Contribution of Myocardium Responsible for Ventricular Tachycardia to Abnormalities Detected by Analysis of Signal-Averaged ECGs

Margaret A. Hood, MB, ChB; Steven M. Pogwizd, MD; Jerome Peirick, MSEE; and Michael E. Cain, MD

Background. Current methods of signal-averaged ECG analysis interrogate the terminal 40 msec of the QRS complex and/or the ST segment and have a low positive-predictive accuracy for detecting vulnerability to sustained ventricular tachycardia (VT). The extent to which abnormalities detected during these ECG intervals are generated by myocardial tissue responsible for VT has not been well defined. The purpose of this study was to determine when, during sinus rhythm, myocardium responsible for VT is activated.

Methods and Results. Three-dimensional ventricular activation maps were analyzed during sinus rhythm and during 10 VTs in eight patients with healed myocardial infarctions undergoing arrhythmia surgery for sustained monomorphic VT. The mechanism of VT was focal in five instances and macroreentrant in five. During sinus beats, myocardium responsible for all focal VTs activated 43±38 msec before the onset of the terminal 40-msec interval of the QRS complex. During sinus rhythm, activation of the myocardium critical to macroreentrant VT began 72±13 msec before the onset of the terminal QRS interval and in only three instances extended 2–25 msec into the terminal 40 msec of the QRS complex. Electrograms recorded during the ST segment represented late activation of epicardial sites overlying zones of infarction that were temporally and spatially remote from tissue critical to VT.

Conclusions. Current methods of signal-averaged ECG analysis limiting interrogation to the terminal QRS/ST segment exclude detection of >95% of the signals generated by myocardium responsible for sustained VT. These results establish a pathophysiological basis for expanding signal-averaged ECG analysis to include more of the cardiac cycle. (Circulation 1992;86:1888–1901)

Key Words • fast Fourier transform • mapping • late potentials

Current methods of analysis of the signal-averaged ECG limit analysis to the terminal 40 msec of the QRS complex and/or portions of the ST segment. Abnormalities detected during these ECG intervals have been well characterized in the time1–7 and frequency8–17 domains and are a manifestation of delayed activation of myocardium. Late potentials recorded from dogs with experimental myocardial infarction correspond in time with fragmented and delayed electrograms recorded from the epicardium.18–25 In humans, late potentials detected in signal-averaged ECGs have been accompanied by late, fragmented electrograms recorded directly from the heart and have been related to the total mass of slowly activated tissue.26,27 Despite the increasing reliance on the signal-averaged ECG for clinical decision making in patients with ischemic heart disease,28 the extent to which abnormalities detected during the terminal QRS complex and ST segment are generated by myocardial tissue responsible for ventricular tachycardia (VT) has not been well defined. Results of computer-assisted analysis of three-dimensional ventricular activation maps during VT have demonstrated that intramural macroreentry and focal mechanisms are responsible for sustained monomorphic VT in experimental animals29–31 and in patients.32,33 The purpose of this study was to determine when, during sinus rhythm, myocardium responsible for VT is activated in patients with healed myocardial infarction undergoing intraoperative mapping.

Methods

Patient Population

The study group was composed of eight patients with ischemic heart disease, a healed myocardial infarction (4 months to 13 years), and sustained monomorphic VT referred for arrhythmia surgery. The mechanism and locus of VT were defined during surgery in each patient by analysis of three-dimensional activation maps (Table 1).33 Each patient underwent cardiac catheterization before surgery. The locus of infarction was anterior in six patients and inferior in two patients. Seven patients had a left ventricular aneurysm. A signal-averaged ECG

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was recorded in all patients before electrophysiological study. Surgical procedures included aneurysmectomy in seven patients, endocardial resection and cryoablation in all patients, epicardial cryoablation in two patients, and placement of cardioverter/defibrillator electrode patches in one patient. Coronary artery bypass graft surgery was performed in four patients. No patient had inducible VT after surgery.

**Preoperative Electrophysiological Study**
Programmed ventricular stimulation and endocardial catheter mapping during VT were performed in seven of the eight patients with the use of standard techniques. Administration of all antiarrhythmic drugs was stopped at least five half-lives before the study with the exception of one patient in whom amiodarone had been discontinued 2 weeks before the study. Sustained monomorphic VT (>30 seconds' duration or associated with hemodynamic compromise) was initiated in six of the seven patients who completed the protocol. The electrophysiological study was not completed in one patient due to the onset of transient neurological symptoms.

**Signal-Averaged ECGs**
ECG signals were recorded and analyzed by the use of time (three of the four patients without intraventricular conduction abnormalities) and frequency (eight patients) domain techniques.

**Time-domain analysis.** Bipolar orthogonal ECGs were recorded over a passband of 0.05–300 Hz, amplified 1,000-fold, and digitized at 2 KHz with 16-bit precision (Corazonix, Inc.). Averaged data were bandpass filtered between 25 and 250 Hz and combined into a vector magnitude. Numerical criteria of abnormality were based on published values for the filtered QRS duration, the root-mean-square voltage in the terminal 40 msec of the filtered QRS complex, and the duration of signals <40 μV in the terminal QRS complex.

**Frequency-domain analysis.** Frank X-, Y-, and Z-lead ECGs were recorded during sinus rhythm over a passband of 0.05–450 Hz, amplified 1,000-fold, digitized at 1 KHz with 12-bit precision, and averaged by the use of methods reported previously. Spectral estimates of a data interval that included the terminal 40 msec of the QRS complex and the entire ST segment of each

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**TABLE 1. Patient Characteristics**

<p>| | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>8</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>61±11</td>
</tr>
<tr>
<td>Myocardial infarction (n)</td>
<td>8</td>
</tr>
<tr>
<td>Anterior</td>
<td>6</td>
</tr>
<tr>
<td>Inferior</td>
<td>2</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>7</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>32±9</td>
</tr>
<tr>
<td>Signal-averaged ECG (n)</td>
<td>8</td>
</tr>
<tr>
<td>Time domain</td>
<td>3</td>
</tr>
<tr>
<td>Frequency domain</td>
<td>8</td>
</tr>
<tr>
<td>Preoperative electrophysiological studies (n)</td>
<td>7</td>
</tr>
<tr>
<td>Programmed ventricular stimulation</td>
<td>7</td>
</tr>
<tr>
<td>Catheter endocardial mapping</td>
<td>6</td>
</tr>
<tr>
<td>Intraoperative electrophysiological studies (n)</td>
<td>8</td>
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<tr>
<td>Epicardial mapping</td>
<td>5</td>
</tr>
<tr>
<td>Transmural mapping</td>
<td>8</td>
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</tbody>
</table>

LVEF, left ventricular ejection fraction.
signal-averaged X, Y, and Z lead were computed by using the fast Fourier transform. A 512-point fast Fourier transform was performed on the data interval after multiplication by a four-term Blackman-Harris window to reduce spectral leakage. Transformed data were expressed as a spectral magnitude and analyzed as
described previously.10,11 The validity of this approach has been established in patients with conduction abnormalities10,14–16 and those with ischemic or nonischemic heart disease.36,37

Three-dimensional Intraoperative Mapping

Ventricular mapping was performed with the use of methods previously described.38–40 After cannulation of the great vessels and institution of normothermic cardiopulmonary bypass, the heart was emptied, and a nylon mesh sock with 96 bipolar (1.5-mm interpole spacing) button electrodes was positioned over the ventricles (five patients). The heart was filled with blood to ensure good electrode contact. The heart was warmed to 37°C, and data were collected during sinus rhythm and during sustained VT.

The sock then was removed. Transmural ventricular mapping was performed (eight patients) with color-coded plunge needle electrodes containing four bipolar pairs (0.5-mm interpole distance) at 4.0-mm intervals. Depending on the size and location of the infarct and the results of the preoperative electrophysiological study, 22–39 plunge needles (representing 88–156 transmural sites) were positioned in and around the infarct/aneurysm at 1–3-cm intervals. In three patients who had infarction of the interventricular septum, the right atrium was opened, and needle electrodes were inserted through the interventricular septum. Transmural and transseptal activation data were collected during sinus rhythm and during VT before ventriculotomy in seven patients. Sustained VT could be induced and mapped only after ventriculotomy in one patient.

Still-frame photographs from a high-resolution video system installed over the operating table were used to localize sock and needle electrode positions and to draw maps to scale using a predetermined coordinate system.33

Electrogram Analysis

Ventricular electrograms were sampled at 2 KHz with 12-bit precision and analyzed off-line using a MICROVAX II (Digital Equipment Corp.) computer with high-resolution graphic capabilities.38–40 Methods of electrogram analysis during VT in these patients have been detailed elsewhere.33 For analysis of sinus beats, a time window that encompassed the QRS complex and T wave was selected, and autocalibrated electrogroms were displayed. Computer-generated activation times were based on a peak criterion1,42 but could be reassigned by the operator. Data were rewindowed to reference activation times to the onset of QRS complex, the onset of the terminal 40 msec of the QRS complex, and the onset of the ST segment (Figure 1). The duration of the QRS complex was determined by two independent observers using surface ECG leads I, aVF, and V1 and V6. The observers reached a consensus decision when the calculated QRS durations differed. Conduction block was defined as either the absence of activation or an activation of >60 msec between electrodes, whereas adjacent electrodes in a less direct spatial path demonstrated sequential activation.33

Epicardial and Three-dimensional Isochronic Maps of Sinus Beats

Hand-drawn epicardial (five patients) and three-dimensional (eight patients) isochronic maps of ventricular activation during sinus rhythm were constructed in 10-msec increments. Epicardial activation times were displayed on a ventricular template drawn in anterior, left lateral, and posterior projections.

Transmural ventricular activation times from the needle electrodes were depicted on five schematized short-axis slices of the heart from base to apex. The wall thickness and shape depicted were representative of the hearts from patients studied in the operating room. The needle electrodes were assumed to be perpendicular to the site of insertion.

Activation of Arrhythmogenic Tissue During Sinus Rhythm

Mechanisms of VT were determined and defined as either macroreentry or focal by analysis of the three-dimensional ventricular isochronic maps.30–33 Reentry was defined as the mechanism when 1) the site of termination of one cycle was immediately adjacent to the initiation of the next and 2) there was evidence of continuous electrical activity reflected by the conduction velocity of the terminal activation wavefront of one cycle being comparable to the conduction velocity from the site of termination to the site of initiation of the next
TABLE 2. Transmural Ventricular Activation During Sinus Rhythm in Patients With Macroreentrant Ventricular Tachycardia

<table>
<thead>
<tr>
<th>Patient</th>
<th>Locus of MI</th>
<th>QRS duration (msec)</th>
<th>Total activation time (msec)</th>
<th>Duration of measured activation (msec) during VT</th>
<th>Activation of myocardium responsible for VT (msec)</th>
<th>Location of myocardium critical to VT activated during term QRS</th>
<th>Location of myocardium activated during term QRS</th>
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<tr>
<td>1</td>
<td>AMI</td>
<td>123</td>
<td>58</td>
<td>0</td>
<td>10</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2</td>
<td>AMI</td>
<td>113</td>
<td>64</td>
<td>2</td>
<td>22</td>
<td>Posterior RVFW, subepicardial, transmural, short-axis 3–4</td>
<td>NA</td>
</tr>
<tr>
<td>3*</td>
<td>IMI</td>
<td>156</td>
<td>126</td>
<td>20</td>
<td>40</td>
<td>Anterolateral LV, transmural, short-axis 2–4</td>
<td>Anterior LV, intramural, short-axis 4</td>
</tr>
<tr>
<td>5</td>
<td>AMI</td>
<td>130</td>
<td>104</td>
<td>20</td>
<td>17</td>
<td>Anterior LV, subepi/transmural, short-axis 2–4</td>
<td>Anterior LV, subepicardial, short-axis 3–4</td>
</tr>
<tr>
<td>6</td>
<td>AMI</td>
<td>156</td>
<td>130</td>
<td>24</td>
<td>31</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Mean±SD 134±20 96±34 13±12 24±12 73±24 72±13 8±10

MI, myocardial infarction; term QRS, terminal 40 msec of the QRS complex; VT, ventricular tachycardia; AMI, anterior myocardial infarction; IMI, inferior myocardial infarction; NA, not applicable; LV, left ventricle; RVFW, right ventricular free wall; subepi, subepicardium.

*No LV aneurysm.

beat. A focal mechanism was assigned when no electrical activity was detectable between the termination of one cycle and the initiation of the next cycle, despite multiple intervening electrodes. This definition does not exclude a microreentrant mechanism.33

The aim of this study was to determine when during sinus rhythm myocardial tissue responsible for sustained VT was activated. In instances of VT resulting from macroreentry, the components of the reentrant circuits were identified by analysis of transmural activation during VT. Sinus rhythm maps from these patients were then analyzed to determine when the components of the reentrant circuit were activated during sinus rhythm (Figure 1). Sinus rhythm maps from patients with VT resulting from focal mechanisms were analyzed to determine when the myocardium that was activated earliest during VT was activated during sinus rhythm.

Results

VT Resulting From Macroreentry

Five VTs resulted from macroreentry. Four patients had a prior anterior myocardial infarction. Each had a left ventricular aneurysm. The remaining patient had a healed inferior infarction but no aneurysm.

Results of transmural/transseptal mapping. Three-dimensional isochronic maps of transmural/transseptal ventricular activation obtained during sinus rhythm from a patient with an inferior myocardial infarction (patient 3) and a patient with an anterior infarction (patient 5) are shown in Figure 2. Both patients had VT due to macroreentry. Regions depicted in yellow indicate myocardium activated during the terminal 40 msec of the QRS complex. The macroreentrant circuits, defined previously by analysis of maps during VT,33 are highlighted in red. For patient 3, the myocardium responsible for VT was located in the interventricular septum. During sinus rhythm, activation of the components of the macroreentrant circuit began 40 msec after the onset of the QRS complex and was complete 59 msec later, 17 msec before the onset of the terminal QRS interval. Myocardium that activated during the last 40 msec of the QRS complex was spatially removed from the reentrant circuit. No activation was recorded during the ST segment.

In patient 5 (Figure 2, right), the myocardium responsible for VT was located in the anterior-apical portion of the left ventricle. During sinus rhythm, activation of the components of the macroreentrant circuit began 73 msec after the onset of the QRS complex, required 84 msec, and extended only 11 msec into the terminal 40 msec of the QRS complex. Although a large volume of tissue activated during the terminal QRS interval, only a portion of this was a component of the reentrant circuit.

The results of transmural/transseptal mapping during sinus rhythm from the five patients with macroreentrant VT are summarized in Table 2 and shown schematically in Figure 3. The mean duration of the QRS complex of sinus beats mapped was 134±20 msec. The total activation time measured with the plunge needles was 96±34 msec. Only 13±12 msec of the transmural activation measured occurred during the terminal QRS interval, and none occurred during the ST segment. During sinus rhythm, activation of the myocardium responsible for VT began 24±12 msec after the onset of the QRS and lasted 73±24 msec. Activation of this tissue began 72±13 msec before the onset of the terminal QRS interval and in two patients was completed 15–17 msec before the onset of the terminal QRS window. In the remaining three patients, activation of components of the macroreentrant circuits extended only 8±10 msec (range, 2–25 msec) into the terminal 40-msec QRS interval. Late intramural activation during the terminal QRS complex was detectable in sinus beats from four of the five patients. In three of these patients, most of this late activation was temporally and spatially removed from the macroreentrant circuits (Figure 2 and Table 2). In the remaining patient, none of the tissue activated...
late was critical to VT. Overall, during sinus rhythm, 92±10% of the electrograms from myocardium responsible for sustained monomorphic VT occurred before the terminal 40-msec interval of the QRS complex.

Results of epicardial mapping. Epicardial activation during sinus rhythm was recorded in three patients with VT resulting from macroreentry. The epicardial and transmural/transseptal maps from patient 6 are shown in Figure 4. Activation extended throughout the terminal QRS interval and 14 msec into the ST segment and was recorded over a large volume of tissue adjacent to the zone of infarction. Most of this late activation was spatially and temporally removed from the components of the macroreentrant circuit.

Data from all three patients with macroreentrant VT in whom epicardial mapping was performed during sinus rhythm are summarized in Table 3 and Figure 3. The mean QRS duration of the sinus beats mapped was 143±14 msec. The total activation time measured with the sock electrodes was 105±21 msec. Mapping confirmed that the epicardium was not critical to VT in two of the three patients. However, activation of the epicardium during sinus beats extended into the terminal 40 msec of the QRS complex in all three patients and into the ST segment in one patient.

VT Resulting From Focal Mechanisms

Five VTs resulted from focal mechanisms. Three patients had prior anterior myocardial infarctions, and two patients had inferior infarctions. Four patients had a left ventricular aneurysm. The focus of the VT was subendocardial in three patients, intramural in one patient, and subepicardial in one patient.

Results of transmural/transseptal mapping. Patient 3 had VTs due to both focal and macroreentrant mechanisms. Figure 5 shows the three-dimensional ventricular activation map obtained during sinus rhythm from patient 3. VT initiated focally in the subendocardium of the anterolateral wall of the left ventricle (red dot). During sinus rhythm, the myocardium responsible for VT activated 13 msec after the onset of the QRS complex and 103 msec before the onset of the terminal QRS interval. In contrast, myocardium activated during the terminal 40 msec of the QRS complex was localized to the posterior base of the right ventricle.

The results of transmural/transseptal mapping during sinus rhythm from the five patients with focal VTs are summarized in Table 4 and Figure 6. The mean duration of the QRS complex of sinus beats mapped was 140±26 msec. The total ventricular activation time that was measured with the plunge needle electrodes was 103±21 msec. Activation of the myocardium responsible for VT was completed 57±45 msec (range, 3–97 msec) after the onset of the QRS complex and 43±38 msec (range, 11–103 msec) before the onset of the terminal QRS interval. For the three patients with an associated aneurysm in whom mapping was performed before the ventriculotomy, activation of the myocardium critical to VT occurred 11–26 msec before the onset of the terminal 40 msec of the QRS complex. Mapping during sinus rhythm was performed after the ventriculotomy in patient 4. The myocardium responsible for VT activated 3 msec after the onset of the QRS complex and 55 msec before the beginning of the terminal QRS interval. Myocardium responsible for VT in patient 3 (no aneurysm) activated 13 msec after the onset of the QRS complex and 103 msec before the terminal QRS interval. For the group, ventricular activation measured with the plunge needles extended 19±4 msec into the terminal QRS complex but not into the ST segment. In each instance, the myocardium responsible for VT was both spatially and temporally removed from the myocardium that activated during the terminal QRS complex.

Results of epicardial mapping. Isochronic maps of epicardial activation during sinus rhythm were recorded from two patients with prior inferior infarction and from one patient with a prior anterior infarction in whom mapping was performed after an apical left ventriculotomy. Data are summarized in Table 5 and Figure 6. The
The mean duration of the QRS complex of the sinus beats mapped was 144±21 msec. The total activation time measured with the sock electrodes was 119±43 msec. All epicardial zones activated late were temporally and spatially removed from the VT focus.

Comparison of the QRS Complex During Sock and Needle Electrode Mapping

Both epicardial and transmural mapping was performed in five patients. The mean durations of the QRS complexes mapped with the sock electrodes and the
plunge needles were similar (145±18 versus 135±28 msec, p=NS). Concordance of both the QRS morphology and frontal plane axis was observed in only one patient for both mapping techniques.

**Signal-Averaged ECGs**

Signal-averaged ECGs were recorded 1±1 day (range, 1–3 days) before the electrophysiological study and 3±3 days (range, 1–10 days) before surgery. Late potentials were detected in the signal-averaged ECG from one of the three patients studied with the use of time-domain methods. Abnormal spectra were detected in the signal-averaged ECGs in seven of the eight patients. An interventricular conduction delay was present in the ECGs from four patients. The mean durations of the QRS complex of sinus beats recorded by the signal-averaged ECG and during intraoperative mapping were similar.

**Signal-averaged ECGs in patients with macroreentrant VT**. All macroreentrant pathways were located intramurally and activated 72±13 msec (range, 51–85 msec) before the onset of the terminal 40 msec of the QRS complex. Intramuraial activation extending 2–25 msec into the terminal QRS complex was observed in four of the five patients and was generated, in part, by myocardium critical to macroreentry in three patients (Table 6). In two patients, this late intramuraial activation was either absent or, when present, spatially removed from components of the reentrant circuit. Epicardial activation during the terminal QRS complex was observed in all three patients in whom epicardial mapping was performed but was only a component of the reentrant circuit in patient 6. Only the epicardium activated during the ST segment. Spectra of the signal-averaged ECGs were abnormal in all five patients. Late potentials were detected in the signal-averaged ECGs from only one of the three patients in whom analysis was also performed in the time domain.

**Signal-averaged ECGs in patients with focal VT**. Late intramuraial activation was observed in all five patients and late epicardial activation was observed in the three patients in whom mapping with the sock electrode was performed (Table 7). Late activation was always adjacent to tissue that had undergone infarction. Intramuraial activation extended 19±4 msec (range, 14–23 msec) and epicardial activation extended 0–21 msec into the terminal QRS complex. Only the epicardium activated during the ST segment. These regions, however, were temporally and spatially removed from the myocardium responsible for VT. Abnormal spectra were detected in the signal-averaged ECG from four of the five patients, including both patients with prior inferior myocardial infarctions. Late potentials were identified in the signal-averaged ECG from one of the two patients with focal VTs in whom analysis was performed in the time domain.

**Table 3. Epicardial Activation During Sinus Rhythm in Patients With Macroreentry Ventricular Tachycardia**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Locus of MI</th>
<th>QRS duration (msec)</th>
<th>Total activation time (msec)</th>
<th>Duration of measured activation (msec)</th>
<th>Location of epicardium activated during term QRS/ST segment</th>
<th>Epicardial critical for VT</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>AMI</td>
<td>135</td>
<td>88</td>
<td>86  2  0</td>
<td>Anterolateral apex LV</td>
<td>No</td>
</tr>
<tr>
<td>3*</td>
<td>IMI</td>
<td>135</td>
<td>99</td>
<td>78  21 0</td>
<td>Posterobasal/lateral LV</td>
<td>No†</td>
</tr>
<tr>
<td>6</td>
<td>AMI</td>
<td>160</td>
<td>129</td>
<td>75  40 14</td>
<td>Middle third anterior/ anterolateral LV</td>
<td>Yes</td>
</tr>
<tr>
<td>Mean±SD</td>
<td></td>
<td>143±24</td>
<td>105±21</td>
<td>80±6 21±19 5±8</td>
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<td></td>
</tr>
</tbody>
</table>

MI, myocardial infarction; term QRS, terminal 40 msec of the QRS complex; VT, ventricular tachycardia; AMI, anterior myocardial infarction; IMI, inferior myocardial infarction; LV, left ventricle.

*No LV aneurysm.
†Overlies subepicardium critical to reentrant pathway.
The signal-averaged ECG has been shown to prospectively identify patients convalescing from myocardial infarction who are prone to life-threatening ventricular arrhythmias. However, only 14–29% of patients recovering from myocardial infarction with late potentials detected by signal-averaged ECG analysis of the terminal QRS complex and/or ST segment will experience VT or sudden death within 1 year. This relatively low predictive accuracy underscores the need for continued refinements of methods for data analysis. Such refinements will depend, in part, on the extent to which ECG intervals interrogated contain signals generated by myocardium responsible for VT.

We tested the hypothesis that during sinus rhythm activation of the myocardium critical to sustained monomorphic VT complicating healed myocardial infarction contributes to ECG intervals in addition to the terminal QRS complex. A major feature of the research is three-dimensional, computer-assisted mapping of transmural and transseptal activation during both VT and sinus rhythm without the need to open the right or left ventricle. Results demonstrate that during sinus rhythm, 96±8% of the intramural signals generated by myocardium responsible for sustained VT are excluded from interrogation using current techniques that limit analysis of the signal-averaged ECG to the terminal QRS complex and/or ST segment. Furthermore, electrograms during the ST segment represent late activation of epicardial sites adjacent to zones of infarction that are temporally and spatially remote from tissue critical to VT. These new observations are pertinent to the pathophysiological basis of late potentials and to the development of improved methods of analyzing the signal-averaged ECG.

**Pathophysiological Significance of Late Potentials**

Late potentials correspond to delayed and fragmented myocardial activation that result from structural changes occurring during the course of infarct healing. They have been observed in epicardial and endocardial electrograms recorded from experimental animals and from patients with ventricular arrhythmias and have traditionally been thought to provide the substrate for reentry. Delayed myocardial activation during sinus rhythm has been correlated with the site of earliest activation during VT and relied on to guide arrhythmia surgery. Aneurysmectomy and/or subendocardial resection that abolishes VT has been associated with a reduction in the incidence of late potentials detected in signal-averaged ECGs recorded after surgery. Based on these published studies, 85–100% of patients who remain inducible into sustained VT after surgery have late potentials detectable in signal-averaged ECGs recorded after surgery. Approximately 90% of the patients in whom results of signal-averaged ECG analysis are normal after surgery have no inducible VT.

Other evidence, however, suggests that late potentials are not specific for arrhythmogenic tissue. After successful arrhythmia surgery for VT, as many as 56% of patients without inducible VT after surgery continue to have abnormalities detectable in signal-averaged ECGs. Furthermore, results of studies in humans and in experimental animals indicate that...
TABLE 4. Transmural Ventricular Activation During Sinus Rhythm in Patients With Focal Ventricular Tachycardia

<table>
<thead>
<tr>
<th>Patient</th>
<th>Locus of MI</th>
<th>QRS duration (msec)</th>
<th>Total activation (msec)</th>
<th>Duration of measured activation (msec) within term</th>
<th>Activation (msec) of myocardium responsible for VT referenced to onset of:</th>
<th>Location of myocardium responsible for VT</th>
<th>Location of myocardium activated during term</th>
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<tbody>
<tr>
<td>3*</td>
<td>IMI</td>
<td>156</td>
<td>126</td>
<td>20</td>
<td>13 -103</td>
<td>Anterolateral LV, subendocardial, short-axis 4</td>
<td>Posterior RV, transmural, short-axis 2</td>
</tr>
<tr>
<td>4†</td>
<td>AMI</td>
<td>98</td>
<td>71</td>
<td>23</td>
<td>3 -55</td>
<td>Posterior IVS, RV side, short-axis 3</td>
<td>Anterior LV/IVS, subepicardial-intramural, short-axis 1</td>
</tr>
<tr>
<td>5</td>
<td>AMI</td>
<td>130</td>
<td>104</td>
<td>20</td>
<td>79 -11</td>
<td>Anteroapical LV, intramural, short-axis 5</td>
<td>Anterior-anterolateral LV, transmural, short-axis 2-4</td>
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<tr>
<td>7</td>
<td>AMI</td>
<td>163</td>
<td>116</td>
<td>16</td>
<td>97 -26</td>
<td>Anterior LV, subepicardial, short-axis 4</td>
<td>Posterior to lateral LV, transmural-subepicardial, short-axis 2-4</td>
</tr>
<tr>
<td>8</td>
<td>IMI</td>
<td>152</td>
<td>99</td>
<td>14</td>
<td>93 -19</td>
<td>Posterobasal IVS, LV side, short-axis 1</td>
<td>Posterior IVS/LFVW, transmural-subepicardial, short-axis 1-2</td>
</tr>
</tbody>
</table>

Mean±SD 140±26 103±21 19±4 57±45 -43±38

MI, myocardial infarction; term QRS, terminal 40 msec of the QRS complex; VT, ventricular tachycardia; IMI, inferior myocardial infarction; AMI, anterior myocardial infarction; LV, left ventricle; RV, right ventricle; IVS, intraventricular septum; LVFW, left ventricular free wall.

*No LV aneurysm. †Mapping performed after ventriculotomy.

delayed activation measured at endocardial and epicardial sites often does not correlate with myocardial tissue activated earliest during VT.

In the present study, detailed analysis of three-dimensional activation maps of sinus beats demonstrated intramural activation during the terminal 40 msec of the QRS complex in seven of the eight patients studied, a finding that was independent of the locus of the infarction. This late activation was generated by myocardium spatially and temporally removed from the myocardium critical for six (five focal VTs and one macroreentrant VT) of the nine VTs mapped in these seven patients. Activation during the terminal 40 msec of the QRS complex of sinus beats was generated by some of the myocardium critical to the remaining three VTs due to macroreentry as well as by myocardium spatially dissociated from the macroreentrant circuit. No late activity was detected in the heart from patient 1 with VT due to a macroreentrant mechanism. Epicardial activation during the terminal QRS complex of sinus beats was detected in each patient from the region of the ventricle that had undergone infarction but was a component of the reentrant circuit in only one patient. Ventricular activation during the ST segment, when detected, arose from the epicardium but was remote from the tissue responsible for VT. These findings

![Figure 6](http://circ.ahajournals.org/)

**Figure 6.** Ventricular activation times recorded during sinus rhythm from the five patients with focal ventricular tachycardia (VT) relative to the QRS onset, the onset of the terminal 40-msec interval of the QRS complex, and the onset of the ST segment. The mean duration of sinus beats was 140±26 msec during transmural mapping and 144±21 msec during epicardial mapping. Top panel: Mean transmural activation time measured with the plunge needles was 103±21 msec (open bar). Only 19±4 msec of this activation occurred during the terminal QRS complex and none occurred during the ST segment. The activation of the myocardium responsible for VT (solid shading) occurred 57±45 msec after the onset of the QRS complex and 43±38 msec before the onset of the terminal QRS interval. Bottom panel: Mean epicardial activation time measured with the sock electrode was 119±43 msec. Although late epicardial activation was detected during the terminal QRS complex and ST segment, these regions were temporally and spatially removed from the site of origin of VT.


**TABLE 5. Epicardial Activation During Sinus Rhythm in Patients With Focal Ventricular Tachycardia**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Locus of MI</th>
<th>QRS duration (msec)</th>
<th>Total activation time (msec)</th>
<th>Duration of measured activation (msec) Before term QRS</th>
<th>Within term QRS</th>
<th>Within ST segment</th>
<th>Location of epicardium activated during term QRS</th>
<th>Epicardium critical for VT</th>
</tr>
</thead>
<tbody>
<tr>
<td>3*</td>
<td>IMI</td>
<td>135</td>
<td>99</td>
<td>78</td>
<td>21</td>
<td>0</td>
<td>Posterobasal/lateral LV</td>
<td>No</td>
</tr>
<tr>
<td>4†</td>
<td>AMI</td>
<td>128</td>
<td>89</td>
<td>0</td>
<td>0</td>
<td>89‡</td>
<td>Entire mapped epicardium</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>IMI</td>
<td>168</td>
<td>149</td>
<td>83</td>
<td>21</td>
<td>26</td>
<td>Posterobasal RV, basal LV</td>
<td>No</td>
</tr>
<tr>
<td>Mean±SD</td>
<td></td>
<td>144±21</td>
<td>119±43</td>
<td>54±47</td>
<td>14±12</td>
<td>38±46</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MI, myocardial infarction; term QRS, terminal 40 msec of the QRS complex; VT, ventricular tachycardia; IMI, inferior myocardial infarction; AMI, anterior myocardial infarction; LV, left ventricle; RV, right ventricle.

*No associated LV aneurysm.
†Mapped after ventriculotomy; no signals recorded over apical third LV/RV.
‡Activation began 194 msec after onset of QRS.

Demonstrate that delayed activation is frequently a nonspecific measure of slowed conduction but not synonymous with myocardial tissue critical to sustained monomorphic VT.

Signal-averaged ECGs were recorded from all eight patients studied. Late potentials were detected in ECGs from one of the three patients without bundle branch block. Abnormal spectra were detected in the signal-averaged ECGs from seven of the eight patients. Abnormalities in the signal-averaged ECGs correlated with late activation in six patients having a total of seven VT morphologies. The late activation was generated by myocardium spatially and temporally remote to that responsible for VT in five of the seven VTs, a finding independent of the mechanism of the tachycardia. Overall, current methods of signal-averaged ECG analysis that limit interrogation to the terminal QRS/ST segment exclude detection of >95% of the signals generated by myocardium responsible for sustained monomorphic VT.

**Implications for Refining Methods of Analysis**

The impetus behind continued refinements in methods of data analysis is to improve the positive-predictive accuracy of the signal-averaged ECG for identifying patients recovering from myocardial infarction at high risk of developing life-threatening ventricular arrhythmias. Approaches that enable direct analysis of signals generated by myocardium critical to VT may improve the diagnostic power of the signal-averaged ECG. Results of this study demonstrate that during sinus rhythm activation of all the arrhythmogenic tissue occurred before the onset of the terminal 40 msec of the QRS complex in all patients with focal VT and in two of the five patients with macroreentrant VT. In the other three patients with macroreentrant VT, only a portion of the reentrant circuit was activated during the terminal 40 msec of the QRS complex of sinus beats. These results provide an objective basis to expand the ECG interval analyzed to include more of the cardiac cycle.

**TABLE 6. Comparison of Results of Three-dimensional Isochronic Mapping During Sinus Rhythm to the Results of Signal-Averaged ECG Analysis in Patients With Macroreentrant Ventricular Tachycardia**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Locus of MI</th>
<th>QRS duration (msec)</th>
<th>Duration of measured activation (msec) within term QRS</th>
<th>Activation of myocardium responsible for VT during term QRS</th>
<th>Location of myocardium activated during term QRS</th>
<th>Location of myocardium critical to VT activated during term QRS</th>
<th>Signal-averaged ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AMI</td>
<td>123</td>
<td>0</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>AMI</td>
<td>113</td>
<td>2</td>
<td>2</td>
<td>Anterior LV, subepicardial, short-axis 3-4</td>
<td>Anterior LV, subepicardial, short-axis 3-4</td>
<td>108</td>
</tr>
<tr>
<td>3*</td>
<td>IMI</td>
<td>156</td>
<td>20</td>
<td>0</td>
<td>Posterior RVFW, transmural, short-axis 2</td>
<td>NA</td>
<td>152</td>
</tr>
<tr>
<td>5</td>
<td>AMI</td>
<td>130</td>
<td>20</td>
<td>11</td>
<td>Anterolateral LV, transmural, short-axis 2-4</td>
<td>Anterior LV, intramural, short-axis 4</td>
<td>176</td>
</tr>
<tr>
<td>6</td>
<td>AMI</td>
<td>156</td>
<td>25</td>
<td>25</td>
<td>Anterior LV, subepi/transmural, short-axis 2-4</td>
<td>Anterior LV, subepicardial, short-axis 3-4</td>
<td>100</td>
</tr>
<tr>
<td>Mean±SD</td>
<td></td>
<td>134±20</td>
<td>13±12</td>
<td>8±10</td>
<td></td>
<td></td>
<td>126±36</td>
</tr>
</tbody>
</table>

MI, myocardial infarction; VT, ventricular tachycardia; term QRS, terminal 40 msec of the QRS complex; AMI, anterior myocardial infarction; IMI, inferior myocardial infarction; NA, not applicable; LV, left ventricle; RVFW, right ventricular free-wall; subepi, subepicardium; +, abnormal signal-averaged ECG; ND, not done.

*No LV aneurysm.
TABLE 7. Comparison of Results of Three-dimensional Isochronic Mapping During Sinus Rhythm to the Results of Signal-Averaged ECG Analysis in Patients With Focal Ventricular Tachycardia

<table>
<thead>
<tr>
<th>Patient</th>
<th>Locus of MI</th>
<th>QRS duration (msec)</th>
<th>Duration of measured activation (msec) within term QRS</th>
<th>Activation of myocardium (msec) responsible for VT referenced to onset term QRS</th>
<th>Location of myocardium responsible for VT</th>
<th>Location of myocardium activated during term QRS</th>
<th>Signal-averaged ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>3*</td>
<td>IMI</td>
<td>156</td>
<td>20</td>
<td>-103</td>
<td>Anterolateral LV, subendocardial, short-axis 4</td>
<td>Posterior RV, transmural, short-axis 2</td>
<td>152</td>
</tr>
<tr>
<td>4†</td>
<td>AMI</td>
<td>98</td>
<td>23</td>
<td>-55</td>
<td>Posterior IVS, RV side, short-axis 3</td>
<td>Anterior LV/IVS, subepicardial-intramural, short-axis 1</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>AMI</td>
<td>130</td>
<td>20</td>
<td>-11</td>
<td>Anterolateral LV, intramural, short-axis 5</td>
<td>Anterolateral LV, transmural, short-axis 2–4</td>
<td>176</td>
</tr>
<tr>
<td>7</td>
<td>AMI</td>
<td>163</td>
<td>16</td>
<td>-26</td>
<td>Anterior LV, subepicardial, short-axis 4</td>
<td>Posterior to lateral LV, transmural-subepicardial, short-axis 2–4</td>
<td>112</td>
</tr>
<tr>
<td>8</td>
<td>IMI</td>
<td>152</td>
<td>14</td>
<td>-19</td>
<td>Posterobasal IVS, LV side, short-axis 1</td>
<td>Posterior IVS/LVFW, transmural-subepicardial, short-axis 1–2</td>
<td>152</td>
</tr>
</tbody>
</table>

Mean±SD 140±26 19±4 43±38 136±35

AMI, myocardial infarction; VT, ventricular tachycardia; term QRS, terminal 40 msec of the QRS complex; IMI, inferior myocardial infarction; AMI, anterior myocardial infarction; LV, left ventricle; IVS, intraventricular septum; RV, right ventricle; LVFW, left ventricular free-wall; ND, not done; +, abnormal signal-averaged ECG; −, normal signal-averaged ECG.

*No LV aneurysm.
†Mapping performed after ventriculotomy.

In support of this hypothesis, we have demonstrated previously undefined alterations in the magnitudes, phase, and spatial distributions of 1–7-Hz, 13–56-Hz, and 70–128-Hz frequencies in the entire cardiac cycle of signal-averaged Frank ECGs from patients with sustained VT.56,59 These new distinguishing spectral, temporal, and spatial features are excluded from detection by available methods of analysis that limit the passband, record data with an uncorrected lead system, or restrict interrogation to selected portions of the cardiac cycle. The extent to which these additional distinguishing features are generated by myocardial tissue critical to VT has not yet been determined.

Study Limitations

Signal-averaged ECGs were recorded before intraoperative mapping. The clinical course and medical management of each patient, however, remained stable during the 3±3 days between procedures. Epicardial and transmural/transseptal mapping was performed sequentially and was associated with some changes in the duration and morphology of the QRS complex of sinus beats. Rotation/displacement of the heart during sock and needle electrode placements or trauma to the conduction system from plunge needle insertion may have contributed to these changes. The mean durations of the QRS complexes measured during both mapping procedures were, however, comparable. Finally, the plunge needle electrodes were concentrated around regions of infarction and were not evenly distributed throughout the left and right ventricles. Accordingly, intramural sites remote from the infarction may have activated late and were undetected. The primary aim of the study, however, was to determine when during sinus rhythm myocardium responsible for VT is activated. It was not our intent to detect all regions of the heart activated during the terminal QRS complex or ST segment.

Summary

These results demonstrate that during sinus rhythm, signals generated by myocardium responsible for sustained monomorphic VT in patients with healed myocardial infarction are excluded from detection with the use of current signal-averaged ECG techniques that limit analysis to the terminal QRS complex and/or ST segment. In most instances, activation of the tissue critical to VT is completed before the onset of the terminal 40 msec of the QRS complex and does not contribute to the delayed ventricular activation detected during this ECG interval or during the ST segment. These findings provide a firm pathophysiological basis to modify the ECG intervals currently analyzed to include more of the cardiac cycle. Further studies are required to determine whether direct analysis of signals generated by the tissue responsible for VT will improve the diagnostic power of the signal-averaged ECG.

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