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STATE-OF-THE-ART REVIEW

Substrate Mapping for Ventricular Tachycardia

Assumptions and Misconceptions

Mark E. Josephson, MD, Elad Anter, MD

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CME Objective for This Article: Upon completion of this activity, the learner should be able to discuss: 1) the factors influencing the size and shape of the bipolar electrogram; 2) the limitations of substrate mapping during sinus rhythm; 3) the role of electrode size and tissue contact on the amplitude and shape of the recorded electrogram; and 4) why the barriers forming the central common pathway of reentrant VT may be functional and not pre-determined by anatomic scar.

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Substrate Mapping for Ventricular Tachycardia

Assumptions and Misconceptions

ABSTRACT

Substrate mapping was developed to treat poorly tolerated infarct-related ventricular tachycardias (VTs). This concept was based on 30-year-old data derived from surgical and percutaneous mapping during sinus rhythm and VT that demonstrated specific electrograms (EGMs) that characterized the "arrhythmogenic substrate" of VT. Electrogram characteristics of the arrhythmogenic VT substrate during sinus rhythm included low-voltage, fractionation, long duration, split signals, and isolated late potentials as well as EGMs demonstrating adjacent early and late activation. Introduction of electroanatomical mapping (EAM) systems during the mid-1990s has allowed investigators to record electrograms in 3 dimensions and to identify sites assumed to represent the central common pathway ("isthmus") during re-entrant VTs. However, several important assumptions and misconceptions make currently used "substrate mapping" techniques inaccurate. These include: 1) re-entrant circuits are produced by fixed barriers of immutable "inexcitable" scar; 2) low voltage amplitude (≤0.5 mV) implies dense "inexcitable" scar; 3) isthmuses identified in patients with tolerated VTs using entrainment mapping are both valid and provide an accurate depiction of isthmuses in less hemodynamically tolerated VTs; and 4) current mapping tools and methods can delineate specific electrophysiologic features that will determine the barriers forming channels during re-entrant VTs. None of these assumptions has been validated and recent experimental and human data using higher resolution mapping with very small electrodes cast doubt on their validity. These data call for re-evaluation of substrate-mapping techniques to characterize the arrhythmogenic substrate of post-infarction VT. Standardization of recording techniques including electrode size, interelectrode spacing, tissue contact, catheter orientation, and wavefront activation must be taken into consideration. (J Am Coll Cardiol EP 2015;1:341–52)

Activation mapping of ventricular tachycardia (VT) is rarely accomplished due to limited temporal and spatial resolution, unacceptably long mapping times, and/or hemodynamic intolerance of the VT. Entrainment mapping is a reasonable approach to identify and target critical sites of the re-entrant VT circuit for ablation in patients with tolerated post-infarction re-entrant VT (1–3). However, at the current time the majority of VTs are not hemodynamically tolerated and therefore do not permit either activation or entrainment mapping. Rapid and hemodynamically nontolerated VTs have become more prevalent during the past 2 decades due to early coronary interventions for acute myocardial infarction (MI). This has led to smaller infarct size, and as a consequence, smaller re-entrant circuits and shorter VT cycle lengths. Substrate mapping has evolved over the past decade and a half as an alternative to activation and/or entrainment mapping to deal with hemodynamically untolerated VTs. This methodology reduces or eliminates that need for mapping during prolonged periods of tachycardia. However, despite acute success, the recurrence rate at 1 year remains unacceptably high, ranging from 50% to 60% (4).

The development of electroanatomic mapping technology by Ben-Haim et al. (5) revolutionized the field as it allowed one to precisely localize the mapping catheter and recorded signals in a 3-dimensional field. The ventricular electrogram characteristics during sinus rhythm in patients with tolerated and nontolerated VTs and cardiac arrest were initially described nearly 3 decades ago. These early catheter mapping studies were performed using nonsteerable catheters with a 2 mm tip electrode separated by 5 mm from a 1 mm ring electrode. These studies were the first to define electrogram characteristics in healthy and infarcted myocardium. The electrogram variables included were signal amplitude, duration, morphology, and activation pattern (6–10).

These studies demonstrated that ≈85% of electrograms at the so-called "site of origin" of VT (defined as sites with pre-QRS complex or mid-diastolic electrograms as well as sites with continuous electrical activity) had abnormal electrograms during sinus rhythm. Most of these abnormal electrograms demonstrated low amplitude (≤3.0 mV) and/or long duration (>70 ms). A small percent of signals were profoundly abnormal and displayed either fractionation (multiple components crossing the baseline), split potentials (electrograms separated

by 30 ms by an isoelectric interval), delayed activation extending beyond the QRS complex, and late potentials separated by 30 to 50 ms of isoelectric interval from the QRS complex. While fractionated electrograms, split and isolated late potentials reflect abnormal signal propagation not seen in normals (i.e., high specificity), they were not seen in all patients with VTs and therefore carried a modest predictive value (approximately ~30%) for defining the so-called site of origin either in the electrophysiology laboratory or the operating room.

Areas of low amplitude and fractionated electrograms were associated with reduced excitability and prolonged dispersion of recovery (11–13). These areas often demonstrated early activation adjacent to areas of late activation, a feature conducive to promoting re-entry. These features were considered to represent electrophysiological milieu for re-entrant ventricular tachycardia. Collaborative work with Dr. Andrew Wit and colleagues demonstrated that the fractionated electrograms noted in these patients were associated with myocyte disarray with bundles of myocytes encased in fibrous tissue that were located primarily in the subendocardial surface of the heart (14,15). Elegant intraoperative studies by Miller et al. (16) demonstrated that the most abnormal electrograms at the "site of origin" (i.e., fractionated, split, and isolated late potentials) were eliminated by resection of 2 to 3 mm of subendocardial tissue and 50% of the subjacent electrograms were normalized. Importantly, subendocardial resection resulted in cure of post-infarction VTs. This study also demonstrated that the subendocardial scar acted as an insulator of subjacent electrograms, resulting in lower amplitude than they truly exhibited with the subendocardium removed.

Based on these data investigators began to use electrogram amplitude and morphology during sinus rhythm and pace mapping to identify the presumed channels forming the central common pathway for re-entrant VTs (17–20). The use of electroanatomic mapping systems allowed for precise localization and annotation of abnormal signals. Electrogram amplitude for normal and abnormal tissue were described using the standard ablation and mapping catheters with 4 mm tip electrode, 1-mm ring electrode and 2 mm interelectrode spacing. Normal ventricular tissue had a bipolar voltage >1.5 mV, dense scar was defined by voltages <0.5 mV, and a border zone was defined by voltages between 0.5 and 1.5 mV. These electrograms were filtered at 10 to 400 Hz (different than the original studies: 30 to 500 Hz). The ability to localize areas of assumed scar and abnormal signals, including late potentials, led to development of substrate mapping as the primary ablation approach for both stable and unstable VTs.

The initial concept of using substrate mapping was based on the hypothesis that channels of viable myocytes within dense scar recorded during sinus rhythm represented isthmuses of re-entrant circuits. Pace mapping at the junction of these channels and the "border zone" produced similar QRS complex morphologies to recorded VTs. These data led to the widespread use of voltage mapping to identify channels of viable myocardium, presumably representing the central common pathway during VT. This stimulated investigators to develop an ablation strategy in which ablation lesions are delivered perpendicular to these channels and/or border, presumably blocking exit from these channels (17–20). Several variations of the theme evolved including changing the windows of "viability" from 1.5 to 0.5 mV and for dense scar to 0.1 to 0.5 mV. In addition to voltage amplitude alone, abnormal electrograms, in particular late potentials have been used to identify the channels.

Despite this "logical" evolution in our ablative strategy, success rates for VT ablation have not increased. In 2 recent randomized and multicenter trials conducted by experienced electrophysiology centers in Europe, the recurrence rate of VT at 1-year follow-up was about 50% (21,22). A systematic review of several single center studies also reported similar VT recurrence rates (4). The SMASH-VT (Substrate Mapping and Ablation in Sinus Rhythm to Halt VT) study, a prospective, randomized, and controlled trial in 127 patients with history of MI and VT who were randomized to implantable cardioverter-defibrillator (ICD) alone or ICD plus substrate ablation demonstrated a 70% reduction in arrhythmic events over a 2-year follow-up period (23). The results of this study were encouraging and created anticipation that percutaneous substrate-based ablation would mimic the excellent results of surgical subendocardial resection without the need for surgery. However, no other group replicated the outcome of the SMASH-VT study, and the overall results of substrate-based ablation remain disappointing.

If the hypotheses on substrate-based ablation strategy were valid, why have the results been so disappointing? We believe 1 of the reasons is that the assumptions on which these hypotheses were based were oversimplified, unfounded, and undermined by misconceptions.

Misconceptions:

1. Re-entrant circuits are determined by a fixed substrate of immutable scar.
2. Low voltage (≤0.5 mV) implies dense scar.

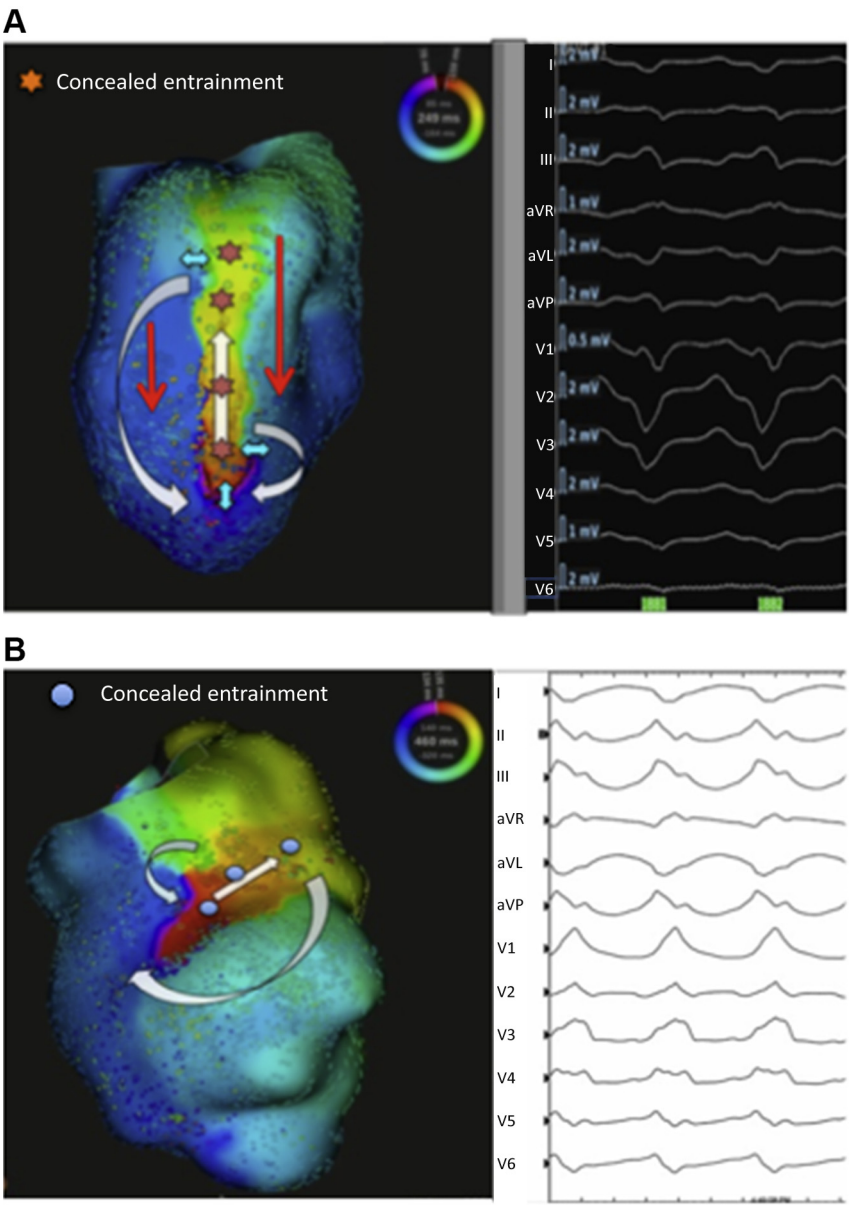
ABBREVIATIONS AND ACRONYMS

MRI = magnetic resonance imaging

MI = myocardial infarction

VT = ventricular tachycardia

FIGURE 1 Overestimation of Isthmus by Entrainment Mapping



Both **panels** show high-resolution activation maps of sustained monomorphic ventricular tachycardia (VT). **(A)** VT map in a porcine model of VT. The **orange stars** mark sites of concealed entrainment. While this corridor of concealed entrainment correlates with the isthmus site, it far exceeds the exit turn around points **(curved large arrow)**. Conduction velocities in outer loops are near normal **(vertical red arrows)**, while velocities at true entrance and exit sites **(broad blue arrows)** are very slow (see text). **(B)** VT map in a human. Concealed entrainment sites are indicated by blue circles. While they approximate the isthmus defined by the **large curved arrow**, they far exceed the exit as denoted by the **small curved arrow**.

3. Isthmuses defined in patients with tolerated VTs using entrainment mapping are both valid and provide an accurate depiction of isthmuses in less hemodynamically tolerated VTs.
4. Current mapping tools and methods can delineate specific electrophysiological features to determine barrier-forming channels during re-entrant VTs.

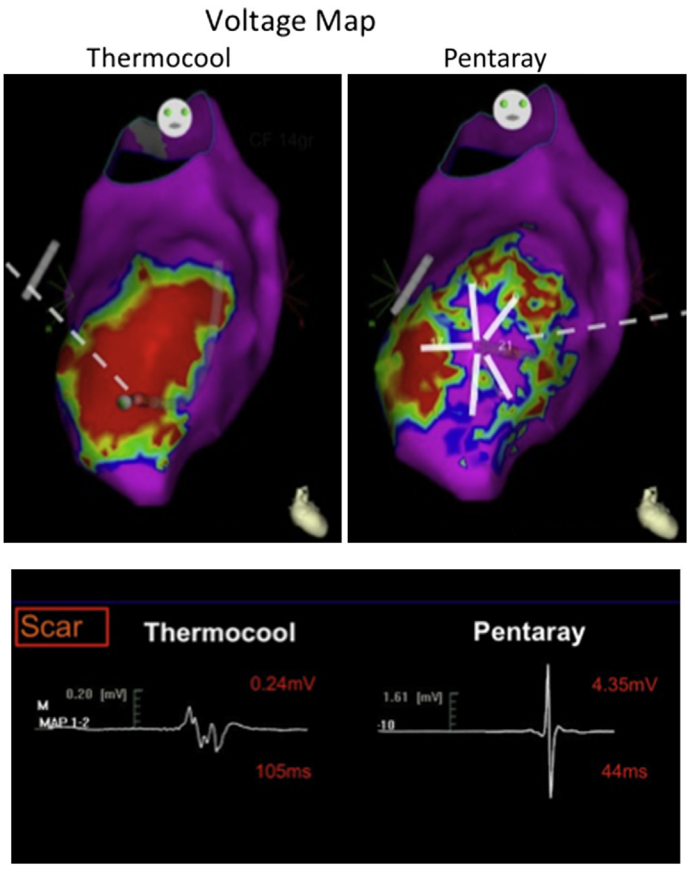
1. Re-entrant circuits are determined by fixed anatomical barriers of inexcitable scar tissue; hence barriers forming the isthmus during VT are present during sinus rhythm.

While fibrosis produced following MI may form anatomic barriers, they themselves are neither sensitive nor specific for defining the borders of the

central common pathway in the VT circuit. Experimental models of VT have shown that the borders of the VT re-entrant circuit are, in large part, functional rather than fixed. Ventricular remodeling following MI has been associated with fibrosis, myocyte disarray, decrease, and redistribution of gap junctions (connexin-43) and ion channel dysfunction, all of which can contribute to slow conduction, heterogeneity of refractoriness, and block (24–29). These abnormalities may be responsible for defining the borders of the central common pathway of the re-entrant circuit. In the 5-day-old canine infarct model of re-entrant VT, marked connexin disarray with *minimal* fibrosis produced a figure of 8 re-entrant circuit (24–26). This phenomenon has been termed "anisotropic re-entry." Impedance mismatch produced by areas of thin tissue or small bundles engaging larger tissue, as well as altered fiber orientation of muscle bundles produced by normal branching or intervening fibrous tissue (myocyte disarray) can also produce slow conduction and block (26,27,30,31). These features are also associated with reduced expression and lateralization of gap junctions (connexin 43) resulting in decreased cell coupling (25,26). This connexin remodeling alters propagation, producing zigzag conduction and fractionated electrograms as well as dispersion of refractoriness, which can lead to block (32–34). Thus, mere presence of scar may be insufficient to produce the electroanatomical milieu required for re-entrant circuits to occur. Instead, the effects of fibrosis on impedance mismatch and remodeling of gap junctions and ion channels can produce the functional abnormalities of propagation to allow re-entry. The "anisotropic" re-entrant circuits were dependent on functional abnormalities producing extremely slow conduction rather than the scar itself (24–27,32). These investigators coined the term "pseudo block" for this very slow conduction produced by zigzag conduction secondary to nonuniform anisotropic conduction associated with connection disarray and heterogeneous coupling. Moreover, ion channel remodeling (I_{Na} and I_{CaL}) also contributed to the formation of functional barriers that stabilize re-entrant circuits (28).

While the canine model in which these data were described is different in some aspects from human post-infarction VT, similar findings (thin/thick relationship, variable fiber orientation, and connexin disarray) have been reproduced in a recent porcine model of infarction that more closely approximates human-related subendocardial infarction and VT (35). Human data also suggest that at least parts of the isthmus boundaries are functional. These include:

FIGURE 2 The Effect of Electrode Size and Interelectrode Spacing on Electrograms



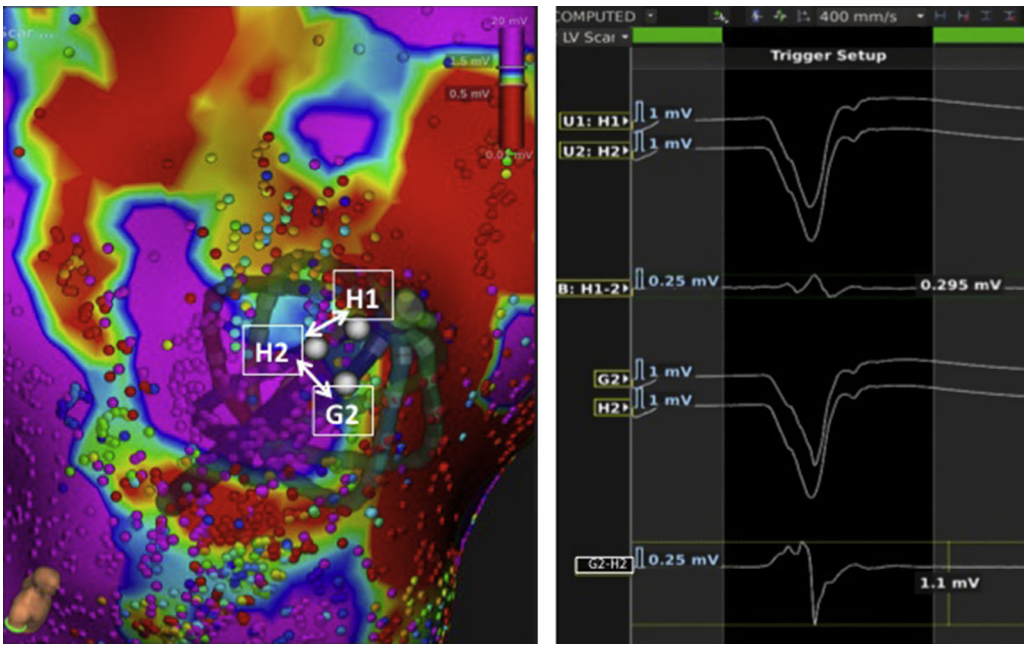
A voltage map with Thermocool (**top left panel**; 3.5 mm tip and 1 mm ring) and Pentaray (**top right panel**; each electrode 0.8 mm^2) are shown. The **red area** is <0.5 mV. The bipolar signal recorded in the red area was 0.24 mV **(top left panel)** and was broad and fragmented. Recordings from the same site with a Pentaray show normal bipolar amplitude and width **(bottom panel)**.

1) no evidence of block during sinus rhythm in areas destined to be the central common pathway; 2) apparent isthmuses based on entrainment mapping exceeding the true isthmus produced by functional slowing of conduction around turning points (**Figure 1**); and 3) differences in resetting curves depending on the site of stimulation (36,37). The very slow conduction at the turning points allow the near-normal conduction velocity in the isthmus to reach longitudinally oriented, rapidly conducting bundles which form the outer loop.

2. Low voltage equals scar and the bipolar amplitude is a reflection of the underlying tissue.

While fibrosis remains an inherent part of the process of remodeling, as stated previously, it is associated with several other processes, all of which can lead to re-entry. Bipolar voltage amplitude alone is the least

FIGURE 3 Effect of Angle of Contact on Amplitude and Voltage



The **left panel** shows voltage map in chronically infarcted swine. The **grey balls** denote unipolar electrodes. If H_1 and H_2 unipolar electrodes create the bipolar signal **(white arrow)**, activation of both electrodes occurs simultaneously, resulting in a significant cancelation effect and a resultant low bipolar voltage of 0.295 mV **(upper right panel)**. If H_2 and G_2 are the unipolar electrodes forming the bipolar signal that is oriented perpendicular to H_1H_2 **(white arrow)**, activation of these electrodes occurs sequentially, resulting in less cancellation and a higher bipolar voltage of 1.1 mV **(lower right panel)**.

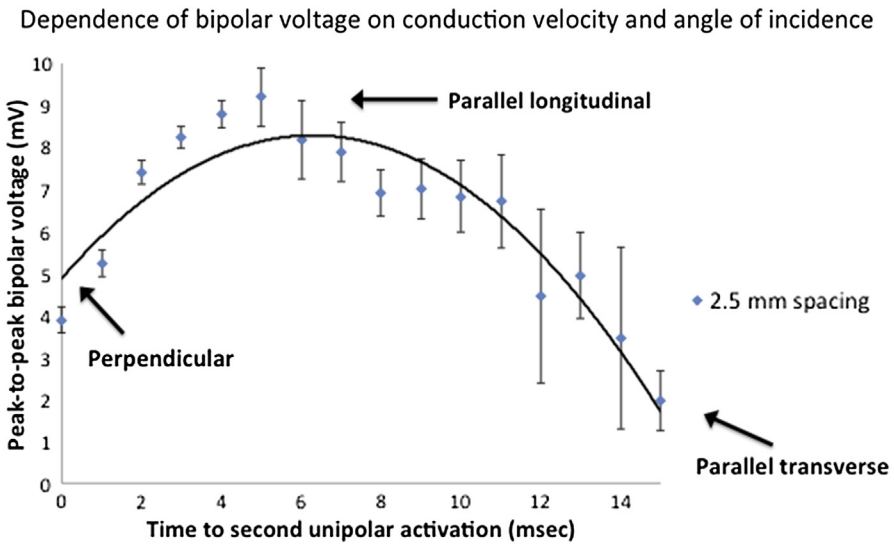
specific variable to consider. It is influenced by many factors including: 1) conduction velocity; 2) fiber orientation and curvature; 3) the relationship of fiber orientation to the propagating wavefront (nonuniform anisotropy); 4) tissue contact; 5) edema; 6) fat; and 7) the characteristics of the recording catheter (electrode size, interelectrode spacing, and orientation relative to the tissue).

Voltage alone should not be a primary measure to define barrier formation or slow conduction. A characterization of the electrophysiologic features of areas destined to form barriers is needed. In the canine VT model areas of fractionated electrograms caused by myocardial fiber and connexin disarray were associated with "barrier" formation. Impedance mismatch secondary to thinning of the myocardium adjacent to the scar border was another important determinant of barrier formation. The seminal study by Dillon et al. (24) demonstrated that sites of turning points at the exit or entrance of an isthmus during VT were associated with fractionated electrograms. Ciaccio et al. (29) subsequently showed that fractionated, long electrograms in sinus rhythm correlated reasonably well with the isthmus barriers. Branching of muscle bundles, which alters axial resistivity, can also give rise to both a decrease in voltage amplitude and increasing complexity of the local electrogram (30). Ciaccio et al. (27) also showed that convex curvature at entry points is often the slowest conducting area and associated with marked nonuniform anisotropic conduction (fractionated electrograms) and that concave curvatures near the exits have more rapid conduction.

Voltage mapping alone has been used to identify "channels" in and around the scar that could be representative of an isthmus during VT. Marchlinski et al. (17) defined "normal" tissue as by bipolar voltages ≥1.5 mV and dense scar by voltages ≤0.5 mV. However unipolar pacing in this area of the so-called dense scar showed local capture, suggesting presence of viable myocardium (38). A bipolar voltage of ≤0.1 mV has been used by our group to define electrical inexcitability. Changing the bipolar viability voltage range to 0.1 to 0.5 mV increased the heterogeneity within the area of previously defined "dense scar."

Attempts using voltage amplitude alone to define barriers and recognize channels are inherently limited by the catheter design and technology.

FIGURE 4 The Effects of Angle of Incidence and Conduction Velocity on Bipolar Voltage



Bipolar voltage is plotted against angle of incidence and activation time between the 2 unipolar signals from which the bipole is derived. Perpendicular refers to the angle of incidence and transverse and parallel longitudinal refer to the relationship of the electrodes to fiber orientation. Adapted with permission from Josephson's Clinical Cardiac Electrophysiology, 5th edition, 2015, Wolters Kluwer Health.

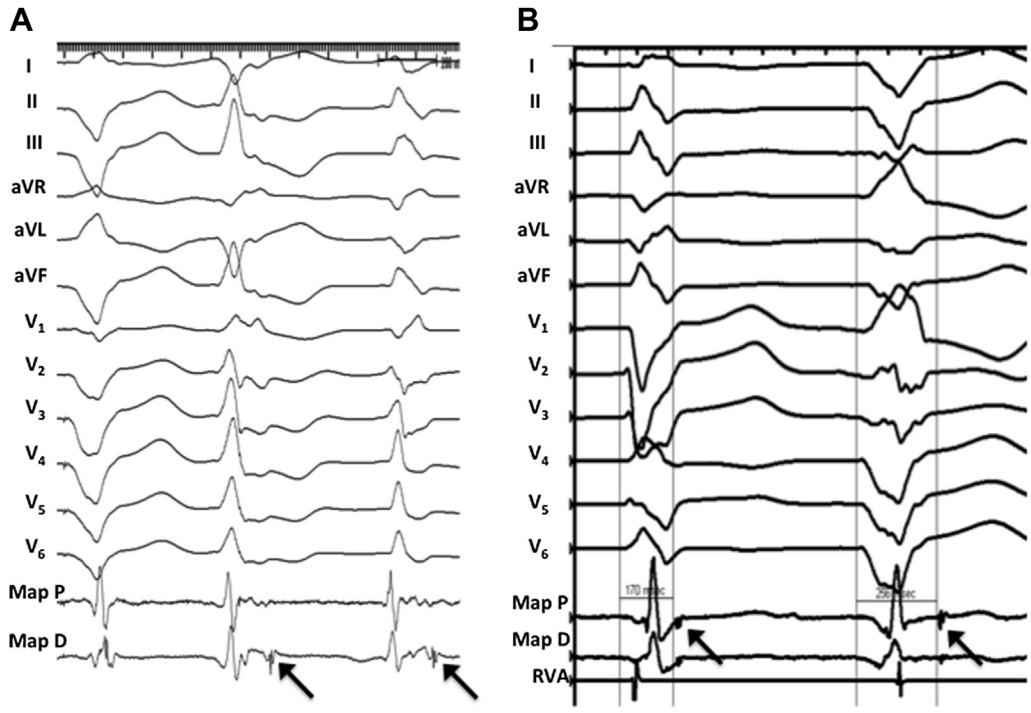
Standard mapping catheters with a 3.5 to 4.0 mm tip electrode have insufficient resolution to detect small viable bundles within heterogeneous scar tissue. These relatively large tip electrodes record activity from over a large area, picking up electrogram data representative of a larger tissue size. For instance, catheters with large-tip electrodes (3.5 to 4.0 mm) often record low amplitude signals in areas of heterogeneous scar, while catheters with smaller electrodes (0.4 to 1.0 mm) record high-voltage signals at similar scar sites, thus identifying surviving myocardial bundles (**Figure 2**). Similarly, decreasing the interelectrode distance may decrease the voltage amplitude and duration, but may better identify near-field obscure activity, increasing the resolution of mapping. Using very small electrodes of 0.4 mm^2 with a 2.5 mm interelectrode distance (Orion catheter, Boston Scientific, St. Paul, Minnesota) or 0.8 mm^2 with 2 mm interelectrode distance (Pentaray, Biosense Webster, Diamond Bar, California), we have been able to demonstrate that in areas of very low voltage, considered "dense scar" when mapped using standard mapping catheters, surviving myocardial bundles with healthy sharp and high-voltage signals could be identified with smaller electrode catheters (38).

Factors that influence bipolar voltage amplitude not only include the electrode size and the interelectrode distance, but also include conduction velocity between the bipolar electrodes, the wavefront of activation, and the angle at which the electrode engage the muscle (39–42). This latter factor has been termed the "the angle of incidence" (42). Blauer et al. (42) found that an angle of contact >30° was associated with a false reduction in bipolar voltage amplitude. In fact, the steeper the angle of contact, the lower the bipolar voltage amplitude due to near simultaneous activation recorded by both poles, resulting in significant cancellation. **Figures 3 and 4** illustrate the affects of angle of incidence and conduction on bipolar voltage amplitude. Importantly, neither the angle of incidence nor the contact force has been controlled during substrate mapping (41).

Additionally, electrogram configuration, in particular fractionated electrograms and late potentials, is markedly influenced by the wavefront activation. This can be illustrated in **Figure 5** in which changes activation produce changes signal amplitude and configuration: multicomponent signals and late potentials can be produced simply by changing in wavefront activation and/or catheter orientation.

Unipolar electrograms recorded from the endocardium have large field of view (antenna) that may potentially be helpful identifying abnormalities extending beyond the endocardium itself. Unipolar endocardial recording are being increasingly used to

FIGURE 5 Effect of Wavefront on Local Electrograms



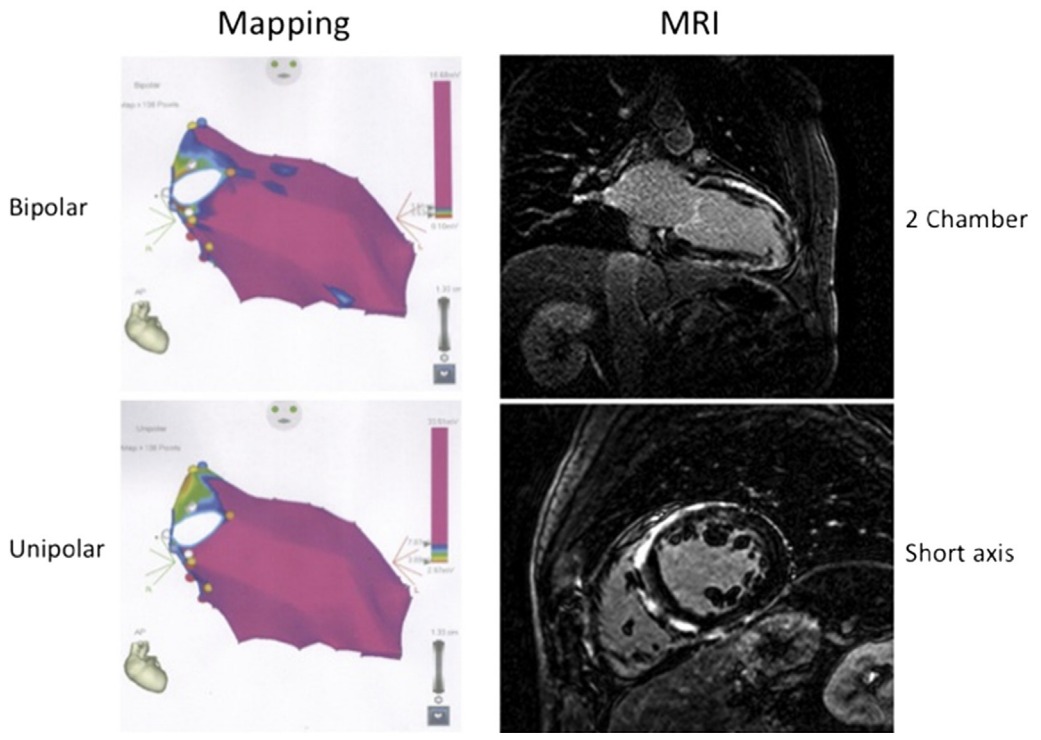
Examples from 2 different patients with history of infarction. **(A)** Pacing the right ventricular apex (RVA) forms the first QRS complex. The distal mapping catheter was positioned at the left ventricular apical septum and recorded a fractionated signal (Map D). The 2 sequential QRS complexes are spontaneous ventricular premature contractions (PVCs) from the basal lateral and septal regions of the left ventricle, respectively. The propagation of these 2 PVCs results in formation of isolated late potential **(arrows)** that was not present during RVA pacing. **(B)** Sinus QRS beat followed by PVC from the left ventricle. Once again, development and timing of the late potential **(arrows)** is influenced by the activation pattern.

evaluate epicardial disease in both patients with ischemic and nonischemic cardiomyopathy, but there are no data that validate the source of the unipolar signal. In post-infarction VT the unipolar signal is likely to reflect the myocardium subjacent to the subendocardium as previously described by Miller et al. (16). However, it is important to emphasize that this technique has significant limitations and is highly nonspecific. Unipolar voltage and configuration are influenced by electrode size, high- and low-pass filters, wavefront of activation, wall thickness, and surrounding anatomical structures. We have found that unipolar voltage is different at different LV walls (septum vs. lateral wall) and is highly influenced by electrode size, with smaller electrode catheters recording smaller unipolar voltage (unpublished data). In the presence of hypertrophy, unipolar voltage can be normal even in the presence of significant midmyocardial or subepicardial scar detected by magnetic resonance imaging (MRI) (**Figure 6**). The significance and role of unipolar mapping with standard catheters requires further evaluation.

3. Isthmuses defined in patients with tolerated tachycardias using entrainment mapping are both valid and provide an accurate depiction of isthmuses in less hemodynamically tolerated patients.

Many of the concepts underlying the "substrate mapping" approach are based on electrogram findings in sinus rhythm in patients with stable VT and channels defined by entrainment mapping. While the previous paragraphs deal mainly with the electrogram aspect of the substrate, the accuracy of entrainment mapping to define the isthmus is accepted as valid. While entrainment mapping can help identify critical sites of the circuits including good sites for ablation, entrainment mapping cannot define the true dimensions of the circuit. We believe that the apparent isthmus as defined by entrainment criteria exceeds the true dimension of the functional isthmus as can be measured by high-resolution

FIGURE 6 Lack of Correlation Between Endocardial Unipolar Voltage Amplitude and Scar of MRI



In this patient with hypertrophic cardiomyopathy and extensive scar as detected diffuse presence of late gadolinium enhancement on magnetic resonance imaging (MRI), the endocardial unipolar voltage amplitude was uniformly >7.5 mV. Bipolar filtering was 30 to 500 Hz and unipolar filtering was 0.05 to 500 Hz.

activation mapping (Figure 1). This occurs because of the nonuniform propagation of the wavefront from the isthmus into the exit area. This has been shown in canine and porcine models and more recently in humans using high-resolution mapping technology. While ablation at these entrainment-defined exit sites can transiently terminate VT, recurrences are common because the functional barriers of the common channel remained unaltered. This also explains why ablation of a single clinical VT can result in appearance of multiple "variants" of the VT following ablation at these exit sites. We have developed and characterized a porcine model of infarction with re-entrant VT that is similar to post-infarction human VT (35). The porcine model displayed myocardial remodeling with disarray in fiber orientation, and connexin content and distribution (lateralization), particularly at curvature points of the isthmus. In the majority of swine in which re-entrant VTs were mapped using in vivo high-resolution mapping systems (Rhythmia, Boston Scientific), boundaries of the isthmus were at least partially functional (9 of 11 VTs; 82%) and displayed an apparent isthmus defined by entrainment criteria that exceeded the true curvature points of the common channel by 1 to 2 cm.

Our animal and human studies display another misconception: that the isthmus is a zone of slow conduction. Data from high-resolution mapping during VT (unpublished observations 2015) demonstrated that the isthmus itself conducts fairly normally (≈0.60 M/s) while the most marked slowing of conduction occurs at turning points (≈0.10 to 15 M/s), in particular at the entrance of the isthmus (Figure 1). Outer loop conduction velocity is normal (≈0.75 M/s).

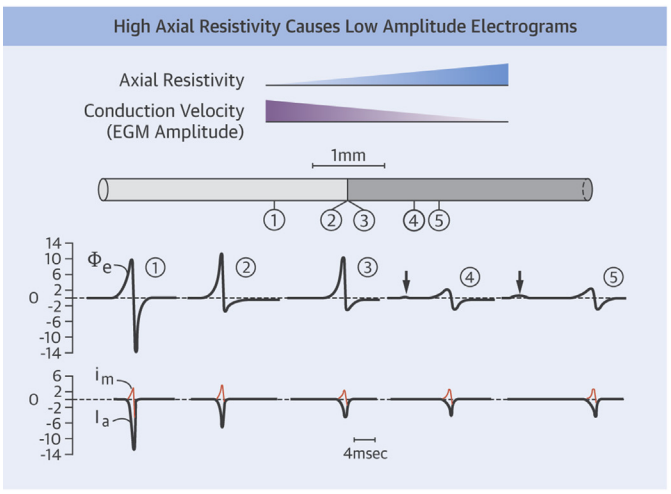
4. Current mapping tools and methods can delineate specific electrophysiological features that will determine the barrier-forming channels during re-entrant ventricular tachycardias.

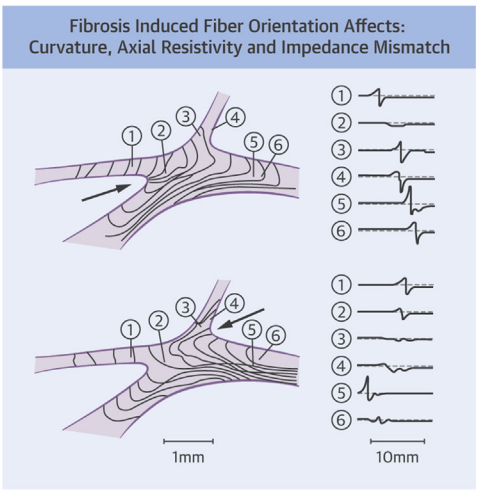
The recorded signals are affected by contact, electrode size, interelectrode distance, angle of contact, and the relationship of the electrodes to the activation wavefront as described previously. The resolution of mapping when using standard catheters with

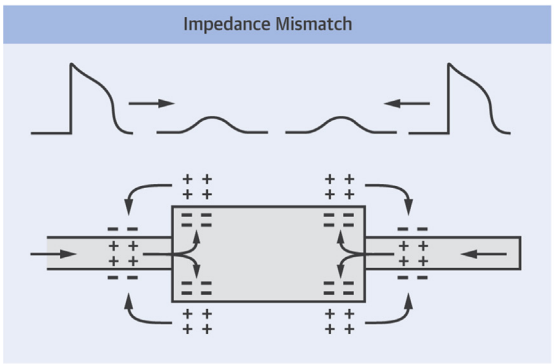
CENTRAL ILLUSTRATION **Factors Affecting the Size and Shape of Electrograms**

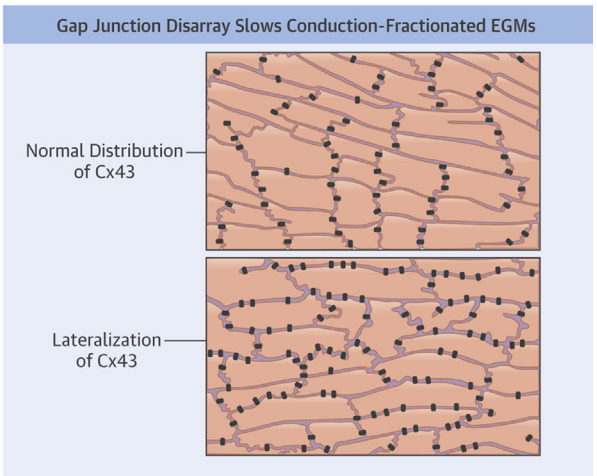
FACTORS AFFECTING SIZE AND SHAPE OF EGM

- Electrode size and interelectrode spacing
- Angle and force of contact
- Wavefront of activation
- Conduction velocity influenced by:
  - reduced sodium channel activity
  - axial resistivity
  - impedance mismatch
  - curvature
- Gap Junction (Connexin-43) disarray
- Insulating tissue: scar, fat, inflammation and edema









Josephson, M.E. et al. J Am Coll Cardiol EP. 2015; 1(5):341–52.

(Top left) Effect of increasing axial resistivity on extracellular waveform. Computed extracellular waveforms (1 to 5) demonstrate a marked reduction in conduction velocity and electrogram (EGM) amplitude distal to an imposed 10-fold increase in internal axial resistivity between sites 2 and 3. Adapted with permission from Spach et al. (30). **(Top right)** Effect of directional differences of wavefront of activation in branching fibers with interstitial fibrosis on extracellular electrograms. Wavefront of activation is shown by **arrows**. Electrograms are shown at **numbered sites**. Adapted with permission from Spach et al. (30). **(Lower left)** Effect of impedance mismatch on electrogram. Conduction from small fiber to larger fiber is markedly impaired due to source-sink mismatch (courtesy of Dr. Andrew Wit). **(Lower right)** Connexin-43 (Cx43) disarray following infarction. Connexins are no longer at the longitudinal ends of muscle fibers but are lateralized. This is associated with zig-zag conduction and fractionated electrograms.

4 mm tip electrode and standard sampling rate allowing significant interpolation is poor and often misleading. Since studies were done using different methodologies not standardized to account for tissue contact, angles of the catheter in relation to the myocardium, and in relation to the wavefront of activation, interpretation is difficult and highly limited. Understanding the underlying substrate can be enhanced using small electrode catheters with closer interelectrode distance, a standard wavefront of activation such as during right ventricular pacing, and with adequate tissue contact force. The smaller the electrode and the smaller the interelectrode distance the more closely the signal approximates the filtered unipolar signal, which is the true local activation. It is hoped that with careful study designs using newer higher-resolution mapping systems, we will be able to better identify areas that may form conduction barriers. Moreover, it may also allow rapid mapping of VTs to better correlate substrate and function and ultimately improve outcomes.

ROLE OF IMAGING

There has been a growing interest in use of MRI and computed tomography to define the electrophysiologic substrate. To date there are no accepted and reproducible data that defines what about a scar is arrhythmogenic. This will require an extremely high-resolution MRI technology capable of at least 100 μm slices that is not available at the present time for human use. Such imaging will need to be correlated with electrophysiologic data during sinus and VT using high-resolution mapping technologies. The sole presence of scar or "channels" of surviving tissue on MRI without electrophysiologic correlation is insufficient. Moreover, as the majority of circuits are at least partially functional, imaging scar geometry using MRI may not be sufficient to identify location of re-entrant circuits and potential ablation targets.

CONCLUSIONS

While the ideas leading to the concept of "substrate based ablation" are rational, they lack scientific support. Many of the limitations of recording techniques can be overcome with the use of new catheters with small electrodes and closer interelectrode spacing, which markedly improve resolution. Factors affecting signal amplitude and morphology need to be taken into consideration (**Central Illustration**). The evaluation of the substrate should include standardization of catheters, wavefront of activation (preferably during right ventricular pacing) and tissue contact. Perhaps the use of filtered unipolar signals in addition to bipolar signals should become a standard. Hopefully these changes will significantly improve our understanding of the arrhythmogenic substrate and improve the results of VT ablation.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Mark E. Josephson, Harvard-Thorndike Electrophysiology Institute, Beth Israel Deaconess Medical Center, 185 Pilgrim Road, Baker 4, Boston, Massachusetts 02215. E-mail: eanter@bidmc.harvard.edu.

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