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ARRHYTHMIAS

Use of MRI to guide electrophysiology procedures

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Cardiac electrophysiology (EP) has rapidly evolved in recent decades from targeting simple arrhythmias such as accessory pathway or nodal re-entry tachycardia to the ablation of more complex substrates. This evolution has been possible due to a better understanding of the anatomical basis, and hence the mechanism, of more complex cardiac arrhythmias. Imaging of the heart has played an important role in defining cardiac structures and characterising the arrhythmic substrates. In this regard, MRI has provided the most comprehensive evaluation of cardiac anatomy, function, and tissue characterisation, and has made a major contribution to the increase in ablation procedures. This article provides a comprehensive overview of the role of MRI in the management of the most common complex arrhythmias: atrial fibrillation (AF) and ventricular tachycardia (VT).

ROLE OF MRI IN THE MANAGEMENT OF PATIENTS UNDERGOING AF ABLATION

AF is the most common arrhythmia in clinical practice and is associated with increased morbidity, mortality, and health care burden.[w1] Catheter ablation has become the standard of care during the past decade for symptomatic drug refractory AF.[w2] Although this treatment option has been amply demonstrated to improve symptoms and quality of life compared with medical treatment, the mid and long term success rate is still moderate.[w3 w4] The EP community has made a great effort to further improve the results of AF ablation by designing new ablation techniques, identifying new ablation targets, and optimising the selection of candidates. In this regard, MRI offers the possibility to evaluate the pathologic substrate and better define the left atrial (LA) structural remodelling, which is closely related to procedural outcome. Evaluation of the LA remodelling after the ablation procedure helps to identify responders presenting a favourable remodelling, which is characterised by a reduction in size and recovery of shape. Additionally, this imaging modality can identify myocardial scarring related to radiofrequency lesions, which provides a non-invasive assessment of pulmonary vein (PV) reconnection after the ablation procedure. The identification of gaps in prior ablation lines by MRI helps to plan the requirements for a repeated procedure, as well as guiding catheter positioning.

Remodelling based risk stratification: improving patient selection

Patient selection is the cornerstone for improved outcome of AF ablation, and avoids unnecessary risks to those unlikely to respond. Although clinical data can be used to identify patients at high risk of recurrence,[1 2 w5] assessment of the LA remodelling stage has refined risk stratification. There is a consistent body of evidence showing that the LA remodelling stage has prognostic value for recurrences, assessed in the majority of studies by the LA dimensions.[2 w6 w7] Recently, the concept of structural remodelling has evolved beyond size. Detailed, non-invasive quantification of LA fibrosis with delayed enhancement cardiac MRI (DE-CMR), as well as an accurate assessment of changes in LA shape (sphericity), have refined the definition of AF related atrial disease and represent a step forward in risk stratification and patient selection for AF ablation.

LA fibrosis

DE-CMR has been widely used to observe fibrotic tissue at the ventricular myocardium. In the past few years, there has been a growing interest in applying this technology at the atrial level to evaluate the arrhythmogenic substrate. Several single centre studies using non-invasive quantification of LA fibrosis have shown the association between the degree of fibrosis and clinical outcome after AF ablation (figure 1).[w8 w9] The authors classified the patients according to four stages of atrial structural remodelling, depending on the percentage of fibrosis of the LA wall volume (Utah classification): <10% (Utah I), 10–20% (Utah II), 20–30% (Utah III), and >40% (Utah IV). They found that the higher the proportion of fibrotic myocardium, the higher the rate of recurrence. The results of the multicentre DECAAF trial have provided more robust evidence on this association.[3] Adjusted for other covariates, a 6% increased risk for recurrence (95% CI 3% to 9%) per each 1% increase in LA fibrosis was reported. In addition, the Utah classification provided good discrimination for recurrence at 1-year follow-up: 15.3% for patients in Utah I, 32.6% for Utah II, 45.9% for Utah III, and 51.1% for Utah IV. Initial data reported by the same group show a correlation between the MRI findings (enhancement) and the histology (fibrosis) in biopsies of patients with AF undergoing heart surgery.[w9] Although this technology provides reliable staging of atrial disease, the inherent technical limitations of the imaging technique, such as the spatial resolution applied to the thin atrial wall, have limited its generalisability. However, research has focused on this topic worldwide. Important contributions, including an automatic quantification tool[w10] and new methods to standardise the intensity thresholds,[w11] will expand the use of this promising technology.

LA shape

Although LA size has classically defined the remodelling stage, size is strongly related to anthropometric

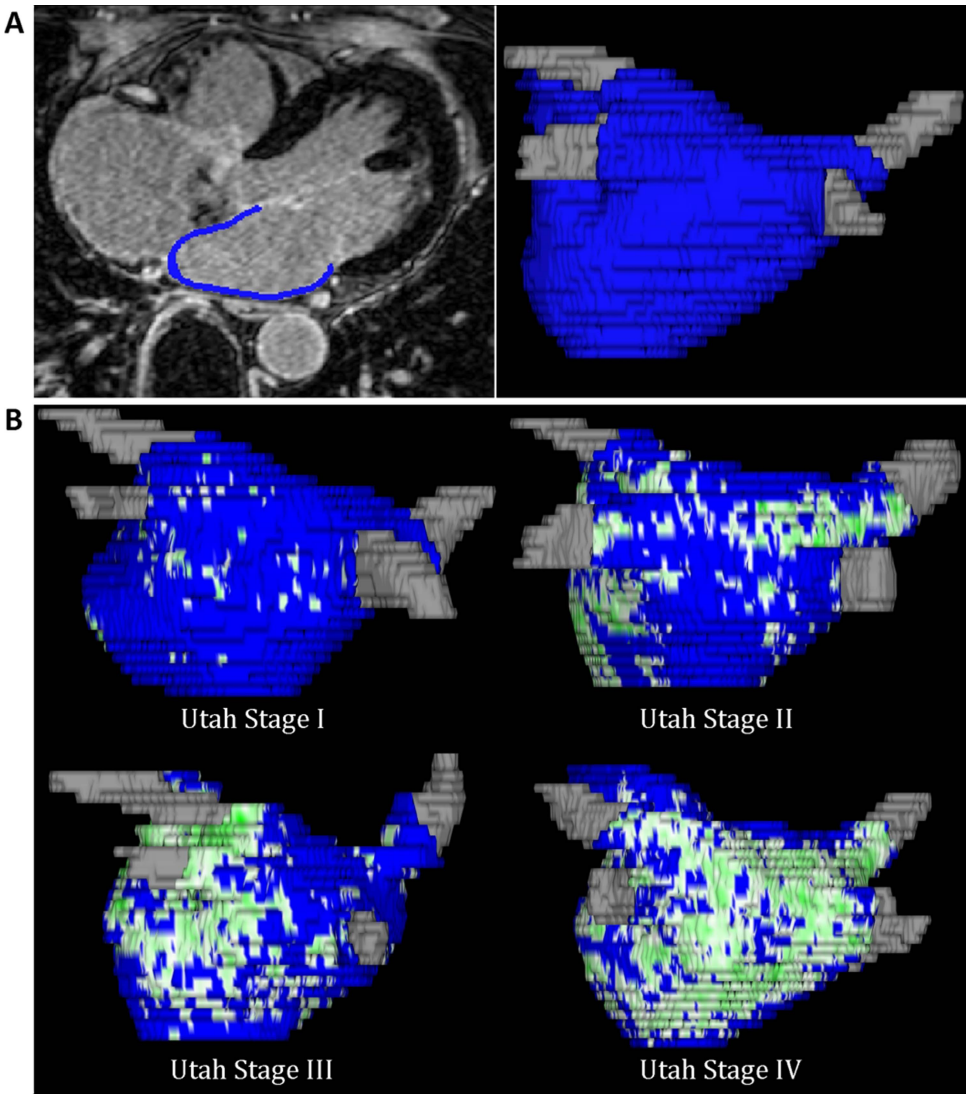

Figure 1 (A) DE-CMR axial slice with the segmented LA wall (left panel) and the resulting three dimensional reconstruction of the LA wall (Coreview, Marrek Inc, Salt Lake City, Utah, USA) (right panel). (B) Utah classification of the LA remodelling based on the percentage of enhancement of the LA wall volume: <10% (Utah I), 10–20% (Utah II), 20–30% (Utah III), and >30% (Utah IV). Courtesy of Nassir F Marrouche, MD. DE-CMR, delayed enhancement cardiac MRI; LA, left atrium.

parameters that do not capture the non-symmetrical three dimensional (3D) structure of the LA. This precludes a sensitive measurement of the subtle geometrical changes during the remodelling process. A new shape-based remodelling parameter, LA sphericity, compares LA geometry and a perfect sphere; sphericity is strongly and independently associated with AF recurrences after PV isolation[4] (figure 2). Patients with a spherical LA had an 11-fold higher chance of recurrence than patients with a discoid LA. This non-invasive parameter uses magnetic resonance angiography and has been shown to be superior to LA size in discriminating patients at risk of recurrence, which may be helpful in selecting the best candidates for ablation.

Post-ablation reverse remodelling: volume, shape, or both?

The meaning of volume reduction after PV isolation remains unclear. While some studies report reduction of LA volume only after successful ablation, others found reduction of the maximum LA volume in all patients, but reduction of minimum LA volume only in patients without recurrence.[w12 w13] This may reflect a scar related retraction of the LA (reduction of maximum volume) but favourable remodelling only after successful ablation (reduction of minimum volume). We recently reported an improvement in LA sphericity in patients with paroxysmal AF (spherical reverse remodelling), but worsening in patients with persistent AF.[5] In our series, there was a trend toward a higher proportion of spherical but not volumetric reverse remodelling in patients without recurrences. Post-ablation volume reduction is likely caused by a combination of scarring and myocardial structural recovery. LA sphericity might be a more subtle index to measure favourable remodelling; while patients with improved sphericity and volume post-ablation may represent responders, those with only volume reduction may suggest scar retraction.

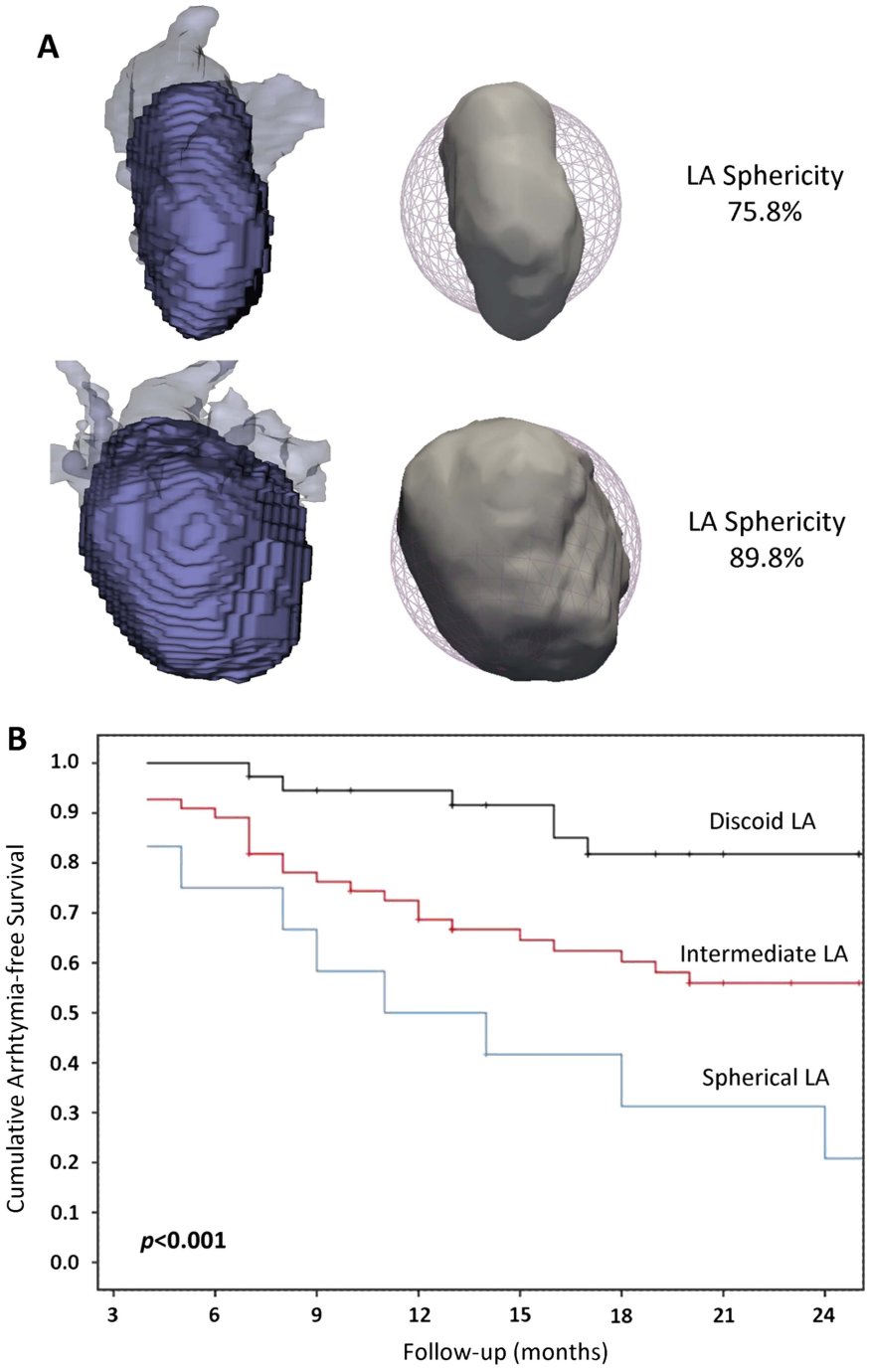

Figure 2 (A) Right lateral projection of the LA three dimensional reconstruction (pulmonary veins and LA appendage shown in transparency) and the integrated sphere that best fitted the LA (shown as a mesh) of a patient with discoid LA (upper panel) and another with spherical LA (lower panel). (B) Kaplan-Meier curves displaying the cumulative arrhythmia-free survival of patients with discoid, intermediate, and spherical LA. LA, left atrium.

MRI guided AF ablation

PV reconnection has been postulated as the main cause of AF recurrences after ablation,[w14] and is often related to gaps in the encircling antral lines.[6] LA ablation lesions and discontinuities in the lines can be identified by DE-CMR,[w15 w16] which may be used as a non-invasive tool to assess post-procedural PV reconnection.

The accuracy of DE-CMR to identify and localise the gaps in prior encircling lesions has allowed the use of this image modality in the re-ablation procedure as the only guide to re-isolate the PVs (figure 3).[7] We reported the first experience of MRI guided PV isolation in humans, in a series of 15 patients undergoing repeated AF ablation. A DE-CMR was performed before the procedure and a 3D DE-CMR model was reconstructed after manually segmenting the LA wall. A pixel signal intensity map was projected on the DE-CMR model and colour coded. The DE-CMR model was imported into the navigation system to directly guide catheter positioning to ablate the anatomic gaps. Importantly, all electrically reconnected PVs had anatomical gaps on DE-CMR. Under the guidance of only the DE-CMR model, re-isolation was achieved in 95.6% of PVs and conduction block through the roofline in all patients, reducing significantly the radiofrequency application time. We found that DE-CMR was more accurate than voltage mapping to assess the location and size of

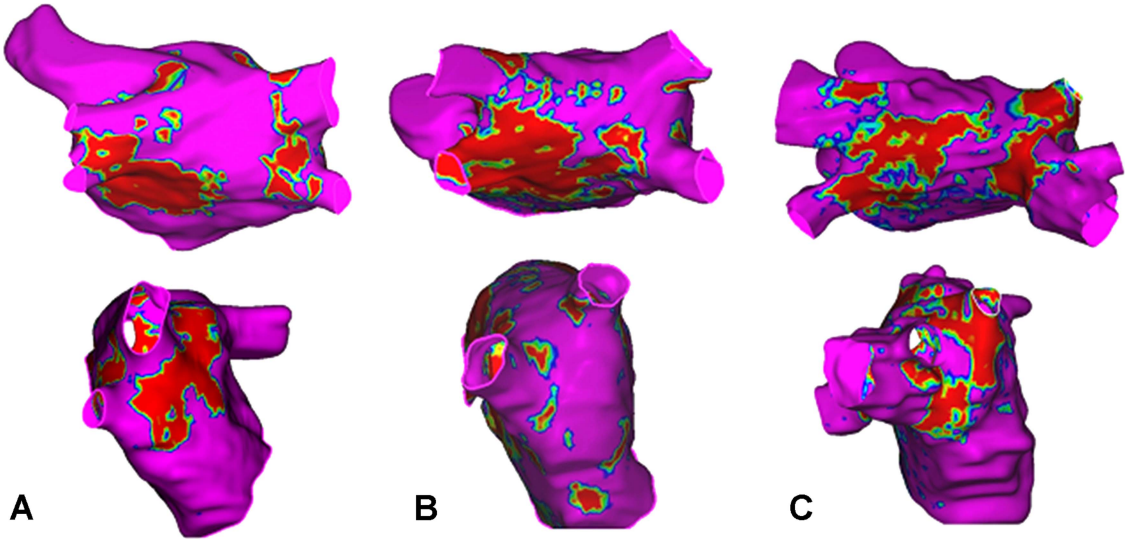

Figure 3 Superior (upper panel) and right lateral (lower panel) views of a three dimensional DE-CMR model of three patients undergoing repeated atrial fibrillation ablation procedure (A–C), where atrial scarring related to prior ablation lesions are depicted in red and healthy tissue in purple. The size of the gaps can vary widely between patients; from a few millimetres (right carina of patient A, left superior PV of patient B, and roofline of patient C) to large areas without any scar (right sided PVs of patient B). DE-CMR, delayed enhancement cardiac MRI; PV, pulmonary vein.

the anatomic gaps (figure 4). Also, the site of electrical reconnection was better determined by the DE-CMR model than by the circular mapping catheter. In those PVs where cannulation was difficult or impossible, DE-CMR allowed the localisation of the site of reconnection.

This 'proof of concept' study opens promising new horizons in the management of patients with AF, not only in redo but also first procedures. Integration and merging of DE-CMR imaging into the navigation system may provide direct visualisation of the pathologic (enhanced) atrial substrate in patients with advanced remodelling stage, allowing the physician to anatomically target these sites ('tailored substrate modification approach').

USE OF MRI IN GUIDING VT ABLATION

Scar related re-entry is the main mechanism for sustained monomorphic VT in patients with structural heart disease. The presence of areas of fibrosis (ie, healed myocardial infarction) with surviving myocardial fibres can promote barriers to conduction block and areas of slow conduction that are the ideal substrate for re-entry.[w17] VT ablation procedures have evolved from conventional mapping techniques, based on pacing manoeuvres during

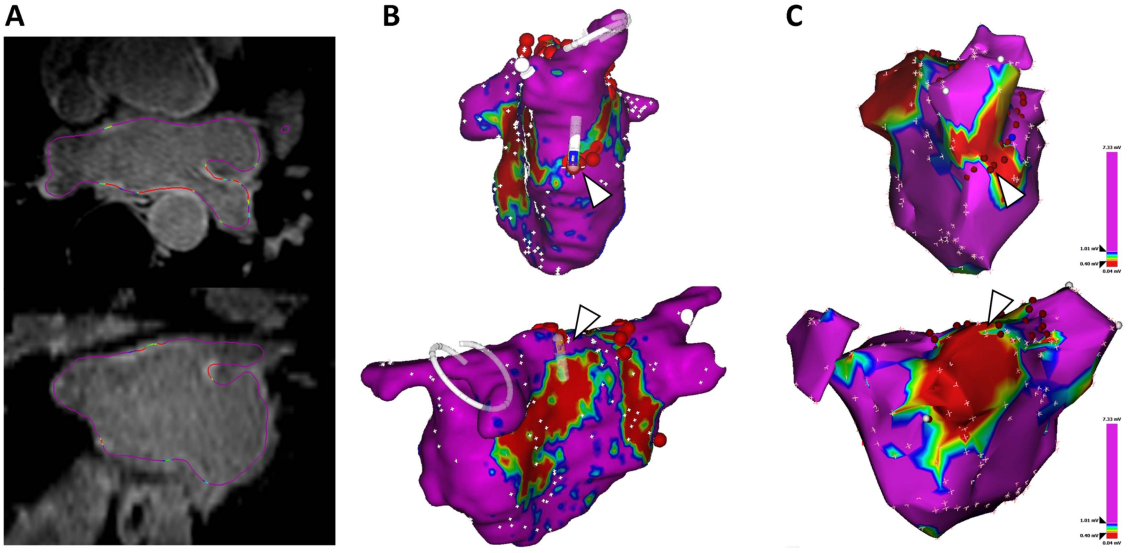

Figure 4 (A) DE-CMR slices in the axial (upper panel) and coronal plane (lower panel) with the segmented left atrial wall and the projected colour coded pixel signal intensity. (B) Right lateral (upper panel) and left posterolateral (lower panel) views of the DE-CMR model during the ablation procedure. The DE-CMR model is integrated in the non-fluoroscopic navigation system (CARTO 3) and guides catheter positioning at the anatomical gaps (white arrowheads). (C) Voltage map (same views as panel B) identified the anatomic gaps less accurately than DE-CMR (arrowheads mark the location of the gaps on the DE-CMR model). DE-CMR, delayed enhancement cardiac MRI.

MRI in atrial fibrillation (AF): key points

- Left atrial (LA) size is currently the standard measurement to stage AF related atrial disease. New MRI based remodelling parameters such as LA fibrosis or LA sphericity have refined the concept of atrial remodelling.
- The degree of atrial remodelling is strongly associated with the clinical outcome of AF ablation; thus, staging the LA disease before ablation is crucial to ensure good results.
- The use of the new remodelling parameters may be useful to select the best candidates and improve AF ablation outcome.
- Catheter ablation of AF may reverse the remodelling process. After the ablation procedure, the assessment of changes in LA size and shape allows the detection of favourable reverse remodelling.
- Gaps in the ablation lines are the main underlying mechanism of pulmonary vein reconnection and AF recurrences. MRI can detect and localise radiofrequency ablation lesions and identify the reconnection sites, and can be a useful tool to guide repeated ablation procedures.

tachycardia using radioscopic guidance, towards the identification and elimination of the arrhythmogenic substrate (ie, areas of low voltage, abnormal electrograms) during stable rhythms using non-fluoroscopic navigations systems.[w18 w19] However, the accuracy of electroanatomic maps for precise scar characterisation is limited and requires long mapping times.

DE-CMR allows a precise reconstruction of cardiac anatomy and permits differentiation between normal myocardium and scar tissue.[w20] Moreover, using appropriate image post-processing, scar tissue can be characterised and categorised in dense scar and heterogeneous tissue (surrogate of viable myocardium).[w21–w23] In recent years, several studies have focused on the utility of DE-CMR to estimate the risk of occurrence of ventricular arrhythmia, to plan ablation procedures, and to guide VT ablation.

Delayed enhancement and susceptibility for ventricular arrhythmia

The presence, extension, and heterogeneity of myocardial fibrosis detected by DE-CMR have been associated with higher susceptibility to ventricular arrhythmia and increased risk of sudden cardiac death. Infarct size is a better predictor for VT inducibility than left ventricular ejection fraction (LVEF) in patients with healed myocardial infarction.[w24] Several studies have shown that the extension of hyperenhancement in patients with coronary artery disease is correlated with a poor prognosis in terms of major cardiovascular events, ventricular arrhythmia, and global mortality.[w25–w27] Klem *et al* highlighted the incremental value of myocardial scarring in risk stratification for placement of an implantable cardioverter defibrillator (ICD).[w28] Patients with LVEF >30% but significant scarring were at high risk; in contrast, patients with LVEF <30% and minimal or no scarring were at low risk, similar to patients with LVEF >30%.[w28]

Similar results have been observed in patients with non-ischaemic cardiomyopathies.[w29–w31] The presence and extension of myocardial fibrosis increased the risk of ventricular arrhythmias and sudden cardiac death in hypertrophic and dilated cardiomyopathies and in cardiac resynchronisation therapy candidates.[w30 w32 w33]

Recent studies have attempted to better characterise myocardial scar by focusing on regions with intermediate signal intensity. It is argued that these border zone areas reflect the presence of viable myocardium within the scar. The amount of border zone predicts the inducibility and occurrence of spontaneous ventricular arrhythmia in patients with structural heart disease.[w21–w23 w33] In a case–control study, corridors of heterogeneous tissue were present more frequently in patients with VT than in controls.[8]

Pre-procedural MRI for planning VT ablation procedure

Ablation of VT in structural heart disease is often challenging. The decision on the appropriate approach (ie, endocardial vs epicardial, right vs left) determines procedural safety and success. Post-myocardial infarction VT can usually be abolished from the endocardium and non-ischaemic patients frequently require epicardial ablation. However, a combined endo- and epicardial substrate ablation could improve the success in ischaemic patients, and epicardial VT has been found in less than half of non-ischaemic patients.[9 w34] Therefore, deciding on the epicardial approach based exclusively on the type of underlying heart disease is insufficient. Several electrocardiographic methods have been developed for identifying epicardial VTs.[w35–w38] However, all these criteria seem to be substrate specific and have several limitations. Scar location on DE-CMR could help to plan whether an endocardial or epicardial approach will be needed, particularly in non-ischaemic patients.[10] We recently reported a series of 80 patients with non-idiopathic ventricular arrhythmia studied with DE-CMR before the ablation procedure. The majority (96%) of ventricular arrhythmias were ablated in segments with hyperenhancement (figure 5). The presence of epicardial scar on DE-CMR identified the epicardial origin of the arrhythmia with a suitable sensitivity (80%) and specificity (89%). In the remarkably challenging case of septal mid-myocardial substrate, the distance from the endocardium to the hyperenhancement area predicted the site (right vs left ventricular septum) of successful VT ablation (figure 6).[9 w39]

MRI guided VT ablation: towards a better characterisation of the arrhythmogenic substrate

Substrate guided ablation allows elimination of non-tolerated or non-inducible VT. This approach tries to precisely characterise and remove the arrhythmogenic substrate during stable rhythms. The standard method for defining areas of scar is the realisation of bipolar voltage maps (areas <0.5–1.5 mV) using 3D mapping systems.[w18 w40] Unfortunately, this technique has many limitations:

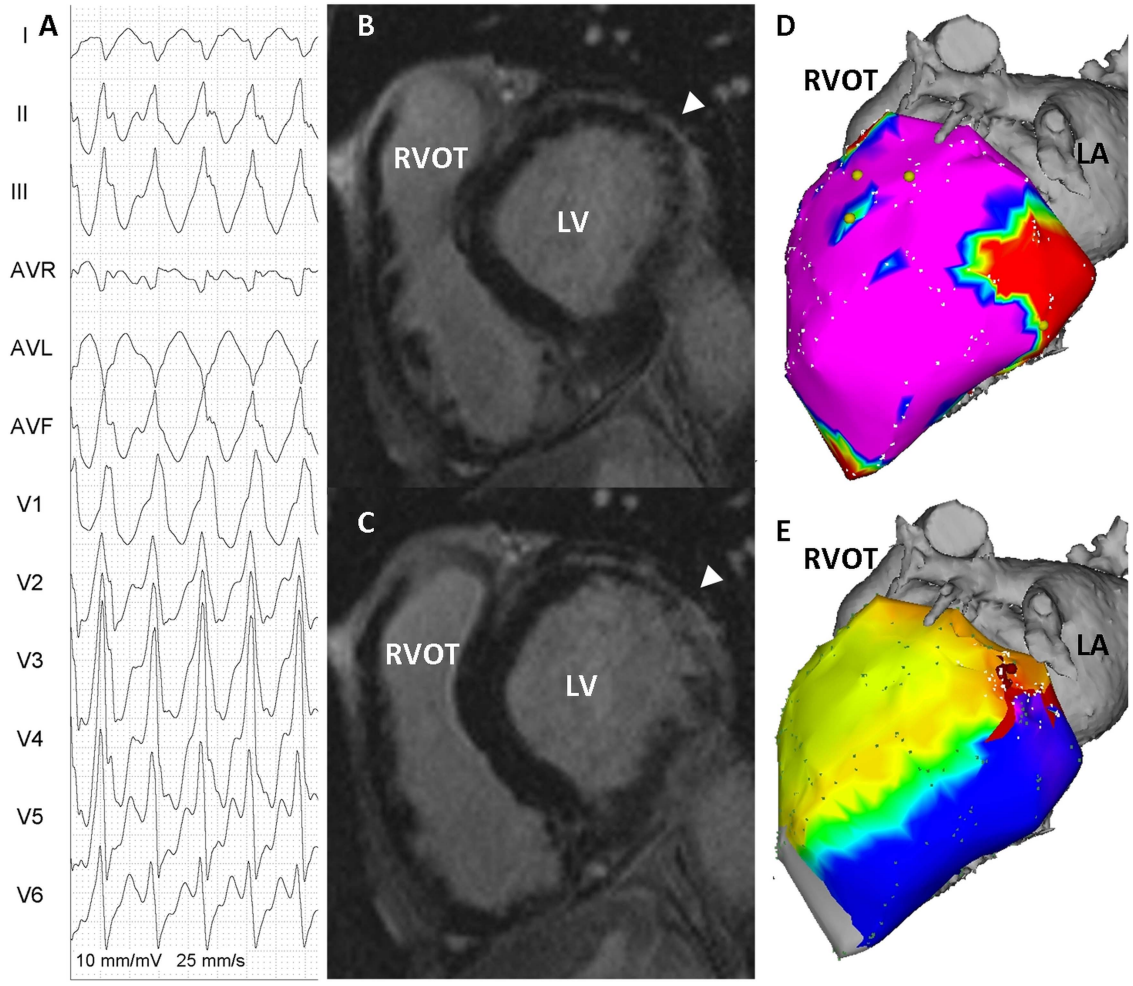

Figure 5 Presence of predominantly epicardial late enhancement in a patient with non-ischaemic cardiomyopathy and epicardial VT. (A) 12-lead ECG of the clinical VT. (B and C) Two basal short axis slices showing a predominant epicardial pattern of late enhancement (white arrows). (D) Bipolar voltage map of the epicardial surface of the LV (lateral view). An area of low voltage (0.5 mV) can be seen in the basal lateral region. Yellow dots indicate sites of phrenic nerve capture. (E) Activation mapping during clinical VT. Radiofrequency ablation at the tachycardia exit site (red dots) terminates the VT. LA, left atrium; LV, left ventricle; RVOT, right ventricular outflow tract; VT, ventricular tachycardia.

(1) it requires obtaining point-to-point maps, which is time consuming; (2) areas with poor catheter contact may be misinterpreted as low voltage areas; (3) due to the size of the electrodes, the spatial resolution is low; (4) the far-field effect of the neighbouring healthy myocardium (in the same plane or in depth) can lead to underestimation of the size of the scar, or even failure to detect small scars; and (5) endocardial bipolar voltage maps are unable to delineate the intramural and epicardial portion of the scar.[11 w41–w43]

Real-time integration into the navigation system

3D DE-CMR reconstructions of the ventricles that display the location of the scar have been integrated into the navigation systems, showing satisfactory correlation with electroanatomic mapping (EAM).[12 w44] Integration of a scar tissue image into the navigation system permits the mapping process to be focused on a particular zone.[w45] Scar components, core and border zone, can be imported separately to guide ablation of VT and scar related premature ventricular complexes (PVC) (figure 6).[11 13] However, standardised methods for the analysis of the DE-CMR derived scar components are lacking.[w22 w23 w46] In a previous study, we obtained the best match between EAM and DE-CMR scar components with an algorithm based on maximal signal intensity.[13]

DE-CMR is widely used for the diagnosis of different forms of non-ischaemic cardiomyopathies. However, limited data are available on DE-CMR derived image integration for VT ablation in non-ischaemic patients.[10 w47] In a series of 29 patients with non-ischaemic cardiomyopathy referred for PVC or VT ablation, 14 of them showed hyperenhancement on DE-CMR that identified the arrhythmogenic substrate and helped in selecting the appropriate approach.[10]

Conducting channels identification on DE-CMR

Surviving myocardial fibres within the scar are the main anatomical substrate for infarct related re-entry.[w17 w48] Those conducting channels, identified by means of bipolar voltage during substrate mapping, are an accepted target for ablation.[w40 w49]

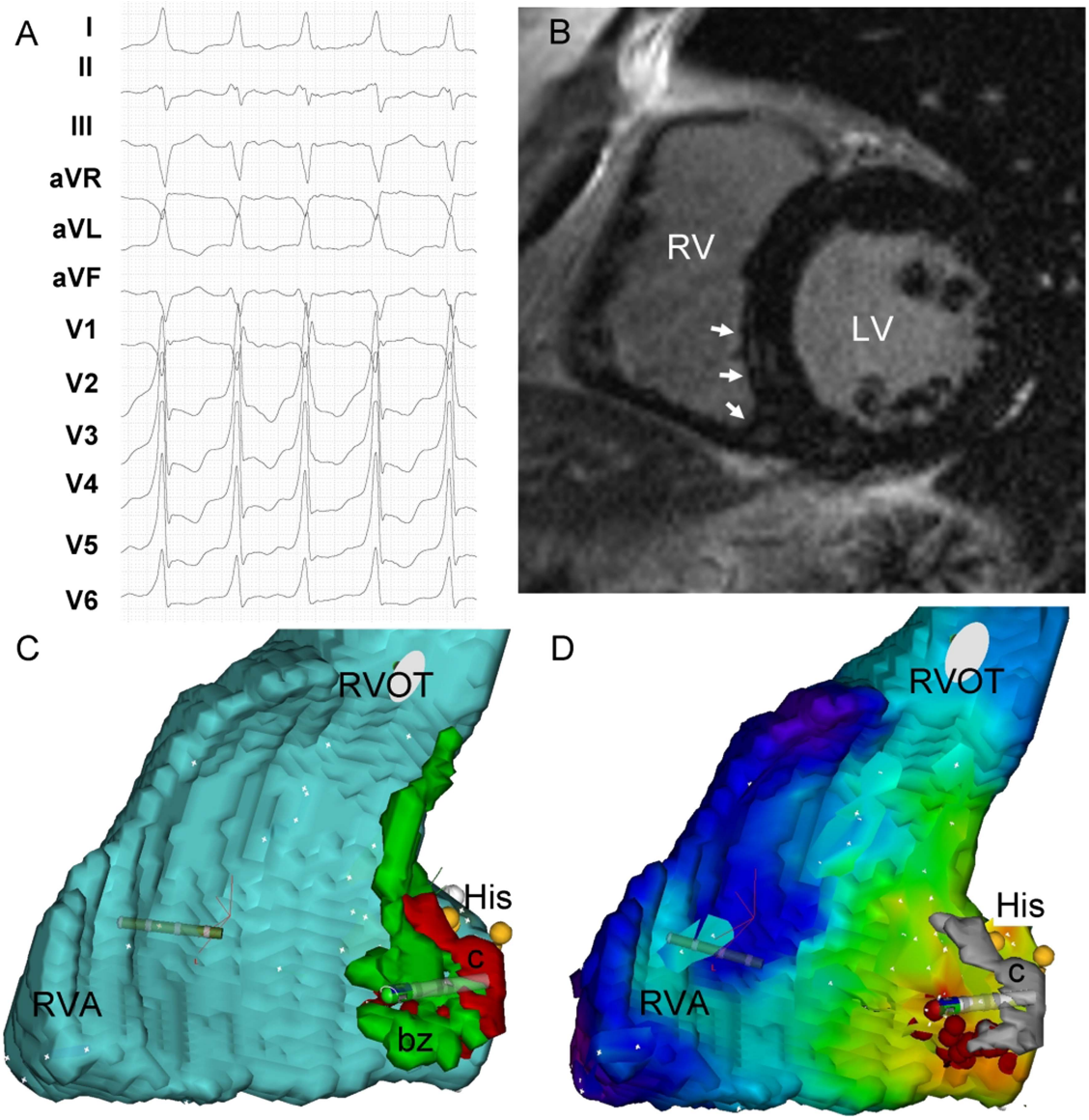

Figure 6 Mid-septal scar and VT. (A) 12-lead ECG of the clinical VT from a patient with non-ischaemic cardiomyopathy. (B) Short axis slice of DE-CMR demonstrates linear mid-myocardial scarring in the basal septum (arrows). Note that the distance between the scar area and the endocardium of the RV is less than the distance to the LV endocardium. (C) Three dimensional DE-CMR reconstruction of the RV and scar tissue (core (c) in red and border zone (bz) in green) located in the basal inferior septum. (D) Endocardial mapping during the VT exposed a focal activation pattern originating from the border zone area. Radiofrequency ablation at this site abolished the VT. Yellow dots indicate His bundle sites. DE-CMR, delayed enhancement cardiac MRI; LV, left ventricle; RV, right ventricle; RVA, right ventricular apex; RVOT, right ventricular outflow tract; VT, ventricular tachycardia.

Animal models using high resolution ex-vivo DE-CMR showed that areas of intermediate signal agreed with bundles of surviving myocytes and predict the location of the VT isthmus.[w50 w51] Recent clinical reports show that border zone channels within the DE-CMR derived scar correlate with conducting channels in EAM.[8 13] These promising results suggest that it is possible to achieve a non-invasive assessment of the VT substrate to guide ablation procedures. However, with the current state of DE-CMR technology (ie, limited spatial resolution, partial volume effect), it is probably not possible to characterise the entire arrhythmogenic substrate accurately. Using high resolution DE-CMR, we recently proposed a shell based approach to better describe the complex 3D structure of the scar and border zone channels in post-myocardial infarction patients (figure 7).[14]

Multimodal image integration

Other imaging modalities, such as positron emission tomography (PET)/CT, have been proposed to identify and characterise scars before VT ablation.[w52] For scar components, image resolution of PET/CT scans is inferior to DE-CMR. On the other hand, CT imaging permits an accurate reconstruction of anatomic structures relevant for ablation, such as epicardial fat or coronary arteries.[w53] Multimodality image integration (ie, CT plus DE-CMR) could offer supplemental information,

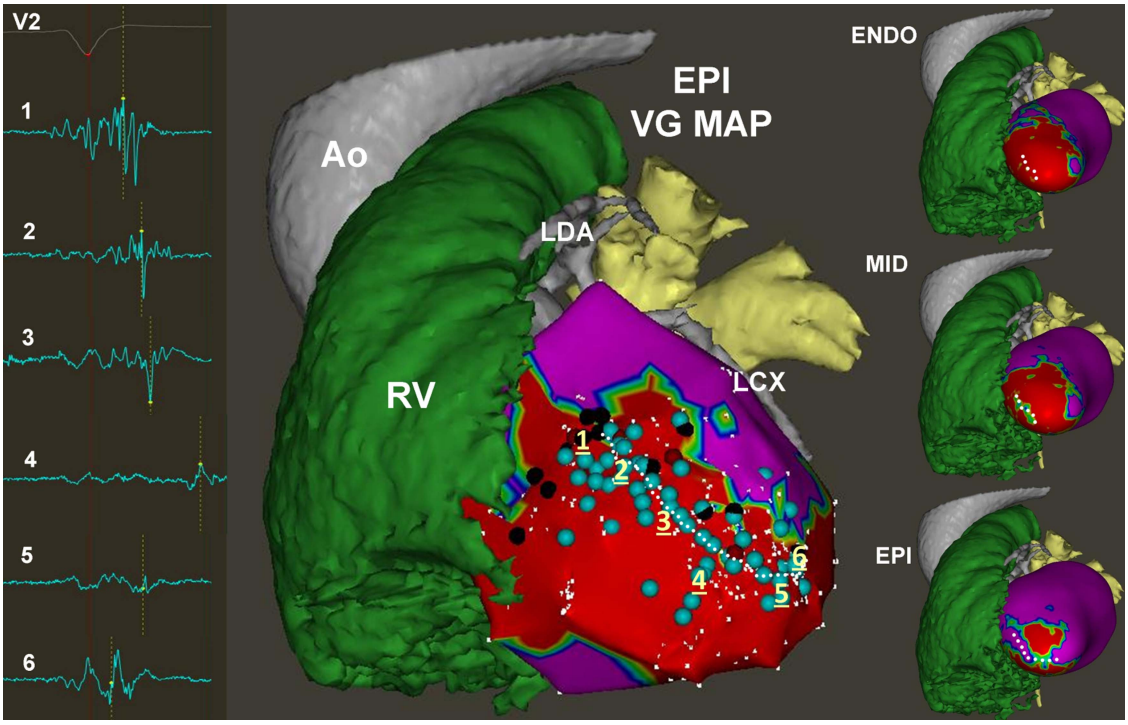

Figure 7 Conducting channel detention in post-myocardial infarction VT. Epicardial bipolar voltage map of the left ventricle merged with CT derived reconstructions of cardiac chambers, aorta, and coronary arteries, shown in the central panel. There is an extensive area of low voltage in the left ventricular apex. A slow conducting channel detected during sinus rhythm is highlighted with a dotted line. Electrograms with delayed components (blue dots) inside the channel (electrograms 1–6) are shown in the left panel. Right panels show signal intensity maps obtained from DE-CMR projected over three dimensional colour coded shells at subendocardium (ENDO), mid-myocardium (MID), and subepicardium (EPI). A large area of scar is seen in the apex. A corridor of border zone (dotted line) reaching the epicardial wall level and matching with the electroanatomic map can be observed. Normal myocardium is coded in purple, core of the infarct in red, and border zone in blue-green-yellow. Ao, aorta; DE-CMR, delayed enhancement cardiac MRI; LCX, left circumflex artery; LDA, left anterior descending artery; RV, right ventricle; VG, voltage; VT, ventricular tachycardia.

improving the safety and results of VT ablation procedures (figure 7).[15 w54]

DE-CMR restrictions: the problem of cardiac devices

The majority of patients with structural heart disease requiring VT ablation have already received an ICD and reported appropriate discharges. The presence of an ICD is considered a contraindication for DE-CMR. Although some studies have reported the safety of DE-CMR in ICD recipients, the presence of relevant artefacts limits the acquisition of quality images, particularly from the anterior myocardial wall.[16] Multimodal image integration and the development of DE-CMR compatible devices may overcome this limitation in the near future. Otherwise, conducting per protocol DE-CMR before ICD implantation would be recommended, with special emphasis on non-ischaemic cardiomyopathies.

EP-MRI SUITE: TOWARDS THE FUTURE OF EP?

The implementation of non-fluoroscopic navigation systems in the EP laboratory has improved anatomic definition of cardiac structures, as well as limiting radiation exposure of both patients and doctors.[w55] Nonetheless, the increased complexity of ablation procedures demands better intra-procedural anatomic definition and improved accuracy in catheter positioning. Reducing the radiation dose also remains an important goal.[w55] Both challenges have led to alternative non-fluoroscopic catheter guidance. Animal data prove the feasibility of catheter tracking, electrogram recording, and radiofrequency energy delivery in a real-time MRI environment.[17 w56–w59] Importantly, the Utah group provided data on intra-procedural tissue characterisation with real-time visualisation of lesion formation during radiofrequency application, which would allow the assessment of lesion depth and transmurality. Ranjan *et al*[17] reported the capability of real-time DE-CMR to identify acute ablation lesions, as well as to identify gaps intra-procedurally and guide catheter positioning to target them. Although important advances have been achieved in animal models, human studies are scarce. Only one study has been published so far showing the feasibility of real-time MRI catheter tracking, pacing, and electrogram recording in humans.[18 w60 w61] Major obstacles need to be overcome to move this technology into the clinical setting: better signal quality on both intracardiac and surface electrograms, improved catheter manoeuvrability, and better visualisation of reference and mapping catheters. However, aside from the technical limitations, this promising technology will provide considerable benefits for patients and their doctors by providing accurate anatomic definition, monitoring radiofrequency lesions, and avoiding x-ray exposure.

MRI in ventricular tachycardia (VT): key points

- The presence of areas of scar tissue with bundles of surviving myocytes is the main underlying substrate for VT in structural heart disease. Cardiac MRI allows precise identification and characterisation of myocardial scar tissue.
- The amount and heterogeneity of scar tissue is strongly related to ventricular arrhythmia susceptibility and adverse outcomes.
- The use of MRI before VT ablation permits focused mapping of the areas of interest and helps in the selection of the appropriate approach (ie, endocardial vs epicardial), particularly in patients with non-ischaemic cardiomyopathy.
- Electroanatomical mapping has several limitations (ie, time consuming, limited accuracy, scar undervaluation) that can be partially overcome by integration of MRI derived scar components into the navigation system.
- MRI postprocessing allows identification and delineation of conducting channels as corridors of border zone within the areas of hyperenhancement.
- Cardiac devices are still the main limitation for using MRI in patients with scar related VT.

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