Characterization of the infarct substrate and ventricular tachycardia circuits with noncontact unipolar mapping in a porcine model of myocardial infarction

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BACKGROUND Conventional mapping of ventricular tachycardia (VT) after myocardial infarction is limited in patients with hemodynamically untolerated or noninducible VT.
OBJECTIVES The purpose of this study was to develop a unique strategy using noncontact unipolar mapping to define infarct substrate and VT circuits.
METHODS Dynamic substrate mapping (DSM) was performed in seven pigs with healed anterior myocardial infarction. This technique defined substrate as the intersection of low-voltage areas identified in sinus rhythm and during pacing around the infarct. Pacing was also performed within the substrate to determine exit sites.
RESULTS Anteroapical transmural scar was identified in all animals. A mean of three pacing sites was used for substrate definition. The mean area (± SD) was 18.4 ± 8.8 cm^2 by DSM and 15.4 ± 6.9 cm^2 by pathology ($P > .5$). A mean of 4.5 sites was paced within substrate. Ten of 18 paced wavefronts exited substrate adjacent to the pacing area, seven exited at distant areas, and one had two exits. VT was induced in five animals (1.6 morphologies per animal). Except for one VT, circuit exit sites were identified at substrate borders on the endocardium. VT exit sites were at (n = 6) or near (n = 3) a pacing exit site. Electrogram voltages differed significantly between substrate, border, and nonsubstrate areas in infarcted animals and in comparison with control animals. No substrate was identified in two control animals.
CONCLUSION DSM is a reliable method for infarct substrate localization in this model. Pacing within substrate can predict VT exit sites and may prove useful for ablation of unmappable VT after myocardial infarction.

KEYWORDS Tachyarrhythmias; Myocardial infarction; Electrophysiology; Ablation; Ventricular tachycardia
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Introduction

Ablation of ventricular tachycardia (VT) following myocardial infarction is modestly effective in well-selected patients. The most successful approach has been based on entrainment mapping of hemodynamically tolerated VT and ablation of a narrow band (isthmus) of viable tissue within scar that is a critical component of the circuit.[1,2] Many patients have multiple morphologies of VT induced during an ablation procedure.[3] If not ablated, nonclinical VT morphologies have a high incidence of recurrence.[4]

Only a limited number of VTs are tolerated by patients for durations sufficient to allow traditional mapping.[5,6] In response, substrate-based ablation of VT has been developed.[7] This approach relies on scar reconstruction using point-by-point voltage mapping and ablation guided by pace mapping of clinical and/or induced VT morphologies. Creation of linear lesions guided by low-voltage areas defined by electroanatomic mapping and pace mapping has allowed

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for treatment of unmappable VT due to either poor hemodynamic tolerance or the inability to induce sustained VT. All known VTs can be targeted, but other possible circuits may be extant.

The acquisition of virtual unipolar electrograms via an expandable multielectrode array has allowed for real-time mapping of many arrhythmias, both focal and reentrant.[8,9] Validation of noncontact electrograms compared with contact electrograms[10–12] and validation of site localization of radiofrequency (RF) lesions[10,13] have been described in animals and humans using a commercially available mapping system. VT exit sites and, to some extent, diastolic pathways for ablation have been identified during VT episodes using noncontact techniques in human cases and in animal models.[9,11,14,15] The current study describes a new strategy for substrate localization and VT circuit characterization using real-time virtual unipolar electrogram mapping with a commercially available noncontact multielectrode array in a porcine model of scar-based VT.

Methods

All methods were approved by the institutional animal care and use committee of the University of Pennsylvania.

Experimental myocardial infarction

Our modification of the closed chest infarction procedure, developed by Eldar et al,[16] was described previously.[17] Nine animals underwent experimental infarction. Using a percutaneous femoral approach, an 8Fr AL1 or AL2 guide catheter was positioned in the left anterior descending coronary artery, and a 2- to 2.5-mm angioplasty balloon was advanced just distal to the second diagonal branch. Thirty seconds after balloon inflation, 300 μL of agarose gel beads (diameter 75–150 μm; Bio-Rad Laboratories, Richmond, CA, USA) diluted in 1.5 mL of saline was injected distal to the site of balloon occlusion. Thirty seconds later, the balloon was deflated and the catheter withdrawn. The evolving anterior infarction was assessed using continuous ECG and hemodynamic monitoring. The animal was maintained under general anesthesia until the arterial sheath was removed 30 minutes after infarction. Animals were housed for 6 to 8 weeks following infarction before undergoing electrophysiologic study.

Dynamic substrate mapping

The process of noncontact mapping has been previously described.[9,12,14] Briefly, a 64-electrode array mounted on a 9Fr catheter (EnSite 3000, Endocardial Solutions, Inc., St. Paul, MN, USA) was positioned in the left ventricle via a retrograde aortic approach. A three-dimensional geometry of the left ventricle was created, and high-density virtual unipolar electrograms were displayed as sequential isopotential maps. Electrograms were filtered between 2 and 150 Hz.

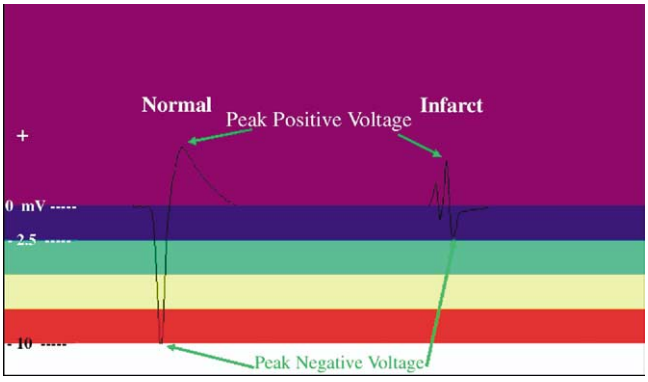

Figure 1 Voltage display on the mapping system. As a wavefront travels toward the virtual electrode on the endocardium, a positive potential is generated; as it passes the electrode (local activation), the electrogram crosses the baseline; and as the wavefront travels away, a negative potential is generated. To focus on the interval encompassing local activation and the receding wavefront, all positive potentials are coded *purple*. As the voltage becomes more negative, the display progresses through the color scheme and back after the peak negative voltage has occurred. The color range is set by the operator, with *white* being the most negative and *purple* the most positive. If an electrogram does not generate a sufficiently low peak negative voltage, it will not progress to white but peaks at an intermediate color. The electrogram on the **left** is an example from normal myocardium; the electrogram on the **right** is an example from infarcted tissue (note the lower voltage and multiphasic morphology). Both electrograms were exported from the mapping system. The peak-to-peak voltage is the difference between the peak positive voltage and peak negative voltage. All electrograms displayed in the figures are filtered between 2 and 150 Hz.

Dynamic substrate mapping (DSM) was performed. *Substrate* was defined as an area of consistently low peak negative voltage (<50% of the largest unipolar deflection recorded on the left ventricular endocardium during the duration of the surface QRS; Figure 1). An area of low voltage was first identified in sinus rhythm (SR). Pacing then was performed at areas in the left ventricle remote to the anteroapical infarct zone as predicted by the coronary occlusion as described earlier. Pacing was performed in at least two sites (one orthogonal to SR activation; one opposite to SR activation) at a cycle length of 500 ms or less (as the animals' native heart rate would allow). At each step, the border of the zone of low peak negative voltage was marked. Substrate was defined as the area that displayed low voltage irrespective of vector of activation (i.e., the overlap of the low-voltage areas determined during SR and the pacing maneuvers; Figure 2). Henceforth, the term *substrate* denotes this area of persistent low voltage as determined by the DSM process. Substrate area was calculated as an idealized ellipse based on the longitudinal (apex to base) and transverse (parallel to the mitral valve) axes (Figure 3).