Electrophysiological Characteristics and Catheter Ablation in Patients With Paroxysmal Right Atrial Fibrillation

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Background—Catheter ablation of the right atrial (RA) substrate has had variable efficacy in curing paroxysmal atrial fibrillation (PAF), suggesting that RA substrate ablation can play an important role in the treatment of atrial fibrillation (AF) in some patients. The aim of this study was to investigate the electrophysiological characteristics and ablation strategy and its results in a specific group of patients with paroxysmal RA-AF.

Methods and Results—The study population consisted of 13 patients (8 men; age, 64±15 years) with drug-refractory (2±1 drugs), frequent episodes of PAF. Provocation maneuvers did not reveal any ectopic beat–initiating AF. However, rapid atrial pacing easily induced AF. Activation mapping during sinus rhythm, atrial pacing, and AF was visualized by using a noncontact mapping system. Noncontact mapping revealed RA reentry (6 patients with single-loop circuits and 7 with double-loop circuits) with conduction through channels between lines of block, crista terminalis gaps, and the cavotricuspid isthmus, which could be identified during sinus rhythm and atrial pacing, resulting in fibrillatory conduction in other parts of the RA. The consistency of wavefront activation was confirmed by frequency analysis from equally distributed mapping sites in the RA. Short lines of ablation lesions were aimed at the conduction channels between the lines of block, crista terminalis gaps, and the cavotricuspid isthmus, resulting in bidirectional block. AF was eliminated in 11 (85%) of 13 patients, and those 11 patients with acute success were free of AF without any antiarrhythmic drugs during the long-term follow-up period (16±6 months).

Conclusions—RA ablation still can cure selected patients with PAF. Linear ablation of the RA substrate guided by the electrophysiological characteristics of RA-AF is an effective approach for treating this specific group of patients with AF. (Circulation. 2005;112:1692-1700.)

Key Words: ablation ■ atrial fibrillation ■ atrium

Several investigators have demonstrated that paroxysmal atrial fibrillation (AF) could be initiated by ectopic beats from the pulmonary veins (PVs) and non-PV areas and that elimination of those ectopic beats could cure the AF.1–3 Compartmentalization of the right atrium (RA) had been previously performed with variable efficacy (the long-term success rate ranging from 6% to 50%),4–6 suggesting that RA substrate ablation could play an important role in the treatment of AF in some patients. However, the AF mechanism and optimal ablation lesions were not validated in those studies with RA substrate ablation. Cox et al7 had demonstrated an important mechanism consisting of a single RA reentrant circuit with fibrillatory conduction by using human epicardial mapping. In our laboratory, we have reported 1 patient who had double-loop reentry with fibrillatory conduction, and the ablation of the crista terminalis (CT) gaps and cavotricuspid isthmus could terminate and prevent further induction of that AF,8 suggesting that the RA was an important substrate for the maintenance of AF in some patients.

In fact, an AF mechanism consisting of a single reentrant circuit with fibrillatory conduction had been proposed in the early twentieth century.9 Dr Lewis9 reported that there was a mother wave of the AF circulating and continuously throwing off a number of centrifugal wavelets, which caused and perpetuated flickering fibrillation. Considering that PV isolation and ablation of non-PV triggers still cannot cure all patients with AF, recent review articles and editorials have again emphasized this concept of atrial reentry with fibrillatory conduction in the animal model and human AF.8,10–13 The aim of the present study was to investigate the electrophysiological characteristics and a new ablation strategy based on the RA activation and substrate characteristics obtained from noncontact mapping in a selected group of patients without ectopy-initiating AF.
Methods

Study Patients
Among 436 patients referred for the ablation of paroxysmal AF, 28 patients who underwent an electrophysiological study and RF ablation under the guidance of noncontact mapping were identified during an electrophysiological study in 13 patients (3%; range, 30 to 81). They had frequent episodes of AF for an average of 4.2 ± 2.7 years (median episode per week in the most recent month) and were refractory to or intolerant of 1 to 3 (mean, 2 ± 1) antiarrhythmic drugs (Figure 1). Eight patients (62%) had an associated cardiovascular disease, including 7 patients (54%) with hypertension and 2 patients (15%) with coronary artery disease. Twelve patients (92%) had a normal left ventricular function, except for 1 patient with mild left atrial dysfunction (LVEF: 38%) due to coronary artery disease. Echocardiography revealed that there were 5 patients (38%) with a mild left atrial enlargement. The mean left atrial dimension was 38 ± 6 mm (range, 26 to 48 mm) (Table 1). To compare the differences in the substrate properties of the RA in these patients with AF, the study population consisted of an additional 28 patients who underwent an electrophysiological study and RF ablation under the guidance of noncontact mapping.

Electrophysiological Study
Each patient underwent an electrophysiological study and catheter ablation in the fasting, nonpaced state after providing written informed consent. As described previously, all antiarrhythmic drugs except for amiodarone were discontinued for at least 5 half-lives before the study.2,3

In all patients, 3 multipolar electrode catheters were positioned in the high right atrium, His-bundle area, and right ventricle through the femoral veins. A 7F, deflectable, decapolar catheter with 5 pairs of electrodes separated by 5 mm and an interelectrode spacing of 2 mm was also inserted into the coronary sinus (CS) through the internal jugular vein. The position of the proximal electrode pair at the ostium of the CS was confirmed with a contrast injection. In the patients with AFL/AF, a 7F, 20-pole, deflectable Halo catheter with a 10-mm paired spacing (Cordis-Webster Inc) was positioned around the tricuspid annulus to simultaneously record the RA activation in the lateral wall and lower right atrial isthmus. A 9F sheath placed in the left femoral vein was used to introduce the noncontact mapping catheter. We tried to find spontaneous ectopic beats initiating the AF before or after the infusion of isoproterenol or by following a designed algorithm for facilitating the initiation of AF.2,3

If no ectopic beat–initiating AF could be demonstrated, atrial burst pacing from the proximal CS or right atrial catheter at progressively shorter cycle lengths until 180 ms and 2:1 atrial capture was used to induce the AF.

During the electrophysiological study, these patients with AF were characterized by (1) no identifiable atrial ectopic beat–initiating AF. During an isoproterenol infusion, short-duration (≤5 seconds) atrial burst pacing with intermittent pauses or electrical cardioversion of the AF did not show any ectopic beat–initiating AF in any of the patients with AF. (2) The mean cycle length obtained during a 1-minute recording from the high RA catheter was significantly shorter than that from the proximal and distal CS catheter recordings (164 ± 27 ms versus 199 ± 28 ms versus 203 ± 30 ms, respectively, p = 0.01). (3) All patients with AF had inducible typical or reverse typical AFL. Therefore, noncontact mapping was used to map the activation pattern during sinus rhythm (SR), atrial pacing, and AF and to guide the RF ablation.

Noncontact Mapping System
A noncontact mapping system was set up in our laboratory; the details were reported previously.4,5 In brief, the system consisted of

TABLE 1. Clinical and Electrophysiological Findings in Patients With Paroxysmal AF Driven by Right Atrial Reentry

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y), Sex</th>
<th>Other CVD</th>
<th>PAF History, %</th>
<th>LA Size, mm</th>
<th>CL of the Reentrant Circuit, ms</th>
<th>LAE of the Reentrant Circuit, ms</th>
<th>Harmonic Index</th>
<th>DF of V(10 Hz)</th>
<th>DTI</th>
<th>Channel Between CBL of the CT and Septum</th>
<th>Channel Between CBL of the CT and Free Wall</th>
<th>Channel Between CBL of the CT and Septum</th>
<th>Follow-Up, mo</th>
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<tr>
<td>1</td>
<td>74, F</td>
<td></td>
<td></td>
<td>48</td>
<td>136</td>
<td>7.3</td>
<td>0.32</td>
<td>6.8</td>
<td></td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>23</td>
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<tr>
<td>2</td>
<td>73, M</td>
<td>HT</td>
<td>3</td>
<td>38</td>
<td>145</td>
<td>6.8</td>
<td>0.32</td>
<td>6.8</td>
<td>+ 4</td>
<td>+</td>
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<td>40</td>
<td>180</td>
<td>5.6</td>
<td>0.37</td>
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<td>+</td>
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<tr>
<td>4</td>
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<td>32</td>
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<td>38</td>
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<td>0.39</td>
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<td>+ 2</td>
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<td>9</td>
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<td>HT</td>
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<td>0.44</td>
<td>5.9</td>
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</tbody>
</table>

Mean ± SD: 42 ± 15; 38 ± 6; 176 ± 35; 6.2 ± 11; 0.34 ± 0.05; 6.2 ± 11.

CAD indicates coronary artery disease; CBL, conduction block line; CL, cycle length; CVD, cardiovascular disease; DLR, double-loop reentry; EF, ejection fraction; HT, hypertension; SLR, single-loop reentry; TA, tricuspid annulus; +, yes; and −, none.
a catheter (9F) with a multielectrode array surrounding a 7.5-mL balloon mounted at the distal end. The system located the 3-dimensional position of the electrodes on any desired catheter relative to the multielectrode array by using a locator signal. Navigation provided the means to define a model of the chamber anatomy and to track the position of the standard contact catheters within the chamber relative to the label points of interest, such as the anatomic structure or critical zones of conduction. Virtual endocardial electrograms were mathematically reconstructed and displayed on the anatomic model, producing isopotential or isochronal color maps.

**Signal Preprocessing**

The unipolar endocardial signals from the noncontact mapping system were sampled at 1.2 kHz and filtered with a second-order Butterworth digital filter with bandwidth between 2 and 300 Hz. The surface ECG lead V½ was also recorded. ECG lead V½ was chosen because it had the largest amplitude of fibrillatory activity. A 7-second segment of raw data downsampled to 600 Hz from 64 equally distributed RA locations (with a mean area of 2.04 cm² for each site) was exported to an external computer program for frequency analysis. The ventricular activity (QRS-T complex) in the signal (endocardial signals and ECG lead V½) was eliminated by using an adaptive cancellation technique. In brief, each R wave in the 6.82 seconds was identified by using a peak detection algorithm. QRS-T segments were aligned on this fiducial point and averaged to create the template. The template was positioned at the location of each QRS complex. Because of the variation in the amplitude of the QRS complex, the template was adjusted accordingly for every beat to form the QRS complex parts of a reference signal. With the reference signal, each QRS-T was adaptively canceled from the original ECG by using a recursive least-squares algorithm.

**Frequency Domain Analysis**

A 4096-point fast Fourier transform (FFT) with a Hanning window was calculated on the resultant data segments (6.82 seconds, 600-Hz sampling rate). The frequency spectra were plotted and analyzed from 2 to 30 Hz to include only the physiological range of practical interest. The remainder ECG of lead V½ was also calculated by FFT. The spectra were normalized by the maximum power of the 64 spectra. For each spectrum, the normalized largest peak, which exceeded 0.2, was identified as the dominant frequency (DF). On the basis of the DF position, the positions of the harmonic peaks were determined.

The total power of the spectrum was calculated from 2 to 30 Hz. The power under the DF and all harmonic peaks from 2 Hz to 30 Hz was determined over a 2-Hz window. The ratio of the power of the DF and its harmonic peaks to the total power was defined as the harmonic index (HI). With a higher number of wavelets, more discrete harmonics represented fewer wavelets circulating within the atria and thus a higher HI. With a higher number of wavelets, more frequency components were added to the atrial signal, which appeared in the spectrum and resulted in a lower HI. A spectrum with a dominant peak and harmonic index (HI), representing the organization of the AF during flutter on a prior ECG or Holter recording. In the electrographic analysis, the 2- to 30-Hz band was used for analysis. For each site, mean MSC was determined by averaging the MSC over all frequencies in the band.

**Definition**

Lines of conduction block were interpreted from the activation patterns observed in the isopotential maps and the associated morphological features of the unipolar electrograms from the noncontact mapping. Local split potentials were always observed in the region of the conduction block (Figure 3).

**Catheter Ablation**

The catheter ablation strategy included the ablation of the cavotricuspid isthmus and critical conduction channels responsible for the AF. The cavotricuspid isthmus was ablated first with bidirectional conduction block; however, burst atrial pacing still induced sustained AF (Figure 1). Therefore, further RF ablation was applied to modify the RA substrate. The critical channels of the AF could be identified between the lines of conduction block during SR and atrial pacing. The ablation catheter (with a 4-mm or 8-mm tip electrode, Mansfield, Boston Scientific) was connected to an EPT-1000 generator (EP Technologies), delivering a 550-kHz sine wave output between the distal electrode of the ablation catheter and a cutaneous patch electrode placed over the left scapula. For the ablation of the CT gap and critical conduction channels, RF energy (through a 4-mm tip electrode; target temperature, 50 to 55°C; power, 50 W) was delivered for 20 to 40 seconds per pulse. For the ablation of the cavotricuspid isthmus (CTI), RF catheter ablation with an 8-mm, electrode-tipped ablation catheter was performed with pacing from the proximal CS and with a preset power, temperature, and duration of each RF pulse of 70 W, 70°C, and 120 seconds, respectively. A continuous application of RF energy during a pullback of the ablation catheter from the right ventricular side of the tricuspid annulus toward the inferior vena cava was used to create linear lesions. The ablation end point for the transverse conduction through the CT gap and CTI was bidirectional conduction block confirmed by noncontact and contact mapping while pacing from both sides of the ablation line. The protocols used to facilitate the AF onset before the ablation were repeated (burst atrial pacing at progressively shorter cycle lengths until 180 ms or 2:1 atrial capture) to assess the effects of the RF ablation. The procedural success of the AF ablation was defined as a duration of induced AF of <30 seconds.

**Postablation Follow-Up**

After discharge, the patients underwent a follow-up (2 weeks after the catheter ablation, then every 1 to 3 months at our cardiology clinic or with the referring physician) without taking any antiarrhythmic drugs, except for the patients with an early recurrence of the AF (defined as <1 month after the ablation) and in which antiarrhythmic drugs were prescribed for 2 to 4 weeks. When the patients had symptoms suggestive of tachycardia, 24-hour Holter monitoring or a cardiac event recorder was used to determine the cause of the clinical symptoms. Twenty-four-hour Holter monitoring was routinely performed at 6 months after the ablation. If more than 1 episode of recurrent AF was documented, antiarrhythmic medications were used to control the AF. If AF still occurred, a repeat electrophysiological study and ablation were recommended.

**Statistical Analysis**

All continuous data are presented as mean±SD values. The differences between 2 groups were analyzed by using the Mann-Whitney test. The differences among 3 or more groups were analyzed by using the Kruskal-Wallis test. The correlation between the surface ECG lead V½ and intracardiac maximal DF was explored by linear regression. Statistical significance was considered when the 2-sided probability value was <0.05.

**Results**

**Baseline Electrophysiological Study**

All 13 patients had clinically documented AF as the dominant arrhythmia. Six of these 13 patients (46%) had transient atrial flutter on a prior ECG or Holter recording. In the electro-
physiological laboratory, all patients had transient typical or atypical AF, and transient AFL spontaneously converted to sustained AF in 8 patients (Figure 1). The mean duration of the transient AFL was 6.0±6.9 seconds. In all patients, rapid atrial pacing easily induced AF. During the entire procedure, no atrial premature beats were observed to initiate AF. The noncontact mapping system was then successfully deployed in the RA to study the activation patterns of the AF in all the patients. No complications occurred during this study.

RA Activation Patterns Before the Induction of AF
Noncontact mapping identified the activation patterns during SR and atrial pacing at a cycle length of 300 ms. Lines of conduction block occurred in the RA, indicated by the isochronal contour lines that converged at the same location where the wavefront was unable to cross over and the local electrograms exhibited split potentials (Figure 3). The patients with RA-AF had more lines of block in the RA than those with AFL or AVNRT (Table 2), indicating that there was a more heterogeneous RA substrate in the patients with RA-AF.

Furthermore, the number of the lines of block in the patients with RA-AF was 1.4±0.7 during SR, 2.6±1.0 during proximal coronary sinus pacing, and 2.3±0.5 during low anterior RA free wall pacing (P<0.01), indicating the functional behavior of the conduction block during different rhythms. The lines of block were located in the low RA in 13 patients (100%), along the CT in 10 patients (77%), the free wall in 9 patients (69%), and the septum in 4 patients (31%). Additionally, transverse conduction through the CT could be identified in all patients (100%), including during coronary sinus pacing in 11 patients (85%), low anterior free wall pacing in 7 patients (54%), and SR in 3 patients (23%).

RA Activation Patterns During AF
The noncontact mapping demonstrated a stable, reentrant conduction around 1 or 2 loops, and unstable conduction outside the loops manifested as an uneven shifting of the activation pattern. Dominant reentrant circuits were identified and are summarized in Table 1. They were composed of a single-loop reentrant circuit (6 patients), or double-loop reentrant circuit (7 patients) with fibrillatory conduction to the rest of the RA (Table 1). The mean fibrillation cycle length measured from the area of the reentrant circuit was 176±35 ms (range, 130 to 235).

In Figure 4, consecutive activation maps show a representative episode of several cycles of atypical atrial flutter (double-loop reentry) with conversion to AF. During AF, the reentry circuit of the AF driver propagated through the CT gap and

![Image](https://example.com/image.png)
channel between the CT and free wall constantly, with splitting of daughter wavefronts (Figure 4B). Local unipolar virtual electrograms demonstrated rhythmic activation within the circuit and irregular activation outside the circuit. Further, the FFT obtained from the main reentrant circuit demonstrated a single peak DF of 5.1 Hz, indicating that rhythmic wavefronts constantly passed through this area (Figure 4C). On the other hand, the rest of the RA was activated passively and irregularly.

**TABLE 2. Number of Conduction Block Lines and Frequency Analysis Results in the Different Groups of Patients**

<table>
<thead>
<tr>
<th></th>
<th>RA Atrial Fibrillation (n=13)</th>
<th>PV Atrial Fibrillation (n=9)</th>
<th>Typical Atrial Flutter (n=11)</th>
<th>Atrioventricular Nodal Reentrant Tachycardia (n=9)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conduction block lines in RA during SR</td>
<td>1.4±0.65</td>
<td>1.4±0.73</td>
<td>0.36±0.51*</td>
<td>0.44±0.51*</td>
<td>0.001</td>
</tr>
<tr>
<td>Conduction block lines in RA during CS pacing</td>
<td>2.6±0.96</td>
<td>2.2±0.75</td>
<td>0.82±0.60*</td>
<td>0.11±0.33†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Conduction block lines in RA during LAL pacing</td>
<td>2.3±0.48</td>
<td>2.2±0.75</td>
<td>0.90±0.74*</td>
<td>0.11±0.33†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dominant frequency of reentry circuit in the RA, Hz</td>
<td>6.3±1.5</td>
<td>Nil§</td>
<td>4.1±0.41*</td>
<td>Nil‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Regional harmonic index in RA</td>
<td>0.38±0.47</td>
<td>0.39±0.46</td>
<td>0.73±0.11*</td>
<td>Nil‡</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LAL indicates low anterior lateral wall.
All continuous data are presented as mean±SD values.
P values for lines of block were obtained from the Mann-Whitney test; P values for the dominant frequency and harmonic index were obtained from the Kruskal-Wallis test.

*P<0.05 compared with patients with atrial fibrillation.
†P<0.05 compared with the patients with typical atrial flutter or atrial fibrillation.
††In patients with AVNRT, the frequency analysis of the atrial depolarization could not be analyzed correctly because of the simultaneous depolarization of the atrium and ventricle.
§§In patients with PV atrial fibrillation, the RA did not show any stable reentry circuit and the highest DF was located in the left atrium.
Figure 4. Activation maps, frequency domain analysis, and intracardiac unipolar electrograms demonstrating the reentrant circuit in the right atrium (RA) during transient atypical flutter and subsequent conversion to AF in patient 11 (surface ECG is shown in Figure 1A). A, Isochronal maps show that the activation propagated through the channels between the lines of conduction block (black lines) during low anterolateral wall pacing before induction of AF. B, Transient atypical atrial flutter converted to AF spontaneously. The time-step for each frame (B1 to B8) is indicated by “1 to 8” on lead aVF. Consecutive isopotential maps show that the macroreentry circuit propagated through the same channels as in A between the lines of block in the CT and free wall to complete the circuit of atypical AFL (frames 1 to 3). During conversion to AF, the reentry circuit repetitively propagated through the channel between the CT and free wall (near site 1) and divided into 2 wavefronts (frame 4). Each of the wavefronts further split into 2 wavelets traveling superiorly and inferiorly, thereby generating fibrillatory conduction in the form of 4 simultaneous wavefronts (frame 5 to 6). The more superior wavefronts (central wavefronts of the driver) fused in the superior RA, whereas the more inferior wavefronts (daughter wavelets, indicated by green arrows) fused and traveled through the cavotricuspid isthmus, which fused with the prior superior wavefronts (frames 6 to 7). Subsequent activation maps show a continuing complex pattern around the 2 conduction block lines in the CT and free wall (frames 7 to 8). C, Local unipolar virtual electrograms demonstrate rhythmic activation along the circuit (sites 1 and 2) and irregular activation outside the circuit (sites 3 and 4). Site 5 was near the margin of the reentrant circuit with a power amplitude of 0.27, which met the criteria of a DF. Regional spectral analysis demonstrated that the maximal DF with the largest power amplitude was along the circuit. Linear ablation (white dashed line in A) connecting the lines of block successfully eliminated and prevented further induction of AF.
resulting in fibrillatory conduction, as confirmed by the results of the FFT in which no DF peaks were available in those areas, indicating a frequency gradient and breakdown of the DF response between the reentrant circuit and the rest of the RA.

**FFT Analysis of the Regional RA**

In the present study, spatial distribution of the DFs (from 64 equally distributed mapping sites in the RA) was used to identify a precise localization of the source of the driver responsible for the AF. All patients with RA-AF demonstrated the highest DF along the identified dominant reentrant circuit (6.24±1.38 Hz, Table 1). The highest DF recorded in the RA septum was not higher than the source frequency in the RA (5.17±1.44 Hz versus 6.24±1.38 Hz, \(P=0.07\)), indicating that the patients did not depend on the left atrium (LA) in maintaining the AF. On the other hand, in the control group with spontaneous initiation of AF from pulmonary veins, there was a frequency gradient from the septal area of the RA (6.1±0.7 Hz) to the rest of the RA (5.0±1.1 Hz, \(P=0.04\)).

In the patients with RA-AF, those with single-loop reentry tended to have a higher DF than those with double-loop reentry (6.6±1.4 Hz versus 5.8±0.71 Hz, \(P=0.12\)). Furthermore, the regional DF exhibited a frequency gradient away from the reentrant circuit (6.24±1.38 Hz to 4.4±0.96 Hz), indicating a frequency gradient and breakdown of the DF response between the reentrant circuit and the rest of the RA. The maximal DF obtained from the dominant reentrant circuit significantly correlated with the DF obtained from the remainder ECG lead V1 (\(r=0.96, P<0.001\), Figure 5). The patients with AF had a higher DF and lower HI in the RA than those with AFL (Table 2).

**Validation of Frequency Spectra**

The values of the DFs measured between the spectra obtained from contact and noncontact electrograms were significantly correlated (5.51±0.75 Hz versus 5.83±0.73 Hz for noncontact and contact electrograms, respectively, \(r=0.9, P<0.01\)). The mean MSC in the 2- to 30-Hz region was obtained at each mapping site. The averaged mean MSC from 18 overall mapping sites was 0.52±0.03.

**Radiofrequency Catheter Ablation and Postablation Follow-Up**

In the patients with RA-AF, ablation was performed along the cavotricuspid isthmus first with bidirectional block. After the cavotricuspid isthmus was ablated, burst atrial pacing still induced sustained AF in all patients (Figure 1B). Further substrate modification was aimed at the conduction channels between the lines of block and CT gap. Of all the patients, ablation was performed along the CT gap in 13 patients (100%), CTI in 13 patients (100%), channels between the CT and line of block at the RA free wall in 9 patients (69%), and channels between the CT and line of block at the septum in 4 patients (31%). Ablation was applied during SR in 11 patients and during AF in 2 patients (patient 7). AF was terminated during the ablation of the critical conduction channel in those 2 patients (patients 7 and 12). Acute success was achieved in 11 patients (85%), with conduction block of all the CTI, CT gaps, and channels. Two patients (patients 1 and 10) could not tolerate the procedure: One patient had severe chest pain during the ablation of the CT gap and in the other, the ablation line in the free wall channel could not be finished because of the long procedure time. The total number of RF ablation pulses was 27±12 (range, 12 to 54). There were no procedure-related complications.

None of the patients with an acute success took any antiarrhythmic drugs, and they were free of AF during long-term follow-up (16±6 months). The 2 patients with incomplete procedures had 1 episode of AF within 1 year after the ablation and required the administration of the previously ineffective antiarrhythmic medications. Twenty-four-hour Holter recordings at 6 months after the ablation revealed only 0.4±0.7 episodes (per patient) of nonsustained atrial arrhythmias (<30 seconds).

**Discussion**

**Main Findings**

Our study presented a new method for atrial substrate mapping and ablation in those patients with AF without any identifiable initiating ectopy, shorter cycle lengths in the high RA recordings as compared with the CS catheter recordings, and inducible typical or reverse typical AFL. Heterogeneous atrial conduction, as confirmed by lines of conduction block in the RA, characterized this specific group of patients with AF. The noncontact mapping during AF revealed that a dominant reentrant circuit in part of the RA could be the driver of AF with fibrillatory conduction to the rest of the RA. The circuits constantly conducted through the channels between the lines of conduction block, which were identified during SR, atrial pacing, and AF. Selective ablation of the conduction channels between the lines of block, CT gap, and CTI successfully eliminated the AF in these patients.

**Comparison With Previous Studies**

Several investigators have reported the results of RA ablation in patients with paroxysmal AF. However, these studies did not identify any specific mechanism of the AF in the RA.
or did not identify the RA substrate properties. Furthermore, the ablation end point was not well defined in those studies. For example, the possible presence of ectopy-initiating AF was not provoked, or the noninducibility of AF was not routinely checked after the ablation. In the present study, the patients were highly selected for substrate modification, because no ectopy-initiating AF could be identified; however, atrial pacing that induced AF and/or AFL that degenerated into AF could reproducibly occur, suggesting the important role of the atrial substrate in this AF. Furthermore, the cycle length of the contact RA recordings was significantly shorter than that of the CS recordings, and the highest DF was not located in the RA septum, suggesting that the driver was from the RA instead of the LA. Therefore, substrate modification was guided by a detailed electrophysiological study and substrate mapping of the RA, and conduction areas between the lines of block were amenable to cure by RF ablation. Strict entry criteria for ablation according to the unique electrophysiological characteristics can explain the high success rate of the catheter ablation in this study as compared with previous reports.

**Mechanism of AF in Patients With Substrate-Dominant AF**

Although single- or double-loop reentry has been presented as atypical AFL, the atrial activation pattern in this group of AF patients differed from that of atypical AFL because of the following reasons. First, unsynchronized and irregular atrial activations manifested as irregular P waves on the surface ECG (Figure 1). Second, the activation mapping from the noncontact mapping showed a fixed pattern of the reentrant circuit in part of the RA with randomly conducted daughter wavefronts to the rest of RA (Figure 4). Third, the FFT also showed areas with a DF gradient or without an identifiable DF in the areas outside the AF reentrant circuit, indicating there was fibrillatory conduction. Fourth, the HI was lower in the patients with AF as compared with the patients with AFL, indicating there were less organized wavefronts during the AF.

Although Jalife et al, Schuessler et al found that sustained AF could be caused by a single reentrant source from the RA inferior wall. Furthermore, Cox et al and Waldo et al also demonstrated the important mechanism of an RA single reentrant circuit with fibrillatory conduction in human AF. In the present study, we used the frequency analysis to identify the precise localization of the source of the driver responsible for AF. The frequency of the surface ECG V1 also reflected the dominant frequency of the activation in the RA, and the result was compatible with the previous study. Furthermore, we demonstrated a wide distribution of frequencies in the RA and could also localize the sites with the highest DF and a frequency gradient to the rest of the RA. These results support that localized sources are responsible for the AF maintenance. Previous work on animal models demonstrated that breakdown of the wave propagation resulting in fibrillatory conduction could occur within the RA. Although this finding did not exclude the dependency of the RA on the LA, the following phenomenon mentioned below strengthened our hypothesis of an AF driver in the RA: (1) Isochronal maps revealed that the activation time of the main reentrant circuit accounted for 100% of the cycle length of the AF in all patients; (2) no approaching wavefronts from the septal areas or coronary sinus ostium with a preceding blanking period of the RA were observed; (3) AF terminated during the ablation of the channels in 2 patients in whom the ablation was performed during the AF; (4) the highest DF recorded in the RA septum was not higher than the source frequency in the RA. According to the previous study, AF waves emanating from the high frequency sources of the LA/PV resulted in a LA-septum-RA frequency gradient across the Bachmann bundle.

Regional frequency analysis showed that the sites with the highest DF and the maximal power amplitude were within the AF driver, according to the activation mapping. However, DF peaks with the same frequency as the driver but with a lower power amplitude may be observed at the reentrant circuit margin. It was possibly due to the far-field effect of the nearby larger signals of the AF driver (as shown in Figure 4, site 5). Therefore, it will not interfere with the identification of the highest and maximal DF of the AF driver. On the other hand, the spectra recorded away from the circuit did not exhibit a dominant DF (a normalized power of the largest peak <0.2), and a single driving rotor was not present there.

**Rationale for Selective Ablation of the RA Substrate**

The noncontact mapping exhibited stable reentrant conduction around 1 or 2 loops and unstable conduction along an alternate loop. Wavefronts split and gave off daughter wavefronts around the conduction block lines, as an uneven shifting of the pattern of activation (Figure 4). Therefore, assuming that a single reentrant circuit or double reentrant circuit with multiple daughter wavelets was the underlying mechanism for the maintenance of AF, the conduction channels between the conduction block lines were targeted as critical areas of the AF reentrant circuits. The rationale for our ablation approach in these patients was to create conduction barriers by connecting the conduction block lines in each patient guided by the noncontact mapping, where only limited ablation lesions were needed. After performing linear ablation over the conduction channels, the possible ectopies coming from PV or non-PV regions could no longer initiate AF.

In the present study, transverse conduction through the CT gap during AF was observed in all patients; therefore, it was important for the maintenance of the AF. Furthermore, CTI ablation was also performed in all patients due to inducible typical and reverse typical AFL. In addition to the CT gap and CTI, the detailed substrate mapping in the present study indicated that more ablation lines in the RA might be required to eliminate the reentrant circuit of AF and prevent further occurrence of AF.

**Limitations**

First, the present study was composed of a small number of patients (3%) from our patients with AF ablation. We did not demonstrate any ectopy-initiating AF in the laboratory; therefore we did not perform PV isolation or superior vena cava isolation in these patients. However, these patients had a significant RA substrate problem. In the present stage,
whether PV isolation can be applied to all patients with AF is still controversial, and some patients have different mechanisms of AF and need different approach techniques. Second, the LA and PVs were not mapped, and the role of the LA substrate was not proven. However, in the study patients, the source of the frequency from the regional spectral analysis, activation mapping, and ablation results did not favor an AF driver in the left atrium. Third, the virtual unipolar electrograms may not have been accurate if the mapping sites were >38 mm from the balloon center. In our previous studies, the overall morphology cross-correlation between the contact and noncontact electrograms during AF was 0.73±0.21. However, in the present study, the mean distance from the mapping sites of the AF driver to the balloon center was 23.4±7.5 mm (over 130 mapping sites in 13 patients). Therefore, we believe the virtual unipolar ECGs were accurate enough for the spectral analysis and activation mapping. In the present study, we further demonstrated that the correlation of the DF value and results of the mean MSC for validation of the spectra from the noncontact and contact electrograms were within an acceptable range.

Conclusions
The present study suggests that a single- or double-loop reentry in the RA may drive the atrium, resulting in AF with fibrillatory conduction. Selective linear ablation of the RA substrate, aimed at targeting the CT gap, CTI, and channels between the conduction block lines guided by noncontact mapping, is an effective approach for treating this specific group of paroxysmal right AF.

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