Cardiac magnetic resonance imaging to detect non-contiguous scar following atrial fibrillation ablation: identifying our knowledge gaps

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This editorial refers to ‘Cardiac magnetic resonance and electroanatomical mapping of acute and chronic atrial ablation injury: a histological validation study’, by J.L. Harrison et al., on page 1486

The advent of catheter ablation for atrial fibrillation (AF) has revolutionized our approach to this most common of arrhythmias, and in selected instances the procedure is now considered first-line therapy. Indeed, over the past decade, tools and techniques have evolved to the stage where this procedure is routinely offered to many patients with refractory paroxysmal and early persistent AF. However, the recurrence rate following ablation continues to present an ongoing challenge with need for repeat ablation procedures in anywhere between 20% and 50% of patients. While there may be many reasons for recurrence, key amongst these is the development of recurrent pulmonary vein (PV) to left atrial (LA) connection. Over recent years, the success in cardiac magnetic resonance (CMR) imaging of ventricular scar has led to attempts to reproduce these results in the atrium.

In particular, a number of studies have used CMR late gadolinium enhancement (LGE) in order to characterize non-invasively the extent and distribution of scarring present following AF ablation.1–3 However, translation of the excellent results obtained from CMR imaging of ventricular scar to the atrium has faced the considerable hurdles associated with image resolution in a thin-walled structure and the absence of a widely available and standardized protocol for analysis of atrial scar. Several studies demonstrated that CMR could identify the extent of LA scarring present at 3 months post-ablation and observed that patients with more extensive scar (or greater percentage scar around the PV circumference) had a lower AF recurrence rate.2,4 In addition, there appears to be a correlation between measured contact force at the time of ablation and the extent of CMR-detected scar development.5 Ultimately the value of CMR in post-ablation imaging would be for identification of regions around the PVS where scar is incomplete with a view to guiding repeat ablation procedures. Badger et al. observed that the extent of CMR scar late after an initial ablation procedure correlated (R² = 0.57) with the low-voltage regions on electroanatomic mapping performed during a repeat ablation procedure.6 No PVS with circumferential scar showed electrical reconnection, but a quantitative correlation of scar gaps with electrical reconnection was not performed. In a preliminary report using CMR to identify incompletely circumferential scar and electroanatomic mapping at a repeat procedure, Bisbal et al. observed a 94% electrical–CMR concordance.7,8 Isolation of all PVS could be achieved guided by the imported MR model to identify the gaps. However, other studies have been less encouraging. While Spragg et al.9 also observed a significant association between scar identified by LGE on CMR and LA low-voltage regions on electroanatomic mapping, they found no association between CMR scar gaps and mapped PV reconnection sites. More disappointingly, a study in 50 paroxysmal AF patients undergoing either wide area or ostial ablation found that the proportion of patients in whom CMR could correctly identify the distribution of ablation lesions varied from as low as 28% to 54% depending on the technique used.10 These authors concluded that LGE imaging of atrial scar was not yet sufficiently accurate to identify ablation lesions reliably or to determine their distribution. While the reasons for the wide variation in reported results remains unclear, in part this may relate to methodology. Furthermore, the extent of the PV circumference reported to show absence of scarring following an initial ablation procedure is at odds with clinical mapping data. In the study by Arujuna et al., in patients with recurrent AF, the average percentage PV antral encirclement by scar was only 34%.11 Figure 1 yet, in repeat ablation procedures, sites of electrical reconnection are frequently focal, with re-isolation achieved in many instances with local radiofrequency applications.8 Large segments where scar is incomplete are infrequently observed clinically, particularly in the era of contact force measurements. Whether CMR will have the resolution to detect such focal regions where scar is incomplete remains uncertain.

In this context, the contribution of Harrison et al. is indeed welcome.11 The authors performed linear intercaval ablation in a series of 16 pigs. Histology was performed after acute sacrifice in...
eight animals and after chronic sacrifice at 3 months in the other eight animals. Using both T2-weighted imaging and LGE, systematic analysis of the signal intensity thresholds from 0 to 15 standard deviations above a blood pool reference were used to determine the threshold that produced a lesion volume most closely correlated to histological lesion volume. The thresholds that best approximated histological volumes varied both between technique and between acute and chronic imaging. Chronically the T2 imaging always underestimated lesion volume. When comparing the LGE average CMR volume divided by the histological volume against the signal intensity threshold, the curve was steep at unity (figure 8 in Harrison et al.11) indicating that minor changes to the signal intensity threshold would result in significant under- or overestimation of scar volume. This study emphasizes the critical importance of appropriately defining this threshold, which in the absence of histological validation is necessarily subjective, and provides some explanation for the variation in reported clinical results.

Additional questions remain. Are these thresholds applicable in the human left atrium and can this model be used to determine the thresholds which best identify electrical gaps in an ablation line? Further, as the authors observed, determining volumes of injury on CMR images in the thin-walled atrium will necessarily require a subjective judgement. Other considerations important to standardize imaging sequences include the optimal contrast dose, the timing of the LGE sequence, and the likelihood of partial volume effects. In addition, the use of the blood pool vs. an area of apparently ‘healthy’ myocardium as the reference region for LGE quantification in the study of Harrison et al. is an important distinction from conventional LGE assessment.

If there has been uncertainty as to how best to identify the dense scar created by ablation in the atrium, then the same methodological questions may be applied to the optimal CMR approach to identify more subtle degrees of pre-existing atrial scarring. In recent years, the group in Utah have pioneered the use of LGE with CMR to characterize the extent of existing atrial fibrosis (graded as minimal, mild, moderate, or extensive) as a predictor of AF recurrence.12,13 In a number of studies they demonstrated a gradation in ablation success in relation to the severity of fibrosis. Importantly, they observed that fibrosis observed on CMR was the most powerful independent predictor of ablation success. While it is recognized that conditions associated with AF such as heart failure, hypertension, valvular disease, and indeed ageing increase the likelihood of finding

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**Figure 1** This figure highlights the differences between the scar gaps seen on cardiac magnetic resonance (CMR) after an atrial fibrillation (AF) ablation procedure (extensive in this case) with the more focal gaps often observed during mapping. Both CMR and electroanatomic mapping define scar by arbitrary cut-off points which may lead to under- or overestimation of scar burden. Identification of conduction gaps is still best achieved with careful mapping. Column 1: The late (>3 months) delayed enhancement (DE) CMR imaging scans post-AF ablation, showing extensive posterior regions around the left and right pulmonary veins (PVs) where no scar is evident. Column 2. (A) Voltage map of a repeat AF ablation procedure. The purple area represents normal atrial myocardium (>0.5 mV amplitude) and the red area represents scar or tissue that has not been activated. There is an area of intermediate voltage in the RSPV due to a focal reconnection (black arrow). In B after a single radiofrequency application, this reconnection is no longer evident and the PV is isolated (black arrow). The colour format of these voltage maps is critically dependent on the thresholds set for normal voltage and for scar. Column 3. PV electrical signals from the patient in column 2. Note that the earliest signal on the PV catheter is at bipoles 1, 2 and 9, 10. A single radiofrequency application at this site resulted in PV isolation. Whether CMR will detect such focal gaps requires further study. CS, coronary sinus; LA, left atrium; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.
atrial scarring, these risk factors do not provide the same individualized risk prediction of the CMR scan. The value of such an approach is clear; those patients with extensive fibrosis and hence low likelihood of ablation success can be stratified prior to invasive mapping. Recently published data support these initial observations. Malcomme-Lawes et al. observed a higher LGE prevalence of pre-ablation scar in patients who subsequently had AF recurrence compared with those who did not. However, the extent of pre-existing scar reported in these studies has varied markedly. In part this may represent different patient populations, but may again relate to the methodological cut-off points in signal intensity used to define scar. This may be all the more critical when attempting to define the imaging characteristics of more subtle regional patchy fibrosis. Post-contrast T1 mapping of the left atrium in humans has recently been shown to correlate with LA voltage maps and, although as yet not widely validated, may also play a role in detection of widespread atrial fibrosis.

The study of Harrison et al. also raises some important questions regarding the relationship between voltage cut-off points used at electroanatomical mapping and presence of scar in the atrium. Widely used cut-off points of 0.05 mV for dense scar and 0.5 mV to identify low-voltage regions presumed to indicate more subtle degrees of fibrosis have been arbitrarily defined. The current study highlights the inaccuracy of these settings and emphasizes the poor resolution of a 4 mm bipole for this purpose, particularly in the context of a long narrow scar. Even in the middle of dense scar, the bipole recorded a voltage amplitude acutely of 0.6 mV and chronically of 0.3 mV, no doubt due to summation of far-field activity. Furthermore, the reverse was also true, as the investigators demonstrated voltage amplitude reduction over normal myocardium at distances of almost 2 cm from the scar centre; presumably due to loss of far-field summation. These observations are more than academic as they raise important questions regarding the use of voltage mapping to validate CMR lesion distribution—to date the clinical gold standard. In a recent CMR study of the atrium, Khurrum et al. defined the signal intensity ratio (defined as atrial myocardial signal intensity divided by blood pool signal intensity) thresholds which correlated with a bipolar endocardial voltage of <0.5 mV (defined as damaged tissue) and <0.1 mV (indicating dense scar). However, the reliability of these bipolar voltages using a 3.5 mm electrode tip for detection of scar is questionable. Further work with closely spaced bipolar recordings and tissue validation is required before we can trust the voltage amplitude as a marker of local fibrosis.

The study by Harrison et al. by providing a validated approach to CMR assessment of scar volume, provides an important step forward in the acceptance and utility of MR imaging in the atrium. For the uninitiated, it also underlines the considerable technical challenges still to be faced in order to achieve accurate and standardized CMR characterization of atrial scar.

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References