International Journal of Surgery Open 10 (2018) 66–71

Contents lists available at ScienceDirect

International Journal of Surgery Open

journal homepage: www.elsevier.com/locate/ijso

Research Paper

Performance characteristics of multiparametric-MRI at a non-academic hospital using transperineal template mapping biopsy as a reference standard

Edwin Michael Chau [a, b, c], Manit Arya [a, b, c], Neophytos Petrides [c], Zaid Aldin [e], Jolanta McKenzie [d], Mark Emberton [b], Jaspal Virdi [c], Hashim Uddin Ahmed [f, g, 1], Veeru Kasivisvanathan [a, b, *, 1]

[a] Division of Surgery and Interventional Science, University College London, United Kingdom
[b] Department of Urology, University College London Hospital, United Kingdom
[c] Department of Urology, Princess Alexandra Hospital, United Kingdom
[d] Department of Pathology, Princess Alexandra Hospital, United Kingdom
[e] Department of Radiology, Princess Alexandra Hospital, United Kingdom
[f] Division of Surgery, Department of Surgery and Cancer, Imperial College London, United Kingdom
[g] Imperial Urology, Imperial Healthcare NHS Trust, United Kingdom

ARTICLE INFO

Article history:
Received 4 January 2018
Accepted 7 January 2018
Available online 31 January 2018

Keywords:
Magnetic resonance imaging
Needle biopsy
Prostatic neoplasm
Predictive value of tests

ABSTRACT

Objectives: To evaluate diagnostic accuracy of mpMRI in a non-academic hospital using transperineal template prostate mapping (TPM) biopsy as a reference standard. Secondary objectives included evaluating why mpMRI missed significant cancer.

Materials and methods: 101 men received pre-biopsy mpMRI and TPM-biopsy over 16 months. Disease status was assigned at hemigland level. Primary histological definition of clinical significance was Gleason grade >/ = 4 + 3 or maximum cancer core length (MCCL) >/ = 6 mm. Positive mpMRI was defined as Prostate Imaging Reporting and Data System (PI-RADS) score >/ = 3.

Results: Median age 69 (IQR 62–76). Median PSA 7 ng/ml (IQR 4.6–9.8). mpMRI had sensitivity 76.9%, specificity 60.7%, PPV 40.4% and NPV 88.3% at primary definitions. For detecting any Gleason >/ = 7 mpMRI had sensitivity 73.2%, specificity 60.3%, PPV 41.4% and NPV 85.4%. Mean MCCL was lower where significant cancer was missed compared to those correctly identified (5.8 mm versus 7.7 mm respectively, p = 0.035).

Conclusion: mpMRI performance characteristics were very encouraging when compared to contemporary clinical trials. In a non-academic hospital setting, negative mpMRI was just as good at ruling-out significant disease, though the ability of positive mpMRI to accurately detect significant disease was lower. An mpMRI-guided diagnostic pathway should be accompanied by appropriate mpMRI protocol optimisation, training, and quality control.

1. Introduction

Transrectal ultrasound (TRUS) guided prostate biopsy is the standard of care for prostate cancer diagnosis in many countries [1]. It is routinely carried out under local anaesthetic and is relatively easily learnt, taught and applied, making it a practical diagnostic strategy. However, it has several recognised limitations and is prone to random and systematic error [2]. Anterior lesions are frequently missed, reducing accuracy [3]. Additionally, they can lead to urosepsis in 1–6% [4].

The use of magnetic resonance imaging (MRI) in the prostate cancer pathway has seen growing interest due to advances in technology using a multiparametric approach (mpMRI). This involves T1 and T2 weighted images (T2W) combined with functional imaging sequences such as diffusion weighted imaging (DWI) and dynamic contrast enhancement (DCE) [5,6]. If biopsy could be avoided in men with negative mpMRI then routine use of pre-biopsy mpMRI could be a cost-effective strategy compared to TRUS-biopsy [7]. However, as a relatively novel modality, routine integration of pre-biopsy mpMRI into national diagnostic cancer pathways has yet to occur.

* Corresponding author. Urology Research Group, Room 4.23, 4th Floor, 132 Hampstead Road, London, NW1 2PT, United Kingdom.
E-mail address: veeru.kasi@ucl.ac.uk (V. Kasivisvanathan).
[1] These authors share joint senior authorship.

https://doi.org/10.1016/j.ijso.2018.01.002

Data from experienced academic centres and contemporary clinical trials show the negative predictive value (NPV) for detection of significant cancer for mpMRI ranges from 72 to 92% [8–11] and targeted-only approaches have been shown to detect similar amounts of significant cancer to systematic biopsy [12,13]. Randomised studies have shown that MRI performance may be influenced by whether the centre was a dedicated high volume mpMRI academic centre or a non-academic centre, with better performance of an MRI-guided pathway demonstrated in the academic centre [14] than outside of one [15]. It is thus known that optimisation of MRI scanners and the centre's experience has an important role in mpMRI performance as a diagnostic tool [16]. However, mpMRI has not been validated in non-tertiary referral ("non-academic") centres against a thorough reference standard of transperineal template mapping biopsy (TPM).

The primary objective of this study was to evaluate the diagnostic accuracy of mpMRI in a non-tertiary referral centre using TPM biopsy as a reference standard. Secondary objectives were to assess: the additional value of DCE and high b-values on DWI in detecting cancer and to explore reasons why mpMRI missed significant cancer.

2. Material and methods

2.1. Setting

Princess Alexandra Hospital (PAH), a non-academic hospital, receiving the majority of its referrals for men with suspected prostate cancer directly from family doctors.

2.2. Patient cohort

All consecutive men who had a TPM biopsy between January 1st, 2015 and April 30th, 2016 were identified from the histopathology database. The population consisted of a representative cohort of all men indicated for prostate biopsy including: 1) biopsy naïve men with suspicion of prostate cancer, 2) men with previous negative biopsy but continued suspicion of prostate cancer and 3) men with known low risk prostate cancer confirmed on a previous biopsy on active surveillance. All men underwent prostate mpMRI and went on to biopsy regardless of mpMRI findings. Men were excluded if the mpMRI was carried out at a different institution or if it was known in advanced that major MRI artefact would be present (e.g. pelvic metalwork).

2.3. Transperineal biopsy

TPM biopsy was performed under general anaesthesia using a modified Barzell technique, reported previously [17]. Biopsy cores were taken approximately every 5 mm on the transperineal grid, aiming for a sampling density of 1 biopsy per ml of tissue. Biopsy cores were potted separately into one of 12 pots. Where mpMRI identified a suspicious lesion, additional targeted biopsies were taken using visual registration technique [12]. One of three experienced surgeons with three to six years of experience in transperineal prostate biopsy carried out the procedures.

2.4. Magnetic resonance imaging

mpMRI was performed with one of two scanners (1.5T Siemens Avanto and 1.5T Siemens Essenza). Sequences included T2W and DWI imaging for all patients, DCE was introduced after January 2015. Contrast used was 15 ml Dotarem® (gadoterate meglumine) administered at 3 mls/sec (concentration 279.32 mg/ml). All cases used a pelvic phased array coil without endorectal coils.

mpMRIs were reported by one of three consultant radiologists with experience in prostate mpMRI ranging from five to twelve years. Prostate lesions were scored using five-level PI-RADS scale (1—cancer highly unlikely, 2—cancer unlikely, 3—equivocal, 4—cancer likely, 5—cancer highly likely) and scores allocated into 27 sectors. Scoring prior to October 2015 was performed using PI-RADSv1 [18]. After this, PI-RADSv2 guidelines were adopted [5]. Dedicated high b-values (>/ = 1000) were introduced from August 2015. Detailed sequence parameters are shown in Supplementary Table 1.

2.5. Prostate specimens

Specimens were analysed according to guidelines set by the Royal College of Pathologists, UK [19].

2.6. Clinical significance

Our primary objective was based on using the validated UCL definition 1 (maximum cancer core length [MCCL] >/ = 6 mm of any grade or any amount of Gleason grade >/ = 4 + 3) and PI-RADS score >/ = 3 on mpMRI [10,20]. As there is no accepted universal definition of clinically significant cancer results were reported secondarily according to UCL definition 2 (MCCL >/ = 4 mm or Gleason grade >/ = 3 + 4) and any amount of Gleason grade >/ = 7.

2.7. Re-review of mpMRI

False negative (FN) mpMRIs were re-reviewed by a senior consultant radiologist with pathology results to explore reasons why the initial report was deemed PI-RADS 1–2. Differences in characteristics (PSA level, PSA density, gland volume, total cancer core length (TCCL), and MCCL) between patients with FN and true positive (TP) mpMRIs were compared to identify features that might predict missing cancer.

2.8. Analysis

Prostates were analysed on hemigland level as consistent with previous studies in this field [10].

Statistical analysis was conducted using Microsoft Excel and SPSS version 22 (release 22.0.0.0). 2 × 2 tables to compare presence or absence of clinically significant cancer were created. Sensitivity, specificity, positive predictive value (PPV), NPV, and difference between proportions with 95% CI were calculated where appropriate. Independent T-tests were performed between TP and FN mpMRI results.

2.9. Ethics

This project was deemed exempt from ethics committee approval by the research and development department at PAH.

3. Results

3.1. Study population details

122 men were identified who underwent TPM within the study period. 21 were excluded (1 had mpMRI from another site, 5 had major artefacts from metalwork, and 15 did not have a pre-biopsy mpMRI). Median age was 69, median PSA was 7.0 ng/ml and median prostate volume was 42 ml 24/101 (24%) had no mpMRI lesion; 76/101 (75%) had a PI-RADS score of >/ = 3 (Table 1).

Overall detection of all cancer on TPM biopsy was 78/101 (77%). 41/101 (41%) had cancer diagnosed with UCL definition 1; 57/101

Table 1
Study population details.

Total number of patients	101
Median age (IQR)	69 (62–76)
Median ml prostate volume (IQR)	42 (30–54)
Median ng/ml PSA (IQR)	7.0 (4.6–9.8)
Median sampling density - number of biopsy cores taken/ml prostate tissue (IQR)	0.94 (0.77–1.3)
Number of mpMRI with contrast enhanced sequences (%)	47 (46.5)
Prior biopsy status (%)	
- Previous positive	64 (63.4)
- Previous negative	12 (11.9)
- Biopsy naive	25 (24.8)
MRI result (%)	
- PI-RADS score 1 - 2	25 (24.8)
- PI-RADS score 3	32 (31.7)
- PI-RADS score 4	23 (22.8)
- PI-RADS score 5	21 (20.8)

(56%) with UCL definition 2; and 43/101 (43%) with any Gleason >/ = 7. Breakdown of cancer detected is given in Table 2.

3.2. mpMRI validity

At primary definitions of clinical significance, mpMRI achieved sensitivity 76.9% (95% CI 66–88), specificity 60.7% (95% CI 53–69), PPV 40.4% (95% CI 31–50) and NPV 88.3% (95% CI 82–95). The performance characteristics of mpMRI according to varied histological thresholds for clinically significant disease is summarised in Table 3.

3.3. Sub-group analysis: dynamic contrast enhancement

No difference in performance characteristics were shown between scans with and without DCE (Table 4).

3.4. Subgroup analysis: sequence parameters

46 men had mpMRI scans with dedicated high b-value as part of the DWI sequences and 55 men had scans prior to use of high b-values. Addition of high b-values demonstrated a higher specificity but lower sensitivity (summarised in Table 5).

3.5. False negative mpMRI

10/12 (83%) hemiglands with significant cancer (UCL definition 1) missed by mpMRI had lesions located in the apex only and 2/12 (17%) had lesions extending through both apex and base of the prostate. No missed cancer was found isolated to the base only. 4/12 (33%) lesions were visible on re-review and were missed on initial reporting (all scoring PI-RADS 1 initially); 6/12 (50%) were difficult to accurately visualise on re-review due to heterogeneous gland appearance; 1/12 was not visible at all (8%); and 1/12 (8%) was due to coding of a midline TPM sector as bilateral disease, therefore no lesion was actually missed.

The key difference in men who had significant disease missed by mpMRIs compared to those who had correctly identified lesions (Table 6) was mean MCCL, which was significantly lower in those cancers missed on mpMRI (means 5.8 mm versus 7.7 mm, difference 1.9 mm, p = 0.035).

4. Discussion

4.1. Summary of main findings

In summary, our study demonstrates that in the context of a non-academic hospital, mpMRI has good performance characteristics for the detection of clinically significant cancer with high sensitivity 76.9% and NPV 88.3%. This is encouraging for the adoption of an MRI-influenced diagnostic pathway outside of academic centres. As with other studies, specificity 60.7% and PPV 40.4% were low indicating the need for histological verification of a suspicious area on mpMRI. We also explored possible reasons for mpMRI missing clinically significant cancer and showed that when mpMRI missed cancer, it tended to be low volume disease, with low maximum cancer core length.

4.2. Clinical implications

mpMRI has been proposed as a triage test for men with suspected prostate cancer, suggesting that men with negative mpMRIs could avoid biopsy altogether [10,12]. Whilst results seen from the literature are primarily from tertiary referral centres or clinical trial settings, there is a distinct lack of results from centres outside these settings. It is in these pragmatic settings that the validity of mpMRI needs to be proven to consider widespread adoption of this strategy as a primary diagnostic approach for suspected cancer.

Table 2
Cancer detection results of transperineal template biopsy.

Number of men with clinically significant cancer (%)	
- UCL definition 1 (Gleason grade >/ = 4 + 3 and/or maximum cancer core length >/ = 6 mm)	41 (40.6)
- UCL definition 2 (Gleason grade >/ = 3 + 4 and/or maximum cancer core length >/ = 4 mm)	57 (56.4)
Biopsy result (%)	
- Gleason grade 3 + 3	35 (34.7)
- Gleason grade 3 + 4	31 (30.7)
- Gleason grade 4 + 3	6 (5.9)
- Gleason grade 4 + 4	6 (5.9)
- Benign	15 (14.9)
- ASAP or PIN[a]	8 (7.9)

[a] ASAP–atypical small acinar proliferation, PIN–prostatic intraepithelial neoplasia.

Table 3
Performance characteristics of multiparametric-MRI in detecting prostate cancer at radiological threshold of PI-RADS score >/ = 3 and varied histological thresholds (95% CI given in parentheses).

	Sensitivity	Specificity	PPV	NPV
UCL definition 1	76.9 (66–88)	60.7 (53–69)	40.4 (31–50)	88.3 (82–95)
UCL definition 2	73.1 (63–83)	66.1 (58–75)	57.6 (48–67)	79.6 (72–87)
Gleason grade >/ = 3 + 4	73.2 (62–85)	60.3 (52–68)	41.4 (32–51)	85.4 (79–92)

Table 4
Performance of multiparametric-MRI in detecting prostate cancer according to biopsy status at clinically significant thresholds of PI-RADS score >/ = 3 and UCL definition 1 (95% CI given in parentheses).

	Prior positive biopsy	No prior biopsy	Prior negative biopsy
Sensitivity	68.4 (54–83)	100 (100–100)[a]	100 (100–100)[a]
Specificity	57.8 (48–68)	54.1 (38–70)	82.6 (67–98)
PPV	40.6 (29–53)	43.3 (26–61)	20 (0–55)
NPV	81.3 (72–91)	100 (100–100)[a]	100 (100–100)[a]
Mean age	68.8	67.9	68
Mean PSA, ng/ml	7.6	7.7	12.1
Mean prostate volume, ml	45.5	36.1	51.6

[a] False negative value of 0.

Table 5
Performance of multiparametric-MRI in detecting prostate cancer according to sequence parameters at clinically significant thresholds of PI-RADS score >/ = 3 and UCL definition 1 (95% CI given in parentheses).

	No high b-values	High b-values	Difference between proportions
Sensitivity	87.1 (75–99)	61.9 (41–83)	25.2 (1.3–49)
Specificity	51.9 (41–63)	70.4 (60–81)	18.5 (3.2–34)
PPV	41.5 (30–54)	38.2 (30–55)	3.3 (−17–24)
NPV	91.1 (83–99)	86.2 (77–95)	4.9 (−7.3–17)
Mean age	67.3	70	2.7
Mean PSA, ng/ml	8.7	7.5	1.2
Mean prostate volume, ml	45.5	41.9	3.6

Table 6
Comparison between true positive and false negative multiparametric-MRI results at clinically significant thresholds of PI-RADS score >/ = 3 and UCL definition 1.

	True positive	False negative	Difference
Mean PSA level (ng/ml)	9.4	6.9	2.5 (p = 0.282)
Mean PSA density (ng/ml/cc)	0.24	0.22	0.02 (p = 0.694)
Mean Gland volume (cc)	41.7	35.4	6.3 (p = 0.299)
Mean TCCL (mm)	23.7	11.6	12.1 (p = 0.152)
Mean MCCL (mm)	7.7	5.8	**1.9 (p = 0.035)**

Bold signifies significant result.

Our results show that approximately 12% of clinically significant cancers (UCL definition 1) would be missed if decisions to avoid biopsy were based on negative mpMRI alone. The value of a negative mpMRI is similar to the PROMIS trial which demonstrated a NPV 89%. The value of a negative mpMRI to rule out significant cancer at the less stringent UCL definition 2 is also similar to PROMIS, with NPV 80%, compared to PROMIS which demonstrated NPV 72%. These results are very encouraging as they demonstrate that mpMRI can have good performance characteristics in a pragmatic setting outside of a tightly regulated clinical trial.

Whilst missing 12–20% (depending on the definition used) of clinically significant disease may seem high, one should consider this in the context of what men would otherwise get. The standard of care for suspected prostate cancer in many countries is TRUS-guided biopsy, which commonly has an NPV lower than that seen for mpMRI in this study, ranging from 36 to 74% for all cancer detected [11,21–23]. In this context, provided that men with negative mpMRIs are kept under PSA surveillance it would appear that mpMRI could have a role in triaging for biopsy. That too, interpreting a negative MRI in conjunction with a low PSA density may further help reassure clinicians that avoiding biopsy is safe and reasonable [24].

However, when comparing the ability of mpMRI to detect clinically significant disease (UCL definition 1) and the value of a positive test result, the results from this study are not as good as those seen in the PROMIS Trial which demonstrated a sensitivity of 93%. Learning from the re-review of mpMRIs where significant cancer was missed, 33% of the FN hemiglands had lesions missed initially, which were then visible on re-review. This confirms the known inter-rater variability [25] and might support the concept of non-suspicious mpMRIs getting a double read if decision about avoiding biopsy is going to be made.

It should also be emphasised that the current study results reflect an on-going optimisation of mpMRI conduct during the study period. The PROMIS trial on the other hand had dedicated quality control of mpMRI conduct and training in mpMRI reporting built in to the study prior to the commencement of the study. So perhaps this difference is to be expected. This suggests that in order to obtain the mpMRI sensitivity seen in contemporary clinical trials, appropriate quality control, optimisation of protocols and training is necessary. Results observed in the PROMIS trial cannot be immediately expected by centres developing an mpMRI service and a period of optimisation should be expected. Future work should focus on establishing what this training and quality control should be and how it should be delivered.

In light of the on-going optimisation of mpMRI conduct during the study we carried out subgroup analyses to explore the effect that this had. The use of long-b values in mpMRI has been shown to

improve diagnostic performance and dedicated high-b values are recommended in PI-RADSv2 [5,26]. The benefit of DCE, however, is not as clear in the literature, with some studies showing no advantage [27,28] and others showing that the combination of sequences improves the performance of the mpMRI [29]. Our data did not show improved performance of mpMRI with DCE and whilst the use of high b-values did show higher specificity, in line with the literature, their use did result in decreased sensitivity.

4.3. Limitations

Radical prostatectomy (RP) specimens would be an alternative reference standard for diagnostic validity of mpMRI. This however would be an imperfect reference standard [11] because it could only be carried out in men who have RP. This would represent selection bias as one could only assess the validity of mpMRI in men with high risk features of prostate cancer that are recommended for RP.

Instead, TPM was chosen as the reference standard as it has been shown to have high diagnostic accuracy and can be applied to all men at risk of prostate cancer, thus reducing selection bias [20,30,31]. Furthermore, TPM was carried out at a high sampling density of almost 1 biopsy per ml of tissue in this study.

We acknowledge that the mpMRI protocols in the study were modified over time, but this reflects continuing development and optimisation of mpMRI at our centre, which is an essential process to optimize cancer detection for any centre wishing to adopt mpMRI. For readers considering adopting their own mpMRI services this shows them progressive steps taken. Further, the influence of changing protocols on the diagnostic performance of mpMRI was explored and shown to have negligible effect.

5. Conclusion

In conclusion, mpMRI performance characteristics in the non-academic setting were very encouraging when compared to contemporary clinical trials. A negative mpMRI was just as good at ruling-out clinically significant disease, though the ability of a positive mpMRI to accurately detect clinically significant disease was lower. This supports the adoption of a mpMRI-driven diagnostic prostate cancer pathway outside of academic centres, though this should be accompanied by appropriate mpMRI protocol optimisation, training and quality control.

Ethical approval

This project was deemed exempt from ethics committee approval by the research and development department at PAH.

Funding

Veeru Kasivisvanathan is funded by a Doctoral Research Fellowship from the National Institute for Health Research. Mark Emberton's research is supported by core funding from the United Kingdom's National Institute of Health Research (NIHR) UCLH/UCL Biomedical Research Centre. He was awarded NIHR Senior Investigator in 2015. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health. Hashim Ahmed receives funding from the Medical Research Council (UK).

Author contribution

Study design: Manit Arya, Zaid Aldin, Veeru Kasivisvanathan, Jolanta McKenzie.

Data collection: Edwin Michael Chau, Neophytos Petrides, Zaid Aldin.

Data analysis: Edwin Michael Chau, Veeru Kasivisvanathan.

Writing: Edwin Michael Chau.

Critical revision of manuscript: Manit Arya, Zaid Aldin, Jolanta McKenzie, Mark Emberton, Jaspal Virdi, Hashim Uddin Ahmed, Veeru Kasivisvanathan.

Supervision: Manit Arya, Zaid Aldin, Jolanta McKenzie, Mark Emberton, Jaspal Virdi, Hashim Uddin Ahmed, Veeru Kasivisvanathan.

Obtaining funding: Veeru Kasivisvanathan.

Conflicts of interest statement

Hashim Ahmed receives funding from Sonacare Medical, Sophiris, and Trod Medical for other trials. Travel allowance was previously provided from Sonacare. Mark Emberton has stock interest in Nuada Medical Ltd. He is also a consultant to Steba Biotech and GSK. He receives travel funding from Sanofi Aventis, Astellas, GSK, and Sonacare. He previously received trial funding or resources from GSK, Steba Biotech and Angiodynamics and receives funding for trials from Sonacare Inc, Sophiris Inc, and Trod Medical. The other authors declare no competing interests.

Guarantor

Veeru Kasivisvanathan.
Edwin Chau.

Research registration number

Research registry 2856.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ijso.2018.01.002.

References

[1] National Institute for Health and Care, Excellence Prostate cancer: diagnosis and management (CG175). Available at: https://www.nice.org.uk/guidance/cg175/resources/prostate-cancer-diagnosis-and-management-pdf-3510975 3913285
[2] Bjurlin MA, Meng XS, Le Nobin J, Wysock JS, Lepor H, Rosenkrantz AB, et al. Optimization of prostate biopsy: the role of magnetic resonance imaging targeted biopsy in detection, localization and risk assessment. J Urol 2014;192(3):648–58.
[3] Wei JT. Limitations of a contemporary prostate biopsy: the blind march forward. Urol Oncol 2010;28(5):546–9.
[4] Rudzinski JK, Kawakami J. Incidence of infectious complications following transrectal ultrasound-guided prostate biopsy in Calgary, Alberta, Canada: a retrospective population-based analysis. Can Urol Assoc J 2014;8(5–6):E301–5.
[5] Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, et al. PI-RADS prostate imaging - reporting and data system: 2015, version 2. Eur Urol 2016;69(1):16–40.
[6] Puech P, Padhani A, Lemaitre L, Betrouni N, Colin P, Villers A. Localization of cancer within the prostate: dynamic contrast-enhanced MRI. In: Ahmed HU, Arya M, Carroll P, Emberton M, editors. Focal therapy in prostate cancer. Oxford: Blackwell Science Publ; 2012. p. 55–65.
[7] Mowatt G, Scotland G, Boachie C, Cruickshank M, Ford JA, Fraser C, et al. The diagnostic accuracy and cost-effectiveness of magnetic resonance spectroscopy and enhanced magnetic resonance imaging techniques in aiding the localisation of prostate abnormalities for biopsy: a systematic review and economic evaluation. Chapter 5, Assessment of cost-effectiveness. Health Technol Assess 2013;17(20):51–88.
[8] Thompson JE, van Leeuwen PJ, Moses D, Shnier R, Brenner P, Delprado W, et al. The diagnostic performance of multiparametric magnetic resonance imaging to detect significant prostate cancer. J Urol 2016;195(5):1428–35.
[9] Villers A, Puech P, Mouton D, Leroy X, Ballereau C, Lemaitre L. Dynamic contrast enhanced, pelvic phased array magnetic resonance imaging of

localized prostate cancer for predicting tumor volume: correlation with radical prostatectomy findings. J Urol 2006;176(6 Pt 1):2432–7.
[10] Abd-Alazeez M, Ahmed HU, Arya M, Charman SC, Anastasiadis E, Freeman A, et al. The accuracy of multiparametric MRI in men with negative biopsy and elevated PSA level–can it rule out clinically significant prostate cancer? Urol Oncol 2014;32(1). 45 e17–45 e22.
[11] Ahmed HU, El-Shater Bosaily A, Brown LC, Gabe R, Kaplan R, Parmar MK, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet 2017;389(10071):815–22.
[12] Kasivisvanathan V, Dufour R, Moore CM, Ahmed HU, Abd-Alazeez M, Charman SC, et al. Transperineal magnetic resonance image targeted prostate biopsy versus transperineal template prostate biopsy in the detection of clinically significant prostate cancer. J Urol 2013;189(3):860–6.
[13] Schoots IG, Roobol MJ, Nieboer D, Bangma CH, Steyerberg EW, Hunink MG. Magnetic resonance imaging-targeted biopsy may enhance the diagnostic accuracy of significant prostate cancer detection compared to standard transrectal ultrasound-guided biopsy: a systematic review and meta-analysis. Eur Urol 2015;68(3):438–50.
[14] Porpiglia F, Manfredi M, Mele F, Cossu M, Bollito E, Veltri A, et al. Diagnostic pathway with multiparametric magnetic resonance imaging versus standard pathway: results from a randomized prospective study in biopsy-naive patients with suspected prostate cancer. Eur Urol 2017;72(2):282–8.
[15] Tonttila PP, Lantto J, Paakko E, Piippo U, Kauppila S, Lammentausta E, et al. Prebiopsy multiparametric magnetic resonance imaging for prostate cancer diagnosis in biopsy-naive men with suspected prostate cancer based on elevated prostate-specific antigen values: results from a randomized prospective blinded controlled trial. Eur Urol 2016;69(3):419–25.
[16] Vargas HA, Akin O, Afaq A, Goldman D, Zheng J, Moskowitz CS, et al. Magnetic resonance imaging for predicting prostate biopsy findings in patients considered for active surveillance of clinically low risk prostate cancer. J Urol 2012;188(5):1732–8.
[17] Barzell WE, Melamed MR. Appropriate patient selection in the focal treatment of prostate cancer: the role of transperineal 3-dimensional pathologic mapping of the prostate–a 4-year experience. Urology 2007;70(6 Suppl):27–35.
[18] Barentsz JO, Richenberg J, Clements R, Choyke P, Verma S, Villeirs G, et al. European society of urogenital r. ESUR prostate MR guidelines 2012. Eur Radiol 2012;22(4):746–57.
[19] Harnden P, Berney D, Shelley M. Royal College of Pathologists. Dataset for histopathology reports for prostatic carcinoma (2nd edition). In: Group CSW; 2009.
[20] Ahmed HU, Hu Y, Carter T, Arumainayagam N, Lecornet E, Freeman A, et al. Characterizing clinically significant prostate cancer using template prostate mapping biopsy. J Urol 2011;186(2):458–64.
[21] Wefer AE, Hricak H, Vigneron DB, Coakley FV, Lu Y, Wefer J, et al. Sextant localization of prostate cancer: comparison of sextant biopsy, magnetic resonance imaging and magnetic resonance spectroscopic imaging with step section histology. J Urol 2000;164(2):400–4.
[22] Salomon L, Colombel M, Patard JJ, Lefrere-Belda MA, Bellot J, Chopin D, et al. Value of ultrasound-guided systematic sextant biopsies in prostate tumor mapping. Eur Urol 1999;35(4):289–93.
[23] Okoro C, George AK, Siddiqui MM, Rais-Bahrami S, Walton-Diaz A, Shakir NA, et al. Magnetic resonance imaging/transrectal ultrasonography fusion prostate biopsy significantly outperforms systematic 12-core biopsy for prediction of total magnetic resonance imaging tumor volume in active surveillance patients. J Endourol 2015;29(10):1115–21.
[24] Distler FA, Radtke JP, Bonekamp D, Kesch C, Schlemmer HP, Wieczorek K, et al. The value of PSA density in combination with PI-RADS for the accuracy of prostate cancer prediction. J Urol 2017;198(3):575–82.
[25] Arumainayagam N, Ahmed HU, Moore CM, Freeman A, Allen C, Sohaib SA, et al. Multiparametric MR imaging for detection of clinically significant prostate cancer: a validation cohort study with transperineal template prostate mapping as the reference standard. Radiology 2013;268(3):761–9.
[26] Zhang K, Shen YG, Zhang X, Ma L, Wang HY, An NY, et al. Predicting prostate biopsy outcomes: a preliminary investigation on screening with ultrahigh B-Value diffusion-weighted imaging as an innovative diagnostic biomarker. PLoS One 2016;11(3):14.
[27] Mirowitz SA, Brown JJ, Heiken JP. Evaluation of the prostate and prostatic-carcinoma with gadolinium-enhanced endorectal coil mr imaging. Radiology 1993;186(1):153–7.
[28] Boni RAH, Boner JA, Lutolf UM, Trinkler F, Pestalozzi DM, Krestin GP. Contrast-enhanced endorectal coil MRI in local staging of prostate carcinoma. J Comput Assist Tomogr 1995;19(2):232–7.
[29] Tanimoto A, Nakashima J, Kohno H, Shinmoto H, Kuribayashi S. Prostate cancer screening: the clinical value of diffusion-weighted imaging and dynamic MR imaging in combination with T2-weighted imaging. J Magn Reson Imag 2007;25(1):146–52.
[30] Crawford ED, Rove KO, Barqawi AB, Maroni PD, Werahera PN, Baer CA, et al. Clinical-pathologic correlation between transperineal mapping biopsies of the prostate and three-dimensional reconstruction of prostatectomy specimens. Prostate 2013;73(7):778–87.
[31] Hu Y, Ahmed HU, Carter T, Arumainayagam N, Lecornet E, Barzell W, et al. A biopsy simulation study to assess the accuracy of several transrectal ultrasonography (TRUS)-biopsy strategies compared with template prostate mapping biopsies in patients who have undergone radical prostatectomy. BJU Int 2012;110(6):812–20.