THE ROLE OF IMAGING IN CATHETER ABLATION OF VENTRICULAR ARRHYTHMIAS

Short Title: Imaging in VT ablation

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ABSTRACT

Late gadolinium enhancement cardiac magnetic resonance (LGE-CMR) and multidetector cardiac computed tomography (MDCT) have emerged as novel, fascinating imaging tools for arrhythmogenic substrate identification and characterization. The role of these techniques for aiding and guiding the catheter ablation of ventricular tachycardia, either as a complement or a surrogate of the electroanatomic map, has been rising in recent years. Integrating pixel signal intensity maps or wall thickness maps delivered from LGE-CMR or MDCT, respectively, into the navigation system has become a cornerstone for VT ablation procedures in a few centers of excellence around the world. The pre-procedure scar characterization offers some advantages, helping decide for the best procedure planning and approach; complete substrate identification and characterization, helping to focus electroanatomical mapping in regions of interest and also has a positive impact in procedure efficiency and outcomes. In the present article, we perform a review of the most practical aspects for using LGE-CMR or MDCT when a VT ablation procedure is planned, from the image acquisition to the integration into the navigation system, analyzing the current role of the LGE-CMR and MDCT for arrhythmogenic substrate characterization as well as for guiding VT ablation.

Keywords: Catheter ablation; ventricular tachycardia; Imaging; Cardiac magnetic resonance; Arrhythmogenic substrate

INTRODUCTION

Catheter ablation of ventricular tachycardia (VT) has notably evolved over the past decades and is approaching its technical maturity. Substrate ablation has become the standard procedure in most of the electrophysiology labs as this approach overcomes the problem of mapping not well-tolerated VTs, and has demonstrated a lower recurrence rate than ablating only the clinical VT (1). Different methodologies for substrate ablation have been described, such as scar homogenization, abolition of late potentials, core isolation or scar dechanneling (2-5). Regardless of the ablation strategy used, the basis for substrate ablation relies on complete arrhythmogenic substrate identification, mostly based on the information of the electroanatomical maps (EAMs). Conventional 3D EAMs generated during ablation procedures have some limitations for substrate characterization: poor catheter contact with the tissue often results in false low voltage areas; depending on the interelectrode distance of the mapping catheter, voltage quantification may be affected by the far-field effect of the surrounding healthy myocardium, thus leading to a smaller EAM-derived low-voltage area; finally, standard bipolar voltage mapping provides limited information regarding tissue that is located deeper to the tip–tissue interface. The last limitation is especially relevant in patients with mid-myocardial scars typically in the basal septum, in which bipolar voltage maps may underestimate the amount of scar, or may display completely normal voltage (6); finally, performing an accurate electroanatomic map of the entire cardiac chamber is time-consuming and requires enough experience and skills.

In the last decade, late gadolinium enhancement cardiac magnetic resonance (LGE-CMR) has emerged as a novel, fascinating imaging tool for aiding and guiding VT ablation procedures and overcoming some of the limitations of the EAM. LGE-CMR has become *the facto* the standard imaging technique to characterize the myocardial scar, not only localizing the scar with exceptional precision, but also allowing for scar quantification and characterization. In the present article, authors analyze the current role of the LGE-CMR for arrhythmogenic substrate characterization as well as during VT ablation procedures. Finally, limitations and future directions of the technique will also be discussed.

LGE-CMR TISSUE CHARACTERIZATION

LGE-CMR capability to distinguish normal myocardium from scarred myocardium is based on the use of gadolinium as a contrast agent to highlight areas of fibrosis. Normal myocardium and scar have different gadolinium washout velocities. Whereas in healthy myocardium the permanence of gadolinium is limited to some minutes, in scarred tissue the washout occurs more slowly. Selecting the correct time to perform a late acquisition is essential to highlight only areas of fibrosis (contrast-enhanced), differentiating them from normal myocardium, which appears black. Several studies have demonstrated the correlation of late gadolinium enhancement with chronic fibrosis (7-8).

The usual image resolution of the LGE-CMR is 1.4 x 1.4 mm. A correct acquisition of the heart images is hampered by its position changes during breathing and the different phases of the cardiac cycle. To overcome this limitation, the standard approach consists in acquiring multiple images during consecutive breath holds, thus obtaining multiple short axis planes along the long axis of the left ventricle. This approach results in an optimal resolution in each single short axis plane but usually with gap distance between slice. On the other hand, the reconstruction of the scar may be difficult due to the existence of partial volume artifact and potential shifting between slices. To control for these limitations, 3-dimensional acquisition protocols have been a great advance. This approach is based on free-breathing imaging using a 3D navigator-gated inversion recovery sequence that allows for 3D reconstructions without slice-shifting artifacts. Our group previously performed a direct comparison between standard 2D and new 3D acquisitions' accuracy to identify and characterize the scarred myocardium and the arrhythmogenic substrate (9); after an automatic imaging post-processing, arrhythmogenic substrate characterization was superior with the 3D technique due to a higher spatial resolution when compared to conventional, 2D sequences.

All methods used for CMR image post-processing are based on the identified pixel signal intensities (PSI). Even if manual depiction of the scar is possible, most groups use a semiautomatic technique that can consist either in: a) a semi-automated standard deviation, defining those pixels with a mean PSI > 2-3 standard deviations as compared with healthy (dark) myocardium; or b) an algorithm based on the maximum pixel intensity (MPI), defining distinct PSI thresholds to differentiate dense scar and heterogeneous scar (border zone). Even though the evidence for choosing one of these post-processing methods is limited, animal studies have reported better correlation when an algorithm based on MPI is used (10). Andreu et al. (11) also studied different algorithms based on the MPI describing that the best correlation with EAM was found by using a 60% cut-off value of the MPI to differentiate the dense and heterogeneous scar.

LGE-CMR IMAGE REGISTRATION AND COMPARISON WITH EAM

An accurate image registration is mandatory for using CMR images for guiding VT ablation procedures. Most of the navigation systems are provided with an automated surface registration algorithm that minimizes the distance from an imaging surface to the EAM surface. The potential error by using these tools has been described to be only about 2-4 mm (12). Still, rotation deviations are possible, especially if the left ventricle is the selected chamber to perform the merge. For this reason, mapping a well-defined anatomical structure, as it is the aortic arch (13), the main left coronary artery (14) or the pulmonary artery can significantly minimize the rotation error. It was suggested that the absence of displacement during the cardiac cycle of the root of the great cardiac vessels makes them optimal structures for merging (15). Figure 1 shows an example of image registration with the aortic root, with the pulmonary artery and finally an example with the left atrium.

An accurate image registration allows performing direct comparison with EAM for arrhythmogenic substrate identification. Wijnmaalen AP et al. (14) studied this correlation in patients with ischemic cardiomyopathy. They found a good correlation of bipolar and unipolar maps amplitudes with the scar areas identified in the LGE-CMR. The standard bipolar voltage cut-off value of <1.5 mV showed good correlation with transmural scar areas, while it did not perform well with small, heterogeneous non-transmural scars. Noteworthy, in this study all VT isthmus sites corresponded with scar areas in the LGE-CMR but some of them were located in areas with normal bipolar voltage. Moreover, the scar area was larger in LGE-CMR than in EAM in one third of the cases, probably due to the far-field effect of the surrounding heathy tissue in the periphery of the scar. Acosta and colleagues previously described that hidden slow conduction areas identified with the multiple extrastimuli technique are located in normal voltage areas in up to one third of cases. In contrast, these areas are frequently located in border zone areas in the LGE-CMR, suggesting a better arrhythmogenic substrate characterization of the scar by the CMR (16). Some strategies to optimize the accuracy of EAM for scar characterization in areas of uncertainty have been described. Tung R. and colleagues described that in patients with a paucity of dense, low-voltage regions in the EAM, an alternate activation wavefront increases the arrhytmogenic substrate detection (17). A preprocedural identification of heterogenous scar by LGE-CMR could potentially select candidates for these maneuvers.

The capability to identify fibrosis areas in patients with non-ischemic cardiomyopathy (NICM) seems to be superior with LGE-CMR than with EAM, too. In an elegant histological study Glashan and coworkers (18) did not find good correlations between fibrosis in NICM patients and any single voltage cut-off value, neither using unipolar or bipolar signals. This fact is not only due to the different fibrosis pattern in NICM patients, described as diffuse with a high heterogeneity, but also to scar distribution; in NICM patients, focal areas of fibrosis are frequently localized in the subepicardial aspect of the left ventricle or mid-septal (19). Dickfeld et al. (6) showed that after integration of LGE-CMR with EAM in NICM patients, a 2-mm rim of viable endocardium, in otherwise transmural scars, results in a falsely normal bipolar voltage that can prevent the detection of up to 60% of transmural mid-myocardial scars. Recently, Marchlinski et al. (20) characterized the arrhythmogenic substrate in a group of 95 NIMC patients. Bipolar mapping was able to accurately identify scar areas in only 61% of the patients with septal involvement. Unipolar voltage better correlated with LGE-CMR scarred area than bipolar voltage.

In summary, LGE-CMR is able to identify areas of scar at least as well as EAM, being clearly superior in cases of non-transmural, small and more heterogeneous scars or in mid-myocardial scars. Figure 2 shows an example of arrhythmogenic substrate characterization with the LGE-CMR reconstruction in patient with a healed myocardial infarction.

HETEROGENEOUS TISSUE CHANNELS IDENTIFICATION USING LGE-CMR

Different myocardial injuries may result in different degrees of cell damage, with also distinct repair mechanisms and, as a consequence, different architectures of fibrosis within the same scar area. Strands of surviving myocardial tissue can cross through the dense scar forming tortuous and slowly conducting channels which support reentry (21), as these channels can be composed by areas with fixed or functional conduction block. These survival myocardial bundles, usually separated by collagenous septa (22), show intermediate degrees of fibrosis. This characteristic makes them identifiable by showing a heterogeneous appearance on the LGE-CMR (23).

As a consequence of the difficulty to obtain direct comparisons of human histology with LGE-CMR, most studies on the matter have validated the accuracy for detecting arrhythmogenic substrate with LGE-CMR imaging against electrophysiological data. Several studies reported that the critical isthmus of reentrant VT in patients with structural heart disease are located in areas of heterogeneous appearance (border zone areas) in the LGE-CMR (24). In a remarkable next step, Perez-David et al. (25) evaluated the capability of LGE-CMR to identify heterogeneous tissue channels (HTC) within the scar in 18 post-infarction patients with monomorphic VTs, considering conduction channels identified by EAM voltage mapping the “gold standard”. They found that all HTC identified in the LGE-CMR corresponded in location and orientation to similar voltage channels in the EAM. Our group have shown that non only voltage channels but also late potential channels identified in the EAM can be identified noninvasively with LGE-CMR. The methodology for channel identification followed by our group is described in detail in Figure 3. Following this approach, Fernández-Armenta et al. (26) studied 21 chronic post-infarction patients undergoing VT ablation with a pre-procedure 3-Tesla LGE-CMR using a high-resolution 3D acquisitions. In this study, LGE-CMR-defined HTCs channels identified 74% of the critical isthmuses of clinical VTs and 50% of all the conducting channels identified in EAMs.

HTCs are usually defined as continuous corridors of border zone surrounded by scar core or scar core and an anatomical barrier (i.e. mitral annulus) connecting two areas of healthy tissue. These HTCs can be identified prior to the ablation procedures and then imported into the navigation system to aid VT ablation procedures. Figure 4 shows an example of LGE-CMR image post-processing for HTCs identification and how this information is imported into the navigation system in a patient with ischemic cardiomyopathy. Due to the thinness of the right ventricular wall, HTCs identification is usually limited to the left ventricular chamber.

USEFULNESS OF LGE-CMR FOR SELECTING THE OPTIMAL ABLATION APPROACH

The selection of the cardiac chamber or the endocardium vs epicardium for mapping and ablation has been usually based on the information of the VT-ECG, the likelihood of the substrate location based on the underlying heart disease, or on the success of a previous endocardial ablation (27). A pre-procedure LGE-CMR has the potential utility of identifying the fibrosis location and, in this way, helping physicians to a better procedure planning (28). In a study by Andreu et al., (29) LGE-CMR studies of 80 patients with structural heart disease undergoing VT ablation were analyzed. Authors reported that gadolinium hyperenhancement was present in 96% of the successful ablation points of clinical VT. Moreover, the presence of subepicardial hyperenhancement showed 85% sensitivity and 100% specificity for predicting an epicardial origin of the VT.

Epicardial access for VT ablation implies performing a subxiphoid puncture into the pericardial space. In ischemic patients, performing a combined endo-epicardial approach was related with a lower recurrence rate during follow-up, either used as a first-line strategy or after a previously failed endocardial ablation (30,31). However, a significant proportion of patients undergoing epicardial mapping do not exhibit epicardial arrhythmogenic substrate, being therefore subjected to a procedure of greater risk but without additional benefit. A decision based on procedural imaging for selecting the best candidates for a first line endo-epicardial approach has shown to be more efficient (32). Figure 5 shows an example of how imaging can accurately predict presence of arrhythmogenic substrate in the epicardium. A combined endo-epicardial approach has been also associated with better outcomes in NICM patients (33). However, this approach has been also related with a higher rate of procedural complications, highlighting the need for an accurate patient selection. Several studies have shown that pre-procedural LGE-CMR is able to identify those NICM patients that could benefit from an epicardial approach based on the LGE distribution (29,34). Moreover, pre-procedural LGE-CMR can also facilitate ablation in NICM patients with predominant intramural scar (35). A biventricular approach guided by LGE-CMR has been also described to be associated with better outcomes in patients with NICM (36). Alternatively, in case of mid septal intramural scar, LGE-CMR can guides the selection of the chamber from which delivery radiofrequency (right ventricle or left ventricle) based on the distance from endocardium to the scar (29). The use of LGR-CMR can be especially useful for selecting the better approach in some kind of NICM due its specific arrhythmogenic substrate distribution,

i.e. cardiac myocarditis or cardiac sarcoidosis (37,38).

CLINICAL USEFULNESS OF LGE-CMR INTEGRATION FOR VT ABLATION

The benefits of using LGE-CMR information for helping during VT ablation procedures go beyond the selection of the best procedure approach: scar location can be depicted right from the beginning of the procedure, helping to focus catheter mapping in this area; scar shape, boundaries, and size are not altered in the LGE-CMR as it occurs in the EAM, due to the far-field effect of the surrounding healthy tissue. This is especially important in small and heterogeneous scars, as previously discussed. Finally, the integration of the HTCs information also permits the identification of the width and depth of the channels, as figure 3 shows, information that cannot be obtained with EAM. In spite of these theoretical advantages, there are no previous randomized studies designed to test the real additional benefits of this approach as compared with the use of the EAM alone. However, evidence is rising. The group of Bordeaux retrospectively analyzed VT-free survival in a consecutive series of 125 ischemic patients undergoing VT ablation (39). They found that the use of real-time integration of CMR was independently associated with less recurrence rate after ablation. Intraprocedural integration of LGE-CMR segmented scar resulted also in better acute outcomes in NICM patients in a retrospective analysis (36). Another recent, prospective analysis of 24 patients with scar-related VT showed that focusing the EAM in those areas with LGE was significantly associated with a lower recurrence rate (40). Our group previously evaluated the benefits of LGE-CMR integration in a consecutive population of 159 patients undergoing VT ablation using the scar dechanneling technique. CMR-aided ablation was performed in 54 (34%) patients. When compared with the remaining 105 patients, aiding the procedure with LGE-CMR integration was associated with a lower need for radiofrequency delivery, higher noninducibility rates after substrate ablation, and a higher VT-recurrence-free survival (41). Recently, our group has reported the results of a LGE-CMR-guided strategy in 28 consecutive patients with scar-related VTs (42). In these patients, no EAM was performed. The LGE-CMR-guided approach showed to be feasible and safe, significantly reducing the procedural, fluoroscopy, and radiofrequency times, and was associated with a low rate of VT recurrence. The novelty of this approach was that the ablation targets were selected based on the LGE-CMR information, suggesting that EAM is not mandatory for substrate identification.

In view of this increasing evidence, the recently published expert consensus statement on catheter ablation of ventricular arrhythmias (43) includes two new indications regarding the use of CMR: 1) the recommendation to perform a preprocedural LGE-CMR in both ischemic and non-ischemic patients undergoing VT ablation to reduce recurrences; and 2) to use the pre-procedural LGE-CMR information for procedural planning. Both indications have a IIa class recommendation.

MULTIDETECTOR CARDIAC COMPUTED TOMOGRAPHY

Multidetector cardiac computed tomography (MDCT) is an imaging tool that, compared to LGE-CMR, presents an important advantage: its greater spatial resolution. Whilst LGE-CMR spatial resolution usually range from 1.4 to 2 mm, MDCT spatial resolution is usually close to 0.5 mm. On the contrary, MDCT presents a lower contrast-to-noise ratio, a characteristic that reduces the MDCT capability for scar characterization.

As consequence of the greater spatial resolution, MDCT allows a high definition of cardiac anatomy. It can accurately define the course of the coronary arteries or the coronary sinus. Moreover, MDCT permits to identify sensitive extracardiac structures, i.e. the left phrenic nerve. Finally, it can detect the presence of fat and calcium with great precision. These capabilities have relevant implications in VT ablation procedures. Yamashita et al. previously showed how MDCT integration during epicardial VT ablation can increase the safety of the procedure by identifying the course of the coronary arteries and phrenic nerve, thus avoiding radiofrequency delivery in close proximity of these structures (44). The group of Katja Zeppenfeld, in Leiden, previously showed how MDCT may help to identify epicardial fat distribution (45), thus facilitating the interpretation of bipolar electrograms and the identification of sites where ablation might be potentially ineffective. Moreover, a recent study by Ustunkaya et al. described a good correlation between the location of the epicardial arrhythmogenic substrate and the presence of right ventricular attenuation in the MDCT after image integration in patients with right ventricular arrhythmogenic cardiomyopathy (46).

MDCT is also useful for helping during ablation procedures of VTs originated from complex intracardiac structures, i.e. the papillary muscles (47), as Figure 6 shows. Finally, the better anatomical definition of MDCT is also used by some groups to supplement the LGE-CMR information, thus performing multimodal image integration, as Figure 4 shows.

The other side of the coin is the low capability of MDCT for distinguishing between normal myocardium and scar due to its low contrast-to-noise ratio. Two main methods have been described for MDCT scar characterization: 1) delayed enhancement areas in late image acquisitions (48); and 2) thinning areas of the ventricular wall (49). When compared with the EAM, MDCT presents a good correlation with the scar in patients with ICM, particularly those with transmural scars, whereas this correlation is weak in non-transmural scars or in patients with NICM (50). Based on the thickness distribution within the scar, conducting channels can be also identified with MDCT. A good correlation between these channels, defined as MDCT-detected myocardial ridges, and VT isthmuses has been described (51). Our group recently reported that MDCT accurately identifies conducting channels in ischemic patients with transmural scars, but when compared with LGE-CMR, the myocardial wall thickness assessment using MDCT fails to detect a significant proportion of arrhythmogenic substrates in patients with subendocardial ischemic scars (52), as Figure 7 shows. MDCT, however, represents a valuable alternative for imaging integration among patients in whom CMR is of suboptimal quality (i.e. ICD carriers), or for whom CMR is contraindicated or unavailable.

LIMITATIONS OF IMAGING INTEGRATION

Currently, the main technical limitation of LGE-CMR is its low spatial resolution, which is usually limited to a maximum of 1.4 x 1.4 x 1.4 mm (voxel resolution), as informed in the clinical reports until now. Theoretically, very small HTCs could be potentially underdetected. The new free-breathing acquisition methods can provide an isotropic spatial resolution of nearly 1 mm^3, but it could be still insufficient to detect very small bundles of surviving myocytes with the potential for sustaining reentry, which have described to be even < 200 µm (21). Further improvements in LGE-CMR spatial resolution are expected to occur in the next years.

Traditionally, LGE-CMR was contraindicated in pacemaker or ICD carriers for safety reasons. However, recent studies have shown that LGE-CMR is safe in these patients (53, 54). Still, artifacts due to the presence of these devices can compromise the quality of the LGE-CMR images, especially in the LV anterior wall. Recently, it has been reported that using a new wideband sequence, a higher proportion of LGE-CMR studies are interpretable by reducing or eliminating these artefacts (55).

Image integration can also be limited by the time lapse between the acquisition and the ablation procedure. Usually, imaging is performed some days before the VT ablation but, in some cases, it can be performed several months before, as for example in case of LGE-CMR acquisition before ICD implantation as primary prevention of sudden cardiac death. It is known that arrhythmogenic substrate may potentially evolve in NICM patients, which suffer from progressive fibrosis. Besides, it was recently reported that arrhythmogenic substrate can also significantly change in chronic post-infarction patients, even years after the ischemic event. (56).

Finally, it is important to take in mind that cardiac image does not contain electrical information. Tissue characterization by the pixel signal intensities permit identifying border zone areas, suggesting that they are composed by dissimilar degrees of fibrosis. However, imaging is not able to provide information on the conduction velocities and slowing of impulse propagation and refractory periods; tissue characteristics which are critical for a given border zone area to become a reentrant arrhythmia circuit. As a consequence, imaging remains an excellent toll for helping VT ablation but cannot substitute electrophysiological information provided by mapping catheters at present.

Main limitation of LGE-CMR and MDTC respectively are summarized in table 1.

FUTURE PRESPECTIVES

Currently, pre-procedure image does not include electrocardiographic information to be used to guide VT ablation. One of the objectives of VT ablation procedures is to localize and ablate the site of origin (isthmus exit site) of the clinical VT, but this is not possible using only imaging data. Surface ECG analysis is useful to anticipate the segment of origin of the VT (57). A new simplified approach for ablation of the clinical TV using the surface ECG and the LGE-CMR information has been described (42). The integration of image and electrocardiographic information in a single platform and the use of machine learning algorithms could potentially allow identifying in advance the channels responsible for the clinical VT, simplifying and increasing the efficiency and efficacy of the VT ablation procedures.

In last years, a new non-invasive strategy for scar-related VT ablation based on stereotactic body radiotherapy has been described (58). Radiation of non-targeted areas (remote myocardium) has limited the application of this technique. Image integration and identification of HTCs or MDCT channels could refine the selection of the ablation targets, minimizing radiotherapy delivery and improving the efficiency of this approach.

Some of the limitations of using LGE-CMR images, like changes in the arrhythmogenic substrate over time or errors in image integration could be overcome by performing CMR directly in the electrophysiology lab with a real-time visualization of catheters inside the heart. The feasibility of this technology has been already reported in the case of atrial arrhythmias (59), but significant issues remain to be applied in VT ablation procedures (60).

Finally, previous studies have shown the feasibility of a post procedure identification of the ablation lesions with LGE-CMR (61,62). Whether characterization of these lesions after ablation, i.e. total block of heterogeneous tissue channels' entrances, can predict outcomes, remains unknown.

Data Availability: Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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Figure 1. Figure 1 shows how image registration can be performed with different cardiac structures.

Figure 1A. Multidetector cardiac computed tomography (MDCT) integration in the navigation system using a fast-anatomical map (FAM) of the aortic root. Note that the entire aortic arch, rather than just the aortic root, was used for merging in order to minimize the rotation deviations. **Figure 1B.** MDCT integration using the trunk of the pulmonary artery. **Figure 1C.** Example of MDCT integration using the FAM of the left atrium and pulmonary veins.

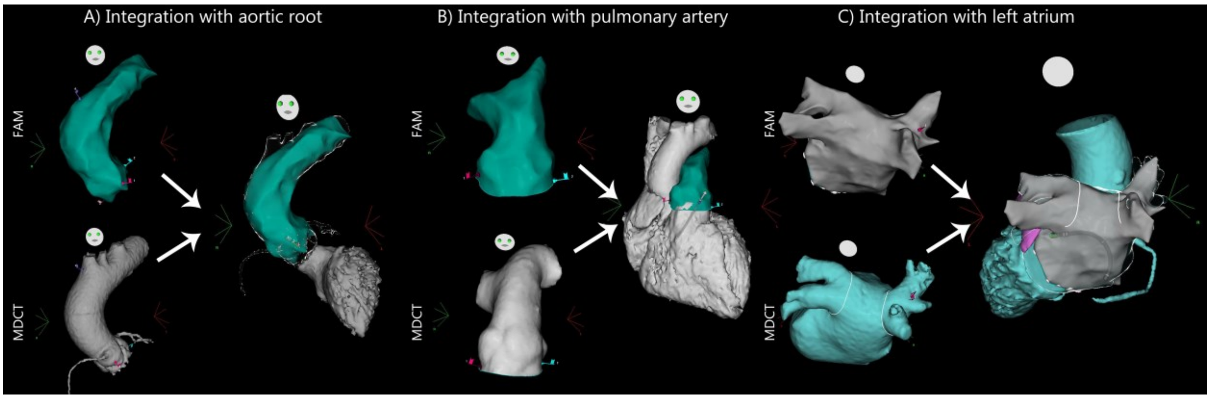

Figure 2. Comparison of arrhythmogenic substrate characterization with the electroanatomical map (EAM) and the pixel signal intensity maps delivered from the late gadolinium enhancement cardiac magnetic resonance (LGE-CMR) in a patient with a healed inferior infarction. On the top and left, posterior view of the voltage map using standard cut-off value for dense scar (0.5 mV) and border zone (1.5 mV), showing an inferior scar involving the basal and medial segments. On the top and right, characterization of the local electrograms (EGMs): blue dots represent EGMs with delayed components; black dots represent EGMs with conduction channel (CC) entrance characteristics; yellow dots represent EGMs with conduction system characteristics. Three CCs are depicted over the reconstruction (white dotted lines), one sub-mitral channel and two channels crossing the scar parallel to the mitral annulus. On the bottom of the figure, pixel signal map delivered from the pre-procedure LGE-CM at 10%, 30%, 60% and 90% of left ventricular wall thickness in the same patient. Note that the same 3 CCs can be easily identified in the 10% endocardial layer.

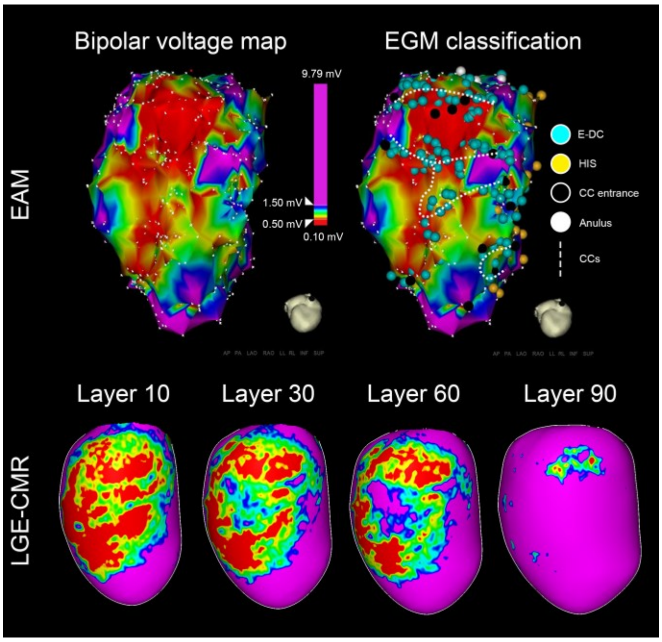

Figure 3. Scar characterization in an ischemic patient with a healed inferior infarction. **Figure 3A,** short axis view of the late gadolinium enhancement cardiac magnetic resonance (LGE-CMR) showing an heterogeneous inferior scar. Healthy myocardium is depicted in purple; border zone (BZ) area is depicted in green; dense scar [core-zone (CZ)] is depicted in red; An heterogeneous tissue channel automatically detected crossing the scar perpendicular to the mitral annulus is depicted in blue. **Figure 3B** shows the 3D reconstruction of the left ventricle using the pixel signal intensity information. The 3D reconstruction renders easier the visualization of the scar architecture, the relationship between the different components of the scar, as well as the course of the channels.

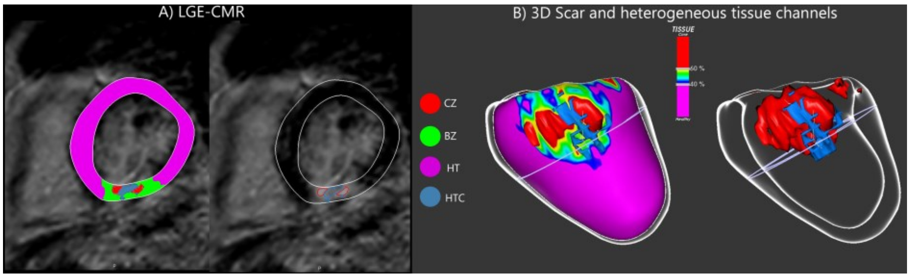

Figure 4. Multimodal image integration. On the left and top, pre-procedure multidetector cardiac computed tomography (MDCT). Note how the high spatial resolution allows to identify, for example, the course of the coronary arteries. On the left and bottom, pixel signal intensity map delivered from the late gadolinium enhancement cardiac magnetic resonance (LGE-CMR). Note how the tissue characterization using the pixel signal information allows the identification of an anterior myocardial scar. Besides, 3 heterogeneous tissue channels were identified (black lines). In the middle, fusion between the anatomical structures extracted from the MDCT and the LGE-CMR. On the right, integration of this information within the spatial reference coordinates of CARTO® system, by performing a fast-anatomical map (FAM) of the aortic root.

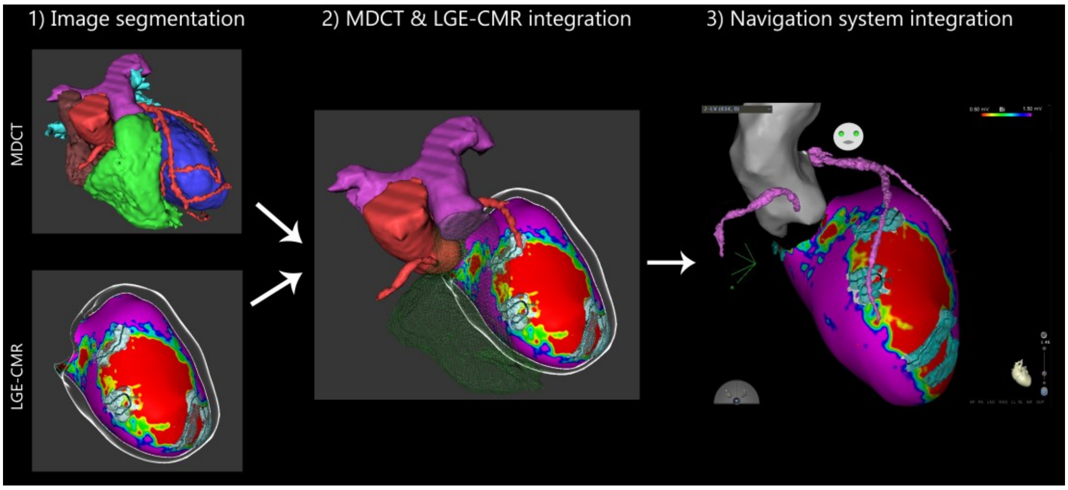

Figure 5. Figure modified from Soto-Iglesias D. et al. Heart Rhythm 2018. Multimodal integration of late gadolinium enhancement cardiac magnetic resonance (LGE-CMR), multi-detector computed tomography (MDCT), and electroanatomical mapping data (EAM) showing two patients with a classical transmural infarction (C-TMI) defined by LGE-CMR which had and not epicardial arrhythmogenic substrate (top and bottom rows, respectively). Scar configuration in the endocardial and epicardial layers, obtained from LGE-CMR, is shown in the two left columns (healthy tissue, border zone and core zone in purple, green and red, respectively). Myocardial wall thickness (WT) extracted from MDCT are mapped onto 9 the epicardial LGE-CMR geometry. Regions with WT 5mm in purple, and 3.59mm<WT are colored in red, WT>5mm in purple, and 3.59mm<WT<5 mm in green. The image "MDCT/LGE-CMR integration" represents scar distribution from LGE-CMR epicardial layer with the contour of the WT area between 3.59 and 5 mm superimposed as a white line. The EAM shows the scar identified from standard voltage values (0.5 and 1.5 mV); electrograms with delayed-components are represented as blue dots.

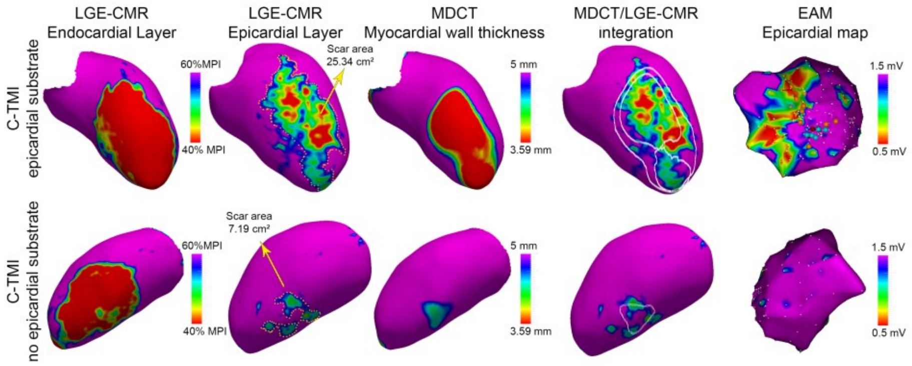

Figure 6. Ablation procedure aided by multidetector cardiac computed tomography (MDCT) integration in a patient with ventricular arrhythmias arising from the infero-septal papillarymuscle. Note how the high spatial resolution of MDCT allows to identify complex intracardiac structures, helping the physician to focus the map in the area of interest and to ensure enough catheter contact with the tissue.

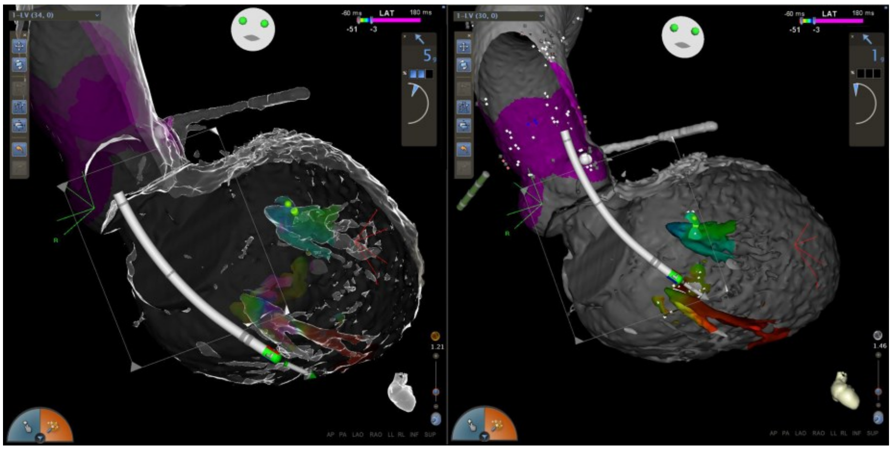

Figure 7. Figure modified from Jauregui B et al. Europace 2020. Multimodal imaging-based channel detection in transmural (top panels) and subendocardial (bottom panels) myocardial infarction. On the top panels, an example of a transmural anterior infarction. Both, late gadolinium enhancement cardiac magnetic resonance (LGE-CMR), on the left, and multidetector cardiac computed tomography (MDCT), on the right, are able to identify 2 channels, one basal and one apical, parallels to the mitral annulus. On the bottom panels, an example of an anterior subendocardial infarction. Only LGE-CMR were able to identify a subendocardial channel whereas no channels were revealed in the MDCT.

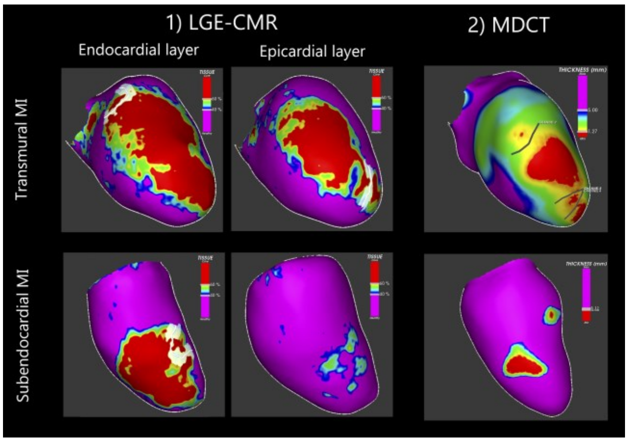

Table 1. Main limitations of LGE-CMR and MDCT for image integration during VT ablation procedures:

Late gadolinium enhancement cardiac magnetic resonance	*Multidetector cardiac computed tomography*
• Low spatial resolution. Spatial resolution is usually limited to 1.2 or 1.4 mm (isotropic voxel resolution) that could be insufficient to detect small bundles of surviving myocytes with the potential for sustaining reentry. • Insufficient spatial resolution to characterize thin structures as the right ventricle wall. • Potential artefacts in patients with cardiac implantable electronic devices. Can be solved by using wideband sequences. • Long acquisition times, especially if high resolution is needed for performing volumetric reconstructions. • Need for optimization of 3D, high resolution, tissue characterization sequences at each center. • Needed of semiautomatic segmentation postprocessing.	• Low contrast-to-noise ratio that minimizes the capability to distinguish between normal myocardium and scar. • Inability to distinguish non-transmural scars and channels when using the myocardial wall thickness for tissue characterization. • Lack of studies validating imaging characterization with human histology. • Increasing the cumulative radiological exposure.