Simultaneous Noncontact Mapping of Left Atrium in Patients With Paroxysmal Atrial Fibrillation
Gerhard Hindricks, MD; Hans Kottkamp, MD

Background—Catheter ablation of pulmonary vein ectopic foci is a potentially curative treatment strategy for patients with atrial fibrillation. However, identification of arrhythmogenic pulmonary veins with conventional mapping is difficult, especially in patients with rare focal activity, multiple active foci, or extrapulmonary foci. The present study was designed to investigate use of simultaneous noncontact mapping in this setting.

Methods and Results—In 17 consecutive patients with paroxysmal atrial fibrillation, a catheter-mounted noncontact multielectrode array positioned in the left atrium was used to reconstruct 3300 electrograms simultaneously from a single beat. Isopotential maps were generated during sinus rhythm and focal activity. After ectopic foci were identified, radiofrequency catheter ablation was performed in patients with 1 or 2 foci. However, in patients who had multiple foci, intraoperative ablation of atrial fibrillation was advised. A total of 28 ectopic foci (25 pulmonary vein foci and 3 extrapulmonary vein foci) were identified by use of isopotential maps generated from a single beat of focal activity. Radiofrequency catheter ablation guided by noncontact mapping was attempted in 12 patients with 1 or 2 ectopic foci. Successful ablation of atrial fibrillation was achieved in 9 of 12 patients (75%).

Conclusions—Noncontact mapping allows rapid and precise identification of arrhythmogenic pulmonary veins in addition to extrapulmonary vein foci. Thus, the present study shows that the technology may be used not only to guide radiofrequency catheter ablation, but also as a diagnostic tool to develop individual treatment strategies. (Circulation. 2001;104:297-303.)

Key Words: arrhythmia • fibrillation • mapping • catheter ablation

Introduction of the concept by Haissaguerre and coworkers1 that rapid discharges of focal triggers in the pulmonary veins represent the source of paroxysmal atrial fibrillation has directed enormous interest toward development of curative ablation strategies. On the basis of the initial description by the group of Haissaguerre, several laboratories have demonstrated that radiofrequency catheter ablation of these focal sources potentially is curative for patients suffering from paroxysmal atrial fibrillation.2–4 However, localization of arrhythmogenic pulmonary veins and mapping of ectopic foci with conventional mapping technologies may be difficult and time consuming. Major problems that limit effective mapping of pulmonary vein foci include unpredictability of sufficient spontaneous ectopic activity to perform sequential mapping of pulmonary veins and occurrence of repetitive episodes of sustained atrial fibrillation that lead to prolonged waiting periods or repeated electrical cardioversions.

A new noncontact mapping technology recently was introduced that allows generation of isopotential maps of a whole cardiac chamber from a single beat by simultaneous reconstruction of >3300 virtual endocardial electrograms.5,6 Previous studies performed in patients with a variety of cardiac arrhythmias have shown that simultaneous noncontact mapping is accurate and reliable.7–9 In the present study, we assessed feasibility of noncontact mapping for localization of pulmonary vein foci that initiate paroxysmal atrial fibrillation.

Methods

Study Patients
Between June 1999 and August 2000, 17 consecutive patients (8 men and 9 women; mean age, 49±16 years) with documented frequent episodes of paroxysmal atrial fibrillation were included in the study. Selection criteria for invasive treatment of atrial fibrillation were (1) documented arrhythmia history of ≥2 years, (2) ≥2 highly symptomatic attacks of atrial fibrillation per week, and (3) proven inefficiency of antiarrhythmic drug therapy. Table 1 presents patient characteristics; 11 had history of arterial hypertension, and left ventricular function was moderately reduced in 2 patients but normal in the others. All patients gave written informed consent for the investigational nature of the left atrial noncontact mapping procedure.

Noncontact Mapping and Catheter Ablation
System components and physical principles of noncontact mapping (EnSite 3000, Endocardial Solutions Inc) previously have been described in detail.8,9 In brief, the EnSite system consists of an array balloon catheter placed in the cardiac chamber of interest that

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TABLE 1. Patient Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>17 (8 men, 9 women)</td>
</tr>
<tr>
<td>Age, y</td>
<td>49±16</td>
</tr>
<tr>
<td>Arterial hypertension, No. of patients</td>
<td>11</td>
</tr>
<tr>
<td>History of atrial fibrillation (range), y</td>
<td>5±4 (3–15)</td>
</tr>
<tr>
<td>No. previous antiarrhythmic medications, (range)</td>
<td>3±2 (1–5)</td>
</tr>
<tr>
<td>Left atrial size (range), mm</td>
<td>41±3 (38–47)</td>
</tr>
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acquires all information necessary to generate isopotential maps from ~3300 reconstructed virtual unipolar endocardial electrograms.

In all patients, a quadripolar electrode catheter was placed in the high right atrium and a bipolar catheter was placed in the right ventricular apex for pacing and conventional electrogram recording. Access to the left atrium was gained by transeptal puncture by use of standard techniques. An SF sheath was introduced to the left atrium for the mapping and ablation catheter (TF; Biosense, Webster). A SF sheath was introduced to place the noncontact mapping electrode array in the left atrium. The balloon was introduced into the left atrium with a wire placed in the left upper pulmonary vein. The sheath was withdrawn, and the balloon was deployed under fluoroscopic control. The deflated balloon was pulled back carefully, the wire was withdrawn, and the balloon was positioned in the center of the left atrium. Before the multielectrode array was deployed, patients were given 10 000 U of heparin, with subsequent boluses to maintain activated clotting time between 300 and 400 s.

Under fluoroscopic guidance, the ablation catheter was positioned at the ostia of all 4 pulmonary veins, and geometry data were acquired at the ostia and several centimeters inside the veins (Figure 1). No further geometry data were obtained. Ostia of the pulmonary veins were labeled, and the smoothing feature of the EnSite geometry algorithm was applied.

In all patients, the first segment of mapping data was recorded during sinus rhythm and analyzed to identify left atrial conduction breakthrough arising from the right atrium. In patients with spontaneous ectopic activity, several recordings were made during successive runs of focal activity. In patients without spontaneous ectopic activity, burst pacing (cycle length, 250 to 300 ms) and isoproterenol infusion (to increase sinus rate to ≥120 bpm) or adenosine (18-mg bolus) was given. After data were acquired, isopotential maps were generated during sinus rhythm, single ectopic beats, nonsustained runs of focal activity, or onset of atrial fibrillation. Virtual electrograms were applied to verify isopotential maps. Software filtering produced a bandwidth of 1 to 300 Hz. When overlap occurred with ventricular repolarization, the software filter setting was adjusted to between 2 or 4 and 300 Hz. Morphology of the virtual electrograms and timing of local atrial activation as evident from reconstructed electrograms in relation to onset of the P wave in the surface ECG and in relation to conventionally recorded right atrial electrograms were analyzed.

The indication for focal catheter ablation was made according to our predefined treatment protocol. This protocol advised focal catheter ablation only for patients with 1 or 2 left atrial foci. The reasons for this rather restrictive treatment strategy were (1) poor outcome of focal catheter ablation performed in patients with >2 foci reported in the literature10 and (2) risk of complications due to pulmonary vein stenosis, which may be critical when radiofrequency is applied to >2 pulmonary veins.11 Thus, in patients with >2 ectopic foci, intraoperative ablation of atrial fibrillation was advised.12 This procedure can be performed in our hospital with minimally invasive surgical techniques.13

In patients in whom catheter ablation was indicated, the mapping and ablation catheter was navigated to the pulmonary vein from which ectopic activity originated and conventionally recorded electrograms were obtained and analyzed. Radiofrequency current (temperature controlled at 60°C; pulse duration, 60 s) was applied in unipolar fashion to sites that displayed spike potentials preceded by left atrial far-field activation during sinus rhythm with conversion of the activation sequence during ectopic beats. In patients in whom no ectopic activity was present while the ablation catheter was in the pulmonary vein, the whole circumference of the pulmonary vein was carefully mapped and ablation was performed along the ostium of the pulmonary vein until no electrical activity could be recorded within the vein during sinus rhythm.

After radiofrequency ablation was applied, the ablation catheter was withdrawn and the patient was monitored for 30 minutes. Isoproterenol infusion, adenosine administration, and burst pacing were applied during the monitoring period to assess residual ectopic activity.

Follow-Up

On days 2 to 4 after ablation, patients underwent 24-hour Holter monitoring and exercise ECG. Before discharge, all patients underwent transthoracic or transesophageal echocardiography. Follow-up visits in the outpatient clinic were advised 3 months and 9 months after ablation or whenever symptoms that indicated arrhythmia...
recurrence were observed. Holter recordings were obtained at the time of follow-up visits by the referring physicians or in our outpatient clinic.

Results

Simultaneous Noncontact Mapping for Identification of Left Atrial Foci

In the 17 patients included in the present study, 19 invasive procedures were performed (1 study in 15 patients and 2 studies in 2 patients). The noncontact balloon was positioned in the left atrium without difficulty in all cases. The balloon was deployed and then positioned in the middle of the left atrium with the distal pigtail-shaped end of the electrode just below the roof of the left atrium (Figure 1). In 18 of 19 studies, position of the balloon remained stable during the whole procedure, whereas during 1 study, displacement of the balloon occurred and repositioning was necessary.

Isopotential maps obtained during sinus rhythm showed earliest left atrial activation at the high left atrium anterior to the right upper pulmonary vein and compatible with conduction over Bachmann’s bundle (Figure 2A). Conventional recordings obtained in the high right atrium preceded earliest left atrial activation by 10 to 20 ms, as evident from analysis of contact and virtual electrograms.

In 17 patients, 28 ectopic foci (25 pulmonary vein foci and 3 extrapulmonary foci) were identified. Frequent focal activity (spontaneously or triggered by isoproterenol) was present during 7 studies, whereas only rare focal activity (single atrial premature beats) was present during 8 studies. During 3 studies, sustained atrial fibrillation occurred during isoproterenol administration and the beats initiating arrhythmia were analyzed. These patients subsequently underwent cardioversion to detect additional foci. In 1 patient, no focal activity was observed during the entire study.

Table 2 shows number of foci identified per patient. Fifteen foci were in right pulmonary veins (11 right upper and 4 right lower pulmonary vein), and 10 were in left pulmonary veins (7 left upper and 3 left lower pulmonary vein). Focal origin could be attributed clearly to pulmonary veins by use of isopotential maps verified by virtual electrograms. At the earliest left atrial activation site during focal ectopy, virtual electrograms displayed either QS morphology or showed a tiny r wave (rS morphology) preceding intrinsic deflection. During consecutive ectopic beats arising from the same pulmonary vein, the breakthrough site to the left atrium, as evident from isopotential maps and virtual electrograms, was

<table>
<thead>
<tr>
<th>TABLE 2. No. of Foci Identified per Patient</th>
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<tr>
<td>No. focal activity, n</td>
</tr>
<tr>
<td>PV foci, n</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>1 PV focus and 1 extra-PV focus</td>
</tr>
<tr>
<td>3 PV foci and 1 extra-PV focus</td>
</tr>
</tbody>
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PV indicates pulmonary vein, extra-PV, extrapulmonary vein; n, No. of patients on all.
always almost identical. Figure 2 depicts a representative example of isopotential maps and virtual electrograms obtained during sinus rhythm and focal ectopy.

In 3 patients, extrapulmonary foci were identified. All extrapulmonary foci displayed repetitive activity during the invasive study, and 1 focus induced an episode of atrial fibrillation. In 2 patients, the focus was in the lower left atrium between and inferior to the lower left and lower right pulmonary veins (Figure 3). In 1 patient, earliest left atrial activation during focal activity was at the septal aspect of the left atrium anterior to the right lower pulmonary vein.

Conventional Mapping to Identify Target Sites for Radiofrequency Ablation and Results of Catheter Ablation

According to our predefined treatment strategy, radiofrequency catheter ablation was attempted in all 8 patients with 1 pulmonary vein focus, in 3 with 2 pulmonary vein foci, and in 1 with 1 pulmonary vein focus and 1 left atrial extrapulmonary focus (Figure 4). Thus, ablation of 15 foci (14 pulmonary vein foci and 1 extrapulmonary focus) was attempted. In these patients, the mapping and ablation catheter was manipulated to pulmonary veins identified by means of noncontact mapping to carry the focus and conventional mapping was applied. Within the pulmonary veins, far-field left atrial activation followed by characteristic spike potentials could be recorded during sinus rhythm in all cases (Figure 5). After the ablation catheter was placed, 9 of 14 pulmonary vein foci displayed activity, with conversion of the activation sequence compared with sinus rhythm (Figure 5). Between 1 and 8 (4±3) radiofrequency applications abolished spike potentials. When no ectopic activity occurred while the ablation catheter was positioned in the vein, the most distal recording site of the spike potential within the pulmonary vein was assessed during sinus rhythm and the mapping catheter was withdrawn slowly. Radiofrequency energy was applied to the most proximal recording site of the spike potential. Between 2 and 9 (5±3) radiofrequency applications applied...
in a parallel, partially circumferential fashion were necessary to abolish conduction to more distal sites within the pulmonary vein.

After completion of radiofrequency application, none of the patients displayed focal activity either spontaneously or that was triggered by burst pacing or isoproterenol or adenosine administration. Total duration of the investigation was 177 ± 31 minutes (range, 140 to 235 minutes), and fluoroscopy exposure time was 32 ± 18 minutes (range, 14 to 61 minutes).

Complications
At 3 hours after the procedure was completed, 1 patient complained of dizziness and blurred vision, which completely resolved 2 hours later. Neurological examination and cranial computed tomography revealed no abnormalities. One patient developed a bleeding complication in the right femoral groin that required a minor surgical intervention. No further complications were observed.

Follow-Up
All patients who underwent catheter ablation were discharged on β-blocker therapy. Two patients with early recurrence of atrial fibrillation after ablation were treated with antiarrhythmic drugs (flecainide 100 mg BID). During long-term follow-up of 8 ± 4 months (range, 2 to 14 months), stable sinus rhythm was documented in 8 of 12 patients who underwent radiofrequency catheter ablation (Figure 4). None of the 8 patients received antiarrhythmic drugs during follow-up.

Curative treatment with a single ablation session was achieved in 6 of 8 patients with 1 focus and in 2 of 3 patients with 2 pulmonary vein foci. In 4 patients, atrial fibrillation recurred 1 day to 4 weeks after the initial ablation session. In 2 patients, a second ablation session using noncontact mapping technology was performed, which was successful in 1 patient. Overall, radiofrequency catheter ablation guided by noncontact mapping resulted in curative treatment in 9 of 12 patients (75%).

Discussion

Main Findings of the Study
The present study is the first to report on the use of simultaneous noncontact mapping of the left atrium in a consecutive series of patients with paroxysmal atrial fibrillation. Analysis of left atrial activation during sinus rhythm and ectopic activity was reliably possible in all cases by use of isopotential maps and virtual electrograms. Because high-resolution maps of the whole left atrium can be created simultaneously from a single beat, the technology allows precise mapping even in patients with rare focal activity. In addition, complex activation sequences due to ectopic activity arising from different pulmonary veins and also extrapulmonary vein foci, which are difficult to map with conventional technologies, could be analyzed and understood. Because mapping data were acquired without conventional electrode catheters being in direct contact with the left atrial endocardium, use of noncontact mapping avoided the mechanical induction of ectopic activity that is frequently seen during conventional mapping of pulmonary veins.
Noncontact mapping allowed identification of left atrial breakthrough sites after pulmonary vein ectopy and identification of extra pulmonary vein foci. Results of noncontact mapping were used to develop individual treatment strategies (ie, to attempt focal catheter ablation in patients with 1 or 2 ectopic foci or intraoperative radiofrequency ablation in patients with >2 ectopic foci). Successful radiofrequency ablation guided by noncontact mapping was achieved in 9 of 12 patients (75%) in whom catheter ablation was attempted.

Mapping of the Left Atrium in Patients With Paroxysmal Atrial Fibrillation

Conventional Mapping
In 1998, Haissaguerre et al reported on 45 patients with paroxysmal atrial fibrillation who underwent conventional mapping of the left atrium to identify potential target sites for curative radiofrequency catheter ablation. Successful ablation of paroxysmal atrial fibrillation was achieved in 62% of patients studied. However, 2 ablation sessions were necessary in almost half and 3 in >10% of the patients. In a subsequent publication, the same group reported the results of mapping and ablation in 110 patients with paroxysmal atrial fibrillation. This patient cohort, 2 procedures were required in nearly all patients to achieve an overall success rate of 69%. In addition, a success rate of only 25% was observed in patients with >2 ectopic foci. These results show that although the concept of focal ablation of the triggers that initiate paroxysmal atrial fibrillation is a potentially curative strategy, technical and methodological improvements are necessary to improve clinical applicability and results of treatment, as recently stated by the inventors of the procedure.

Simultaneous Noncontact Mapping
Results of the present study show that some of the difficulties related to conventional mapping and ablation of atrial fibrillation described above can be overcome by use of simultaneous noncontact mapping. One significant advantage of the system is the ability to provide a global, simultaneous view of arrhythmia activation. This is of particular importance for the analysis of unstable or nonsustained arrhythmias such as focal atrial fibrillation. The virtual unipolar electrograms obtained at the earliest site of activation during ectopic activity were characterized by QS or rS morphology, with the intrinsic deflection inscribing earlier compared with all adjacent sites, a characteristic comparable to what could be expected with contact unipolar electrograms recorded at the exit site of activation to the left atrium. Amplitude of the r wave of the virtual electrograms recorded at breakthrough sites and at distant sites was variable (see Figure 2). Thus, for correct interpretation of the virtual unipolar electrograms, both morphology and timing criteria must be applied. The dV/dt of the virtual unipolar electrograms differed markedly at different recording sites. This phenomenon can be explained in terms of the variable distance and orientation of the center of the EnSite balloon electrode to the recording sites. No specific pulmonary vein spike potentials preceding onset of left atrial activation during ectopy could be visualized with virtual electrograms in the present study. However, recent data from Schneider et al indicate that pulmonary vein potentials can be recorded with the noncontact mapping system when the balloon electrode is placed close to a pulmonary vein that displays ectopic activity. In our present study, the balloon electrode was positioned in the center of the left atrium; this may explain the lack of pulmonary vein potential recording. Thus, ectopic activity that arises in the pulmonary veins but is not conducted to the left atrium may not be obtained with noncontact mapping. This is a noteworthy limitation of the mapping technology.

Comparison With Other New Mapping Strategies
Haissaguerre et al recently introduced circumferential mapping of the ostia of the pulmonary veins to identify and ablate connection sites of the left atrial musculature to the pulmonary veins. Significant advantages of this technique are that the ablation procedure can be performed during sinus rhythm and no focal activity is required. However, the initial experience with disconnection of the pulmonary veins showed a high recurrence rate (44%). In addition, patients with extrapulmonary vein foci may not benefit from the procedure. Whether an ablation concept guided by identification of focal triggers or an anatomically based treatment strategy that aims for isolation or disconnection of the pulmonary veins will prove superior is unclear.

Radiofrequency Catheter Ablation

Patient Selection for Radiofrequency Catheter Ablation
In the present study, the indication for catheter ablation was based on number of pulmonary vein foci identified during the diagnostic part of the study. Although the results of focal ablation of atrial fibrillation reported in the literature are variable, general agreement seems to be that the success rate of the procedure is significantly lower in patients with multiple foci versus those with 1 or 2 ectopic foci. In addition, incidence and risks of pulmonary vein stenosis after radiofrequency application inside the pulmonary veins is still unclear, and we did not want to take the risk of radiofrequency application to multiple pulmonary veins in our patients. On the basis of these issues, our treatment protocol advised ablation only in patients with 1 or 2 left atrial foci. To the other patients obviously more difficult to treat with focal ablation, we recommended intraoperative radiofrequency ablation of atrial fibrillation, which can be performed with minimally invasive techniques in our hospital and has been shown to be highly effective.

The mean procedure duration of our studies was slightly shorter than for other current approaches to cure atrial fibrillation. This difference may have occurred because the present investigation was terminated after the diagnostic part and no ablation was attempted in approximately one third of the patients included in the present study.

Study Limitations
Data published in the present article represent our initial results with the use of noncontact mapping in patients with atrial fibrillation. The number of patients included is small, and more experience is needed before the role of noncontact mapping applied in patients with paroxysmal atrial fibrilla-
tion can be defined securely. The procedure is highly invasive and bears the risk of significant complications. Special attention and care are necessary during placement of the large balloon electrode in nondilated left atria. In addition, a few specific limitations need to be addressed. Reconstruction of left atrial geometry limited to the tagging of pulmonary veins provides only a rough estimation of true left atrial geometry. The approach proved feasible for identification of breakthrough sites from the pulmonary veins to the left atrium and of extrapulmonary vein foci. However, no exact electroanatomical reconstruction of the pulmonary vein ostia was performed. Thus, it was not possible to define target sites for catheter ablation on the basis of the geometry data. A success rate of 75% to cure patients of paroxysmal atrial fibrillation was achieved in the present study. However, the patients treated with focal ablation in the present study represent a selected subgroup and conventional ablation may have been performed with comparable success rates. Although obvious advantages of noncontact mapping could be demonstrated, one cannot conclude from the present study that noncontact mapping is superior to conventional mapping strategies to cure patients of atrial fibrillation. Finally, although mechanical induction of ectopic activity frequently seen during conventional mapping of the pulmonary veins is avoided by noncontact mapping, the noncontact balloon electrode itself, when placed in the left atrium, may induce atrial arrhythmias.

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