Radiology

REVIEWS AND COMMENTARY • RESEARCH IN PRACTICE

MRI-guided Minimally Invasive Focal Therapies for Prostate Cancer

Mostafa Alabousi, MD • *Sangeet Ghai, MD* • *Masoom A. Haider, MD*

From the Joint Department of Medical Imaging, University Health Network, University of Toronto, 263 McCaul St, 4th Floor, Toronto, ON, Canada M5T 1W7 (M.A., S.G., M.A.H.); and Lunenfeld-Tanenbaum Research Institute, Sinai Health System, Toronto, Ontario, Canada (M.A.H.). Received February 27, 2023; revision requested March 29; final revision received May 26; accepted June 7. **Address correspondence to** M.A. (email: *mostafa.alabousi@medportal.ca*).

Conflicts of interest are listed at the end of this article.

See also the editorials "Mentoring Radiologists and Imaging Scientists in the Postpandemic Digital Era" by Lee et al and "The Future Impact and Role of the Journal *Radiology* in Latin America" by Silva and Elizondo-Riojas in this issue.

Radiology 2023; 309(3):e230431 • https://doi.org/10.1148/radiol.230431 • Content codes: GU MR

Two cases involving patients diagnosed with localized prostate cancer and treated with MRI-guided focal therapies are presented. Patient selection procedures, techniques, outcomes, challenges, and future directions of MRI-guided focal therapies, as well as their role in the treatment of low- to intermediate-risk localized prostate cancer, are summarized.

Supplemental material is available for this article.

Case 1 Presentation (Dr Mostafa Alabousi)

A 65-year-old male patient presented with an elevated prostate-specific antigen (PSA) level and mildly enlarged prostate at digital rectal examination. Multiparametric MRI (mpMRI) of the prostate demonstrated a suspicious lesion (Fig 1). Subsequent MRI-guided targeted and systematic biopsies demonstrated localized grade group (GG) 2 prostatic adenocarcinoma.

The patient proceeded with a minimally invasive focal therapy (FT) with MRI-guided laser ablation (Fig 2), without significant postprocedural complications. PSA, mpMRI, and biopsy were negative for prostate cancer (PCa) at 6- and 24-month follow-up. Urinary and sexual function was preserved at 24 months. Overall, favorable oncologic and functional outcomes were achieved without the need for salvage therapy at 2 years.

Case 2 Presentation (Dr Mostafa Alabousi)

A 72-year-old male patient presented with an elevated PSA level. mpMRI demonstrated a suspicious lesion (Fig 3). MRI-guided targeted and systematic biopsies demonstrated GG2 adenocarcinoma. MRI-guided high-intensity focused ultrasound (HIFU) treatment was performed via transrectal approach, without significant postprocedural complications (Fig 4). At 24-month follow-up mpMRI, a suspicious lesion was identified in the treatment zone (Fig 4), and a targeted biopsy demonstrated disease recurrence at the posterior margin of the original tumor, necessitating salvage radiation therapy.

Case Discussion (Dr Sangeet Ghai and Dr Masoom A. Haider)

PCa is one of the most common malignancies affecting men (1). Disease grade and extent can significantly impact patient morbidity and mortality (2). As a result, the use of TNM staging, grade (Gleason score), and PSA levels is critical for risk stratification and management of PCa (3–7). Table 1 provides a breakdown of the GG and Gleason score classification for PCa (4).

Whole-gland treatment options, including radical prostatectomy and pelvic radiation therapy, are definitive approaches for organ-confined PCa management (8). However, they can result in significant morbidity: Erectile dysfunction occurs in more than half of patients treated with radical prostatectomy and radiation therapy, while many experience long-term urinary dysfunction (9). At 5 years after diagnosis, up to 14% of men experience treatment-related regret following whole-gland therapy, generally related to posttreatment functional outcomes and patient expectations (10). In contrast, active surveillance removes the morbidity of whole-gland therapies without a significant effect on oncologic outcomes for most low-risk and some favorable intermediate-risk PCa (11,12). A small risk of disease progression remains with active surveillance, and it is not considered standard-of-care management for intermediate-risk PCa (11,12).

The 2022 American Urological Association/American Society for Radiation Oncology guidelines (3) for localized PCa note that minimally invasive FTs may be considered for low- and intermediate-risk—but not high-risk—PCa, with satisfactory clinical outcomes and reduced morbidity compared with whole-gland therapies (13). The objective of FT is to eradicate all identified clinically significant PCa (csPCa) lesions, while minimizing treatment of normal prostatic tissue and surrounding structures, including the sensitive neurovascular bundles and urinary sphincter, when achievable (14,15). This approach reduces postprocedure recovery times and risk of injury to sexual and urinary function compared with whole-gland therapies (16,17). Essentially, FTs offer the chance of curing csPCa, unlike active surveillance, with improved morbidity compared with whole-gland therapies; however, long-term studies are still required to assess whether there is an impact on oncologic outcomes. Furthermore, salvage whole-gland therapy may still be performed if FT is unsuccessful.

Abbreviations

csPCa = clinically significant PCa, FDA = Food and Drug Administration, FT = focal therapy, GG = grade group, HIFU = high-intensity focused ultrasound, MRgFLA = MRI-guided focal laser ablation, MRgFUS = MRI-guided focused ultrasound, MRgTULSA = MRI-guided transurethral ultrasound ablation, mpMRI = multiparametric MRI, PCa = prostate cancer, PSA = prostate-specific antigen

Summary

MRI-guided minimally invasive therapies for localized prostate cancer in appropriately selected low- and intermediate-risk patients produce good oncologic outcomes with better quality-of-life outcomes compared with whole-gland therapies.

Teaching Points

- MRI-guided minimally invasive focal therapies (FTs) have shown reasonable oncologic and functional outcomes in the treatment of low- and intermediate-risk prostate cancer (PCa) in short-term follow-up.
- MRI-guided FTs, unlike active surveillance, offer a chance of curing PCa and have lower morbidity (eg, erectile dysfunction, urinary incontinence) than whole-gland treatment.
- Compared with US guidance, MRI guidance for FTs enables more selective targeting of clinically significant PCa and real-time thermometry monitoring of the treatment zone.
- Energy sources for MRI-guided minimally invasive therapy for PCa include high-intensity focused ultrasound, cryoablation, and laser ablation.
- Other uses of MRI-guided FTs have also been explored, including in benign prostatic hyperplasia and salvage therapy for PCa recurrence.

Table 2 illustrates general inclusion and exclusion criteria for determining which patients with PCa are candidates for FT (18). While the intent of FT may be to target the index lesion (ie, the "dominant" lesion in terms of grade and size), PCa is often a multifocal disease (15,19). The sensitivity and negative predictive value of mpMRI for secondary foci are limited, with about half of secondary csPCa lesions being missed (20). Thus, systematic biopsy may be important prior to FT, especially in higher-risk patients.

In terms of imaging guidance for PCa FT, US or MRI may be utilized, and each modality presents benefits and drawbacks. Overall, MRI guidance enables more effective targeted therapy and normal tissue preservation (21). Energy sources for FT include HIFU, high-intensity directional ultrasound, cryoablation, irreversible electroporation, and laser ablation, among others (22). This article reviews the treatment approaches and techniques, as well as oncologic and functional outcomes of MRI-guided minimally invasive FT for localized PCa.

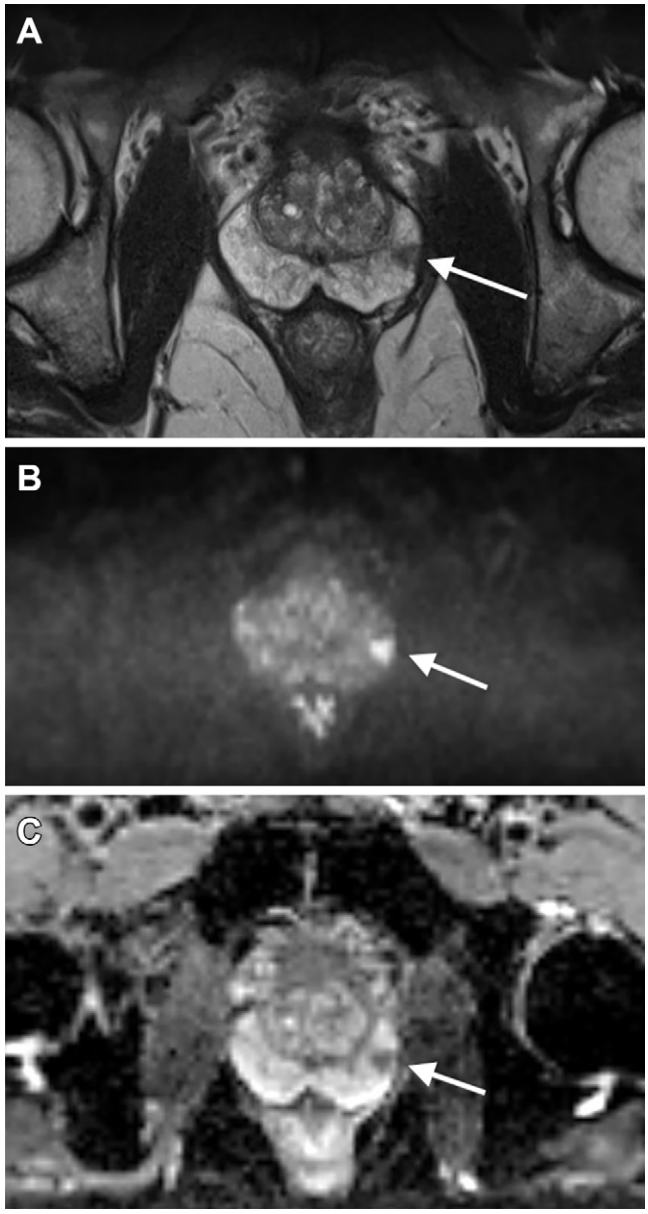

Figure 1: Multiparametric MRI (mpMRI) of the prostate prior to MRI-guided focal laser ablation (MRgFLA). mpMRI scans demonstrate a suspicious lesion (arrow) in the prostate apex left peripheral lateral and anterior zone that is **(A)** hypointense on the T2-weighted scan, **(B)** hyperintense on the diffusion-weighted (b = 1600 sec/mm^2) scan, and **(C)** hypointense on the apparent diffusion coefficient scan. The lesion measured less than 15 mm (Prostate Imaging Reporting and Data System, or PI-RADS, category 4). No other suspicious lesion was seen in the prostate at mpMRI. No extraprostatic extension, neurovascular bundle invasion, or seminal vesicle involvement was seen. Staging imaging workup was negative for metastasis. MRI-guided biopsy demonstrated prostate adenocarcinoma, grade group 2. The patient subsequently underwent MRgFLA.

MRI versus US Guidance

Minimally invasive FT for localized PCa was first performed under US guidance via transrectal approach with multiple devices approved by the U.S. Food and Drug Administration (FDA) (Ablatherm Integrated Imaging and Focal One, EDAP Technomed; Sonoblate HIFU, Sonoblate). However, MRI guidance has emerged as an alternative method performed via a transrectal, transurethral, or transperineal approach. MRI guidance presents some limitations, including a higher cost, greater resource utilization, and a need for dedicated expertise. US is more portable and more familiar to urologists (14). Reported median "magnet" treatment times (MRI to recovery room) for MRI-guided FT are also higher (256 minutes) (14) compared with US-guided FT (<120 minutes) (17,23,24).

On the other hand, MRI guidance presents several advantages over US guidance for FT. Improved localization of tumor in three planes reduces overall ablation volumes, leading to decreased

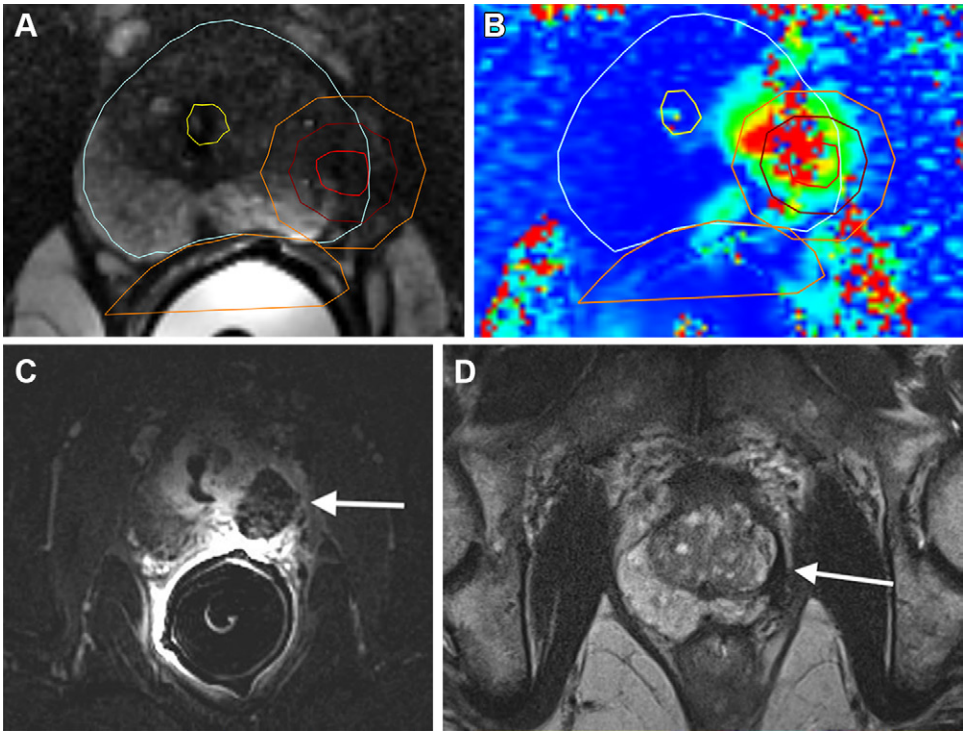

Figure 2: MRI-guided focal laser ablation of grade group 2 prostatic adenocarcinoma. **(A)** Axial MRI scan obtained during MRI-guided focal laser ablation shows the contoured rectal wall (lower orange contour), urethra (yellow), prostate margin (blue), region of interest for treatment (bright red), and 5-mm (dark red) and 10-mm (orange) margins surrounding the treatment zone. **(B)** Map from MRI thermometry obtained during treatment depicts the temperature, with heat deposition color coded. The hottest to coldest temperatures are shown in red, yellow, green, and blue. **(C)** Axial contrast-enhanced MRI scan obtained immediately after treatment shows the devascularized ablated volume (arrow). **(D)** Axial T2-weighted MRI scan at 24 months after ablation shows involution and volume loss (arrow) in the prostate apex left peripheral zone. Targeted biopsy of the treatment zone and systematic biopsy of the remainder of the gland were negative for malignancy.

adverse effects and a faster recovery time (25,26). Furthermore, MRI thermometry enables real-time feedback and modification to optimize temperatures for tissue ablation (14). Following FT, MRI can be used to assess the ablation zone with dynamic contrast-enhanced imaging to identify nonperfused tissue volumes (14). Of note, while MRI helps accurately localize areas of disease, it may lead users to underestimate the total extent; thus, margins of 8–9 mm surrounding the MRI-visible tumor have been suggested for successful FT (27,28). Overall, the advantages of MRI guidance in terms of precise tissue targeting suggest that it may be a more effective option than US guidance (29).

MRI-guided High-Intensity Ultrasound

High-intensity ultrasound, including HIFU and high-intensity directional ultrasound, represents one of the energy sources used for MRI-guided FT of localized PCa. It uses acoustic energy produced by piezoelectric transducers to thermally ablate tissue (21,26,30). Temperatures above 55°C are targeted for a period of a few seconds to establish coagulative tissue necrosis without significantly affecting the surrounding tissue (31,32). Multiple sonications (ie, energy deposition into tissue) are performed, with pauses in between to limit heat accumulation and injury to surrounding tissue (21,33).

There are two FDA-approved MRI-guided high-intensity ultrasound devices: a transrectal device utilizing HIFU (Exablate 2100; Insightec) and a transurethral device utilizing high-intensity directional ultrasound (TULSA-PRO; Profound Medical). Although both devices utilize focused ultrasound as the energy source to thermally ablate the prostate gland, their techniques differ.

Transrectal MRI-guided focused ultrasound (MRgFUS) utilizes an endorectal phased-array ultrasound transducer consisting of 1000 elements operating at 2.3 MHz (frequency) and 30 W (power) (34,35). During treatment planning, T2- and diffusion-weighted images are obtained, and the prostate gland, tumor site, urethra, neurovascular bundle, and rectal wall are manually contoured. A 10-mm margin is incorporated beyond the MRI-visible tumor targeted for treatment, where possible; attention should be given to surrounding sensitive structures, including the rectal wall, external sphincter, and bladder wall (36). The prostatic urethra may be included in the treatment area, if necessary, as it may grow a new epithelial lining over time (36). The bladder is continuously drained throughout the procedure with a urinary catheter, or a suprapubic catheter if the urethra is included in the treatment plan. Degassed water (14°C) fills the endorectal probe for protective rectal cooling, and to eliminate air within the treatment path (36). Subtherapeutic sonications are initially administered to confirm the target, followed by multiple consecutive, overlapping therapeutic sonications for tissue ablation (35). MRI thermometry is utilized during thermal ablation to provide real-time temperature feedback for the treated area and to ensure that tissue-ablative temperatures are achieved (35). Postablation dynamic contrast-enhanced MRI is used to confirm the nonviability and devascularization of the treatment area (34).

MRI-guided transurethral ultrasound ablation (MRgTULSA) utilizes a rigid ultrasound applicator that incorporates 10 independent ultrasound transducers in a linear array (37). The transducers emit high-intensity ultrasound energy in a directional manner, rather than a focal manner as seen with MRgFUS, directly into the prostate (37). This allows the high-energy beams to interact with a larger volume of tissue to reduce overall treatment times and produce more consistent thermal ablation, making timely whole-gland treatment an option for patients with multifocal disease (37). Similar to MRgFUS, MRgTULSA utilizes MRI for PCa localization, as well as MRI thermometry

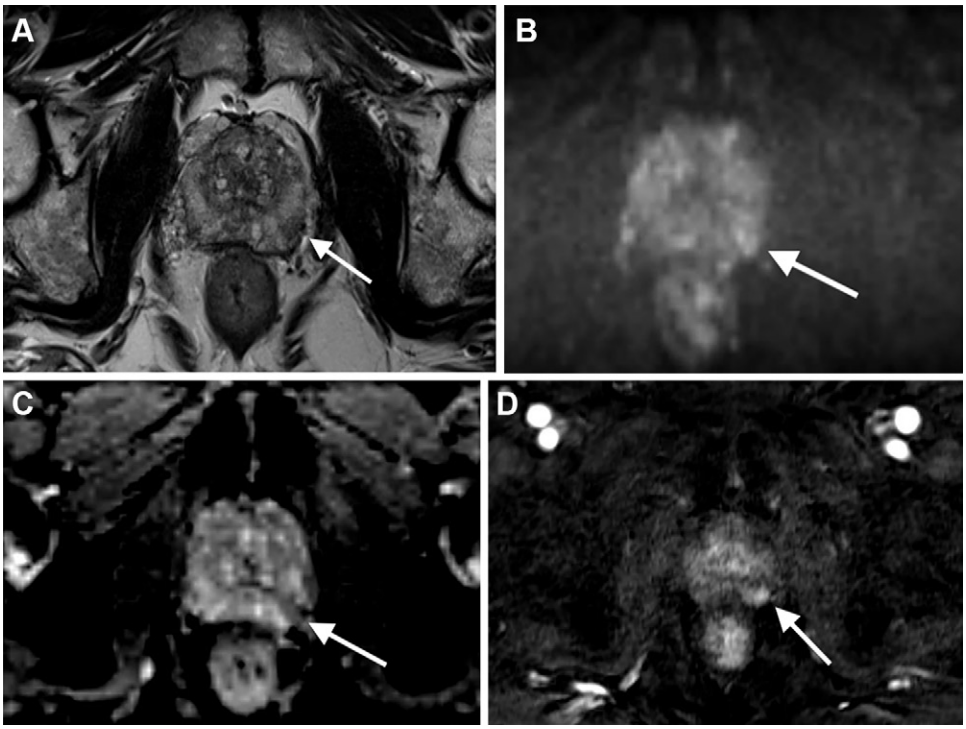

Figure 3: Multiparametric MRI (mpMRI) of the prostate prior to transrectal MRI-guided focused ultrasound (MRgFUS). mpMRI scans demonstrate a suspicious lesion (arrow) in the mid prostate left posterolateral peripheral zone measuring less than 15 mm that was **(A)** hypointense on the T2-weighted scan, **(B)** hyperintense on the diffusion-weighted scan, and **(C)** hypointense on the apparent diffusion coefficient scan, with **(D)** early enhancement on the dynamic contrast-enhanced sequence, consistent with a Prostate Imaging Reporting and Data System, or PI-RADS, category 4 lesion. No other suspicious lesions were seen in the prostate at mpMRI. No extraprostatic extension, neurovascular bundle invasion, or seminal vesicle involvement was seen. Staging imaging workup was negative for metastasis. MRI-guided biopsy demonstrated prostatic adenocarcinoma, grade group 3. The patient subsequently underwent MRgFUS.

(Movie) (38). During MRgTULSA, the ultrasound applicator is positioned within the prostatic urethra. A safety margin of 3 mm between the ultrasound applicator and the sphincter at the prostate apex is generally advised (37). A suprapubic catheter is placed prior to the procedure for continuous bladder drainage and to limit prostate gland movement during treatment (37). During the procedure, high-intensity ultrasound energy is delivered into the target prostate volume by rotation of the ultrasound applicator, with simultaneous MRI thermometry (38). Rectal and urethral cooling is performed throughout the procedure (22,38). Posttreatment dynamic contrast-enhanced MRI is performed to assess the nonperfused treatment area (37). The suprapubic catheter is usually left in place for up to 2 weeks after the procedure to limit acute urinary retention secondary to edema from thermal injury (37).

MRI-guided Focal Laser Ablation

MRI-guided focal laser ablation (MRgFLA) (Visualase, Medtronic; Tranberg Thermal Therapy System, Clinical Laserthermia Systems—both FDA-approved devices) of PCa may be performed via transperineal or transrectal approach (39–41). Usually, a 15-W, 980- or 1063-nm diode laser is utilized for ablation, and real-time monitoring is performed with MRI thermometry (Fig 5) (41–43). Each laser applicator achieves an ablation diameter of 10–15 mm; multiple applicator positions are required for successful tumor ablation with adequate margins. Bladder catheterization is performed for continuous drainage during the procedure. The prostate gland, tumor target, rectal wall, and urethra are manually contoured on T2-weighted images obtained at the start of the procedure. Initially, a coaxial catheter with an MRI-compatible titanium obturator is inserted transperineally or transrectally under MRI guidance to the target region (39,41). The titanium obturator is then replaced with an optical fiber with a 10–15-mm cylindrical diffusing tip (39,41). Initially, subtherapeutic power is applied at 3 W to ensure correct positioning of the applicator, followed by higher tissue-ablative energies confirmed with real-time MRI thermometry (39,41,43). Once the desired volume of tissue ablation is achieved, postablation MRI is performed (44).

MRI-guided Cryoablation

Cryoablation utilizes a freeze-thaw cycle; fast freezing and slow thawing are performed to achieve the most efficient ablation, with a target low temperature of −40°C (45). Although immediate cell damage occurs, the main mechanism of cell death is delayed vascular injury (45). An MRI-compatible cryoablation system (Visual Ice, Boston Scientific—FDA-approved device) is used with a transperineal approach under real-time MRI guidance using a template grid (46–48). A rectal balloon and urethral warming catheter are inserted to protect these structures (47,48). When the correct positioning of the cryoneedle or cryoneedles has been confirmed with multiplanar MRI sequences, two freezing cycles lasting 10 minutes are performed, separated by 2-minute passive and 1-minute active thaw intervals (46,47). Continuous T1-weighted gradient-echo MRI monitoring is used, with the cryoablation "iceball" appearing as an area of signal-intensity void, while the margin surrounding the iceball (reaching cooled but nonfreezing temperatures < 20°C) demonstrates a hyperintense rim (Fig 6) (49). The iceball shape and size can be modified through regulation of gas flow to the cryoneedle until complete coverage of the treatment target is ensured (46–48). Freezing is continued until the iceball covers 5 mm beyond the target margin or until the iceball reaches the urethral or rectal wall (46,47). Following the final thaw period, the cryoneedles are removed and postablation MRI is performed (46–48,50).

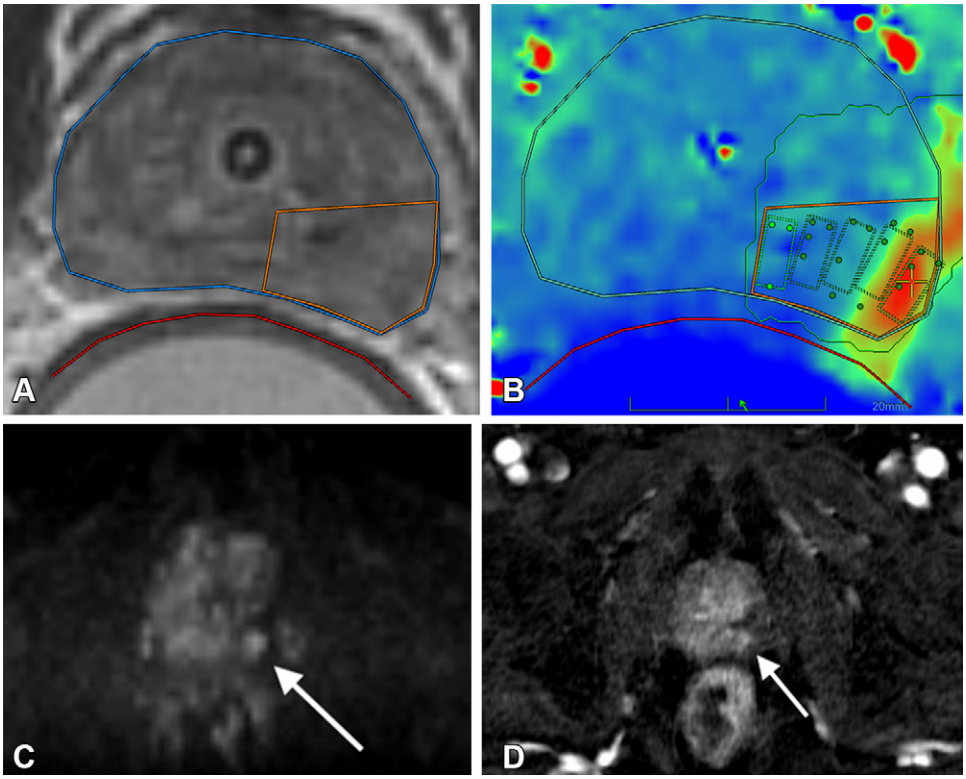

Figure 4: MRI-guided focused ultrasound (MRgFUS) for grade group 3 prostatic adenocarcinoma. **(A)** Axial MRI scan obtained during transrectal-approach MRgFUS ablation shows the rectal wall (red), prostate margin (blue), and the region of interest for treatment (orange). **(B)** Map from MRI thermometry obtained during treatment depicts the temperature, with heat deposition color coded. The hottest to coldest temperatures are shown in red, orange, yellow, green, and blue. Heat deposition is color coded, with red indicating the hottest temperatures and blue indicating the coldest temperatures. Rectangles represent nominal sonication spots, and dots represent each of the prescribed focal points. **(C, D)** At 24 months after ablation, there are imaging findings suspicious for recurrent disease (arrow) at the medial aspect of the ablation zone, including **(C)** focal hyperintensity on axial diffusion-weighted MRI scan, with **(D)** associated early enhancement on axial dynamic contrast-enhanced image. Targeted biopsy of the suspicious area in the treatment zone was positive for disease recurrence, and the patient subsequently underwent salvage radiation therapy.

Table 1: Grade Group and Gleason Score Classification for Prostate Cancer

Grade Group	Gleason Score	Grade Description
1	≤6	Low grade
2	7 (3+4)	Intermediate grade
3	7 (4+3)	Intermediate grade
4	8	High grade
5	9 or 10	High grade

Source.—Reference 4.

Posttreatment Follow-up: Role of PSA Level, mpMRI, and Biopsy

Following FT, using the appropriate test to monitor for residual and/or recurrent disease is essential. For whole-gland therapies for PCa, PSA level is a good predictor of recurrent disease (42,51). In contrast, FT spares normal prostatic tissue, which will continue to produce PSA. This limits the efficacy of PSA monitoring for the follow-up of FTs.

mpMRI follow-up has been recommended at 3–6 months, 12–24 months, and 5 years after FT (52). mpMRI has outperformed PSA monitoring in detecting residual and/or recurrent disease following FT (42,51). A challenge of interpreting mpMRI scans following FT is the lack of a standardized approach to reporting. Although the Prostate Magnetic Resonance Imaging for Local Recurrence Reporting (PI-RR) guidelines have recently emerged, they specifically apply to PCa recurrence after radiation therapy and radical prostatectomy (53,54). Standardized reporting guidelines for using mpMRI to monitor for PCa recurrence following FT are warranted. Moreover, there may be a role for prostate-specific membrane antigen (PSMA) PET in monitoring patients following FT (55,56). Finally, targeted biopsy of the treated zone is recommended within the first year following FT, and additional systematic biopsy is recommended at 12–24 months and 5 years (52). Any suspicious new lesions seen at follow-up mpMRI should also be sampled (52).

Oncologic and Functional Outcomes

Compared with US-guided FTs for PCa, initial experiences with MRI-guided therapies have demonstrated good success rates. This may in part be due to precise tumor targeting, with real-time treatment-zone monitoring using MRI thermometry (57). Multiple safety and feasibility pilot studies have been performed with MRgFUS, MRgTULSA, MRI-guided cryoablation, and MRIgFLA with promising results, which support further investigation of these minimally invasive therapies (13,35,38–40,46,58–62).

Two major prospective, phase II MRgFUS trials have shown that MRI-guided FTs are safe treatment options for low- and intermediate-risk localized PCa (8,14). Ghai et al (14) assessed 44 patients with intermediate-risk PCa (36 with GG2 disease, eight with GG3 disease) treated with MRgFUS. At 5 months, three of the 44 participants had residual disease at targeted biopsy and 41 were free of csPCa. No patients had any csPCa outside the treatment zone (14). At 5 months, erectile and urinary function scores were similar to baseline (14). Ehdaie et al (8) conducted a multicenter trial assessing 101 individuals with intermediate-risk PCa (79 with GG2 disease, 22 with GG3 disease) and found that 96 of 101 individuals at 6 months and 78 of 89 individuals at 24 months had no GG2 or higher disease in the treatment zone. Meanwhile, 77 of 101 individuals at 6 months and 59 of

98 individuals at 24 months had no GG2 or higher disease anywhere in the prostate gland (8). At 24 months, preserved urinary function and a slight decrease in sexual function was noted (8). With MRgTULSA, large-scale phase II trials have assessed only whole-gland ablation (37,63,64), but proof-of-concept FT trials have been promising (13,38,59).

Table 2: Recommended Eligibility Criteria for Prostate Cancer Focal Therapy Candidates

Category and Criteria
Inclusion criteria
Pretreatment assessment with mpMRI and systematic biopsy
Clinical stage T1c to T2a*
MRI-visible lesion up to 15 mm in size
GG2 or GG3 disease
Life expectancy > 5 years
PSA level < 15 ng/mL; PSA level ≥ 15 may be considered with caution and appropriate workup (ie, to exclude metastasis)
Exclusion criteria
Local extraglandular tumor growth (eg, extracapsular extension, seminal vesicle or neurovascular bundle invasion)
Metastases (eg, lymph node or bone)
Multiple sites of clinically significant disease; these would be more amenable to whole-gland treatment approach (eg, MRgTULSA)
Contraindication to MRI or gadolinium contrast agent
Clinically significant disease detected at systematic biopsy, but not visible at MRI for targeted focal therapy
Significant calcifications along the treatment path for MRgFUS and MRgTULSA
Visible tumor > 5 cm from the rectum excludes MRgFUS with transrectal approach as the ultrasonic beam cannot be appropriately focused to attain therapeutic temperatures beyond this distance; these anterior lesions may be more amenable to MRgTULSA (transurethral approach)

Note.—GG = grade group, mpMRI = multiparametric MRI, MRgFUS = MRI-guided focused ultrasound, MRgTULSA = MRI-guided transurethral ultrasound ablation, PSA = prostate-specific antigen.

* MRI-guided therapies may also be used for salvage and whole-gland treatment, which may apply to cases outside the given clinical stages.

Multiple phase II MRIgFLA trials have been performed in patients with low- to intermediate-risk PCa (65–67). Lepor et al (65) assessed 25 individuals who underwent MRIgFLA, of whom 96% had no evidence of PCa at 3-month targeted biopsy, with preserved sexual and urinary function. Eggener et al (66) performed MRIgFLA in 27 patients (23 with GG1 disease, three with GG2 disease, one with GG3 disease). At 3-month targeted biopsy, 26 of 27 individuals were free of PCa at the treatment site. At 12-month systematic biopsy, three of 27 individuals had residual PCa within the treatment zone, and 10 of 27 individuals had residual PCa anywhere in the prostate. Urinary and sexual function were preserved at 12 months (66). Walser et al (67) performed MRIgFLA and/or hemiablation in 120 patients (37 with GG1 disease, 56 with GG2 disease, 27 with GG3 disease). At 12-month MRI, with biopsy of suspicious lesions anywhere in the prostate, 22 of 120 individuals had PCa, with 18 of these individuals having csPCa. Urinary and sexual function were preserved at 12 months (67).

MRI-guided cryoablation has predominantly been assessed as a salvage therapy for recurrent disease, or for whole-gland ablation (46–48,50,68,69). However, Gangi et al (61) performed a pilot assessment of MRI-guided focal cryoablation in 11 individuals with PCa with contraindications to surgery and found it to be a feasible and promising alternative.

The most common complications of FT usually occur within 30 days and include infection (urinary tract infection, epididymo-orchitis), hematuria, and catheter-related issues (pain, discomfort, urethral sloughing) (70). Less common complications include urinary incontinence, erectile dysfunction, ejaculatory dysfunction, penile numbness, and penoscrotal swelling. Rectourethral fistula is a rare complication (70).

Challenges of MRI-guided FT

For successful MRI-guided FT for PCa, appropriate treatment population selection is essential. FT is most likely to succeed in individuals with well-defined, MRI-visible low- to intermediate-risk PCa measuring up to 15 mm (13). Moreover, some studies have reported a high number of patients with csPCa outside the treatment area at follow-up imaging (8). This may, in part, be due to the performance of only MRI-guided targeted biopsy at the time of PCa diagnosis, with omission of systematic biopsies. This practice may be problematic, as a recent trial suggested that forgoing systematic biopsies should be considered only in patients with a prior negative systematic biopsy or in patients with a large area of disease who would not be candidates for FT (71). Some studies have also demonstrated an improvement

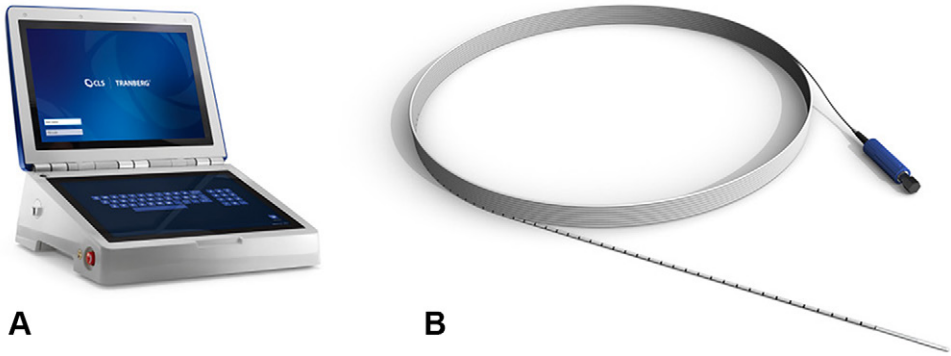

Figure 5: **(A)** Monitoring workstation and **(B)** laser fiber applicator for MRI-guided focal laser ablation.

in the diagnostic performance of PSMA PET/MRI over MRI alone in assessment for PCa, and adoption of this additional imaging test may further benefit the selection process (8,16).

There may also be an added benefit of screening patients for intraprostatic calcifications with CT. Similar to diagnostic US, the passage of HIFU sound waves is limited by dense structures and air. Thus, intraprostatic calcifications in the treatment path may limit MRgFUS and MRgTULSA therapy, resulting in suboptimal treatment (22). Appropriate screening allows for the selection of an alternative energy source in patients with intraprostatic calcifications, such as MRgFLA.

Another potential challenge may be the location of the treatment target relative to the energy source. For example, transrectal MRgFUS may have limited utility in targeting the anterior gland, due to the anatomic distance from the HIFU source with a transrectal approach, resulting in a higher loss of ablative energy (72). In this scenario, MRgTULSA may be ideal, as it would reduce the gap between the energy source and the lesion of interest.

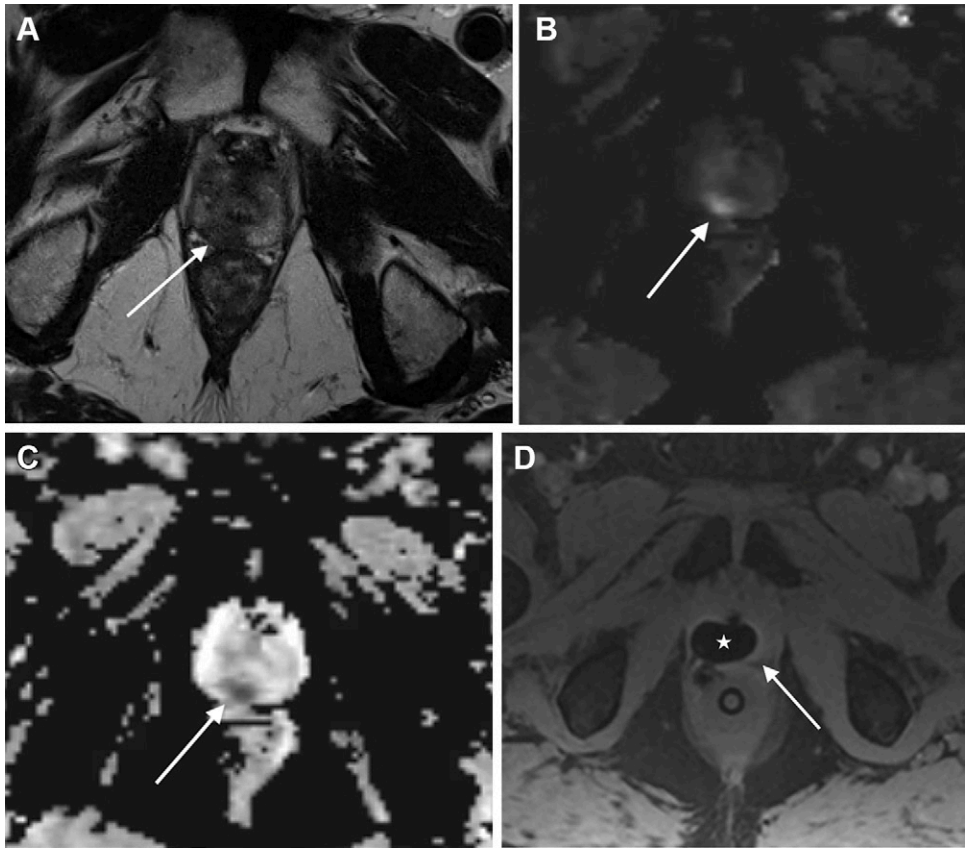

Figure 6: MRI-guided focal cryoablation of grade group 2 prostate adenocarcinoma. **(A–C)** Multiparametric MRI (mpMRI) scans demonstrate a suspicious lesion (arrow) in the prostate base right posteromedial peripheral zone measuring less than 15 mm that is **(A)** hypointense on the T2-weighted scan, **(B)** hyperintense on the diffusion-weighted scan, and **(C)** hypointense on the apparent diffusion coefficient scan, consistent with a Prostate Imaging Reporting and Data System, or PI-RADS, category 4 lesion. **(D)** T1-weighted gradient-echo mpMRI scan from continuous monitoring during MRI-guided cryoablation demonstrates the treatment-zone "iceball" appearing as an area of signal intensity void (★), while the margin surrounding the iceball demonstrates a hyperintense rim (arrow).

Future Directions and Other Uses of MRI-guided FT

Overall, minimally invasive MRI-guided FTs have demonstrated promising results for low-risk and favorable intermediate-risk PCa as a safe and effective treatment with acceptable short-term oncologic profiles and reasonable functional outcomes (8,14,37,63,64). In comparison to US-guided FTs, early results for MRI-guided FTs have demonstrated improved eradication of unifocal csPCa and improved functional outcomes, which may justify the additional cost and resources associated with MRI guidance (8,14,17,23,24,73). Given the indolent nature of PCa, long-term follow-up studies are still needed, including randomized controlled trials comparing the oncologic outcomes of MRI-guided FTs to those of active surveillance and whole-gland therapies. Multiple registered trials are ongoing, which are necessary to support the implementation of MRI-guided FTs in routine PCa care *(https://clinicaltrials.gov)*.

Aside from the use of MRI-guided FTs for PCa treatment at initial diagnosis, their use in other clinical scenarios has also been explored. Multiple studies have assessed MRgTULSA, cryoablation, and MRgFLA as a salvage therapy for recurrent PCa, with promising results (46–48,50,74–76). Early studies of MRgTULSA for the treatment of symptomatic benign prostatic hyperplasia have shown improvements in urinary function and symptom relief (77,78). Future trials will continue to explore the value of MRI-guided therapies in various clinical scenarios *(https://clinicaltrials.gov)*.

Disclosures of conflicts of interest: M.A. Former deputy editor on *Radiology* In Training Editorial Board. **S.G.** No relevant relationships. **M.A.H.** No relevant relationships.

References

1. Nam R, C, Milot L, et al. Prostate MRI versus PSA screening for prostate cancer detection (the MVP Study): a randomised clinical trial. BMJ Open 2022;12(11):e059482.
2. Weinreb JC, Barentsz JO, Choyke PL, et al. PI-RADS Prostate Imaging - Reporting and Data System: 2015, version 2. Eur Urol 2016;69(1):16–40.
3. Eastham JA, Boorjian SA, Kirkby E. Clinically localized prostate cancer: AUA/ASTRO guideline. J Urol 2022;208(3):505–507.
4. Epstein JI, Egevad L, Amin MB, et al. The 2014 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma: definition of grading patterns and proposal for a new grading system. Am J Surg Pathol 2016;40(2):244–252.

5. Alabousi M, Salameh JP, Gusenbauer K, et al. Biparametric vs multiparametric prostate magnetic resonance imaging for the detection of prostate cancer in treatment-naïve patients: a diagnostic test accuracy systematic review and meta-analysis. BJU Int 2019;124(2):209–220.
6. Carroll PH, Mohler JL. NCCN guidelines updates: prostate cancer and prostate cancer early detection. J Natl Compr Canc Netw 2018;16(5S):620–623.
7. Mohler J, Bahnson RR, Boston B, et al. NCCN clinical practice guidelines in oncology: prostate cancer. J Natl Compr Canc Netw 2010;8(2):162–200.
8. Ehdaie B, Tempany CM, Holland F, et al. MRI-guided focused ultrasound focal therapy for patients with intermediate-risk prostate cancer: a phase 2b, multicentre study. Lancet Oncol 2022;23(7):910–918.
9. Hoffman KE, Penson DF, Zhao Z, et al. Patient-reported outcomes through 5 years for active surveillance, surgery, brachytherapy, or external beam radiation with or without androgen deprivation therapy for localized prostate cancer. JAMA 2020;323(2):149–163.
10. Wallis CJD, Zhao Z, Huang LC, et al. Association of treatment modality, functional outcomes, and baseline characteristics with treatment-related regret among men with localized prostate cancer. JAMA Oncol 2022;8(1):50–59.
11. Morash C, Tey R, Agbassi C, et al. Active surveillance for the management of localized prostate cancer: guideline recommendations. Can Urol Assoc J 2015;9(5-6):171–178.
12. Hamdy FC, Donovan JL, Lane JA, et al. 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. N Engl J Med 2016;375(15):1415–1424.
13. Ramsay E, Mougenot C, Staruch R, et al. Evaluation of focal ablation of magnetic resonance imaging defined prostate cancer using magnetic resonance imaging controlled transurethral ultrasound therapy with prostatectomy as the reference standard. J Urol 2017;197(1):255–261.
14. Ghai S, Finelli A, Corr K, et al. MRI-guided focused ultrasound ablation for localized intermediate-risk prostate cancer: early results of a phase II trial. Radiology 2021;298(3):695–703.
15. Postema AW, De Reijke TM, Ukimura O, et al. Standardization of definitions in focal therapy of prostate cancer: report from a Delphi consensus project. World J Urol 2016;34(10):1373–1382.
16. Ghai S, Perlis N. Beyond the AJR: MRI-guided focused ultrasound focal therapy for intermediate-risk prostate cancer. AJR Am J Roentgenol 2023;220(4):610.
17. Ahmed HU, Dickinson L, Charman S, et al. Focal ablation targeted to the index lesion in multifocal localised prostate cancer: a prospective development study. Eur Urol 2015;68(6):927–936.
18. van den Bos W, Muller BG, Ahmed H, et al. Focal therapy in prostate cancer: international multidisciplinary consensus on trial design. Eur Urol 2014;65(6):1078–1083.
19. Donaldson IA, Alonzi R, Barratt D, et al. Focal therapy: patients, interventions, and outcomes—a report from a consensus meeting. Eur Urol 2015;67(4):771–777.
20. Lee MS, Moon MH, Kim YA, et al. Is Prostate Imaging Reporting and Data System version 2 sufficiently discovering clinically significant prostate cancer? Per-lesion radiology-pathology correlation study. AJR Am J Roentgenol 2018;211(1):114–120.
21. Zini C, Hipp E, Thomas S, Napoli A, Catalano C, Oto A. Ultrasound- and MR-guided focused ultrasound surgery for prostate cancer. World J Radiol 2012;4(6):247–252.
22. Galgano SJ, Planz VB, Arora S, Rais-Bahrami S. MR-guided high-intensity directional ultrasound ablation of prostate cancer. Curr Urol Rep 2021;22(1):3.
23. Feijoo ERC, Sivaraman A, Barret E, et al. Focal high-intensity focused ultrasound targeted hemiablation for unilateral prostate cancer: a prospective evaluation of oncologic and functional outcomes. Eur Urol 2016;69(2):214–220.
24. Ahmed HU, Hindley RG, Dickinson L, et al. Focal therapy for localised unifocal and multifocal prostate cancer: a prospective development study. Lancet Oncol 2012;13(6):622–632.
25. Siddiqui MM, Rais-Bahrami S, Turkbey B, et al. Comparison of MR/ultrasound fusion-guided biopsy with ultrasound-guided biopsy for the diagnosis of prostate cancer. JAMA 2015;313(4):390–397.
26. Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med 2018;378(19):1767–1777.
27. Priester A, Natarajan S, Khoshnoodi P, et al. Magnetic resonance imaging underestimation of prostate cancer geometry: use of patient specific molds to correlate images with whole mount pathology. J Urol 2017;197(2):320–326.
28. Le Nobin J, Rosenkrantz AB, Villers A, et al. Image guided focal therapy for magnetic resonance imaging visible prostate cancer: defining a 3-dimensional treatment margin based on magnetic resonance imaging histology co-registration analysis. J Urol 2015;194(2):364–370.
29. Tan N, Margolis DJ, Lu DY, et al. Characteristics of detected and missed prostate cancer foci on 3-t multiparametric mri using an endorectal coil correlated with whole-mount thin-section histopathology. AJR Am J Roentgenol 2015;205(1):W87–W92.
30. Jolesz FA. MRI-guided focused ultrasound surgery. Annu Rev Med 2009;60(1):417–430.
31. Simon CJ, Dupuy DE, Mayo-Smith WW. Microwave ablation: principles and applications. RadioGraphics 2005;25(Suppl 1):S69–S83.
32. Napoli A, Anzidei M, Ciolina F, et al. MR-guided high-intensity focused ultrasound: current status of an emerging technology. Cardiovasc Intervent Radiol 2013;36(5):1190–1203.
33. Napoli A, Alfieri G, Scipione R, et al. High-intensity focused ultrasound for prostate cancer. Expert Rev Med Devices 2020;17(5):427–433.
34. Ghai S, Louis AS, Van Vliet M, et al. Real-time MRI-guided focused ultrasound for focal therapy of locally confined low-risk prostate cancer: feasibility and preliminary outcomes. AJR Am J Roentgenol 2015;205(2):W177–W184.
35. Ghai S, Perlis N, Lindner U, et al. Magnetic resonance guided focused high frequency ultrasound ablation for focal therapy in prostate cancer—phase 1 trial. Eur Radiol 2018;28(10):4281–4287.
36. Orihuela E, Pow-Sang M, Motamedi M, Cowan DF, Warren MM. Mechanism of healing of the human prostatic urethra following thermal injury. Urology 1996;48(4):600–608.
37. Chin JL, Billia M, Relle J, et al. Magnetic resonance imaging-guided transurethral ultrasound ablation of prostate tissue in patients with localized prostate cancer: a prospective phase 1 clinical trial. Eur Urol 2016;70(3):447–455.
38. Chopra R, Colquhoun A, Burtnyk M, et al. MR imaging-controlled transurethral ultrasound therapy for conformal treatment of prostate tissue: initial feasibility in humans. Radiology 2012;265(1):303–313.
39. Raz O, Haider MA, Davidson SRH, et al. Real-time magnetic resonance imaging-guided focal laser therapy in patients with low-risk prostate cancer. Eur Urol 2010;58(1):173–177.
40. Lindner U, Lawrentschuk N, Weersink RA, et al. Focal laser ablation for prostate cancer followed by radical prostatectomy: validation of focal therapy and imaging accuracy. Eur Urol 2010;57(6):1111–1114.
41. Mehralivand S, George AK, Hoang AN, et al. MRI-guided focal laser ablation of prostate cancer: a prospective single-arm, single-center trial with 3 years of follow-up. Diagn Interv Radiol 2021;27(3):394–400.
42. Paxton M, Barbalat E, Perlis N, et al. Role of multiparametric MRI in long-term surveillance following focal laser ablation of prostate cancer. Br J Radiol 2022;95(1131):20210414.
43. van Luijtelaar A, Greenwood BM, Ahmed HU, et al. Focal laser ablation as clinical treatment of prostate cancer: report from a Delphi consensus project. World J Urol 2019;37(10):2147–2153.
44. Westin C, Chatterjee A, Ku E, et al. MRI findings after MRI-guided focal laser ablation of prostate cancer. AJR Am J Roentgenol 2018;211(3):595–604.
45. Lodeizen O, de Bruin M, Eggener S, et al. Ablation energies for focal treatment of prostate cancer. World J Urol 2019;37(3):409–418.
46. Woodrum DA, Kawashima A, Karnes RJ, et al. Magnetic resonance imaging-guided cryoablation of recurrent prostate cancer after radical prostatectomy: initial single institution experience. Urology 2013;82(4):870–875.
47. Overduin CG, Jenniskens SFM, Sedelaar JPM, Bomers JGR, Fütterer JJ. Percutaneous MR-guided focal cryoablation for recurrent prostate cancer following radiation therapy: retrospective analysis of iceball margins and outcomes. Eur Radiol 2017;27(11):4828–4836.
48. Bomers JGR, Yakar D, Overduin CG, et al. MR imaging-guided focal cryoablation in patients with recurrent prostate cancer. Radiology 2013;268(2):451–460.
49. Overduin CG, Bomers JGR, Jenniskens SFM, et al. T1-weighted MR image contrast around a cryoablation iceball: a phantom study and initial comparison with in vivo findings. Med Phys 2014;41(11):112301.
50. Bomers JGR, Overduin CG, Jenniskens SFM, et al. Focal salvage MR imaging-guided cryoablation for localized prostate cancer recurrence after radiotherapy: 12-month follow-up. J Vasc Interv Radiol 2020;31(1):35–41.
51. Dickinson L, Ahmed HU, Hindley RG, et al. Prostate-specific antigen vs. magnetic resonance imaging parameters for assessing oncological outcomes after high intensity-focused ultrasound focal therapy for localized prostate cancer. Urol Oncol 2017;35(1):30.e9–30.e15.
52. Tay KJ, Amin MB, Ghai S, et al. Surveillance after prostate focal therapy. World J Urol 2019;37(3):397–407.

53. Panebianco V, Villeirs G, Weinreb JC, et al. Prostate Magnetic Resonance Imaging for Local Recurrence Reporting (PI-RR): international consensus-based guidelines on multiparametric magnetic resonance imaging for prostate cancer recurrence after radiation therapy and radical prostatectomy. Eur Urol Oncol 2021;4(6):868–876.
54. Pecoraro M, Turkbey B, Purysko AS, et al. Diagnostic accuracy and observer agreement of the MRI Prostate Imaging for Recurrence Reporting assessment score. Radiology 2022;304(2):342–350.
55. Farolfi A, Calderoni L, Mattana F, et al. Current and emerging clinical applications of PSMA PET diagnostic imaging for prostate cancer. J Nucl Med 2021;62(5):596–604.
56. Duan H, Ghanouni P, Daniel B, et al. A pilot study of 68Ga-PSMA11 and 68Ga-RM2 PET/MRI for evaluation of prostate cancer response to high-intensity focused ultrasound therapy. J Nucl Med 2023;64(4):592–597.
57. Alabousi M, Ghai S. Magnetic resonance imaging-guided ultrasound ablation for prostate cancer—a contemporary review of performance. Front Oncol 2023;12:1069518.
58. Napoli A, Anzidei M, De Nunzio C, et al. Real-time magnetic resonance-guided high-intensity focused ultrasound focal therapy for localised prostate cancer: preliminary experience. Eur Urol 2013;63(2):395–398.
59. Anttinen M, Mäkelä P, Suomi V, et al. Feasibility of MRI-guided transurethral ultrasound for lesion-targeted ablation of prostate cancer. Scand J Urol 2019;53(5):295–302.
60. Bomers JGR, Cornel EB, Fütterer JJ, et al. MRI-guided focal laser ablation for prostate cancer followed by radical prostatectomy: correlation of treatment effects with imaging. World J Urol 2017;35(5):703–711.
61. Gangi A, Tsoumakidou G, Abdelli O, et al. Percutaneous MR-guided cryoablation of prostate cancer: initial experience. Eur Radiol 2012;22(8):1829–1835.
62. Oto A, Sethi I, Karczmar G, et al. MR imaging-guided focal laser ablation for prostate cancer: phase I trial. Radiology 2013;267(3):932–940.
63. Klotz L, Pavlovich CP, Chin J, et al. Magnetic resonance imaging-guided transurethral ultrasound ablation of prostate cancer. J Urol 2021;205(3):769–779.
64. Nair SM, Hatiboglu G, Relle J, et al. Magnetic resonance imaging-guided transurethral ultrasound ablation in patients with localised prostate cancer: 3-year outcomes of a prospective phase I study. BJU Int 2021;127(5):544–552.
65. Lepor H, Llukani E, Sperling D, Fütterer JJ. Complications, recovery, and early functional outcomes and oncologic control following in-bore focal laser ablation of prostate cancer. Eur Urol 2015;68(6):924–926.
66. Eggener SE, Yousuf A, Watson S, Wang S, Oto A. Phase II evaluation of magnetic resonance imaging guided focal laser ablation of prostate cancer. J Urol 2016;196(6):1670–1675.
67. Walser E, Nance A, Ynalvez L, et al. Focal laser ablation of prostate cancer: results in 120 patients with low- to intermediate-risk disease. J Vasc Interv Radiol 2019;30(3):401–409.e2.
68. De Marini P, Cazzato RL, Garnon J, et al. Percutaneous MR-guided whole-gland prostate cancer cryoablation: safety considerations and oncologic results in 30 consecutive patients. Br J Radiol 2019;92(1097):20180965.
69. Kinsman KA, White ML, Mynderse LA, et al. Whole-gland prostate cancer cryoablation with magnetic resonance imaging guidance: one-year follow-up. Cardiovasc Intervent Radiol 2018;41(2):344–349.
70. Rakauskas A, Marra G, Heidegger I, et al. Focal therapy for prostate cancer: complications and their treatment. Front Surg 2021;8:696242.
71. Deniffel D, Perlis N, Ghai S, et al. Prostate biopsy in the era of MRI-targeting: towards a judicious use of additional systematic biopsy. Eur Radiol 2022;32(11):7544–7554.
72. Huber PM, Afzal N, Arya M, et al. Focal HIFU therapy for anterior compared to posterior prostate cancer lesions. World J Urol 2021;39(4):1115–1119.
73. Guillaumier S, Peters M, Arya M, et al. A multicentre study of 5-year outcomes following focal therapy in treating clinically significant nonmetastatic prostate cancer. Eur Urol 2018;74(4):422–429.
74. Anttinen M, Mäkelä P, Viitala A, et al. Salvage magnetic resonance imaging-guided transurethral ultrasound ablation for localized radiorecurrent prostate cancer: 12-month functional and oncological results. Eur Urol Open Sci 2020;22:79–87.
75. Mäkelä P, Wright C, Anttinen M, Boström PJ, Blanco Sequeiros R. Safety and efficacy of MRI-guided transurethral ultrasound ablation for radiorecurrent prostate cancer in the presence of gold fiducial markers. Acta Radiol 2023;64(3):1228–1237.
76. Magee D, Perlis N, Corr K, et al. Salvage interstitial laser thermal therapy under MRI guidance (MRgFLA) for high-intensity focal ultrasound (HIFU) recurrences: feasibility study. Clin Imaging 2021;76:217–221.
77. Viitala A, Anttinen M, Wright C, et al. Magnetic resonance imaging-guided transurethral ultrasound ablation for benign prostatic hyperplasia: 12-month clinical outcomes of a phase I study. BJU Int 2022;129(2):208–216.
78. Elterman D, Li W, Hatiboglu G, et al. Relief of lower urinary tract symptoms after MRI-guided transurethral ultrasound ablation for localized prostate cancer: subgroup analyses in patients with concurrent cancer and benign prostatic hyperplasia. J Endourol 2021;35(4):497–505.

Dr Mostafa Alabousi is a clinical fellow in abdominal and breast imaging in the University Health Network, University of Toronto, Canada. He received the RSNA Roentgen Resident/Fellow Research Award in 2022. He has a special interest in studying multiparametric versus biparametric MRI use in prostate cancer, as well as MRI-guided focal therapies. Dr Alabousi has served as a deputy editor on the *Radiology* In Training Editorial Board.

Dr Sangeet Ghai is a professor in the Department of Medical Imaging at the University of Toronto and research director of the Joint Department of Medical Imaging at University Health Network–Mount Sinai Hospital–Women's College Hospital. He leads a team in MRI-guided interstitial laser thermal therapy and MRgFUS ablation for prostate cancer. Dr Ghai's primary research focus is prostate imaging and intervention, and he holds the Trachtenberg/Haque Chair in Image Guided Prostate Therapy Research.

Dr Masoom Haider is a professor in the Joint Department of Medical Imaging at the Princess Margaret Cancer Center and Mount Sinai Hospital at the University of Toronto, Canada. His research focuses on multiparametric MRI in prostate cancer and machine learning–based imaging biomarker discovery. Dr Haider is the director of the Radiomics and Machine Learning Lab at the Lunenfeld-Tanenbaum Research Institute and was an inaugural member of the ACR PI-RADS steering committee.