Feasibility of Contrast-Enhanced and Nonenhanced MRI for Intraprocedural and Postprocedural Lesion Visualization in Interventional Electrophysiology

Animal Studies and Early Delineation of Isthmus Ablation Lesions in Patients With Typical Atrial Flutter

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Background—Imaging of myocardial ablation lesions during electrophysiology procedures would enable superior guidance of interventions and immediate identification of potential complications. The aim of this study was to establish clinically suitable MRI-based imaging techniques for intraprocedural lesion visualization in interventional electrophysiology.

Methods and Results—Interventional electrophysiology was performed under magnetic resonance guidance in an animal model, using a custom setup including magnetic resonance–conditional catheters. Various pulse sequences were explored for intraprocedural lesion visualization after radiofrequency ablation. The developed visualization techniques were then used to investigate lesion formation in patients immediately after ablation of atrial flutter. The animal studies in 9 minipigs showed that gadolinium-DTPA–enhanced T1-weighted and nonenhanced T2-weighted pulse sequences are particularly suitable for lesion visualization immediately after radiofrequency ablation. MRI-derived lesion size correlated well with autopsy ($R^2=0.799/0.709$ for contrast-enhanced/nonenhanced imaging). Non–contrast agent–enhanced techniques were suitable for repetitive lesion visualization during electrophysiological interventions, thus allowing for intraprocedural monitoring of ablation success. The patient studies in 24 patients with typical atrial flutter several minutes to hours after cavotricuspid isthmus ablation confirmed the results from the animal experiments. Therapeutic lesions could be visualized in all patients using contrast-enhanced and also nonenhanced MRI with high contrast-to-noise ratio (94.6±35.2/111.1±32.6 versus 48.0±29.0/68.0±37.3 for ventricular/atrial lesions and contrast-enhanced versus nonenhanced imaging).

Conclusions—MRI allows for precise lesion visualization in electrophysiological interventions just minutes after radiofrequency ablation. Nonenhanced T2-weighted MRI is particularly feasible for intraprocedural delineation of lesion formation as lesions are detectable within minutes after radiofrequency delivery and imaging can be repeated during interventions. (Circ Cardiovasc Imaging. 2011;4:282-294.)

Key Words: atrial flutter • cardiac electrophysiology • catheter ablation • interventional MRI • MRI

Today, electrophysiological examinations and interventions are usually performed under fluoroscopic guidance. Among the main weaknesses of this imaging technique is the inability to generate sufficient soft tissue contrast. Therefore, these procedures are increasingly complemented by additional imaging modalities, allowing for the acquisition of additional 3-dimensional anatomic information, such as preprocedural MRI and electroanatomic mapping. However, even with the use of such complex and time-consuming additional techniques, the inability to directly visualize therapeutic effects remains, which is one of the main weaknesses in present interventional electrophysiology. Intraprocedural MRI has been proposed as an alternative imaging modality for guiding and monitoring electrophysiological investigations. Magnetic resonance technology provides superior 3-D anatomic and functional information and avoids ionizing...
radiation or iodine contrast agents. Compared with fluorosco-
scopic imaging, MRI potentially offers a broad spectrum of
additional data. Allowing 3-D data acquisition, MRI enables
exact anatomic visualization and precise catheter guidance
to specific target regions, which potentially increases patient
safety. Providing unsurpassed soft tissue contrast, MRI may
also help identifying the arrhythmogenic substrate or even
directly visualize therapeutic lesions after interventional elec-
physiological procedures, as demonstrated before.\textsuperscript{1–8} In-
traprocedural accurate feedback of lesion formation during
therapy could reduce procedural time and patient risk and
increase efficacy of electrophysiological interventions. These
potential advantages position magnetic resonance–guided
electrophysiology uniquely for complex interventions in the
near future.\textsuperscript{9}

Clinical Perspective on p 294

Therefore, the field has been actively working on overcom-
ing the various technical challenges to use MRI for real-time
guidance of electrophysiological interventions. First studies
reported on feasibility of real-time MRI for catheter guidance
in diagnostic electrophysiology\textsuperscript{10} and electroanatomic
mapping with magnetic resonance–based catheter tracking.\textsuperscript{11}

Just recently, even complex electrophysiological interven-
tions such as AV modulation\textsuperscript{12} and isthmus ablation\textsuperscript{13} under
magnetic resonance guidance have been performed using a
magnetic resonance–conditioned electrophysiology setup.

The aim of the current study was to establish intraproce-
dural visualization of therapeutic electrophysiological lesions
in MRI. Various pulse sequences were first tested in a large
animal model. The developed imaging techniques were then
used to visualize therapeutic lesions in patients with atrial
flutter shortly after cavotricuspid isthmus ablation. We antic-

Ablation Protocol for Animal Experiments

Before the magnetic resonance experiments, the animals were
sedated by intramuscular injection of 10 mg ketamine and set to 1%
isoﬂurane. An intravenous line was established, and an 8F Terumo
catheter introducer sheath was inserted in the left jugular vein. With
the animal ventilated by an Oxylog ventilator (Dräger Medical,
Luebeck, Germany) under general anesthesia (midazolam/fentanyl/
rcuronium bromide) in the scanner, the catheter was inserted
through the sheath from the jugular vein under magnetic resonance
guidance using a passive catheter tracking technique. Initially, a
stack of catheter tracking images was acquired 90° to the supposed
catheter direction. An image showing the catheter longitudinally was
then acquired positioning the slice vertically over the catheter, which
was repeated with the catheter approaching to the target to keep it in
plane. A basic diagnostic electrophysiology routine was performed,
including determination of sensing and pacing thresholds in the
atrium and ventricle. In each animal, one predefined region, either in
the right atrium, right ventricular free wall, septum, or coronary sinus
approximately 3 cm behind the ostium, was chosen for ablation to
simulate different interventional approaches and include ablation
lesions in several ventricular and atrial myocardial tissues. The
predefined ablation site was then targeted under magnetic resonance
guidance. Once the catheter tip had reached the desired region, focal
radiofrequency ablation was performed with maximum power of 75
W/60 s and a temperature cut off at 65°C. Several radiofrequency
ablation cycles of 1 minute each were performed. The primary end
point of radiofrequency delivery was a significant reduction (>80%) of
the intracardiac electrogram (IEGM) amplitude. Radiofrequency
delivery was stopped immediately if bradycardia or tachycardia
occurred.

Imaging Protocol for Animal Experiments

MRI was performed at 1.5 T. Pulse excitation used the integrated
radiofrequency body coil, and signal was received with a dedicated
cardiac surface coil, including a custom-made 32-channel surface
coil to improve signal-to-noise ratio (SNR) for visualization of small
atrial ablation lesions.

As previously described, fast non–ECG-triggered images—that is,
using steady-state free precession (SSFP) (echo time, 1.33 ms;
repetition time, 2.69 ms; flip angle, 80°; slice thickness, 4 to 8 mm;
matrix, 168 × 256; total acquisition time, 0.7 seconds) or fast low-
angle shot (FLASH) pulse sequences—were repeatedly acquired to
guide the catheter to the target region using passive catheter
tracking.\textsuperscript{12}

Lesion visualization began directly after radiofrequency delivery
with the catheter still in place, using various experimental and
manufacturer-supplied pulse sequences, most importantly, none-
hanced T2-weighted and contrast agent–enhanced T1-weighted
(inversion recovery) gradient echo, turbo spin-echo, and FLASH
imaging techniques. For contrast agent–enhanced imaging,
gadolinium-DTPA was administered at 0.1 mmol/kg body weight,
unless stated otherwise. High-resolution images were acquired in
diastole and end-diastole, using an ECG trigger module and a
breath-hold technique. Generally, the imaging protocol started with
enhanced pulse sequences, subsequently followed by contrast
agent–enhanced T1-weighted imaging techniques. Gadolinium-
DTPA was injected between 15 minutes and 45 minutes after
ablation, and imaging thereafter was performed at different time
points after administration of the contrast agent (0 to 120 minutes).

After the electrophysiology and magnetic resonance experiments,
the animals were euthanized, and the hearts were excised and
sectioned. Location and extend of the radiofrequency lesion were
determined at gross examination and compared with the findings on
MRI. Lesion size is given as maximum diameter and maximum
depth as assessed by MRI. At autopsy, hearts were sliced parallel to

Methods

The experimental protocol was approved by the local ethics com-
mittee and the governmental animal care and use committee (Regier-
ung von Unterfranken, approval No. 54-2531.01-63/04). Written
informed consent was obtained from all patients on all procedures.

Experimental Setup for Animal Experiments

To establish an applicable intraprocedural imaging protocol, targeted
ablation of selected regions and subsequent lesion imaging was
performed in 9 minipigs weighing 40 to 55 kg. A custom electro-
physiology platform including a custom steerable nonmetallic abla-
tion catheter (7F, bipolar, with 4-mm tip and 2-mm ring electrode)
and custom radiofrequency filters for use in the MRI environment
were used for ablation to prevent unintended interactions of the
electromagnetic fields inherent in MRI technology with the electro-
physiology equipment. The catheter is feasible for passive catheter
tracking techniques. A commercially available electrophysiology
platform (LabSystem Duo, BARD Electrophysiology, Lowell, MA)
and radiofrequency generator were used for electrophysiological
investigations and radiofrequency ablation. Electrophysiology setup/

Technical equipment for the animal experiments have been described
in detail before.\textsuperscript{12}
magnetic resonance acquisition using landmarks as orientation (eg, right ventricular apex or papillary muscle) to allow direct comparison of lesion size acquired by MRI with the measurement results from pathology.

Clinical Studies
After experimental validation of contrast-enhanced and nonenhanced imaging techniques, we explored the use of sequences successfully tested in animals for intraprocedural visualization of radiofrequency lesions in patients after interventional therapy of atrial flutter. All patients were referred to the magnetic resonance scanner 1 to 3 days before ablation therapy, running a basic imaging protocol to investigate heart morphology and function, including T2-weighted imaging but excluding contrast-enhanced imaging techniques due to contrast agent delivery restrictions. Radiofrequency ablation of typical right atrial flutter was then performed using standard techniques and fluoroscopic guidance. A diagnostic 6F electrophysiological catheter was placed in the coronary sinus. In the case of bradycardia, a second diagnostic catheter was placed in the right ventricular outflow tract for backup pacing. Ablation was done with a standard 8-mm-tip ablation catheter (AI Cath black, gold tip, Biotronik, Berlin, Germany). Temperature and power maximum were set to 65°C and 75 W, respectively. The end point of ablation was confirmation of bidirectional isthmus blockade by differential pacing on both sites of the ablation line. All patients were monitored several hours after the procedure. Patients were followed up in the outpatient clinic 3 months after ablation.

Lesion Visualization in Patients After Atrial Flutter Ablation
Patients were imaged as soon as clinically feasible at the physician’s discretion and <24 hours after ablation to assess myocardial damage at 1.5 T, using a Gyroscan ACS NT Intera R12 (Philips Medical, Best, The Netherlands) with the integrated body coil for radiofrequency excitation and a 5-channel cardiac array for signal reception, starting with the nonenhanced imaging techniques. A T2-weighted ECG-triggered turbo spin-echo sequence with a black blood pulse was used for nonenhanced lesion visualization (echo time, 90 ms; repetition time, ~1850 ms; flip angle, 90°; slice thickness, 4 to 8 mm; field of view, ~340 mm; matrix, 236*195; bandwidth, 481). Delayed-enhancement imaging for lesion visualization was starting with a delay of 12 minutes after application of 0.1 mmol/kg body weight gadolinium-DTPA, using a breath-hold ECG-gated inversion prepared 3-D FLASH pulse sequence (echo time, 1.1 ms; repetition time, 2.1 ms; flip angle, 8°; slice thickness, 4 to 10 mm; field of view, ~260 mm; matrix, 256*128; inversion time, 220 to 300 ms). Both short- and long-axis slices were acquired for lesion visualization.

Lesion depth was examined separately at the cavotricuspid isthmus just outside the tricuspid valve (atrial side). This region was selected because the landmark of the connective tissue skeleton of the tricuspid valve could be identified easily. Maximum lesion depth and diameter were measured separately from several measurements in each patient (both contrast-enhanced and non–contrast-enhanced).

Data and Statistical Analysis
Lesion size and signal intensity were quantitatively measured directly from the corresponding MRIs using the scanner system console and Philips ViewForum R6.3. The sequence specific 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 divided by the standard deviation of the background noise. Magnetic resonance lesion size was determined by the maximum outer margins of the lesion contrast enhancement or signal void. Lesion size was then measured ex vivo at gross examination and compared to the results from the magnetic resonance measurements using linear regression. SPSS 18 (SPSS Inc, Chicago, IL) was used for statistical analysis. The Student t test for paired comparisons was used for comparisons between 2 groups/imaging techniques; changes over time were evaluated by repeated-measures ANOVA followed by Greenhouse-Geisser/Huynh-Feldt correction. For comparisons of the multiple imaging techniques, an ANOVA was first used to compare among all groups (with the probability values shown in the top right corner of the graphs), which in the case of significance was then followed by a paired post hoc comparison using Bonferroni-Holm correction. Unless noted otherwise, results are reported as mean ± standard deviation (SD).

Results
Catheter Tracking and Ablation in Animals
Guidance of the catheter to the target ablation region (including the right atrium, right ventricular free wall, septum, and coronary sinus) could be achieved in all animals using short pulse sequences for passive in vivo catheter tracking as described. A representative series of images demonstrating passive catheter tracking is given in Figure 1.

Sensing and pacing testing was successful in all animals. Ablation lesions could be created in 8 of 9 animals, as demonstrated by a decrease in IEGM amplitude. One animal died directly after the beginning of radiofrequency ablation in the right ventricle as the result of ventricular fibrillation.

Assessment of Native T2-Weighted and Delayed-Enhancement T1-Weighted MRI
Intraprocedural magnetic resonance–based lesion visualization was successful in all 8 surviving animals. No catheter-induced artifacts occurred unless the catheter itself caused partial signal void if inside the slide (Figure 1).

From the broad spectrum of contrast agent–enhanced and nonenhanced imaging techniques in use, administration of gadolinium-DTPA allowed for particularly precise lesion visualization directly and several minutes after contrast agent delivery. First-pass hypoenhancement clearly indicating myocardial damage with the catheter still in place after ablation is shown exemplary in Figure 1E and 2B and online-only Data Supplement Movie 1. Delayed hyperenhancement is demonstrated in Figure 3G and 3H. We found advantageous lesion visualization starting MRI 12 minutes after contrast agent injection using a breath-hold ECG-gated inversion prepared 3-D FLASH pulse sequence (echo time, 1.1 ms; repetition time, 2.1 ms; flip angle, 8°; slice thickness, 4 to 10 mm; field of view, ~260 mm; matrix, 256*128; inversion time, 220 to 300 ms). Compared with early/first-pass contrast-enhanced MRI, lesion CNR using delayed-enhancement MRI was >10-fold higher (7.89 ± 1.76 versus 114.66 ± 32.81, P < 0.001), mostly because of a much higher imaging robustness (provided comparable image resolution).

Nonenhanced T1-weighted pulse sequences were also used successfully to visualize radiofrequency lesions directly after ablation (Figure 2A) but provided only relatively poor tissue contrast (CNR, 8.57 ± 1.88 versus 108.59 ± 25.38; P < 0.001, for nonenhancement versus late enhancement in the respective group). Nonenhanced lesion visualization as achieved using a T2-weighted ECG-triggered turbo spin-echo sequence with a black blood pulse is shown exemplarily in...
In Figure 1 and Figure 3. Additional fat suppression further enhanced CNR (54.99 ± 19.90 versus 35.90 ± 12.32, P = 0.003, in sequential imaging) and therefore lesion visibility. The calculated CNR values for lesion visualization using different imaging techniques are summarized in Figure 4A.

Intraprocedural Lesion Mapping in Animals: Spatial and Temporal Development

All lesions could be detected successfully using contrast agent–enhanced T1 contrast as well as using nonenhanced T2 contrast immediately after radiofrequency delivery. Except for the investigations on sequence-specific temporal lesion visualization, which were done using either repetitive T1- or T2-weighted imaging over time, both contrast-enhanced and nonenhanced images were achieved in the first hour after ablation, starting with nonenhanced imaging.

Experiments on temporal development of lesion size showed that lesion size as determined by MRI was not significantly different immediately after ablation and during subacute follow-up but remained almost the same after the initial measurements (Figure 3). Temporal development of lesion size was determined using native T2-weighted imaging sequences. The average lesion size was 31.3 ± 1.6 mm² after 3 minutes, 33.0 ± 1.8 mm² after 5 minutes, 32.3 ± 2.0 mm² after 10 minutes, 33.2 ± 1.7 mm² after 30 minutes, 31.3 ± 1.5 mm² after 60 minutes, and 33.3 ± 1.6 mm² after 360 minutes and therefore did not differ significantly over time (P = 0.277, Figure 4B).

Compared with the corresponding pathological specimen (32.4 ± 7.3 mm²), comparable lesion sizes (maximum length × maximum depth) were observed in the delayed contrast-enhanced T1-weighted images (n = 8, 32.8 ± 5.3 mm², P = 0.75), with a tendency for a slightly larger lesion size in the native T2-weighted images (n = 8, 35.9 ± 6.2 mm², P = 0.006). Linear regression analyses of the lesion diameter measured by MRI showed good agreement of both imaging techniques compared with pathology (r² = 0.709, P = 0.017 for T2 and r² = 0.799, P = 0.007, for T1 LE [late enhancement], Figure 4).
Temporal lesion visibility was also investigated using T1-weighted delayed enhancement protocols. In both atrial and ventricular tissue, not only late-enhancement signal intensity but also visible lesion size decreased over time after contrast agent injection (Figure 3G and 3H). Specifically, 2 hours after injection, mean lesion signal intensity decreased from 1073±93 to 662±114 (P<0.001), but only 775±52 for the lesion center (P=0.02 for SI difference), meaning that small central lesion parts could still be visualized without further contrast agent injection but not the lesion in total (Figure 3H).

Lesion Imaging in Patients
A total of 24 patients were examined. Patient characteristics are given in the Table. Preprocedural MRI showed no morphological specificities at the cavitricuspid isthmus in any patient before ablation therapy using nonenhanced imaging techniques. All patients had atrial flutter and underwent standard radiofrequency ablation therapy to achieve complete bidirectional conduction block of the cavitricuspid isthmus. Ablation details are given in online-only Data Supplement Table 1. In all patients, cardiac MRI could then successfully be performed within 24 hours after ablation of the cavitricuspid isthmus.

Thermal lesions after interventional electrophysiology could be visualized in all patients after ablation with a T1-weighted delayed-enhancement technique (starting MRI 12 minutes after application of 0.1 mmol/kg gadolinium-DTPA) as well as using nonenhanced T2-weighted imaging performed directly before contrast agent delivery. Hyperenhancement in the right atrium at the cavitricuspid isthmus was seen in all these patients after radiofrequency ablation with both contrast-enhanced and nonenhanced MRI. Examples of contrast-enhanced lesion visualization after atrial flutter ablation are given in Figure 5. Nonenhanced lesion visualization after atrial flutter ablation is demonstrated in Figure 6 and Figure 7. Mean SNR and CNR for all patients was higher for T1 LE imaging compared with T2 imaging (P<0.001, Figure 8). T2 CNR values showed higher relative variations compared with T1 LE between the patients, as apparent in the higher relative standard deviation of T2 CNR. Perfusion imaging for lesion visualization was not performed in patients because of lower CNR/resolution and higher susceptibility to image artifacts.

Lesions were found not only at the (atrial) isthmus itself but additionally covering parts of the right ventricular base adjacent to the cavitricuspid isthmus in most cases (Figures 5C, 6, and 7). These ventricular lesions showed a tendency for lower SNR and CNR values compared with the respective atrial ablation (CNR, 94.6±35.2 versus 111.1±32.6, P=0.42 for T1 LE, and 48.0±29.0 versus 68.0±37.3, P=0.012 for T2), which had not been seen in the animal experiments (Figure 8). Lesion depth acquired by both imaging techniques showed good agreement with a trend for higher values using native T2-weighted imaging (r²=0.790, P<0.001 for linear regression analysis, Figure 8C), and excellent agreement for lesion diameter (r²=0.992, P<0.001, Figure 8D). Serial image acquisitions over time in single patients showed an excellent reproducibility for native T2-weighted imaging with only minimum changes in lesion CNR (Figure 8E). Serial image acquisitions using T1 LE adopting only the inversion over time showed a small additional increase in CNR from 15 to 25 and 35 minutes (P=0.003, Figure 8E).

Clinical Investigations: Patient Outcome
In 2 patients, atrial flutter could not be terminated successfully by radiofrequency ablation during the first intervention. The first patient underwent DC cardioversion to establish sinus rhythm; this case is demonstrated in Figure 7. Failure of successful ablation was confirmed through intracardiac ECG tracings, showing the absence of split potentials in the MAP (mapping) catheter when pacing from the coronary sinus as sign of incomplete isthmus block. Postablation imaging with both contrast-enhanced and nonenhanced MRI revealed an
incomplete ablation line with interruption in the otherwise clearly visible hyperintense ablation line (Figure 7A and 7B). After recurrence of a second episode of atrial flutter, the patient again received radiofrequency ablation using irrigated radiofrequency ablation technique. Successful bidirectional isthmus block was confirmed during the electrophysiological study. Subsequently, a continuous ablation line could also be demonstrated in the MRI (Figure 7C) after the second

Figure 3. Temporal development of ablation lesions using nonenhanced T2-weighted and contrast-enhanced MRI. A through C, Lesion visualization after ablation in the coronary sinus. Intraprocedural nonenhanced MRI sequences using black blood T2 contrast show undamaged myocardium in the porcine model before ablation (A) and reveal myocardial damage 3 minutes after ablation in the coronary sinus as hyperintense area (B). C, Epicardial view on the ablation lesion at gross examination. White arrows indicate the ablation area. D through I, Intraprocedural radiofrequency ablation lesion visualization at the interventricular septum (IV) using T1-weighted delayed-enhancement and nonenhanced T2-weighted magnetic resonance techniques. D, Nonenhanced lesion visualization in the ventricular short axis 5 minutes after radiofrequency ablation using a T2-weighted black blood TSE (turbo spin echo) sequence with fat suppression. E, Same lesion and pulse sequence 2 hours after radiofrequency ablation. F, Pathological view on the respective ablation lesion. G, T1-weighted gradient-echo sequence showing the ablation lesion (white circle) at the lower ventricular septum in the long axis 35 minutes after radiofrequency ablation and 12 minutes after contrast agent injection (0.1 mmol gadolinium-DTPA/kg body weight). The catheter is still in place, even though not well visible using this sequence. H, 2 hours after radiofrequency delivery and administration of the contrast agent, visualization of the lesion using the same imaging technique was less prominent because of wash-out of the medium. Small central enhancement is still visible. I, Ablation lesion at the interventricular septum at gross examination. The ablation scar at the lower septum and surrounding edema are visible. Note there is a small thrombus directly in the center of the lesion. RV indicates right ventricle; LV, left ventricle.
intervention. Calculations of this lesion’s signal intensity showed a further signal increase and lower signal variation at the atrial isthmus which had been targeted by reablation (1926±238 after 2nd versus 1253±339 after 1st ablation, \( P < 0.001 \)). Contrarily, signal intensity in the ventricular lesion part that had not been targeted during the second ablation showed a signal decrease (1073±223 versus 1213±142, \( P < 0.001 \)) (Figure 8F).

In a second patient, there was also no complete isthmus blockade as indicated by missing split potentials and MRI. This patient refused further treatment using radiofrequency or cryoablation. All other patients were free of atrial flutter in the postablation 3-month interval (online-only Data Supplement Table 2). Thus, there was a good correlation between bidirectional isthmus block during the electrophysiological study with the findings from the magnetic resonance study.

**Table. Patient Characteristics of the 24 Patients Who Underwent Radiofrequency Isthmus Ablation for Atrial Flutter, Followed by Postprocedural MRI**

<table>
<thead>
<tr>
<th>Patients</th>
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<tbody>
<tr>
<td>Age, y</td>
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</tr>
<tr>
<td>Sex</td>
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<td>Male</td>
<td>12</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
</tr>
<tr>
<td>Disease</td>
<td></td>
</tr>
<tr>
<td>CAD</td>
<td>15</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5</td>
</tr>
<tr>
<td>DCM</td>
<td>4</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>42±13</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
</tr>
<tr>
<td>( \beta )-blocker</td>
<td>21</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>7</td>
</tr>
<tr>
<td>Cycle length of flutter</td>
<td>232±22 ms</td>
</tr>
<tr>
<td>Functional class</td>
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<tr>
<td>NYHA I–II</td>
<td>16</td>
</tr>
<tr>
<td>NYHA III–IV</td>
<td>8</td>
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</table>

CAD indicates coronary artery disease; DCM, dilated cardiomyopathy; LVEF, left ventricular ejection fraction; and NYHA, New York Heart Association.

**Figure 4.** Signal characteristics and correlation of ablation lesion size determined by different imaging techniques in the animal model. A, Comparison of the lesion CNR using different imaging techniques. CNR for ventricular and atrial lesions is shown separately. All values are mean±SD. B, Time course of lesion size (mm²) as visualized using nonenhanced T2-weighted MRI in a minipig. 0 indicates end of radiofrequency ablation. C and D, Linear regression analysis of the lesion diameter as determined using different imaging protocols (contrast-enhanced T1-weighted and nonenhanced T2-weighted MRI), compared with the lesion size measured in the pathological examination.

**Discussion**

**MRI for Guidance of Electrophysiological Interventions**

A major obstacle in ablation procedures is the inability to gain information on the extent of the thermal lesion after delivering radiofrequency energy, although this is crucial to determine the success or failure of the procedure. Especially in case of long linear lesions, the possibility for direct lesion visualization would be helpful to find remaining gaps. We now extended the potential of magnetic resonance–guided electrophysiology, showing that ablation lesions can be directly visualized after ablation in good agreement with anatomic findings, using an animal model of targeted ablation.
with the catheter still in place. Various regions in right atrium, ventricle, and coronary sinus were successfully targeted and ablated in living animals using steerable catheters with real-time magnetic resonance fluoroscopy pulse sequences. The high-resolution images of endocardial anatomy considerably improved targeting and accurate lesion placement (Figures 1 through 3), whereas standard x-ray fluoroscopy, in contrast, generally delivers poor tissue contrast.

Animal Experiments: Procedural Safety and Adverse Events

There is a substantial danger for technical equipment to interfere with the electromagnetic fields inherent in MRI technology.14 Regarding magnetic resonance–guided interventional electrophysiology, there are particular safety concerns regarding unintended catheter heating caused by radiofrequency coupling (which can be difficult to foresee15,16), and electrophysiological device malfunction, for example, through electric interference during imaging. Additionally, magnetic resonance–compatible equipment or specific imaging sequences are warranted to avoid imaging artifacts. Recently, substantial improvements of hardware and software enabled diagnostic10 and even interventional electrophysiology in the MRI environment in animals for the first time.12

Even though to date there still is no electrophysiology setup officially approved for magnetic resonance–guided electrophysiological interventions in patients, there are several groups actively working to overcome the remaining issues. The present animal experiments provide evidence for applicability and safety of magnetic resonance–guided electrophysiological interventions in a clinical setup, including intraprocedural magnetic resonance lesion visualization. One animal of 9 died as the result of ventricular fibrillation. However, this event was directly related to radiofrequency ablation and can therefore not be attributed to the use of MRI. The species-specific high susceptibility of pigs to ventricular tachycardia is well known. No further adverse events occurred in the present study.

MRI for Electrophysiological Lesion Visualization

The current study showed that MRI can visualize acute and subacute ablation lesions not only in an experimental setup but also in patients after cavotricuspid isthmus ablation. Delayed enhancement imaging has been shown to be suitable to detect subacute and chronic lesions with high resolution and good precision.1,2,5–8 Our findings are in good agreement with these reports, now adding evidence that even acute lesions can be successfully visualized with contrast-enhanced MRI both in an experimental and clinical setup. In general, contrast-enhanced MRI is a valuable tool for lesion visualization, being a standard procedure offering relatively easy visualization of ablation lesions with good detectability even of small atrial lesions in patients.7,8 On the other hand, this approach is more suitable for postprocedural imaging and would be problematic in a real-time interventional approach because of limitations in the amount of contrast agent.

Figure 5. Contrast-enhanced lesion visualization in patients after atrial flutter ablation. A, Right ventricular (RV) 2-chamber view in a female patient 45 minutes after ablation of the cavotricuspid isthmus. Delayed enhancement clearly marks the area of ablation (T1-weighted gradient-echo sequence with inversion recovery) 15 minutes after application of 0.1 mmol gadolinium-DTPA/kg body weight. In this case, lesion size is comparably small. Using a slightly increased inversion pulse time compared with conventional late-enhancement techniques allows for better discrimination of the endocardial lesion at the expense of a decreased blood/myocardium contrast. B, Maximum intensity projection of the same lesion allowing for lesion size measurements. C, Ventricular short-axis view in a second patient showing transmural late enhancement at the crossing from the RV to the cavotricuspid isthmus. The lesion was frequently found to reach into the RV basis after atrial flutter ablation. D, Subendocardial late enhancement in the ventricular short-axis view in a third patient. Arrows indicate lesion areas. RA indicates right atrium; Ao, aorta.
delivery and imaging problems if multiple contrast agent boluses are needed. Therefore, nonenhanced imaging is desirable in an interventional approach.

**Contrast-Enhanced Versus Nonenhanced Lesion Visualization**

It has been recently shown in an animal model that exposure of epicardial ablation lesions is even possible with nonenhanced MRI, for example, using T2-weighted pulse sequences, which could be advantageous not only for fast lesion detection but also for lesion characterization. The potential of T2-weighted MRI to detect myocardial injury is particularly well investigated in patients with myocarditis and after myocardial infarction. In our experiments, we were able to detect small lesions of only several millimeters in diameter with good precision 2 minutes after ablation using T2-weighted pulse sequences with a black blood technique and fat suppression. Moreover, in a patient with incomplete isthmus block after ablation as determined by IEGM, we were able to visualize an incomplete ablation lesion line with a non–contrast agent–enhanced imaging technique. This demonstrates the potential of nonenhanced MRI for lesion visualization, even though further efforts are warranted to increase imaging technique robustness, particularly at the desired high spatial resolutions.

In our experience, delayed enhancement imaging using contrast agent generally was more suitable for postprocedural lesion mapping, particularly because of their robustness, whereas nonenhanced T2 imaging techniques are highly advantageous for intraprocedural mapping because they do not rely on time consuming contrast agent washout and can be repeated as often as needed during interventions. Meanwhile, combining several

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**Figure 6.** Nonenhanced lesion visualization in patients after atrial flutter ablation. Demonstration of nonenhanced isthmus ablation lesion visualization in a female patient in the right ventricular 2-chamber view. A, Anatomic overview before isthmus ablation. This isthmus is marked by an arrow. B, Preprocedural T2-weighted black blood gradient echo sequence. Because of the low signal intensity, the isthmus is hardly visible. C, Same pulse sequence 45 minutes after isthmus ablation. The isthmus is well visible, but lesion contrast to surrounding myocardium and discrimination to connective (fatty) tissue is limited. D and E, By using additional SPIR (spectral presaturation inversion recovery) fat suppression, lesion contrast is greatly increased. F, Maximum intensity projection showing the ablation lesion at the cavotricuspid isthmus. The small cavity inside the lesion is the coronary sinus.
MRI techniques (nonenhanced T2, early and late contrast-enhanced T1, perfusion) could be suitable not only to visualize ablation lesions but also to allow for further ablation characterization. During in vivo endocardial ablation the intensity of tissue-catheter contact changes; therefore, usually lesion sites after endocardial ablation are heterogeneous because the targeted tissue is damaged to a different extent. Areas of necrosis, hemorrhage, and edema are in close proximity or even merged. This might result in complex wash-in and wash-out kinetics of contrast agents, which—in combination with changing contrast behavior in nonenhanced imaging—potentially allow for differentiation of temporal from permanent myocardial damage. In our setup, nonenhanced T2 and first-pass T1 contrast delivering gadolinium-DTPA visually revealed slightly different lesion

Figure 7. Visualization of incomplete isthmus block by contrast-enhanced and nonenhanced MRI. A-1, Nonenhanced T2-weighted gradient echo sequence with black blood pulse and fat suppression in a female patient after frustrating cavotricuspid isthmus ablation. Incomplete conduction block after ablation was verified by a lack of split potentials in the IEGM (A-2). The maximum intensity projection reveals an insufficient ablation lesion (solid arrows) with a gap at the cavotricuspid isthmus (dotted arrow). A-3, Lesion close-up. B-1, Inversion recovery delayed-enhancement MRI showing the same lesion. B-2, Maximum intensity overlay of nonenhanced T2 signal and delayed enhancement imaging. Both imaging techniques suggest a gap (dotted arrow) in the ablation line (solid arrows) at the cavotricuspid isthmus (B-3). C-1, Postprocedural nonenhanced T2-weighted gradient echo sequence with black blood pulse and fat suppression in the same patient after the second ablation procedure using a cooled tip ablation technique. C-2, Maximum intensity projection after the second ablation process. Complete conduction block is demonstrated in the IEGM (C-2). The small cavity in the lesion middle is the coronary sinus (C-3). Because the patient had already received 3 doses of contrast agent in different magnetic resonance investigations over a very short period of time before, we did not perform late-enhancement imaging after this second ablation procedure.
patterns (Figure 1). One study has reported on differences in peripheral “delayed enhancement” and central “very delayed” enhancement of ablation lesions, possibly caused by different degrees in myocardial damage. Similarly, in our study, contrast agent washout appeared to be slower in parts of larger lesions, possibly because of the development of central necrosis (Figure 3). The ability to directly visualize temporal myocardial damage would be a major advance in interventional electrophysiology.

Theoretical assumptions suppose changes in lesion size over time as inflammation and healing appear, and this has just recently been reported regarding long-term follow-up of ablation lesions, and also in the short-term follow-up. In contrast, investigations in our setup showed that the visualized lesion size was not significantly changing over time immediately after ablation and during subacute follow-up but remained constant during the first hours after the initial measurements (Figure 3 and Figure 4).

Limitations and Perspective
Only endocardial lesions were investigated in the current setup and therefore the results should not be extended to epicardial lesions, which may show different behavior especially over time because of differences in tissue and perfusion.

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**Figure 8.** Signal characteristics, correlation of ablation lesion size, and signal time course determined by different imaging techniques in patients. A and B, Comparison of the lesion SNR and CNR using different imaging techniques in patients. SNR and CNR for ventricular and atrial lesions are shown separately. All values are mean±SD. C and D, Linear regression analysis of the lesion depth and diameter as determined using contrast-enhanced T1-weighted and nonenhanced T2-weighted MRI. E, Time course of lesion CNR using native and contrast-enhanced MRI in patients over time; 0 minutes corresponds to the contrast agent delivery for the T1 LE imaging. The inversion time was adopted over time. Native T2 imaging was performed before contrast agent delivery. F, Repetitive T2-weighted lesion imaging in a patient before and after 2 ablation procedures at the cavotricuspid isthmus, signal intensity ±SD is shown for the atrial and ventricular ablation site and remote ventricular and atrial myocardium separately. Incomplete conduction block after the first ablation therapy required a second ablation, after which a further increase in atrial but not ventricular signal intensity was found.
characteristics. Furthermore, only lesions from standard radiofrequency ablation were investigated. Based on the results, MRI has proven to be an expedient tool for immediate visualization of therapeutic lesions after radiofrequency ablation. Particularly, nonenhanced MRI has the potential to improve future complex electrophysiological interventions because it is repeatable multiple times during interventions and lesions are visible only minutes after radiofrequency delivery. Further advances in imaging techniques have to be established to use MRI-guided electrophysiological interventions to full capacity. In particular, there is a desire not only for exact visualization but also characterization of ablation lesions, that is, a clear discrimination between permanent ablation lesions and regions with transient cardiac edema. Although MRI guidance of electrophysiological interventions is applicable to all cardiac arrhythmias, it may be particularly well suited for more complex arrhythmias that require the accurate placement of multiple, linearly arranged lesions, with the benefit to facilitate real-time detection (and possibly prevention) of complications. Combining several imaging techniques (eg, adding MRI thermometry) would enable the electrophysiologist to assess additional information that could improve electrophysiological procedures, increasing the success rate while decreasing procedural duration.

Conclusion
Real-time MRI for guidance of interventional electrophysiology is an area of great potential that is expected to further enhance the abilities in interventional approaches of complex arrhythmias. As a further component in solving the remaining technical challenges, the current study provides evidence that intraprocedural MRI is feasible for visualization of acute radiofrequency ablation lesions in an experimental model and subacute lesions in patients directly after ablation therapy of typical atrial flutter. Not only contrast agent–enhanced but particularly nonenhanced imaging techniques are suitable for real-time ablation lesion visualization, allowing for sequential intraprocedural lesion imaging, which could be crucial for the decision on further ablation strategies during interventional electrophysiology.

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Disclosures
Dr Jakob serves as scientific advisor for Siemens; Dr Bauer and Dr Ritter serve as scientific advisors for Biotronik.

References

CLINICAL PERSPECTIVE

To date, the inability to directly visualize ablation lesions during interventions is one of the main shortcomings in interventional electrophysiology. Conventional fluoroscopy provides insufficient soft tissue contrast, limited imaging capabilities of the heart and adjacent organs, and no spatial 3-dimensional information. Therefore, recovery of tachycardia after ablation due to unrecognized incomplete lesions is not uncommon, often resulting in the need for repeat procedures. Furthermore, there is little intraprocedural feedback on possible unintended ablation damage to adjacent organs. MRI has been proposed as a beneficial imaging modality for guiding electrophysiological procedures because it provides excellent soft tissue contrast and allows for 3-dimensional spatial imaging without exposing the patient and investigator to ionizing radiation. Recent reports describe successful MRI guidance of diagnostic electrophysiological investigations and even complex interventions such as AV-node modulation. Other studies have shown potential of MRI to visualize therapeutic lesions after radiofrequency ablation, mostly using delayed-enhancement imaging. The current study shows accurate visualization of ablation lesions in an animal model as well as in patients immediately after electrophysiological interventions. Not only contrast-enhanced but also nonenhanced MRI was feasible for immediate lesion visualization, which enables constant surveillance by repeated lesion imaging during interventions. Combining MRI catheter guidance with the ability to visually characterize myocardium and adjacent structures to discriminate viable tissue from lesions during ablation in real time has the potential to greatly improve safety and procedural success of electrophysiological interventions. Further technical improvements are expected to make real-time magnetic resonance-guided electrophysiological procedures a useful alternative to fluoroscopic guidance, especially for complex interventions.
Feasibility of Contrast-Enhanced and Nonenhanced MRI for Intraprocedural and Postprocedural Lesion Visualization in Interventional Electrophysiology: Animal Studies and Early Delineation of Isthmus Ablation Lesions in Patients With Typical Atrial Flutter

Peter Nordbeck, Karl-Heinz Hiller, Florian Fidler, Marcus Warmuth, Natalie Burkard, Matthias Nahrendorf, Peter M. Jakob, Harald H. Quick, Georg Ertl, Wolfgang R. Bauer and Oliver Ritter

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Supplementary Table 1. Patient ablation details

24 patients were examined in the MRI after successful ablation of atrial flutter. Time points for MRI examination of different patients were between 15 minutes and 24 h after ablation. In patients no. 8 and 21 no bidirectional isthmusblock could be achieved at the end of the procedure.

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**Supplementary Table 2. Procedural success**

Success was defined as freedom of atrial flutter after 3 months. 2 out of 24 patients had recurrence of atrial flutter. In both patients there was no bidirectional block across the cavo-tricuspid isthmus at the end of the invasive procedure. MR visualisation revealed a discontinuous ablation line in both patients.

<table>
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Supplementary Movie. Lesion visualization using contrast enhanced first pass perfusion imaging

First pass perfusion imaging after delivery of Gadolinium-DTPA in a short axis imaging slice near the atrioventricular sulcus. Directly after RF ablation in the coronary sinus of a mini pig, the ablation lesion is marked by a pronounced perfusion deficit (arrow).