Modification of the Substrate for Maintenance of Idiopathic Human Atrial Fibrillation

Efficacy of Radiofrequency Ablation Using Nonfluoroscopic Catheter Guidance

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Background—Catheter ablative techniques to modify the substrate to maintain atrial fibrillation (AF) require the creation of continuous radiofrequency current-induced ablation lines. This study was designed to assess the efficacy and safety of nonfluoroscopic mapping in this setting.

Methods and Results—A total of 45 consecutive patients with idiopathic AF were studied. The first 13 underwent ablation confined to the left atrium by creating a circular line isolating the pulmonary vein ostia and a second line connecting the former with the mitral annulus. Subsequently, 12 of these patients underwent a procedure confined to the right atrium (RA), where attempts were made to create an isthmus line between the inferior vena cava and the tricuspid annulus, an anterior line connecting the tricuspid annulus with the superior vena cava, and an intercaval line between the ostia of the inferior and superior venae cavae. In the last 32 patients, only the RA approach was performed. Technical difficulties prevented the creation of the intended left atrial line pattern: all patients experienced recurrences. A 100% recurrence rate was also observed after subsequent RA ablation, despite creation of a complete line pattern in 4 of 12 patients. Of the final 32 patients, AF recurred in 94%; a complete ablation line pattern had been achieved in 18 patients (56%), 16 of whom had recurrences.

Conclusions—The electroanatomically-guided creation of extended radiofrequency current lesions is technically feasible only in the RA. However, procedural success in the RA does not suppress recurrences of AF in the majority of patients.

(Key Words: atrial fibrillation • catheter ablation • mapping)

Curative nonsurgical treatment of atrial fibrillation (AF) is still a challenge. Interventional electrophysiologists presently concentrate their efforts on combining the principles of 2 successful therapeutic approaches: surgery and catheter ablation. Cardiac surgeons have succeeded in preventing the initiation and maintenance of AF by dissecting both atria into small, electrically insulated compartments. Initial attempts at emulating the surgical approach to treatment of AF in the catheter laboratory have met with limited success. The major obstacle has been the need to create long radiofrequency (RF) current–induced lesions in the atria that are both continuous and transmural.

Recently, a novel system (CARTO, Biosense Ltd) for mapping cardiac chambers has been introduced into clinical practice. Forgoing fluoroscopy, it enables a precise determination of the spatial location and orientation of the catheter tip inside the heart, with simultaneous assessment of the endocardial electrical activation at that point in space; from a multitude of points sampled, a sophisticated computer system reconstructs and displays the 3D endocardial contour of the targeted cardiac chamber, superimposed with a color-coded map of pertinent electrical information.

The purpose of this study was to assess the feasibility and safety of RF current-induced compartmentalization of both the left and right atrium in patients with idiopathic AF using the CARTO system.

Methods

Between June 1997 and June 1998, 45 consecutive patients (37 men and 8 women aged 58±8 years) underwent attempts at primary ablation of symptomatic, idiopathic AF at our institution. AF was documented as the sole underlying arrhythmia at the time of palpitations in all patients. AF had recurred intermittently in 37 patients (82%), with a mean number of 12.4±7.9 episodes per month, and a maximum duration of episodes of 25±20 hours. In the remaining 8 patients, AF had become chronic. A median number of

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Baseline Patient and Procedure Data

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AA indicates antiarrhythmic medication; AVN, atrioventricular node; LA, left atrium; LAT, left atrial tachycardia; and Rpt, repeat ablation.

4 (range, 1 to 7) antiarrhythmic agents at therapeutic doses had been ineffective (Table). On admission, a detailed history was taken from all patients, and a physical examination was performed. Previous anticoagulation therapy (aspirin, Coumadin) was switched to a continuous infusion of heparin (200 to 300 IU · kg$^{-1}$ · day$^{-1}$). Before the electrophysiological investigation, patients underwent transthoracic and/or transesophageal echocardiography. Antiarrhythmic medication was maintained throughout hospitalization and after discharge.

All patients were informed in detail about the investigational nature of this study and gave their written consent. The protocol was approved by the Freiburg Ethics Committee.

Mapping and Ablation
The physical principles of the CARTO system have been described in detail elsewhere. Using a special mapping catheter (NAVISTAR, 7 or 8F, 4-mm tip electrode; Cordis Webster), 2 types of electroanatomical maps were assessed. They displayed either the spatial distribution of local endocardial activation relative to the stimulus artifact on the coronary sinus electrogram (activation map) or the spread of electrical activation over the targeted chamber throughout the cardiac cycle (propagation map).

Although the CARTO system was designed specifically to minimize fluoroscopy time, in this study, fluoroscopy was used to introduce catheters into the heart and to gain experience with nonfluoroscopic catheter guidance. Thus, particularly in the early study phase, the mapping catheter was first positioned under fluoroscopic guidance and then verified by CARTO.

Left Atrial Procedure
Access to the left atrium was gained by way of a patent foramen ovale or by transseptal puncture using either a single 9-French sheath (SL2, Daig Corporation) or (in patients 12 and 13) a custom-made 2-sheath system (Cordis Webster). Additional catheters were positioned inside the coronary sinus (Jackman, Cordis Webster) and at the bundle of His (standard decapolar).

Acquisition of the baseline map was performed during coronary sinus pacing at a cycle length of 600 to 700 ms or during AF. The anatomical locations of the mitral annulus (displayed as a ring) and pulmonary veins (displayed as tubes) were determined first; thereafter, as many points as deemed necessary were taken to reconstruct the left atrial cavity.

After completion of the CARTO map, the intended ablation lines were drawn into it as a series of contiguous marker dots. Lines included a circular line isolating the ostia of the pulmonary veins and a curvilinear line along the lateral atrial wall connecting the circular pulmonary line with the mitral annulus (Figure 1).

For RF current application, different approaches were taken, depending on whether the procedure was performed during coronary sinus pacing or during AF. In the former case, the local electrogram at each marker dot was assessed for its morphology (single or double potential). At sites where a single potential was recorded, current delivery was started at a power of 20 W and gradually increased during continuous monitoring of impedance, temperature, and local electrogram. Current delivery (maximum 50 W, 60 to 180 s) at each site was terminated if one of the following end points was reached: (1) the occurrence of a widely separated double potential; (2) a decrease in local electrogram amplitude by ≥70%; (3) failure to reach either end point after two 180-s current pulses; and (4) a sudden impedance rise. During AF, the same power titration technique was used, but current was always delivered for 60 to 180 s.

In patients in whom the procedure was performed during coronary sinus pacing, CARTO mapping was repeated after ablation to validate the ablation lines for completeness. Complete lines of conduction block were characterized on the activation map by an abrupt color change from shades of light colors (red or yellow) to purple, representing sites of early and late activation on either side of the line.
Right Atrial Procedure
Catheters positioned in the right atrium included a Jackman catheter advanced into the coronary sinus, a 7-French catheter with 20 electrodes (A20, Cordis Webster) placed along the lateral right atrial (RA) wall, and a His bundle catheter. The NAVI-STAR catheter was introduced by way of the right femoral vein or the right internal jugular vein.

To enable ablation in the right atrium during coronary sinus pacing, all efforts were undertaken to restore and maintain sinus rhythm throughout the procedures. RA lesions included 3 lines (Figure 2). The first line bridged the isthmus between the tricuspid annulus and the ostium of the inferior vena cava (isthmus line). The second line connected the ostium of the superior vena cava with the anterior aspect of the tricuspid annulus (anterior line). The third line was begun at the ostium of the inferior vena cava and directed toward the ostium of the superior vena cava (intercaval line).

An intended gap of 2 to 3 cm was left in the superior part of the intercaval line in all patients; exceptions were patients in whom persistent gaps in the anterior line could not be closed. In those patients, the intercaval line was intentionally closed.

The following modalities were used to validate the completeness of RA linear lesions during coronary sinus pacing. Conduction block across the isthmus line was assessed using the conventional criterion of a change in the activation sequence recorded by the A20 catheter.6

To validate the completeness of the anterior and intercaval lines, the CARTO activation and propagation map features were used. Whenever unintended gaps were found along the ablation lines, current was again applied. If single potentials persisted, the line was regarded as incomplete.

Follow-Up
Postablation, a 12-lead ECG was recorded daily, and ≥1 Holter recording (48-hour) was taken. Transthoracic echocardiography was repeated to monitor procedure-related pericardial effusions. Overlapping with continued heparin infusion (partial thromboplastin time, 60 to 100 s), anticoagulation therapy with Coumadin (international normalized ratio, 2 to 3) was initiated.

After hospital discharge, ≥1 ECG (12-lead) and 24-hour Holter recording were obtained at months 1, 3, and 6. During follow-up, patients were asked to report all episodes of recurrent symptoms suggestive of AF.

Study Endpoint
The study endpoint was the recurrence of documented AF or of symptoms suggestive of AF.
Statistics
Continuous variables are presented as mean±1SD, where appropriate. In cases with a non-Gaussian distribution, median and range are given.

Results
Initial Left Atrial Ablation
In the first 13 patients enrolled in this study (11 men and 2 women aged 60±8 years), the initial ablation procedure was performed in the left atrium. Mapping and ablation was done during AF and coronary sinus pacing in 7 (54%) and 6 patients (46%), respectively. In all patients, catheter manipulation and stable positioning along the septum, the inferior septal pulmonary vein, and the anterior left atrial wall were technically difficult, if at all possible. The mean number of RF current applications was 49±11; procedure duration and fluoroscopy time amounted to 7.9±1.4 hours and 105±22 minutes, respectively.

Line Validation
Postablation line validation could be performed in a total of 7 patients. A complete pattern of left atrial lines was not achieved in any patient.

Figure 2. Anatomical reconstruction of right atrium in right anterior oblique projection, with intended ablation lines superimposed (pale dots). Tricuspid annulus (TA), superior vena cava (SVC), and inferior vena cava (IVC) are represented by colored rings. Foreshortened yellow tube represents coronary sinus (CS). Ablation lines include isthmus line, anterior line, and intercaval line.
Complications
Patient 3 developed a pericardial tamponade requiring immediate pericardiocentesis; the ablation procedure was repeated 2 weeks later. Patient 12 suffered a cerebral infarction 2 days after the procedure in the region subtended by the right posterior cerebral artery. This resulted in left-sided hemianopsia, which resolved gradually.

Follow-Up
During a median follow-up of 26 days (range, 1 to 47 weeks), all patients had recurrent episodes of AF (Figure 3).

RA Ablation After Left Atrial Ablation
In 12 of the 13 patients (the exception was patient 12), 1 or 2 RA ablation procedures were performed within a median of 29 days (range, 1 to 39 weeks) of the left atrial ablation procedure (Table). Mapping and ablation were performed during coronary sinus pacing and AF in 9 and 3 patients, respectively. In 2 patients, the anterior line could not be closed and, therefore, no intentional gap was left in the intercaval line. The mean number of RF current applications was 31 ± 16; procedure duration and fluoroscopy time amounted to 6.6 ± 2.0 hours and 41 ± 26 minutes, respectively.

Line Validation
Postablation line validation was done in 8 patients. Three patients had a complete pattern of ablation lines. Of the remaining 5 patients, all had complete isthmus lines, but unintended gaps were present in the anterior line when the intercaval line was intentionally left open (n = 4) or multiple gaps were left in the anterior line in the presence of a totally blocked intercaval line (n = 1).

Complications
Postablation pericardial effusions were observed in 2 patients; neither required pericardiocentesis. A procedure-related false aneurysm of the left femoral artery occurred in 1 patient.

Follow-Up
Of 4 patients with complete line patterns (including 1 patient in whom remapping after 6 months revealed that the intended gap in the intercaval line had closed but a single gap was still left in the anterior line), all experienced recurrent episodes of AF (Figure 4). Recurrences of AF were also observed in all 8 patients in whom either ablation line patterns were incomplete or line validation was not performed. Thus, the recurrence rate of AF after RA ablation after left atrial ablation was 100%. Pacemakers were eventually implanted in 3 patients.

Initial RA Ablation
In the remaining 32 patients enrolled in this study (26 men and 6 women aged 57 ± 8 years), the initial ablation procedure was performed in the right atrium. Mapping and ablation were done during AF in the first 2 patients and during coronary sinus pacing in all other patients. Postablation line validation was done in 27 patients (84%); in the other 5 patients, several attempts at achieving sinus rhythm after ablation failed, and line validation could not be performed.

The mean number of RF current applications was 37 ± 16; procedure duration and fluoroscopy time were 7.4 ± 1.6 hours and 14.2 minutes (range, 5.7 to 70.0 minutes), respectively. Fluoroscopy time tended to get lower as more patients were studied: median fluoroscopy times in the first 5 and last 5 of the 32 patients were 44 and 12 minutes, respectively.

Line Validation
Postablation line validation (Figures 5 and 6) revealed that complete lines had been achieved in 16 of 27 patients (59%). They were the isthmus line in all 16 patients, the anterior line in 12 patients, and the intercaval line in the remaining 4 patients. Of the 11 patients with incomplete lines, unintended gaps were present in either the anterior line (n = 7) or the intercaval line when the anterior line could not be closed (n = 4); the isthmus line was complete in all 11 patients.

Complications
Despite postablation demonstration of conduction gaps in either the anterior or the intercaval line, RA isolation was observed within 48 hours in 3 patients. In these patients, sinus node activity was not conducted to the atroventricular node. Right/left atrial dissociation existed, with the right atrium in sinus rhythm and the atrial septum and left atrium activated by a junctional or atrial escape rhythm or AF; because atrioventricular nodal conduction was not impaired, escape rhythm or AF was conducted to the ventricles (Figure 7). RA isolation was permanent in 2 patients, which necessitated pacemaker implantation, and transient (for 4 days) in the other patient. AF recurred in all 3 patients.
Pacemakers were implanted in a further 4 patients. Other complications were clinically irrelevant pericardial effusions in 3 patients and a retroperitoneal hematoma and a pneumothorax in 1 patient each.

**Follow-Up**

Two of the 16 patients with an initially complete RA line pattern underwent repeat RA ablation, which was unsuccessful in 1, leaving 15 patients with complete line patterns (Figure 8). Of the other 16 patients in whom right ablation lines after the initial session were either incomplete or not validated, 3 underwent successful attempts at the ablation of focal left atrial ectopy triggering left-sided AF, and 4 underwent repeat RA ablation; in 3 of the latter patients, a complete pattern of ablation lines could be achieved. Thus, after $1$ RA ablation procedures, 18 of the 32 patients (56%) had a complete pattern of RA linear lesions. Of these, 16 (89%) still had recurrences of AF. All 14 patients with lines that were incomplete or not validated had recurrences of AF. Thus, the total recurrence rate in the 32 patients undergoing initial RA ablation was 94%.

**Discussion**

Recent therapeutic studies have suggested that different electrophysiological substrates may exist for the initiation and maintenance of human AF. The initiation of AF has been shown to originate from rapidly firing foci predominantly located inside the pulmonary veins. If suppression of the substrate for initiation of AF cannot be achieved using a catheter-based approach, then modification of the substrate for maintenance of AF presents itself as an important therapeutic alternative.

In an animal study, a critical number of reentrant wavelets, which required a critical mass of atrial myocardium, was necessary to maintain AF. Therefore, the surgical approaches were designed to divide atrial mass into several compartments that, by themselves, could not maintain AF. However, by isolating the ostia of the pulmonary veins from the remainder of the left atrium, the surgeons may have inadvertently blocked foci inside the pulmonary veins. Because electrophysiological mapping has not been performed in any of the surgical studies, the true mechanism underlying the surgeons’ therapeutic success has not been elucidated.

Transferral of the surgical approach to fluoroscopy-guided RF current catheter ablation techniques has previously been attempted. However, catheter positioning after displacement is imprecise under fluoroscopy and renders the creation of long linear lesions extremely difficult. Validation of ablation lines for completeness has not been reported. Therefore,
electrophysiological endpoints that would allow a systematic and reproducible therapeutic approach have not been defined.

The present study used a novel technique for 3D electroanatomical reconstruction of the targeted atrium and catheter guidance, which allowed precise positioning and, even more important, repositioning. The rationale for line design in both left and right atrium was to implement electrical barriers that prevent single macroreentrant wavefronts from circulating.

**Figure 6.** Validation of anterior line by means of CARTO propagation map. All panels show cranial left anterior oblique views and represent freeze frames from animated sequence obtained during coronary sinus (CS) pacing. Shades of red on blue background represent local activation times, which span an interval of 30 ms (red bar on the time scale under each panel). Top, Spread of stimulated wavefront before ablation shows homogeneous activation of anterior aspect of right atrium from inferoposterior to superolateral. Bottom, Spread of stimulated wavefront after achievement of complete conduction block (light blue dots) along anterior line. Stimulated wavefront reaches line of conduction block (second panel) and then activates RA regions distal to line of conduction block after traveling along the posterior wall. S indicates stimulation artifact. Other abbreviations as in Figure 5.

**Figure 7.** Postablation surface electrocardiographic leads in patients in whom RA ablation resulted in RA isolation. A, Sinus rhythm (SR; cycle length, 920 ms) with biphasic P-wave morphology (arrows) in lead II, which is indicative of prolonged interatrial conduction after RA ablation but before onset of RA isolation. First P-wave component represents RA activation, and second P-wave component represents left atrial activation. B, Same patient as in A. RA sinus node activation is shown (cycle length, 1000 ms) represented by monophasic P-waves (arrows) independent of junctional escape rhythm (JER; cycle length, 1630 ms) activating atrial septum, left atrium, and ventricles. C, Surface leads II and V1 in another patient, showing RA sinus node activation at cycle length of 600 ms (arrows in lead V1) and irregular R-R intervals indicative of AF activating atrial septum, left atrium, and ventricles.
around the ostia of the pulmonary veins, the mitral valve annulus, the ostia of the caval veins, and the tricuspid valve annulus and to prevent random microreentry secondary to multiple wavelets.

**Initial Left Atrial Ablation**
A complete pattern of left atrial ablation lines could not be achieved in any of the 13 patients studied. Incomplete lines were particularly present along the septum, the inferior septal pulmonary vein, and the anterior left atrial wall. With the conventional transseptal sheath technology used in the majority (85%) of patients, those regions were either difficult to reach or did not allow stable catheter-wall contact for longer periods of time. All patients continued to have episodes of AF, and 2 patients also developed gap-related atrial tachycardias.

**RA Ablation After Left Atrial Ablation**
In none of the 12 patients who subsequently underwent RA ablation did the substrate for maintenance of AF change; all 12 patients experienced recurrences of AF.

**Initial RA Ablation**
In the final 32 patients, every effort was made to validate ablation lines for completeness. No attempts were made to detect asymptomatic episodes of AF because they were considered to be of secondary importance as long as symptomatic episodes were not suppressed.
Recurrences of AF were observed in all but 2 of the 32 patients, despite the fact that an RA ablation line pattern, as intended, was achieved in 18 patients (56%). Sixteen of these 18 patients (89%) had recurrences, suggesting that the entire left atrium plus the septal compartment of the right atrium provide a mass that is sufficiently large to maintain AF. This was strikingly demonstrated by the 4 patients who developed either permanent or transient RA isolation within 2 to 4 days of the ablation procedure.

**Limitations**
Fluoroscopy was used to verify catheter positions on the CARTO maps. Therefore, fluoroscopy times reflect the operators’ learning curve; they decreased with growing experience. Long procedure durations were a consequence of the sequential CARTO mapping modality and the need for postablation remappings. On-line assessment of line completeness could possibly reduce procedure duration markedly. All procedures were performed under maintenance of the patients’ antiarrhythmic medication, which was also continued after ablation. Therefore, a proarhythmic effect of the individual patient’s medication cannot be excluded.

**Conclusions**
This study demonstrates that by using electroanatomical mapping, continuous lines of conduction block can be created in the right atrium. However, successful creation (as achieved in 22 of the 45 patients) of the 3-ablation-line pattern in the right atrium that was designed for this study does not suppress clinical recurrences of AF in the majority of patients; AF may even recur in the presence of RA isolation. The practical realization of the left atrial pattern of ablation lines designed for this study could not be achieved due to technical difficulties.

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