Electrical Remodeling of the Atria Associated With Paroxysmal and Chronic Atrial Flutter

Paul B. Sparks, MBBS, PhD; Shenthar Jayaprakash, MD; Jitendra K. Vohra, MD; Jonathan M. Kalman, MBBS, PhD

**Background**—Atrial electrical remodeling may be important for the initiation and perpetuation of atrial arrhythmias. Whether paroxysmal atrial flutter (AFL) and chronic AFL cause electrical remodeling of the atria has not been conclusively determined.

**Methods and Results**—Before radiofrequency ablation of paroxysmal AFL, 15 patients in sinus rhythm were evaluated under autonomic blockade. Lateral right atrial (LRA) effective refractory periods (ERPs) at 600 and 450 ms were measured before and at 1-minute intervals for 10 minutes after spontaneous or pace termination of a 5- to 10-minute period of induced AFL. In 10 patients with chronic AFL, LRA, septal, and coronary sinus (CS) ERPs and corrected sinus node recovery times (cSNRTs) at 600 and 450 ms were measured under autonomic blockade 15 minutes, 30 minutes, and 3 weeks after termination of chronic AFL by ablation. In the paroxysmal AFL group, LRA ERPs decreased by 18% at 600 ms and 12% at 450 ms (P < 0.01) after induced AFL and recovered to baseline over ~5 minutes. Atrial fibrillation developed during AFL in 3 patients and during ERP testing in 3 patients when refractoriness was at its nadir. In the chronic AFL group, LRA, septal, and CS ERPs at 3 weeks were significantly greater than at 15 and 30 minutes after termination of chronic AFL at both cycle lengths (P < 0.01). Three weeks after ablation, cSNRT decreased 35% at 600 ms (P < 0.05) and decreased 44% at 450 ms (P < 0.05). Both ERPs and cSNRTs measured 15 and 30 minutes after ablation of chronic AFL were not significantly different.

**Conclusions**—Both paroxysmal AFL and chronic AFL cause reversible electrical remodeling of the atria but demonstrate different time courses of recovery. (*Circulation. 2000;102:1807-1813.*)

**Key Words:** ablation ■ fibrillation ■ atrial flutter ■ remodeling

Electrical remodeling of the atrium has been clearly demonstrated both in animal models and in humans.1–4 Experimental studies have shown that atrial fibrillation (AF) begets AF predominantly because of a fall in atrial effective refractory periods (ERPs), suggesting that this may contribute to the development of the chronic form of the arrhythmia.1,2 Several minutes of pacing-induced AF in humans is sufficient to abbreviate atrial refractoriness for up to 8 minutes, facilitating the subsequent induction and perpetuation of AF.3,4 However, these studies have been performed mostly in patients without clinical AF, and there is a relative lack of data demonstrating the phenomenon of electrical remodeling in humans with paroxysmal or chronic atrial arrhythmias.

Atrial flutter (AFL) accounts for ~15% of supraventricular arrhythmias and frequently coexists with or precedes AF.5–10 Recent data suggest that chronic AFL may also produce electrical remodeling in a fashion similar to that observed with AF, but whether this is a reversible phenomenon and whether paroxysmal AFL is also associated with electrical remodeling are unknown.11 This is of importance because it raises the hypothesis that AFL might contribute to the development and/or maintenance of AF by way of electrical remodeling.

We prospectively evaluated the effects of both paroxysmal and chronic AFL on atrial electrophysiological properties to determine whether this arrhythmia produces electrical remodeling. Studies were performed in patients undergoing radiofrequency ablation (RFA) of AFL.

**Methods**

**Paroxysmal AFL Group**

The study population comprised 15 patients undergoing RFA of paroxysmal AFL (Figure 1). Demographic details are presented in Table 1. Antiarrhythmic drugs, including calcium blockers, were ceased >5 half-lives before ablation, and no patients received amiodarone in the 6 months before study. Patients gave written informed consent to the study, which was approved by the Board of Medical Research of Royal Melbourne Hospital.

**Paroxysmal AFL Definition**

Paroxysmal AFL was defined by a history of ≥3 episodes of typical AFL confirmed by its characteristic ECG appearance.6,12,13 Patients in this group had reverted spontaneously or were overdrive paced or electrically cardioverted >1 month before RFA. All patients were in sinus rhythm immediately before ablation, and no patient described symptoms referable to paroxysmal AFL in the 4 weeks before
Ablation. Paroxysmal AFL duration was defined as the time between the initial diagnosis and the time of ablation.

**Electrophysiological Study**

Intracardiac electrodes were placed in the lateral right atrium (LRA), coronary sinus (CS), His bundle, and tricuspid annulus positions as previously described. An 8F ablation catheter was positioned in the subeustachian isthmus for entrainment mapping and RFA. Pharmacological autonomic blockade was administered (atropine 0.04 mg/kg IV and propranolol 0.2 mg/kg IV) over 10 minutes. The doses of atropine and propranolol were 24 ± 6 mg and 12.5 ± 3.0 mg, respectively.

Ten minutes after autonomic blockade, ERPs were evaluated from the LRA and distal CS at twice the diastolic threshold (for a pacing threshold of 0.2 mA) at cycle lengths (CLs) of 600 and 450 ms. Baseline ERPs were measured 3 times and averaged. The ERP was determined by use of an 8-beat S1 drive and an incremental technique starting with an S2 coupling interval of 160 ms and increasing by 5 ms. This technique was used to minimize the possibility of inducing AF or AFL. ERP was defined as the longest S1 S2 coupling interval failing to propagate to the atrium. Archived digital images were used to ensure stable catheter positioning during the study.

**AFL Induction**

After baseline ERP measurement, typical AFL was induced by pacing from the CS. Incremental pacing was performed until unidirectional block in the isthmus was demonstrated by a change in activation sequence on the tricuspid annulus catheter (Figure 2). Pacing was discontinued immediately when this was observed. AFL was induced without the development of transitional AF so that the effects of AFL on refractoriness could be evaluated in isolation.

<table>
<thead>
<tr>
<th>TABLE 1. Paroxysmal AFL Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, n</td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>Male, n</td>
</tr>
<tr>
<td>History of paroxysmal AFL, mo</td>
</tr>
<tr>
<td>Paroxysmal AF, n</td>
</tr>
<tr>
<td>Ischemic heart disease, n</td>
</tr>
<tr>
<td>ASD repair, n</td>
</tr>
<tr>
<td>Aortic valve replacement, n</td>
</tr>
<tr>
<td>LA, cm</td>
</tr>
<tr>
<td>LVEDD, cm</td>
</tr>
</tbody>
</table>

ASD indicates atrial septal defect; LA, left atrial; and LVEDD, left ventricular end-diastolic diameter.

Patients in whom AFL could not be induced (n = 4) or in whom AF developed during the induction protocol (n = 2) were excluded. The flutter mechanism was confirmed on the basis of counterclockwise activation sequence in the RA in the frontal plane, manifest entrainment from the high right atrium, and concealed entrainment from the isthmus.

**AFL Termination and ERP Assessment**

After 10 minutes of AFL, the arrhythmia was pace terminated with a 1- to 8-beat train delivered from the isthmus at a CL 40 to 60 ms below the flutter CL. Because pace termination of AFL may be associated with intra-atrial reentry lasting >1 second (considered unlikely to have a significant effect on refractoriness), a transitional atrial rhythm lasting >1 second before termination of AFL did not exclude patients from subsequent evaluation (Figure 3). Patients developing longer-lasting AF during pace termination were excluded from further assessment because of the known effects of AF on atrial refractoriness (n = 2). If AFL terminated spontaneously 5 to 10 minutes after its initiation, ERP measurements were made at that time.

On reversion to sinus rhythm, ERPs from the LRA were evaluated at alternating drive CLs of 600 and 450 ms. Measurement of ERP was made at each CL immediately on reversion and at 1-minute intervals for 10 assessments after termination of AFL. These measurements are designated ERP1 through ERP10. To estimate the temporal change in ERP, the time from reversion of AFL to each ERP was measured to the
nearest second. Development of AF during AFL or induction of AF during ERP determinations precluded subsequent measurements.

### Chronic AFL Group

The study population comprised 10 patients undergoing RFA of chronic AFL (Figure 1). The patients had documented AFL for 17±18 months (range, 2 to 60 months) and had failed a mean of 2.1±0.4 antiarrhythmic drugs before ablation (Table 2). Antiarrhythmic drugs, including calcium blockers, were stopped ≥5 half-lives before ablation. No patients were taking amiodarone.

#### Chronic AFL Definition

Typical AFL was defined by its characteristic 12-lead ECG.6,12,13 Chronicity was defined by the presence of AFL on ECG on ≥2 separate occasions separated by ≥1 month ≥1 month before ablation. All patients were in AFL at the time of the study and at the time of ablation. Duration of chronic AFL was defined as the time from initial diagnosis to the time of ablation.

#### Mechanism and Ablation of AFL

Intracardiac electrodes were placed in the LRA, CS, His, and tricuspid annulus positions as described above. An ablation catheter positioned in the subeustachian isthmus was used for entrainment mapping and delivery of radiofrequency energy.6,12,13 Digital images were archived to help replicate catheter locations for a follow-up study performed 3 weeks after ablation. After confirmation of the flutter mechanism, an anatomic approach was used to create a line of conduction block between the tricuspid annulus and the eustachian ridge.12 In all patients, ablation was performed during AFL. On termination of AFL, atrial electrophysiological properties were evaluated as described below.

#### Atrial Electrophysiology After AFL Ablation

On termination of AFL, pharmacological autonomic blockade was administered over 10 minutes as described above.14 The doses of atropine and propranolol were 2.3±0.7 and 12.2±4.5 mg, respectively.

Fifteen and 30 minutes after termination of AFL, ERPs were evaluated from the LRA, CS, and right atrial septum (RAS) via repositioning of the radiofrequency catheter at CLs of 600 and 450 ms. To estimate the variability of ERP assessments associated with catheter repositioning, the following was performed in 6 patients. After the 30-minute ERP measurements were completed, the LRA electrode was withdrawn into the inferior vena cava and then repositioned at the original LRA site as determined by archived digital images. The intrastudy variability was 4.8% for ERPs at 600 ms and 4.2% for ERPs at 450 ms.

The corrected sinus node recovery time (cSNRT) was assessed at CLs of 600 and 450 ms after a 30-second S1 pacing train 15 and 30 minutes after ablation. Pacing was performed twice from the LRA site and averaged.

### Results

#### Paroxysmal AFL Group

**Induction, Duration, and Termination of AFL**

Sustained AFL of ≥5 minutes was achieved in 15 patients. The duration of induced AFL was 8.6±2.4 minutes, excluding the time required to induce AFL (0.5±0.3 minutes). The mean CL of induced AFL was 241±14 ms. Spontaneous termination of AFL occurred in 8 patients (53%) after a period of AFL ranging from 5.2 to 9.0 minutes. Pace termination of AFL was required in 4 patients (27%) after a total AFL duration of 10 minutes. AFL degenerated into AF in 3 patients (20%) after a mean AFL duration of 7.7±1.5 minutes (Figure 4). These patients required electrical cardioversion after 15 minutes of AF and were excluded from subsequent evaluation because of the known effects of AF on atrial refractoriness.3,4

#### Atrial ERPs

Data are summarized in Tables 3 and 4 and illustrated in Figures 5 and 6. In the 12 patients in whom sinus rhythm was established after induced AFL, the LRA ERP at 600 ms decreased from 243±34 ms before AFL to 200±33 ms immediately after AFL (P<0.01). The LRA ERP at 450 ms decreased from 225±33 ms before AFL to 198±32 ms immediately after AFL (P<0.01). In 2 patients, the first captured extrastimulus after a 600-ms drive...
(at 180 and 185 ms, respectively) induced AF, and subsequent ERP determinations were not performed. In 1 patient, sustained AF was induced with the fifth ERP determination (ERP4) after a 450-ms drive (at 175 ms), and subsequent ERP testing was not performed.

Serial ERPs were measured in the remaining 9 patients, permitting estimation of the temporal recovery of atrial refractoriness (Figures 5 and 6). At 600 ms, post-AFL ERPs were lower than pre-AFL ERPs for up to 260±55 seconds (ERP4) after AFL termination (P<0.01). At 450 ms, post-AFL ERPs were lower than pre-AFL ERPs for up to 304±53 seconds (ERP4) after AFL termination (P<0.05). In 4 patients, ERPs at drive CLs of 600 and 450 ms did not return to within 10 ms of pre-AFL values after the final ERP determination.

The AFL CL did not change significantly between immediately after induction and immediately before termination of AFL (241±14 versus 239±16 ms, P=0.83).

Development of AF
Six patients developed AF during AFL or during atrial ERP determination. Of these 6, 3 patients had a history of paroxysmal AF, 2 developed AF during AFL, and 1 developed AF during ERP testing. There were no significant differences between patients who developed AF and those who did not in terms of age (61.2±10.0 versus 59.8±11.1 years, P=0.84) or left atrial size (4.2±0.5 versus 4.1±0.5 cm, P=0.72).

Chronic AFL Group

ERPs and Adaptation to Rate After Termination of Chronic AFL
The mean AFL CL of the population was 257±25 ms. RFA was successful in terminating AFL, and bidirectional isthmus block was achieved in all patients.

Complete data were available for all patients at the LRA and CS sites. ERP data at the RAS were available for 6 patients at 15 and 30 minutes and 4 patients at 3 weeks after ablation. ERPs measured 15 and 30 minutes after AFL termination were not significantly different. Results were consistent at LRA, RAS, and distal CS sites at both measured CLs (Table 5 and Figures 7 and 8). Atrial refractoriness increased significantly 3 weeks after ablation compared with ERPs measured 15 and 30 minutes.

### TABLE 3. LRA ERP at 600 ms in the Paroxysmal AFL Group

<table>
<thead>
<tr>
<th>Patients, n</th>
<th>LRA ERP at 600-ms CL, ms</th>
<th>P vs Pre-AFL ERP</th>
<th>Time Post-AFL Conversion, s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-AFL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate post-AFL</td>
<td>12</td>
<td>200±33</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ERP1</td>
<td>10</td>
<td>204±36</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ERP2</td>
<td>10</td>
<td>207±38</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ERP3</td>
<td>10</td>
<td>212±33</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ERP4</td>
<td>10</td>
<td>217±37</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ERP5</td>
<td>9</td>
<td>226±37</td>
<td>NS</td>
</tr>
<tr>
<td>ERP6</td>
<td>9</td>
<td>226±39</td>
<td>NS</td>
</tr>
<tr>
<td>ERP7</td>
<td>9</td>
<td>229±33</td>
<td>NS</td>
</tr>
<tr>
<td>ERP8</td>
<td>9</td>
<td>228±34</td>
<td>NS</td>
</tr>
<tr>
<td>ERP9</td>
<td>9</td>
<td>228±35</td>
<td>NS</td>
</tr>
<tr>
<td>ERP10</td>
<td>9</td>
<td>231±34</td>
<td>NS</td>
</tr>
</tbody>
</table>

### TABLE 4. LRA ERP at 450 ms in the Paroxysmal AFL Group

<table>
<thead>
<tr>
<th>Patients, n</th>
<th>LRA ERP at 450-ms CL, ms</th>
<th>P vs Pre-AFL ERP</th>
<th>Time Post-AFL Conversion, s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-AFL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate post-AFL</td>
<td>11</td>
<td>198±32</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ERP1</td>
<td>10</td>
<td>200±35</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ERP2</td>
<td>10</td>
<td>201±33</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ERP3</td>
<td>10</td>
<td>203±34</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ERP4</td>
<td>10</td>
<td>208±39</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ERP5</td>
<td>9</td>
<td>215±39</td>
<td>NS</td>
</tr>
<tr>
<td>ERP6</td>
<td>9</td>
<td>217±29</td>
<td>NS</td>
</tr>
<tr>
<td>ERP7</td>
<td>9</td>
<td>221±32</td>
<td>NS</td>
</tr>
<tr>
<td>ERP8</td>
<td>9</td>
<td>218±31</td>
<td>NS</td>
</tr>
<tr>
<td>ERP9</td>
<td>9</td>
<td>221±30</td>
<td>NS</td>
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<tr>
<td>ERP10</td>
<td>9</td>
<td>222±31</td>
<td>NS</td>
</tr>
</tbody>
</table>
after ablation. At LRA, RAS, and CS sites, ERPs were consistently less at a drive CL of 450 ms compared with 600 ms. This relationship was maintained at 15 and 30 minutes and 3 weeks after termination of AFL, suggesting rate adaptation of refractoriness at the CLs measured.

**SNRT After Chronic AFL Ablation**

No patients were excluded from analysis on the basis of SNRTs $>$ 1500 ms at baseline. cSNRTs 15 and 30 minutes after termination of chronic AFL were comparable (Table 5). However, a significant decrease in cSNRT 3 weeks after termination of chronic AFL at 450 and 600 ms drive CLs was demonstrated.

**Chronic Versus Paroxysmal AFL**

LRA ERPs at 600 and 450 ms 30 minutes after termination of chronic AFL were not significantly different from those measured immediately after termination of induced AFL in the paroxysmal AFL group (600 ms: 215±20 versus 200±33 ms, $P=0.22$; 450 ms: 205±16 versus 198±32 ms, $P=0.65$).

LRA ERPs at 600 and 450 ms 3 weeks after RFA of chronic AFL were not significantly different from those measured in the paroxysmal AFL group before AFL induction (600 ms: 250±16 versus 254±32 ms, $P=0.75$; 450 ms: 241±20 versus 242±20 ms, $P=0.93$). A trend toward a longer flutter CL was observed in patients with chronic AFL (239±16 ms) compared with that immediately before flutter termination in the paroxysmal group (239±25 ms, $P=0.069$).

**Discussion**

This study of patients with paroxysmal and chronic AFL presents new information regarding electrophysiological remodeling of the atria in humans. The processes of acute and

| TABLE 5. ERPs at LRA, Septum, and CS and cSNRTs (600 ms/450 ms) at 15 Minutes, 30 Minutes, and 3 Weeks After Termination of Chronic AFL |
|---------------------------------------------------------------|-------|-------|-------|-------|-------|
|                  | 15 min, ms | 30 min, ms | 3 wk, ms | $P$, ANOVA |
| LRA at 600 ms | 213±18 | 215±20 | 235±23 | <0.01 |
| LRA at 450 ms | 207±16 | 205±16 | 229±20 | <0.01 |
| Septum at 600 ms | 228±17 | 229±19 | 251±10 | <0.01 |
| Septum at 450 ms | 217±13 | 215±15 | 236±12 | <0.01 |
| CS at 600 ms | 218±18 | 215±22 | 250±16 | <0.01 |
| CS at 450 ms | 207±19 | 203±17 | 241±20 | <0.01 |
| cSNRT at 600 ms | 320±60 | 308±72 | 205±72 | <0.05 |
| cSNRT at 450 ms | 370±131 | 380±140 | 213±77 | <0.05 |
chronic atrial electrical remodeling were examined in patients with clinical atrial arrhythmias under standardized levels of autonomic tone in the absence of antiarrhythmic agents and cardioverting DC energy.

In patients with paroxysmal AFL, a 5- to 10-minute period of induced AFL is associated with a significant reduction in atrial refractoriness. This “electrical remodeling” reverses within 5 minutes of resumption of sinus rhythm in most patients.

In patients with chronic AFL, atrial refractoriness increases significantly 3 weeks after AFL termination compared with 30 minutes after cessation of the arrhythmia. However, there was no difference between ERPs measured 15 and 30 minutes after reversion. Three weeks after termination of AFL, cSNRT increases significantly compared with values soon after reversion. These findings suggest that chronic AFL promotes reversible remodeling of atrial electrical properties with a time course of recovery distinctly different from that of paroxysmal AFL.

Previous Studies of Atrial Electrical Remodeling Associated With AFL
Franz et al11 examined the monophasic action potential duration at 90% repolarization (MAPd90) in patients 15 to 30 minutes after cardioversion of AFL and compared measurements with patients cardioverted from AF and control subjects. Chronic AFL was clearly associated with shortening of the MAPd90 and depressed atrial MAPd-CL relations paralleling those observed in patients cardioverted from AF. However, serial measurements were not made to determine whether MAPd90 changed after cardioversion, and an assessment of the temporal recovery of refractoriness was not possible.16

Electrical Remodeling Associated With Paroxysmal Atrial Arrhythmias in Man
Studies in humans have demonstrated that a 5- to 10-minute period of AF produces a fall in atrial ERPs that reverses over a similar period after resumption of sinus rhythm.3,4 The magnitude and duration of ERP reduction were similar to those observed in most patients in the present study as a result of paroxysmal AFL. As in prior studies, autonomic blockade was administered to control for potential fluctuations in autonomic tone resulting from the induced arrhythmia.3 Our observations suggest that paroxysmal AFL is of sufficiently short CL (241 ± 14 ms) to induce atrial electrical remodeling. However, prior studies of short-duration AF have been conducted in patients without atrial arrhythmias or structural heart disease. In the present study, electrical remodeling was observed in patients with a clinical history of paroxysmal AFL as a result of a paroxysm of their clinical arrhythmia.

The observed interpatient variability in baseline and subsequent ERP measurements from a single fiducial right atrial site probably reflects the considerable electrical heterogeneity that exists in patients with atrial arrhythmias.17 However, the dynamic trends in refractoriness after a paroxysm of AFL were consistent across the study population, suggesting that electrical remodeling develops regardless of baseline ERPs. No specific reason for failure of refractoriness to return to normal after AFL induction could be delineated in the 4 patients in whom this was observed. Age and left atrial size were comparable to those in whom refractoriness returned to baseline. Failure to observe a return to baseline may have been a function of the time limits of our clinical protocol.

Electrical Remodeling Associated With Chronic Atrial Arrhythmias in Humans
That atrial electrical remodeling develops as a consequence of chronic AFL may be inferred from the observation that refractoriness increases 3 weeks after termination of the arrhythmia. In contrast to the rapid restitution of atrial refractoriness occurring after termination of paroxysmal AFL, significant shortening of refractoriness persisted for ≥30 minutes in the chronic AFL group. This suggests that more prolonged AFL is associated with more slowly reversing electrical remodeling and possibly a different mechanism. Because autonomic blockade was administered at the time of ERP assessments, changes in autonomic tone are unlikely to have contributed to the changes in refractoriness. Our obser-
vations support other evidence from humans demonstrating that chronic AF–related electrical remodeling develops and may reverse after cardioversion.18

The present study suggests that adaptation of ERP to rate is present after termination of chronic AFL. This observation is consistent with the work of Pandozzi et al14 and Kamalvand et al15 who demonstrated ERP adaptation to rate after cardioversion of AF. However, our observations contrast with those of Franz et al11 and Attuel et al12 in humans and of animal studies that demonstrate loss or reversal of rate adaptation.1,2

After termination of chronic AFL, cSNRT increased after 3 weeks of sinus rhythm. This finding is consistent with animals studies demonstrating reversible sinus node dysfunction after a period of chronic AF and suggests that AFL may also induce reversible remodeling of sinus node function.21 The persistence of sinus node dysfunction in the presence of autonomic blockade also suggests that AFL causes significant depression of sinus node automaticity and/or sinoatrial conduction.

Relationship Between AFL and AF
Several studies have attempted to clarify the mechanistic relationships between AFL and AF. AFL may serve as a trigger for AF, with organized macro-reentrant wave fronts of AFL splitting over anatomic obstacles such as the crista terminalis or pectinate muscles to generate daughter wavelets of AF or short-circuiting through gaps in constraining barriers to yield tighter reentrant circuits.22–24 AFL may disorganize into AF through a reduction in the length of functional barriers around which atrial wave fronts propagate.25 Cheng et al23 and Scheinman et al26 have hypothesized that some forms of atypical AFL may develop when caudal boundaries of the crista terminalis are breached during times of reduced atrial refractoriness. A reduction in atrial ERP like that found in the present study after a paroxysm of AFL might contribute to the promotion of AF soon after AFL onset and possibly some atypical forms of AFL by decreasing the size of such functional barriers in the human heart. The present study also suggests that AF inducibility may be heightened for up to 10 minutes after a paroxysm of AFL and for 30 minutes after termination of chronic AFL owing to the effects of electrical remodeling. This process may contribute in part to the high rates of AF inducibility observed immediately after AFL ablation.7–9

Study Limitations
The present study did not control for the potential confounding effect of multiple ERP determinations on refractoriness. No significant changes in atrial ERPs were demonstrated after repeated ERP assessments in previous studies, suggesting that the methodology used in this study was unlikely to influence the observed changes in refractoriness.3,4 In the chronic AFL group, a threshold <2 mA at the septal site could be achieved in only 6 patients at 15 and 30 minutes and in 4 patients at 3 weeks. Hence, electrical remodeling of the septum has not been conclusively demonstrated.

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References
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