Noninvasive identification of epicardial ventricular tachycardia substrate by magnetic resonance–based signal intensity mapping

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BACKGROUND Endo–epicardial substrate ablation reduces ventricular tachycardia (VT) recurrences; however, not all patients in whom the epicardium is explored have a VT substrate. Contrast-enhanced magnetic resonance imaging (ceMRI) is used to characterize VT substrate after myocardial infarction.

OBJECTIVE The purpose of this study was to determine if epicardial VT substrate can be identified noninvasively by ceMRI-based endo–epicardial signal intensity (SI) mapping.

METHODS Myocardial infarction was induced in 31 pigs. Four or 16 weeks later, ceMRI was obtained, and the averaged subendocardial and subepicardial SIs were projected onto 3-dimensional endocardial and epicardial shells in which dense scar, heterogeneous tissue (HT), and normal tissue were differentiated. An HT channel was defined as a corridor of HT surrounded by dense scar and connected to normal tissue. A "patchy" scar pattern was defined as the presence of at least 3 dense scar islets surrounded by HT forming $\geq$2 HT channels. Electrophysiologic study was performed after ceMRI.

RESULTS Thirty-three different sustained monomorphic VTs (291 $\pm$ 49 ms) were induced in 25 pigs. Mid-diastolic electrograms were recorded in the endocardium (endocardial VT) in 17 and in the epicardium (epicardial VT) in 13. Epicardial SI mapping showed that scar area was similar in animals with and without epicardial VT (24 $\pm$ 6 cm^2 vs 25 $\pm$ 12 cm^2), but HT covered a higher surface of the epicardial scar in animals with VT (76 $\pm$ 6% vs 61 $\pm$ 10%, $P = .03$). A patchy scar pattern was observed in all animals with epicardial VT but only in 3 animals without VT ($P < .001$).

CONCLUSION CeMRI-based SI mapping allows identification of the epicardial VT substrate.

KEYWORDS Epicardium; Magnetic resonance imaging; Ventricular tachycardia; Arrhythmogenic substrate

ABBREVIATIONS **3D** = 3-dimensional; **CC** = conduction channels; **ceMRI** = contrast-enhanced magnetic resonance imaging; **CL** = cycle length; **EIC-LP** = electrograms with isolated components/late potentials; **ENDO** = entire endocardium; **ENDO-50%** = internal half of the endocardium; **EPI** = entire epicardium; **EPI-50%** = external half of the epicardium; **HT** = heterogeneous tissue; **LV** = left ventricle; **MRI** = magnetic resonance imaging; **PES** = programmed electrical stimulation; **SI** = signal intensity; **SMVT** = sustained monomorphic ventricular tachycardia; **VT** = ventricular tachycardia

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Introduction

The substrate of most sustained monomorphic ventricular tachycardias (SMVTs) is located in the endocardium, but some ventricular tachycardias (VTs) can only be ablated from the epicardium.[1–4] A combined endo–epicardial substrate ablation approach reduces VT recurrences; however, $<$30% of patients in whom the epicardium was explored had an epicardial VT substrate.[5] In addition, epicardial fat may reduce voltage mapping accuracy to delimit epicardial scars.

Contrast-enhanced magnetic resonance imaging (ceMRI) reliably identifies scars and VT substrate: (1) infarct morphology, scar surface extension, and heterogeneous tissue (HT)

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mass are predictors of VT inducibility and mortality[6–8]; and (2) VT-related endocardial slow conduction channels (CC)[9,10] correspond with HT channels that are detected by ceMRI-based signal intensity (SI) mapping, a method in which the averaged subendocardial tissue SI is projected onto a 3-dimensional (3D) left ventricular (LV) endocardial shell.[11,12]

We hypothesized that epicardial SMVT substrate can be identified by ceMRI-based endo–epicardial SI mapping. This hypothesis was assessed in a swine model of postinfarction VT. The purposes of the study were (1) to evaluate the capability of SI mapping to identify epicardial VT substrate, (2) to compare the characteristics of epicardial and endocardial VT substrates, and (3) to determine the time to epicardial VT substrate appearance.

Methods

Experimental protocol

The study protocol was approved by the Institutional Animal Care and Use Committee (Centro de Cirugía de Mínima Invasión Jesús Usón). Experimental details are available in the Online Supplementary Material.

Thirty-one domestic pigs weighing 29 to 37 kg were used for this study. To induce closed chest myocardial infarction, the left anterior descending coronary artery was occluded transiently by a balloon catheter placed just distal to the first diagonal branch for 150 minutes, followed by reperfusion. CeMRI and electrophysiologic study were performed either 4 weeks (group 1) or 16 weeks (group 2) later in order to establish the time to epicardial VT substrate appearance.

MRI acquisition and processing (Online Supplementary Material)

The animals underwent ceMRI with a 1.5-T scanner (Intera, Philips Medical Systems, Best, The Netherlands). All images were obtained with ECG gating and breath-holding.

The MRI study consisted of cine steady-state free-precession imaging of LV function and late enhancement imaging of myocardial scar tissue. Late-enhanced images were obtained 15 minutes after a total injection of 0.2 mmol/kg of gadobutrol (Gadovist, Bayer Shering Pharma AG, Berlin, Germany) and were used for infarct characterization. Delayed enhancement data acquisition provided a pixel resolution of 1.29 × 1.29 mm in-plane and a slice thickness of 2.5 mm, which corresponds to approximately 40 slices covering the LV. We used previously defined SI thresholds to quantify 2 different areas within the infarct zone: (1) the scar core defined by a SI >3 SD above the mean of the remote normal myocardium, and (2) HT (i.e., gray zone) defined by an SI between 2 and 3 SD.[7,8]

Magnetic resonance based endo–epicardial SI mapping

The myocardial wall was divided into 2 equal parts: subendocardium and subepicardium. The averaged SI of the internal half of the subendocardium (ENDO-50%), the entire subendocardium (ENDO), the entire subepicardium (EPI), and the external half of subepicardium (EPI-50%) were projected respectively onto 3D endocardial and epicardial shell reconstructions of the LV to identify the endocardial and epicardial VT substrate. LV endocardial/epicardial contours were manually defined on contiguous short-axis slices using QMass MR 7.0 and imported into our tool in which 3D endocardial/epicardial reconstructions were computed offline from a short-axis ceMRI image volume using custom software developed in the MATLAB environment (Mathworks, Natick, MA). The 3D visualization interface was implemented in Java (Sun Microsystems, Santa Clara, CA) using VTK (Kitware, Clifton Park, NY) visualization algorithms.[11] These 4 surface maps were analyzed to determine the structure of the scar (endo–epicardial SI mapping; Figure 1, A–D). These surfaces were color coded to provide information on SI. The red area represented dense scar and was defined by SI ≥ minimal SI in the core of the scar; the magenta area represented normal myocardium (SI ≤ peak SI in normal myocardium); and the area between these extremes represented HT. In all SI maps, the extension of scar, dense scar, and HT were measured using custom-developed software. An HT channel was defined as a corridor of HT differentiated by a SI lower than the surrounding scar tissue (Figure 1). A patchy scar pattern was defined by the presence of at least 3 dense scar islets surrounded by HT; this implied the existence of at least 2 HT channels. For side-to-side comparison with voltage mapping, the scar extension and the orientation referred to the mitral annulus and segment location of each HT channel were determined.[13] Two independent investigators blind to the electrophysiologic study analyzed the SI maps.

Electrophysiologic study and electroanatomic mapping

The animals underwent electrophysiologic study 2 days after ceMRI. A quadripolar catheter was placed at the right ventricular apex against the distal septum close to the infarct area. A multipolar catheter was placed in the pericardial sac as previously described.[14]

Point-by-point sequential endocardial and epicardial mapping was performed during sinus rhythm or right ventricular pacing using the CARTO system (XP version, Biosense Inc, Diamond Bar, CA) with the NaviStar ThermoCool catheter (Biosense Inc). Multiple sites were explored to obtain a minimal fill threshold of 10 mm in the low-voltage area; 0.5 and 1.5 mV were the limits to define dense scar and scar areas, respectively. As the upper and lower limits of the color range were set at 1.51 and 1.5 and then lowered in steps of 0.1 mV to 0.11 and 0.10 mV, 30 voltage maps were analyzed for each animal: 15 maps from the endocardium and 15 from the epicardium.

Slow CC and the activation sequence within CC were defined as referred[9] and tagged in the scar. In those cases in which voltage mapping was performed during sinus rhythm, CC were reviewed during right ventricular pacing to uncover electrograms with isolated components/late potentials (EIC-LP).[15] HT conduction velocity was estimated in CC in which