Cryothermal mapping of recurrent ventricular tachycardia in man

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ABSTRACT Intraoperative reversible cryothermal mapping of recurrent ventricular tachycardia was performed in seven patients with left ventricular aneurysms with use of a 0°C ice probe. A single, reproducible cryotermination site was found in each patient. The cryotermination site was uniformly located in an area where local electrograms obtained during ventricular tachycardia showed electrical activation during the diastolic portion of the surface electrocardiogram, and was different than the site of activation coincident with the onset of the QRS complex on the surface electrocardiogram (earliest reactivation site or ERS) by 4.5 ± 2.7 cm (mean ± SD) in five of seven patients. Sinus rhythm late potentials were recorded at the cryotermination site in five of six patients and from the ERS in one. In five patients, extensive subendocardial resection including both the ERS and cryotermination sites was performed. In two patients only the cryotermination site was excised. In six survivors, including one in whom only the cryotermination site was excised, ventricular tachycardia could not be induced 2 weeks after surgery and has not recurred during the follow-up period of 7 to 17 months (12 ± 4.5 months, mean ± SD). Reversible cryothermal mapping may provide additional important information not obtained by standard electrogram mapping of ventricular tachycardia that may help guide surgical therapy of recurrent ventricular tachycardia.

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LEFT VENTRICULAR aneurysmectomy with activation mapping-guided endocardial resection has improved the surgical cure rate for patients with recurrent ventricular tachycardia.1 Usually the area surrounding the site recording the earliest occurring electrogram during ventricular tachycardia is related to the onset of the QRS complex on the surface electrocardiogram and is identified and excised.1 However, treatment failures occur. Failure is sometimes attributed to an unresectable location of the site identified by activation mapping, for example, the base of a papillary muscle, but unexpected failures suggest an incomplete understanding of the mechanisms responsible for reentrant ventricular tachycardia.2 Recently, Gessman et al.3 and El-Sherif et al.4 used reversible cryothermal mapping in dogs to localize a site at which cooling reproducibly terminated ventricular tachycardia. We have demonstrated, in a canine infarct preparation, that this cryotermination site may be distant from the site showing activation coincident with the onset of the QRS complex on the surface electrocardiogram5 and hypothesized that cryothermal mapping might provide additional important information that could be used in guiding surgical therapy of ventricular tachycardia in man.

We describe our experience with reversible cryothermal mapping in seven patients and demonstrate the validity and utility of this mapping method.

Methods

This study was approved by the institutional human studies committee and informed written consent was obtained from each of seven patients scheduled for left ventricular aneurysmectomy. The indication for surgery in each patient was recurrent refractory ventricular tachycardia. Two patients also had congestive failure severe enough to warrant aneurysmectomy. All had coronary artery disease and myocardial infarctions from 1 month to 7 years before surgery (mean ± SD, 34 ± 43.8 months, median 10 months). Electrocardiographic examination showed sinus rhythm and evidence of the prior myocardial infarction in each. Three patients had disturbances of intraventricular conduction. Six patients previously required cardioversion, and in five patients cardiac arrest had occurred. All were considered New York Heart Association class III or IV. Before surgery, six of seven patients had ventricular tachycardia induced by single or double premature ventricular extrasystoles

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introduced during sinus rhythm or during right ventricular pacing at a cycle length of 600 msec. In one patient (No. 2) nonsustained ventricular tachycardia of multiple morphologies and sustained ventricular tachycardia of two distinct morphologies was induced. The seventh patient had repeated episodes of spontaneous ventricular tachycardia that were not responsive to drug therapy and this patient was scheduled for surgery on an urgent basis without preoperative programmed stimulation.

After anesthesia was induced and normothermic (37°C) right atrial-to-aortic cardiopulmonary bypass was begun, normal sinus rhythm mapping, activation mapping of ventricular tachycardia, and cryomapping during ventricular tachycardia were performed as follows.

**Mapping in patients during normal sinus rhythm.** Seventy-two bipolar electrograms (interelectrode distance five mm) were recorded from the epicardial and endocardial surfaces of the heart, three at each ‘‘hour of the clock’’ around the epicardial and endocardial perimeters of the ventricular aneurysm (figure 1), with use of a hand-held roving probe with three bipolar electrode pairs. Electrograms were recorded simultaneously with two surface electrocardiographic leads and, in five patients, a right ventricular reference lead was also obtained. Recordings were made on an Electronics for Medicine (Pleasantville, NY) VR-12 recorder at paper speeds of 100 mm · sec⁻¹ with filter settings of 0.1 to 100 Hz (electrocardiogram) and 30 to 500 Hz (electrograms). After epicardial mapping, the aneurysm was opened in an apical-basal direction to facilitate endocardial mapping. Local electrogram duration was measured by the method of Cassidy et al. as the time from the earliest electrical activity that deviated from baseline to the onset of the amplification signal decay artifact. Electrograms were examined for late potentials, which were defined as discrete potentials at the terminal portion of the local electrogram extending beyond the QRS duration on the surface electrocardiogram.

**Electrogram mapping of ventricular tachycardia.** Bipolar silver plunge electrodes (two patients) or a quadrapolar transvenous pacing catheter (five patients) was positioned in the right ventricular apex or mid right ventricle to allow intraoperative programmed stimulation. With a Bloom Stimulator (Bloom Associates Ltd., Reading, PA), sustained ventricular tachycardia was induced by introducing single or double premature extrastyles during sinus rhythm or during right ventricular drive pacing for 8 beats at 100 beats · min⁻¹ or by 3 to 6 beat bursts of rapid right ventricular pacing at heart rates of 150 to 250 beats · min⁻¹.

After ventricular tachycardia of a similar rate and surface electrocardiographic morphology as that recorded before surgery was induced, 72 point epicardial and endocardial electrogram hour of the clock mapping was repeated. Attempts were made to place the middle bipole of the mapping electrode over the visible border of the aneurysm. Activation time at each site was measured as the time from the onset of the surface QRS to the first deflection in the local electrogram. In four patients discrete double potentials were recorded during ventricular tachycardia, with the first deflection being associated with electrical systole on the surface electrocardiogram and a later diastolic potential. In these cases, activation was timed to both the discrete diastolic and systolic potentials and the electrogram was considered to be a composite recording of electrophysiologically heterogeneous tissue. Twenty millisecond isochronal maps were constructed from the 72 electrograms obtained. The site showing activation coincident with the onset of the QRS complex (±10 msec) on the surface electrocardiogram was identified and defined as the earliest reactivation site (ERS). Sites from which electrograms were recorded that preceded the QRS complex on the surface electrocardiogram by 0 to 25 msec also were identified because it has been suggested that excision of these sites is likely to cure ventricular tachycardia if fragmented diastolic activity cannot be identified.

**Cryothermal mapping of ventricular tachycardia.** Ice probes (0°C) were made by freezing water, under sterile conditions, into cubes 1.5 × 1.5 × 1.5 cm. After electrogram mapping, when the duration of ventricular tachycardia exceeded 2 min, cryomapping was begun. The ice probe was held along the border of the aneurysm for 10 sec sequentially at each hour of the clock on the epicardial and then endocardial surfaces. Each cryomapping site covered the area of the three electrographic recording sites at each hour of the clock. When a site was found that terminated the arrhythmia, the arrhythmia was reinduced at least once more to assess the specificity and reproducibility of cryomarketerination. A site was called a cryomarketermination site if cooling at that site terminated the arrhythmia at least twice, if at no time did cooling of the site fail to terminate the ventricular tachycardia, and if no other site was found from which the arrhythmia could be terminated.

The ERS and cryomarketermination site were considered identical if they were within one hour of the clock (approximately 1.5 cm) from each other and were considered ‘‘different’’ if they were two or more hours of the clock apart. Distances between sites were measured circumferentially around the border of the aneurysm.

**Operative procedure.** After completion of mapping, systemic hypothermia was induced, the aorta was cross-clamped, and cold potassium cardioplegic solution was administered. Left ventricular aneurysmectomy and extensive subendocardial excision of the cryomarketermination site and, when possible, of the ERS was performed. These sites were excised generously, and

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**FIGURE 1.** Hour of the clock scheme used for epicardial and endocardial mapping. Circumflex and occluded left anterior descending coronary arteries are depicted along with the left ventricular aneurysm (cross-hatched area). Ventriculotomy was performed to facilitate endocardial mapping. Proximal, mid, and distal bipolar electrograms (interelectrode distance 5 mm) were recorded at ‘‘X’’ sites from each ‘‘hour’’ on the epicardial and endocardial surfaces.
at least one hour of the clock surrounding each site was excised, resulting in excision of approximately 25% to 40% of the endocardial perimeter of the aneurysm. If indicated aortocoronary saphenous vein grafts were placed and then the surgical procedure was completed.

Ten days to two weeks after surgery electrophysiologic examinations were performed in the six surviving patients in an attempt to reinduce ventricular tachycardia with right ventricular endocardial pacing.

**Results**

No patient suffered adverse sequelae attributable to the cryothermal mapping procedure. In one patient a sustained ventricular tachycardia not seen clinically was initially induced. This was terminated by programmed extrastimuli. In patient 2, who had two morphologically distinct ventricular tachycardias, only one type could be induced intraoperatively. Mapping required 20 to 40 min, with cryothermal mapping contributing 5 to 10 min. (Each cryothermal map required a maximum of 4 min, with most of this time spent reinducing the ventricular tachycardia.) An example of electrograms recorded from the endocardial surface during ventricular tachycardia in patient 1 are displayed in figure 2. Activation time (in msec) at each recording site follows the electrogram. The ERS was located at between 12 and 2 o’clock on the endocardial surface and activation occurred during electrical systole on the surface electrocardiogram at from 2 to 7 o’clock. Between 7 and 12 o’clock, double electrical potentials appeared, with the second potentials occurring during diastole on the surface electrocardiogram. Activation times for the systolic potentials are omitted for clarity. All epicardial potentials in this patient occurred during surface electrophysiographic electrical systole. Twenty millisecond isochronal activation maps were constructed from electrographic recordings; an example is shown in figure 3. In this endocardial isochronal representation from patient 1, corre-

![FIGURE 2. Endocardial electrogram map from patient 1. Surface electrocardiographic leads II and V5 during ventricular tachycardia are displayed along with the middle bipolar electrogram from each hour of the clock along the endocardial perimeter of the aneurysm. Time and amplitude references are shown and the vertical line represents surface QRS onset. Numbers following each electrogram represent local activation time (in msec; referenced to surface QRS onset). Earliest activation occurs at 12 o’clock, with electrograms occurring during electrical systole at between 1 and 7 o’clock. Between 7 and 12 o’clock slowing of conduction, manifested as the appearance of double electrical potentials (outlined with rectangle) with the second potentials occurring during diastole, as observed on the surface electrocardiogram, was seen. Activation time to the first potential was omitted for clarity. All epicardial potentials occurred during inscription of the QRS on the surface electrocardiogram.](http://ahajournals.org)
grams were recorded during ventricular tachycardia. In three of seven patients the cryotermination site was different than the site showing activation 25 msec before surface electrocardiographic onset of the QRS.

In each of six patients in whom sinus rhythm mapping was performed, late potentials were recorded at multiple sites. Table 2 summarizes results of sinus rhythm mapping. Late potentials were recorded at one to 12 sites (4.8 ± 4.2, mean ± SD, median 3) in each patient. In patient 3, ERS and cryotermination sites were identical, and a late potential was recorded at this site (figure 4, A). In patients 1, 2, 5 (figure 4, B), and 6, late potentials were recorded from the cryotermination site, but not the ERS. In patient 7, late potentials were not recorded at either the ERS or cryotermination site.

**Modes of cryotermination.** Figure 5 shows the cryotermination sequence in patients 3 and 6. In six of seven patients the cycle length of tachycardia increased over several beats before cryotermination. In one patient (No. 5) electrical activity became increasingly disorganized, approaching the appearance of ventricular fibrillation before reverting to sinus rhythm. In patients 2, 4, 6 (figure 5, A), and 7 one or two ventricular contractions of a different morphology than that of the underlying ventricular tachycardia occurred before cryotermination. In patients 1 and 3 (figure 5, B) ventricular tachycardia progressively slowed until sinus rhythm supervened.

Table 3 summarizes the intraoperative and postoperative courses of the patients. One to four aortocoronary saphenous vein grafts were placed in six patients (mean ± SD, 1.7 ± 1.1 grafts). In patients 1, 3, 5, 6, and 7 both the ERS and cryotermination site were excised. In patients 2 and 4, the location of the earliest reactivation site precluded excision, so only the cryotermination site was excised. Patient 4 died 4 days after surgery as a result of severe heart failure despite vasopressor therapy and intra-aortic balloon counterpulsation. The other six patients are alive 7 to 17 months after surgery (mean ± SD, 12 ± 4.5 months, median 12 months). During electrophysiologic studies performed 2 weeks after surgery, ventricular tachycardia was not inducible in any of the six surviving patients.

No patient has required antiarrhythmic therapy since discharge from the hospital, but one has required hospital admission for congestive heart failure.

**TABLE 1**

Results of intraoperative electrogram and cryo thermal mapping of ventricular tachycardia (VT)

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>VT cycle length (msec)</th>
<th>ERS Site of CT</th>
<th>25 msec site</th>
<th>Distance between CT and ERS sites (cm)</th>
<th>Distance between CT and 25 msec sites (cm)</th>
<th>Activation time at CT site (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>275</td>
<td>Endo 12–2</td>
<td>Endo 8</td>
<td>Endo 12</td>
<td>4.5</td>
<td>5.0</td>
</tr>
<tr>
<td>2</td>
<td>325</td>
<td>Endo 2</td>
<td>Endo 9</td>
<td>Endo 2</td>
<td>7.5</td>
<td>7.5</td>
</tr>
<tr>
<td>3</td>
<td>240</td>
<td>Endo 9</td>
<td>Endo 9</td>
<td>Endo 9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>245</td>
<td>Epi 2</td>
<td>Endo 2</td>
<td>Endo 1</td>
<td>6.0</td>
<td>0–1.5</td>
</tr>
<tr>
<td>5</td>
<td>280</td>
<td>Endo 2</td>
<td>Endo 12</td>
<td>Endo 12</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>290</td>
<td>Endo 12</td>
<td>Endo 8</td>
<td>Endo 5–6</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>190</td>
<td>Endo 4</td>
<td>Endo 3</td>
<td>Endo 4</td>
<td>0–1.5</td>
<td>0–1.5</td>
</tr>
</tbody>
</table>

Endo = endocardial surface; Epi = epicardial surface; CT = cryotermination.

Numbers represent hour of the clock locations of sites of origin or cryotermination.
TABLE 2  
**Data from sinus rhythm mapping**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>n</th>
<th>Location</th>
<th>Electrogram duration (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Surface ECG QRS duration</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>Endo 8</td>
<td>110</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>Epi 12, 1, 11</td>
<td>120</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Endo 2, 3, 6, 7, 8, 9, 10, 11</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>Endo 10, 9</td>
<td>130</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>Epi 2, 5</td>
<td>120</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Endo 1, 4, 7, 8, 9, 10, 12</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>Endo 8, 9</td>
<td>110</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>Epi 6</td>
<td>130</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Endo 7, 9, 11</td>
<td></td>
</tr>
</tbody>
</table>

Endo = endocardial surface; Epi = epicardial surface; ECG = electrocardiographic.

Numbers represent hour of the clock locations.

Cryotermination site and ERS identical.

Discussion

Three cases of cryotherapy for recurrent ventricular tachycardia have been reported previously. In 1977, Gallagher et al. were able to terminate ventricular tachycardia arising from an automatic focus with 60 sec of cooling. After 10 sec of rewarming, the arrhythmia recurred. Microreentry could not be ruled out, but the immediate recurrence after rewarming suggested an automatic focus. Cryoablation at $-60^\circ$ C cured the arrhythmia. Camm et al. terminated ventricular tachycardia in a patient by cooling ($0^\circ$ to $-10^\circ$ C) the site of earliest septal activation. Mason et al. reported in 1981 that cooling ($2^\circ$ C) of the slow-conducting area of tissue in a patient terminated ventricular tachycardia. However, tachycardia recurred promptly upon rewarming, a phenomenon similar to that of the automatic ventricular tachycardia cryoablative by Gallagher et al.In contrast, after cryotermination, presumed reentrant tachycardia always required reinduction by programmed stimulation in our patients.

The mechanism of cryotermination has been evaluated. Gessman et al. found that conduction in excised canine cryotermination zone tissue was abnormally depressed and became increasingly slow to the point of complete conduction block as temperature was decreased from $37^\circ$ to $30^\circ$ C. Wallace and Mignonne found that cooling prolonged the local effective refractory period, with consequent conduction delays and block. In our patients, cycle length characteristically increased before cryotermination and this implied that local cooling slowed conduction at the cryotermination site. Horowitz et al. have reported that pressure applied at certain sites may terminate ventricular tachycardia. Pressure applied during cryomapping was the same or less than during activation mapping, which did not predictably terminate tachycardia at the cryotermination sites. It is therefore unlikely that pressure played a major role in cryotermination.

Our choice of 10 sec cooling duration was made based on canine studies in which cryotermination occurred in $7.7 \pm 0.9$ sec (mean $\pm$ SEM). Epicardial cooling of the canine heart in both normal and infarcted tissue was limited to a 3 mm depth during the initial 10 sec. After longer cooling periods, cooling spread to deeper levels, decreasing the localizing specificity of the technique. Sterile ice provided a convenient, in-

![FIGURE 4. Sinus rhythm electrograms from patients 3 and 5. A. Surface electrocardiographic leads I and V8 are shown along with a right ventricular (RV) reference and the local electrogram recorded at 9 o'clock on the endocardial surface (ERS-CT). High-frequency fractionation of the terminal portion of the electrogram extending 30 msec beyond surface QRS duration is seen. Time and amplitude calibrations are included. ERS and cryotermination sites were identical in this patient. B. The ERS is different from the cryotermination site (CT). The late potential at the CT site extends 90 msec beyond duration of the surface QRS.](http://ahajournals.org)
expensive cryoprobe since it held constant temperature (0°C) and could not produce irreversible cryothermal damage.

In our patients, cryotermination occurred at sites at which local electrograms showed electrical activation during the diastolic portion of the surface electrocardiogram during ventricular tachycardia. Gessman et al.\(^3\) found in dogs that the cryotermination site correlated with the site at which mid to late diastolic electrical activity was recorded during activation mapping of the tachycardia. El-Sherif et al.\(^4\) further characterized the cryotermination site as an area where the reentry loop was narrow and surrounded by an arc of functional conduction block. Cooling the earliest reactivation site failed to interrupt reentry because other sites near this site were reactivated without changing the overall reentry pattern.\(^4\)

Josephson and Seides\(^10\) have suggested that if low-amplitude, fragmented diastolic activity is not identified, sites showing activation within 25 msec before onset of the surface QRS complex should be excised. Others have used definitions similar to that for the ERS to guide surgical excision.\(^16\) Cryomapping often identifies different sites of earliest reactivation and cryotermination. In four of our seven patients the ERS was more than two hours of the clock distant from the cryotermination site. In two of seven patients, the site from which electrograms were recorded 25 msec before surface electrocardiographic onset of the QRS was more than two hours of the clock distant from the cryotermination site.

Sinus rhythm recordings showed the presence of late potentials at the cryotermination site in five of six patients in whom these recordings were obtained. Late potentials appeared at the ERS in only one of six patients (patient 3) in whom both ERS and cryotermination sites were identical. Late potentials represent delayed depolarization of a mass of slowly conducting ventricular tissue and suggest increased susceptibility to ventricular tachycardia in patients with ventricular aneurysms.\(^17\) Cassidy et al.\(^7\) recorded abnormal sinus rhythm electrograms at 88 of 102 sites showing diastolic potentials during ventricular tachycardia in 52

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**TABLE 3**

**Outcome of treatment**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>ERS</th>
<th>Cryotermination site excised</th>
<th>Postoperative electrophysioligic study</th>
<th>Duration of follow-up (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>No inducible VT</td>
<td>17</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
<td>Yes</td>
<td>No inducible VT</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>Yes</td>
<td>No inducible VT</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>Yes</td>
<td>Died 4 days postop of pump failure</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>Yes</td>
<td>Yes</td>
<td>No inducible VT</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td>Yes</td>
<td>Yes</td>
<td>No inducible VT</td>
<td>8</td>
</tr>
<tr>
<td>7</td>
<td>Yes</td>
<td>Yes</td>
<td>No inducible VT</td>
<td>7</td>
</tr>
</tbody>
</table>

Postoperative electrophysiologic study was performed 2 weeks after surgery.
patients undergoing endocardial catheter mapping. In our patients, the cryotermination site was located in an area showing diastolic potentials during ventricular tachycardia so that the occurrence of late potentials at these sites was not unexpected.

Although present at five of six cryothermal sites, late potentials were also present at other sites in five of six patients. In three of six patients, however, a limited number of contiguous sites recording late potentials were identified. The cryotermination site was located in this area in all three and at the earliest reactivation site in one of three. In patients in whom ventricular tachycardia cannot be induced in the operating room, excision of the site recording late potentials during sinus rhythm may effectively guide the surgeon to excise the same area as that which would be identified by cryomapping.

Cryomapping provides an identifiable, reproducible end point: termination of ventricular tachycardia. In contrast, electrogram mapping depends on the ability to locate sites of fragmented diastolic electrical activity or sites from which electrograms coincident with surface onset of the QRS are recorded. This requires skilled interpretation and, as Mason et al. suggest and we and others have demonstrated in dogs, the concept of a "site of origin" or a focus of ventricular tachycardia origin is misleading in some cases. It may not be necessary to excise the ERS to cure ventricular tachycardia surgically. In our patient 2, excision of the cryotermination site only was curative of ventricular tachycardia. Our data suggest that the cryotermination site correlates with the area of diastolic electrical activation of ventricular tachycardia, and may be the most vulnerable part of the reentrant loop of tachycardia.

However, whenever possible in our patients, extensive endocardial resection of both the ERS and cryomapping site was performed. Until optimal probe size and cooling duration are known, and larger numbers of patients are studied, it is premature to suggest that excision of the cryotermination site only is sufficient.

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References