Electrically Unexcitable Scar Mapping Based on Pacing Threshold for Identification of the Reentry Circuit Isthmus
Feasibility for Guiding Ventricular Tachycardia Ablation
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Background—We hypothesized that delineating electrically unexcitable scar (EUS) within low-voltage infarct regions will locate reentry circuit isthmuses by defining their borders. The pacing threshold and electrogram amplitude that best determines EUS is unknown.

Methods and Results—The change in dimension of the virtual electrode was estimated in 11 patients and observed to increase by $4.4 \pm 2.5$ mm as stimulus strength increases from threshold ($2.9 \pm 1.8$ mA) to 10 mA. EUS was defined as a threshold $>10$ mA. In 14 consecutive patients, mapping and ablation of ventricular tachycardia (VT) were performed using an electroanatomic mapping system. During sinus rhythm, unipolar pacing was performed at sites with bipolar electrogram amplitude $<1.5$ mV. EUS regions were marked on the maps. Reentry circuit isthmuses were identified by entrainment mapping or pace mapping, and ablation was performed. EUS was identified in the infarct in all 14 patients $(11.8 \pm 13.9$ cm$^2$). All 20 VT circuit isthmuses identified were adjacent to EUS. Although electrogram amplitude correlated with pacing threshold ($r=0.64$, $P<0.0001$), many isthmuses had very low-amplitude electrograms, and EUS could not be identified from electrogram amplitude alone. RF ablation lines connecting selected EUS regions abolished all inducible VTs in 10 patients (71%); spontaneous VT was markedly reduced during follow-up (from $142 \pm 360$ to $0.9 \pm 2.0$ episodes per month, $P=0.002$).

Conclusions—This new method of identifying EUS provides complimentary information to the electrogram amplitude in delineating potential reentry circuit paths, potentially facilitating ablation during sinus rhythm. (Circulation. 2002;106:1678-1683.)

Key Words: ventricles ▪ tachycardia ▪ catheter ablation

Reentry is the major mechanism of ventricular tachycardia (VT) associated with myocardial infarction scar. The reentry circuits can be large, extending over several centimeters. The circuits often contain critical isthmuses or channels that can be identified from entrainment mapping, where focal ablation lesions can interrupt the circuit. However, radiofrequency ablation for VT is often difficult, in part because of the frequent presence of multiple reentry circuits giving rise to multiple VTs and to unstable VTs that do not allow extensive mapping.1,2 Therefore, a method to identify potential reentry circuit isthmuses during stable sinus rhythm is of interest.

The borders of reentry circuit isthmuses are defined by conduction block. In animal models studied several days after infarction, this block is often functional in nature.3,4 In human hearts explanted many years after the infarction, extensive fibrosis creating areas of fixed conduction block is often present.5,6 These observations suggest that reentry circuit isthmuses can potentially be defined during sinus rhythm by delineating the areas of dense, fibrous scar. How best to accomplish this task with catheter mapping has not been established. Infarct scars, comprised of excitable and unexcitable tissue, are characterized by low-amplitude electrograms. A minimum electrogram amplitude that distinguishes excitable tissue from unexcitable scar has not been established.

We hypothesized that capture of tissue during pacing could be used to distinguish electrically unexcitable scar (EUS) from excitable tissue that forms part of a reentry circuit. A high pacing threshold may indicate EUS. This assessment depends on the pacing stimulus strength. Capturing stimuli directly depolarize tissue beneath the stimulating electrode, creating a “virtual electrode” in the tissue. The size of this virtual electrode is not known. To provide some approximation of the size of the virtual electrode achieved with unipolar pacing from an ablation catheter, we studied changes in ventricular conduction time over a range of stimulus strengths in the right ventricle. In infarct regions, the relation between...
the pacing threshold and electrogram amplitude was evaluated. Three-dimensional ventricular reconstructions incorporating electrogram amplitude and high threshold information were created, revealing isthmuses between EUS regions, some of which were causing VT that was abolished by ablation through the isthmus.

Methods

Studies were performed during electrophysiological study in consenting patients referred for catheter ablation according to protocols approved by the Brigham and Women’s Hospital human subject protection committee.

Effect of Stimulus Strength on the Virtual Electrode

The study evaluated the change in size of the virtual electrode as stimulus strength increased from threshold to 20 mA in 11 patients with supraventricular tachycardias (age 42.6±13.2 years, 5 male) and normal RV electrograms (>1.5 mV). Quadrupolar catheters at the His-bundle recording site and septal RV apex were used as reference catheters, and the mapping catheter with 4-mm distal electrode was positioned at the RV septum between the reference catheters. Distances between the pacing and reference sites were measured with a mapping system that has a spatial resolution of 0.42±0.05 mm.7 During pacing at threshold, the conduction time (T ×1000) from the pacing site to the reference sites was measured. The mean conduction velocities (CVs) in the directions toward the reference catheters were measured as the distance divided by the conduction time (T ×1000). The conduction times during pacing at stimulus strength (T’) of 5, 10, 15, and 20 mA were then measured. Assuming that the conduction velocity remains the same, then the decrease in conduction time with increasing stimulus strength is attributable to capture of tissue farther from the pacing electrode (increase in the dimension of the virtual electrode in that direction) and the increase in the radius of the tissue (ΔR) captured as CVx(T ×1000−T’).

Electrically Unexcitable Scar in Patients With Infarcts and Ventricular Tachycardia

The study population consisted of 14 consecutive patients (11 male; age 65.4±11.5 years; myocardial infarction location: 5 inferior, 2 anterior, and 7 both; ejection fraction 28.9±8.4%) referred for radiofrequency (RF) ablation of VT associated with myocardial infarction. An electroanatomic mapping system (CARTO, Biosense, Inc) was used to construct three-dimensional plots of electrophysiological data.1 Left ventricular mapping was performed with 7F steerable catheter with a 4-mm distal electrode or external irrigation catheter with a 3.5-mm distal electrode (Cordis-Webster). Bipolar electrograms filtered at 10 to 400 Hz were recorded on the electroanatomic mapping system and were also filtered at 30 to 500 Hz and recorded on a separate digital system (Prucka Engineering Inc). For pace mapping, entrainment mapping, and measurement of threshold, unipolar pacing from the distal electrode of the pacing catheter was used to avoid confounding effects of capture at the proximal electrode.

The mapping and ablation protocol is shown in Figure 1. Programmed stimulation was performed from the right ventricle (RV) with up to 3 extra stimuli with 2 different basic cycle lengths to induce VT and obtain the QRS morphology to compare with pace mapping. VT was terminated by pacing or cardioversion, and the ventricle of interest was mapped during sinus rhythm to construct a voltage map displaying peak to peak electrogram amplitude with color range set for maximal voltage of 1.5 mV on the basis of a previous study that found >95% of electrograms recorded with this methods in normal ventricles had amplitudes exceeding this limit.3 Thus, purple areas represent normal-amplitude electrograms, and electrogram amplitude progressively diminishes as colors proceed to blue, green, yellow, and red. Electrogram amplitude <1.5 mV is defined as low amplitude.

At low-amplitude sites, pacing was performed with 10-mA, 2-ms pulse-width unipolar stimuli. If pacing did not capture, the contact of the catheter was confirmed by observing the response to gentle manipulation. Stability was assessed by monitoring position on biplane fluoroscopy and on the electroanatomic mapping system and by continuous monitoring of electrogram morphology and timing. Sites with pacing threshold >10 mA were tagged as “electrically unexcitable scar,” marked as gray regions. Anatomic isthmuses were identified on the basis of sinus rhythm mapping data as regions between two areas of EUS or between EUS and an anatomic obstacle such as the mitral or aortic valve annulus, where the pacing threshold was <10 mA.

In 6 patients, more detailed assessment of pacing threshold was obtained at the initial sites around the low-voltage areas by decreasing the stimulus output from 10 mA to threshold. Sites acquired after RF ablation in a region were excluded from voltage maps.

Delineation of the VT Reentry Circuit Isthmuses

After completion of the voltage map, VT was reinitiated. If the initial VT was hemodynamically stable, the VT activation sequence map was reconstructed and entrainment mapping was performed. If the initial VT was incessant, the VT activation sequence map was constructed before the sinus rhythm map. For stable VTs, reentry circuit isthmuses were defined from entrainment mapping as sites where pacing entrained VT with concealed fusion, a postspacing interval equal to the VT cycle length, and stimulus-QRS interval <70% of the VT cycle length.8 For unstable VTs, reentry circuit isthmuses were defined on the basis of the results of pace mapping as sites where the QRS morphology matched that of VT with a stimulus-QRS >40 ms. Although confirmation that the site was in the reentry circuit was not directly obtained, these findings have been shown to be related to the reentry circuit exit and sites where ablation abolishes inducible VT.9,10

Catheter Ablation

A series of ablation lesions were made to transect isthmuses. RF lesions were applied to the region until pacing with 10-mA/2-ms-strength stimuli failed to capture. After completion of the initial set of RF lesions, programmed stimulation (1 to 3 extra stimuli after a 600-ms and then 400-ms basic drive from the RV apex and outflow tract) was repeated. If any monomorphic VT was inducible, the mapping and ablation process was repeated.

The procedure ended when no monomorphic VT was inducible, hemodynamically stable VT was inducible but an endocardial site for the VT circuit could not be found on the endocardium, or only unstable VT that was faster than any of the previous VTs was inducible.
The acute effects of the ablation procedure were defined as success if no monomorphic VT was inducible; modified if monomorphic VT was inducible but different and faster than VTs induced at the beginning of the procedure; and failure if VT inducible at the beginning of the procedure remained inducible. After ablation, patients received anticoagulation with warfarin for 1 month or aspirin chronically.

Data Analysis

Areas of low voltage or EUS were calculated on the basis of measurements approximating the area as a rectangle or ellipse, as appropriate. The threshold for sites with threshold >10 mA was assigned a value of 10 mA. Statistical analyses were performed using SAS (SAS Statistical Software Version 6.12, SAS Institute). Continuous data are expressed as mean ± SD. Fisher’s exact test was used when the data were categorical; t tests and Wilcoxon rank-sum tests were used for comparison of normal and abnormal continuous data, respectively. The correlation of electrogram amplitude and threshold was evaluated with the Spearman rank correlation. Receiver operating characteristic curves were used to assess the relation of electrogram amplitude for predicting high pacing threshold. Generalized estimating equations were used to adjust for multiple observations in individual patients.

Results

Effect of Stimulus Strength on Virtual Electrode Dimension

The mean unipolar pacing threshold was 2.9 ± 1.8 mA. The radius of the virtual electrode increased by a mean of 2.0 ± 2.1 mm at 5 mA, by 4.4 ± 2.5 mm at 10 mA, and by 8.4 ± 1.5 mm at 20 mA stimulus strength.

Mapping and Ablation of Ventricular Tachycardia

Sinus rhythm maps were constructed from a mean of 164.7 ± 52.9 sites per patient (range, 72 to 244). Low-amplitude (<1.5 mV) regions of infarction were present in all patients with endocardial areas of 41.1 ± 20.4 cm² (range, 12.6 to 77.0). Pacing at 10 mA with 2-ms pulse width to assess presence or absence of capture was performed at 1641 sites in the low-amplitude area. The pacing threshold was >10 mA at 2-ms pulse width for 204 (12%) sites. In 6 patients, more detailed pacing thresholds were measured when pacing at 10 mA captured for 397 low-amplitude sites. The mean threshold at these sites was 6.6 ± 6.1 mA.

Isthmuses Defined by Electrically Unexcitable Scar

At least one area of EUS (threshold >10 mA) was identified in each patient. The average number of EUS areas was 2.9 ± 1.0 per patient (range, 2 to 6), and the average total endocardial area of EUS was 11.8 ± 13.9 cm² per patient. More than one potential isthmus was identified during sinus rhythm in all patients.
Relation to Isthmuses During Ventricular Tachycardia

A total of 20 VT circuit isthmuses were identified, 12 by entrainment mapping (Figure 2) and 8 by pace mapping (Figure 3). Of these isthmuses, 16 were between two areas of EUS, 3 were between EUS and a valve annulus, and 1 was adjacent to EUS with a normal voltage area on the other border. These isthmuses were 1.9\(\pm\)1.1 cm in width and 2.6\(\pm\)1.4 cm in length.

A total of 24.1\(\pm\)10.0 RF applications per patient were made, including an average of 12.8\(\pm\)8.8 applications in each isthmus to achieve a pacing threshold >10 mA in the isthmus. After ablation, all inducible VTs were abolished in 10 patients; different and faster VT was inducible in 2 patients. The same VT remained inducible in 2 patients, who appeared to have an isthmus deep to the endocardium.

At 11 of the 12 VT circuit isthmuses identified by entrainment mapping, RF application was delivered during a VT and the VT terminated. These isthmuses were between two areas of EUS (9 isthmuses) or between EUS and the valvular annulus (2 isthmuses). Eleven isthmuses in 8 patients seemed to be shared by >1 VT circuit. Ablation across the region containing these isthmuses abolished a total of 30 different morphologies of VT. Ablation lesions extended outside the identified isthmuses, however, so it is possible that adjacent isthmuses as well as shared single isthmuses might have been interrupted.

Electrogram Amplitude at EUS and Isthmus Sites

For sites in the low-amplitude (<1.5 mV) infarct region, the pacing threshold correlated with bipolar electrogram amplitude (Figure 4) \(r=0.64, P<0.0001\). Although the bipolar
The bipolar electrogram amplitude and percentage of the sites in EUS and excitable scar. The electrogram amplitude was significantly less at EUS sites (0.18±0.14 mV) compared with sites with lower pacing thresholds (0.52±0.36 mV, P<0.0001), electrogram amplitude alone had limited ability to distinguish EUS sites from isthmus sites (Figure 5). An electrogram amplitude of <0.25 mV provided 84% specificity and 81% of sensitivity for predicting EUS, with a good negative predictive value of 93% but a positive predictive value of only 62%. An electrogram amplitude <0.1 mV had specificity of 98%, sensitivity of 81%, positive predictive value of 64%, and negative predictive value of 76% for identifying EUS.

The sinus rhythm electrogram amplitude at sites in VT circuit isthmuses was 0.32±0.16 mV, ranging from 0.08 to 0.91 mV (21 of 48 [44%] sites were <0.25 mV). Thus, use of a low-amplitude electrogram alone to indicate scar misses some isthmuses. This is illustrated by retrospective analysis of additional sinus rhythm maps constructed by labeling sites with electrogram amplitude <0.25 mV (the electrogram amplitude cutoff with the optimal performance of sensitivity and specificity for EUS) as gray dense scar. The resulting maps show substantially larger areas tagged as scar compared with the EUS defined by the pacing threshold (17.7±15.5 versus 11.8±13.9 cm², P<0.05). The VT isthmus was located within a dense scar area and no longer evident from the maps for 8 of 20 VT circuit isthmuses.

Discussion
Recently, an approach using an electroanatomic mapping system to delineate areas of low-voltage infarction or scar to guide ablation has been described to facilitate ablation of unstable and multiple VTs.1,2 The low-voltage infarct areas are, however, relatively large (average area, 38.6±34.6 cm²; range, 6.4 to 205.4 cm²),1 such that complete encirclement with catheter ablation is likely to be difficult. A more limited approach, placing ablation lines through regions where an isthmus is identified, has been shown to reduce VT episodes,1,2 but identification of isthmuses can be challenging, and means to guide placement of RF lines during sinus rhythm are desirable. Reentry circuit isthmuses can be bordered by unexcitable scars that create conduction block.5,6 Our study shows that VT reentry circuit isthmuses can be identified from delineation of electrically unexcitable scar defined by a high pacing threshold. RF ablation in these regions abolished inducible VT in 10 of 14 patients and abolished or markedly reduced spontaneous VT during follow-up. This approach is promising, but several caveats and methodological issues require consideration.

Virtual Electrode
The tissue directly depolarized by the pacing stimulus is referred to as the virtual electrode. The size and shape of the virtual electrode is influenced by stimulus strength, the size of the pacing electrode, pacing configuration (unipolar versus bipolar), and tissue contact and has not been previously studied using ablation catheters in humans. Our calculations suggested that the radius increases by 4 to 5 mm as the stimulus strength increases from threshold to 10 mA. This radius is likely to be in the range of size of RF ablation lesions.12,13 Thus, it seems likely that sites with such elevated thresholds are relatively large areas of scar where ablation is
likely not needed but that may form the border of a reentry circuit.

Our methods may overestimate the increase in virtual electrode dimension because the curvature of the excitation wavefront produced may decrease with increasing virtual electrode size, potentially increasing conduction velocity. Also, the virtual electrode is not a regular shape, but complex and irregular. We assessed the dimension in only 2 approximately opposite directions. Our findings apply to unipolar pacing. The virtual electrode measure was assessed for the normal right ventricular septum rather than areas of infarct.

Although this pacing method likely identifies large unexcitable areas of scar, small strands of fibrosis, which may still create important conduction block, would likely escape detection. Although all patients in this study had EUS detected, it is likely that large sheets of surviving endocardial myocardium occur in some patients with circuits created by functional block during tachycardia and no endocardial EUS.16

Bipolar Electrogram Amplitude

Compared with unipolar, unfiltered signals, bipolar recordings reduce the contribution of far-field signal and are preferred for mapping scar-related VT. Although the amplitude of the signal is influenced by the direction of the wavefront relative to the recording dipole, there is a good correlation between the bipolar amplitude recorded during atrial and RV apex pacing and between the electrogram amplitude and the location of areas of infarct. The present study showed that a bipolar electrogram amplitude <0.25 mV provided 84% specificity and 81% sensitivity for detection of EUS. Only 2% of sites with amplitude >0.5 mV had a pacing threshold >10 mA. Interestingly, a substantial number of very low-amplitude sites have low pacing thresholds, and many sites in reentry circuit isthmuses have very low amplitudes. Thus, pacing provides complementary information to electrogram amplitude. Plots of electrogram amplitude alone did not adequately identify VT circuit isthmuses. Electrogram amplitude is influenced by the precise recording methods, and filter settings.

The number of patients studied was relatively small. Ablation targeting anatomic isthmuses using sinus rhythm mapping alone was not prospectively performed. Many patients have multiple potential isthmuses identified during sinus rhythm by this method (Figures 2 and 3). Whether ablation of all potential isthmuses is warranted is unknown.

Conclusions

Pacing in regions of low-amplitude electrograms (<0.5 mV) can identify areas of EUS that delineate isthmuses for some VT circuits, which can be transected with a modest number of RF lesions during sinus rhythm. This method may facilitate ablation of multiple and unstable VTs during sinus rhythm.

References


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