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### Authors

Muller, Berrend G  
Fütterer, Jurgen J  
Gupta, Rajan T  
et al.

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## The role of magnetic resonance imaging (MRI) in focal therapy for prostate cancer: recommendations from a consensus panel

Berrend G. Muller<sup>1</sup>, Jurgen J. Fütterer<sup>2,3</sup>, Rajan T. Gupta<sup>4</sup>, Aaron Katz<sup>5</sup>, Alexander Kirkham<sup>6</sup>, John Kurhanewicz<sup>7</sup>, Judd W. Moul<sup>8</sup>, Peter A. Pinto<sup>9</sup>, Ardeshir R. Rastinehad<sup>10</sup>, Cary Robertson<sup>10</sup>, Jean de la Rosette<sup>1</sup>, Rafael Sanchez-Salas<sup>11</sup>, J. Stephen Jones<sup>12</sup>, Osamu Ukimura<sup>13</sup>, Sadhna Verma<sup>14</sup>, Hessel Wijkstra<sup>1,15</sup>, and Michael Marberger<sup>16</sup>

<sup>1</sup>Department of Urology, AMC University Hospital, Amsterdam <sup>2</sup>Department of Radiology, Radboud University Nijmegen Medical Centre, Nijmegen <sup>3</sup>MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, the Netherlands <sup>4</sup>Department of Radiology, Duke University Medical Center, Durham, NC <sup>5</sup>Department of Urology, Winthrop University Hospital, New York, NY, USA <sup>6</sup>Department of Radiology, University College Hospital, London, UK <sup>7</sup>Department of Radiology, University of California UCSF, San Francisco, CA <sup>8</sup>Division of Urology and Duke Cancer Institute, Duke University Medical Center, Durham, NC <sup>9</sup>Department of Urology, National Cancer Institute, Bethesda, MD <sup>10</sup>Department of Urology/Radiology, Smith Institute for Urology, New York, NY, USA <sup>11</sup>Department of Urology, Institut Montsouris, Paris, France <sup>12</sup>Department of Urology, Cleveland Clinic Foundation, Cleveland, OH <sup>13</sup>Department of Urology, University of Southern California, Norris Cancer Center, Los Angeles, CA <sup>14</sup>Department of Radiology, University of Cincinnati, Cincinnati, OH, USA <sup>15</sup>Department of Electrical Engineering, Eindhoven University of Technology, Eindhoven, the Netherlands <sup>16</sup>Department of Urology, Medical University of Vienna, Vienna, Austria

### Abstract

#### Objective—

- To establish a consensus on the utility of multiparametric magnetic resonance imaging (mpMRI) to identify patients for focal therapy.

#### Methods—

- Urological surgeons, radiologists, and basic researchers, from Europe and North America participated in a consensus meeting about the use of mpMRI in focal therapy of prostate cancer.
- The consensus process was face-to-face and specific clinical issues were raised and discussed with agreement sought when possible. All participants are listed among the authors.

- Topics specifically did not include staging of prostate cancer, but rather identifying the optimal requirements for performing MRI, and the current status of optimally performed mpMRI to (i) determine focality of prostate cancer (e.g. localising small target lesions of 0.5 mL), (ii) to monitor and assess the outcome of focal ablation therapies, and (iii) to identify the diagnostic advantages of new MRI methods.
- In addition, the need for transperineal template saturation biopsies in selecting patients for focal therapy was discussed, if a high quality mpMRI is available. In other words, can mpMRI replace the role of transperineal saturation biopsies in patient selection for focal therapy?

### Results—

- Consensus was reached on most key aspects of the meeting; however, on definition of the optimal requirements for mpMRI, there was one dissenting voice.
- mpMRI is the optimum approach to achieve the objectives needed for focal therapy, if made on a high quality machine (3T with/without endorectal coil or 1.5T with endorectal coil) and judged by an experienced radiologist.
- Structured and standardised reporting of prostate MRI is paramount.
- State of the art mpMRI is capable of localising small tumours for focal therapy.
- State of the art mpMRI is the technique of choice for follow-up of focal ablation.

### Conclusions—

- The present evidence for MRI in focal therapy is limited.
- mpMRI is not accurate enough to consistently grade tumour aggressiveness.
- Template-guided saturation biopsies are no longer necessary when a high quality state of the art mpMRI is available; however, suspicious lesions should always be confirmed by (targeted) biopsy.

### Keywords

prostate cancer; focal therapy; consensus; multiparametric magnetic resonance imaging; prostate biopsies

### Introduction

Current treatment in prostate cancer aims at systemic or whole gland/radical procedures, with significant side-effects, i.e. erectile dysfunction and/or incontinence [1]. Consistent with rising awareness and new and improved imaging methods, small tumours occupying <5–10% of the prostate volume are detected earlier than in the past. Concerns have been raised about the diagnosis and over-treatment of these small tumours. These concerns led to the concept of focal therapy, a selective ablation targeted to specific sites in the prostate gland, reducing lifetime morbidity and side-effects without compromising life expectancy for patients with low- and selected patients with intermediate-risk prostate cancer [2]. These techniques include cryotherapy, high-intensity focused ultrasound (HIFU), laser ablation

therapy, radiofrequency ablation, irreversible electroporation (IRE) and photodynamic therapy (PDT). The first two methods have emerged as alternative therapeutic options in patients with clinically localised prostate cancer by the European Association of Urology (EAU) and the American Urological Association (AUA). The others are still considered experimental.

Imaging criteria in focal therapy for prostate cancer differ from imaging criteria for whole gland treatment. Eligible patients who are offered focal treatment are already diagnosed with prostate cancer, which has been confirmed by TRUS-guided prostate biopsies. The objective of imaging is therefore accurate location and contour (boundary) of the target lesion, rather than just identifying or staging of a lesion. However, several key issues remain to be addressed for successful focal therapy: (i) Can cancers of clinical significance be reliably identified? (ii) Can such lesions be accurately localised? (iii) Can these lesions be targeted and ablated with lower morbidity than that associated with whole-gland therapy? (iv) Can complete ablation be monitored to determine treatment success and what are the optimal parameters to measure success? [2]. Considering morbidity and potential pitfalls of repeated multiple core prostate biopsies, imaging technology that enables reduction or replacement of these invasive interventions is always advantageous. Moreover, there is a paucity of information about the concept of focal therapy in the current urological guidelines. Therefore, a meeting was organised to achieve consensus among experts on the use of mpMRI in focal therapy for prostate cancer. The objectives of this meeting were to establish a consensus on: (i) the utility of mpMRI to identify patients for focal therapy (e.g. can mpMRI accurately localise small target lesions of 0.5 mL), (ii) to determine criteria for monitoring of focal therapy and follow-up after focal therapy, and finally (iii) whether mpMRI can replace the need for invasive transperineal template saturation biopsies. The topic of prostate cancer diagnosis by mpMRI, was specifically not discussed, as patients eligible for focal therapy already have biopsy confirmed prostate cancer. This subject was recently discussed in a meta-analysis by Moore et al. [3] and is therefore not further covered in this article.

## Methods

The consensus meeting was held 6 June 2012 (Durham, NC, USA: <http://www.focaltherapy.org>). The meeting focused on optimising methods and indications of mpMRI in the localisation and follow-up of prostate cancer in patients eligible for focal therapy. A multidisciplinary board of international contributors was selected based on their expertise in the topics discussed. Professor Michael Marberger (Vienna, Austria) chaired the meeting; participants are listed among the authors.

The conduct of the meeting conformed to an informal consensus process, for which no formal scoring system to measure the level of agreement was used [4]. However, the process did conform to generally accepted stages of a consensus process [5]. Items for discussion were preselected beforehand and discussed by three individual groups. These topics were assigned a specific time for general discussion during the meeting. A representative of each group gave a brief presentation. A moderated discussion took place using the presentation as a basis (Level 1). Discussed issues were resolved within this session of the meeting (Level

2). A consensus was established by noting any individuals who did not agree to the general view on specific items (Level 3). Items selected for discussion are shown in the headlines of the results section. All contributors to the consensus process have read and approved the present manuscript and, by agreeing to authorship, concur with the essential contents of this article. Dr Peter Pinto chaired the discussion on item number 1, Dr Jurgen Fütterer chaired the discussion on item number 2, and Professor Osamu Ukimura chaired the discussion on item number 3.

## Results

### 1. What Are the Optimal mpMRI Requirements for Selecting Patients for Focal Therapy in Prostate Cancer, and Can This Technology Replace Template Saturation Biopsies?

Over the last 6 years, several studies have been published comparing preoperative MRI to histopathological specimens from radical prostatectomies (RPs) for definition of the diagnostic accuracy [6–19]. Reports of similar consensus meetings about imaging and focal therapy for prostate cancer have been previously published [2,20]. However, these were mainly directed at diagnosing and staging prostate cancer, and not so much on locating small lesions amenable to focal therapy. Therefore, the results from these meetings were still unsuited for use in clinical practice [21]. The most reliable approach to assess the diagnostic accuracy of mpMRI is by comparing mpMRI results with histological finding in whole mounted and close step-sectioned RP specimens. As prostate cancer is often multifocal in nature, correlation of mpMRI is not straightforward, e.g. differentiation of index lesions from other smaller lesions is often difficult. Limitations in studies assessing accuracy of MRI with histopathology arise from free-hand slicing of the specimens (deformation and variable slice thickness) and non-uniform shrinkage during fixation (distortion). It was therefore difficult to determine the true accuracy of mpMRI for localisation of lesions [16,22,23]. Turkbey et al. [24] found a potential solution for this problem in 2011 by slicing the histopathological specimen exactly according to the mpMRI images by using a customized three-dimensional mould. This mould, for standardised slicing, enabled accurate comparison of RP specimen with histopathology. Good positive predictive values for mpMRI at 3T were found (98%, 98%, and 100% in the overall prostate, peripheral zone and central zone, respectively). According to the consensus meeting, this study represents an accurate representation of the available evidence for validation of mpMRI in focal therapy of the prostate. The results of the study are shown in Table 1 [6–24]. This data was supported by the data from a study by Villers et al. [23]. These mpMRI data, which were acquired on a 1.5 T device, instead of the 3 T device in the study of Turkbey et al. [24], and compared with whole-mount histopathology without a customised mould, showed a sensitivity, specificity and positive and negative predictive values for detection of prostate cancer by mpMRI of 77%, 91%, 86% and 85% for foci of >0.2 mL, and 90%, 88%, 77%, and 95% for foci of >0.5 mL, respectively.

Given the variation of sensitivity and specificity for different quality mpMRIs, the general opinion in the consensus meeting was that optimal MRI technology and protocols should be defined to select patients for focal therapy, rather than defining minimal criteria. The optimum approach to achieve the objectives needed for focal therapy was considered a 3T

mpMRI, regardless of use of a transrectal or whole body coil. The highest signal-to-noise ratio is achieved using 3T MRI with an endorectal coil (Figure 1). This is about five-times higher than when solely a surface coil is used. There is currently no data showing equivalent signal strengths between the two different approaches. The clinical difference between the two approaches may be minimal. However, a 1.5T system can only be used considered an optimal alternative if used with a transrectal coil. One person (Dr Kirkham) was opposed to this motion, as in his opinion 1.5T devices have enough diagnostic accuracy for focal therapy. However, the others strongly disagreed on this point and felt that with less than optimum technology, additional measures, i.e. template biopsies are absolutely needed. Spectroscopy at this time is still under investigation and suffers from the inability of multiple institutions being able to perform it reproducibly. As the decision for focal therapy relies on the mpMR examination, only better developed technology should be used for decision making in focal therapy.

Considering artefacts induced by previous biopsies, it was decided that any previous biopsies should have been taken at least 8 weeks before mpMRI, as biopsy artefacts disturb tumour visibility.

There was consensus that mpMRI and 12-core TRUS-guided biopsies, do not show contradictory findings, when exporting TRUS images to MRI [25]. It can therefore be concluded that template biopsy is not a strong prerequisite, as long as there is a high quality mpMRI available. Consequently, consensus was reached on the following topic: in presence of any doubt on the MRI image, a MRI-guided biopsy should be considered instead of a template biopsy. However, due to clinical importance of mpMRI, the consensus meeting decided that it should preferably be assessed by two 'blinded' readers with a minimum experience of 50 studies under appropriate monitoring each. Furthermore, elastically fused MRI-TRUS can also be performed to guide lesion biopsy [26], but on this topic no consensus was reached. Important information from this paragraph is summarised in Table 1.

## **2. What Is the Diagnostic Accuracy of mpMRI Defined as Necessary for Answering the Demand for Focal Therapy for Localising Focal Cancer, Predicting the Progressive Potential of Small Lesions and What Are the Limitations from Previous Biopsies?**

Focal therapy is defined as treatment to a segment of tissue; ideally patients have low-volume, unilateral, preferentially unifocal disease. However, multifocal prostate cancer is common, present in 67–87% of all pathological specimens after a RP, even among men with small cancer volumes (<0.5 mL) [27]. Multifocal prostate cancer does not necessarily represent a contraindication for focal therapy. An index lesion (defined as the largest and usually considered the highest grade) is frequently identified and may represent the most important determinant of prognosis. Even when the cancer is multifocal, most non-index lesions appear to be biologically indolent on the basis of small size and low grade. Eggener et al. [28] found that among patients with multifocal disease, 80% of the total tumour volume was present in the index lesion. In 92% of patients, extracapsular extension arose only from the largest lesion [28]. It is generally accepted that tumour progression is usually mediated by index lesions of larger volume (>0.5 mL) and higher grade (Gleason score 7).

For effective treatment, accurate localisation and characterisation of the index lesion in candidates for focal therapy on mpMRI is a prerequisite. Therefore, diagnosis of evident high-volume lesions, as well as small lesions on mpMRI is paramount. According to the Epstein criteria of significant prostate cancer, a tumour of >0.5 mL is already significant [29]. Consequently, MRI must be accurate in diagnosing tumours of >0.5 mL, particularly those with a primary or secondary Gleason pattern 4.

Recent studies that compare mpMRI to whole-mount histopathology for disease detection report maximum sensitivities and specificities of 80–88% and 96–100%, respectively, with 3T MR systems. However, only tumours of >0.5 mL were included in the analyses [13,30]. The accuracy of mpMRI for detecting tumours of <0.5 mL is less well established. MRI information using a four prostate quadrants localisation showed low sensitivity of 2–20%, but high specificity (91–95%) [31]. MRI improved the prediction of minimal disease that included clinical and pathological preoperative data. These data do not support the use of T2-weighted (T2w) endorectal MRI without functional parameters to localise small tumours for focal therapy as a single sequence compared with mpMRI. However, this suggests that T2w MRI is useful to exclude patients for focal therapy trials based on radiological evidence of more extensive disease [31].

T2w MRI without functional parameters, i.e. diffusion-weighted imaging (DWI) or dynamic contrast material-enhanced MRI (DCE-MRI), is not sufficient for accurate diagnosis and measurement of small tumours eligible for focal therapy [31]. Tumour volume measurements made based only on T2w MRI are not reliable for clinical decision making [32–35]. As a result, functional MR methods, i.e. DWI [36], MR-spectroscopic imaging (MRSI) [37] and DCE-MRI [23] have been investigated for their capability to improve prostate tumour volume measurement. DWI is a noninvasive technique that is sensitive to random thermal movement of water molecules and is capable of probing the structure of biological tissue at a microscopic level [36]. Several studies [33,38–41] report on the added value of apparent diffusion coefficient (ADC) maps calculated from DWI on clinical decision making in prostate cancer diagnosis. Using an ADC threshold value at  $0.0016 \text{ mm}^2$ , the analysis showed a sensitivity of 95% and specificity of 65% [42]. DWI and MRSI have shown significant incremental value to clinical variables in predicting organ-confined and insignificant prostate cancer [43,44].

As the diagnostic accuracy of only T2w imaging is too low for use in focal therapy, the incremental value of mpMRI such as DCE-MRI, DWI, and MRSI has been investigated. Studies reporting on the combination of these techniques describe the additional value in diagnostic yield [9,16,45–51]. Fütterer et al. [9] reported an area under the curve (AUC) of 0.90 when T2w, DWI and DCE-MRI were combined in localising prostate cancer. The meeting therefore recommended performing mpMRI, using T2w, DCE-MRI, and DWI (Figure 1). Especially for less experienced readers of MRI in staging prostate cancer, DCE-MRI could be of added diagnostic value [52].

The consensus meeting decided that 3T mpMRI (T1, T2, DCE, DWI), regardless of use of a transrectal or whole body coil, should be used. A 1.5T system can only be considered an alternative when performed with a transrectal coil. However, compared with a 3T device

there is a clear limitation in signal that results in a relative decrease in cancer detection of 40% [16]. Spectroscopy suffers from the inability of multiple institutions being able to perform it reproducibly, and therefore the consensus was to not discuss it at this time.

Although studies that report on comparison of Gleason grade with MRI are limited, a significant negative correlation between Gleason grade and ADC value has been found with DWI [53–55]. Furthermore, choline plus creatine-to-citrate ratios determined by MRSI have also been correlated with Gleason grade [56,57]. One study even reported on the correlation of signal intensities on T2w imaging with Gleason grade [58]. Correlation can be found, but Gleason grade can still not be accurately determined by mpMRI, as ADC values overlap between different Gleason grades. Therefore, more research needs to be done with regard to what role mpMRI can play in the differentiation of small high-grade cancers (target lesions) in contrast to small low-grade lesions (insignificant lesions).

For the diagnostic accuracy of small tumours, the consensus meeting decided that mpMRI has sufficient potential to detect a lesion of  $\approx 0.5$  mL with sensitivity as well as specificity of  $\approx 90\%$  (Tables 2 [24] and 3 [23]). For smaller tumours of  $\approx 0.2$  mL, the sensitivity of MRI decreased from 90.0 to 76.0% compared with tumours of  $>0.5$  mL, but specificity remained in the same range (87.9 and 91.2%, respectively). This means that detection rate decreases as the size of the tumour decreases. For these very small tumours, mpMRI can only be used to exclude patients from focal therapy.

Upon the issue of reporting of the results, the consensus meeting decided the following: Structured reporting of the results is of utmost importance to increase sensitivity and specificity and to diminish inter-observer variability. The lack of consensus in imaging protocols (i.e. with/without endorectal coil, field strengths, b-values, post-processing methods) makes defining guidelines for mpMRI troublesome. The PI-RADS classification, which resulted from the 2011 consensus meeting among uro-radiologists, is a useful tool for standardised reporting of mpMRI. Using this classification as a guideline is strongly recommended [59]. There is little evidence about learning curves for mpMRI reading, but the consensus panel agreed on a number of 50 patients.

### **3. What Is the Role of MRI in Monitoring and Defining Successful Focal Therapy and Follow-up?**

MRI could have a potential role in real-time monitoring of thermal focal ablation, namely MR thermometry [60]. The technology is based on temperature sensitive MR parameters, i.e. proton resonance frequency, diffusion coefficient, T1, T2 relaxation times, magnetisation transfer, proton density, as well as temperature-sensitive contrast agents [60]. This non-invasive way of monitoring thermal focal therapies is fairly accurate provided that the target does not move. With transrectal ablation this is virtually impossible to avoid. The technique is validated both with image-guided focal laser therapy of the prostate [61], and transurethral HIFU of the prostate [62]. Siddiqui et al. [63] showed in 2010 that MR thermometry could show excellent results in real-time treatment monitoring for thermal therapy in the canine prostate. Preliminary results of this monitoring option in humans look promising. However, these results were only achieved when the prostate is secured in place, i.e. by using a transurethral probe. The challenges of movement in MR thermometry have



not been resolved for transrectal ablation technologies and to date no data have been published. Until these issues have been resolved, the meeting does not recommend this technology for monitoring focal therapy.

In the follow-up of focal treatment, mpMRI can also be an accurate diagnostic tool. Depending on the extent of treatment, loss of zonal differentiation, thickening of the prostatic capsule, periprostatic fibrosis and scarring may be present after focal therapy. After cryotherapy, heterogeneous enhancement intermixed with areas of necrosis and thickening of the prostatic capsule, urethra and rectal wall are seen on T1-weighted (T1w) images [64]. After HIFU, ablation-induced changes in the region of the lesions appear on contrast enhanced T1w images as non-enhancing hypointense regions with 3–8 mm thick peripheral rims of enhancement that resolve within 3–5 months [65]. Kirkham et al. [66] showed that at 6 months, the prostate is of predominantly low signal intensity on T2w images and that there is a median volume reduction of 61%. They also concluded that the volume of enhancing prostate tissue on the initial image after treatment correlated well with serum PSA level nadir (Spearman's  $r = 0.90$ ,  $P < 0.001$ ) and with volume at 6 months (Pearson's  $r = 0.80$ ,  $P = 0.001$ ). After photodynamic therapy, MRI may be used to assess the extent and distribution of the expected necrosis in the target region. In one study [67], most patients showed marked irregularity at the treatment boundary, that was best appreciated on T1w images after i.v. administration of contrast material, with areas of enhancement (viable tissue) interposed between non-enhancing low-signal-intensity regions (necrosis) [68].

Enhancing soft tissue lesions after focal treatments should be considered suggestive of residual/recurrence, just as they are after other forms of treatment. It is important to be aware that a recurrent lesion may present in conjunction with normal post-treatment appearances. Furthermore, the characteristics typically associated with recurrence on T2w images may not represent recurrence in some cases. In some cases of recurrence, these features simply fail to appear [64]. Some authors suggest that MRSI is superior to MRI for the differentiation of cancer voxels from necrosis voxels [69], but at present, MRSI is not widely used to aid clinical decision making and is therefore insufficient to give a conclusive statement. In one study, postoperative contrast-enhanced MRI up to 3 weeks after surgery was used in an attempt to predict the success of cryoablation, as determined with tissue sample results at 6 months after treatment and follow-up PSA levels; however, no significant correlations were found between MRI findings, biopsy results and PSA levels [70]. After HIFU, the detection of recurrent or residual disease could be hindered by diffuse or multifocal areas of low signal intensity on T2w MRI [65]. A short time to peak enhancement, early washout, and other pharmacokinetic parameters seen on DCE-MRI in patients with untreated prostate cancer can also be present in cases of recurrence after HIFU [69]. A recent study showed that, for prediction of local tumour progression of prostate cancer after HIFU, DCE-MRI was more sensitive but less specific than the combination of T2w and DWI [71]. In a study by Rouvière et al. [72] on the use of T2w and DCE-MRI in 59 patients suspected of having recurrence after HIFU, the odds ratio of the probability of finding viable cancer and viable prostate tissue (benign or malignant) during routine biopsy was 1.38; this odds ratio increased to 3.35 when biopsies were targeted at lesions identified on T2w and DCE-MRI [68].

Rouvière et al. [72] showed in 2010 that in men with PSA elevation after whole gland HIFU-MR targeted biopsy detected more cancer than when the biopsies were taken by someone who was 'blinded' from the MRI images. The odds ratio of the probability of finding viable cancer at MRI targeted vs routine biopsy was 3.35. Punwani et al. [73] showed that DCE-MRI has similar sensitivity and specificity and receiver operating characteristic performance to serial PSA. They support surveillance with serial PSA measurements, then in cases of biochemical recurrence, use of MRI to detect local recurrence and guide biopsy. The trend is that with the increasing use of focal therapies, the significance of PSA is decreasing, although the percentage decrease of PSA from before and after focal therapy may have a role in predicting successful ablation of the index lesion. The role of DCE-MRI in focal therapy for prostate cancer is becoming more and more important [73]. Ahmed et al. [74] showed in 2012 with mpMRI after HIFU that cancer can be reliably be detected. Kim et al. [71] showed in 2008 that for prediction of local tumour progression after HIFU ablation, DCE-MRI was more sensitive than T2w MRI with DWI, but T2w MRI with DWI was more specific than DCE-MRI.

For above reasons, the conclusion of the consensus panel was that the diagnostic accuracy of loss of enhancement in MRI immediately after treatment, could suggest 'Technical successful' targeting, but there is yet too little evidence to correlate histological success to MRI images. Therefore, more data are required of post-MRI findings in the long term, namely after 6 months, to draw solid conclusions about MR follow-up of focal therapy. The consensus panel decided also that preoperative MRI is mandatory, to compare with focal therapy results. This MRI should ideally be taken before biopsy, but MRI before focal therapy is acceptable, if done 8 weeks after the last biopsy. Finally, the consensus panel agreed that follow-up MRI of the prostate should be taken 6 months after therapy. Some voices also opted for a MRI immediately after surgery, 2 weeks, for comparison, but in this topic no consensus was reached.

## Conclusions

Focal therapy in prostate cancer is a new and developing field of research. The present evidence for MRI in focal therapy is limited, as studies are not uniformly executed with different technologies (1.5–3T), different protocols (mpMRI, DCE-MRI, DWI, MRSI, T1-T2) and MRI results are not uniformly reported. Therefore, limited evidence is available to make firm statements. mpMRI is the optimum approach to achieve the objectives needed for focal therapy, if made using a high-quality machine (3T with/without endorectal coil or 1.5T with endorectal coil) and judged by an experienced radiologist. Structured and standardised reporting of prostate MRI is paramount. However, when mpMRI is compared with Gleason grade, the technology is not yet accurate enough to consistently grade tumour aggressiveness. Template-guided saturation biopsies for selecting patients for focal therapy can be discarded if a high-quality MRI is available; however, suspicious lesions should always be confirmed by (targeted) biopsy. In this rapidly developing field, most research is based on expert opinion and performed only in centres of excellence. Therefore there is a need for large standardised studies.

## Acknowledgments

### Conflict of Interest

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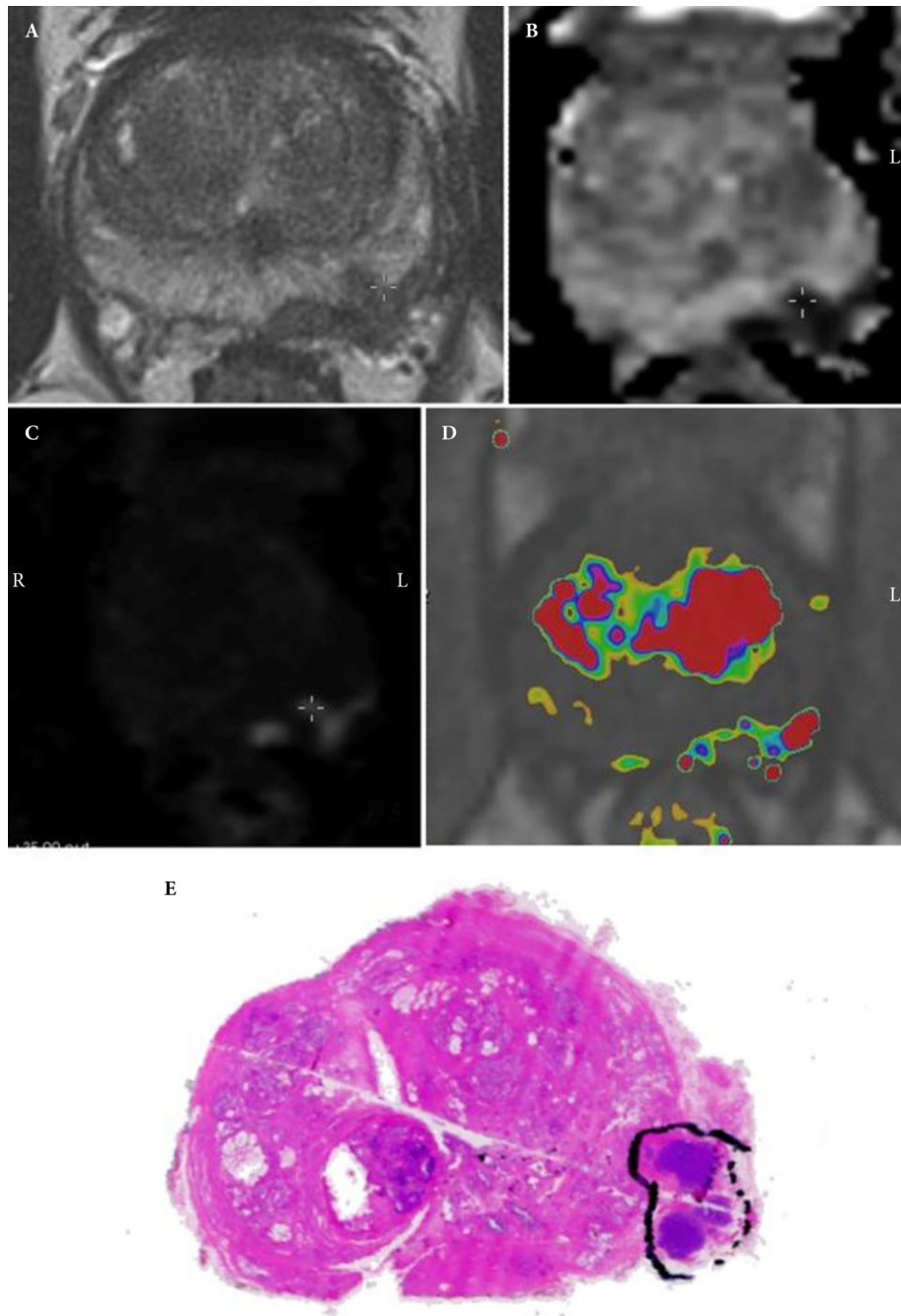
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## Abbreviations

<b>ADC</b>	apparent diffusion coefficient
<b>DCE-MRI</b>	dynamic contrast material-enhanced MRI
<b>DWI</b>	diffusion-weighted imaging
<b>HIFU</b>	high-intensity focused ultrasound
<b>IRE</b>	irreversible electroporation
<b>mpMRI</b>	multiparametric MRI
<b>MRSI</b>	MR-spectroscopic imaging
<b>PDT</b>	and photodynamic therapy
<b>RP</b>	radical prostatectomy
<b>T1w</b>	T1-weighted
<b>T2w</b>	T2-weighted



**Fig. 1.** Prostate cancer in a 67-year-old patient with a PSA level of 6.23 ng/mL and Gleason 7. (a) Axial T2-weighted MRI of the prostate showing a low signal intensity area in the left peripheral zone. (b) ADC and the high b-value (c) images show restriction and high signal in the left peripheral zone, respectively. The perfusion MRI shows high Ktrans (transfer constant) in the left peripheral zone (d). The whole-mount section histopathology slide on the same level as (a–d) shows Gleason 7 cancer in this MRI-positive area (e).



Table 1

Outcomes of studies from paragraph 1 summarised. (–) means that no data on this variable was provided in the study.

Reference	N	MRI	Sequence	ERC	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %	PA
Kim et al. [6]	20	3T Intera Achieva, Philips	T2w, T1w, DCE	No	73	77	78	72	75	TRUS-Biopsy
Torricelli et al. [7]	29	3T Intera, Philips	T2w, T1w	Yes	83	90	90	81	–	Whole-mount HP
Park et al. [8]	54	3T Intera Achieva, Philips	T2w, T1w	Yes	81	67	–	–	72	Whole-mount HP
Fütterer et al. [9]	34	1.5 T Sonata, Siemens	T2w, T1w, DCE, MRSI	Yes	–	–	–	–	69	Whole-mount HP
Kim et al. [10]	20	3T Intera Achieva, Philips	T2w, T1w, DCE	No	55	88	83	63	70	TRUS-biopsy
Ocak et al. [11]	50	3T Intera, Philips	T2w, T1w, DCE	Yes	70	88	75	74	–	TRUS-biopsy
Scheenen et al. [12]	45	3T Magnetom, Siemens	T2w, T1w, MRSI	No	78	81	–	–	–	Whole-mount HP
Heijmink et al. [13]	46	3T Magnetom, Siemens	T2w, T1w	Yes	80	100	100	91	93	Whole mount HP
Miao et al. [14]	37	3T Magnetom, Siemens	T2w, T1w, DWI	No	84	81	81	84	82	TRUS-biopsy
Zhang et al. [15]	158	1.5T Signa, GE Medical Systems	T2w, T1w, MRSI	Yes	–	–	–	–	80	Whole-mount HP
Turkbey et al. [16]	70	3T Achieva, Philips	T2w, T1w, MRSI, DCE	Yes	73	89	–	–	–	Whole-mount HP
Rosenkrantz et al. [17]	38	1.5T Magnetom Avanto, Siemens	T2w, T1w	No	67.4	71.1	58.6	78.3	69.7	Whole-mount HP
Riches et al. [18]	20	1.5T	T2w, T1w, DWI, DCE	Yes	–	–	–	–	–	Whole-mount HP
Kitajima et al. [19]	53	3T Magnetom Trio Tim, Siemens	T2w, T1w, DWI, DCE	No	80.8	95.7	85.1	95.4	92.2	TRUS-Biopsy
Scheidler et al. [22]	53	1.5T Signa, GE Medical Systems	T2w, T1w, MRSI	Yes	95	41	76	82	77	Whole-mount HP
Villers et al. [23]	24	–	T2w, T1w, DCE	No	77	91	86	85	–	Whole-mount HP
Turkbey et al. [24]	45	3T Intera Achieva, Philips	T2w, T1w, DWI, DCE, MRSI	Yes	58	100	93	90	–	Whole-mount HP

N, number of patients included in the study; MRI, type and strength of MRI device; ERC, endorectal coil; PPV, positive predictive value; NPV, negative predictive value; PA, the manner in which histopathology was compared to MRI footage.

**Table 2**

The individual sensitivity, specificity, and positive (PPV) and negative predictive values (NPV) of the four MRI sequences for the peripheral zone (PZ), central gland (CG), anterior horns of the peripheral zone and central gland (A&CG), and overall prostate gland (from [24]).

	<b>PZ</b>	<b>CG</b>	<b>A&amp;CG</b>	<b>Overall gland</b>
<b>% Sensitivity (P)</b>				
T2w	0.65 (0.04)	0.15 (0.08)	0.38 (0.07)	0.58 (0.04)
DWI	0.57 (0.04)	0.22 (0.09)	0.44 (0.07)	0.53 (0.04)
MRSI	0.17 (0.04)	0.08 (0.06)	0.15 (0.05)	0.16 (0.04)
DCE	0.39 (0.05)	0.22 (0.09)	0.31 (0.07)	0.38 (0.05)
<b>% Specificity (P)</b>				
T2w	0.9 (0.02)	1 (0)	0.98 (0.01)	0.93 (0.01)
DWI	0.93 (0.02)	0.97 (0.01)	0.97 (0.01)	0.95 (0.01)
MRSI	1 (0)	1 (0)	1 (0)	1 (0)
DCE	0.97 (0.01)	0.99 (0)	0.99 (0)	0.98 (0.01)
<b>% PPV (P)</b>				
T2w	0.69 (0.05)	0.87 (0.1)	0.73 (0.09)	0.7 (0.05)
DWI	0.74 (0.04)	0.63 (0.13)	0.75 (0.06)	0.73 (0.04)
MRSI	0.94 (0.04)	0.89 (0.1)	0.96 (0.04)	0.93 (0.04)
DCE	0.86 (0.05)	0.86 (0.07)	0.89 (0.04)	0.86 (0.04)
<b>% NPV (P)</b>				
T2w	0.89 (0.02)	0.92 (0.02)	0.93 (0.01)	0.9 (0.01)
DWI	0.87 (0.02)	0.92 (0.02)	0.94 (0.01)	0.89 (0.01)
MRSI	0.8 (0.02)	0.91 (0.02)	0.91 (0.01)	0.83 (0.01)
DCE	0.84 (0.02)	0.92 (0.02)	0.92 (0.01)	0.87 (0.01)

**Table 3**

Sensitivities, specificities, positive predictive values (PPV) and negative predictive values (NPV) of small and large tumour detection on DCE-MRI correlated with whole gland histopathology (from [23]).

	<b>MRI performance for detecting 56 cancer foci according to tumour volume in regions</b>		
	<b>% foci (95% CI)</b>		
	<b>&gt;0.2 mL</b>	<b>&gt;0.5 mL</b>	<b>All cancers</b>
Sensitivity	76.6 (68.5–85.3)	90.0 (84–96)	55.4 (45–65)
Specificity	91.2 (85.5–96.9)	87.9 (81.3–94.4)	90.0 (84–96)
PPV	85.7 (78.7–92.7)	77.1 (68.7–85.5)	88.6 (82–95)
NPV	85.2 (78.1–92.3)	95.1 (90.6–99.3)	59.0 (49.2–68.8)