeal et al in 1988<sup>4</sup> demonstrated trends in the zonal origin of PCa, particularly the predominance of malignancy within the peripheral zone (PZ) and hence its amenability to detection on digital rectal examination (DRE) and TRUS-guided biopsy. However, a minority of cancers arose from more anterior regions of the prostate leading to a newly articulated phenomenon “prostatic evasive anterior tumor syndrome (PEATS).” PEATS describes a subset of PCa which, due to anatomical location, may be missed by traditional investigations such as DRE and TRUS biopsy, both of which primarily focus on the PZ, but may be detected by multiparametric magnetic resonance imaging (mpMRI) or transperineal biopsy (TPB).<sup>5</sup>

Management of PCa depends on risk stratification, most commonly the Gleason score, TNM staging, and PSA level. Lower risk cancers may be indolent and require active surveillance (AS) involving (with local variation) monitoring PSA levels (serial PSA tests), DRE, biopsy, and possibly mpMRI or watchful waiting for

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patients deemed not suitable for active treatment with curative intent by their treating clinician. Higher risk cancers may be treated with radical prostatectomy (RP), external beam or interstitial (brachytherapy) radiotherapy, androgen deprivation therapy, or a combination of these. Newer focal therapies are under investigation.<sup>3</sup>

This literature review aims to describe mpMRI and to explore the evolving role for PCa diagnosis and staging.<sup>6</sup> The sensitivity and specificity of mpMRI reported in the literature is approximately 80–90% and 50–90%, respectively, when compared with RP and template TPB (TTPB) specimens.

## 2. Materials and methods

MEDLINE and PubMed database searches were conducted from August 2014 to January 2015 using combinations of the MeSH terms “prostate,” “prostatic neoplasia,” “diagnosis,” “magnetic resonance imaging,” and using specific search terms such as “mpMRI,” “multiparametric,” or “erMRI.”

## 3. Discussion

Multiparametric MRI (mpMRI) is an emerging technique that aims to improve upon the diagnostic sensitivity of prostate biopsy, and ultimately reduce the number of biopsies performed and better direct management decisions. The recently released 2014 National Institute for Health and Care Excellence (NICE) guidelines for management of PCa in the United Kingdom recommended an increasing role for mpMRI based on clinical and cost effectiveness. However, these guidelines recommended against utilizing mpMRI before biopsy due to insufficient cost benefit.<sup>3</sup> It is important to distinguish multiphasic MRI from conventional 1.5-T MRI techniques without dynamic contrast-enhanced MRI (DCE-MRI) or diffusion-weighted imaging (DWI), which have been shown not to provide sufficiently reliable information for clinical decision making.<sup>7</sup> The sequences involved in mpMRI are detailed in [Table 1](#). [Tables 2 and 3](#) summarize the literature regarding the diagnostic utility of mpMRI for PCa.

### 3.1. MRI after a negative TRUS

The NICE guidelines recommended consideration of an MRI after negative TRUS biopsy to assess the requirement for an additional biopsy.<sup>3</sup> This particularly relates to PEATS, because anterior or apical tumors may be missed by TRUS biopsy but still be visible on mpMRI.<sup>5,8</sup>

### 3.2. Active surveillance

mpMRI has an emerging role within AS for low-grade disease, partly to minimize morbidity due to repeat biopsy.<sup>9,10</sup> The Prostate Cancer Research International: Active Surveillance (PRIAS)—guideline and study for the expectant management of localized prostate cancer with curative intent study is a multicenter, international, ongoing study that includes a subgroup of men undergoing mpMRI as part of their AS for low-risk PCa. The PRIAS protocol includes an MRI 3 months after diagnosis, similar to the NICE guidelines recommending mpMRI for all men commencing AS.<sup>3</sup> In addition, PRIAS includes yearly mpMRI and some targeted biopsies. The number, size, and prostate imaging-reporting and data system (PI-RADS) progression of visible lesions direct whether targeted biopsy is undertaken and longitudinal information will be collected regarding correlation of MRI with biopsy and RP specimens. PRIAS is expected to conclude in 2021 and may dictate the future role of mpMRI in AS.<sup>11,12</sup>

### 3.3. Preoperative staging

The NICE guidelines recommended mpMRI to investigate for regional nodal disease and the extent of the primary tumor in men with histologically proven PCa if the tumor growth affects management, such as in preoperative staging.<sup>3</sup> Organ-confined disease enables an operative approach to spare the neurovascular bundle, minimizing concerns regarding positive surgical margins, and thereby reducing postoperative morbidity relating to erectile dysfunction without increasing mortality risk.<sup>13</sup> mpMRI has been

**Table 1**  
Details of magnetic resonance sequences.

Magnetic resonance sequence	Technical details	Clinical implications
DWI/ADC	The apparent diffusion coefficient (ADC) of a tissue dictates Brownian motion of water molecules within that tissue. <sup>15</sup> Lower ADC within PCa may result from the replacement of fluid containing ducts with tightly packed glandular tissue. <sup>17</sup>	ADC negatively correlates with tumor grade. <sup>18,19</sup> DWI is more sensitive for tumors of a higher grade, stage and volume. <sup>20</sup>
DCE	Malignant tissue has increased permeability and vascularity relative to normal tissue causing early enhancement and washout of the contrast agent. <sup>15</sup>	Higher tumor grades correlate with proportionately earlier enhancement and washout. <sup>21</sup> DCE-MRI may reduce accuracy within the TZ. <sup>21,22</sup>
Magnetic resonance spectroscopy	Magnetic resonance spectroscopy detects increasing (choline + creatinine)/citrate ratios, which have been correlated with Gleason score. <sup>23</sup>	A large clinical trial suggested that magnetic resonance spectroscopy provides little additional information compared with T2WI. <sup>23</sup> Magnetic resonance spectroscopy may not be included in mpMRI sequences <sup>16,24</sup> and is optional in the PIRADS scoring system. <sup>15</sup>
T1WI	Detects postbiopsy hemorrhage, which confounds other sequences. <sup>25</sup>	
T2WI	Delineates the zonal anatomy of the prostate and capsule, and helps elucidate extracapsular extension. <sup>15</sup> Suspicious characteristics include homogenous areas of low signal with ill-defined margins. <sup>15,26</sup>	

*Note.* From “The role of magnetic resonance imaging in the diagnosis and management of prostate cancer,” by J. Thompson, N. Lawrentschuk, M. Frydenberg, L. Thompson, and P. Stricker, *USANZ*, 2013, *BJU Int*, 112, p. 6–20; Also from “MRI for men undergoing active surveillance or with rising PSA and negative biopsies,” O. Raz, M. Haider, J. Trachtenberg, D. Leibovici, and N. Lawrentschuk, 2010, *Nat Rev Urol*, 7, p. 543–51.

ADC, apparent diffusion coefficient; DCE, dynamic contrast enhanced; DWI, diffusion-weighted imaging; mpMRI, multiparametric magnetic resonance imaging; MRI, magnetic resonance imaging; PCa, prostate cancer; PIRADS, Prostate imaging and reporting data system; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; TZ, transition zone.

**Table 2**  
mpMRI with RP reference standard.

Reference	Thompson et al <sup>19</sup>	Chamie et al <sup>41</sup>	Junker et al <sup>23</sup>	Hoeks et al <sup>40 a)</sup>	Delongchamps et al <sup>22</sup>	Yoshizako et al <sup>29 a)</sup>	Villers et al <sup>43</sup>
Year	2014	2014	2014	2013	2011	2008	2006
Retrospective /prospective	Prospective	Retrospective	Prospective	Retrospective	Retrospective	Retrospective	Prospective
Age (y)	62	61, mean	63, mean	67	63	65	63
Prostate-specific antigen	5.6	5.6, mean	7.3, mean	9	7	NR	9.9
Sensitivity (%)	98	96	97	65	78	69	77
Specificity (%)	43	46	79	67	97	94	91
Negative predictive value (%)	75	92	NR	NR	NR	NR	NR
Positive predictive value (%)	91	66	NR	NR	NR	95	NR
N	48	115	50	63 <sup>a)</sup>	57	35 <sup>a)</sup>	24
MRI sequence	T2, DWI, DCE	T2, DWI	T2, DWI, DCE	T2, DWI, DCE	T2, DWI, DCE	T2, DWI, DCE	T2, DCE
Field strength (T)	1.5/3 alternating	3	3	3	1.5	1.5	1.5
Coil	PPA	ERC	PPA	ERC	ERC	PPA	PPA
No. of readers, experience	2, 1,000+ prostate MRI reported	1, Experienced	1, Experienced	4, 3–10 y	2, Experienced	2 y, 13 y, and 15 y	2 y, 15 y, and 4 y
Radiologist blinding	NR	Blinded to clinical	Blinded to clinical	PCa known, not location	Blinded to clinical	PCa known, not location	Blinded to biopsy and histopathology
Time from MRI to RP	NR	NR	1 d	NR	NR	1–7 wk, median 4	30 d, mean
Reporting system	PI-RADS	Epstein criteria or ADC < 850 mm <sup>2</sup> /s	PI-RADS	Likert	Likert	Likert	Likert
Significant cancer definition	GS ≥ 7, GS = 6 CL ≥ 5 mm or 20% cores positive <sup>b)</sup>	pT3, GS ≥ 4+3, GS = 3 + 4 and ≥ 1.3 mL	Any PCa	Any PCa	Any PCa	Any PCa	Any PCa

Age and PSA are median values unless labeled as mean. PIRADS 3–5 was considered positive.

<sup>a)</sup> Only considers TZ PCa.

<sup>b)</sup> Paper reports other definitions.

ADC, apparent diffusion coefficient; CL, core length; DCE, dynamic contrast enhanced; DWI, diffusion-weighted imaging; ERC, endorectal coil; GS, Gleason score; mpMRI, multiparametric magnetic resonance imaging; MRI, magnetic resonance imaging; NR, not recorded; PCa, prostate cancer; PI-RADS, prostate imaging-reporting and data system; RP, radical prostatectomy; TZ, transition zone; UCL, University College London.

**Table 3**  
mpMRI with TPB reference standard.

Reference	Pepe et al <sup>42</sup>	Thompson et al <sup>19</sup>	Grey et al <sup>34</sup>	Abd-Alazeez et al <sup>25</sup>	Abd-Alazeez et al <sup>32</sup>	Arumainayagam et al <sup>31</sup>
Year	2014	2014	2014	2014	2014	2013
Retrospective/prospective	Prospective	Prospective	Prospective	Retrospective	Prospective	Retrospective
Age (y)	65	62	65, mean	62	61	64, mean
Prostate-specific antigen	10.4	5.6	11.7, mean	5.8	10	8.2, mean
Sensitivity (%)	83	93	97	98, 94	90, 76	64–81, 58–73 <sup>a)</sup>
Specificity (%)	72	53	60	22,23	42,42	68–80, 71–83 <sup>a)</sup>
Negative predictive value (%)	88	52	98	98, 89	95, 79	91–94, 84–89 <sup>a)</sup>
Positive predictive value (%)	79	98	49, 58, 84 <sup>b)</sup>	21, 34	26, 38	35–45, 49–63 <sup>a)</sup>
N	168	150	201	129	54	64
N with prostate cancer	66	150	77	141 (two sectors)	34	54
MRI sequence	T2, DWI, DCE, MRS	T2, DWI, DCE	T2w, DWI	T2, DWI, DCE	T2, DWI, DCE,	T2, DWI, DCE
Field strength (T)	3	1.5/3 alternating	1.5	1.5	1.5	1.5
Coil	PPA	PPA	PPA	PPA	PPA	PPA
No of readers, experience	2, NR	2, 1,000+ prostate MRI reported	1, 4 y	5, 100 + mpMRI/y	8, 3–8 y	3, 3–10 y
Radiologist blinding	Blinded to clinical	NR	Blinded to clinical	Blinded to biopsy	Blinded to biopsy	Blinded to biopsy
Time from MRI to TPB	3–10 d	NR	43 d, median	<1 y	NR	106 d, median
Reporting system	NR	PI-RADS	PI-RADS	PI-RADS	PI-RADS	Likert
Number of cores	6–35, median 28	median 30, two targeted	24–40, two to four targeted	20–93, median 41	minimum 10–12	29–41, median 34
Prior negative biopsy	Yes	Mainly No	Mixed	No	Yes	Mixed
Significant cancer definition	NR	GS ≥ 7, GS = 6 CL ≥ 5 mm or 20% cores positive <sup>d)</sup>	GS ≥ 7, GS = 6 CL ≥ 6 mm	UCL 1, UCL 2 <sup>c,d)</sup> , and PIRADS 4	UCL 1, UCL 2 <sup>c)</sup>	UCL 1, UCL 2 <sup>c)</sup>

a) Range is from different radiologists

b) PPV for PIRADS 3,4, and 5, respectively.

c) UCL 1: Gleason score of over 4 + 3 and/or maximum cancer core length (CCL<sub>max</sub>) of 6 mm or more; UCL 2: Gleason score of 3+4 or more and/or CCL<sub>max</sub> of 4 mm or more.<sup>33,36,37</sup>

d) Paper reports other definitions.

DCE, dynamic contrast enhanced; DWI, diffusion-weighted imaging; GS, Gleason score; mpMRI, multiparametric magnetic resonance imaging; MRI, magnetic resonance imaging; MRS, magnetic resonance spectroscopy; NR, not recorded; PI-RADS, prostate imaging-reporting and data system; PPA, pelvic-phased array; TPB, transperineal biopsy; UCL, University College London.

Age and PSA are median values unless labeled as mean. PIRADS 3–5 was considered positive.

shown to have a high positive predictive value (PPV) of around 90% in a high-risk cohort and a negative predictive value (NPV) of around 90% in a low-risk cohort for predicting extracapsular extension versus organ-confined disease.<sup>13–15</sup> However, Billing et al<sup>16</sup> reported a PPV and NPV of approximately 70% in the general case, which serves to remind that all MRI reports must be viewed in their clinical context.

### 3.4. mpMRI sequences

A 2014 European Consensus Panel and the European Society for Urogenital Radiology (ESUR) agreed that multiphase MRI should involve various submodalities such as T1-weighted images (T1WIs), T2-weighted images (T2WIs), DWI and DCE as different sequences provide an additive benefit to accuracy.<sup>17,18</sup> The role of MR spectroscopy is less clear.<sup>18</sup> The 2014 NICE guidelines only recommend obtaining T2WI and DWI images and provide no recommendations regarding field strength or the use of an endorectal coil (ERC).<sup>3</sup>

### 3.5. Magnetic field strength and ERCs

3-T MRI may be preferred due to increased spatial resolution and signal-to-noise ratio.<sup>17,18</sup> However, this may not improve diagnostic accuracy.<sup>19,20</sup> ERC, compared with a pelvic-phased array (PPA), may be used to locally increase spatial resolution while also causing significant patient discomfort.<sup>7</sup> Improvements in diagnostic accuracy are less clear.<sup>20</sup> A 2014 International Consensus Panel recommended the use of ERC at 1.5 T, but considered 3 T as optional; by contrast, the ESUR considers them entirely optional.<sup>17,18</sup>

### 3.6. Scoring system for image interpretation

In 2012, the ESUR published a structured reporting system known as the PI-RADS and recommendations on standardizing the mpMRI protocol.<sup>17</sup> The aim of these guidelines was to improve the diagnostic accuracy of mpMRI for PCa, to improve communication between radiologists, and to standardize the literature for better comparisons between studies. A PI-RADS score has components from different MRI sequences and an overall score from one to five, with higher numbers reflecting an increasing probability of PCa risk and aggression.<sup>17</sup> Prior to these publications, many studies used more subjective Likert scales, which have subsequently shown to have greater interobserver variability.<sup>21</sup>

Some authors describe the PI-RADS system as a work in progress due to ongoing controversy surrounding MRI protocols and the definition and treatment of clinically significant PCa.<sup>22–24</sup> PI-RADS 3 is considered “equivocal” and it is unclear whether this should be considered positive or not; in particular, the morbidity due to overtreatment of PCa is a concern. The trend is that if equivocal results are included, sensitivity is higher while specificity is lower. Some authors report both and the difference in quantitative results is substantial. For example, Abd-Alazeez et al<sup>25</sup> reported, for University College London (UCL) definition 2, sensitivities of 94% and 68% with specificities of 23% and 69% for PI-RADS of 3 or more and 4 or more, respectively.

Typically, it is local practice in Melbourne, Australia, for a radiologist to recommend a biopsy of a PI-RADS 3 lesion. Fig. 1 illustrates the correlation between a PI-RADS 5 lesion identified on mpMRI and an RP specimen.

### 3.7. Reference standard controversy

There is an ongoing controversy surrounding the reference standard to which mpMRI is compared.<sup>26</sup> Various authors advocate

comparing MRI with transrectal biopsy, TPB, or whole-mounted prostatectomy specimens. Transrectal biopsies miss 20–30% of clinically significant tumors, typically caused by undersampling of the apex, transition zone (TZ), and anterior horns of the PZ.<sup>2</sup> Template-guided TPB provides a more comprehensive sample.<sup>27</sup> RP whole-mount specimens minimize any sampling error, but exacerbate selection error because men with low-risk disease, who are unfit for surgery, who choose alternative treatments, or those without PCa are not sampled.<sup>26</sup> By focusing on men with high-risk PCa, this approach limits the investigation of the NPV and the role for MRI to reduce unnecessary biopsies.<sup>19</sup> Thompson et al<sup>19</sup> used TTPB and RP and reported similar results.

### 3.8. Benign disease mimicking carcinoma

Benign disease such as benign prostatic hyperplasia, biopsy changes, fibrosis, prostatitis, and prostatic intraepithelial neoplasia can mimic the appearance of cancer on mpMRI.<sup>20</sup> However, Junker et al<sup>23</sup> demonstrated that such mimics are almost exclusively mistaken low-grade carcinoma as indicated by a PI-RADS score of 3 or less.

### 3.9. Timing of MRI postbiopsy

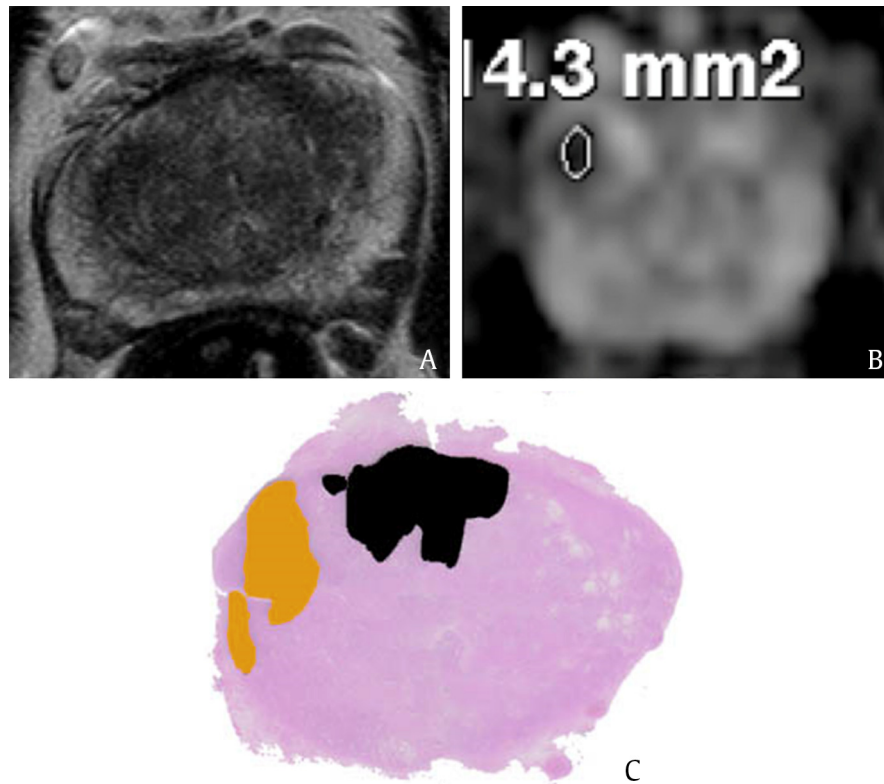
A 2014 European Consensus recommended that mpMRI should be conducted at least 8 weeks after the biopsy to minimize the confounding effect of postbiopsy hemorrhage.<sup>18</sup> Hemorrhage can cause decreased T2 signal potentially masking or mimicking tumors and can involve areas quite distant from the needle trajectory.<sup>28</sup> However, a 2012 study by Rosenkrantz et al<sup>28</sup> involving 44 patients showed that lengthy delay might not be necessary, as hemorrhage can reliably be demonstrated on T1WI.

### 3.10. Definition of clinically significant PCa

As mentioned earlier, PCa can range from indolent to lethal. Appropriate risk stratification is critical to guiding management, to both reduce morbidity from overtreatment and mortality from undertreatment. There is considerable variation in the definition of “clinically significant” PCa.<sup>9</sup> For example, in 2008, Yoshizako et al<sup>29</sup> included cancers with Gleason score 3 + 3 and no size restrictions. In 2011, Haffner et al<sup>30</sup> defined clinically significant as either core length of over 5 mm or Gleason score of 3 + 4 or more. In 2015, Junker et al<sup>23</sup> defined low grade as 3 + 4 or less and high grade as 4 + 3 or more without mention of core length. In 2014, Abd-Alazeez et al<sup>25</sup> reported results for five different definitions of clinical significance based around the Gleason score (either  $\geq 4 + 3$  or  $\geq 3 + 4$ ) and individual cancer core length (either  $\geq 6$  mm or  $\geq 4$  mm) or combinations of the two. More recently, papers from UCL have attempted to standardize reporting with the following definitions. UCL 1: Gleason score of over 4 + 3 and/or maximum cancer core length (CCL<sub>max</sub>) of 6 mm or more; UCL 2: Gleason score of 3 + 4 or more and/or CCL<sub>max</sub> of 4 mm or more.<sup>25,31,32</sup> More exclusive definitions of clinically significant PCa tend toward higher sensitivities compared with more inclusive definitions, with small decreases in specificities. Arumainayagam et al<sup>31</sup> and Abd-Alazeez et al<sup>25,32</sup> compared the more exclusive UCL 1 with the more inclusive UCL 2, and showed that sensitivity increases by 4–16% and specificity decreases by 0–3%. Thompson et al<sup>19</sup> analyzed four definitions and reported smaller differences of 0–3% for both sensitivity and specificity.

### 3.11. Blinding

The studies in Tables 2 and 3 all used some form of blinding, but the details varied. One would expect that a stricter blinding



**Fig. 1.** Prostate imaging-reporting and data system 5 lesion histologically proven to be prostate cancer. (A) Focal, irregular hypointensity on T2-weighted imaging, (B) focal restricted diffusion on an apparent diffusion coefficient map, and (C) correlation with radical prostatectomy (index lesion marked in yellow and other foci marked in black).

protocol results in less diagnostic accuracy, but this is not evident in these tables so the effect is likely small.

### 3.12. Patient population and biopsy indication

By definition, sensitivity and specificity are independent of disease prevalence, whereas PPV and NPV are not. Despite this, the differing indications for mpMRI alter the diagnostic accuracy. For example, Grey et al<sup>34</sup> reported sensitivity varying from 85% to 100% across primary biopsy, AS, and previous negative biopsy groups. The effects were more pronounced for NPV varying from 27% to 77%.<sup>33,34</sup> The two 2014 studies by Abd-Alazeez et al<sup>25,32</sup> primarily differ in the MRI indication as they are from the same institution over similar periods. In the primary biopsy setting, with significant PCa defined by UCL 2, sensitivity and specificity were reported as 94% and 23%, respectively, compared with 76% and 42% respectively in the repeat biopsy setting. This variation may be accounted for by the systematic differences between the groups in terms of tumor size and location such as PEATS being more common in the previous negative biopsy group.<sup>5</sup>

### 3.13. Comment on specific papers

Tables 2 and 3 summarize the literature regarding the diagnostic utility of mpMRI for PCa. They demonstrate the wide range of results and heterogeneity in terms of patient population, test indication, study design, MRI protocol, scoring system, radiologist experience, biopsy protocol, significant cancer definition, and reference standard, all of which confound direct comparison. Several papers were excluded as they only investigated the MRI sequences individually and not their combined utility.<sup>35–37</sup> A 2014 meta-analysis by de Rooij et al<sup>38</sup> and a 2015 meta-analysis by

Fütterer et al<sup>39</sup> were excluded as the relevant studies were already included, and thus, the information was considered redundant. The results of the meta-analyses largely agree with Tables 2 and 3 with some differences as other reference standards such as TRUS biopsy or MRI-guided biopsy were included.

The difficulty in imaging the TZ was illustrated by Hoeks et al<sup>40</sup> as they reported disappointing results, with no significant improvement in mpMRI (including both DCE and DWI–MRI) compared with T2WI MRI alone with accuracies of 66% and 68%, respectively. These numbers are comparable to those obtained by a smaller study Yoshizako et al<sup>29</sup> where accuracy decreased from 83% to 79% after DCE was added to T2WI and DWI for TZ PCa. Delongchamps et al<sup>22</sup> again showed the difficulty in imaging the TZ, reporting a maximum sensitivity and specificity of 71% and 98% for the TZ (results not statistically significant), which is less favorable than the PZ with 80% and 97%, respectively. This suggests that PCa location is another confounding factor for comparing studies.

Delongchamps et al<sup>22</sup> found that the addition of DCE to an mpMRI protocol reduces accuracy within the TZ and reported sensitivity and specificity of 53% and 83%, respectively, if DCE was included; however, upon excluding DCE, they reported sensitivity and specificity of 71% and 98%, respectively.<sup>22</sup> This was supported by Junker et al<sup>23</sup> who reported a sensitivity and specificity within the TZ as 53% and 83%, respectively, if DCE was included compared with 71% and 98% if DCE was excluded.<sup>23</sup> Junker et al<sup>23</sup> subsequently recommended that the PI-RADS score developed in 2012 by the ESUR be amended to reflect this finding.

Chamie et al<sup>41</sup> demonstrated that the additional benefit of DWI in mpMRI is most significant for higher grade disease, which is particularly relevant as overtreatment of clinically insignificant disease is a concern. Pepe et al<sup>42</sup> also reported that the diameter of lesions identified on mpMRI correlated with aggressiveness. Grey

et al<sup>34</sup> reported that out of 88 patients with a negative MRI, only two had low-volume Gleason score 3 + 4 PCa on TPB (98% NPV). In addition, Thompson et al<sup>19</sup> suggested that avoiding biopsy of PI-RADS 1 or 2 MRI lesions may reduce unnecessary biopsies by 50% at the cost of delaying diagnosis of Gleason score 3 + 4 in 1% of patients. In both papers, no higher-grade disease was missed. This suggests that MRI may have a role in reducing unnecessary biopsies and associated morbidity.<sup>34</sup>

The two oldest studies by Villers et al<sup>43</sup> and Yoshizako et al<sup>29</sup> illustrated the evolution of mpMRI protocol across time. Villers et al<sup>43</sup> did not include DWI as their study preceded a number of guidelines advocating its use.<sup>3,18,43</sup> Further, both authors used a 1.5-T field strength without an ERC, which results in a lower spatial resolution and is now perhaps thought to be insufficient.<sup>18</sup>

Grey et al<sup>34</sup> described a particular patient whose PCa was missed by mpMRI. The reference test (TPB) was performed 10 months after the MRI (compared with the mean of 43 days) so it is possible the cancer had either increased in volume or progressed in grade and the original PI-RADS score of 1 or 2 may have been accurate at the time.<sup>34</sup> This case suggests that an additional confounding factor is the time from MRI to biopsy and then to RP.

### 3.14. Interobserver variability and a learning curve

Interobserver variability and learning curves are likely contributing factors to the diversity of results in different studies of mpMRI. The effects are greater when Likert scale scoring systems are employed, as they rely heavily on the experience of senior radiologists, and the effects are lessened for more well-defined scoring systems, such as PI-RADS. Gaziev et al<sup>44</sup> demonstrated a significant learning curve for PCa detection with MRI reporting on a Likert scale. The 2-year prospective study reported an increase in cancer detection from 42% to 81%. Vaché et al<sup>21</sup> compared different scoring systems for the diagnosis of PCa on mpMRI. Significant interobserver variability occurred with the subjective Likert scoring system with area under the curve (AUC) scores varying from 0.88 to 0.81. Interobserver variation was minimal across the more rigid scoring systems as PI-RADS AUC varied from 0.75 to 0.76. Pokorny et al,<sup>45</sup> using PI-RADS, demonstrated no significant difference in accuracy between junior and senior radiologists and a urologist after the protocol had been implemented for 18 months. Accuracy did not increase with time across the 6-month study.

### 3.15. Future studies

The UCL Hospital is undertaking the Prostate Imaging Compared to Transperineal Ultrasound Guided Biopsy for Significant Prostate Cancer Risk Evaluation (PICTURE) study and the multicenter PROstate MRI Imaging Study: Evaluation of Multi-parametric Magnetic Imaging in the Diagnosis and Characterisation of Prostate Cancer (PROMIS) designed to prospectively assess the NPV of mpMRI and the role to reduce biopsies.<sup>46</sup> Both studies are expected to be completed in 2014/2015.<sup>47</sup>

### 3.16. MR-guided biopsy

Lawrence et al<sup>48</sup> electronically aligned and fused mpMRI images with three-dimensional real-time TRUS imaging for targeted biopsy. Pokorny et al<sup>45</sup> described in-bore MR-guided prostate biopsy reporting sensitivity and specificity of 92% and 97%, respectively, for intermediate and high-grade PCa.<sup>45</sup>

In conclusion, mpMRI has an increasing role for PCa diagnosis, staging, and directing management toward improving patient outcomes. The sensitivity and specificity of mpMRI reported in the literature is approximately 80–90% and 50–90% when compared

with RP and TTPB specimens. This is less than what some expect, possibly reflecting a learning curve for the technique of mpMRI.

### Conflicts of interest

None declared.

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