Automated analysis of atrial late gadolinium enhancement imaging that correlates with endocardial voltage and clinical outcomes: A 2-center study

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BACKGROUND For late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) assessment of atrial scar to guide management and targeting of ablation in atrial fibrillation (AF), an objective, reproducible method of identifying atrial scar is required.

OBJECTIVE To describe an automated method for operator-independent quantification of LGE that correlates with colocated endocardial voltage and clinical outcomes.

METHODS LGE CMR imaging was performed at 2 centers, before and 3 months after pulmonary vein isolation for paroxysmal AF (n = 50). A left atrial (LA) surface scar map was constructed by using automated software, expressing intensity as multiples of standard deviation (SD) above blood pool mean. Twenty-one patients underwent endocardial voltage mapping at the time of pulmonary vein isolation (11 were redo procedures). Scar maps and voltage maps were spatially registered to the same magnetic resonance angiography (MRA) segmentation.

RESULTS The LGE levels of 3, 4, and 5SDs above blood pool mean were associated with progressively lower bipolar voltages compared to the preceding enhancement level (0.85 ± 0.33, 0.50 ± 0.22, and 0.38 ± 0.28 mV; $P = .002$, $P < .001$, and $P = .048$, respectively). The proportion of atrial surface area classified as scar (ie, >3 SD above blood pool mean) on preablation scans was greater in patients with postablation AF recurrence than those without recurrence (6.6% ± 6.7% vs 3.5% ± 3.0%, $P = .032$). The LA volume >102 mL was associated with a significantly greater proportion of LA scar (6.4% ± 5.9% vs 3.4% ± 2.2%; $P = .007$).

CONCLUSIONS LA scar quantified automatically by a simple objective method correlates with colocated endocardial voltage. Greater preablation scar is associated with LA dilatation and AF recurrence.

KEYWORDS Atrial fibrillation; Delayed-enhancement magnetic resonance imaging; Radiofrequency ablation

ABBREVIATIONS **2D** = 2-dimensional; **AF** = atrial fibrillation; **CMR** = cardiovascular magnetic resonance; **ECG** = electrocardiogram; **LA** = left atrial/atrium; **LGE** = late gadolinium enhancement; **MRA** = Magnetic resonance angiography; **PAF** = paroxysmal atrial fibrillation; **RF** = radiofrequency; **SD** = standard deviation

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Introduction

Success rates for catheter ablation of atrial fibrillation (AF) are approximately 50%–75%[1] and remain largely unchanged despite efforts to improve targeting and delivery of ablation. Improved outcomes require better understanding of the patient's atrial myocardial substrate for case selection, tailored ablation therapy, and better evaluation of the resulting tissue injury. Several recent studies suggest that high-spatial-resolution late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) imaging can be used to visualize preexisting atrial fibrotic change and evaluate radiofrequency (RF) lesions.[2–8]

Current methods to identify atrial scar rely on operator judgement to define the level of enhancement assigned as scar.[2–8] One approach is to look for a bimodal distribution of intensity to define the threshold of scar as the trough between the peaks.[3] In many patients, however, the distribution of

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intensity is not bimodal, preventing this from being a universally applicable technique. An alternative approach is to manually select regions of scar and nonscar tissue in order to define a patient-specific threshold above which enhancement is defined as scar.[9] However, in many patients, scar may be patchy and different observers may choose different regions to define scar. Despite the operator dependence of these methods, visually appreciable correlations between regions of scar and low voltage (<0.5 mV) have been demonstrated.[10,11] Furthermore, blinded scoring systems have been used to show an association between total atrial scar and the total burden of low voltage in a given patient, but these measures lack the ability to confirm the colocality of scar and low voltage.[11]

In this study, we examine the use of the blood pool mean as an intensity reference in an automated process that expresses atrial myocardial intensity as multiples of standard deviation (SD) above blood pool mean. We tested the hypothesis that this method will identify LGE with a level of consistency that will enable both point-by-point correlation with colocalized voltage and correlation with procedural and patient characteristics.

Methods

Patients undergoing first ablation for paroxysmal atrial fibrillation (PAF) were recruited. LGE CMR scan was performed before and 3 months after either cryoballoon or conventional RF ablation. A randomly selected subset of patients underwent endocardial voltage mapping during the ablation procedure. All CMR scans and voltage maps were performed in sinus rhythm. Patients were followed up with electrocardiogram (ECG) and clinical history at 3, 6, and 12 months and with 24-hour Holter monitor at 6 months. The study was approved by the local research ethics committees (UK). Written informed consent was obtained. All patients included in the study had diagnostic quality images and completed 12-month follow-up.

LGE CMR protocol

A Philips Achieva 1.5-T MRI system and a 5- or 32-element phased-array cardiac coil was used for LGE imaging, as described previously.[3] Fifty-phase 2-dimensional (2D) cine-determined time delay for ECG gating. The anatomic details of the left atrium (LA) and pulmonary veins (PVs) were obtained by using non-ECG-gated 3D spoiled gradient-echo contrast-enhanced timing robust angiography (CENTRA) during the first pass of 20-mL gadobenatedimeglumine-enhanced contrast. A 3D left ventricular LGE breath-hold sequence, approximately 9-minute postcontrast, was used to identify optimal nulling time for the left ventricular.

ECG-triggered, free-breathing navigator-gated whole-heart 3D spoiled gradient-echo acquisition was performed in axial orientation, with resolution approximately $1.5 \times 1.5 \times 4$ mm, reconstructed to $1.25 \times 1.25 \times 2$ mm. Complete LA coverage was obtained with 40–50 slices. Data were acquired within 100–150-ms window for each RR interval, with a low-high k-space ordering and spectral presaturation with inversion recovery for fat suppression. Inversion recovery delay, determined from the Look-Locker sequence,[12] was chosen to null the myocardial signal. Navigator inflow artifact was reduced by lowering the navigator rescale factor and positioning the Navigator away from the right-sided PVs. Free-breathing images acquired 12–20-minute postinjection depending on the successful leading navigator placement, aiming for a Navigator efficiency of $>30\%$.

Voltage mapping

Patients underwent voltage mapping either during the initial procedure or the redo procedure for recurrent AF. The LA segmentation was imported into Ensite NavX (St Jude Medical, St. Paul, MN) or CARTO 3 (Biosense Webster, Diamond Bar, CA). The LA geometry was collected by using the duodecapolar AFocus catheter (St Jude Medical) or 20-pole lasso catheter (Biosense Webster). The electroanatomical geometry was registered to the imported LA segmentation using surface registration. Peak-to-peak voltages were collected from the 10 bipoles of the circular mapping catheter. Bipolar electrogram amplitudes can be influenced by catheter orientation and the direction of wave-front propagation.[13] We therefore performed additional unipolar recordings in 5 patients using a single reference electrode within the inferior vena cava. Bipolar (16–500 Hz) and unipolar (2–240 Hz) filter settings were used.

Automated method of scar mapping

LA segmentation was performed on a Philips Healthcare workstation by using the maximum intensity projection view to remove structures external to the LA blood pool. This surface was the reference anatomy on which LGE and voltage were compared. Automated software written in C++ was used to perform rigid or nonrigid registration[14] (depending on atrial wall overlap) between the segmented magnetic resonance angiography (MRA) and LGE surfaces.

The LA blood pool was used as a nonenhancing region against which the LA wall enhancement could be compared and normalized. The blood pool was identified automatically by shrinking the LA segmentation using mathematical morphology, and mean (M_{BP}) and standard deviation (SD_{BP}) intensity of the blood pool were calculated. The maximum LA wall intensity (I_{LA}) was determined along the normal to the wall at each location, 3 mm inside and outside the LA surface[15] to allow for wall thickness and minor registration mismatch. LA wall intensities were expressed as multiples of SD_{BP} above the blood pool mean to provide a normalized LA wall intensity (N_{LA}), such that $N_{LA} = (I_{LA} - M_{BP})/SD_{BP}$.

Comparison of LGE and voltage

The registered voltage map was exported for offline comparison with the atrial scar map. Each electrogram was assumed to represent a region of 2-mm radius from the point of endocardial contact, given the electrode spacing of the catheters used. The mean intensity of the surface "cells" within the 2-mm radius was used to compare with colocated