Radiofrequency ablation for atrial fibrillation (AF) has become a widely accepted therapy, but despite technological and procedural advances, long-term freedom from AF remains modest.1 The most common approach is the electric isolation of pulmonary veins (PV) via circular ablation lines around the PV ostia or antra. In some centers, additional linear lesions are placed along the left atrial (LA) roof and mitral isthmus especially in patients with persistent AF. Despite successful acute PV isolation and conduction block along ablation lines, failure to maintain sinus rhythm is commonly seen during follow-up2. Mechanistically, electric PV reconnection represents the predominant cause for the ablation failure and has been reported in 54% to 71% of patients at 5-year follow-up.3,4 Reversible edema rather than permanent radiofrequency-induced tissue necrosis is thought to result in gaps within the ablation lines leading to PV reconnection.5 Indeed, tissue temperatures >45°C result in a marked decrease in conduction velocity and transient conduction block. However, full-tissue recovery occurs up to the heat-induced tissue necrosis during the course of 1 to 4 weeks.6 Identification of such gaps by noninvasive techniques, such as cardiac magnetic resonance imaging (CMR), would have high clinical utility.7–11

In this issue, Harrison et al12 present data on 20 patients with a prior AF ablation who underwent a redo ablation because of recurrence of AF or atrial tachycardia. Index lesion sets consisted of wide area encirclement with optional stepwise CAFE (complex atrial fractionation electrodegram) ablation and linear lesions along the LA roof, mitral, and cavotricuspid isthmus for persistent AF. End point of the repeat procedure was electric PV isolation and electrically confirmed block of any prior linear ablation lesion set. A CMR was performed before the repeat ablation in all patients, but was unavailable to the treating electrophysiologist. After the repeat ablation, the point-by-point Carto 3 electroanatomical maps (averaging 342 points per LA) were coregistered with the 3-dimensional (3D) CMR reconstructed data sets using custom-made software. First, the investigators compared the unipolar/bipolar voltages of the resulting 6767 mapping points with the corresponding late gadolinium (LGE) signal intensities to assess the correlation between decreasing voltage and increasing CMR scar. They found a surprisingly weak correlation (weighted means of −0.17 to −0.21), even when including surrounding 2.5- and 5-mm LGE areas. Discouragingly, neither the traditionally used threshold of <0.05 mV nor the cut-off of <0.3 mV derived from animal work by the same investigators11 performed well in predicting CMR-defined scar. Second, the authors compared the mean and minimum LGE signal intensity along a 20-mm wide path of the prior linear ablation lesions around the PV antra, LA roof, and mitral isthmi. The mean signal intensity was analyzed as a measure of total scar burden, whereas the minimum signal intensity was measured to identify the weakest link within the line, representing the possible site of electric reconnection. At repeat ablation, 50% of the PVs and 36% of LA roof/mitral isthmus lines demonstrated electric reconnection. Neither the mean nor minimum LGE signal intensity was different between isolated/reconnected PVs or the blocked/unblocked linear lines. Interestingly, in the 13 PVs with a single discrete electric gap, the minimum LGE intensity correlated in only 1 case with the electric breakthrough site. Moreover, the average LGE intensity at the breakthrough sites was actually 4× higher than the measured minimum LGE signal.

This carefully conducted study by Harrison et al12 highlights the challenges that still exist in the field of atrial ablation imaging. Since Peters et al13 first demonstrated the feasibility of LA scar imaging, a variety of publications have examined the clinical applicability of LA fibrosis imaging. However, attempts to detect conducting gaps by CMR have shown conflicting results (Table).

Although LA scar imaging developed as an extension of the well-established LV fibrosis imaging, its technical complexity remains high and may well explain some of the discrepant results. Similar to LV scar imaging, a Look-Locker T1 mapping sequence must be applied to null the myocardium rendering normal myocardium black and fibrotic myocardium white. Compared with the thick LV myocardium, most investigators feel that the LA wall thickness of only 1 to 4 mm does not allow a direct application in the LA myocardium and therefore use surrogate measurements of the LV or even the LA blood pool instead. Indeed, an accurate delineation of the myocardial LA boundary is challenging even to the experienced imaging specialist. However, the inclusion of blood pool with high signal intensity may result in false-positive scar or inversely assigning high signal areas to extramyocardial structures may eliminate true LA fibrosis. To compensate for the high degree of technical complexity, various centers have developed center-specific imaging acquisition and processing protocols (Table). Despite those improvements, an important number of LA CMR studies are

In this issue, Harrison et al12 present data on 20 patients with a prior AF ablation who underwent a redo ablation because of recurrence of AF or atrial tachycardia. Index lesion sets consisted of wide area encirclement with optional stepwise CAFE (complex atrial fractionation electrodegram) ablation and linear lesions along the LA roof, mitral, and cavotricuspid isthmus for persistent AF. End point of the repeat procedure was electric PV isolation and electrically confirmed block of any prior linear ablation lesion set. A CMR was performed before the repeat ablation in all patients, but was unavailable to the treating electrophysiologist. After the repeat ablation, the point-by-point Carto 3 electroanatomical maps (averaging 342 points per LA) were coregistered with the 3-dimensional (3D) CMR reconstructed data sets using custom-made software. First, the investigators compared the unipolar/bipolar voltages of the resulting 6767 mapping points with the corresponding late gadolinium (LGE) signal intensities to assess the correlation between decreasing voltage and increasing CMR scar. They found a surprisingly weak correlation (weighted means of −0.17 to −0.21), even when including surrounding 2.5- and 5-mm LGE areas. Discouragingly, neither the traditionally used threshold of <0.05 mV nor the cut-off of <0.3 mV derived from animal work by the same investigators11 performed well in predicting CMR-defined scar. Second, the authors compared the mean and minimum LGE signal intensity along a 20-mm wide path of the prior linear ablation lesions around the PV antra, LA roof, and mitral isthmi. The mean signal intensity was analyzed as a measure of total scar burden, whereas the minimum signal intensity was measured to identify the weakest link within the line, representing the possible site of electric reconnection. At repeat ablation, 50% of the PVs and 36% of LA roof/mitral isthmus lines demonstrated electric reconnection. Neither the mean nor minimum LGE signal intensity was different between isolated/reconnected PVs or the blocked/unblocked linear lines. Interestingly, in the 13 PVs with a single discrete electric gap, the minimum LGE intensity correlated in only 1 case with the electric breakthrough site. Moreover, the average LGE intensity at the breakthrough sites was actually 4× higher than the measured minimum LGE signal.

This carefully conducted study by Harrison et al12 highlights the challenges that still exist in the field of atrial ablation imaging. Since Peters et al13 first demonstrated the feasibility of LA scar imaging, a variety of publications have examined the clinical applicability of LA fibrosis imaging. However, attempts to detect conducting gaps by CMR have shown conflicting results (Table).

Although LA scar imaging developed as an extension of the well-established LV fibrosis imaging, its technical complexity remains high and may well explain some of the discrepant results. Similar to LV scar imaging, a Look-Locker T1 mapping sequence must be applied to null the myocardium rendering normal myocardium black and fibrotic myocardium white. Compared with the thick LV myocardium, most investigators feel that the LA wall thickness of only 1 to 4 mm does not allow a direct application in the LA myocardium and therefore use surrogate measurements of the LV or even the LA blood pool instead. Indeed, an accurate delineation of the myocardial LA boundary is challenging even to the experienced imaging specialist. However, the inclusion of blood pool with high signal intensity may result in false-positive scar or inversely assigning high signal areas to extramyocardial structures may eliminate true LA fibrosis. To compensate for the high degree of technical complexity, various centers have developed center-specific imaging acquisition and processing protocols (Table). Despite those improvements, an important number of LA CMR studies are
deemed of insufficient diagnostic quality even in highly experienced centers.13

Both topics investigated by Harrison et al.,12 namely the atrial voltage cut-off for scar and gap imaging, are of high clinical importance for electrophysiologists. The commonly used threshold of 0.05 mV to define LA scar in many studies lacks histopathologic validation. Recent animal and human CMR studies have suggested new cut-off values for atrial endocardial bipolar voltages: 0.3 mV from the animal data and 0.25 mV at the LA/PV junction in human atria.11,14 However, application of the cut-off of 0.3 mV derived from the animal scar model of the same investigators did not perform well in this study. Differences between right and LA tissue, porcine versus human myocardium and variable imaging quality may explain some of the differences. The ability to perform gap visualization post ablation remains an issue of ongoing debate, and in this study similar to the study by Sprague et al.,8 CMR was not able to reliably identify conducting gaps. In contrast, studies by Bisbal et al.,7 Badger et al.,9 and Taclas et al10 showed good correlation between electroanatomic mapping and LGE CMR to predict gap location (Table). Some reasons may be technical and the different image acquisition protocols, scar reconstruction algorithms, LGE and electroanatomic mapping threshold values, scan resolution and magnetic resonance imaging scan timing make a comparison difficult. However, this study highlights the difficulties that still exist today with this challenging application. In addition, modeling experiments have shown that conduction block can exist despite presence of small gaps in ablation lesions (1.4–4 mm) as long as reduced tissue conductivity is maintained.15 A scenario of incomplete ablation line and electric isolation is therefore possible.

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients (n)</th>
<th>Atrial Scar Threshold (mV)</th>
<th>LGE Threshold Method</th>
<th>Scanner Type/Timing of Scan After First Ablation</th>
<th>LA Endocardial Mapping/Ablation Method</th>
<th>Voxel Size (mm³)</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harrison et al12</td>
<td>20</td>
<td>&lt;0.3 mV</td>
<td>Minimum/mean LGE signal intensity in preablated areas of LA</td>
<td>1.5T, 32-channel cardiac phased array col/not specified</td>
<td>Point-by-point, &gt;300 points per LA, 3.5-mm irrigated catheter</td>
<td>1.3×1.3×4</td>
<td>Poor correlation between LGE CMR and LA voltage (correlation coefficient of −0.17). LGE signal intensity at sites of PV reconnection was greater than the overall lower LGE signal intensity (3.08 vs 0.76)</td>
</tr>
<tr>
<td>Bisbal et al7</td>
<td>15</td>
<td>NA</td>
<td>40±5 of the maximum voxel signal intensity in LA, derived from an automated pixel SI-based algorithm</td>
<td>3.0T, 12-element phased array col/15 mo post</td>
<td>Point-by-point, &gt;800 points per LA, 3.5-mm irrigated contact sensing catheter</td>
<td>1.4×1.4×1.4</td>
<td>PV reconnection match of 79% between LGE CMR and LA voltage. Median voltage for LGE CMR scar areas was 0.21 mV</td>
</tr>
<tr>
<td>Spragg et al8</td>
<td>10</td>
<td>&lt;0.5 mV</td>
<td>Visually estimated LGE hyperenhancement</td>
<td>1.5T, 12-channel phased array col/16 mo post</td>
<td>Point-by-point, &gt;100 points per LA, 3.5-mm irrigated catheter</td>
<td>1.3×1.3×2</td>
<td>Poor correlation between LGE CMR and LA voltage PV reconnections. Good correlation between LA voltage and LGE CMR scar (0.84). Mean LA voltage in LGE CMR scar areas was 0.39 mV</td>
</tr>
<tr>
<td>Badger et al9</td>
<td>13</td>
<td>&lt;0.1 mV</td>
<td>Bimodal distribution of pixel intensity in the LA scar defined as 3 SD above normal mean tissue pixel intensity values</td>
<td>1.5T, phased array col/3 mo post</td>
<td>Point-by-point, &gt;100 points per LA, 3.5-mm irrigated catheter</td>
<td>1.25×1.25×2.5</td>
<td>Positive quantitative correlation between LGE CMR and PV antral voltage scar ($R^2=0.57$). Qualitative correlation between gaps on LGE CMR and EAM in 7/7 patients after second AF ablation</td>
</tr>
<tr>
<td>Taclas et al10</td>
<td>19</td>
<td>&lt;0.05 mV</td>
<td>Visually estimated LGE hyperenhancement and manually selected ROI (LA and PV ostia)</td>
<td>1.5T, 5-element cardiac col/3 mo post</td>
<td>Point-by-point, number of LA points not specified, 3.5-mm irrigated and 8-mm nonirrigated catheters</td>
<td>1.3×1.3×4</td>
<td>Visual quantitative correspondence between voltage map and LGE CMR post ablation of 80%. Qualitative good EAM/LGE CMR correlation for gap visualization</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; CMR, cardiac magnetic resonance imaging; EAM, electroanatomic mapping; LA, left atrial; LGE, late gadolinium; PV, pulmonary veins; and ROI, region of interest.
Despite its rigorous methodology, the study by Harrison et al is not without limitations. The CMR area assigned to each mapping point taken with a 3.5-mm tip can be argued, but the investigators also assessed 2.5- and 5-mm radius areas without improving correlation between voltage and CMR intensity. A recent study by Karim et al examines efforts toward standardization and validation of LA imaging protocols are needed and underway. A recent study by Karim et al suggested that clinical implementation of novel technology is often a hard-won token. Joint and collaborative efforts toward standardization and validation of LA imaging protocols are needed and underway. A recent study by Karim et al16 offered a challenge to compete for the best magnetic resonance imaging LA fibrosis algorithm with participation of 7 leading centers in the field assessing 8 imaging algorithms. Sixty magnetic resonance imaging scans were used to compare the performance of each center’s scar segmentation algorithm(s). Interestingly, all of the algorithms performed similarly, showing room for further collaboration and synergistic improvement to arrive at a generally agreed reference standard. The 2012 expert consensus on catheter ablation for AF17 stated that the technical aspects of magnetic resonance–based imaging of atrial fibrosis and ablation lesions make it difficult to adapt these techniques for clinical use today. Three years on we still have work to do.

Disclosures

Dr Dickfeld receives grant funding from Biosense Webster and GE Healthcare and is a consultant for Biosense Webster. Dr Jimenez reports no conflicts.

References


Keywords: Editorials • ablation techniques • atrial fibrillation • gadolinium
Closing the Knowledge Gaps
Alejandro Jimenez and Timm M. Dickfeld

Circ Arrhythm Electrophysiol. 2015;8:252-255
doi: 10.1161/CIRCEP.115.002783
Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circep.ahajournals.org/content/8/2/252

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Arrhythmia and Electrophysiology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Arrhythmia and Electrophysiology is online at:
http://circep.ahajournals.org/subscriptions/