Programmed Electrical Stimulation at Potential Ventricular Reentry Circuit Sites
Comparison of Observations in Humans With Predictions From Computer Simulations

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The purpose of this study was to define specific types of resetting responses to programmed electrical stimulation during human ventricular tachycardia and to use computer simulations of reentry circuits to assess the possible mechanisms and pacing site location relative to the reentry circuit for each type of response. The effects of scanning single stimuli at 35 left ventricular endocardial sites during sustained monomorphic ventricular tachycardia in 12 patients were studied. In considering alterations in QRS configuration and the delay between the stimulus and the advanced QRS, we identified three types of resetting responses to scanning stimuli consistent with stimulation at sites in or near the reentry circuit at 12 abnormal endocardial sites in eight patients. Type 1: all capturing stimuli were followed after a delay by early QRS complexes that had the same configuration as the tachycardia complexes. Type 2: late stimuli reset tachycardia as in type 1 but early stimuli reset the tachycardia after altering the QRS configuration. Type 3: late stimuli reset tachycardia as in type 1, but early stimuli advanced tachycardia with a short stimulus to QRS delay without altering the configuration of the advanced QRS. In the simulations, premature depolarization of sites in the circuit produced orthodromic and antidromic wavefronts. The orthodromic wavefront propagated through the circuit and exited the circuit at the same site as did the previous tachycardia wavefronts and advanced the tachycardia without altering the configuration of the advanced QRS. The antidromic wavefront of relatively late stimuli was confined within or near the circuit by collision with the orthodromic wavefront of the preceding tachycardia beat and failed to alter ventricular activation distant from the circuit. Therefore, the QRS configuration after the stimulus was unchanged. A type 1 response occurred when all capturing stimuli produced this effect. However, with increasing stimulus prematurity, the antidromic wavefront propagated farther before colliding with an orthodromic wavefront, and under some conditions, it exited the circuit from a site other than the original circuit "exit," and altered the ventricular activation sequence distant from the circuit and, therefore, the QRS configuration, producing a type 2 pattern. The type 3 pattern occurred when the antidromic wavefront of early premature beats captured the original circuit exit. The effect of a stimulus was dependent on the stimulus prematurity, the relative conduction times from the stimulation site to the potential sites of "exit" from the circuit, and the timing of the excitable gap at the stimulation site. In the figure-eight reentry circuit simulations, the type 1 response tended to occur during stimulation within, the type 2 response near the entrance to, and the type 3 response outside but near the exit from the slowly conducting central common pathway. Type 2 responses could also occur with stimulation at a site that was close to but not within the circuit. The recognition of specific responses characteristic of programmed stimulation at reentry circuit sites is feasible in humans and may improve ventricular reentry circuit localization by catheter techniques. However, at some circuit sites, stimulation may alter ventricular activation distant from the circuit and falsely suggest that the site is not within the circuit. The potential variability of electrophysiologic and spatial factors that influence the response to programmed stimulation may limit precise determination of the stimulation site location relative to critical areas in the circuit. (Circulation 1989;80:793–806)
Success of catheter ablation techniques for treatment of reentrant ventricular tachycardia is likely to depend on localization of critical sites in the reentry circuit. Evaluating the effect of electrical stimuli on ventricular tachycardia during catheter mapping has been suggested as a possible method of determining whether or not the stimulation site is participating in the tachycardia circuit.\(^1\)\(^-\)\(^4\) We hypothesized that electrical stimulation during ventricular tachycardia would produce specific patterns of response while resetting the tachycardia, depending on the location of the stimulation site relative to the reentry circuit, the stimulus timing, and the electrophysiologic characteristics of the circuit. The purpose of this study was to determine whether or not specific types of resetting responses can be identified during catheter endocardial mapping studies in humans. Computer simulations of programmed stimulation within and near reentry circuits were used to assess the possible mechanisms of the responses observed in humans and to evaluate the potential relation between the type of response and the pacing site location relative to the circuit.

**Methods**

**Endocardial Stimulation in Patients**

Studies were performed in 12 consecutive patients undergoing evaluation for recurrent sustained monomorphic ventricular tachycardia due to prior myocardial infarction. Patient characteristics are shown in Table 1. After informed consent was obtained, electrode catheters were inserted into a femoral artery and one or more femoral veins and positioned in the left ventricle, at the right ventricular apex, and at the His bundle. Three to five surface electrocardiogram leads (I, aV\(_5\), V\(_1\), and V\(_3\)) were recorded simultaneously with endocardial electrograms at a paper speed of 100 mm/sec (VR-16, Electronics for Medicine, Pleasantville, New York). Endocardial recordings were filtered from 30 to 500 Hz. Endocardial mapping was performed with 6F quadripolar catheters having a 1-cm interelectrode spacing. During sinus rhythm, areas of potentially abnormal conduction as indicated by the presence of fractionated electrograms, and evidence of slow conduction during ventricular pacing\(^6\) were identified. The paced QRS and tachycardia QRS configurations were compared. Ventricular tachycardia was then initiated by programmed electrical stimulation. During ventricular tachycardia, programmed electrical stimulation was performed at selected sites, concentrating on those sites suspected of participating in the tachycardia circuit based on electrograms and pace mapping.\(^1\)\(^,\)\(^2\)\(^,\)\(^5\) The cardiac cycle was scanned in 10-msec decrements with bipolar electrical stimuli that had a pulse width of 2 msec and an amplitude of 10 ma (Bloom Associates, Reading, Pennsylvania). Programmed stimulation was performed at 35 left ventricular sites during 19 distinct, sustained monomorphic ventricular tachycardias (Table 2).

**Computer Simulations**

Computer simulations of a simple, protected reentry circuit and a figure-eight type of reentry circuit\(^6\) were performed. In the simple circuit (Figure 1, Panel A), reentry occurs around a central area of block. The circuit is relatively protected from the surrounding myocardium by two arcs of conduction block that allow excitation wavefronts to enter and exit the circuit from two possible areas (at sites 1 and 4) as has been suggested by Josephson and coworkers.\(^7\)\(^,\)\(^8\) In the figure-eight circuit (Figure 1, Panel B), two wavefronts of excitation circulate around two arcs of conduction block sharing a common central path of slow conduction.\(^6\) For the purposes of these studies, the position of the reentry circuit and the areas of conduction block that define the reentrant paths are fixed. The length of the circuit is determined by specifying the diameter of each circular path. Conduction through the scar in which the circuit is contained is assumed to produce low-amplitude electrical activity that is not detectable from the surface electrocardiogram.\(^5\)\(^-\)\(^9\)\(^-\)\(^11\) The QRS complex then occurs when the excitation wavefront emerges from the circuit at site 1 or site 4 and propagates out to the more normal myocardium. The mean conduction velocities and absolute refractory periods that exist during stable tachycardia are specified for segments in the circuit. During stable tachycardia, the conduction velocity through normal tissue was 1 m/sec.\(^10\) In the slowest segment of the

**TABLE 1. Patient Characteristics**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr) and sex</th>
<th>Heart disease</th>
<th>Antiarrhythmic drug at study</th>
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<tr>
<td>1</td>
<td>75 F</td>
<td>Inf MI</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>2</td>
<td>63 M</td>
<td>Inf MI</td>
<td>Sotalol</td>
</tr>
<tr>
<td>3</td>
<td>54 M</td>
<td>Ant MI</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>4</td>
<td>50 M</td>
<td>Ant MI</td>
<td>...</td>
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<tr>
<td>5</td>
<td>63 F</td>
<td>Ant MI</td>
<td>Amiodarone + Mexiletene</td>
</tr>
<tr>
<td>6</td>
<td>56 M</td>
<td>Inf MI</td>
<td>...</td>
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<tr>
<td>7</td>
<td>55 M</td>
<td>Ant MI</td>
<td>Procaimidine</td>
</tr>
<tr>
<td>8</td>
<td>71 M</td>
<td>Ant MI</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>9</td>
<td>48 M</td>
<td>Ant MI</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>10</td>
<td>62 M</td>
<td>Inf MI</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>11</td>
<td>71 M</td>
<td>Ant + Post MI</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>12</td>
<td>63 M</td>
<td>Ant MI</td>
<td>Propafenone</td>
</tr>
</tbody>
</table>

Ant MI, anterior myocardial infarction; Inf MI, inferior myocardial infarction; Post Inf, posterior myocardial infarction.
TABLE 2. Programmed Electrical Stimulation Results in Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>VT configurations evaluated</th>
<th>VT cycle length (msec)</th>
<th>Sites paced (n)</th>
<th>Response type</th>
<th>Reset only with QRS alteration</th>
<th>No reset</th>
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<td>1</td>
<td>510</td>
<td>1</td>
<td>...</td>
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</tr>
<tr>
<td>2</td>
<td>2</td>
<td>375, 380</td>
<td>4</td>
<td>1 2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>440</td>
<td>1</td>
<td>1 ...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>260</td>
<td>3</td>
<td>1 ...</td>
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<td>1</td>
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<td>7</td>
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<td>...</td>
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<tr>
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<td>380, 650</td>
<td>2</td>
<td>... 1</td>
<td>...</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>4</td>
<td>360, 460, 520, 540</td>
<td>5</td>
<td>... 1</td>
<td>4</td>
<td>0</td>
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<td>450</td>
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<td>... ... 2</td>
<td>2</td>
<td>...</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>35</td>
<td>4 7 1</td>
<td>13</td>
<td>10</td>
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</tr>
</tbody>
</table>

VT, ventricular tachycardia.

circuit (typically from site 5 to site 1 in the figure-eight model), basal conduction velocities ranging from 0.05 to 0.4 m/sec were specified. In faster areas in the scar, conduction velocities of up to 0.8 m/sec were used. Changes from basal conduction velocities and refractory periods are modeled as exponential functions of the diastolic interval (see Appendix).

Orthodromic wavefront propagation in both circuit types is illustrated in Figure 1. Sites 8–13 are located in normal tissue distant from the circuit (not shown). Site 14 is located adjacent to the entrance to an area of slow conduction in the circuit but is not in the circuit itself. The computer simulation uses an iterative program written in BASIC. For each 10-msec period of tachycardia, the status of each of six sites in the circuit (sites 1–6 in Figures 1 and 2) and site 14 outside the circuit is evaluated. The activation times, direction of activation (orthodromic, antidromic, or from a stimulus), and recovery times are determined. A sample of the data generated is shown in Table 3.

A Normal

B Normal

QRS onset

Scar

Figure 1. Schematics of the protected, simple reentry circuit and the figure-eight reentry circuit in Panels A and B, an area of scar is present inferior to and to the right of the dashed line. Areas of fixed conduction block are indicated by the hatched rectangles. Solid arrows indicate propagation of excitation wavefronts through the circuits. Sites for which activation times were calculated and for which programmed stimulation was simulated are indicated as 1–6 and 14. Panel A: The protected, simple reentry circuit. Reentry occurs around a central area of conduction block (hatched ellipse). Arcs of block (hatched rectangles) allow wavefronts to enter and exit the circuit only at site 1 and site 4. The onset of the QRS complex (vertical line) occurs when the excitation wave exits the circuit at site 1 and propagates to the myocardium outside the scar. Depending on the circuit characteristics, collision of wavefronts from within the circuit with the wavefront propagation from site 1 to site 14 occurs either within (near site 4) or outside the circuit (near site 14). Panel B: The figure-eight reentry circuit. Two excitation wavefronts propagate from site 1 to site 4 around two lines of block. Propagation from site 1 to site 14 in the edge of the scar is associated with activation of myocardium outside the scar. Propagation from sites 1–4 is confined within the scar.
TABLE 3. Computer Simulation Output

<table>
<thead>
<tr>
<th>Cycle</th>
<th>1 Expected</th>
<th>Site</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>14</th>
<th>Fusion</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Activation time (sec)</td>
<td>000</td>
<td>000</td>
<td>0.035</td>
<td>0.070</td>
<td>0.094</td>
<td>0.143</td>
<td>0.273</td>
<td>0.065</td>
<td>0</td>
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<tr>
<td></td>
<td>Direction</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2</td>
<td>Activation time (sec)</td>
<td>0.404</td>
<td>0.404</td>
<td>0.439</td>
<td>0.474</td>
<td>0.498</td>
<td>0.508</td>
<td>0.660</td>
<td>0.469</td>
<td>0</td>
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<tr>
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<td>Direction</td>
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<td>1</td>
<td>1</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Activation time (sec)</td>
<td>0.808</td>
<td>0.803</td>
<td>0.835</td>
<td>0.871</td>
<td>0.902</td>
<td>0.912</td>
<td>1.064</td>
<td>0.873</td>
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<tr>
<td></td>
<td>Direction</td>
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<td>1</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Activation time (sec)</td>
<td>1.207</td>
<td>1.183</td>
<td>1.239</td>
<td>1.256</td>
<td>1.276</td>
<td>1.333</td>
<td>1.485</td>
<td>1.277</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Direction</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Computer-generated data used to produce Figure 5 tracing in Panel A are shown. Activation time at sites 1–6 and 14 are shown. Calculations start at time 0, which is activation of site 1 at the exit from the common path of slow conduction in the figure-eight circuit. Beneath each activation time, the direction from which the wavefront arrived to activate the site is coded as 1 is orthodromic, 2 is antidromic, 3 is direct activation by a stimulus at that site, and 5 is activation of site 4 by the wavefront from site 14. The third column from the left shows the expected activation time at the “exit” from the circuit if there is no change from the basal conditions, that is, if the tachycardia circuit is not perturbed by a stimulus. The last column on the right (fusion) shows the calculated antidromic activation of the arc from site 14 to site 1 outside the scar. In this circuit, the orthodromic wavefront from site 1 to 14 arrives at site 4 before the orthodromic wavefront from site 3 (at site 4, direction=3). During the second cycle a stimulus at time 0.508 second captures site 5 (direction=3). The following activation of site 1 is advanced, occurring at 0.803 second rather than the expected time of 0.808 second. Because of decremental conduction properties in this circuit and shortening of refractoriness in some areas after the premature stimulus, conduction time through the slow area of the circuit shortened during cycle 2, and the fourth QRS is also early at 1.183 second. There is no alteration of the ventricular activation sequence distant from the circuit (fusion=0). See text for discussion.

When a wavefront exited the scar from site 14 and propagated to myocardium outside the scar, the sequence of ventricular activation distant from the circuit was altered, and therefore, by definition, the surface electrocardiogram “QRS” configuration was altered. As an index of the alteration in distant ventricular activation due to fusion of antidromic and orthodromic wavefronts, the fraction of the path from site 1 to site 14 that was activated antidromically (by a wavefront propagating from site 14 toward site 1) was calculated (Table 3). Circuit sizes and conduction velocities were specified to produce ventricular tachycardias with cycle lengths ranging from 280 to 520 msec, and a range of circuits was evaluated. At sites 1–6 and 14, programmed electrical stimulation with scanning premature stimuli was simulated. The cardiac cycle was scanned with a single stimulus that depolarized the site when the site had recovered from its prior depolarization. Stimuli scanned 1 cardiac cycle in 10–20-msec decrements. After each stimulus, the tachycardia was returned to the basal state by restarting the simulation.

Results

Observations in Patients

During ventricular tachycardia, four types of response patterns to scanning single stimuli were identified. These could be distinguished from analysis of the surface electrocardiogram QRS configuration and timing of the beats after the stimuli.

Type 1. Resetting without QRS alteration. In the type 1 response, all capturing stimuli that reset the tachycardia have the same effect. The tachycardia is reset with little or no detectable alteration of the QRS configuration of the beats after the stimulus and with a delay between the stimulus and the advanced tachycardia beat. An example of this pattern of response in a patient is shown in Figure 2. Sustained monomorphic ventricular tachycardia with a cycle length of 440 msec is present. In Panel A, a stimulus at left ventricular site 1–2, 30 msec after the onset of the left ventricular electrogram, does not change the tachycardia QRS configuration. However, the subsequent beat is advanced after a substantial delay of 360 msec between the stimulus and the advanced beat. With increasingly premature stimuli (Figure 2, Panel B), the response is similar. The tachycardia is reset without alteration of the QRS configuration. This response was observed during stimulation at four sites in four patients (Table 2).

Type 2. Resetting with variable QRS alteration. In the type 2 response, late stimuli advance the tachycardia as in the type 1 response without altering the QRS configuration. However, earlier stimuli are followed by a change in the QRS configuration and a shorter interval between the stimulus and the altered QRS. The subsequent QRS is advanced without a change in QRS configuration. An example of this pattern of response in a patient is shown in Figure 3. This pattern of response was observed during stimulation at seven sites in five patients (Table 2).

Type 3. The stimulus to QRS delay decreases with early stimuli. In the type 3 response, late stimuli reset the tachycardia as in response type 1, with a relatively long delay between the stimulus and the advanced beat and no change in the QRS configuration. However, sufficiently early stimuli advance the tachycardia after a markedly shorter delay between the stimulus and advanced beat. The advanced beat still has a QRS configuration similar to that of the tachycardia beats. This is an espe-
FIGURE 2. Tracings of type 1 pattern of response in a patient with recurrent ventricular tachycardia. From the top of Panels A and B are 50-msec time lines, surface electrocardiographic leads I, aVF, and V1, and intracardiac recordings from the right ventricle (RV), stimulus marker channel (LVs), and the proximal electrode pair of the left ventricular catheter (pLV1-2). Sustained monomorphic ventricular tachycardia at a cycle length of 440 msec is present. In Panel A, a stimulus (S) 30 msec after the ventricular electrogram fails to alter the configuration of the QRS immediately after the stimulus. The subsequent QRS is advanced (from 440 to 380 msec) and also has the same configuration as the tachycardia beats. Slight changes in QRS configuration due to superimposition of dissociated P waves are evident in the second and fourth QRS complexes. The delay from the stimulus to the onset of the advanced left ventricular electrogram is 360 msec. In Panel B, a stimulus (S) 30 msec earlier than in Panel A (LV−S=0 msec) is shown. Tachycardia is advanced from 440 to 390 msec after a delay between the stimulus and advanced QRS that has increased to 400 msec. These findings are consistent with further slowing of conduction in the circuit with earlier stimuli.

Computer Simulations

In reentry circuit simulations, the effect of a stimulus on the tachycardia depended on the stimulus prematurity, the location of the stimulus site, and the characteristics of the reentry circuit. Scanning reentry circuit sites with single stimuli was able to reproduce the types 1, 2, and 3 responses observed in the patient studies. Similar results were obtained with both the figure-eight and the simple, protected reentry circuits and are illustrated using the figure-eight circuit in the following examples.

Resetting without QRS alteration (type 1 response). In the computer simulations, tachycardia resetting without alteration of the QRS configuration after the stimulus occurred when the stimulated wavefronts exited from the circuit only from the same exit site as the tachycardia beats. That is, the antidromic wavefronts were confined in or near the circuit. This is illustrated in Figure 5 during stimulation at site 5, within the common central path of slow conduction in the figure-eight circuit. A portion of the computer-generated data from which Figure 5 was constructed is shown in Table 3. Capturing stimuli produce excitation wavefronts that propagate in both the orthodromic and antidromic striking occurrence because the delay between the stimulus and advanced QRS complex usually increases with increasing stimulus prematurity. This pattern of response was observed and reproduced in one patient and is shown in Figure 4.

Resetting with QRS alteration after all capturing stimuli. Resetting with QRS alteration after all capturing stimuli is a familiar pattern of resetting observed during pacing at the right ventricular apex, distant from the presumed tachycardia circuit. All capturing stimuli are followed by a paced QRS complex, the configuration of which is different from that of the tachycardia and which may reflect some degree of fusion between the paced QRS and the tachycardia QRS, depending on stimulus prematurity. This pattern of resetting was observed at 13 sites in six patients (Table 2) and has been extensively discussed elsewhere.
mic directions. In the antidromic direction, the wavefront encounters the returning wavefront from the preceding tachycardia beat. These two wavefronts collide and are extinguished near the "entrance" to the common path of slow conduction at site 4 (thin solid lines). Therefore, the antidromic wavefront does not propagate out beyond the circuit (the path from site 1 to site 14 is activated entirely orthodromically), and there is no change in the tachycardia QRS produced by the antidromic wavefront. The orthodromic wavefront produced by the stimulus propagates from site 5 to site 6 and site 1 and then into the myocardium beyond the scar, producing the next QRS. This orthodromic wavefront also propagates around the arcs of conduction block and reenters the area of slow conduction. If the area of collision of the prior orthodromic and antidromic wavefronts has recovered, the orthodromic wavefront "reenters" this area continuing the tachycardia. Thus, the orthodromic wavefront advances and resets the tachycardia. The point of exit of the orthodromic wavefront from the area of slow conduction at site 1 is the same as that of the regular tachycardia wavefronts, and hence, the QRS configuration of the advanced beat is similar to that of the other tachycardia beats. There is, however, a delay between the stimulus and the advanced QRS because of slow conduction between the stimulus site (site 5) and site 1. With progressively earlier stimuli (Figure 5, Panel B), the antidromic wavefront propagates farther before colliding with the returning orthodromic wavefront. However, if this collision still occurs in or near the common path of slow conduction in the scar, there is little or no
effect of the antidromic wavefront on activation of the myocardium distant from the circuit. Therefore, there is no change in the configuration of the surface electrocardiogram after the stimulus other than the premature occurrence of the reset tachycardia beat. When all capturing stimuli produce this effect, the result in the surface electrocardiogram is identical to the type 1 response identified in our patient studies during endocardial mapping (Figure 2).

**QRS alteration during pacing at a site within the circuit (type 2 response).** When the reentry circuit can communicate with the surrounding myocardium from a site other than the exit of the tachycardia beats, such as from site 4 in our simulations, the potential exists for stimulation at a site in the circuit to alter the QRS configuration. This is illustrated schematically in Figure 6 derived from results obtained in a reentry circuit that has a cycle length of 520 msec. A premature stimulus at site 5 in the slow, common central pathway produces orthodromic and antidromic wavefronts. Relatively late stimuli at this site reset the tachycardia without altering the QRS configuration as in the type 1 response because the antidromic wavefront collides with the returning orthodromic wavefront in or near the circuit. The orthodromic wavefront propagates to site 1 and advances the tachycardia after a delay due to slow conduction from site 5 to site 1. However, compared with the circuit in Figure 5, the conduction time from site 5 to site 4 in this circuit is shorter relative to the conduction time from site 5 to site 1. This allows the antidromic wavefronts from earlier stimuli to propagate farther to site 14 and then out from the scar before colliding with an orthodromic wavefront. The antidromic wavefront alters the sequence of ventricular activation distant from the circuit and the QRS configuration after the stimulus is thereby altered as a result of fusion between orthodromic and antidromic wavefronts in myocardium distant from the circuit. The stimulated orthodromic wavefront again exits from site 1 after a delay and advances the tachycardia without altering the QRS configuration of this advanced beat compared with that of the previous tachycardia beats. If the antidromic wavefront exits the circuit shortly after the preceding orthodromic wavefront exits from site 1, the altered QRS will appear to be on time. If the antidromic wavefront exits the circuit before the orthodromic wavefront, the altered QRS will be premature.

Thus, stimulation at reentry circuit sites from which the antidromic wavefront could propagate beyond the circuit from site 4 produces a type 2 response (Figure 3). This type of response occurs when the conduction time in the antidromic direction between the stimulus site and the myocardium

**Figure 4.** Tracings of type 3 pattern of response in a patient with recurrent ventricular tachycardia. From the top of Panels A and B are 50 msec time lines, surface electrocardiographic leads I, aVF, and V1, and intracardiac recordings from the stimulus marker channel (S), and the proximal electrode pair of the left ventricular catheter (LV8p). Single stimuli at the left ventricular site during sustained monomorphic ventricular tachycardia at a cycle length of 390 msec are shown. Panel A: A stimulus (S) 330 msec after the QRS onset fails to alter the configuration of the immediately following QRS complex. The subsequent QRS is advanced (from 390 to 375 msec) and is similar in configuration to the other tachycardia beats. Panel B: The stimulus is 30 msec earlier than that in Panel A. The stimulus is followed after 80 msec by an early QRS (380 msec after the previous tachycardia beat) that is similar in configuration to the tachycardia QRS. This reproducibly terminated the tachycardia.
outside the circuit (such as from site 4 to site 14) is relatively short compared with the orthodromic conduction time from the stimulation site to the circuit exit at site 1. In contrast to the first pattern of response, this response was also observed during stimulation at site 14. This site is just outside the circuit, near the “entrance” to the common pathway of slow conduction but is not participating in the tachycardia circuit itself. Thus, the type 2 response may not reliably indicate that the stimulation site is a critical site in the circuit.

**Antidromic capture of the circuit exit (type 3 response).** In the computer simulations, response type 3 can occur when an antidromic, stimulated wavefront captures the exit from the circuit (site 1). This is illustrated in Figure 7. Stimulation is performed at site 2 in the figure-eight circuit. As in responses types 1 and 2, the excitation wavefronts from late stimuli at site 2 propagate in orthodromic and antidromic directions in the circuit. In the antidromic direction, the wavefront collides with an orthodromic wavefront and is extinguished between sites 1 and 2. In the orthodromic direction, the wavefront propagates through the circuit to sites 3, 4, 5, 6, and 1 and advances the tachycardia. As the orthodromic wavefront reaches site 4, it propagates toward site 14 and toward site 5. However, the wavefront propagating from site 4 to site 14 encounters the returning orthodromic wavefront and is extinguished in or near the circuit preventing antidromic activation from extending outside the circuit. With progressively earlier stimuli, the antidromic wavefront propagates farther toward site 1 until site 1 is depolarized by the antidromic wavefront. When this occurs, there is a decrease in the interval between the stimulus and the first advanced QRS because of the short antidromic conduction time from site 2 to site 1. The advanced QRS configuration is not altered because the ventricle is still activated from site 1. Antidromic capture of site 1 was frequently followed by tachycardia termination because the antidromic wavefront propagating from site 1 toward site 6 collided with the orthodromic wavefront propagating from site 5 toward site 6, and the stimulated orthodromic wavefront often encountered refractory tissue on reaching the area of collision between site 1 and site 6.

Antidromic capture of the circuit “exit” (site 1) tended to occur when the antidromic conduction time from the stimulation site to site 1 was relatively short compared with the orthodromic conduction time from the stimulus site to site 1. Although no alteration of QRS configuration was observed in the patient described (Figure 4), in some computer simulations, the stimulated orthodromic wavefront depolarized site 4 sufficiently early to allow propagation of this wavefront from site 4 to site 14 and out to the more normal myocardium, altering ventricular activation distant from the scar.

**Resetting only after QRS alteration.** Depolarization of large portions of the ventricle by a stimulated wavefront that alters the sequence of ventricular activation and therefore the QRS configuration immediately after the stimulus occurs commonly during stimulation at sites distant from the reentry circuit. However, in some reentry circuit simulations, this was observed when stimulation was performed at a site located in the circuit. In such cases, the stimulation site was at the “entrance” to the circuit (e.g., near site 4 in Figure 1), and the conduction time from the stimulation site to the adjacent myocardium beyond the scar was short. All capturing stimuli then produced the same effect as did early stimuli in the type 2 response (Figure 6, Panel B). The antidromic wavefront propagated to

**Figure 5.** Schematic and tracings of the type 1 response to scanning stimuli in a figure-eight circuit. The specifications for this circuit were a diameter of 2 cm (for the path 1-2-3-4-5-6-1), conduction velocity from site 1 to site 5 of 0.3 m/sec and conduction velocity from site 5 to site 1 of 0.08 m/sec. The resulting tachycardia cycle length was 404 msec. Single stimuli at site 5 (S) produced wavefronts traveling in the antidromic and orthodromic directions (indicated by the open arrows). In the antidromic direction (from site 5 to site 4), the stimulated wavefronts collide with the orthodromic wavefronts (solid arrows) of the preceding tachycardia beat and are extinguished at the thin irregular lines near site 4. The orthodromic stimulated wavefront propagates from site 5 to site 6 and to site 1 and then exits the circuit, producing the advanced QRS without altering the QRS configuration compared with the tachycardia beats. At the bottom of the figure tracings, the predicted electrocardiographic effects are indicated. Panel A: A stimulus 104 msec after the QRS onset advances the tachycardia by 5 msec (from 404 to 399 msec) with a delay of 292 msec from the stimulus to the QRS onset of the advanced beat. Panel B: A stimulus 40 msec earlier (64 msec after the QRS onset) advances the tachycardia by 11 msec (from 404 to 393 msec). The delay from stimulus to advanced QRS has increased to 329 msec with the earlier stimulus. See text for discussion.
site 14 and beyond the scar 3 and altered the sequence of ventricular activation distant from the circuit. The QRS complex immediately after the stimulus is altered because of fusion of orthodromic and antidromic wavefronts in myocardium distant from the circuit. The following QRS is advanced and has the same configuration as the other tachycardia beats. Thus, as in the type 2 response, alteration of the QRS after a stimulus may not always indicate that the stimulation site is distant from the tachycardia circuit.

**Influence of the electrophysiologic characteristics of the circuit.** As illustrated in the examples above, the effect of a stimulus at a site in the circuit depends not only on the stimulus timing but also on the orthodromic and antidromic conduction times between the stimulus site and the areas of exit from the circuit. These conduction times are determined by the distance between the stimulation site and the circuit exits and by the conduction velocity through the intervening tissue. In the simulated figure-eight circuit, the stimulus site location relative to the slowly conducting central common pathway was a major determinant of the response type. Type 1 responses tended to occur at sites within the central common pathway. Type 2 responses tended to occur at sites near the entrance to this central pathway. Type 3 responses tended to occur at sites outside but close to the exit from the central pathway. However, Figures 5 and 6 illustrate that stimulation performed at the same site in circuits with different conduction velocities can produce different types of response. In addition, when conduction through the circuit behaves in a decremental fashion and slows further as the diastolic interval decreases, earlier stimuli produce progressively longer delays between the stimulus and the advanced QRS. When conduction slows markedly, the delay between the stimulus site and the subsequent QRS onset may greatly exceed the tachycardia cycle length producing either no apparent change in the tachycardia or an increase in the tachycardia cycle length for one beat. This is illustrated from simulation data in Figure 8. Simulations were performed with the same tachycardia circuit as in Figure 5. However, in Figure 5, the function relating conduction velocity and the diastolic interval had a relatively flat slope for the slow common pathway from site 5 to site 1 (curve 1 in Figure 8, Panel A). The bottom panel of Figure 4 shows the results of an increase in the slope of conduction velocity plotted against diastolic interval (curve 2 in Figure 8, Panel A). Evidence of decremental conduction properties between the stimulus site and the "exit" from the circuit was observed in three of the four patients during type 1 responses. The duration of the "excitable gap," during which a stimulus is able to depolarize the myocardium, also determines the type of response observed. The timing of excitable gaps at sites 1–6 in a figure-eight circuit is shown in Figure 9. The timing of the excitable gap is determined by the refractory period and the time of arrival of the tachycardia wavefront at that site in the circuit. During stimulation in the circuit, the distance that the antidromic wavefront propagates

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**Figure 6.** Schematic and tracings of the type 2 response to scanning stimuli in a figure-eight circuit. Specifications for this circuit were a diameter of 2 cm (for the path 1-2-3-4-5-6-1), conduction velocity from site 1 to site 5 of 0.6 m/sec, and conduction velocity from site 5 to site 1 of 0.05 m/sec that produced a tachycardia cycle length of 520 msec. The stimulated excitation wavefronts are indicated by the open arrows. Panel A: A stimulus at site 5 (S) 20 msec after the QRS onset. The stimulus propagates through the circuit in orthodromic and antidromic directions as in the type 1 response, advancing the tachycardia from 520 to 509 msec without altering the QRS. Panel B: A stimulus 80 msec earlier (QRS-S=440 msec) produces an antidromic wavefront that propagates to site 14 and through myocardium outside the scar. This alters the QRS configuration immediately after the stimulus. The following QRS is advanced (603 msec after the stimulus) and is similar in configuration to the tachycardia QRS complexes because of the exit of the orthodromic stimulated wavefront from site 1. Although the circuit size and stimulation site are the same as in the circuit shown in Figure 5, the conduction velocities and timing of excitable gaps differ from those in the Figure 5 circuit. Consequently, the response to programmed stimulation at the same site is different in the two simulations.
before colliding with an orthodromic wavefront is determined by the premature of the stimulus and the antidromic conduction velocity. If the excitable gap is very short, only relatively “late” stimuli capture, and collision of the antidromic and orthodromic wavefronts will occur relatively close to the circuit, tending to produce a type 1 response. A longer excitable gap allows earlier stimuli to capture, and more time is available for the antidromic wavefront to propagate from the stimulus site before colliding with an orthodromic wavefront. This increases the possibility that the antidromic wavefront will reach the entrance or exit from the circuit producing a type 2 or 3 response.

**Discussion**

Recently, programmed electrical stimulation has been used to localize critical areas of slow conduction in reentry circuits. At present, the mechanisms by which electrical stimuli act on tachycardia circuits in humans are largely speculative, based on analysis of the surface electrocardiogram and a limited number of endocardial recordings during catheter mapping. Intraoperative mapping studies are likely to allow more detailed analysis. However, even with sophisticated multiplexing systems, the entire reentry circuit may be difficult to define. Computer simulations, although speculative, provide the opportunity to evaluate the effects of premature depolarization at any site in a variety of reentry circuits. Our simulations in relatively simple reentry models show that responses to electrical stimuli at sites in the reentry circuit can be complex. That responses strikingly similar to those predicted from the models were observed in patients with ventricular tachycardia supports the relevance of these studies to human ventricular tachycardia. However, our computer simulations have several limitations, and other mechanistic explanations for our findings in patients probably exist.

**Estimation of the Stimulation Site Location Relative to the Circuit**

Electrical stimuli that prematurely depolarize a portion of the reentry circuit during ventricular tachycardia may produce two basic effects that are easily detectable from the surface electrocardiogram and a limited number of intracardiac recordings. First, a change in the activation sequence of the myocardium distant from the scar may be produced and alter the configuration of the QRS complex. Second, the expected timing of a following QRS complex may be altered. Combinations of these two effects produce the characteristic patterns observed as stimuli scan the cardiac cycles. When stimulation is performed at a site distant from the tachycardia circuit, alterations in the sequence of ventricular activation distant from the tachycardia circuit occur and alter the surface electrocardiogram. With very late stimuli, this may be difficult to detect because the stimulated wavefront may collide close to the stimulation site with the excitation wavefront from the tachycardia circuit. However, as stimuli become earlier, progressively more myo-

**FIGURE 7.** Schematic and tracings of the type 3 response to scanning stimuli in a figure-eight circuit. Specifications for this circuit were the same as those in Figure 2. Single stimuli are given at site 2. Stimulated excitation wavefronts are indicated by the open arrows. Panel A: Stimulus 364 msec after the QRS onset produces antidromic and orthodromic excitation wavefronts. Propagating toward site 1 is the orthodromic direction, the stimulated wavefront collides with the orthodromic wavefront emerging from site 1 and is extinguished along the irregular thin line. The orthodromic wavefront propagates through the circuit advancing the tachycardia as in the type 1 pattern. Panel B: The effects of a stimulus 20 msec earlier than that in Panel A are shown. The stimulated antidromic wavefront depolarizes site 1 and propagates toward site 6 and also into the myocardium outside the scar, producing an early QRS complex. The early QRS follows the stimulus after a relatively short interval (38 msec) because of the proximity of the pacing site to site 1. In addition, the advanced QRS is similar in configuration to the tachycardia beats. The stimulated orthodromic wavefront propagates through the circuit and encounters tissue in the region where the antidromic and orthodromic wavefronts collided (thin line between site 1 and site 6) that has not yet recovered its excitability, terminating the tachycardia.
Figure 8. Plot and tracings of the effect of increasing the dependence of conduction velocity in the circuit on the diastolic interval. Panel A: Two curves of conduction velocity (c.v.) (y axis) plotted against diastolic interval (x axis) are plotted. Curve 1 is the conduction curve generated for propagation from site 5 to site 1 in the circuit illustrated in Figure 5. Curve 2 has a steeper average slope throughout the range of diastolic intervals illustrated. Panels B and C illustrate the effect of using the curve B function to describe conduction from site 5 to site 1 in the figure-eight circuit from Figure 1. Panel B: A stimulus at site 5, 104 msec after the QRS onset captured and propagated through the circuit in the manner illustrated in Figure 2. However, the delay in conduction from site 5 to site 1 increased to 302 msec and the following QRS occurs only 2 msec later than expected, 406 msec after the preceding QRS. Thus, the effect of the stimulus on tachycardia would probably not be recognized from analysis of the surface electrocardiogram. Panel C: A stimulus 40 msec earlier produced further slowing of conduction in the circuit, and the following QRS was actually delayed, occurring 458 msec after the preceding QRS.

Figure 9. Graph of the duration of the “excitable gap” during which a site is recovered sufficiently to be depolarized (x axis) plotted against the conduction time in the orthodromic direction between the site and site 1. Data are derived from the figure-eight reentry circuit shown in Figure 5. The tachycardia cycle length is 520 msec. For reference, the electrocardiogram is inscribed at the bottom of the graph. Time 0 on the x axis (off scale) is the onset of the preceding QRS complex. The excitable gaps for sites 1–6 are shown. The excitable gap begins after recovery of the site and lasts until the site is depolarized by the next tachycardia wavefront. During stable tachycardia, sites 2–4 have refractory periods of 300 msec and an excitable gap of 220 msec. Sites 1, 5, and 6 have refractory periods of 330 msec and shorter excitable gaps of 190 msec.

cardiurn is depolarized by the stimulated wavefront and produces the commonly observed alteration in the QRS complex.7,12–18 When a stimulus in the reentry circuit produces wavefronts that exit from the circuit only at the same exit site as that of the tachycardia beats (site 1 in our model), the QRS of the stimulated beat will resemble that of the tachycardia beats, although slight QRS changes may be produced by the superimposition of the early QRS on a different portion of the preceding ST segment and T wave. However, if the reentry circuit communicates with the surrounding myocardium at points other than the original “exit” and if a stimulated wavefront exits the circuit from such a site, the QRS configuration may be altered compared with that of the tachycardia beats. Our computer simulations suggest that the type 1 and 3 responses in which the QRS configurations are not altered after a stimulus are more likely to indicate that the pacing site is in the circuit than does the type 2 response that in the simulations occurred at sites in and adjacent to the circuit.

When the stimulation site is located within the circuit, the relative conduction times from the stimulus site to the “entrance” to and “exit” from the circuit determine the pattern of response to scanning stimuli. These conduction times are determined by the distance and conduction velocity. Conduction times are unlikely to directly reflect distance because of heterogeneous conduction velocity in the circuit.10 The situation is further complicated by potential changes in conduction velocity that may occur as stimuli vary in prematurity. With marked conduction slowing in response to stimulus prematurity, delays between the stimulus and exit of the orthodromic wavefront from the circuit may be sufficient to produce very little change in the tachycardia cycle length and prevent detection of an effect of the stimulus on the circuit (Figure 8, Panel B). Greater conduction slowing may actually prolong the QRS to QRS interval beyond that of the tachycardia cycle length.3 From these consider-
ations, it follows that when the pacing site is in the circuit, analysis of stimulus to QRS intervals may provide only an estimate of the pacing site location relative to areas of slow conduction in and exit sites from the circuit. In the figure-eight type of circuit, El-Sherif et al.22 have shown that ablation of a site in the slow common pathway is required for tachycardia termination. In our simulations, stimulation in the slow common pathway most frequently produces a type 1 response. However, further studies are required to determine the relation of the response type to the likelihood of successful catheter ablation.

Limitations

We considered only two reentry circuit configurations: the figure-eight type of circuit that has been well characterized in animal models6,21–24 and that has recently been shown to occur in humans11,20 and the simple circuit with two possible pathways to the surrounding myocardium suggested by Rosenthal et al.7 However, other reentry circuit configurations probably occur that could allow other response patterns to stimulation or similar patterns resulting from mechanisms other than those defined in our simulations. For example, we performed only limited simulations of stimulation at sites of slowly conducting tissue that communicate with but are not participating in the tachycardia circuit (site 14 in our simulations). Although we observed only type 2 responses at these sites, stimulation at such areas could theoretically produce type 1 and 3 responses if the site were relatively protected from the myocardium distant from the scar.25 However, the existence of such areas in human myocardial scars is speculative at present. We also assumed that the figure-eight reentry circuit was located in the border of a myocardial scar with one loop of the circuit (the loop from sites 1–3 in Figure 1) relatively protected from the surrounding myocardium by the arcs of block and the common central pathway of slow conduction. We did not study other geometric placements of the figure-eight circuit relative to the scar that may alter the response patterns at a given site, especially during stimulation in the relatively protected loop.

We assumed that antidromic propagation of a wavefront from site 4 to site 14 and then beyond the scar would alter the ventricular activation sequence sufficiently to alter the QRS configuration. However, if the tachycardia circuit is very small or if the sites of exit from the circuit are very close, such an event may produce little detectable change in the QRS configuration. Thus in small circuits, the type 1 response may theoretically be observed in the surface electrocardiogram even though the stimulated antidromic wavefront propagates beyond the circuit. Intraoperative mapping studies suggest that both relatively large and small reentrant circuits occur in humans.10,11

In our simulations the arcs of conduction block that determine the path of reentry are anatomically fixed. This is an oversimplification because conduction block is often functional and because in some cases apparent block may be due to collision of opposing wavefronts rather than true failure of conduction.23 However, shifts in the arcs of block that determine the reentry path are likely to alter the tachycardia cycle length and QRS configuration. Restricting the model to one in which the reentrant path remains fixed is consistent with human studies in which pacing during ventricular tachycardia entrains or resets the tachycardia without disturbing the tachycardia cycle length and QRS configuration after pacing termination.7,12–18 Our observations in patients were consistent with this model, although we cannot exclude the possibility that small alterations in the reentrant path occurred during pacing and could have contributed to the long delays between stimuli and advanced tachycardia beats or alterations in QRS configuration after a stimulus.

Although infarct scars that give rise to reentry circuits are physiologically heterogeneous,10 our model divides the reentry circuit into electrophysiologically homogeneous segments. Thus, the characteristics specified for each segment represent the “means” for a complex heterogeneous system. This was done for simplicity because data on intercellular conduction in human myocardial scars are limited, but empiric information is available to allow approximations of conduction characteristics over larger distances.10 Similarly, data on refractoriness in human myocardial scar is limited, especially at heart rates comparable to those occurring during ventricular tachycardia.10,26 Therefore, we studied a range of parameters for these characteristics. As supported by studies in animal models and in humans, we also assumed that depolarization of the slow pathways in the simulated circuits generated low-amplitude electrical signals that would not be detected on the standard surface electrocardiogram.5,9,10,23,27–29

In our patient studies, a limited number of surface electrocardiogram leads were recorded, and we cannot exclude the possibility that subtle changes in QRS configuration would have been detected had we recorded a greater number of electrocardiographic leads. During bipolar pacing, as was used during our patient studies, the precise site of stimulation can change because of varying contributions of the cathode and anode to ventricular excitation.30 This could theoretically produce small changes in activation sequence and was not considered in the computer simulations. For a small reentry circuit, simultaneous activation of sites inside and outside the circuit could theoretically produce alterations of the QRS configuration and a type 2 response.

Conclusions

During ventricular tachycardia in humans, scanning the cardiac cycle with electrical stimuli can produce complex patterns of resetting and QRS fusion consistent with stimulation at sites in or near
the tachycardia circuit.Resetting the tachycardia by stimuli over a range of coupling intervals that do not alter the sequence of ventricular activation distant from the circuit suggests that the stimulation site is located within the circuit. However, alteration of the QRS configuration by a stimulus does not always indicate that the stimulation site is outside the circuit. Analysis of responses to premature stimuli may aid in further defining the characteristics of reentry in humans and in localizing critical sites in the circuit for catheter ablation and warrants further investigation.

**Appendix, Modeling Responses to Cycle Length Changes**

**Refractory Periods**

Refractory periods are modeled as an exponential function of the diastolic interval after the formula for action potential duration derived by Elharrar et al. The diastolic interval was defined as the difference between the activation time and the end of the refractory period after the previous activation:

\[ \text{RP} = \text{RPmax} \cdot [1 - A1 \cdot \exp(-D1/T1) - A2 \cdot \exp(-D1/T2)] \]  

where RP is the refractory period, DI is the diastolic interval, A1, A2, T1, and T2 are constants 0.38, 0.12, 0.097, and 1.46, respectively. The tachycardia cycle length is determined by the conduction velocities and length of the reentry circuit. The basal refractory periods that exist during the stable tachycardia are specified for each site and Equation 1 is solved for RPmax. Subsequent refractory periods at each site are calculated from Equation 1.

**Conduction Velocity**

Mathematical descriptions of conduction through infarct scars in humans are not available. However, conduction slowing through the AV node in response to premature stimuli can be modeled as an exponential function of the form: Conduction time = A \cdot \exp(-n \cdot DI) + C. Therefore, we modeled changes in conduction velocity as a monoeponential function of the diastolic interval:

\[ \text{CV} = \text{CVnormal} \cdot [1 - \exp(-N1 \cdot (DI \cdot F1 + F2))] \]  

CVnormal is the normal conduction velocity (1 m/sec in these simulations), DI is the diastolic interval, and N1, F1, and F2 are constants. F1 is a specified constant between 0 and 1 that is used to set the mean slope of the function. F2 is the basal diastolic interval multiplied by (1 - F1), and therefore, the term (DI \cdot F1 + F2) is equal to the diastolic interval in the basal state. Conduction velocities and refractory periods are specified for the stable tachycardia, and Equation 2 is then solved for N1. Conduction velocities for subsequent diastolic intervals are determined from Equation 2.

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KEY WORDS • ventricular tachycardia • mapping, endocardial • catheter ablation • programmed electrical stimulation
Programmed electrical stimulation at potential ventricular reentry circuit sites. Comparison of observations in humans with predictions from computer simulations.
W G Stevenson, K Nademanee, J N Weiss, I Wiener, K Baron, L A Yeatman and C T Sherman

Circulation. 1989;80:793-806
doi: 10.1161/01.CIR.80.4.793

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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