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Review Article

Ventricular tachycardia in ischemic heart disease substrates



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ABSTRACT

Advances in the treatment of myocardial infarction (MI) have improved survival after ischemic cardiac injury. Post-infarct structural and functional remodeling results in electrophysiologic substrates at risk for monomorphic ventricular tachycardia (MMVT). Characterization of this substrate using a variety of clinical and investigative tools has improved our understanding of MMVT circuits, and has accelerated the development of device and catheter-based therapies aimed at identification and elimination of this arrhythmia.

This review will discuss the central role of the ischemic heart disease substrate in the development MMVT. Electrophysiologic characterization of the post-infarct myocardium using bipolar electrogram amplitudes to delineate scar border zones will be reviewed. Functional electrogram determinants of reentrant circuits such as isolated late potentials will be discussed. Strategies for catheter ablation of reentrant ventricular tachycardia, including structural and functional targets will also be examined, as will the role of the epicardial mapping and ablation in the management of recurrent MMVT.

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1. Introduction

Significant improvements in the prevention, diagnosis, and treatment of coronary artery disease have resulted in higher rates of survival following acute myocardial infarctions (MIs).¹ As a result of rapid reperfusion, increased implementation of hemodynamic support devices, and adherence to antiplatelet and neurohormonal therapies, an increasing number of patients with healed myocardial infarcts require electrophysiologic management for the treatment and prevention of ventricular arrhythmias.²

This review will concentrate on the structural and functional features of ischemic myocardial substrates in the genesis of ventricular arrhythmias after healed MI. Polymorphic ventricular tachycardia and ventricular fibrillation, which are more prevalent in the acute to sub-acute ischemic period, will not be discussed. Components of the ischemic cardiomyopathic substrate, which facilitate the reentrant pathways characteristic of monomorphic ventricular tachycardia (MMVT) will be discussed, along with implications for catheter-based management of these arrhythmias. Automatic ventricular tachycardia, which may appear monomorphic, will not be discussed in this review.

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2. Post-infarct myocardial remodeling

2.1. Structural remodeling

The healing phase of infarcted myocardium is characterized by infiltration of the infarcted myocardial tissue by inflammatory cells. Necrotic myocytes are cleared by macrophages, and replaced fibrous tissue, consisting of collagen, is deposited by fibroblasts over the next days, weeks, and months. The ischemic wavefront of necrosis proceeds from the subendocardium to epicardium during myocardial ischemia,³ and scar deposition parallels this sequence. Critical elements arise during this process, which permit the reentrant circuits that characterize MMVT. The heterogeneous process of myocyte resorption and collagen deposition results in islands of surviving myocardial cells within healed infarct scars as shown in Fig. 1.⁴ These preserved myocardial bundles exist as a “labyrinth” in three dimensions, involving the endocardium, mid-myocardium, and epicardium. The functional electrophysiologic characteristics of these channels will be discussed in detail later in this review.

Channels that facilitate or sustain MMVT, consist of an entry site, a protected isthmus, and a breakthrough exit site that activates the ventricles.⁵ Functional or fixed conduction slowing and block in a channel can result in an excitable gap for reentry. These localized regions of slow conduction within scar exhibit “zig-zag” conduction during normal sinus rhythm through heterogeneously connected myocytes traversing dense unexcitable scar⁶ (Fig. 1). Post-infarct structural

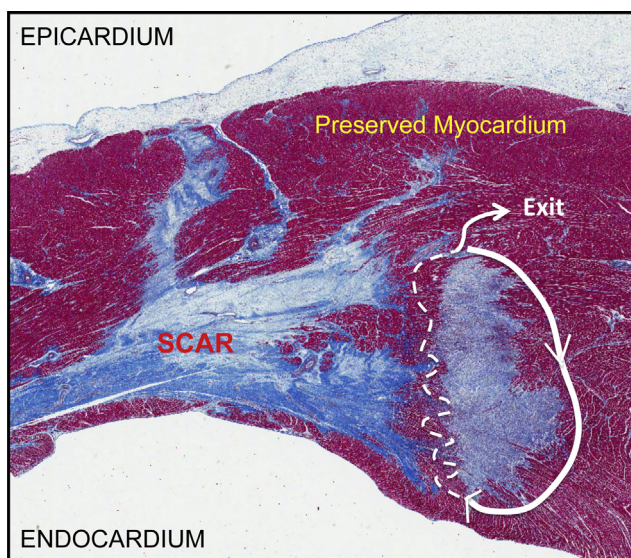


Fig. 1 – Histologic characterization of ischemic heart disease substrates. Masson trichrome stain of infarcted myocardium with “islands” of preserved myocardium surrounded by scar tissue (blue). A schematized representation of a possible ventricular tachycardia circuit is depicted with the white lines. Slowed “zig-zag” conduction through the “isthmus” of the circuit is represented by the broken white lines. Adapted from Tung R, Boyle NG, Shivkumar K. *Circulation*. 2011; 123(20):2284–2288.

remodeling may also involve deposition of adipose tissue in the infarcted bed. A recent report showed that electrophysiologic consequences of post-infarct myocardial fatty replacement in ovine MI included decreased conduction velocity, and reduced bipolar electrogram amplitude.⁷ The presence of inducible VT in MI animals was associated with greater adipose content and slower conduction velocity in the border zones of infarcts.

These structural changes alter local “source–sink” mismatch (in favor of the “source”), given the diminution in electrotonic forces that minimize membrane voltage deviations in one (or a few) myocytes exerted via gap junctions. Reductions in source–sink mismatch facilitate the genesis of premature ventricular depolarizations, which trigger VTs.

2.2. Functional cellular remodeling

Remodeling of other important elements within and beyond the infarcted myocardial bed also occur, and add further complexity to the post-MI substrate. These include remodeling of myocyte ionic currents and gap junctions, direction of activation propagation, and intra-myocardial nerve fibers. Although human data are lacking, studies in animal models have provided insight into how ventricular myocyte action potential (AP) remodel in cardiomyocytes adjacent to a healed MI. These include reduction in the duration, upstroke amplitude, and velocity of border zone myocyte AP.⁸ Reductions have also been reported in peak calcium currents in surviving border zone cells. In addition, refractoriness in the infarcted animal heart is known to be more nonuniform compared to normal hearts, with varying degrees of AP prolongation exhibited by individual surviving myocytes adjacent to and remote from the infarcted myocardium. In the border zones of infarcts, this worsens heterogeneity in refractoriness, and facilitates the development of unidirectional block, critical to genesis and perpetuation of VT.

The distribution of connexin 43 gap junctions in the border zone of the infarcted human heart is also aberrant. Fewer gap junctions are organized into transverse (side-to-side) connections, rather the gap junctions are redistributed in a longitudinal fashion.⁹ Detailed animal studies support light microscopy findings in humans, with altered anisotropic conduction in the healed infarct heart. In addition, interstitial fibrosis results in displacement of myocytes from each other, and a significant decrease in the syncytial connection of myocytes in the infarct border zone.¹⁰

Another component of post-MI functional change is neural remodeling. Nerve endings in the infarcted bed are resorbed, however, since the neuronal cell body from which these nerves originate is removed from the infarcted territory, plastic growth is driven at the most distal intact endings adjacent to the infarcted tissue. This nerve sprouting in the border zone is heterogeneous, and is unable to penetrate scar tissue. The presence of these sprouts has been associated with ventricular arrhythmias and sudden death in humans,¹¹ likely related to local heterogeneity in myocyte electrophysiological properties. We have demonstrated that the border zone of infarcts exhibits variable responses to autonomic stress (Fig. 2).¹² Remodeling within stellate ganglia, which partly control myocardial excitability, has also been reported, and

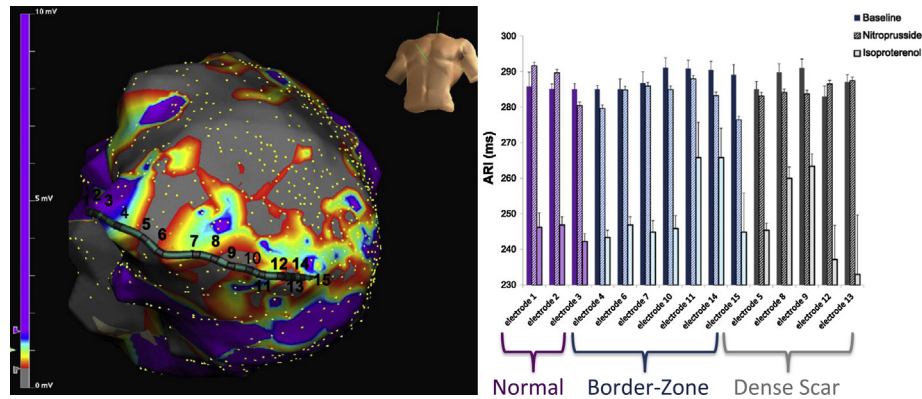


Fig. 2 – Heterogeneous responses to direct and reflex sympathetic nerve stimulation in scar, border zone, and preserved myocardium. Image on the left depicts an electroanatomic map of a patient with a large anterior wall infarction (with dense scar in gray, preserved myocardium in purple, and border zone in other colors) and the location of a multi-electrode catheter. The image on the right shows the activation recovery interval (ARI) at baseline and in response to reflex (nitroprusside) and direct (isoproterenol) sympathetic stimulation. In preserved myocardium, direct activation via adrenergic receptors is fairly uniform, however in the border zone and scar regions, this response is heterogeneous, reflecting varying degree of adrenergic receptor responses in adjacent myocardium. In response to reflex sympathetic stimulation induced by cardiac sympathetic nerves, significant heterogeneity is seen across the entire spectrum of scar, border zone, and even “preserved” myocardium. Adapted from Vaseghi M, Lux RL, Mahajan A et al. *Am J Physiol Heart Circ Physiol* 2012, 302(9):H1838–46.

likely contributes to enhanced sympathetic tone and electrical heterogeneity seen after MI.¹³

In summary, the healed infarct heart exhibits changes in the structural and functional characteristics of the myocardial substrate. These alterations facilitate the conditions required for initiation and maintenance of sustained reentrant ventricular arrhythmias.

3. Characterization of ischemic heart disease substrates

3.1. Role of imaging

Myocardial imaging has an increasing role in the diagnosis and treatment of VT in the ischemic heart disease substrate. Contrast enhanced-magnetic resonance imaging (MRI) appears to provide the most valuable information on cardiac structure, owing to its superior resolution (Fig. 3A) over positron emission tomography (PET) and computed tomography (CT).¹⁴

Pre-procedurally, imaging is used to identify the location and transmuralty of scar. Patchy scars (which may support VT) and border zones of scar (where VT exit sites are typically located) can be identified prior to the procedure to guide mapping. Scar transmuralty has been correlated to sites of VT termination, as are sites with late potentials.^{15,16} A recent study using CT showed consistent findings with MRI data, with regards to post infarct wall thinning.¹⁷ Regions of heterogeneity in contrast enhanced MRI, also known as “gray zones”, have been related to MMVT inducibility.

The resolution of in vivo MRI still has limitations, due to partial volume effects from cardiac motion, making determinations of transmuralty suboptimal. The presence of ICDs in most patients undergoing VT ablation raises concerns

about performing MRIs. At our center we have routinely performed MR imaging in this patient population (except when abandoned leads are present, or when the patient is pacing-dependent) without adverse outcomes. Image artifacts created by the device can also be minimized (Fig. 3B) to improve the quality and usefulness of images obtained in patients with devices.¹⁸ Intra-procedural imaging in contemporary VT ablation can be achieved with ICE,¹⁹ although its utility extends beyond ablation of the ischemic substrate. Intra-procedural MRI remains under development, however its role in real-time characterization of lesion formation, and ischemic substrate homogenization remains promising.²⁰

3.2. Electrophysiologic characterization

3.2.1. Development and validation of electrogram amplitude
The characteristics of bipolar electrograms recorded from normal myocardium and scar are distinct. This difference is the basis of voltage mapping. Electrical signals are recorded from cardiac tissue using catheters fitted with bipolar (or multipolar) electrodes. These signals are filtered at 30–40 Hz to 400–500 Hz, and bipolar electrograms demonstrating sharp bi or tri-phasic waveforms with amplitudes greater than 3 mV and durations under 70 ms are consistent with normal myocardium. Bipolar electrograms with amplitudes less than 0.5 mV, showing durations >133 ms, and showing fractionations are consistent with recordings from regions of myocardial scar.²¹ Current mapping cut-offs utilize bipolar electrogram amplitudes of >1.5 mV and <0.5 mV²² to delineate normal myocardium and dense scar respectively, with regions demonstrating intermediate amplitudes designated as border-zone areas (Fig. 4). These voltage thresholds have been validated in multiple studies. In a porcine healed infarct model, Callans et al showed that bipolar electrograms <1 mV in

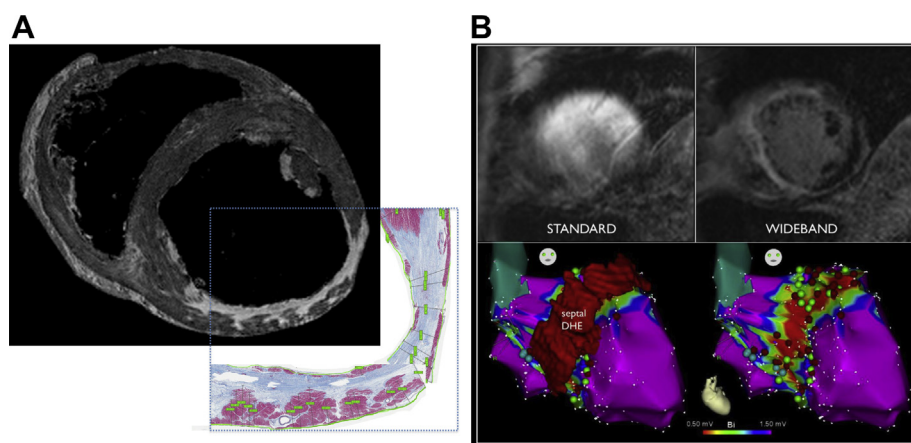


Fig. 3 – Characterization of ischemic heart disease substrates – magnetic resonance imaging. A An ex vivo magnetic resonance image (MRI) of an infarcted porcine heart is shown (top image), with the corresponding Masson's trichrome stain of the same region shown in the inset. The high resolution of this MRI image relative to the histologic image can be readily recognized. It should be noted that artifacts created by cardiac motion and presence of thoracic structures are not present in ex vivo MR images. B The top left and right images depict an MR image before and after application of the WIDEBAND method of device artifact attenuation. The bottom left and right images depict the corresponding voltage map (right anterior oblique projection of left ventricular endocardium) showing consistency between the WIDEBAND (left) and electroanatomic (right) location of scar. Adapted from Stevens SM, Tung R, Rashid S et al. *Heart Rhythm* 2013 in press.

amplitude correlated with regions of infarction.²³ Wroblewski et al²⁴ similarly correlated such areas in chronic infarcted porcine heart with bipolar electrograms <1.5 mV and under ≥ 50 ms in duration. More detailed validation of electroanatomic data recorded in humans has been performed using imaging modalities such as MRI, PET,²⁵ and CT.^{17,26}

3.2.2. Electroanatomic mapping

Electroanatomic mapping systems are capable of creating 3-D myocardial geometry based on tissue contact, and superimpose color-coded characterization of normal, border zone, and

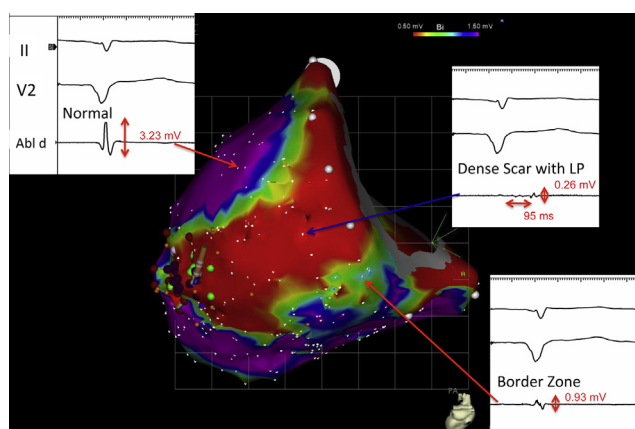


Fig. 4 – Bipolar electrogram morphology in ischemic heart disease substrates. Representative examples of bipolar electrograms (and amplitudes) recorded from regions of “normal”, dense scar, and border zone myocardium are shown superimposed onto a voltage map (0.5–1.5 mV). A significant portion of the electrograms recorded in the dense scar region are “late” (i.e. occur well after the surface QRS) and are very low in amplitude (<0.5 mV).

dense scar myocardial regions (Fig. 4). Myocardium is sampled point-by-point, with the corresponding bipolar voltage amplitude binned into scar (<0.5 mV), border zone (0.5–1.5 mV), or normal (>1.5 mV) tissue. Intra-procedural characterization of the myocardial substrate using one of the two available platforms (magnetic-based CARTO, Biosense Webster, Diamond Bar, CA and electrofield-based Ensite NaVX, St Jude Medical, Minneapolis, MN) is the standard in contemporary VT ablation.

The correlation between EAM data and CE-MRI delineation of myocardial substrates remains imperfect. In a study by Wijnmaalen et al, although there was excellent correlation between infarcted regions on CE-MRI and electrical infarct localization (bipolar electrogram <1.5 mV), scar areas on MRI were significantly larger than scar areas delineated by EAM.²⁷ In this study, approximately 20% of points taken in MRI-designated regions of dense transmural scar recorded “normal” bipolar electrograms (>1.5 mV). The converse may also account for poor correlation between EAM and other imaging modalities or histopathology i.e. bipolar electrograms <1.5 mV recorded from areas with normal tissue. The latter issue may arise due to poor catheter tissue contact or stability, changes in the volume loaded state of the patient (increased during EAM relative to imaging), inadequate delineation on CE-MRI.

4. Treatment of ventricular tachycardia in ischemic substrates

4.1. Pharmacologic therapy

Despite decades of intense research and development, few effective drugs with minimal side effects are available for the

treatment of recurrent MMVT. Beta-adrenergic receptor blockers have been studied in a variety of post-myocardial infarction trials, demonstrating substantial reduction in the risk of sudden death and recurrent VT^{28,29}. The efficacy of beta blockers in stable MMVT is however limited. Sotalol demonstrates greater efficacy compared to beta blockers, however, the risk of prolonged QT and PMVT restricts its use. The proarrhythmic risk of anti-arrhythmics drugs in the post-infarct setting have long been recognized,^{30,31} with amiodarone demonstrating a safer risk profile.^{32–34,23} Given the long-term risk of side effects, amiodarone is a less favorable choice for long-term management of VTs in ICM patients. Newer agents such as ranolazine have shown some promise in reducing VT and ICD shocks in ICM patients without significantly increased risk profile.³⁵

4.2. Defibrillator therapy

Implantable cardioverter-defibrillators have been demonstrated in multiple trials to reduce the risk of sudden death in patients with ischemic heart disease substrates.³⁶ Although defibrillators save lives, they do not prevent the initiation of VT, and patients frequently present to medical attention with repetitive ICD shocks. Defibrillator shocks are associated with significant medical and psychiatric morbidity. Post hoc analysis of ICD studies demonstrate that patients who receive appropriate ICD shocks have clinical outcomes that are less favorable than those patients without VT and who do not receive ICD shocks.³⁷ While the underlying reason for this phenomenon is not clear, it emphasizes that although defibrillators have a role in preventing sudden death from ventricular arrhythmias, adjunctive therapies are required to mitigate arrhythmogenesis.

4.3. Surgical treatment

In contemporary management of recurrent MMVT, surgical therapy has a limited role. Although intraoperative mapping studies provided substantial insights into the mechanisms underlying scar-related VT,^{38,39} it has fallen out of favor due to the morbidity of surgical exposure of the heart for mapping and ablation.⁴⁰ This is especially true in the era of minimally based access to the endocardium and epicardium, and mini-thoracotomy for epicardial access, which is increasingly implemented.^{41,42} However, it is important to note that the advent of border zone ablation was an attempt to mimic encircling ventriculotomy and subendocardial resection.^{43,44}

4.4. Catheter ablation

Catheter-based management of MMVT is an increasingly adopted strategy, with a number of studies supporting its role over antiarrhythmic drugs.^{45–48} It requires careful patient selection, pre-procedural planning and imaging, procedural substrate characterization, induction and mapping of tolerable MMVTs, ablation of electrophysiologic and substrate targets, and careful post-procedural care, while minimizing risks of complications. Catheter ablation is often reserved for patients with ischemic heart disease who suffer ICD shocks or recurrent arrhythmias (including electrical storm), although a growing trend is the early introduction of catheter ablation of VT.

4.4.1. Identification of clinical VT

Patients may be inducible for multiple VT morphologies, however, only one, or a few, may be responsible for the patient's presentation. Identification of clinically relevant VT by 12-lead electrocardiogram, if possible, is important, as it

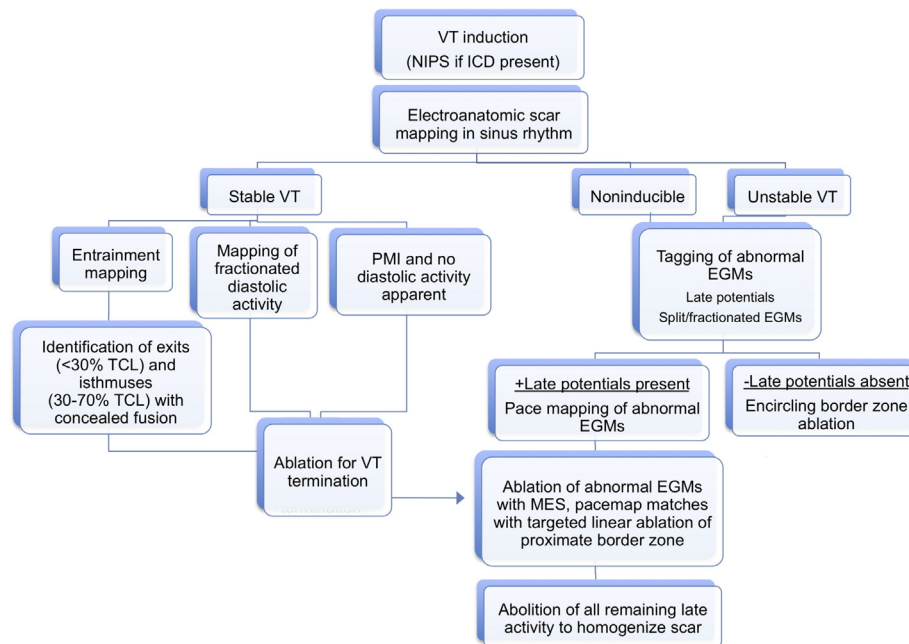


Fig. 5 – Approach to catheter mapping and ablation of ventricular tachycardia (VT). EGM: electrogram. ICD: implantable cardioverter-defibrillator; NIPS: noninvasive programmed stimulation; TCL: tachycardia cycle length. Adapted from Tung R, Mathuria N, Michowitz Y et al. *Circ Arrhythmia Electrophysiol* 2012;5:264–272.

provides a target, and meaningful endpoint for the procedure. The ventricular site of origin of the clinical VT deduced from a 12-lead ECG may also guide procedural planning and approach. If the 12-lead ECG suggests an epicardial exit, preparatory measures for epicardial access can be performed before the procedure.^{49,50}

For some patients, only ICD recordings of the clinical VT may be available. The VT cycle length may be a useful clue to the clinically relevant VT. Patients with devices can also undergo a noninvasive programmed stimulation (NIPS) in the day(s) prior to VT ablation, or at the start of the procedure. The morphologies of inducible VTs can be noted on the electrophysiologic recording systems, and used as templates during the procedure, when the patient is typically under deeper sedation. The morphologies of induced VTs can also be compared to ICD recordings in terms of morphology and CL for VTs that were monitored, or for which therapies were delivered.⁵¹

4.4.2. Procedural strategy

The major determinant of mapping strategy is whether the VT is hemodynamically tolerated. An approach, used at our center, is detailed in the chart shown in Fig. 5.⁵² For hemodynamically tolerated VTs, activation mapping is preferable, as the origin of the VT can be mapped in detail for exit sites and critical isthmuses showing diastolic potentials (Fig. 6).

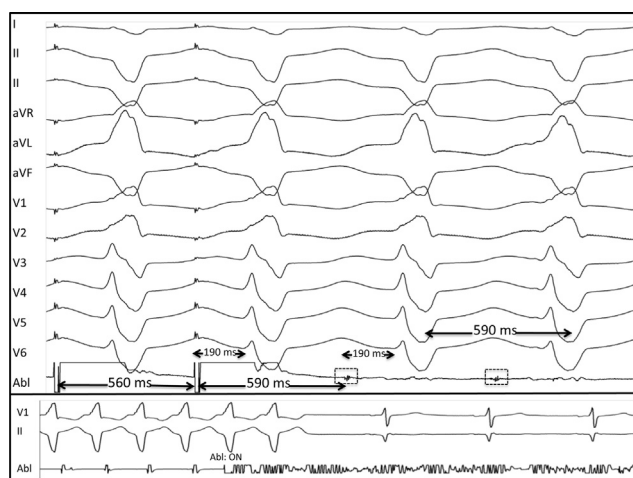


Fig. 6 – Entrainment and ablation of monomorphic ventricular tachycardia (MMVT). Top panel: an MMVT with a cycle length of 590 ms is entrained at 560 ms. The post-pacing interval (PPI) is 590 ms, and exactly matches the TCL. The stimulus to QRS (Stim-QRS) interval shown on the last paced complex is 190 ms, which also exactly matches the electrogram to QRS (EGM-QRS) interval at 190 ms. The entrainment demonstrated here is also concealed (paced QRS morphology is identical to MMVT QRS morphology, i.e. no evidence of QRS fusion) These conditions (PPI = TCL, Stim-QRS = EGM-QRS, and concealed entrainment) confirm that the site is a protected and critical isthmus for this MMVT. Lower panel: Ablation at the site with entrainment characteristics demonstrated above terminates MMVT immediately. Adapted from Tung R, Boyle NG, Shivkumar K. *Circulation*. 2011;123(20):2284–2288.

Entrainment mapping during VT can be performed to confirm critical isthmuses or exit sites, and ablation performed. Attention can then be focused on addressing the substrate facilitating the clinical VT.

As most VTs are poorly tolerated hemodynamically, a substrate mapping approach is more commonly used to guide ablation. Strategies include anatomic and electrogram-based approaches.

4.4.3. Substrate mapping – anatomic strategies

4.4.3.1. Border zone ablation & scar homogenization. Border zone tissue has been shown to harbor both isthmus and exit sites for MMVT.^{53,54} The strategy of border zone ablation relies upon adequate mapping and electrophysiologic characterization of the substrate, which can be facilitated by multipolar catheters. Strategies to achieve border zone homogenization include creating linear lesions,⁴⁵ transecting the scar with a “T” shaped lesion set, in addition to encircling.⁴⁶ Substrate homogenization involves eradicating regions of preserved voltage within dense scar regions, which may serve as isthmuses or exit sites, and can be guided by abnormal electrograms.⁵⁵

4.4.3.2. Identification and ablation of channels. As described previously, channels bordered by electrically unexcitable scar tissue form the basis for the majority of MMVTs. Adjusting voltage settings during mapping may identify macroscopic channels. Arenal et al demonstrated 23 channels in 20 patients using a tiered voltage threshold of 0.1–0.5 mV. Twenty of such channels were related to a VT morphology. In another study utilizing a tiered scar display, a mean voltage threshold of 0.33 ± 0.15 mV was found to be optimal for identifying channels, with an average observed channel length of 32 ± 21 mm (range 12–87 mm).⁵⁴

Channels have been alternatively identified by electro-anatomic mapping during hemodynamically tolerated MMVT. Channel characteristics identified include a mean length and width of 31 ± 7 mm and 16 ± 8 mm respectively. In addition, the location of the circuit was associated with channel orientation, with perimitral circuits demonstrating channels parallel to the mitral annulus, while all other channels were oriented perpendicular in 21 studied patients. Confirming the concept, ablation lesions transecting the narrowest portion of a common channel terminated VT in 97% of cases. In contrast to these studies, others have failed to find strong associations between channels and critical isthmuses of VTs. Mountantonakis and colleagues demonstrated that 88% of scar maps contained channels using tiered voltage settings, however, only 30% were shown by entrainment to contain the isthmus.⁵⁶

As noted earlier, these channels exist as a labyrinth in 3-D, and may be interconnected. Our group assessed the connectivity between channels, such that ablation of a critical LP reflecting the common isthmus of these channels, causes eradication of multiple channels (Fig. 7A).⁵⁷

4.4.3.3. Multiple exit sites. Akin to multiple interconnected channels, complex scars may also contain protected isthmuses that are provided spatially distinct exits. This phenomenon results in ≥ 2 distinct QRS morphologies from a single stable pacing site, indicating multiple exits sites (MES)

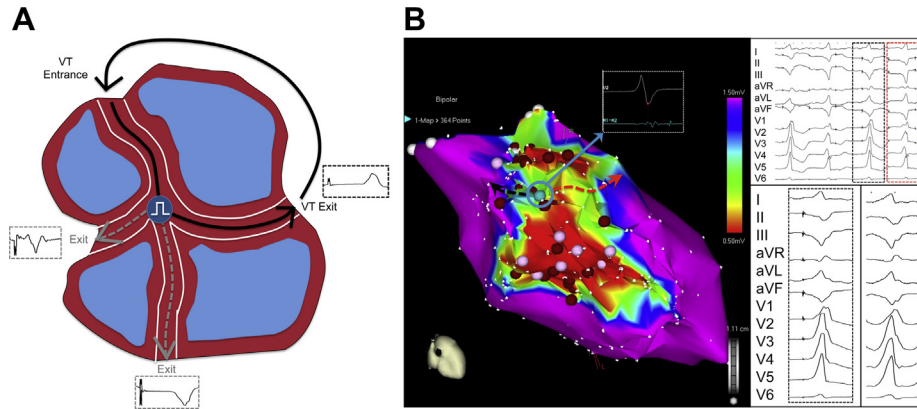


Fig. 7 – Multiple exit sites and channels. A Schematic representation of interconnected channels with a common isthmus, and three spatially separate exits, each producing a distinct QRS morphology. **B** The image on the left depicts the electroanatomic map from a patient with inferior wall low voltage areas (0.5–1.5 mV). The electrogram recorded at an isthmus site (inset, indicated by blue circle and arrow) with two exits is shown. Pacing at this site produced two distinct QRS morphologies and two stimulus to QRS intervals (black and red box in top right tracing). One of the paced QRS morphologies (black box) matches the clinical VT (shown in right lower tracing). Adapted from Tung R, Mathuria N, Michowitz Y et al. *Circ Arrhythmia Electrophysiol* 2012;5:264–272.

are available to this common isthmus (Fig. 7A and B). In a recent report,⁵² our group defined an MES site as an abnormal EGM site that produces ≥ 2 distinct QRS complexes with at least three leads showing distinct QRS complexes qualitatively (Fig. 7B). When MES sites are identified and ablated, a greater freedom from recurrent VT was seen, suggesting that these are surrogates for critical isthmuses.⁵²

4.4.4. Functional strategies

4.4.4.1. Late and abnormal potentials. Bipolar recording over dense scar typically demonstrates late or absent activation, owing to slower or absent conduction in this tissue. Local low amplitude fractionated bipolar electrograms that have a distinct onset after the end of the QRS complex are classified as isolated late potentials (Fig. 8) in sinus or paced rhythm or diastolic potentials in VT. These signals identify sites that are activated later than the bulk of the ventricular tissue and have been shown to have specificity as sites critical for reentry. Ablation strategies specifically targeted at LPs have been demonstrated to be effective in eradicating and preventing recurrent VT.^{58,59}

In the ischemic substrate, sites with LPs are encountered more frequently than in the non-ischemic substrate. Nakahara et al,⁶⁰ showed that “very” late potentials (occurring greater than 100 ms after the surface QRS complex) were three and two-fold more common in the endocardium and epicardium respectively, of ischemic cardiomyopathy patients relative to non-ischemic patients. Interestingly, when high-density electroanatomic mapping was performed in patients with ICM, heterogeneous islets (HI) (Fig. 8) with relatively preserved voltage amplitudes were observed deep within dense infarct scar.⁶¹ Fifty seven percent of sites demonstrating vLPs were encountered within or adjacent to an HI. This electrophysiologic finding is consistent with histologic characterization of the healed infarct heart, as islands of surviving myocardium are frequently encountered.

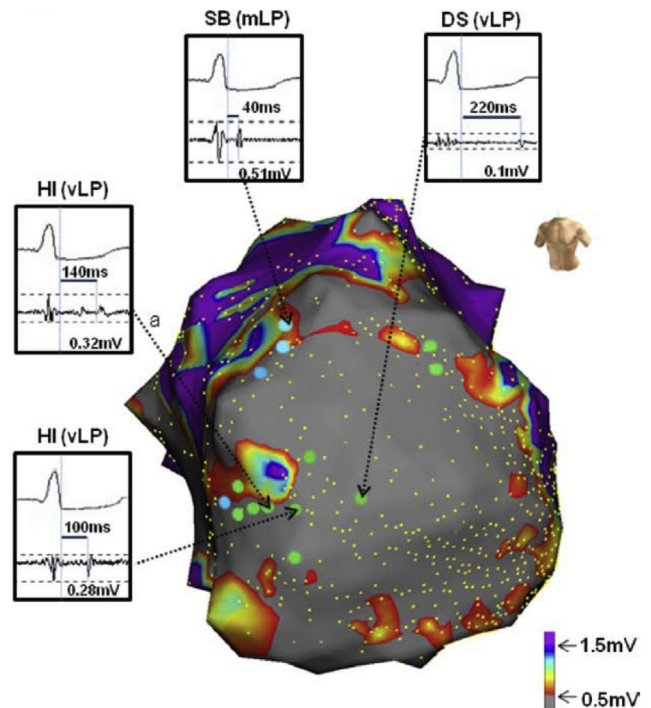


Fig. 8 – Distribution of late potentials in ischemic heart disease substrates. An electroanatomic map is shown in antero-posterior view depicting an anterior myocardial infarction, with heterogeneous islets (HIs, regions of preserved voltage within dense scar) shown. Very late potentials (VLPs, green tags) were recorded around HIs or dense scar (DS) areas. Mid-late potentials (MLPs, blue tags) were recorded at scar border SB between DS and normal tissue. Yellow dots reflect electrogram sampling points. Adapted from Nakahara S, Tung R, Ramirez RJ et al. *Heart Rhythm* 2010;7:1817–1824.

4.4.4.2. *Pace map induction.* Induction of VT during pace-mapping at a site of abnormal electrograms has been termed pace map induction (PMI) (Fig. 9). The significance of this finding is the identification of a functionally important site for MMVT. The requisite for VT induction from this site is unidirectional block, supporting unique characteristics of a critical isthmus. Other features that may be observed during PMI are concealed entrainment and longer stimulus to QRS interval, further indications of MMVT isthmus sites. In our report, ablation at a PMI site successfully terminated VT in 93% of cases.⁵² Multiple distinct QRS morphologies may also be observed during PMI, and PMI may identify more relevant VTs. Entrainment maneuvers can be performed after PMI to confirm that a critical isthmus has been identified.^{5,62} Ablation can be initiated rapidly, with the goal of terminating the VT during energy delivery (Fig. 9, lower panel).

An often sought or important endpoint during ablation is termination of VT early during RF delivery. Whether or not this has any relationship to VT inducibility after RF delivery is unclear. As most clinical MMVTs are poorly tolerated, mechanical hemodynamic support to permit mapping and ablation during VT has been advocated by some. These include intra-aortic balloon pump (IABP), TandemHeart & Impella ventricular assist devices, and extra-corporeal membrane oxygenation (ECMO). Whether clinical outcomes are significantly improved in patients with poorly tolerated VT who undergo substrate-based ablation compared to ventricular assist devices is unclear.

4.4.5. *Epicardial mapping and ablation*

In patients with ischemic heart disease substrates, an epicardial approach is often favored after previous failed endocardial approach. This is in contrast to other substrates such as Chagas cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy (ARVC), or idiopathic dilated cardiomyopathies where epicardial VT substrates are encountered more frequently. The pericardial space is typically accessed via subxiphoid puncture using a Tuohy needle as shown in Fig. 10, with an anterior or posterior entrance into

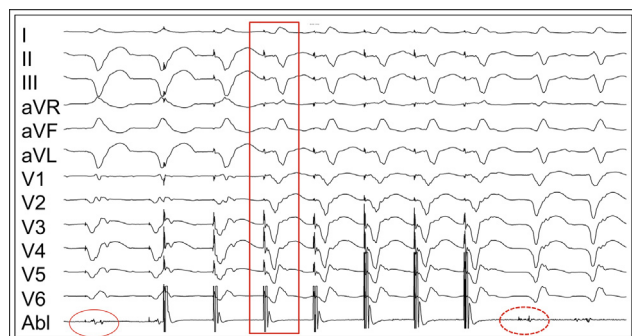


Fig. 9 – Pace map induction (PMI). A representative tracing showing PMI. Low amplitude electrograms with split potentials (solid red circle on ablation catheter, Abl) recorded at a site from which pacing induced a monomorphic ventricular tachycardia (MMVT). The red box indicates the first beat of MMVT. The split potentials become diastolic potentials during MMVT (broken red circle).

the pericardial space selected based on whether the posterior or anterior myocardium respectively, is the most likely origin of VT. In most cases, use of angled sheaths and deflectable catheters enables access to all aspects of the epicardium. In patients who have had prior cardiac surgery, prior epicardial access, or prior pericarditis, focal or global adhesions may be present, restricting access to the pericardial space. Limited surgical exposure can be utilized to gain epicardial access in these cases.

The true incidence of epicardial VTs in ICM remains unknown. As circuits may be transmural, termination of VT on a given surface is an imperfect gold standard. Additionally, 12-lead ECG localization only assists in determining the exit site, which can be spatially remote from the critical isthmus. Martinek et al demonstrated that traditional 12 lead criteria lacked specificity in ICM substrates.⁶³

Additionally, selection and referral bias are present in reports from experienced tertiary centers. In patients referred after failed endocardial ablation, epicardial substrate was found in 71%. In our experience, where 81% of ICM patients had failed a prior ablation, the long-term freedom from VT was improved with combined endocardial-epicardial ablation strategy.⁶⁴ Di Biase et al⁵⁵ demonstrated that a combined endo-epicardial approach was better in ICM patients with electrical storm, although a homogenization strategy was also employed in this study, making it unclear whether critical sites were on the endocardium or epicardium. The role of combined endocardial-epicardial ablation as an initial strategy requires further prospective investigation.

Risks of epicardial access include cardiac perforation and/or tamponade, phrenic nerve palsy, hepatic laceration, bowel perforation, pericarditis, and epicardial coronary artery

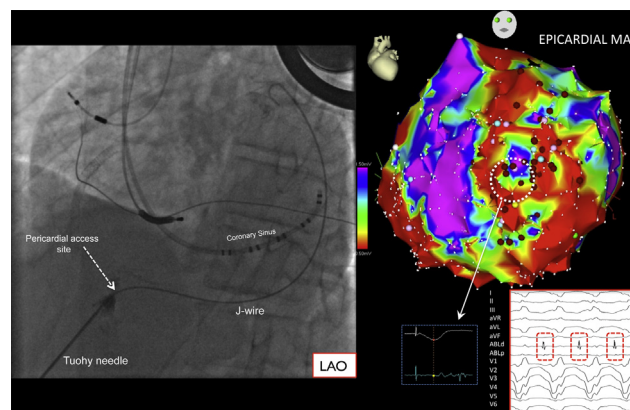


Fig. 10 – Epicardial access and mapping for ventricular tachycardia (VT). The left panel depicts an image of epicardial access in the left anterior oblique (LAO) projection. The Tuohy needle is seen entering the pericardium as indicated, small amounts of contrast are injected during the course of the needle to identify structures passed in its trajectory. A J-tipped wire passed through the needle into pericardial space outlines the lateral heart border in LAO. The right panel image depicts an epicardial voltage map in the LAO projection. A site with late potentials during baseline paced rhythm is shown (broken white circle and inset), as well as the diastolic potentials recorded during VT.

injury. At our center, of 95 patients who underwent epicardial access, complications were seen in 8.8% of cases (eight patients), including six (6.7%) cases of epicardial bleeding (one confirmed RV puncture), and two patients with phrenic nerve palsy. These complication rates are in line with multicenter experience detailing the safety of epicardial mapping and ablation of VT.⁶⁵

5. Conclusion

After infarction, the myocardial substrate undergoes significant structural and functional alterations, from a molecular to macroscopic level, resulting in substrates capable of facilitating MMVT. The morbidity and mortality associated with VT in this substrate cannot be overstated. Pharmacologic, and catheter-based approaches to treating VT specific to this substrate have evolved since the initial intraoperative mapping studies detailing critical elements of the ischemic substrate. While the structural elements of the ischemic heart disease substrate are well understood, the chronic functional changes that permit unidirectional block and other key electrophysiologic phenomena, as well as the acute functional changes that initiate MMVT remain poorly understood. Improving our understanding of this new frontier will undoubtedly improve our ability to prevent and care for patients with ischemic heart disease substrates suffering from recurrent MMVT.

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Conflicts of interest

All authors have none to declare.

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