Static Relationship of Cycle Length to Reentrant Circuit Geometry

Edward J. Ciaccio, PhD; Constantino Costeas, MD; James Coromilas, MD; Andrew L. Wit, PhD

Background—Knowledge of the pathway common to both wave fronts in figure-8 reentrant circuits (ie, the isthmus) is of importance for catheter ablation to stop reentrant ventricular tachycardia. It was hypothesized that quantitative measures of isthmus geometry were interrelated and could be correlated with tachycardia cycle length.

Methods and Results—A canine infarct model of reentrant ventricular tachycardia in the epicardial border zone with a figure-8 pattern of conduction was used for initial analysis (experiments in 20 canine hearts with monomorphic reentry). Sinus-rhythm and reentry activation maps were constructed, and quantitative (skeletonized) geometric parameters of the isthmus and border zone were measured from the maps. Regression equations were used to determine significant correlation relationships between skeletonized variables, which can be described as follows. Tachycardia cycle length, measured from the ECG R-R interval, increases with increasing isthmus length, width, narrowest width, angle with respect to muscle fibers, and circuit path length determined by use of sinus-rhythm measurements. After this procedure, in 5 test-set experiments, tachycardia cycle length measured from the R-R interval, in combination with regression coefficients calculated from initial experiments, correctly predicted isthmus geometry (mean estimated/actual isthmus overlap 70.5%). Also, the circuit path length determined with sinus-rhythm measurements correctly estimated the tachycardia cycle length (mean error $2.5 \pm 2.5$ ms).

Conclusions—Correlation relationships derived from measurements using reentry and sinus-rhythm activation maps are useful to assess isthmus geometry on the basis of tachycardia cycle length. Such estimates may improve catheter ablation site targeting during clinical electrophysiological study.

Key Words: catheters $\bullet$ ablation $\bullet$ reentry $\bullet$ tachycardia $\bullet$ ventricles

For treatment of reentrant ventricular tachycardia, catheter ablation is often the method of choice because it does not involve surgery, there is low morbidity, and it is frequently effective at stopping tachycardia and preventing recurrence.¹ The target site for ablation of reentry is the central common pathway, or isthmus, which is a protected region through which the propagating wave front is constrained by arcs of conduction block.² Some reentrant circuits are difficult to ablate during clinical electrophysiological study because it is problematic to ascertain the precise location and/or geometric characteristics of the isthmus.³–⁵ Concealed entrainment procedures are an important method to pinpoint the location of the standard ablation catheter tip with respect to the isthmus entrance or exit; however, isthmus shape is not discerned.⁶–⁸ Therefore, the best ablation lesion (length and orientation) to block the impulse as it traverses the isthmus cannot presently be determined by a standard mapping catheter except by either trial and error or use of extensive, time-consuming mapping procedures.⁹ Currently, even when an ablation lesion terminates reentry, it does not always preclude reinitiation of the same reentry morphology,¹⁰ suggesting that such lesions may be off center with respect to the optimal target site.

Improved knowledge of circuit geometry before catheter ablation can potentially increase the success rate for terminating reentrant ventricular tachycardia without recurrence of the same or another morphology, because ablation site targeting can be achieved in part on the basis of assessment of isthmus shape. This study tested the hypothesis that ventricular tachycardia cycle length can be correlated with reentrant circuit geometry and with sinus-rhythm activation characteristics in a canine model. If tachycardia cycle length, in conjunction with measurements made during sinus rhythm, could be used to estimate geometric properties of the reentrant circuit during clinical electrophysiological study, it would potentially enhance the speed and accuracy of ablation therapy even under circumstances of hemodynamic intolerance in which extensive mapping information is unobtainable before tachycardia termination.

Methods

Myocardial infarcts were created within the subepicardium of in situ canine hearts by ligation of the left anterior descending coronary...
Electrophysiological study was done 4 to 5 days after LAD ligation. Dogs were anesthetized with sodium pentobarbital, the chest was opened and positive-pressure ventilation applied, and recordings were made from the epicardial border zone of the anterior left ventricle with a 196- to 312-channel array. The distance between poles of each bipolar electrode was 3 mm, and the spacing between bipolar electrodes was 4 to 5 mm. A fixed signal gain of $100 was used for first-stage amplification, and a $128 gain determined automatically by computer software was used for second-stage amplification, so that the final signal peak-to-peak level was between 2 and 8 V. The signal pass band was 2 to 500 Hz. For 20 training-set canine heart experiments, data were acquired during sinus rhythm, pacing, and monomorphic reentrant ventricular tachycardia with figure-8 conduction pattern that was induced by programmed electrical stimulation (10 S pacing cycles followed by a premature stimulus). Activation maps were made by automatically marking activation times of electrogram signals by slope and peak criteria and printing the times for all sites on a computerized map grid. Arcs of block separated sites in which activation differed by 40 ms and where wave fronts on opposite sides of the arcs moved in different directions in the maps.

Figure 1A shows, for a selected canine heart experiment, the reentry activation map for the first cycle of tachycardia after onset in which the cycle length had stabilized, which was determined as described previously for this model. Activation maps were made by automatically marking activation times of electrogram signals by slope and peak criteria and printing the times for all sites on a computerized map grid. Arcs of block separated sites in which activation differed by 40 ms and where wave fronts on opposite sides of the arcs moved in different directions in the maps.

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Figure 1. Maps used for skeletonization procedures. A, Reentry activation map. B, Skeletonized reentry map. C, Sinus-rhythm pace map. D, Sinus-rhythm electrogram duration map. Locations of recording sites are shown by small numbers that indicate activation time (C), and anatomic landmarks are labeled (A). See text for abbreviations.
to areas of short (<40-ms) electrogram duration. Path length was then equal to the summed lengths of the piecewise linear segments.

The above mapping and skeletonization procedure was initially done by one person (observer 1). Best-subsets linear regression (SigmaStat V2.0, Jandel Scientific) was used to describe significant relationships ($P<0.001$) between the skeletonized parameters and the tachycardia cycle length, which was measured from the R-R interval of the ECG. To assess measurement reproducibility, another arbitrary cycle of sinus rhythm and a cycle of tachycardia near termination were mapped and skeletonized by the same person (observer 1). Thereafter, a second person (observer 2) mapped, for skeletonization, the same cycles of sinus rhythm and ventricular tachycardia as observer 1. The Pearson product moment correlation (SigmaStat V2.0, Jandel Scientific) was used to analyze the agreement in skeletonized parameters measured for different cardiac cycles by the same observer and also between the 2 observers.

The significant correlation coefficients ($P<0.001$) determined from the 20 training-set canine heart experiments were used to assess 5 test-set canine heart experiments. For each test-set experiment, the reentry cycle length measured from the ECG R-R interval, in conjunction with the linear regression coefficients determined from the training-set experiments, was used to provide an estimate of the isthmus geometry (shape and orientation). Because the estimate of skeletonized angle with respect to muscle fiber orientation was unsigned, for simplicity it was chosen in the direction for best overlap with the actual reentry arcs of block determined from activation mapping. To quantify overlap, the isthmus centers were made coincident on the computerized grid, and as a first approximation, the narrowest width was drawn at the center of the estimated isthmus. The center of the actual isthmus was taken as the mean XY location of the 4 end points of the arcs of block, and the center of the skeletonized isthmus was taken as the midpoint of the angle vector. The area percent by which the skeletonized isthmus overlapped the actual isthmus was then computed for each test set.

### Results

Figure 2 shows maps of selected skeletonized isthmus parameters for each experiment, from the measurements of observer 1, with the maps ordered according to cycle length. The reentry circuit of Figure 1 is shown in panel I. Isthmus with greatest cycle length tended to be larger in both length and width (A through L). In many of the maps, the wave front propagates through the reentry isthmus toward the LAD basal margin. There is no evident relationship of cycle length with XY location. The mean skeletonized circuit from the 20 training-set experiments is shown in Figure 3. Mean skeletonized isthmus length, width, and narrowest width were 20.3 mm, 18.4 mm, and 10.8 mm, respectively, and mean tachycardia cycle length was 198.8 ms. The mean isthmus angle was $23.4^\circ$ to the left of vertical in the map, approximately in line with muscle fiber orientation at the mean XY isthmus location for all experiments. The isthmus is narrowed near its center, and slower conduction occurs there and at the pivot points around the arcs of block. Conduction velocity is rapid at the isthmus exit and along the straightaway locations outside the isthmus.

![Figure 2. Summary of skeletonized geometric variables for 20 canine experiments (isthmus length, width, narrowest width, angle, and XY location in infarct border zone are shown in each panel). Narrowest width is drawn at isthmus center for simplicity.](http://circ.ahajournals.org/content/multimedia/CIR-1083-Fig2.jpg)

![Figure 3. Mean skeletonized reentry circuit parameters from measurements of all experiments. LAT indicates lateral.](http://circ.ahajournals.org/content/multimedia/CIR-1083-Fig3.jpg)
The Table shows significant correlation relationships between skeletonized variables at the onset of stable tachycardia cycle length. Tachycardia cycle length (CL) is highly correlated with the path length (PL) determined during sinus rhythm (Equation $\alpha$). There is a second-order relationship between skeletonized isthmus length and width (Equation 1), isthmus length and angle are correlated with cycle length (Equations 2 to 4), and narrowest width is correlated with width (Equation 5). The correlation in skeletonized parameters measured for different cardiac cycles by the same observer, and also between the 2 observers, was significant ($P<0.02$).

From the reentry cycle length measured by use of the R-R interval of the ECG and the coefficients of Equations 1 and 3 to 5 in the Table, isthmus geometry was assessed for 5 test-set experiments, and the result is shown in Figure 4. In each experiment, the original arcs of block locations from the reentry activation maps are shown as black, and the estimated locations from skeletonized geometry coefficients are shown as gray. The actual and estimated arcs of block are more nearly coincident when the actual arcs of block were approximately parallel (A through C), because the skeletonization process did not account for relative differences in orientation between the 2 arcs. There was a mean overlap of 70.5% for the 5 test-set experiments. Equation $\alpha$ was then used to estimate tachycardia cycle length from the path length determined from sinus-rhythm data in each test-set experiment, with good agreement with the actual cycle length (mean difference between estimated/actual cycle length was $6.2\pm2.5$ ms).

**Discussion**

**Tachycardia Cycle Length and Skeletonized Parameters**

The skeletonized length and angle in tandem were highly correlated with cycle length (Table, Equation 2), as might be anticipated because isthmus length contributes to the circuit path length, whereas isthmus angle contributes to conduction velocity around the path; path length and conduction velocity

![Table: Significant Correlation Relationships Between Variables](image)

<table>
<thead>
<tr>
<th>Equation</th>
<th>$r^2$</th>
<th>Relationship</th>
<th>Regression Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$</td>
<td>0.90</td>
<td>Cycle length, path length</td>
<td>$CL = 89.91 + 0.64PL$</td>
</tr>
<tr>
<td>1</td>
<td>0.83</td>
<td>Isthmus width, length</td>
<td>$W = -6.77 + 2.66L - 0.061L^2$</td>
</tr>
<tr>
<td>2</td>
<td>0.75</td>
<td>Cycle length, isthmus length, angle</td>
<td>$CL = 130.16 + 1.79L + 0.87A$</td>
</tr>
<tr>
<td>3</td>
<td>0.54</td>
<td>Isthmus angle, cycle length</td>
<td>$A = -48.34 + 0.43CL$</td>
</tr>
<tr>
<td>4</td>
<td>0.54</td>
<td>Isthmus length, cycle length</td>
<td>$L = -21.32 + 0.21CL$</td>
</tr>
<tr>
<td>5</td>
<td>0.37</td>
<td>Isthmus narrowest width, width</td>
<td>$W_n = 0.80 + 0.59W$</td>
</tr>
</tbody>
</table>

See text for abbreviations. Length is expressed in millimeters.
are the determinants of tachycardia cycle length. As skeletonized isthmus length increased, tachycardia cycle length tended to increase (Equation 4). Hence, isthmus length is likely to be constrained by the possible range in cycle lengths. The length of the isthmus cannot increase such that it prolongs the tachycardia cycle length beyond the time that a sinus escape beat would occur. Also, isthmus length cannot decrease below a level at which it would result in arrival of the activating wave front at a particular portion of the circuit during the relative refractory period (causing slowed conduction) and/or during the absolute refractory period (causing block). As conduction velocity diminished with increasing angle of the isthmus away from muscle fibers, tachycardia cycle length also increased (Equation 3), in agreement with experimental and theoretical studies of the anisotropic relationship between these variables.14,15 In the present study, the single cycle (static case) tachycardia cycle length near the onset of stability and also near tachycardia termination were found separately over many experiments to be directly proportional to the isthmus length during those cycles. During a particular reentry experiment, however, it was shown elsewhere in this same animal model that over many cardiac cycles (dynamic case), there is a reverse relationship between tachycardia cycle length and isthmus length because of changes in conduction velocity of the activation wave front as it traverses the slow conduction zone that occur over the course of tachycardia (ie, the isthmus lengths when cycle length decreases and shortens when cycle length increases).11

By definition, the sinus-rhythm electrogram duration parameter was a measurement of the electrical activity occurring in proximity to the recording electrode and did not include isolated late potentials (see Methods); hence, this measurement would be expected to be influenced by factors affecting local activity only, such as wave-front conduction velocity near the recording site. At tachycardia onset for the experiment whose activation map is shown in Figure 1A, relatively rapid conduction occurred as the propagating wave front coursed around the left block line (A), and sinus-rhythm electrogram duration there was relatively short (path denoted PL in D), whereas relatively slow conduction occurred around the right block line, particularly along the lateral edge of the map grid (A), and sinus-rhythm electrogram duration there was relatively long (D). The left wave front crossed the isthmus entrance ≈20 ms before the right wave front; hence, the left loop along which the electrogram duration is relatively short can be said to drive the reentry circuit and therefore the tachycardia cycle length (CL). Therefore, heterogeneity of the border zone substrate is probably reflected in the spatial variability of the electrogram duration maps (see Figure 1D) and manifested as conduction velocity variations along the path. For all experiments, conduction velocity during reentry was observed to be rapid along tracts of short sinus-rhythm electrogram duration. If such tracts, and the rapid wave fronts associated with them, extended far from the isthmus toward the periphery of the border zone, then wave-front components crossing areas of longer electrogram duration, although moving more slowly, could potentially arrive at the isthmus entrance more rapidly, thereby skewing the linearity of the CL-PL relationship (Table, Equation α).

**Interrelationships Between Skeletonized Parameters**

Figure 3 shows the mean skeletonized parameters; the mean isthmus from all experiments approximately aligns with muscle fiber orientation at the mean XY location. This phenomenon may be related to the setup of tachycardia: during premature stimulation leading to reentry onset, a unidirectional arc of block forms, and the wave front bifurcates and proceeds around it. The same wave front coalesces on the other side of the unidirectional arc and breaks through to reenter the previously excited tissue if there is sufficient delay for recovery of excitability. Wave front traversal around the arc will be slowest (hence, the greatest chance for delay necessary for reentry induction) if it propagates perpendicular to muscle fiber orientation. To meet this condition, the isthmus long axis, which generally aligns in parallel with the direction of reentry breakthrough during the premature cycle,13 would most commonly reside in parallel with muscle fiber orientation, as was observed. Also in Figure 3, the narrowest portion of the isthmus is coincident with the zone of slow conduction. This may be the result of an aperture effect in which insufficient current is available for normal activation as the wave front proceeds out of the aperture and into an area of distal expansion.16

Correlation between the skeletonized variables can potentially provide information concerning the range of possible shapes that the reentry isthmus may possess. The strong second-order relationship between skeletonized isthmus length and width (Table, Equation 1) can be stated as follows. When the reentry isthmus is narrow in this canine model, it tends to be either long or short in length, and when it is wide, it tends to be of intermediate length. An isthmus having large dimensions of both length and width may be uncommon, because the path length could prolong tachycardia cycle length to the extent that a sinus-rhythm escape beat would capture conduction of the heart. Were the isthmus very short and wide, which is also uncommon in this model, the activating wave front would no longer be constrained to enter the isthmus at an angle approximately in parallel with the bounding arcs of block. One end of the wave front, for example, might cross the isthmus exit while the other edge lagged behind at the isthmus entrance. This could act to destabilize the excitable gap,17 which depends in part on synchronicity of conduction along symmetrical portions of the circuit to be maintained, and therefore act to destabilize the functional arcs of block that bound the reentry isthmus. The relationship between isthmus width and narrowest width (Equation 5) suggests that block lines bounding the isthmus are often tapered inward by a constant proportion, regardless of the magnitude of isthmus width.

**Clinical Implications of Skeletonized Geometry**

When a standard ablation catheter is used during clinical electrophysiological study, most methods for targeting sites rely on measurement of border-zone parameters that can be related to reentry isthmus geometry.1–3 For example, concealed entrainment methods are based on timing considerations between electrical activation at the pace site and features of the ECG signal,1,3–6 but the success rate is varied.
Depending on isthmus width, if the site location were within the isthmus but off center with respect to the midline, the ablation lesion could actually serve to reinforce any arc of block bounding the isthmus that is adjacent to the ablation electrode. It could also potentially constrict the isthmus without complete interruption of the circuit. The effect of any such isthmus stricture caused by an ablation lesion might be to decelerate conduction velocity and prolong cycle length, as has been observed during a clinical study, because current infused to areas distal to the stricture in the circuit is diminished. If for clinical study, isthmus shape could be estimated by use of skeletonized regression coefficients in conjunction with a measurement of tachycardia cycle length from the ECG R-R interval, it would be of potential benefit for targeting ablation sites to know a priori the characteristics of the isthmus that are of importance for determining the best lesion length and orientation. Ideally, measurement of tachycardia cycle length from the patient’s ECG would be done before electrophysiological study, recorded, for example, with a Holter monitor, so that ablation therapy could be planned accordingly. The skeletonized isthmus angle estimate described here is unsigned; hence, there are 2 possible orientations with respect to muscle fiber direction (+/−). For the measurement to be useful, therefore, it would be necessary during clinical therapy to have some knowledge of the propagation direction through the isthmus, for example, by consideration of proximal and distal activation times when the catheter tip is located in proximity to the reentry circuit.

The reentry circuit path length, which was measured by use of the sinus-rhythm electrogram duration parameter, was also found to be highly correlated with tachycardia cycle length measured from the ECG R-R interval. On the basis of the correlation coefficient derived from this measurement and the path length determined from sinus-rhythm electrogram duration maps, tachycardia cycle length was correctly estimated (mean error 6.2±2.5 ms). Estimation of tachycardia cycle length before tachycardia induction during clinical study, using isthmus boundaries determined from sinus rhythm measurements, is potentially useful to gauge toleration of the tachycardia by the patient and the effect of any arrhythmic drug to be administered during tachycardia, both of which are in part rate-dependent.

**Limitations and Future Directions**

Isthmus arcs of block were localized by spline interpolation to 0.1 mm, which was beyond the 4- to 5-mm resolution of the multielectrode array but consistent from one activation map to the next. Any inaccuracy in placement of the arcs of block may serve to decrease the significance of correlation between variables; higher electrode spatial resolution may reveal other geometric variables with significant correlation. The simple measurements used to gauge isthmus geometry are not indicative of subtle features of the circuit. For improved representation, more sophisticated geometric measurements might be useful; however, the complexity of analysis would increase. At present, it is unknown how the properties of functional circuits for the canine model described here might apply to ventricular tachycardia circuits in human patients, in whom the isthmus may more frequently be bounded by anatomic arcs of block. Use of an anatomic model of reentry in canine hearts might better serve to describe some reentry episodes in humans with parameters of skeletonized geometry. Skeletonized geometry methods may also be useful to assess the effect of isthmus orientation with respect to muscle fibers on the action of antiarrhythmic drugs that preferentially impede conduction in either the longitudinal or transverse direction.

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