Characterization of acute and subacute radiofrequency ablation lesions with nonenhanced magnetic resonance imaging

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BACKGROUND Magnetic resonance imaging (MRI) has the potential to visualize radiofrequency (RF) ablations, which have become the preferred strategy for treatment of many arrhythmias. However, MRI patterns after RF ablation have not been well investigated.

OBJECTIVE The purpose of this study was to define the characteristic appearance and the effect of time and energy on noncontrast-enhanced MRI of RF ablation.

METHODS Using a power-controlled, cooled-tip ablation system, RF ablation lesions (5–50 W for 45 seconds) were created on the right ventricular epicardium in 10 mongrel dogs. T1- and T2-weighted MR images were obtained during 12-hour follow-up and compared with gross anatomy and histopathology.

RESULTS Lesions were successfully visualized with T2- and T1-weighted images 30 minutes to 12 hours after RF ablation. T2 images were more consistent and displayed a characteristic ellipsoid, high-signal core (contrast-to-noise-ratio [CNR] = 18.9 ± 8.4) with a surrounding 0.5-mm low-intensity rim that on histopathology corresponded to the central tissue necrosis and the transition zone, respectively. T1 images showed a less remarked increase in signal intensity (CNR = 9.6 ± 7.4) without a surrounding rim. Lesion size and appearance were well defined and unchanged during the 12-hour follow-up (analysis of variance). CNR was independent of applied RF energy and allowed accurate assessment of RF ablation at all time points (r = 0.87 and r = 0.83 for T2 and T1 images, respectively). Transmurral lesions, interstitial gaps, and intrallesional pathology could be reliably predicted in >90%.

CONCLUSION Noncontrast-enhanced MRI allows accurate assessment of RF ablation and its intrallesional pathology during 12-hour follow-up. This finding confirms a possible role of MRI in guiding and evaluating RF application during electrophysiologic ablation procedures.

KEYWORDS Catheter ablation; Magnetic resonance imaging; Ablation lesion; Electrophysiology; Arrhythmia

Introduction

Over the last two decades, radiofrequency (RF) ablation has become first-line therapy for many cardiac arrhythmias, including atrioventricular nodal reentrant tachycardia, atrial flutter, and accessory pathway–mediated arrhythmias.1

As ablation protocols have become increasingly complex and anatomically based, such as for ablation of atrial fibrillation and nonmappable ventricular tachycardia,2,3 the need for newer imaging technology that can assess the anatomic location and extent of ablation lesions has become evident.3,4 However, currently used guiding tools, such as fluoroscopy and three-dimensional mapping devices, have limited ability to confirm the exact location, presence, and extent of ablation lesions, which are indicators of procedural success.2,5

Over the last 10 years, cardiac magnetic resonance imaging (MRI) has evolved as a standard diagnostic tool for the evaluation of ischemic heart disease6,7 and has been used successfully to guide cardiac interventions, such as right heart catheterization,8 but its application in electrophysiology has been limited. Because heat-related changes in T1 and T2 parameters should allow visualization of the location and extent of ablation lesions within the myocardium,4 MRI has the potential to guide RF ablation, evaluate treatment progress, and reduce radiation exposure. Therefore, the purpose of the study was to establish the role of noncontrast-enhanced MRI in the assessment of acute and subacute RF lesions.

Methods

Animal preparation

Ten mongrel dogs (weight 35–40 kg) were injected with ketamine 10 mg intramuscularly and maintained on 1% to
2% isoflurane gas (Narkomed Draeger, Telford, PA, USA). End-tidal CO₂ as well as ECG leads I, II, and III were monitored throughout the experiment. Vascular access was obtained by percutaneous puncture or cutdown of the right jugular vein. Midline thoracotomy was performed using clinical grade surgical equipment, and the pericardium was removed. Using a 4-mm-tip, 7Fr ablation catheter with an open irrigation system (0.9% normal saline at a flow rate of 5 mL/min), single RF lesions were created along the epicardial surface of the right ventricle (RV) using a clinical RF generator (Atakr, Medtronic, Inc., Minneapolis, MN, USA). Ablation lesions were created in a linear interrupted fashion using a power-controlled mode at 5, 10, 20, 30, 40, and 50 W for 45 seconds each. All ablation sites were >2.5 cm from any epicardial fat deposits. After the ablation, the animals were closely monitored hemodynamically, and the live animals were transported to the MRI scanner without closing the thoracotomy. All animal protocols were reviewed and approved by the Animal Care and Use Committee at the Johns Hopkins University and conformed to the guidelines published in the “Position of the American Heart Association on Research Animal Use.”

Imaging protocol
MRI was performed using a 1.5-T magnetic resonance scanner (Signa XL, GE, Waukesha, WI, USA) using a standard surface phase-array coil. First, the correct imaging plane of the ablation lesions was identified with standard T1- and T2-weighted scout images. Continuous long-axis images were obtained in the area of RF ablations with 3-mm slice thickness at 30 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, and 12 hours after RF ablation with a T2-weighted fast spin-echo sequence (TR = 1,200 ms, TE = 68 ms, echo train length = 32, field of view = 18 cm, readout bandwidth = 62.5 kHz, 512 × 256 matrix, nexus = 5, slice thickness = 3 mm). For comparison, imaging was repeated using an intrathoracic, 3-inch high-resolution coil, which was placed directly over the RV wall.

Similarly, T1-weighted images were acquired along this slice prescription at the same time intervals using a spoiled gradient recall acquisition (SPGR) protocol (TR = 9 ms, TE = 4.3 ms, readout bandwidth = 31.25 kHz, field of view = 20 cm, 256 × 192 matrix, flip angle = 20°, nexus = 1, slice thickness = 3 mm). Animals were monitored and alive during all follow-up imaging sequences. All images were visually inspected to rule out the presence of susceptibility artifacts caused by the air–tissue interface of the open chest preparation.

Postmortem examination
After the experiment, the animals were sacrificed with an intravenous injection of 3M KCl solution. The hearts were excised and sectioned through the RV lesions into slices corresponding to the tomographic MR images. Lesion size, diameter, location, morphology, and transmural extent were measured at autopsy and photographed for later comparison with MR images. Histologic staining with Masson trichrome and hematoxylin–eosin was performed on sections of the thermally damaged tissues and analyzed for global morphologic changes using light microscopy.

Data analysis
Using an offline quantitative analysis package (version 1.53, e-film, Merge Technology, Milwaukee, WI, USA), lesion size, characteristics, and signal intensity were measured directly from the corresponding MR images. The signal-to-noise ratio (SNR) was calculated as the signal intensity of the lesion divided by the standard deviation of the background noise. The contrast-to-noise ratio (CNR) was measured as the signal intensity of lesion minus the signal intensity of the adjacent myocardium over the standard deviation of the background noise.

Lesion parameters at gross examination were measured independently of MR lesion parameters and compared.

Statistical analysis
Changes in lesion size, signal intensity, and heterogeneity during the time course were analyzed and compared between the various energy groups. P < .05 by paired t-test was considered significant (analysis of variance [ANOVA]). Comparisons of the pathologic specimens and the ablation lesions assessed by MRI were performed using linear regression after an adjusted analysis with a generalized estimating equation approach to control for a potential cluster effect. P < .05 was considered significant. Unless noted otherwise, results are reported as arithmetic mean ± SD.

Results
Lesion characteristics and lesion size
In T2-weighted images, the lesions appeared as conus- or oval-shaped areas of high signal intensity (SNR = 73.4 ± 29.6), which were well demarcated compared with the surrounding myocardium (CNR = 18.9 ± 8.4). Identification was further facilitated by the existence of a small rim of low signal intensity (~0.5 mm wide) in >80% of the lesions (Figure 1). In the pathologic specimen, the center with increased signal corresponded to a macroscopically darker inner zone demonstrating coagulation necrosis and an adjacent lighter zone displaying contraction band necrosis. The low-intensity rim seen on MRI correlated to a macroscopically small and darker outward rim that showed interstitial edema and hemorrhage. Lesion size as assessed with MRI increased with the amount of RF energy applied and correlated well with the tissue specimen (r = 0.87, P < .05; Figure 3). T2-weighted images overestimated the lesion size by 0.2 ± 1.5 mm.

In T1-weighted images, RF lesions had a similar cone or oval-like shape. They appeared as areas of high signal intensity compared with the adjacent myocardium (SNR 34.5 ± 26.0), but image quality was less consistent than in the T2-weighted images (Figure 2). The ablation lesions showed CNR = 9.6 ± 7.4 compared with the adjacent myocardium. This high-signal area corresponded to the two central concentric zones on the pathologic specimen with
coagulation and contraction band necrosis. No surrounding rim of low density was seen using the T1 protocols. The lesion size on T1-weighted MR images correlated well with the gross specimen ($r = 0.83$, $P < .05$; Figure 3). Using the SPGR imaging protocol, lesion size was underestimated by 1.1 ± 1.4 mm.

Slice acquisition in T2-weighted protocols required more time (32 vs 13 seconds, $P < .01$), but the higher CNR allowed better and more consistent visualization in the individual experiments.

Use of the 3-inch high-resolution MR coil increased SNR by 46% to 107.5 ± 45.7 ($P < .001$) and CNR by 44% to 27.3 ± 20.7 ($P < .001$) in the T2-weighted images. During the T1-weighted protocols, SNR and CNR increased by 42% and 44% to 48.9 ± 22.8 and 13.8 ± 10.6, respectively ($P < .001$). No changes in imaging characteristics or lesion size were seen when comparing the standard surface phase-array coil and the intrathoracic high-resolution coil.

**Time course**

Over the course of the 12-hour follow-up, the typical appearance of the RF lesions on T2-weighted images remained unchanged, displaying a core of high signal intensity and an adjacent low-intensity rim (Figure 1). CNR and SNR decreased nonsignificantly to 17.4 ± 12.4 (−7.9%) and 68.8 ± 35.9 (−6.2%), respectively (Figure 4). RF lesion size on the MRI did not significantly change over the time course ($P = \text{NS, ANOVA}; $Figure 5$)$.

Similar observations were made for the T1-weighted sequences. The characteristic appearance of RF lesions did not change (Figure 2), and assessment of lesion size did not vary significantly during follow-up ($P = \text{NS ANOVA}; $Figure 5$)$). However, SNR decreased to 29.6 (−14%) and CNR diminished to 8.1 (−16%), which represented a nonsignificant trend ($P = .08$ and $P = .06$, respectively; Figure 4).

![Figure 1](image1.png) Time course of radiofrequency lesions. Shown are 30-W, 40-W, and 50-W epicardial ablation lesions after 30 minutes, 1 hour, 3 hours, 6 hours, and 12 hours of follow-up using T2-weighted magnetic resonance imaging and the corresponding pathologic specimen. EN = endocardium; EP = epicardium; RV = right ventricular wall.

![Figure 2](image2.png) Time course of radiofrequency ablation lesions. Shown are 30-, 40-, and 50-W epicardial ablation lesions at 30 minutes, 1 hour, 3 hours, 6 hours, and 12 hours of follow-up using T1-weighted magnetic resonance imaging and the corresponding pathologic specimen. EN = endocardium; EP = epicardium; RV = right ventricular wall.
Energy dependency and intralesional pathology

As expected, RF lesion size increased with the amount of applied RF energy ($P < .05$; Figure 5). However, SNR and CNR within the RF lesion did not depend on the energy used to create the lesion in either the T2 or T1-weighted protocols ($P = \text{NS ANOVA}$; Figure 4). However, with higher RF energy, the lesion appearance became increasingly heterogeneous, displaying adjacent areas of high and low signal intensity, which was a significant change in the T2-weighted images and showed a trend for the T1-weighted protocols (Figure 6). At pathologic and histologic examination, heterogeneous areas corresponded to regions of necrotic cavity formation and/or intralesional hemorrhage (Figure 7). Location and size of intralesional necrotic cavities correlated well with the pathologic specimen and appeared as areas of increased signal intensity on T2-weighted images and decreased signal intensity on T1-weighted images.

Assessment of transmural extent or intralesional gaps

Transmural extent was assessed with T2-weighted and T1-weighted images in 39 and 27 RF lesions, respectively. All...
10 transmural lesions were correctly identified on T2-weighted images, but two nontransmural lesions appeared transmural on MR images (sensitivity 100%, specificity 93%). SPGR images correctly identified all 20 nontransmural lesions but did not accurately describe two transmural lesions (sensitivity 71%, specificity 100%).

Twenty-nine intralesional gaps were assessed with T2-weighted images, which underestimated the gap by 0.8/1.3 mm compared with the pathologic specimen. T1-weighted images were used to evaluate 23 intralesional gaps and overestimated the gap size by 0.3/1.9 mm.

Discussion
Main findings
The findings of this study suggest that (1) RF lesions have a characteristic appearance and can be visualized with non-contrast-enhanced MRI over a time course of at least 12 hours using T2- and T1-weighted images; (2) ablation size, intralesional gaps, and degree of transmurality can be predicted using T2- and T1-weighted protocols; (3) CNR is independent of applied energy allowing visualization over a wide energy spectrum; and (4) MRI can successfully visualize changes in intralesional morphology.

Noncontrast-enhanced MRI of cardiac RF lesions
RF lesions could be visualized with noncontrast-enhanced MRI during the entire 12 hours of follow-up. This is due to specific changes in the T1 and T2 relaxation parameters, which result from a variety of heat-induced biophysical changes in cardiac tissue, such as interstitial edema, hyperemia, conformational changes, and tissue coagulation. In T2-weighted images, the area of increased signal intensity correlated with the histologic picture of coagulation and contraction band necrosis and is predominantly caused by an increase in unbound proteins representing interstitial edema after tissue damage and hyperemic response. Although not statistical significant, the decrease of signal intensity at the end of the observation period may indicate a gradual resolution of the edema after the acute phase of injury. Heat-related products of hemoglobin, such as deoxyhemoglobin, display decreased signal intensity on T2-weighted images and might be responsible for the low-signal-intensity rim frequently observed in the transition zone.

These findings extend the observations of the only previously published study in which T2-weighted imaging of RF lesions in the RV apex of six mongrel dogs were limited to the first ~20 minutes of the acute phase. Ablation lesions could be visualized after 2 minutes and demonstrated a linear increase in signal intensity up to 1.9 ± 0.4 times greater than baseline after 12 ± 2.1 minutes. In the current study, T2-weighted MRI allowed accurate assessment of RF lesion size at any time point during follow-up and did not significantly change during the course of the study. This is consistent with the findings of Lardo et al., who showed that lesion size obtained by MRI ~20 minutes postablation correlated well with actual postmortem size.

Although two canine series reported MRI of ablations using contrast agents such as gadolinium, the current study is the first to evaluate the visualization of RF lesions using T1-weighted, noncontrast-enhanced MRI. This is of interest because imaging times were significantly less compared with T2-weighted protocols. Ablations appeared as homogeneous areas of increased signal intensity, which correlated well with the pathologic lesion size and did not change significantly during follow-up of 12 hours. The increased signal intensity on T1-weighted images likely reflects changes in T1 relaxation parameters due to configuration changes of the denatured proteins in the necrotic areas as well as the heat-induced formation of methemoglobin from deoxyhemoglobin. However, CNR was decreased in comparison with T2-weighted images, and image quality was less consistent between individual experiments.

Both imaging protocols were able to accurately assess the transmural extent of the lesions and to identify non-ablated gaps between the ablation lesions, which might be useful for noninvasive assessment of complex RF lesions. This would be facilitated by the observation that RF energy over a wide range resulted in the same characteristic appearance in both imaging protocols, enabling its use in a wide variety of ablation procedures.

MRI slightly overestimated the pathologic lesion size on T2-weighted images. This would be consistent with the

![Figure 7](http://example.com/figure7.jpg) Intralesional pathology. Necrotic cavities within high-energy radiofrequency ablation lesions and corresponding pathologic specimen. Typical appearance of intralesional necrotic cavities as areas of increased signal intensity on T2-weighted magnetic resonance images (A) and decreased signal intensity on T1-weighted magnetic resonance images (B), corresponding gross pathology (C), and histology with Masson trichrome stain (D).
hypothesis that unbound proteins in the interstitial edema are responsible for the signal increase as the edema extends beyond the actual necrosis borders in the adjacent, heated, but still viable myocardium. As such, some of the peripheral ablated tissue visualized with T2 protocols may be able to regain electrical conductivity after the healing process is complete. T1-weighted images, on the other hand, slightly underestimated the lesion size. As the increased signal intensity is likely due to denatured protein within the ablation lesion, this may more accurately describe the truly necrotic area of the RF lesion. This difference of the imaging protocols was also reflected in the transmurality and gap measurements and resulted in either high sensitivity or specificity, respectively. This raises the intriguing question of whether specific MRI protocols might be able to differentiate histologic properties of the myocardium (e.g., reversible edema vs permanent necrosis), providing a potential tool for evaluating procedural success and enabling a future application of “MR histology.”

MRI was able to identify and characterize intraleSIONal pathology in this study. When applying higher energy (i.e., >30–40 W), creation of necrotic cavities was frequently noted on the pathologic specimen, which corresponded to areas of heterogeneous signal intensities on MRI (Figures 6 and 7). With sufficiently high-energy delivery, intracellular and interstitial fluid is heated beyond its boiling point, resulting in the creation of gas and steam, which can create intramyocardial cavities and may even suddenly evaporate out of the myocardium. This phenomenon has been described in ultrasound-guided ablation series as “bubbles formation” and may correlate to occasionally audible “pops” during RF delivery in our experiments. Postablation intracellular edema develops, leaving these holes filled with fluid.

Consistent with those findings, we observed that these intraleSIONal cavities displayed an increased signal intensity on T2-weighted images as the unbound protons in water would be mostly responsible for the increased T2 signal intensity. Correspondingly, in the T1 protocols those areas appeared as islets of less signal intensity. As the higher T1 signal of the RF lesion is likely due to the denatured proteins in the ablated area, fluid-filled cavities would be expected to display little or less T1 signal.

MRI of noncardiac RF lesions
Multiple studies have examined the MRI characteristics of RF ablations in noncardiac tissue. However, reports on the appearance of ablation lesions using T1 protocols vary. Naour et al reported decreased signal intensity of 2-hour-old RF ablations in tongue muscle of 10 swine, whereas Oyama et al described isodense properties in 69 lung lesions after 1 day with slight signal increase after 1 week. On the other hand, several other studies reported an increased signal intensity, which is similarly thought to be due to hemorrhage or aproteinaceous material within the RF lesion. Comparison of the MRI with the pathologic preparation demonstrated that T1 images correlated reasonably well with histology (r = 0.69–0.85).

Different imaging characteristics have been described for imaging of ablation lesions with T2-weighted studies. Kim et al described ablations of VX2 carcinomas in rabbit muscle, which appeared as hyperintense on T2-weighted MR images and were surrounded by a 1- to 2-mm-thick rim of higher signal intensity. In RF treatment of liver cancer, Dromain et al reported that most of the areas were hypointense on T2-weighted images, possibly representing a dehydrating effect of RF-induced thermal damage. However, marked hyperintensity found in 14% of the successful ablations might have been due to bilomas or liquefying necrosis. Several other studies reported the appearance of a low-signal center with a high-signal border. Similarly, T2 images correlated reasonably well with pathology (r = 0.62–0.83).

MRI of contrast-enhanced RF lesions
Two studies reported the visualization of RF lesions using delayed enhancement with gadolinium. Lardo et al reported hyperenhancement of the ablation site occurring as early as 1 minute during a 12-minute follow-up of RF lesions in the RV of six mongrel dogs. Lesions correlated well with the pathologic lesion size and achieved a signal intensity of 1.55 ± 0.16 times the preinjection values. In a recent study, we found a characteristic four-phase enhancement pattern reflecting the prolonged wash-in kinetics of gadolinium. Although CNR allowed good delineation of the ablation lesions, contrast-enhanced imaging was unable to further describe the intraleSIONal pathology. Although the contrast-enhanced area likely represents cell necrosis as well, the postinjection change of T1 and T2 parameters renders visualization of histologic processes, such as edema vs necrosis, unreliable.

Study limitations
Several limitations with regard to this study should be considered. Although clinical RF lesions usually are delivered endocardially, ablations in this study were created on the epicardium to allow controlled delivery of a wide range of RF energies and to guarantee lesion development. Although the macroscopic and histologic appearance of the ablation lesions was similar to the lesions described for endocardial ablations and included >50% of the myocardial wall thickness, differences related to factors such as blood supply and cooling effects cannot be excluded.

Because of the experimental design, which included post-RF ablation animal transport and scanner setup, the MRI follow-up did not start until 30 minutes after ablation. Although previous work has suggested that RF lesions can be visualized already minutes after ablation on T2-weighted images, no experience with nonenhanced T1-weighted protocols has been reported. However, given that MRI might be used to evaluate the procedural progress of complex and prolonged procedures, a postprocedural imaging time frame of several hours appears realistic.
Conclusion
The results of this study demonstrate that acute and subacute RF ablation lesions can be reliably evaluated with noncontrast-enhanced MRI. Although three-dimensional mapping devices and image integration have been a significant improvement, none of the currently used modalities can visualize the RF lesions and potentially allow assessment of procedural success. As RF ablations have become increasingly complex and anatomically based, such as for ablation of atrial fibrillation or nonischemic ventricular tachycardia, imaging of ablation lesions may shorten the procedure times and increase safety and treatment success. Different MRI protocols might be able to differentiate between acute ablation results due to reversible surrounding edema and long-term success due to tissue necrosis, as well as assess transmural extent, interlesional gaps, and intraleSIONAL characteristics. With further progress in the emerging field of real-time MR guidance, these assessments potentially could be performed during the ablation procedure.

Additional studies are needed to delineate its clinical applicability in electrophysiology and possibly open another application of MRI in the field of cardiology.

References