Electroanatomic Mapping of Entrained and Exit Zones in Patients With Repaired Congenital Heart Disease and Intra-Atrial Reentrant Tachycardia

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Background—Characterization of reentrant circuits and targeting ablation sites remains difficult for intra-atrial reentrant tachycardias (IART) in congenital heart disease (CHD).

Methods and Results—Electroanatomic mapping and entrainment pacing were performed before successful ablation of 18 IART circuits in 15 patients with CHD. Principal features of IART circuits were atrial septal defect (4 patients), atriotomy (3 patients), other atrial scar (3 patients), crista terminalis (3 patients), and right atrioventricular valve (5 patients). A median of 176 sites (range, 96 to 317 sites) was mapped for activation and 13 sites (range, 9 to 28 sites) for entrainment response. Postpacing intervals within 20 ms of tachycardia cycle length and stimulus–to–P-wave intervals of 0 to 90 ms (exit zones) were mapped to atrial surfaces generated by electroanatomic mapping. Criteria for entrainment were met over a median of 21 cm² of atrial surface (range, 2 to 75 cm²), 19% (range, 1% to 81%) of total area tested. Using integrated data, relations between activation sequence and protected corridor of conduction could be inferred for 16 of 17 IARTs. Successful ablation was achieved at a site distant from the putative protected corridor in 9 of 18 (50%) circuits.

Conclusions—The right atrium in CHD supports a variety of IART mechanisms. Fusion of activation and entrainment data provided insight into specific IART mechanisms relevant to ablation. (Circulation. 2001;103:2060-2065.)

Key Words: atrial flutter ■ heart defects, congenital ■ catheter ablation

Considerable knowledge has been developed regarding the causes of intra-atrial reentrant tachycardia (IART) in congenital heart disease (CHD). Awareness of the morbid significance of IART has prompted application of a variety of therapies, but none has proved highly effective for arrhythmia suppression. Catheter ablation has been used to target specific arrhythmia circuits. Although short-term ablation outcomes are satisfactory,1-3 long-term recurrence is common.4 Knowledge of recurrent IART patterns and underlying atrial features1 and application of new electrophysiological imaging technologies that are well referenced to the spatial geometry of the mapped atrial chamber may improve these outcomes. However, the complexity of the atrial substrate renders even these data ambiguous in many cases.

The current study investigates the application of data fusion techniques to characterize specific IART circuits, with particular reference to the location and geometry of protected conduction corridors that may be arrhythmogenic or vulnerable to ablation. Electroanatomic IART activation maps were combined with functional electrophysiological measurements, made at multiple sites, consisting of the response to entrainment pacing and identification of P-wave exit zones related to emergence of the IART wave front from protected conduction corridors.

Methods

Patient Population

The study group consisted of patients with CHD referred to Children’s Hospital, Boston, Mass, before April 2000 for ablation of IART. This study includes patients in whom electroanatomic mapping and systematic entrainment pacing studies were performed, followed by successful short-term termination of IART by ablation. Informed consent was obtained in accordance with Hospital policies. Patients were studied under general anesthesia after hemodynamic evaluation.

Electroanatomic Mapping

IARTs were mapped using the CARTO system ( Biosense Webster). Validation of this technology and of its use in CHD has been reported.5-8 An interscapular location reference sensor was applied and an atrial reference electrode placed to record left atrial activation, either from the coronary sinus or transesophageally. Activation mapping was performed by initial systematic sampling of the entire atrial endocardial surface, followed by more detailed mapping of areas of interest and entrainment pacing. Simultaneous recordings of
in intracardiac electrograms and 12-lead surface ECG were obtained (CardioLab, Prucka Engineering, Inc). Recordings from the 2 systems were cross-referenced manually.

**Entrainment Pacing**

Entrainment pacing was performed at a variable number of sites in the right atrium. Each site was paced at a cycle length 5 to 25 ms shorter than the tachycardia cycle length. If capture was demonstrated by shortening of the paced intervals, and the tachycardia cycle length, P-wave morphology, and intracardiac activation sequence were identical, then the postpacing interval was determined as the return cycle length at the distal electrode of the pacing catheter. If a return cycle electrogram was not visible on the distal electrode, the proximal electrode pair electrogram was used under the following conditions: (1) a recording immediately before pacing demonstrated the temporal relation between the distal and proximal electrograms, and (2) the morphology of the proximal electrogram was unchanged with pacing. If the difference between the postpacing interval and the tachycardia cycle length was ≤20 ms, the point was deemed to lie within the entrained zone comprising the primary tachycardia circuit.

**Determination of Exit Zones**

An idealized model of the IART mechanism and its relation to the measurements described below is presented in Figure 1. Stimulus–to–P-wave intervals were determined by inspection of the P wave in 12 leads during tachycardia and identification of the electrocardiographic signature of baseline inflections. If an identical electrocardiographic pattern of P-wave onset could be identified during an entrainment pacing sequence, the duration from stimulus to P wave was recorded. The exit zone from a protected conduction corridor was defined as the region of the atrium with stimulus–to–P-wave intervals of 0 to 90 ms.

**Spatial Measurements**

The density and homogeneity of sampling of the atrial surface with entrainment pacing were estimated by point-to-point measurements obtained using the CARTO system. Entrainment sampling density (D) was calculated as the mean proximity of each entrained point to its 3 nearest neighbors. Each point was considered to sample a circular area A, calculated as \( A = \pi (D/2)^2 \) cm². Total coverage of the atrium by entrainment study was calculated as the sum of areas covered by entrainment.

**Data Fusion**

Activation sequence maps were overlaid with electroanatomic maps of entrained and exit zones. These maps were created by using the CARTO system to map binarized entrainment pacing data onto the spatial framework that had been developed during activation mapping (Figure 2) and overlaid on activation sequences using Photoshop (Adobe). For entrainment, points that were in the circuit were mapped in red, whereas those out of the circuit were mapped in purple. For identification of exit zones, points with a stimulus–to–P-wave interval of 0 to 90 ms were mapped in red, whereas other points were mapped in purple. Colors were linearly interpolated between adjacent points.

**Statistics**

Data are summarized as mean±SD or median (range). Comparisons of means and medians are made using t test and Wilcoxon rank-sum test as appropriate, with P<0.05 considered significant.

**Results**

**Patient Population**

Fifteen patients were studied (5 female; median age, 24 years; range, 3 to 50 years). Six patients had had biventricular surgical repairs for tetralogy of Fallot (2 patients), total anomalous pulmonary venous connection (1 patient), atrial septal defect (1 patient), pulmonary atresia with ventricular septal defect (1 patient), and corrected transposition of the great vessels with ventricular septal defect (1 patient). One patient had unrepaird biventricular anatomy (Ebstein’s anomaly variant with giant right atrium). Seven patients had had a Fontan procedure by creation of either a right atrial–pulmonary artery anastomosis or right atrial–right ventricular conduit: tricuspid atresia (4 patients) and single ventricle (3 patients). One patient with single right ventricle had had a bidirectional Glenn anastomosis.

**Descriptions of Tachycardia Circuits**

Entrainment mapping was performed for 18 IART circuits. One patient had 3 and another had 2 circuits mapped. Median
tachycardia cycle length was 313 ms (range, 177 to 384 ms). A median of 176 sites per circuit (range, 96 to 317 sites per circuit) was mapped for activation, and a median of 13 sites per circuit (range, 9 to 28 sites per circuit) was mapped for entrainment. Entrainment pacing cycle lengths were chosen to be 10 to 20 ms shorter than tachycardia cycle length; this resulted in observed entrainment pacing cycle lengths with a mean prematurity of 15 ms (5.3% of mean tachycardia cycle length) that ranged from 86% to 98% of the tachycardia cycle length.

Dimensions, Locations, and Coverage of Tachycardia Circuits

Linear dimensions and volumes of the atria studied are presented in Table 1. Indexed for body surface area, the volumes of the atria of Fontan procedure patients were nearly twice those of biventricular repair patients. Two hundred seventy entrainment sites were evaluated, 103 of which met criteria for entrainment. The mean interpoint distance measured for entrained points was 2.2 ± 1.0 cm, versus 2.8 ± 1.2 cm for nonentrained points (P < 0.001). This difference suggests an operator bias to sample areas of the heart demonstrated to be in circuit more thoroughly than those not in circuit. A median of 89 cm² of right atrial endocardial surface (range, 19 to 178 cm²) was evaluated by entrainment pacing (Table 2). Although total atrial surface area is not available by this technique, these values are of comparable magnitude and somewhat smaller than the surface area of a sphere with a 7-cm diameter (154 cm²). A median of 4.5 sites per circuit mapped met entrainment criteria (range, 1 to 13 sites per circuit), covering a median of 21 cm² (range, 2 to 75 cm²) and accounting for 19% of the total mapped right atrial surface area (range, 1% to 81%).

Location of Entrained and Exit Zones in Isthmus-Dependent Atrial Flutter

Five patients had isthmus-dependent atrial flutter confirmed by activation mapping and response to ablation. In 4 cases, the entrained zone completely or nearly encircled the atrioventricular (AV) valve annulus, with variable posterior extension of the zone to include portions of the septum, right atrial free wall, and lateral right atrial wall. Exit zones were observed at the medial isthmus and atrial septum. In 1 case, the entrained zone failed to include the isthmus but did include the superior aspect of the tricuspid annulus. An example of isthmus-dependent atrial flutter from the present series is given in Figure 3.

Case Examples

Figure 4 demonstrates entrainment mapping of IART in a patient who had had a Fontan procedure. The activation sequence had 2 conduction pathways, indicated by yellow arrows. Mapping of entrained and exit zones demonstrated that the lower loop was primary, with a presumed corridor extending anteriorly in this region from the crista terminalis. Ablation at the site of the yellow star resulted in abrupt slowing, with shift of the entrained zone to the upper limb of the circuit. IART was terminated by cephalad extension of the radiofrequency (RF) application.

Figure 5 demonstrates complex activation in the lateral right atrium of a patient who had had a Fontan procedure. White arrows highlight an apparent corridor (left) where unsuccessful RF applications were made. Mapping of entrainment revealed that only a small area (∼1% mapped atrial surface) met entrainment criteria. The exit zone encompassed much of the anterior right atrial surface, which activated rapidly. Successful RF applications were made in the gap between entrained and exit zones.

### TABLE 1. Dimensions and Volumes of Mapped Atria

<table>
<thead>
<tr>
<th>Dimension of Axes, cm</th>
<th>Median</th>
<th>Range</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major</td>
<td>9.2</td>
<td>4.8–11.4</td>
<td></td>
</tr>
<tr>
<td>Semi-minor</td>
<td>7.0</td>
<td>3.3–9.4</td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>5.6</td>
<td>3.1–8.0</td>
<td></td>
</tr>
<tr>
<td>Measured right atrial volume, cm³</td>
<td>199</td>
<td>23–433</td>
<td></td>
</tr>
<tr>
<td>Indexed right atrial volume,† cm³/m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biventricular repair (n=6)</td>
<td>70</td>
<td>37–136</td>
<td>0.032</td>
</tr>
<tr>
<td>Fontan palliation (n=7)</td>
<td>133</td>
<td>94–223</td>
<td></td>
</tr>
</tbody>
</table>

*Wilcoxon test.
†Two patients who had neither Fontan procedure nor repaired biventricular anatomy are not included in comparisons of indexed atrial volume.

### TABLE 2. Coverage of Atrial Surface by Entrainment Mapping

<table>
<thead>
<tr>
<th>Entrainment Sites Per Circuit, n</th>
<th>Total</th>
<th>In Circuit</th>
<th>Percentage of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entrainment sites per circuit</td>
<td>13 (9–28)</td>
<td>4.5 (1–13)</td>
<td>31% (8%–73%)</td>
</tr>
<tr>
<td>Endocardial area tested for entrainment, cm²</td>
<td>89 (19–178)</td>
<td>21 (2–75)</td>
<td>19% (1%–81%)</td>
</tr>
</tbody>
</table>

*Values are median (range) or percentage.
Relation of Successful Ablation Sites to Entrained and Exit Zones

The location of successful ablation sites in relation to entrained and exit zones is presented in Figure 6. Entrained zones are diagrammed as outlined areas, exit zones are vertically hatched, and an arrow represents the direction of the activation wave front. These 3 features of the IART circuit defined a path that included the successful ablation site in 17 of 18 circuits. In 13 circuits, the entrained and exit zones overlapped (Figure 6B), and in 4 circuits a gap existed between the two (Figure 6A). A single isthmus-based atrial flutter (see above) had a site of successful ablation that was not clearly related to the mapped circuit. When supported by data from activation mapping, overlaps or gaps were considered likely to represent protected conduction corridors, as per the schema presented in Figure 1. Eight of 18 circuits were successfully targeted in this area, including 4 of 5 isthmus-dependent atrial flutters. Six circuits were successfully targeted in the entrained zone at sites distant from the presumed protected area. Three circuits were successfully targeted in neither the entrained nor the exit zones but in an area lying between the two, which was plausibly included in the circuit by activation sequence mapping.

Discussion

In this report, atrial reentrant tachycardias were mapped in patients with a broad spectrum of repaired CHD by superimposition of data describing the functional properties of the tachycardia circuit—response to entrainment pacing—onto activation sequence maps of those tachycardias. The validity of this approach was tested in 5 patients who had a right AV valve (4 tricuspid and 1 mitral). These patients had maps constructed of isthmus-dependent atrial flutter, ie, counterclockwise rotation of an activation wave front around the right AV valve annulus. In 4 of 5 cases, the entrained zones encircled (or nearly encircled) the right AV annulus, were bounded posteriorly by the inferred location of the crista terminalis, and demonstrated exit zones at the base of the atrial septum.

Extension of these observations to complex circuits anchored to central obstacles other than the AV valve annulus allowed distinction of bystander tissue from atrial tissue critical to the arrhythmia circuit. We were also able to infer the locations of protected conduction corridors and their relations to anatomic and presumed surgical lines of conduction block. Identification of these areas sometimes showed that sites that might have been deemed optimal for attempted RF ablation were not, in fact, those locations in which successful ablation lesions were placed. Mapping the atria in this manner also revealed that entrainable wave fronts in atrial reentrant tachycardias may in places be broad and that fractional right atrial surface area that is considered in circuit is sizable. This may explain why favorable entrainment responses during atrial reentrant tachycardias do not necessarily have a high positive predictive value, although...
Characterization of IART Circuits

A variety of anatomic substrates were characterized underlying this relatively small sample of arrhythmias by superposition of activation latency and multisite entrainment mapping data. A complex and effective example of this is demonstrated in Figure 7, which shows the use of entrainment mapping to characterize a macroreentrant circuit using segments of the atrial septum and the left atrium. Prior studies suggest diverse arrhythmogenic substrates for IART. Central obstacles presumably related to surgical and hemodynamic injury include fixed lines of conduction block at atriotomy and cannulation sites and areas of electrically silent and presumably inexcitable tissue traversed by channels of surviving atrial myocardium.8 Isthmus-dependent atrial flutter circuits are often identified in patients with CHD (particularly after biventricular repairs) and are successfully ablated in the smallest demonstrated circuits using an atrial septal defect patch and right pulmonary veins as central obstacles. Lateral left (LA) and right (RA) atria, right pulmonary veins, and superior right septal surface fail to meet an entrainment criterion of difference between postpacing interval and tachycardia cycle length of <20 ms. IVC indicates inferior vena cava.

Unfavorable entrainment responses have a high negative predictive value for ablation success.2

Positive Predictive Value of Entrainment Pacing

The size of measured entrained zones in these macroreentrant circuits varied widely, signifying diverse right atrial mechanisms. The fraction of atrial endocardial points meeting the common entrainment criteria used in this study was generally large, averaging ≈30%. Operator bias in favor of checking points likely to meet entrainment criteria is a potential limitation of this study. However, examination of the interval between entrained and nonentrained areas indicates that this effect was minor, and the fraction of the endocardial surface tested for entrainment that was in circuit was still ≈20%. This suggests that targeting sites for ablation solely by entrainment may have a low positive predictive value for success.

Anatomic visualization of entrainment zones may thus have practical value for our understanding of entrainment as a clinically useful technique. No standard criterion for the difference between the postpacing interval and the tachycardia cycle length signifying in-circuit response to entrainment has been validated experimentally. At any entrained site, this difference is a function of both distance of the site from the tachycardia circuit and conduction velocity between the site and the circuit. Mapping of entrainment in the proposed manner allows the tradeoff between sensitivity and positive predictive value of entrainment pacing to be visualized anatomically. As the criterion for entrainment is relaxed (eg, from 20–30 ms), the entrained area, channel width and, hypothetically, the sensitivity of the technique will also increase. At the same time, relaxation of the entrainment criterion will diminish its positive predictive value and
probably increase the need for additional criteria for choice of ablation site, such as observation of mid-diastolic potentials.19 Conversely, imposing a more stringent criterion for entrainment (eg, from 20 to 10 ms) will have the opposite effects. In our experience, measurements of entrainment made at a single site may vary by as much as 5 to 10 ms, and our choice to designate entrainment as occurring with a threshold of 20 ms in timing difference reflects both a balance between these 2 competing issues and concordance with the range of values used by other investigators.19,20

Limitations

Entrainment maps were constructed after ablation, and entrained sites were sampled in a sparse and inhomogeneous distribution. This was because of the intermittent inability to capture atrial tissue or to measure accurately low-amplitude, postentrainment atrial signals. Mapping of 10 to 20 points may be insufficient to completely define circuits by entrainment mapping. In this study, anatomic understanding of these lower resolution maps was enhanced by superposition of the data onto higher-resolution activation maps.

There was an apparent bias to map entrainable sites more densely in areas considered by other criteria (eg, activation sequence and anatomic knowledge) to represent plausible target sites for ablation. A geometric correction based on the distance between each point and its nearest neighbors was made in an effort to correct for this, but there remains an unknown amount of error in the estimates of entrained and nonentrained surface area.

Acknowledgments

Dr Alexander was supported in part by a grant from the National Heart, Lung, and Blood Institute (RO1-HL02385); Dr Bevilacqua was supported by a grant from the Hood Foundation; and Dr Berul was supported by grants from the National Institutes of Health (K08-HL03607 and P50-HL61036).

References

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Circulation. 2001;103:2060-2065
doi: 10.1161/01.CIR.103.16.2060
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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