Magnetic Resonance Image–Guided Focal Prostate Ablation

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Semin Intervent Radiol 2016;33:206–216

Abstract

Keywords

- magnetic resonance imaging
- prostate cancer
- ablation
- interventional radiology

Prostate cancer is the most common cancer (other than skin cancer) in American men, with one in seven men being diagnosed with this disease during his lifetime. The estimated number of new prostate cancer cases in 2016 is 180,890. For the first time, imaging has become the center of the search for contained, intraglandular, small-volume, and unifocal disease, and an increasing number of academic institutions as well as private practices are implementing programs for prostate multiplanar magnetic resonance imaging (MRI) as parts of their routine offerings. This article reviews the role of MRI-guided focal prostate ablation, as well as opportunities for further growth in this minimally invasive therapy of prostate cancer.

Objectives: Upon completion of this article, the reader will be able to discuss the role of MRI-guided focal prostate ablation, as well as its current limitations and potential for further growth.

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Prostate cancer is the most common cancer (other than skin cancer) in American men, with one in seven men being diagnosed with this disease during his lifetime. The estimated number of new prostate cancer cases in 2016 is 180,890. With 26,120 estimated deaths from this disease during the same year, prostate cancer ranks as the second deadliest cancer in American men after lung cancer.^{1,2}

Prostate cancer should, however, be viewed as a spectrum of diseases ranging from a very indolent low-risk process to an aggressive high-risk, potentially fatal disease. The likelihood that a “true” low-risk prostate cancer progresses to metastatic disease is very slim. Much more likely, a high-risk cancer has been present and undetected from the beginning.³ Over the past several years, there has been a growing concern that patients with true low-risk prostate cancer are being overtreated. Several randomized controlled trials provided a level-1 evidence of the lack of benefit from radical therapy in patients with low-risk prostate cancer.^{4–6} Miller et al⁷ studied the incidence of initial local therapy among men with low-risk prostate cancer in the United States and found that only 45% of a population of 24,405 patients have received expectant management for their low-risk disease. They quantified the remaining 55% of patients who were treated with radical prostatectomy or radiation therapy as a target population for whom a greater use of conservative approaches may reduce overtreatment and improve the quality of care for their localized prostate cancer.

On the other hand, the current lack of validated selection criteria for active surveillance, the lack of methods to reliably monitor progression and initiate timely interventions, and the anxiety associated with the presence of known untreated

cancer⁸ all contribute to an existing dilemma in the management of low-risk prostate cancer and constitute the grounds for an increasing excitement about the role of focal ablative therapy in this subset of the prostate cancer population.

Pathologic Basis of Focal Therapy

The notion of focal therapy applied to treat a neoplastic process that is notoriously known for its multifocal organ involvement warrants a close understanding of the pathologic landscape of prostate cancer. Several studies have highlighted the concept of “index tumor” in prostate cancer, where many patients with “*pathologically multifocal*” disease can be considered to have a “*biologically unifocal*” disease. Those patients are found to have a dominant focal tumor along with a smaller burden of nondominant tumors that rarely contain higher-grade disease than the main tumor and are therefore not considered the denominators for disease progression and are unlikely to affect the treatment outcome. Eliminating that dominant tumor focus with targeted therapy that spares the rest of the gland is therefore hypothesized to markedly reduce tumor burden and eradicate the likely source of extracapsular tumor extension while potentially reducing morbidity and preserving the sexual, urinary, and bowel function.^{8–12}

These pathologic grounds for focal prostate cancer therapy have, however, been challenged by the lack of reliable means for accurate in vivo mapping of intraprostatic disease. The clinical and systematic biopsy information are typically suboptimal in identifying small volume or unifocal disease⁸ due to the random nature of sampling and the poor performance of transrectal ultrasound (TRUS) guided biopsy techniques in detecting cancers in the anterior and apical gland. The role of imaging in prostate cancer care has long been limited to detecting locally invasive disease and identifying nodal metastases. The commencement of multiparametric magnetic resonance imaging (mpMRI) in the recent few years has exploited the benefits of combining functional information along with high-resolution anatomical scans and resulted in a conceptual shift in the role of imaging in prostate cancer care. For the first time, imaging has become the center of the search for contained intraglandular small volume and unifocal disease, and an increasing number of academic institutions as well as private practices are implementing programs for prostate mpMRI as parts of their routine offerings.

Role of MRI in Candidate Selection for Focal Prostate Ablation

The concept of ablative therapy for focal prostate cancer has evolved from a whole-gland treatment offered for localized cancer to hemiablation of the side of the prostate harboring the tumor, and eventually to selective targeting of the index tumor (or tumors). This evolution mirrors a parallel development of the techniques available for cancer detection and characterization.¹³

A key point to the decision making of ablative therapy is the ability to generate a reliable belief that low-risk, small volume cancer is present and is confined to a certain part(s) of

the gland. This description identifies what most experts agree on as the appropriate candidate who is likely to benefit from focal prostate ablation. The real challenge, however, lies in the question: “How to generate this reliable belief of confined disease?” When the information about cancer grade, volume, and location is derived from a systematic 12-core ultrasound-guided biopsy along with clinical and laboratory assessment, ablative therapy is typically directed to a larger part of the gland (e.g., hemiablation) due to the limitation of the random sampling approach in the presence of a potentially multifocal neoplastic process.

Three-dimensional (3D) pathologic mapping of the prostate was proposed by Barzell and Melamed¹⁴ using transperineal brachytherapy grids to obtain template mapping biopsies of the prostate. This has improved the reliability of identifying true unilateral disease to 45%¹⁵ compared with 22.6%¹⁶ on 24-core TRUS biopsies and has been advocated as a more reliable method for mapping of prostate disease prior to embarking in focal therapy. Transperineal 3D mapping biopsy does, however, entail obtaining a median number of 46 (SD ± 19) core biopsies.

There has been a growing interest in the recent few years in integrating advanced imaging technology, exemplified by mpMRI, in the evaluation paradigm of patients considered for focal prostate cancer ablation. The negative predictive value (NPV) of mpMRI in ruling out clinically significant prostate cancer has been reported at 88 to 100% when systematic biopsy is used as the reference test^{17–21} and at 79 to 89% when transperineal template mapping biopsy is used as the reference test.^{17,22–24} MpMRI is therefore poised to play a crucial role in selecting candidates who are likely to benefit from focal ablation by accurately locating the index lesion(s) and, equally important, by ruling out additional undetected aggressive cancer.

It is important, however, to understand that although mpMRI is currently the best available imaging tool for evaluating patients for focal ablation, the current imaging technology is still not quite optimized. de Rooij and colleagues²⁵ recently published a meta-analysis assessing the diagnostic accuracy of MRI for local prostate cancer staging, using prostatectomy (rather than biopsy) as the reference standard. The analysis covered 9,796 patients included in 75 studies performed between the years 2000 and 2014. The pooled sensitivity and specificity of MRI for overall stage T3 detection were 0.61 and 0.88, respectively.

In addition to its diagnostic value, MRI is being increasingly utilized to improve the yield of biopsies by directing tissue sampling toward focal abnormalities during MRI-guided prostate biopsies. MRI-guided biopsies of cancer-suspicious areas detected on multiparametric prostate MRI have been reported to detect cancer in 37 to 59% of patients with elevated prostate-specific antigen (PSA) level and one or more previous negative TRUS biopsy sessions.²⁶ More importantly, the implementation of MRI-guided biopsy of cancer-suspicious areas has been associated with the detection of predominantly (87–93%) clinically significant prostate cancer,^{26,27} compared with an estimated 56% of clinically significant cancers for repeat TRUS biopsy.²⁸

The author therefore believes that MRI evaluation of patients considered for focal prostate cancer ablation should not only include a high-quality diagnostic prostate mpMRI but also involve direct tissue sampling of cancer-suspicious areas with in-bore MRI-guided biopsy or at least an MRI/TRUS fusion biopsy.

The next layer of challenge is typically related to selecting the proper targets for biopsy in a manner that ensures accurate localization of the index tumor(s) and excludes the presence of additional aggressive disease. There have been continuous efforts to use MRI to assign cancer suspicion levels for various findings in the prostate in a standardized fashion. These efforts have resulted in establishing version 1 of the PI-RADS (Prostate Imaging-Reporting and Data System) guidelines in 2012 by the European Society of Urogenital Radiology (ESUR),²⁹ followed by an updated version 2 in 2015 as a combined effort of the American College of Radiology, ESUR, and the AdMeTech Foundation.³⁰ At the time of writing this article, the updated PI-RADS (version 2) guidelines have been out for less than 6 months and there is no evidence yet available as to which PI-RADS Assessment Categories should or should not be targeted for biopsy. The PI-RADS version 2 document does not include recommendations for management and states that biopsy may or may not be appropriate for PI-RADS Assessment Categories 2 or 3 (i.e., low and intermediate suspicion for cancer).³⁰ In their recently published work, Cash and colleagues³¹ correlated the older PI-RADS (version 1) assessment categories with the results of MRI/TRUS fusion prostate biopsies. They did find that, overall, cancer detection rate (CDR) was strongly correlated with a rising PI-RADS score and also found that CDR for PI-RADS Assessment Categories 2 and 3 were 16% (with 60% rate of significant tumors) and 26% (with 66% rate of significant tumors), respectively.

At the author's institution, patients evaluated for MRI-guided focal prostate ablation are subjected to in-bore MRI-guided biopsies, targeting foci at all levels of cancer suspicion. In fact, acknowledging the current limitations in imaging technology, patients with clearly unifocal disease on MRI do receive random contralateral sampling as well prior to their final approval for focal therapy.

Choice of Focal Ablative Therapy

As the interest in focal ablative therapy for prostate cancer grows, so does the curiosity about the ablation modality best suited for effective control of localized prostate cancer. Currently available ablative modalities for prostate cancer are cryoablation, high-intensity focused/directional ultrasound, laser, and irreversible electroporation (IRE). At the existing level of knowledge with limited expertise and lack of long-term outcome data, there is no sufficient evidence accrued to support the use of one modality versus another for focal ablative therapy. Indeed, the ablative strategies currently offered at various institutions are largely related to device and skill availability rather than established practice guidelines. The efficacy of prostate ablative therapy will likely follow the collected experience with ablative treatments in other body organs, where proper candidate selection, sound

ablative technique, and reliable monitoring of energy deployment proved to be more important factors for favorable outcome than the choice of ablative modality itself.

MRI has been reported to guide cryo, ultrasound, and laser ablations of the prostate gland. There have been no reports so far, to the author's best knowledge, describing the use of MRI to guide prostate irreversible electroporation (IRE) ablation.

Prostate cryoablation has been practiced as a whole-gland treatment under TRUS guidance and without much emphasis on imaging for ablative device placement or treatment monitoring.^{32,33} Limited data are available on the use of MRI guidance during cryoablation or on its use for focal therapy. Gangi et al³⁴ used MRI to place 4 to 7 cryoprobes into the prostate gland, spaced 1 cm apart, via a transperineal approach using the free-hand technique. They performed whole-gland ablations to treat 11 patients with contained multifocal prostate cancer (Gleason scores: 5–8). They reported one case of biochemical failure at 1 month posttreatment. Bomers et al³⁵ reported the results of MRI-guided focal cryoablation performed on 10 patients with locally recurrent prostate cancer after radiation therapy. They used the transperineal template approach to place two to four cryoprobes into the recurrent prostate tumor and applied two freeze–thaw cycles (►Fig. 1). Spacing of cryoprobes was not described. They reported recurrent/residual tumors detected in 2 of 10 patients after 6 months and in a third patient after 12 months. Woodrum et al³⁶ performed MRI-guided cryoablation for recurrent prostate carcinoma on 18 post-radical prostatectomy patients. They used the transperineal grid guidance system to insert the two to eight cryoprobes into the biopsy-proven recurrent cancer nodules within the prostatectomy beds. In the first group of nine patients, the cryoprobes were spaced 1 cm apart and two freeze–thaw cycles were applied. In the second group of nine patients, the cryoprobes were spaced 0.5 cm apart and three freeze–thaw cycles were applied. Group I patients demonstrated an immediate decrease followed by a slow and steady rise in PSA over the course of 15-month follow-up, while group II patients demonstrated an immediate decrease which was relatively stable over the course of 15-month follow-up.

Similar to cryoablation, there is sparse literature data on the use of MRI to guide prostate ultrasound ablation compared with the relative abundance of literature on nontargeted ultrasound ablation.^{37,38} Ghai et al³⁹ reported a small series of four patients who underwent MRI-guided focused ultrasound ablation for focal prostate cancer (Gleason score: 3 + 3 = 6). They used an endorectal focused ultrasound ablation system (ExAblate 2100; InSightec, Haifa, Israel) integrated within a 1.5-T MRI unit (►Fig. 2). They achieved 83% recurrence-free rate at the 6-month follow-up time point. Chin et al⁴⁰ recently reported the results of a phase I multicenter study evaluating MRI-guided transurethral whole-gland ultrasound prostate ablation on 30 patients with low- and intermediate-risk prostate cancer. They used a rigid transurethral high-intensity directional (rather than focused) ultrasound system (TULSA-PRO; Profound Medical Inc., Toronto, CA) integrated with a 3-T MRI system. At

Fig. 1 A 76-year-old man with histopathologically proven prostate cancer recurrence (Gleason score: $3 + 4 = 7$) 16 months after radiation therapy. (a) Axial dynamic contrast-enhanced MR image (36/1.41; flip angle, 14 degrees; temporal resolution, 3.5 seconds). Tumor is located in the right peripheral zone (oval). Prostate is delineated by red line. Images obtained during MR imaging-guided cryoablation. (b) Axial T2-weighted MR image (5,000/107; flip angle, 150 degrees) shows cryoneedles in situ (circles). (c–e) Axial T1-weighted MR images obtained with a volumetric interpolated gradient-echo sequence (4.81/1.96; flip angle, 6 degrees) show growing ice ball (black signal intensity void), which eventually covered entire tumor (f) Axial dynamic contrast-enhanced MR image (36/1.41; flip angle, 14°; temporal resolution, 3.5 seconds) demonstrates no enhancement in treatment area. (Modified with permission from Bomers et al.³⁵)

12-month follow-up, biopsies were positive for clinically significant disease in 9 of 29 patients (31%) and for any disease in 16 of 29 patients (55%).

Laser ablation is a newer modality in the realm of prostate thermal therapy with no much experience reported prior to the era of MRI-guided focal prostate ablation. Preclinical feasibility testing was performed on canine models⁴¹ and human cadavers⁴² that paved the road to subsequent clinical investigations. Raz et al⁴³ published a case study describing an initial experience of two patients with low-risk prostate cancer who were treated with outpatient in-bore MRI-guided focal laser ablation. They used the MRI-guided transperineal template approach. No follow-up data are available from this case study. Subsequently, Oto et al⁴⁴ published their results on nine patients treated with transperineal MRI-guided focal laser ablation for prostate cancer (Gleason score ≤ 7) in ≤ 3 cores limited to one sextant (→ Fig. 3). At 6-month follow-up, MRI-guided biopsy of the ablation zone showed no cancer in seven patients (78%) and Gleason 6 cancer in two patients (22%). Natarajan et al⁴⁵ recently reported their series of eight patients treated with focal laser ablation for Gleason $3 + 4 = 7$ (or less) prostate cancer diagnosed by MR-US fusion biopsy within a single MR-visible lesion (and no GS > 6 elsewhere in the prostate). They used the transrectal prostate access utilizing the Dyna-TRIM system (Invivo Corp, Gainesville, FL). Follow-up MR-US fusion

biopsies performed 6 months after ablation showed evidence of malignancy within the treated area in three of eight patients and within the treatment margin in six of eight patients.

MRI Guidance for Device Placement during Focal Ablative Therapy

Performing minimally invasive image-guided thermal ablation generally entails three distinct processes: (1) guiding the ablative device to the target; (2) confirming placement relative to the 3D geometry of the target; and (3) deploying the ablative energy with the goal of achieving complete tissue necrosis of the tumor along with a rim of adjacent normal tissue.⁴⁶

In contrast to ablations in other parenchymal body organs (e.g., liver or kidney) where CT or ultrasound are usually sufficient to visualize the target tumor and guide the placement of ablative device, MRI guidance represents a necessity for device placement during focal prostate ablation. Technically, MRI guidance can be performed in most body organs using the free-hand technique,^{47,48} which is also applicable for guidance in the prostate gland via the transgluteal approach as shall be discussed later. Most prostate ablations are, however, performed with the target tumor accessed via the transperineal, transrectal, or transurethral approach. For MRI-guided focal prostate ablation, the magnetic field strength used is more important than the availability of a

Fig. 2 A 64-year-old man with biopsy-confirmed Gleason 6 prostate carcinoma. (a, b) Pretreatment axial T2-weighted fast spin-echo MR image (repetition time/echo time [TR/TE], 3,500/116) and corresponding axial apparent diffusion coefficient map (TR/TE, 5,800/73; b values 0, 100, 400, and 800 mm/s²) show well-demarcated visible lesion (arrow) in right medial posterior peripheral zone at midgland level. (c) Dynamic contrast-enhanced subtraction MR image shows increased early nodular enhancement (arrow) at the site of tumor. (d) Intraoperative MR image shows focused ultrasound beam path (blue) overlaid on treatment plan. (e) Thermal map image obtained during treatment shows areas of heat deposition color coded in red (arrow) overlaid on sonication spot. (f) Axial gadopentetate dimeglumine-enhanced subtraction MR image obtained immediately after treatment highlights devascularized ablated volume (arrow) and shows no damage to rectal mucosa or neurovascular bundle. (Reproduced with permission from Ghai et al.³⁹)

wide-bore configuration or the access to other interventional accessories. High-field 3T MRI guidance is indeed preferred in these procedures due to the improved delineation of target lesion(s) leading to more accurate ablative device placement. The simple setup for these procedures renders them applicable virtually in any practice with standard MRI capabilities and facilitates their incorporation into existing workflow paradigms.

In the transperineal approach, the patient is placed in the supine lithotomy position on the MRI table. A needle guide grid/template carrying three fiducial markers (Visualase, Inc., Houston, TX) is placed against the perineum and an MRI scan is performed to localize the grid relative to the prostate target(s) in a manner similar to the earlier concept of MRI-guided breast biopsies. The integrated software application facilitates fiducial localization within the stack of axial scans and calculates the guidance trajectories and appropriate depth of insertion.^{42,49} A transperineal free-hand technique has also been described.³⁴

In the transrectal approach, the patient is placed in the prone position on the MRI table. A rectal needle holder/

fiducial marker is then placed and connected to the rest of the MRI-compatible table-mount system. Preliminary images are obtained to identify the transrectal fiducial line, the target lesion(s), and to calculate the trajectory angles in three planes (►Fig. 4). The actual coordinates have to then be dialed manually. Two commercially available systems are currently available that employ this approach: Dyna-TRIM (Invivo Corp) and Sentinelle (Hologic, Toronto, Canada). Several robotic systems have also been developed for prostate interventions but are not commonly used in clinical settings.^{50–52}

In the author's experience, the transrectal approach works best for deep and anterior tumors, particularly in larger glands.⁵³ It can, however, be challenging when attempting posterior capsular-based prostate neoplasms. Inserting the ablative device through the rectal needle holder inevitably lifts up a fold of the rectal wall against the prostate gland. When the holder is aligned along the tumor trajectory, this rectal wall fold is essentially squeezed between the tip of the needle holder (posteriorly) and the posterior capsular-based tumor (anteriorly). This arrangement precludes a complete

Fig. 3 Images on a 55-year-old man with biopsy-proved prostate cancer with Gleason score of 6 in a single core from left lateral base of peripheral zone of prostate. (a) T2-weighted axial fast spin-echo image through prostate base shows focal hypointense area within left peripheral zone anteriorly (circle), which is indicative of cancer. (b) Apparent diffusion coefficient map through same level shows a concordant focal area of low signal intensity (arrow). (c) MR image demonstrates how prostate cancer is targeted with transperineal grid and software. Green circle (arrow) indicates appropriate hole for insertion of trocar. After a test dose of laser energy, which was sufficient to cause detectable thermal change but insufficient to cause injury, an axial image plane was used to visualize thermal changes and damage estimates during treatment. (d) MR thermography image shows increased temperature in target areas (circle), which are updated every 3–5 seconds. Black pixels in heated region likely indicate artifacts. (e) Axial T2-weighted fast spin-echo image obtained 6 months after ablation but before MR imaging-guided biopsy shows near-complete resolution of lesion (circle). MR imaging-guided biopsy of that location revealed no cancer. (Reproduced with permission from Oto et al.⁴⁴)

ablation of the posterior aspect of the tumor, let alone creating a safety margin, while maintaining the rectal wall integrity.

For those posterior capsular-based tumors, we prefer using the transgluteal approach. In this technique, the patient is placed in the prone position on a wide-bore (ideally 3T) MRI scanner equipped with interventional accessories. A free-hand technique is then used to insert a 14 g MRI-compatible introducing needle into the target tumor under “MR-fluoroscopy” using triorthogonal image plane guidance⁵⁴ to interactively monitor the needle on continuously updated sets of true fast imaging with steady state precession (true-FISP) images. Once the introducing needle position is deemed satisfactory, we then replace the introducer stylet with a laser applicator to conduct the thermal ablation.

The MRI-guided transurethral approach for prostate ablation has been specifically reported with high-intensity ultrasound prostate ablation.^{40,55} The TULSA-PRO system (Profound Medical Inc., Toronto, Canada) is currently an investigational device that involves a rigid ultrasound applicator carrying an array of 10 independent ultrasound transducers. The patient is placed on the supine position on the

MRI table. A suprapubic catheter is inserted to avoid prostate displacement between the treatment planning and execution. The rigid ultrasound applicator is then inserted manually into the urethra. MRI is then used to refine the position of the ultrasound applicator within the prostatic urethra to maintain a 3-mm safety margin between the ultrasound transducers and sphincter plane at the prostate apex.⁴⁰

MRI Monitoring during Focal Ablative Therapy

After the ablative device has been guided into the target tumor/location and its placement has been deemed satisfactory on high-resolution MRI scans, the final phase of the process, that is, deploying the ablative energy, is another task where MRI adds a significant value by titrating the ablation dose and determining the treatment endpoint.

Using MRI to interactively monitor the effect of thermal ablation allows the detection of any area(s) of undertreatment or resistance to thermal damage. The ability to identify these areas and to use MRI to accurately redirect additional treatment represents a significant improvement of image-

Fig. 4 (a) Axial T2-weighted image from multiparametric MR acquired on a 50-year-old man prior to MRI-guided transrectal focal laser ablation. It shows a 1.7-cm left central midgland localized lesion (arrows), pathologically proven to represent a Gleason 3 + 3 = 6 prostate cancer. (b) Posttreatment gadolinium-enhanced T1-weighted image showing the generated laser ablation zone (arrow), replacing the target tumor. Intraprocedural real-time temperature (c) and cumulative damage estimate (d) maps allowing interactive online assessment of the extent of ablation and determination of treatment endpoint.

guided thermal ablation technology in general and certainly a new era of procedural refinement compared with the earlier versions of prostate ablations performed without imaging control. This approach for controlled ablation may not only guard against potential treatment failures but also allow a confident cessation of therapy once the appropriate coverage is achieved and therefore minimize the risk of complications from disproportionately aggressive therapy.

Much of the knowledge available on interactive MRI monitoring during cryoablation is derived from the experience with earlier MRI-guided renal ablations,^{56–58} where MRI was reported to provide reliable visualization of the growing iceball on all pulse sequences. A similar experience has been reported during MRI monitoring of cryoablations of prostatectomy bed recurrences³⁶ and of focal recurrences in native prostates after radiation treatment,³⁵ where the size and shape of the iceball could be crafted by adjusting the gas flow to individual cryoprobes based on interactive monitoring of treatment response to maximize tumor coverage and avoid rectal wall injury. An important limitation of cryoablation monitoring with MRI is that the visualized size of the iceball may represent a slight overestimation of the final

ablation zone size. The visualized leading edge of the iceball during the procedure corresponds to 0°C, indicating a need to extend the visualized iceball margin beyond the desired treatment area to ensure adequate delivery of the lethal isotherms (−4°C) to the tumor border. Experts recommend at least 5-mm margin which may be increased in the vicinity of large vessels, urethral warmers, or other factors that may confound the cooling process.^{59–61}

Temperature-sensitive MRI sequences have been developed to enable direct on-line monitoring of heat deposition^{62–64} and are typically used for interactive treatment monitoring during MRI-guided ultrasound and laser thermal ablation procedures. A commonly used technique is the proton resonance frequency shift method^{65–67} that measures the temperature-induced changes in chemical shift from continuously acquired phase-sensitive images and displays a color-coded thermal map to visually delineate the temperature distribution over the treatment area. The time-varying temperature maps may be used to calculate a thermal dose map⁶⁸ that can be displayed over the magnitude (i.e., anatomic) image featuring the target tumor to facilitate an overall estimate of thermal tissue destruction.

MR imaging can also detect the actual lethal effect of hyper- (or hypo-) thermia on viable tissues rather than measuring the temperature change itself, through detecting the changes in the tissue relaxation parameters that accompany the phase transition from the viable to the necrotic state.^{69,70} The ability of MR imaging to reliably define the extent of thermally induced tissue necrosis using various sources of energy has been repeatedly demonstrated and correlated with histopathologic analysis.^{71–75} The development of tissue necrosis associated with thermal ablation involves several processes at the cellular level, including^{76,77} denaturation, shrinkage, aggregation of cytoplasmic proteins, and increased hydrophobic interactions resulting in the extrusion of water. The latter effect, along with binding between the denatured proteins and any residual free water, most likely represents the underlying cause for the shortening of the T2 relaxation time after thermal ablation, which ultimately leads to the uniform hypointense appearance of ablation zones seen on the T2-weighted (and STIR) images acquired intermittently during the procedure. In the author's experience, this signal change is less conspicuous during prostate ablations compared with other parenchymal organ ablations, but it does allow a crude estimate of the size and configuration of the developing thermal ablation zone and permit the identification of undertreated and thermally resistant foci where additional treatment may be directed.

MR Imaging Follow-up after Focal Ablative Therapy

Follow-up after focal prostate ablative therapy should include mpMRI scans, ideally reproducing the same protocol obtained prior to treatment, and interpreted in conjunction with serum PSA trend analysis.

The MRI appearance and signal characteristics of focal prostate ablation zones generally follow postablation changes in other parenchymal organs. On precontrast T1-weighted MR imaging, the thermal ablation zone may demonstrate a hypointense, isointense, slightly hyperintense, or markedly hyperintense signal. Inevitable hemorrhage occurs within the target tissues during the ablation process. The amount of ablation-related parenchymal hemorrhage appears to correlate with the degree of target tissue vascularity⁷⁷ and is believed to be responsible for the reduction of T1 relaxation time following thermal ablation procedures. These T1-weighted signal changes are usually observed as early as the intraprocedural or immediate postprocedure scans and typically involute gradually over several months following the ablation procedure.

On T2-weighted images, the uniform hypointense appearance of the ablation zone noted during the ablation procedure as described earlier continues to evolve and becomes more conspicuous on the early follow-up scans before it starts to gradually decrease in size with the involution of the ablation zone. The ablative device track(s) is typically seen as a linear high T2-weighted signal within the ablation zone, particularly on the early postablation follow-up scans.

Thermal ablation zones are typically associated with acute inflammatory reaction that encircles the ablation site and

comprises edema, hyperemia, and foci of hemorrhage on histopathologic analysis.^{75,78–81} This inflammatory response presents as a bright rim encircling the area of necrosis on T2-weighted scans and demonstrates enhancement on the postgadolinium T1-weighted scans. The inner margin of this rim is typically sharp, whereas its outer margin usually fades gradually into the adjacent intact tissues.⁸² Although we have previously demonstrated that the extent of actual cell death does eventually extend to the outer margin of the inflammatory rim,⁷⁵ we do use the sharp inner margin as an unequivocal indicator of the definite extent of tissue necrosis to ensure complete treatment of the targeted tumor.

As the thermal ablation zone matures, the surrounding reactive tissue inflammation subsides and starts to gradually be invaded by granulation tissue laid concentrically around the necrotic ablated center. This granulation tissue ring subsequently undergoes active organization resulting in progressive maturation into fibrous tissue in a concentric fashion proceeding from the periphery of the ablation zone toward the center.⁸⁰ On follow-up MRI, these changes result in resolution of the T2 hyperintense rim. Unlike the previously reported gradual resolution over ~3 months following renal ablations,⁸² it has been our experience that this T2 hyperintense reactive rim is soon replaced by a thick T2 hypointense (most likely fibrotic) rim as early as 3 weeks following prostate focal ablations.

Posttreatment and subsequent follow-up scans should not demonstrate any focal hyperperfusion at the ablation site on DCE-MRI. Residual vessel enhancement may, however, be normally seen for several months in cryoablation beds.⁸³ Delayed postgadolinium scans will demonstrate rim enhancement around the thermal ablation zone that is explained during the early postablation period by the enhancing granulation tissue and later by the enhancing mature fibrotic tissue and is seen for extended periods during the follow-up course.

Any pretreatment focal-restricted diffusion on diffusion weighted imaging (DWI) scans should not be identified on the immediate postablation or on any subsequent follow-up scans. Ultimately, the chronic thermal ablation zone involutes into an area of featureless “mummified” coagulated tissue encased by a variable amount of fibrous tissue. The latter may further progress to replace the entire ablation zone, producing a linear, contracted scar and resulting in asymmetric reduction in the overall prostate volume.

Complications and Morbidity after Ablative Therapy

MRI-guided prostate ablative therapy emerges as a generally safe and low morbidity procedure that can be offered on an outpatient basis or with a short hospital stay. The most significant complication reported in the literature was a single case of urethrorectal fistula following MRI-guided whole-gland cryoablation³⁴ that healed on conservative management after 8 weeks. Progressive urine incontinence was reported in three of nine patients who underwent an aggressive protocol of MRI-guided cryoablation to treat prostatectomy bed recurrences.³⁶ Mild

urine incontinence was reported in three of four patients who received MRI-guided transrectal focal ultrasound ablation.³⁹ Mild and moderate urine incontinence was reported in 4 of 30 patients who received MRI-guided transurethral whole-gland ultrasound ablation. Of these, only one patient continued to have mild pad-free incontinence at 12 months.⁴⁰ Erectile dysfunction was reported in 47% of patients who received MRI-guided transurethral whole-gland ultrasound ablation after 1 month. This percentage decreased to 35% after 3 months, 29% after 6 months, and 15% after 12 months.⁴⁰

Additional minor complications reported following MRI-guided prostate ablations include (in decreasing frequency) hematuria, urinary tract infection, urine retention, obstructive micturition, urinary stricture, mild proctalgia, transient dysuria, scrotal pain, focal paresthesia of the glans penis, and epididymitis.^{34–36,39,40,44}

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