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The Transatlantic Recommendations for Prostate Gland Evaluation with Magnetic Resonance Imaging After Focal Therapy (TARGET): A Systematic Review and International Consensus Recommendations

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Abstract

Background and objective: Magnetic resonance imaging (MRI) can detect recurrences after focal therapy for prostate cancer but there is no robust guidance regarding its use. Our objective was to produce consensus recommendations on MRI acquisition, interpretation, and reporting after focal therapy.
Methods: A systematic review was performed in July 2022 to develop consensus statements. A two-round consensus exercise was then performed, with a consensus meeting in January 2023, during which 329 statements were scored by 23 panellists from Europe

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and North America spanning urology, radiology, and pathology with experience across eight focal therapy modalities. Using RAND Corporation/University of California-Los Angeles methodology, the Transatlantic Recommendations for Prostate Gland Evaluation with MRI after Focal Therapy (TARGET) were based on consensus for statements scored with agreement or disagreement.

Key findings and limitations: In total, 73 studies were included in the review. All 20 studies (100%) reporting suspicious imaging features cited focal contrast enhancement as suspicious for cancer recurrence. Of 31 studies reporting MRI assessment criteria, the Prostate Imaging-Reporting and Data System (PI-RADS) score was the scheme used most often (20 studies; 65%), followed by a 5-point Likert score (six studies; 19%). For the consensus exercise, consensus for statements scored with agreement or disagreement increased from 227 of 295 statements (76.9%) in round one to 270 of 329 statements (82.1%) in round two. Key recommendations include performing routine MRI at 12 mo using a multiparametric protocol compliant with PI-RADS version 2.1 standards. PI-RADS category scores for assessing recurrence within the ablation zone should be avoided. An alternative 5-point scoring system is presented that includes a major dynamic contrast enhancement (DCE) sequence and joint minor diffusion-weighted imaging and T2-weighted sequences. For the DCE sequence, focal nodular strong early enhancement was the most suspicious imaging finding. A structured minimum reporting data set and minimum reporting standards for studies detailing MRI data after focal therapy are presented.

Conclusions and clinical implications: The TARGET consensus recommendations may improve MRI acquisition, interpretation, and reporting after focal therapy for prostate cancer and provide minimum standards for study reporting.

Patient summary: Magnetic resonance imaging (MRI) scans can detect recurrent of prostate cancer after focal treatments, but there is a lack of guidance on MRI use for this purpose. We report new expert recommendations that may improve practice.

1. Introduction

Focal therapy for localised prostate cancer is increasingly performed [1]. Observational data show that focal ablative modalities, including high-intensity focused ultrasound (HIFU) and cryotherapy, can produce oncological outcomes that are comparable to those for whole-gland treatments but with lower toxicity [2–5]. However, close surveillance of patients is needed after focal therapy in case of cancer recurrence or the development of a new tumour focus requiring further treatment. Prostate magnetic resonance imaging (MRI) is routinely used to evaluate the treated gland, with previous studies describing imaging findings that reflect treatment-related changes and changes suspicious for cancer recurrence [6–8]. Despite this, the role of MRI in this setting is poorly established and there is limited evidence supporting specific clinical practice [9]. Consequently, multiple guidelines advocate for routine ablation zone biopsies post-treatment regardless of MRI findings [10–13]. These biopsies carry risks and have had poor patient acceptance in previous focal therapy series [3,14,15].

In other treatment settings, MRI interpretation is guided by scoring systems. For example, the 2021 Prostate Magnetic Resonance Imaging for local Recurrence Reporting (PI-RR) consensus guidelines give a 5-point scoring system for MRI after radical prostatectomy and radiotherapy [16]. In the primary diagnostic setting, the consensus-derived Prostate Imaging-Reporting and Data System (PI-RADS) guidance is now widely used [17]. Similar guidance for MRI assessment after focal therapy is needed [9]. If MRI use can be optimised via improved image interpretation, this could reduce the number of unnecessary protocol biopsies performed, reflecting what has been achieved with better imaging in the primary diagnostic and active surveillance settings [18–20].

In the absence of high-quality evidence, a consensus approach can generate preliminary guidance that can be validated and refined in later stages. If carried out judiciously, this approach can also identify areas of uncertainty and set priorities for future research. Here, we describe the results of a systematic review, followed by consensus recommendations for the acquisition and interpretation of MRI after focal therapy for prostate cancer. The results are summarised as the Transatlantic Recommendations for Prostate Gland Evaluation with MRI after Focal Therapy (TARGET) consensus recommendations.

2. Materials and methods

2.1. Systematic review

A systematic review was performed to identify the scope of MRI practice (PROSPERO registration: CRD42022338740). An initial literature review with broad eligibility criteria is recommended by the RAND Corporation/University of California-Los Angeles (RAND/UCLA) appropriateness method to synthesise all relevant data available. This review informed consensus item development and its results were presented to panel members during the consensus exercise [21].

MEDLINE, Embase, and Web of Science databases were searched on July 18, 2022. Members of the study team (H. U.A., T.T.S.) were also consulted and references from relevant reviews were screened. When searches returned a relevant conference abstract, a manual search was performed to identify a corresponding full-text article if not already identified.

Articles detailing MRI use after primary focal therapy at any time interval were included. Studies evaluating whole-gland and salvage treatment were excluded. The search string is included in the Supplementary material and Supplementary Table 1 lists the full eligibility criteria. Two authors (A.L., N.M.) screened each abstract and reviewed full-text articles for inclusion, with any disagreement settled via discussion.

This review had three main outcomes chosen to inform the subsequent development of consensus statements: (1) to identify the range of MRI acquisition protocols used, including MRI timing after treatment; (2) to identify the range of MRI interpretation criteria used; and (3) to determine the diagnostic accuracy of MRI acquisition and interpretation protocols for detecting recurrence, measured against a histological reference. For outcome (3), a meta-analysis was planned, but after data extraction it was decided to omit this because of wide between-study variation for biopsy protocols, definitions of cancer, MRI timing, and MRI indications. Studies also varied considerably regarding indications for performing biopsy after MRI.

The risk of study bias was assessed with the QUADAS-2 tool [22].

2.2. Consensus exercise

The RAND/UCLA appropriateness method was then applied to conduct a two-round consensus study [21]. Using the systematic review and clinical experience, a list of 295 statements was drafted by a core group (A.L., A.P., A.K., H. U.A., T.T.S.). These statements spanned six categories pertaining to MRI after focal therapy: (1) timing; (2) technical parameters; (3) interpretation; (4) structured minimum reporting data set; (5) capabilities; and (6) study minimum reporting standards.

These statements assume that a single focal treatment has been adequately performed in a previously untreated gland in patients eligible for focal treatment as determined via preoperative MRI and biopsy. The statements are intended to apply across all focal therapy modalities rather than being specific to any one modality. The statements also assume that all MRI techniques are available and that all images obtained are of adequate quality. Unless otherwise stated, the purpose of MRI after focal therapy is to detect disease recurrence within the focal ablation zone and its margins. Panellists were asked not to consider cost, in line with RAND/UCLA guidance [21].

Panellists rated their agreement with each statement using a 9-point scale, where 1 represents strong disagreement, 5 represents neither disagreement nor agreement, and 9 represents strong agreement. Abstention was permitted. After both rounds, it was established whether the panellists as a group agreed or disagreed with each statement and whether there was consensus among the panellists. A group median score of 1–3 indicated disagreement, 4–6 indicated uncertainty, and 7–9 indicated agreement. The presence of consensus was determined using the interpercentile range adjusted for symmetry (IPRAS) method [21]. Further details on this method are given in the Supplementary material and Supplementary Figure 2. The final recommendations presented are based on statements scored with agreement or disagreement for which consensus was achieved after round two. During manuscript drafting, linguistic modifications were made in conjunction with panellists and the chair to improve the clarity of statements 102 and 106 for readers, without changing the fundamental meaning of the statements. These two statements pertain to dynamic contrast-enhanced (DCE) sequence interpretation for readers (Supplementary Table 13).

Details for panellists and their experience are given in Supplementary Table 9. A total of 35 panellists were invited, of whom 24 panellists from seven countries agreed to participate. These panellists comprised 13 radiologists, ten urologists, and one pathologist. One panellist was a dual-trained urologist-radiologist who performs focal therapy and one radiologist also performs focal therapy. Panellists had experience across eight focal therapy modalities. Of the 24 panellists, 20 (83%) had experience with cryotherapy and 18 (75%) had experience with HIFU (Supplementary Table 9). The other six modalities represented were irreversible electroporation (IRE; ten panellists; 42%), vascular-targeted photodynamic therapy (VTP; six panellists; 25%), radiofrequency ablation (RFA; four panellists; 17%), transurethral ultrasound ablation of the prostate (TULSA; four panellists; 17%), focal laser ablation (FLA; three panellists; 13%), and microwave treatment (one panellist; 4%). All 24 panellists participated in round one and 23 participated in round two.

In round one (December 2022 to January 2023), panellists were e-mailed statements to score, along with a summary of the systematic review. Panellists were also asked to suggest statement modifications, additions, and deletions.

Round two (January 2023) comprised a hybrid consensus meeting. Eight panellists and the chair participated in person in London, UK, and 15 panellists participated via Zoom online video. The meeting was chaired by an independent, nonscoring clinical epidemiologist (J.v.d.M.) with significant experience in both prostate cancer research and chairing of consensus meetings. After alterations to round one statements, 334 statements were discussed. Each statement was presented with a histogram of round one scores and an indication of the degree of agreement with the statement and consensus among the panellists. Each statement was then discussed before being rescored. Further modifications, additions, and deletions were permitted if approved by the chair.

3. Results

3.1. Systematic review

From the 3916 articles identified, 73 unique studies spanning 113 articles were included (Supplementary Fig. 1). Of

these 73 studies, 45 (62%) were prospective observational studies and one (1%) was a randomised controlled trial. The remaining 27 studies (37%) were retrospective. Ten focal therapy modalities were included, with HIFU (25 studies; 34%) and cryotherapy (14 studies; 19%) the most common.

3.1.1. MRI timing

A total of 68 studies reported on MRI timing (Supplementary Table 3). Of these 68, 18 studies involved "early" MRI performed within 1 mo after focal therapy, with two early MRI examinations performed in one study. The aim of this examination was to identify complete ablation of the target rather than to diagnose recurrence. The most common time point was 7 d (seven studies; 39%), followed by 28 d to 1 mo (four studies; 22%; Supplementary Table 4).

MRI was performed after 1 mo to assess for recurrence in 67 studies. The most common time point was 6 mo (30 studies; 45%), followed by 12 mo (12 studies; 18%) and then 6–12 mo (6 studies; 9%; Supplementary Table 5). In one of 67 studies (1%) MRI was only performed on a for-cause basis. Nineteen studies performed more than one surveillance MRI examination. Between the first and second MRI examinations, the most common interval was 6 mo (nine studies; 47%), followed by 12 mo (four studies; 21%; Supplementary Table 6).

3.1.2. MRI technical specifications

The MRI sequences used were described in 71 studies, with 65 (92%) using a multiparametric protocol. Among the 30 studies that reported on field strength, 17 (57%) used 3.0 T only, three (10%) used 1.5 T only, and ten (33%) used either 1.5 or 3.0 T. Among the 19 studies that reported on coil use, three (16%) used an endorectal coil.

3.1.3. MRI interpretation

Twenty studies discussed imaging findings suspicious for recurrence (Supplementary Table 7). The most cited was focal enhancement on the DCE sequence (20 studies; 100%), while ten (50%) specifically stated early enhancement and two (10%) stated early enhancement with washout. The second most-cited finding was restricted diffusion on diffusion-weighted imaging (DWI; eight studies; 40%). A focal low and/or intermediate signal on T2-weighted (T2W) imaging was deemed suspicious in five studies (25%).

A total of 31 studies reported assessment criteria for ablation zone lesions (Table 1). The most-cited criterion for assessment was the PI-RADS score (20 studies; 65%), followed by a 5-point Likert score (six studies; 19%). Only two studies (3% each) detailed individualised sequence-specific scores [23–26].

3.1.4. MRI diagnostic accuracy

Supplementary Table 8 lists biopsy data and Table 2 summarises studies reporting both MRI and biopsy data at 1 mo after focal therapy, grouped by MRI interpretation criteria [3,8,15,23–54]. The 1-mo cutoff here was chosen to exclude studies focusing on interpretation of early MRI, when genuine recurrent tumour is not expected and the intention is instead to confirm complete ablation of the target area and evaluation of margins via characteristics such as oedema, inflammation, and lack of perfusion. Among the 12 studies that used PI-RADS, a suspicious in-field MRI lesion was observed in 0–60% of cases and in-field cancer was detected on biopsy in 0–57%. Among the four studies that used a 5-point Likert score, a suspicious in-field MRI lesion was observed in 18–50% of cases and in-field cancer was detected on biopsy in 17–100%. Table 2 details data for individual studies using a 3-point Likert, binary, and individualised scores.

Table 1 – Summary of magnetic resonance imaging scoring criteria for suspicious ablation zone lesions after focal therapy for prostate cancer as identified in the systematic review. 31 studies reported assessment criteria for ablation zone lesions.

Assessment system used	Studies, *n* (%)
PI-RADS score	20 (65)
5-point Likert score	6 (19)
Binary score: suspicious vs nonsuspicious	2 (6)
3-point Likert score	1 (3)
Individual sequence scores [23]: 4-point T2W score: 0 = ill-defined scaring; 1 = ill-defined scarring with atrophy; 2 = well-defined scarring; 3 = scarring with cystic changes 2-point DWI score: 0 = no restricted diffusion; 1 = restricted diffusion 3-point DCE score: 0 = hypoenhancement; 1 = isoenhancement; 2 = hyperenhancement	1 (3)
Individual sequence scores [24–26]: 3-point T2W: 0 = heterogeneous or homogeneous very low signal intensity; 1 = uniform intermediate or low signal intensity, wedge-shaped or circumscribed; 2 = uniform intermediate or low signal intensity, irregular or invasive margins 3-point DWI: 0 = low signal intensity; 1 = intermediate signal intensity; 2 = high signal intensity 3-point DCE: 0 = nonenhancing or hypoenhancement; 1 = isoenhancement or progressive enhancement; 2 = early hyperenhancement with washout	1 (3)

DCE = dynamic contrast-enhanced; DWI = diffusion-weighted imaging; PI-RADS = Prostate Imaging-Reporting and Data System; T2W = T2-weighted.

3.1.5. Risk of bias

Results for the risk of bias assessment are shown in Supplementary Table 9. Of 73 studies, 43 (59%) were deemed to be at high risk for the flow and timing domain, the majority because only a proportion of patients who underwent MRI were subsequently biopsied (Supplementary Tables 7 and 8).

3.2. Consensus recommendations

Supplementary Table 11 summarises the statement scoring. For round one, there was consensus for 227 of 295 statements (76.9%) scored with either agreement or disagreement. After round one, 17 statements were altered and 39 statements were added (Supplementary Table 12). Therefore, 334 statements were discussed in the round two consensus meeting, during which 57 statements were altered and five statements were deleted, meaning that 329 statements were scored (Supplementary Table 12). Consensus was achieved for 270 of 329 (82.1%) statements, scored either with agreement or disagreement. These 270 statements form the basis of the recommendations. Supplemen-

Table 2 – Summary of studies reporting on both MRI and biopsy findings (performed after >1 mo) specifically within the ablation zone (in-field), grouped by MRI interpretation criteria used.

MRI interpretation criteria	Study	Focal therapy modality	Patients	MRI sequences used	Biopsy technique	Men with suspicious in-field MRI findings, *n*/*N* (%)	Men with in-field recurrence on biopsy, *n*/*N* (%)
PI-RADS	[27]	Brachytherapy (LDR)	26	T2W, DWI, DCE	SBx ± TBx	12–18 mo: 0/21 (0)	12–18 mo: 12/21 (57)
	[28]	Cryotherapy	75	T2W, DWI, DCE	SBx or TBx	12 mo: 16/70 (23)	>12 mm: 19/75 (25)
	[29,30]	Cryotherapy	55	T2W, DWI, DCE	SBx or TBx	6 mo: 14/31 (45)	6 mo: 7/31 (23)
	[31]	IRE	12	T2W, DWI, DCE	SBx ± TBx	6 mo: 2/12 (17) 12 mo: 2/12 (17)	12 mo: 3/12 (25)
	[32]	PAE	10	T2W, DWI, DCE	SBx ± TBx	6 mo: 6/10 (60)	6 mo: 5/10 (50)
	[33]	Brachytherapy (LDR)	17	T2W, DWI, DCE	SBx ± TBx	12 mo: 1/17 (6)	12 mo: 3/17 (18)
	[34]	Brachytherapy (LDR)	31	T2W, DCE	SBx	24 mo: 2/26 (8)	24 mo: 3/26 (12)
	[35]	Brachytherapy (LDR)	5	T2W, DWI, DCE	SBx	12 mo: 1/3 (33) 24 mo: 1/2 (50)	24 mo: 0/2 (0)
	[36]	Cryotherapy	27	T2W, DWI, DCE	SBx ± TBx	24 mo: 0/27 (0)	24 mo: 4/27 (15)
	[37]	HIFU	21	T2W, DWI, DCE	SBx ± TBx	6–12 mo: 2/21 (10)	6–12 mo: 4/21 (24)
	[8,38]	HIFU	51	4 centres: T2W, DWI, DCE 1 centre: T2W, DCE	SBx ± TBx	12 mo: 8/48 (17)	12 mo: 13/49 (27)
	[39]	FLA	120	T2W, DWI, DCE	TBx	Time NR: 44/120 (37)	Time NR: 22/120 (18)
5-point Likert	[3]	HIFU	100	T2W, DWI, DCE	SBx ± TBx	6–12 mo: 18/61 (30)	6–12 mo: 10/58 (17)
	[40,41]	IRE	30	T2W, DWI, DCE	SBx	6 mo: 6/30 (20) 12 mo: 9/18 (50)	12 mo: 3/5 (60)
	[42]	IRE	34	T2W, DWI, DCE	TBx	6 mo: 6/34 (18)	>6 mo: 1/1 (100)
	[43–53]	HIFU	118	T2W, DWI, DCE	NR	6 mo: 38/109 (35)	6 mo: 28/109 (26)
3-point Likert	[54]	Cryotherapy	90	T2W, DWI, DCE	NR	Time NR: 22/27 (82)	Time NR: 5/11 (46)
Binary	[15]	VTP	41	T2W, DWI, DCE	SBx ± TBx	12 mo: 2/21 (10) 24 mo: 0/5 (0)	12 mo: 4/21 (19) 24 mo: 3/5 (60)
Individualised	[23]	FLA	54	T2W, DWI, DCE	4–8 mo: TBx 21–101 mo: SBx ± TBx	4–8 mo: DCE: 4/28 (14); DWI: 3/28 (11) 21–101 mo: DCE: 8/20 (40); DWI: 6/21 (29)	4–8 mo: 5/51 (10) 21–101 mo: 8/21 (38)
	[24–26]	FLA	18	T2W, DWI, DCE	TBx	6 mo: 17/18 (94) 12 mo: 16/17 (94)	6–12 mo: 11/18 (61)

DCE = dynamic contrast-enhanced; DWI = diffusion-weighted imaging; FLA = focal laser ablation; HIFU = high-intensity focused ultrasound; IRE = irreversible electroporation; LDR = low-dose rate; MRI = magnetic resonance imaging; NR = not reported; PAE = prostatic artery embolisation; PI-RADS = Prostate Imaging-Reporting and Data System; SBx = systematic biopsy; TBx = targeted biopsy; T2W = T2-weighted; VTP = vascular-targeted photodynamic therapy.

tary Table 13 details the final statements and scores and Table 3 summarises key recommendations.

3.2.1. *MRI timing*

3.2.1.1. Early MRI. Early MRI was defined as MRI performed within 30 d after focal therapy to confirm complete treatment of the target area. It was uncertain if early MRI should be performed at all. Furthermore, if early MRI is desired, it was uncertain at what time point this should be performed. It was argued that, although desirable for comparison to later imaging, this examination rarely impacts clinical management and could strain resources in an era when prostate MRI is increasingly performed across multiple indications. However, it was acknowledged that early MRI is useful for feedback and learning for inexperienced focal therapists, such as those undertaking their first 30–50 cases.

3.2.1.2. Surveillance MRI. Surveillance MRI was defined as MRI performed after 1 mo after focal therapy to identify recurrence. Here, this pertains specifically to protocol-specified MRI examinations rather than examinations performed on a for-cause basis. A first protocol MRI should be performed at 12 mo after focal therapy; this should minimise any treatment-induced necrosis and inflammation that can mask recurrent disease at earlier time points [55]. The point was also raised that early prostate-specific antigen (PSA) kinetics after focal therapy can be erratic and challenging to interpret, which tends to stabilise at 12 mo [51]. The 12-mo point therefore provides the first good opportunity to assess MRI and PSA together, with minimal treatment artefacts.

If a patient has negative first MRI findings and a normal PSA, then further surveillance MRI should be scheduled for 12 mo after the previous examination, irrespective of whether the patient had a biopsy after the first MRI, even if that biopsy was negative. However, it was acknowledged that increases in PSA after 12 mo have high sensitivity for recurrence and are a useful indication for performing for-cause MRI [51]. Exact guidance on what determines a normal PSA after focal therapy was not decided. The inherent nature of focal treatment makes interpretation of PSA more difficult in comparison to whole-gland therapies such as radical prostatectomy. PSA will certainly vary between patients, depending on factors such as the ablation pattern, the presence and characteristics of cancer in untreated tissue (whether already identified or not), and prostate size. A previous study concluded that PSA nadir + $\geq$1.0 ng/ml

Table 3 – Summary of the key TARGET consensus recommendations.

Area	Recommendation
MRI timing	Perform MRI at 12 mo to assess for recurrence.
	If a patient has negative MRI and normal PSA at 12 mo and (1) no protocol biopsy was performed or (2) protocol biopsy was negative, then further surveillance MRI should be scheduled.
	Further surveillance MRI should be scheduled at an interval of 12 mo after the previous MRI.
	The duration for ongoing surveillance MRI should depend on the clinical and pathological characteristics of the patient's cancer.
MRI technical parameters	Full multiparametric MRI including T2W, DWI, and DCE sequences is mandatory.
	MRI can be performed with a 1.5 T or 3.0 T scanner, but 3.0 T is preferred.
	In addition to use of an external (surface) phased array coil, an endorectal coil is neither mandatory nor preferred.
	Technical specifications for T1W, T2W, DWI, and DCE sequences should match the PI-RADS version 2.1 standard.
	If the T2W or DWI sequence is omitted or of inadequate quality on MRI before focal therapy, the sequence should be repeated preoperatively to allow for image comparison.
	If the T2W, DWI, or DCE sequence is omitted or of inadequate quality on MRI after focal therapy, the sequence should be repeated.
Treatment-related MRI findings	Possible treatment-related imaging findings on early MRI include haemorrhage/haematoma, oedema, necrosis, diffuse contrast enhancement, rim-like contrast enhancement, and loss of zonal differentiation. Fibrosis is not expected.
	Possible treatment-related imaging findings on later MRI include necrosis (uncommon at 12 mo), fluid-filled cavities, fibrosis, and diffuse contrast enhancement. Oedema is not expected.
MRI interpretation within the ablation zone	Lesions within the ablation zone should be scored out of 5 using the criteria in Figure 1.
	DCE is the major sequence and should be graded out of 3 as shown in Figure 1.
	DWI and T2W sequences are joint minor sequences. These sequences should be graded out of 3, but specific assessment criteria are not recommended.
MRI interpretation outside the ablation zone	Lesions outside the ablation zone should be scored using both PI-RADS version 2.1 and Likert scores.
Other considerations	The MRI after focal therapy should be compared to the most recent MRI before focal therapy.
	Clinical details should be available for MRI readers, including focal therapy details, recent PSA values, and Gleason scores before focal therapy.
	MRI readers should have experience of reading at least 20 prostate MRI examinations after focal therapy every year.
	For new readers, a proportion of their output should be independently double-reported by another reader.
MRI reporting	MRI after focal therapy should be reported according to the structured minimum reporting data set in Figure 2.
Minimum standards for study reporting	Studies that report on outcomes for MRI after focal therapy should include items listed in the checklist in Table 4.

DCE = dynamic contrast-enhanced; DWI = diffusion-weighted imaging; MRI = magnetic resonance imaging; PI-RADS = Prostate Imaging-Reporting and Data System; PSA = prostate-specific antigen; T1W = T1-weighted; T2W = T2-weighted.

at 12 mo, PSA nadir + ≥1.5 ng/ml at 24 mo, and PSA nadir + ≥1.5 ng/ml at 36 mo were thresholds that each had 100% sensitivity for a composite treatment failure outcome [51].

There was no agreement on how many years patients should receive protocol MRI surveillance for, although this duration should depend on the patient's clinicopathological disease characteristics.

3.2.2. *MRI technical specifications*

A multiparametric protocol that includes T2W, DWI, and DCE sequences is required. Owing to the importance of the DCE sequence in this setting, a biparametric protocol that omits DCE images cannot be used. Adequate imaging can be performed at either 1.5 or 3.0 T, but 3.0 T is preferred. An endorectal coil is neither mandatory nor preferred at either field strength. Sequence technical parameters should match PI-RADS version 2.1 (v2.1) standards [17]. However, the importance of high-quality images was emphasised; parameters should ultimately be optimised for whatever scanner is available.

The DCE sequence is most important for detecting recurrence. The temporal resolution, spatial resolution, and signal-to-noise ratio are all important, especially the latter two in the post-ablation setting. The panel was uncertain whether the DCE slice thickness should preferably be ≤2 mm versus the PI-RADS v2.1 recommendation of 3 mm. In comparison to the PI-RADS v2.1 recommendation of ≤15 s, the panel was also uncertain whether a temporal resolution of ≤10 s is preferable, although panellists agreed that ≤7 s is not preferable. An increase in slice thickness to improve temporal resolution, or a reduction in temporal resolution to improve spatial resolution and the signal-to-noise ratio, should not be pursued. Quantitative or semi-quantitative imaging assessments are also not required.

In the event of a missing or inadequate T1-weighted (T1W) sequence on pretreatment MRI, then a repeat pretreatment MRI examination is unnecessary. However, if the T2W or DWI sequence is missing or inadequate, this sequence should be repeated before treatment so that images can be compared with post-treatment MRI scans. It was acknowledged that repeating the DWI sequence would not be appropriate in certain patients, such as patients with a hip replacement.

If the DCE sequence is missing or inadequate on pretreatment MRI, the panel was uncertain whether the MRI should be repeated before treatment. Some panellists argued that good-quality biparametric MRI, as some centres now perform, is sufficient to offer focal therapy. It was also argued that early contrast enhancement in the ablation zone after treatment is suspicious irrespective of whether this was present on the pretreatment MRI.

For post-treatment MRI examinations, if the T2W, DWI, or DCE sequence is missing or inadequate, these sequences should be repeated. A missing or inadequate T1W sequence does not need to be repeated; the precontrast phase of the DCE sequence has sufficient spatial resolution for interpretation.

3.2.3. MRI interpretation

3.2.3.1. Treatment-related imaging findings. The treatment-related findings discussed here reflect features that may be observed rather than those that should be expected on all examinations.

Haemorrhage/haematoma, oedema, necrosis, diffuse contrast enhancement, rim-like contrast enhancement, and loss of zonal differentiation are possible early MRI findings. Fibrosis is not expected. DCE images are needed to establish the extent of necrosis [55,56].

Necrosis, fluid-filled cavities, fibrosis, and diffuse contrast enhancement are possible findings on MRI performed later, such as 6–12 mo after focal therapy. Oedema is not expected. Necrosis is less likely with later MRI examinations and is rarely seen at 12 mo [55].

3.2.3.2. Ablation zone lesions. A 5-point score should be used to denote suspicion of recurrence within the ablation zone on a per-lesion basis. PI-RADS v2.1 scoring criteria should not be used. Instead, Figure 1 shows the recommended TARGET score design and examples of its use. This two-tier algorithm incorporates a major DCE sequence and joint minor DWI and T2W sequences. Each sequence should be individually assessed on a scale from 1 to 3: 1 = nonsuspicious; 2 = equivocal; and 3 = suspicious. Once each sequence has been scored out of 3, the overall score out of 5 can be calculated. The overall score should be interpreted as follows: 1 = very low suspicion; 2 = low suspicion; 3 = equivocal; 4 = high suspicion; and 5 = very high suspicion.

The ability to discriminate between suspicious and normal tissue on DCE images is better after focal therapy than for treatment-naïve glands. The choice of DCE as the major sequence reflects strong agreement that it is the most important sequence in this setting.

The ability to discriminate between suspicious and normal tissue on DWI and T2W sequences is lower after focal therapy. Although there was agreement that the DWI sequence is more important than the T2W sequence, there was also agreement that these should be joint minor sequences in the chosen two-tier scoring algorithm.

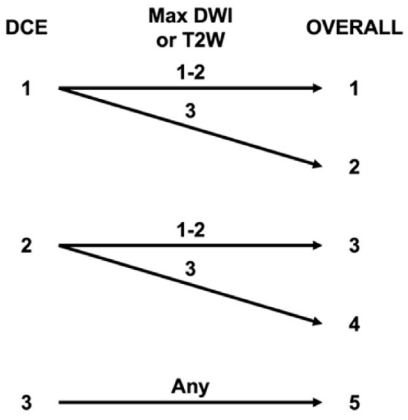
The panel considered whether to introduce new statements describing more complex three-tier algorithms that separate DWI and T2W sequences, but ultimately this was avoided. Although the panel agreed that all three sequences should be included in the scoring design, panellists considered that the DCE sequence has substantially greater importance than either the DWI or the T2W sequence. The chosen design reflects this notion, with the overall suspicion of recurrence primarily driven by DCE findings; DWI and T2W findings influence the overall score to a much lesser degree. In this design, nonsuspicious DCE findings (1/3) can never lead to an overall score greater than 2/5 (low suspicion), even if DWI and/or T2W findings are suspicious (3/3). Equivocal DCE findings (2/3) will give an overall score of either 3/5 (equivocal) or a maximum of 4/5 (high suspicion) if DWI and/or T2W findings are deemed suspicious (3/3). Last, regardless of the DWI and T2W sequences, suspicious DCE findings (3/3) can never be downgraded and will always give an overall score of 5/5 (very high suspicion). It was argued that a three-tier design would be unnecessarily more complex; distinguishing between DWI and T2W findings in a three-tier design would be unlikely to have a substantial impact on the overall score from the simpler two-tier design with joint minor DWI and T2W sequences.

The recommendation for scoring of DCE images is given in Figure 1. Focal nodular strong early enhancement was considered the most suspicious finding, giving a DCE score of 3/3. This reflects malignant vascular perfusion and permeability properties in a morphology that resembles tumour [57]. Early enhancement here reflects greater influx of contrast through a greater number of arterioles associated with recurrent tumour formation. In the presence of recurrent tumour with associated neoangiogenesis, strong enhancement is coupled with early enhancement, reflecting greater retention of contrast in the interstitial space, arising from leakage associated with the hyperpermeable tumour vasculature. The first time point at which the panel recommends protocol surveillance MRI is 12 mo, which should be sufficient time for recurrent tumour neoangiogenesis yielding strong early enhancement. Furthermore, by this time point it would be expected that treatment-induced inflammatory vascular changes that may cause diffuse contrast enhancement should have minimised via fibrosis. Early enhancement that is not coupled with strong enhancement and/or early enhancement in a morphology that is atypical for tumour, are more ambiguous findings and would give a score of 2/3 (equivocal). No early enhancement, or focal late enhancement, is in keeping with ablation zone fibrosis, the end result of successful ablation that would give a score of 1/3 (nonsuspicious).

Six statements outlining specific criteria for scoring of DWI sequences and six for T2W sequences were proposed. However, there was no consensus achieved for any of these statements rated as having agreement. Consequently, no granular guidance for interpreting these two sequences is explicitly recommended and individual readers are asked to make their own judgement as to whether these sequences are nonsuspicious, equivocal, or suspicious in conjunction with DCE imaging findings.

Panellists did acknowledge the lack of evidence supporting the diagnostic importance of different DWI and T2W findings in the post-ablation setting; this is likely to have led to the lack of any statement being scored with overall agreement and consensus. Although the panel could not agree on specific criteria for these sequences, panellists did discuss the importance of different imaging findings. For the DWI sequence, it was postulated that post-treatment fibrosis should result in a low signal on both apparent diffusion coefficient (ADC) maps and high b-value images. The difficulty in distinguishing between fibrosis and a genuine low signal from diffusion-restricted tumour on ADC maps was acknowledged. High b-value images may be more useful; a focal high signal against a background appearance of fibrosis could strongly suggest recurrence, particularly with corresponding focal early enhancement. The significance of a milder and/or more dif-

A



DCE score	Interpretation	Criteria
1	Non-suspicious	No early enhancement OR Focal late enhancement OR Any other finding not meeting criteria for score 2 or 3
2	Equivocal	Focal nodular mild early enhancement OR Thin linear early enhancement OR Curvilinear early enhancement
3	Suspicious	Focal nodular strong early enhancement

B

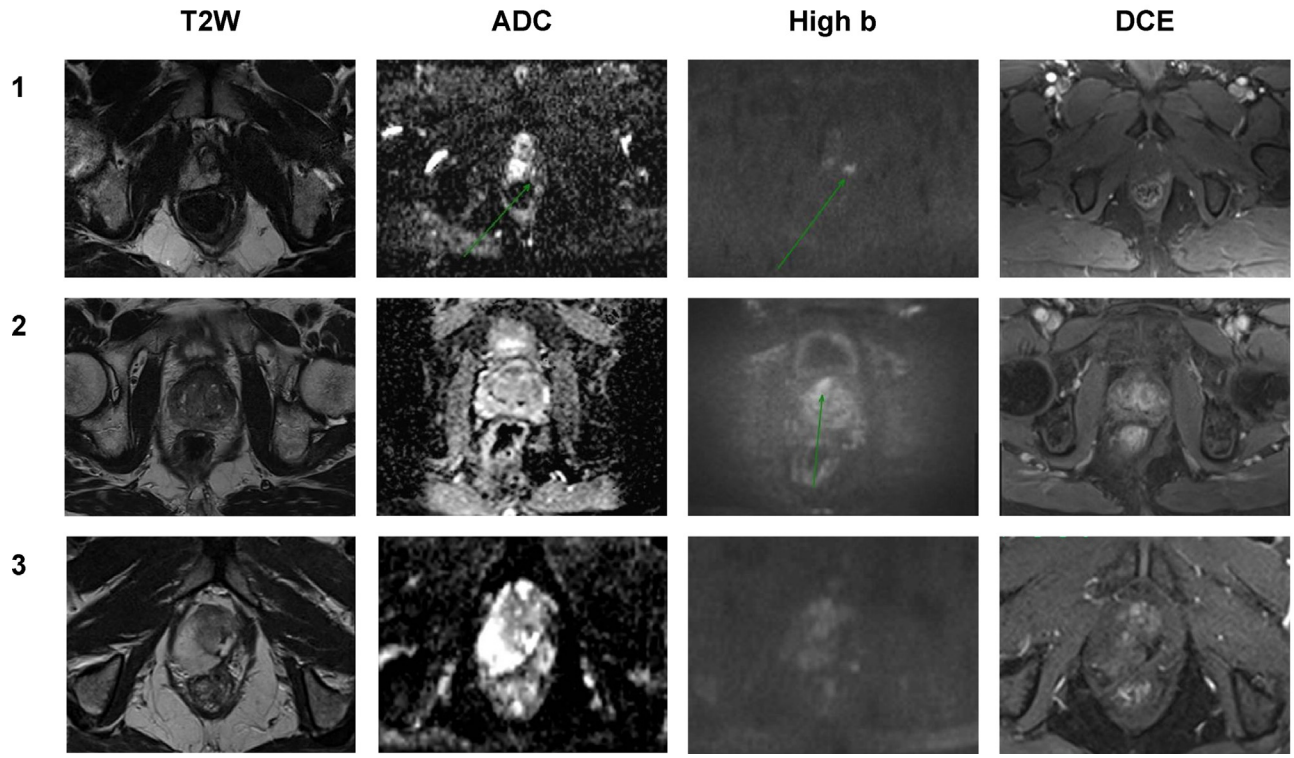


Fig. 1 – (A) Recommended 5-point magnetic resonance imaging scoring system for assessment of lesions within the ablation zone after focal therapy for prostate cancer. The DCE sequence is the major sequence and the DWI and T2W sequences are joint minor sequences. The overall score should be interpreted as follows: 1 = very low suspicion; 2 = low suspicion; 3 = equivocal; 4 = high suspicion; and 5 = very high suspicion. Each sequence should be individually assessed with a score out of 3. Criteria for DCE interpretation are given in the adjacent table. No agreement could be reached for specific criteria for DWI and T2W interpretation. During discussions on DWI it was suggested that a focal high signal on high b-value images could be suggestive of recurrent tumour and this may be more reliable than using ADC maps to identify restricted diffusion. For T2W sequences, a low to intermediate signal that is slightly higher than for fibrotic tissue but lower than for untreated tissue could be deemed more equivocal and possibly suspicious. Comparison should be made to DWI and DCE findings. (B) Examples of MRI scans after focal therapy with varying findings within the ablation zone. Row 1: MRI performed 20 mo after left-quadrant ablation with HIFU. At the posterior aspect of the left apex, there is a focal lesion with restricted diffusion on ADC and high-b images (DWI 3/3), with corresponding early enhancement (DCE 3/3). This would give an overall score of 5/5. Targeted biopsy of this lesion was positive for seven of 12 cores, revealing grade group 3 cancer with a maximum cancer core length of 12 mm. Row 2: MRI performed 43 mo after right-quadrant ablation with cryotherapy. At the anterior aspect of the right transition zone there is a lesion with restricted diffusion on the high b-value image (DWI 3/3), but no contrast enhancement (DCE 1/3). This would give an overall score of 2/5. Targeted biopsy of this lesion was negative for all six cores sampled. Row 3: MRI performed 18 mo after left-quadrant ablation with HIFU. There is no diffusion restriction (DWI 1/3) or contrast enhancement within the ablation zone (DCE 1/3), giving an overall score of 1/5. Template biopsies sampling the whole prostate were all negative. ADC = apparent diffusion coefficient; DCE = dynamic contrast-enhanced; DWI = diffusion-weighted imaging; HIFU = high-intensity focused ultrasound; T2W = T2-weighted.

fuse signal on high b-value images was less clear amongst panellists, although this could be considered more equivocal.

Of the six statements on DWI scoring criteria (statements 109–111***), all were rated overall as having disagreement with consensus, or uncertainty. When considering radiologist scores as a subgroup, all statements were rated the same (Supplementary Table 14). However, when considering urologist scores only, statement 111*** was rated as having agreement with consensus (median score 8), with five of nine urologists (56%) voting in agreement. This statement prioritises high b-value images in scoring, posing that individual lesions should be rated out of 3 as: 1 = nonsuspicious (no elevated signal on high b-value DW images OR not meeting criteria for 2 or 3); 2 = equivocal (focal mildly elevated signal on high b-value DW images); or 3 = suspicious (focal moderately or intensely elevated signal on high b-value DW images). By contrast, the same statement was rated as uncertain by radiologists (median score 6), with only five of 13 radiologists (38%) voting in agreement. Nonetheless, given the discussion points and the urologist voting pattern, high b-value images could have value and this should be investigated in future validation work.

For T2W scoring criteria, all six statements (statements 114–116***) were rated overall as having disagreement with consensus, or uncertainty. In subgroup analysis of radiologist versus urologist scores, no group individually voted any of these statements as having agreement with consensus (Supplementary Table 14). As with the DWI sequence, the lack of evidence supporting the diagnostic utility of different T2W findings may explain why panellists were unable to reach consensus. Furthermore, one panellist suggested that T2W images should be used primarily to assess for fibrosis and for residual prostate tissue and that its utility in detecting recurrent cancer should be considered limited. Nonetheless, panellists did discuss that focal intermediate signal intensity on T2W images could be considered equivocal and possibly suspicious. Specifically, this would be regions with a signal slightly higher than fibrosis (low or very low signal intensity), but lower than untreated prostate. Comparison of any focal low to intermediate signal against DWI and DCE findings would be important for clarifying the significance of this T2W finding.

3.2.3.3. Lesions outside the ablation zone. Lesions outside the ablation zone should be scored using PI-RADS v2.1 criteria and a 5-point Likert score.

3.2.3.4. Other considerations. The post-treatment MRI should be compared to the most recent pretreatment MRI. Aside from treatment details, other clinical data should be available to readers, such as recent PSA values with kinetics and the tumour Gleason score. For readers new to MRI after focal therapy, a proportion of their output should be independently double-reported.

Readers should have experience of reporting at least 20 MRI examinations per year in the post–focal therapy setting, although the panel was uncertain whether this should be 50 per year. For less experienced and/or lower-volume centres that do not meet these numbers, it was suggested that the development of an educational online portal could provide additional training, as has been created in the primary diagnostic setting [58].

3.2.4. Structured minimum reporting data set

In order to standardise reporting and to provide greater clinical context within the report, MRI after focal therapy should be reported using a structured minimum reporting data set, as outlined in Figure 2. Details such as recent PSA and biopsy data should be provided on the imaging request form or separately by the referring clinician, rather than the onus being on the radiologist to obtain this information.

3.2.5. MRI capabilities

As an imaging modality, MRI is not sufficient to detect recurrence of any grade or length after focal therapy. However, it is able to detect cancer defined as grade group $\geq$2 and/or a maximum cancer core length $\geq$4 mm (PROMIS definition 2) [18]. The panel agreed that MRI and PSA density together, but not MRI alone, can determine if a subsequent biopsy is needed. The panel was uncertain whether PSA density alone is an important parameter in assessing recurrence, given gland shrinkage and the difficulties in calculating prostate volume after focal therapy, which could lead to large inter- and intra-reader variability in calculations. Despite this, PSA density kinetics after focal therapy could be a useful metric warranting future study. Further research is also needed to ascertain the diagnostic accuracy of MRI and other imaging modalities, such as prostate-specific membrane antigen (PSMA) positron emission tomography/-computed tomography (PET/CT), after focal therapy. Accordingly, the panel was uncertain whether use of PSMA PET/CT alongside MRI could improve detection of localised recurrences. Ultimately, current data on the use of PSMA PET/CT after focal therapy are too scarce for comment [59,60].

3.2.6. Minimum reporting standards

Table 4 provides a checklist of minimum reporting standards for studies detailing outcome data for MRI after focal therapy, given the heterogeneity in reporting noted in our systematic review. The aim of these standards is to supplement, but not replace, well-established guidance for specific study designs such as CONSORT [61] and STROBE [62].

Certain items were altered during round two to note that they should be included "where available". These items pertain to the number of patients for whom MRI was omitted and the reasons for omitting MRI, which were considered to be difficult to determine in retrospective studies. Furthermore, maximum cancer core length is not routinely reported by all centres and should not be mandated.

4. Discussion

4.1. Key recommendations

Our systematic review highlights that while focal contrast enhancement is the most-cited suspicious imaging finding after focal therapy, most studies used PI-RADS scoring. PI-

TARGET Structured Minimum Reporting Dataset Form

Patient name	
Hospital number	
Date of birth	

Reporting radiologist	
Date of scan	
Date of report	

Indication for scan	

1. INITIAL DIAGNOSIS

Lesion	Location	PI-RADS / Likert score	Cancer on biopsy?	Grade group	MCCL (mm)	Other information
1						
2						
3						

2. FOCAL THERAPY

Date of focal therapy	
Focal therapy energy	
Location and ablation pattern	
Adjuvant treatments	
Most recent PSA (ng/mL)	
Other information	

3. POST-ABLATION MRI

Sequences used	
Prostate volume (mL)	
PSA density (ng/mL^2)	
No. lesions inside ablation zone	
No. lesions outside ablation zone	
Other information	

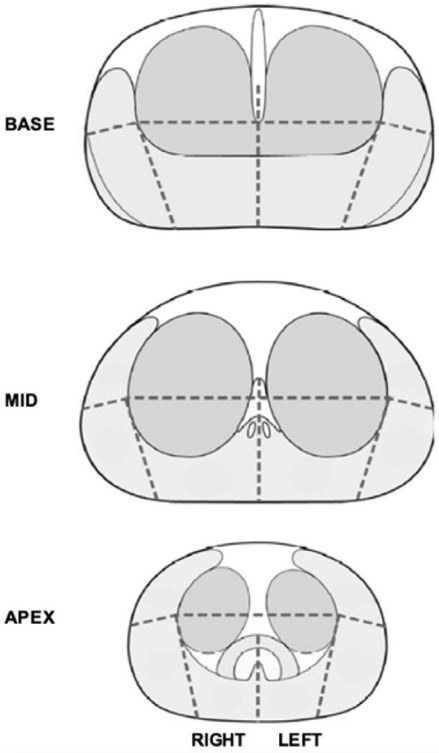
3a. Inside the ablation zone

Lesion	Visible on pre-operative MRI?	Dimensions (*x-y-z*; mm)	TARGET score (1-5)	Other information
IN-1				
IN-2				
IN-3				

Treatment-related imaging findings	

3c. Prostate map

For the post-ablation MRI, please annotate the location of the ablation zone (with a dashed line), any lesions inside it (with IN-1, IN-2 etc.), and any lesions outside it (with OUT-1, OUT-2 etc.)



3b. Outside the ablation zone

Lesion	Visible on pre-operative MRI?	Dimensions (*x-y-z*; mm)	% change in volume*	PI-RADS v2.1 score (1-5)	Likert score (1-5)	Other information
OUT-1						
OUT-2						
OUT-3						

*If lesion was visible on pre-operative MRI

Fig. 2 – Recommended structured minimum reporting data set for MRI after focal therapy. Key images within the imaging viewing software can be highlighted in addition or as an alternative to annotation of a prostate map. MCCL = maximum cancer core length; MRI = magnetic resonance imaging; PI-RADS = Prostate Imaging-Reporting and Data System.

Table 4 – Minimum reporting standards for studies detailing outcomes related to MRI performed after focal therapy for prostate cancer.

Area	Item
Methods	
Study methodology	Setting of the study centre(s), for example, academic (tertiary) centre
	Location of the study centre(s)
	Study dates for recruitment and follow-up
	Whether data collection was retrospective or prospective
	Study design, for example, cohort study or randomised-controlled trial
	Study inclusion and exclusion criteria
	Whether any of the study patients were included in previous publications, with references provided for the previous publications
Focal therapy	Focal therapy modalities used in the study, with the number of men per modality reported
	Focal therapy techniques performed, for example, quadrant ablation, measured as the number of men per focal therapy technique
	A description of how patients were selected for specific focal techniques, for example, quadrant versus hemi ablation
	Number of patients undergoing more than one focal therapy procedure
	Details of any neoadjuvant or adjuvant treatments, measured as the number of men per neoadjuvant or adjuvant treatment
	For each focal therapy modality in the study, the experience of study centre(s) in terms of (1) years performing each modality and (2) number of procedures performed per year
	Number of surgeons performing focal therapy in the study
	For each focal therapy modality in the study, the experience of each surgeon in terms of (1) years performing each modality and (2) number of procedures performed per year
Conduct of MRI after focal therapy	MRI field strength
	Coils used
	Sequences used
	Slice thickness
	T2W sequence: planes used
	DWI sequence: b-values used
	DWI sequence: whether an ADC map was calculated
	DCE sequence: temporal resolution used
	Adherence to PI-RADS standards for scan technical parameters
Assessment of MRI after focal therapy	Whether details of MRI before focal therapy and treatment details were made available to readers of MRI after focal therapy
	Total number of readers reporting MRI after focal therapy in the study
	Number of readers reporting each MRI examination after focal therapy in the study
	If more than one reader interpreted each MRI, (1) whether the MRI was reported independently by each reader and (2) how discrepancies in interpretation were handled
	Experience of each MRI reader in terms of (1) years reporting prostate MRI; (2) years reporting prostate MRI specifically after focal therapy; and (3) number of prostate MRI examinations after focal therapy reported per year
	MRI criteria used to denote suspicion of recurrence inside the ablation zone
	MRI criteria used to denote suspicion of recurrence outside the ablation zone
Conduct of biopsy after focal therapy	Experience of the biopsy operator in terms of (1) years performing prostate biopsy; (2) years performing prostate biopsy specifically after focal therapy; (3) number of prostate biopsies performed per year; and (4) number of number prostate biopsies performed per year specifically after focal therapy
	Biopsy route, for example, transperineal or transrectal
	Biopsy technique, for example, template, systematic, targeted, or combined, measured as the number of men undergoing each biopsy technique
	A description of the intended biopsy strategy, split by targeted and systematic cores, for example, 4–6 biopsy cores from each MRI target
	Criteria for selection of a lesion as a biopsy target
	Method for registration and guidance of MRI-targeted biopsy, for example, visual or software registration, ultrasound guidance or MRI guidance
	Description of the location of any targeted biopsies in terms of in-field vs out-of-field
	Description of the location of any systematic biopsies in terms of in-field vs out-of-field
	Comment on whether any systematic biopsies sample the same area as targeted biopsies
	Whether the biopsy operator was blinded to information regarding the focal therapy treatment and the most recent MRI
Assessment of biopsy after focal therapy	Number of pathologists reporting each biopsy after focal therapy in the study
	Experience of pathologists reporting biopsy after focal therapy in terms of (1) years reporting prostate biopsy; (2) years reporting prostate biopsy specifically after focal therapy; (3) number of prostate biopsies reported per year specifically after focal therapy
	If used, the definition of clinically significant cancer
Results	
Initial diagnosis	Age of participants, reported as the mean/median
	PSA, reported as the mean/median
	Maximum Gleason score for any lesion(s) subsequently treated with focal therapy, reported as the number of men per Gleason score
	Where available, MCCL for any lesion(s) subsequently treated with focal therapy, reported as the mean/median
	Location of any lesion(s) subsequently treated with focal therapy per patient, reported as the number of men per location
	Maximum Gleason score for any lesion(s) not treated with focal therapy, reported as the number of men per Gleason score
	Where available, MCCL for any lesion(s) not treated with focal therapy, reported as the mean/median
	Stage, reported as the number of men per stage
MRI after focal therapy	Most recent PSA value before MRI after focal therapy, reported as the mean/median
	Time between the focal therapy procedure and MRI after focal therapy, reported as the mean/median
	Number of men undergoing prostate MRI after focal therapy and, where available, the number of men for whom prostate MRI has been omitted

Table 4 (*continued*)

Area	Item
	Indications for MRI after focal therapy, for example, routine scan or rising PSA, reported as the number of men per indication
	Where available, the reason for omission of study patients in whom MRI has not been performed, reported as the number of men per reason
	Prostate volume, reported as the mean/median
	PSA density, calculated using the most recent PSA value before MRI after focal therapy and the prostate volume calculated on this scan, reported as the mean/median
In-field lesions on MRI after focal therapy	Number of suspicious lesions per patient, reported as the mean/median
	Number of patients with at least one suspicious lesion
	An overall score per patient used to denote suspicion, reported as the number of men with each score
Out-of-field lesions on MRI after focal therapy	Number of suspicious lesions per patient, reported as the mean/median
	Number of patients with at least one suspicious lesion visualised
	Where possible, comment on whether any lesions outside the ablation zone were visible on MRI performed before focal therapy
	An overall score per patient used to denote suspicion, reported as the number of men with each score
Biopsy after focal therapy	Number of men undergoing prostate biopsy following MRI after focal therapy and the number of men for whom prostate biopsy has been omitted
	Indication for biopsy, for example, protocol biopsy or suspicious lesion visualised on MRI after focal therapy, reported as the number of men per indication
	Reason for omission of study patients in whom a biopsy has not been performed, for example, no suspicious lesion visualised on MRI after focal therapy, reported as the number of men per indication
	Time between MRI after focal therapy and biopsy, reported as the mean/median
	Total number of cores per patient, reported as the mean/median
	Number of positive cores per patient, reported as the mean/median
	Overall Gleason grade group per patient, reported as the number of patients per Gleason grade group
	MCCL per patient, where available, reported as the mean/median
Biopsy of the ablation zone	Total number of cores per patient, both overall and split by targeted and systematic cores, reported as the mean/median
	Number of positive cores per patient, both overall and split by targeted and systematic cores, reported as the mean/median
	Overall Gleason grade group per patient, both overall and split by targeted and systematic cores, reported as number of patients per Gleason grade group
	MCCL per patient, both overall and split by targeted and systematic cores, where available, reported as the mean/median
Biopsy outside the ablation zone	Total number of cores per patient, both overall and split by targeted and systematic cores, reported as the mean/median
	Number of positive cores per patient, both overall and split by targeted and systematic cores, reported as the mean/median
	Overall Gleason grade group per patient, both overall and split by targeted and systematic cores, reported as the number of patients per Gleason grade group
	MCCL per patient, both overall and split by targeted and systematic cores, where available, reported as the mean/median
Study outcomes	The number of men with any cancer on biopsy after focal therapy, overall and for each focal therapy modality individually
	The number of men with any recurrent cancer on biopsy after focal therapy specifically inside the ablation zone, overall and for each focal therapy modality individually
	The number of men with any cancer on biopsy after focal therapy specifically outside the ablation zone, overall and for each focal therapy modality individually
	The number of men with any cancer on biopsy after focal therapy, split by targeted and systematic biopsy cores, overall and for each focal therapy modality individually
	For lesions inside the ablation zone overall and for each focal therapy modality individually, the number of men with any cancer on biopsy found at the same location as on biopsy at initial diagnosis
	For lesions outside of the ablation zone overall and for each focal therapy modality individually, the number of men with any cancer on biopsy found at the same location as on biopsy at initial diagnosis
	Sensitivity, specificity, PPV, and NPV of MRI after focal therapy for cancer detection anywhere in the prostate, using a biopsy reference standard
	Sensitivity, specificity, PPV, and NPV of MRI after focal therapy for recurrence specifically within the ablation zone, using a biopsy reference standard
	Sensitivity, specificity, PPV, and NPV of MRI after focal therapy for lesions specifically outside the ablation zone, using a biopsy reference standard
Impact	Number of men proceeding to receive further treatment, with indication provided
	Number of men not receiving further treatment, with reasons provided (eg, no cancer detected on biopsy)

ADC = apparent diffusion coefficient; DCE = dynamic contrast-enhanced; DWI = diffusion-weighted imaging; MCCL = maximum cancer core length; MRI = magnetic resonance imaging; NPV = negative predictive value; PI-RADS = Prostate Imaging-Reporting and Data System; PPV = positive predictive value; T2W = T2-weighted.

RADS is designed to be used for imaging of treatment-naïve glands, with DCE a minor sequence used only to upgrade equivocal peripheral zone lesions. The use of PI-RADS scoring for treated tissue is therefore inappropriate and this was a key recommendation.

For lesions within the ablation zone, the panel recommends use of the alternative 5-point TARGET system, with DCE more appropriately positioned as the major sequence, and DWI and T2W as joint minor sequences (Fig. 1). The importance of DCE images here is consistent with PI-RR guidance, in which DCE is the dominant sequence after both radiotherapy and prostatectomy [16]. Although the DWI sequence was considered more important than the T2W sequence, the chosen design considers these as joint minor sequences. This reflects the notion that overall suspicion should be primarily driven by DCE findings and only

marginally augmented by DWI and T2W findings. Validation of this system will be crucial before clinical implementation.

Lesions outside the ablation zone should be assessed as for primary diagnostic MRI and the panel recommends giving both PI-RADS and 5-point Likert scores. MRI should be performed routinely at 12 mo after focal therapy and PI-RADS parameters should be followed for image acquisition. MRI results should also be reported using a new structured minimum reporting data set (Fig. 2). This data set not only standardises imaging reports but also promotes routine interpretation of imaging findings within the context of important clinicopathological data.

Last, heterogeneity in study reporting precluded a robust synthesis of published data in the systematic review, so the panel recommends minimum reporting guidelines for studies detailing MRI data after focal therapy (Table 4). It should be noted that there is little high-quality evidence in this field and that standardisation of study reporting may improve this situation.

4.2. Further research

First, validation of the recommended 5-point score is needed before clinical implementation. Ideally, this would involve assessment against a protocol ablation zone biopsy reference performed regardless of MRI score. This should include assessment of the diagnostic accuracy across different treatment modalities and for detection of cancer according to different definitions. Inter-reader agreement will also be important, especially as no specific criteria have been recommended for DWI and T2W assessment.

Second, it will be vital to consider the diagnostic utility of MRI and the TARGET score in the context of the wider diagnostic pathway. For example, it would be useful to develop a model predicting the presence of recurrent cancer that incorporates the TARGET score and other metrics, such as PSA kinetics and PSA density, and potentially other imaging modalities such as PSMA PET/CT. The latter has high sensitivity for diagnosing intraprostatic disease in both untreated and irradiated prostates, which increases further when used in conjunction with MRI [63,64]; it would be reasonable to expect comparable performance in the post-ablation setting. However, data on the use of PSMA PET/CT after focal ablation are currently scarce [59,60].

Third, an assessment of how TARGET scores impact clinical decision-making is needed, balancing the biopsy burden with early detection of recurrences. An integrated diagnostic strategy incorporating TARGET scores and other diagnostic data such as PSA may have clinical benefit in informing decisions on whether to biopsy versus "biopsy-all" strategies.

Last, an investigation of how TARGET scores correlate with longer-term oncological outcomes would be of value. As a parallel, a higher PI-RADS score at initial diagnosis is associated with a greater risk of biochemical recurrence after radical prostatectomy and radiotherapy [65].

Our consensus exercise also identified areas of uncertainty that should inform future research. The panel agreed that PI-RADS criteria for DWI and T2W assessment should be avoided, but no agreement on alternative sequence-specific criteria could be reached. Before future modification of these recommendations, readers are asked to make their own judgement as to whether these sequences are nonsuspicious, equivocal, or suspicious, a system equivalent to a 3-point Likert score. Likert systems are intuitive and are more flexibly interpreted in the context of other imaging sequences; thus, they are used in multiple diagnostic applications and are frequently applied in the primary diagnostic setting, for which comparable performance to PI-RADS has been demonstrated [66,67]. Our systematic review identified fewer studies describing suspicious DWI and T2W features in comparison to the number of studies describing DCE features. Nonetheless, discussions during the consensus meeting aligned with features cited by studies, such as a focal high signal on high b-value images, but this did not translate into overall consensus among panellists. In order to develop specific DWI and T2W criteria, greater focus on these sequences is required and studies evaluating specific imaging findings against a histological reference are needed. For example, the comparative value of high b-value images versus ADC maps should be established. This is especially important given subgroup analysis demonstrated that urologists rated statement 111***, a statement that emphasised the relative importance of high b-value images in DWI assessment, as having agreement with consensus (Supplementary Table 14). Although DCE is the major sequence in the post-ablation setting, outlining specific criteria for DWI and T2W sequences may be most useful for newer and less experienced readers. It is possible that the DCE sequence has greater sensitivity for detecting recurrence than DWI and T2W sequences, which instead have greater specificity [68].

Following initial validation studies, the TARGET working group will apply further consensus methodology to refine the TARGET score. Establishing the diagnostic accuracy of individual sequences and specific imaging findings will facilitate a data-driven approach for adjusting the current two-tier design with regard to how imaging findings from different sequences are integrated and what these specific imaging findings should be.

On a related note, the panel recommends repeat examinations if a key imaging sequence is of inadequate quality. However, panellists did not discuss how to proceed if repeat MRI is not possible or practical, such as for patients with a hip replacement and the artefact this generates. The PI-RADS v2.1 guidance advises readers how to alter their assessment in the presence of inadequate sequences [17]; future work evaluating specific imaging findings and sequences would inform the development of similar guidance for the post–focal therapy setting. An area of uncertainty is also whether a pretreatment DCE sequence is needed as biparametric MRI use increases. A future validation study could selectively blind readers to preoperative DCE images to evaluate how biparametric MRI impacts post-treatment MRI interpretation and outcomes.

MRI timing is another area of uncertainty. Further work is required to establish when early MRI is best performed and how early MRI findings can guide management decisions. The panel was also uncertain on how long patients should undergo protocol MRI surveillance for. Long-term

outcomes following focal therapy are not well established. An observational study using multicentre UK registry data with the longest known follow-up reported failure-free survival rates of 96% at 2-yr and 69% at 7-yr follow-up [53]. In this study, MRI was performed routinely between 6 and 12 mo after focal therapy and on a for-cause basis thereafter. It is unclear if longer-term routine MRI surveillance would have detected late failures earlier in comparison to only performing for-cause MRI. It is equally unclear if earlier detection of late failures would significantly improve subsequent clinical outcomes. Furthermore, the panel acknowledges that there is an increasing demand for prostate MRI across indications and recommending serial MRI examinations needs to be balanced against this demand. However, there was consensus among panellists that tumour characteristics at diagnosis should influence the duration of scheduled MRI surveillance. Evaluation of surveillance protocols tailored to prognostic risk groups should therefore be considered. A parallel could be drawn to studies detailing risk-stratified active surveillance protocols [69,70].

4.3. Limitations

The major limitation of consensus recommendations is that they are ultimately driven by expert opinion rather than by data. Validation is therefore required before clinical use. Nonetheless, in the absence of high-quality data, consensus recommendations derived using robust methodology are valuable for guiding practice and highlighting areas of uncertainty that are priorities for future research. As with previous image interpretation systems, presentation of consensus recommendations is the first step before validation and eventual clinical implementation [16,71,72].

A strength of the study is the inclusion of an experienced impartial chair and a diverse panel from predominantly high-volume European and North American centres with clinical expertise in urology, radiology, and pathology and with experience spanning eight focal therapy modalities. However, a limitation is that panellists outside of Europe and North America were not included. Furthermore, the recommendations may not be fully generalisable to newer or lower-volume centres. As such centres are an important target audience for these recommendations, attempts were made to take this into account for certain areas, for example by advocating the use of 1.5 T scanners and discussing methods to supplement lower-volume MRI readers.

Focal therapy experience among the panellists comprised mostly cryotherapy and HIFU, the two energies that constitute the majority of global focal therapy practice. It is common for centres to offer both treatments, with the specific choice based primarily on anatomic factors such as tumour location, prostate size, and the presence of calcifications [2,52,73]. Although our recommendations are intended to be applied across focal therapy modalities, they may be less generalisable to modalities that were less represented in our panellists' experience. Despite this, it should be acknowledged that thermal modalities (HIFU, cryotherapy, FLA, TULSA, RFA, and microwave) and VTP all induce tissue death via coagulative necrosis [74–78]. While it is possible that IRE may have a thermal effect and induce coagulative necrosis, it predominantly induces nonthermal apoptosis by irreversibly increasing cell membrane permeability and causing osmotic disequilibrium [79–81]. Regardless, the final pathological effect of adequate ablation is fibrosis of the treated area; therefore, while differences between modalities may lead to variation in treatment-related imaging findings shortly after treatment, interpretation of MRI performed at a later time point should be more uniform across modalities [78,82]. Genuine and "typical" recurrent tumour within the ablation zone should exhibit the same hallmark imaging characteristics, such as focal nodular strong early contrast enhancement on a background of a fibrosed ablation zone, regardless of the initial ablation energy. Until data emerge to the contrary, the panel argues that these recommendations can be applied regardless of the ablation energy used.

5. Conclusions

The TARGET consensus recommendations have been produced to guide the use of MRI after focal therapy for prostate cancer. A 5-point MRI assessment score has been designed alongside guidance for MRI timing, image acquisition, and reporting. Minimum study reporting guidelines are also presented. Validation studies are now required before clinical implementation. Following validation, application of further consensus methodology is planned to refine further this recommended scoring system.

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Study concept and design: Light, Ahmed, Shah.
Acquisition of data: All authors.
Analysis and interpretation of data: Light, Mayor, Ahmed, Shah.
Drafting of the manuscript: Light, Mayor, Ahmed, Shah.
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