Atrial Linear Ablations in Pigs
Chronic Effects on Atrial Electrophysiology and Pathology

Lior Gepstein, MD, PhD; Gal Hayam, BSc; Shlomo Shpun, DSc; David Cohen, MD; Shlomo A. Ben-Haim, MD, DSc

Background—Generation of long and continuous linear ablations is required in a growing number of atrial arrhythmias. However, deployment and assessment of these lesions may be difficult, and there are few data regarding their short- and long-term effects on atrial electrophysiology and pathology.

Methods and Results—A nonfluoroscopic mapping and navigation technique was used to generate 3-dimensional (3D) electroanatomic maps of the right atrium in 8 pigs. The catheter was then used to deliver sequential radiofrequency (RF) applications (power output gradually increased until 80% reduction in the amplitude of the unipolar electrogram) to generate a continuous lesion between the superior and inferior venae cavae. The animals were remapped 4 weeks after ablation during septal pacing. Lesion continuity was confirmed in all cases by the following criteria: (1) activation maps indicating conduction block [significant disparities in activation times (52.0±16.0 ms) and opposite orientation of the activation wave front on opposing sides of the lesion], (2) evidence of double potentials (interspike time difference of 52.3±17.1 ms), and (3) low peak-to-peak amplitude of the bipolar electrograms (0.7±0.6 mV) along the lesion. At autopsy, all lesions were continuous and transmural, averaged 50.5±6.7 mm, and were characterized histologically by transmural fibrosis throughout the length of the lesion.

Conclusions—Long linear atrial ablation, created by sequential RF applications (using unipolar amplitude attenuation as the end point for energy delivery), results in long-term continuous and transmural lesions. Lesion continuity is associated with evidence of conduction block in the 3D activation maps and the presence of double potentials and low electrogram amplitude along the lesion. (Circulation. 1999;100:419-426.)

Key Words: catheter ablation ■ electrophysiology ■ arrhythmia ■ atrium

Catheter ablation procedures have evolved in recent years to become an established treatment for a variety of supraventricular and ventricular arrhythmias.1-2 Although some arrhythmias can be managed with the application of focal ablations,3 others may require the formation of continuous longitudinal lesions.3-6 Generation of such lesions, aiming at creating continuous lines of conduction block, may be mandatory for the treatment of a variety of arrhythmias such as atrial flutter,4 reentrant arrhythmias with broad isthmuses,3 and most likely for the curative treatment of atrial fibrillation.6 The recent paradigm shift from application of focal ablations to continuous longitudinal lesions, although it significantly increased the spectrum of treatable arrhythmias, has also raised several issues regarding the application and short- and long-term electrophysiological and pathological consequences of these lesions. However, data regarding these issues are lacking in the literature.7 Such information may be crucial for optimal treatment of various arrhythmias and for better understanding of the mechanisms involved in arrhythmia recurrences.

Recently, a nonfluoroscopic, catheter-based, electroanatomic mapping method was introduced.8-12 This method uses magnetic fields to accurately determine the 3-dimensional (3D) location of a mapping and ablation catheter. More recently, it has been shown that this technique can be used to generate precise continuous and longitudinal lesions.10

In this study, we used this technique to study the chronic effects of the generation of longitudinal lesions on the electrophysiological and pathological properties of the atrium. Specifically, we tried to investigate whether chronic healing of an acute lesion may result in the appearance of discontinuities along the line, and also to describe the spatial and electrophysiological parameters associated with the presence of a continuous lesion.

Methods

Mapping System

The nonfluoroscopic electrophysiological mapping and navigation system (CARTO, Biosense) has been described elsewhere.8-12 In brief, the system uses ultralow magnetic fields to accurately determine the location and orientation of the tip of the mapping and ablation catheter. The catheter’s location is determined relative to a reference catheter (fixed to the subject’s back) and gated to a fiducial point in the
cardiac cycle. This information allows real-time tracking of the tip of the mapping catheter while it is deployed within the heart.

**Animals**

Studies were performed on 8 healthy male pigs weighing 25 to 40 kg. Animals were anesthetized with pentobarbital 30 mg/kg, intubated, and ventilated. Vascular access was obtained by vascular cutdown of the jugular veins. A 100-U/kg IV bolus of heparin was given shortly thereafter. The experimental protocol was approved by the Animal Study Committee of the Technion Faculty of Medicine.

**Mapping Procedure**

The mapping procedure was based on sequential sampling of the location of the roving catheter simultaneously with the local electrogram recorded from its tip, at several endocardial sites. In our experience, sampling of '50 points was needed to accurately reconstruct the 3D geometry of the right atrium (RA). The local activation time (LAT) at each site was determined as the time interval between a fiducial point on the body-surface ECG and the steepest negative intrinsic deflection in the unipolar recordings. We report results that were collected from unipolar and bipolar recordings filtered at 0.5 to 400 Hz and 30 to 400 Hz, respectively. The activation map was then color-coded and superimposed on the 3D geometry.

**Radiofrequency Energy Application**

Radiofrequency (RF) energy was delivered from the distal tip electrode (4 mm) of the mapping catheter, and the ground electrode was a large patch placed on the animal’s back. RF ablation was performed with a 500-kHz RF generator (RFG-3C; Radionics) with power output increased gradually (maximum temperature, 60°C) for up to 60 seconds, or 10 seconds after 80% reduction in the unipolar amplitude.

**Experimental Protocol**

After creation of the RA electroanatomic map during sinus rhythm, the catheter was navigated to the most distal site of the planned ablation path. RF energy was delivered to create a point ablation at that site. The catheter was withdrawn slightly and then navigated to a nearby site, where another ablation point was created (Figure 1, left). Each ablation site was tagged on the map, resulting in a complete and continuous lesion (Figure 1, right). After completion of the line, the catheter was navigated back along the entire lesion to assess the presence of low-amplitude electrograms (bipolar amplitude, <0.5 mV) and the presence of double potentials. If “viable” electrograms that did not comply with these criteria were noted, additional energy was delivered at these sites. Consequently, a lesion extending from the superior vena cava (SVC) to the inferior vena cava (IVC) was created in all animals.

Four weeks after the first procedure, the RA was remapped during septal pacing. Between 30 and 50 points were sampled along the lesion, providing a high-density map (distance of 2 to 5 mm between adjacent points) of this region.

**Electrophysiological Verification of the Lesion**

We investigated 3 different electrophysiological methods for the determination of lesion continuity.

**Activation Mapping to Determine Conduction Block**

A high-density RA activation map was generated by use of LATs determined from the unipolar recordings. When split electrograms were recorded, the LAT was derived from the steeper of the two. Conduction block was defined as a LAT difference >30 ms between adjacent points on opposite sides of the lesion (<10 mm apart) and opposite orientation of the wave front on opposing sides of the lesion.

**Presence of Double Potentials Along the Line**

The presence of double potentials in the local unipolar electrogram and their spatial distribution relative to the lesion was assessed at all sampled sites.

**Amplitude of the Bipolar Electrogram**

The peak-to-peak amplitude of the local bipolar electrogram was determined at each sampled site.

**Pathological Verification**

At the end of each study, the animals were killed and the hearts excised. Histochemical staining was obtained with 2,3,5-triphenyltetrazolium chloride (TTC), followed by preservation in 4% neutralized formalin for further analysis. The length, shape, location, and continuity of each ablation line was measured on the fresh tissue and compared with the line demonstrated on the electroanatomic map. After fixation, each lesion was blocked and sectioned into a number of longitudinal cuts parallel to the long axis of the lesion, and

![Figure 1. Generation of linear lesion. After creation of 3D map of the RA (posteroanterior view), the catheter is navigated along a predetermined path where sequential point ablations are generated (left). Each point is tagged, resulting in a complete and continuous lesion (right).](http://circ.ahajournals.org/Download/july271999)
the sections were then stained with hematoxylin-eosin and Masson's trichrome for microscopic examination.

Statistical Analysis
Results are reported as mean±SD. Unpaired t test or ANOVA was used to determine statistical significance.

Results
Mapping and Ablation Procedure
Mapping and ablation of the RA were performed rather easily. Fluoroscopy was used only for the introduction of the catheter. Baseline maps consisted of an average of 69.6±41.1 points. The time required to acquire the baseline maps and to generate the lesions was 10±5 and 26±6 minutes, respectively. The Table describes the number of RF applications required for the generation of each line and the length of the line as assessed from the maps and from pathology. Average line length in the maps was 52.8±6.9 mm and consisted of 16.3±1.8 applications per lesion.

The reduction in the amplitude of the local electrogram during energy delivery was evident in all lesions (Figure 2). The characteristic morphological changes in the unipolar electrogram consisted of an initial ST-segment elevation, followed by a gradual decrease in the amplitude of the intrinsic atrial deflection. Thus, in most sites (>95%), RF application lasted <60 seconds before the threshold criterion was achieved (80% reduction in the unipolar amplitude).

In the majority of animals studied, no additional RF applications were needed before the completeness criteria were met. In 3 animals, a number of RF applications (1 to 4) were applied to ensure completeness of the lesion in sites at which viable electrograms were recorded. Interestingly, these sites were usually located at the middle of the SVC-IVC line, which suggested a possible problem of inadequate catheter-wall contact in this area. After these additional applications, lesion continuity was ensured in all animals.

Electroanatomic Maps in the Chronic Stage
Four weeks after ablation, the RA was remapped during pacing from the fossa ovalis. The following electrophysiological parameters were assessed to define the lesion continuity.

Presence of Conduction Block
Figure 3 shows a posteroanterior view of a typical activation map of the pig's RA during pacing. The earliest activation (red) was located at the inferoseptal aspect of the atrium. Note the appearance of a well-defined line of block with very late LATs (blue and purple) located at the lateral aspect of the lesion just adjacent to sites with early LATs. The presence of conduction block can also be viewed in the propagation map (Figure 4). Note that activation originates at the pacing site and then propagates medially, upward, and downward along the posterior wall but is blocked laterally. The activation is then directed around the lesion, using the roof and floor of the atrium, terminating with collision of the 2 wave fronts on the lateral aspect of the lesion.

A line of conduction block characterized by significant LAT differences (52.0±16.0 ms) and by opposite orientation of the activation wave front on opposing sides of the lesion was noted in all animals.

Spatial Distribution of Double Potentials
As can be seen from Figure 5, most double potentials were located at the posterior intercaval area straddling the ablation

<table>
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<tr>
<th>Pig</th>
<th>Line Length, mm, Map</th>
<th>No. of Applications</th>
<th>Lesion Length, mm, Pathology</th>
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<td>1</td>
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<tr>
<td>Mean±SD</td>
<td>52.8±6.9</td>
<td>16.3±1.8</td>
<td>50.5±6.7</td>
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</table>
The double potentials in the 2 deflections (23.4 ± 6 ms). The double potentials located at areas not related to the lesion displayed the shortest interval between the 2 components (52.3 ± 17.1 ms), those located at the edges of the lesion had an interspike interval of 37.1 ± 10.5 ms, and double potentials located at areas not related to the lesion displayed the shortest interval between the 2 deflections (23.4 ± 8.3 ms). The double potentials in the third group accounted for 11.3% of the points in the map not related to the lesion and were associated with the presumed anatomic location of the crista terminalis, the eustachian ridge, and areas of activation wave collision.

Voltage Maps
Figure 6 presents a typical voltage map of the RA, depicting the peak-to-peak bipolar amplitude at each site. Note that the low voltage (red, bipolar amplitude <0.5 mV) located in the posterior wall depicts the lesion. This phenomenon was noted in all maps, with the average amplitude along the lesion (0.7 ± 0.6 mV) being significantly lower (P < 0.01) than that found at other sites (2.3 ± 1.5 mV).

Pathological Examination
Pathological examination revealed the presence of complete, continuous, and transmural lesions in all animals. Average lesion length was 50.5 ± 6.7 mm. A typical lesion stained with TTC is shown in Figure 7. Note that the lesion is continuous, with no apparent gaps, and that it extends in the smooth posterior RA from the SVC to the IVC.

Histological examination of the lesions (Figure 8) revealed transmural myocardial fibrosis with areas of chronic inflammatory cell infiltration. Occasionally, foci of preserved myocardium could be observed within the necrotic zones, which, however, were continuous.

Discussion
Generation of long linear ablations, in an attempt to create continuous lines of block, is required in a growing number of atrial arrhythmias.4–6 In this study, we examined the long-term effects of these lesions on atrial electrophysiology and pathology. Our results demonstrate that generation of continuous lesions acutely results in long-term electrophysiological and pathological evidence of conduction block. We have also shown that lesion continuity can be assessed by the presence of conduction block in the activation maps and by the appearance of double potentials and low-amplitude electrograms along the lesion.

Chronic Pathological Changes
Using the ability of the new technique to accurately combine sequential point ablations into continuous lesions, we were able to generate an anatomic and electrophysiological model to study the chronic changes of such lesions. We found that the initial linear ablations resulted in long-term continuous and transmural lesions as assessed by TTC staining and serial pathological examination. Histologically, all lesions were characterized by well-defined transmural fibrosis, similar to the histological changes described for focal ablations.13,14

Use of Atrial Local Electrogram Attenuation for Energy Titration
Throughout the years, a number of techniques were developed for energy titration during RF application. These include power titration,14 temperature control,15 and impedance measurements.16 Common to all strategies is the aim of creating transmural atrial lesions with minimal risk (of endocardial charring, thromboembolism, barotrauma, and damage to adjacent structures). Nevertheless, the information acquired by these techniques is restricted to the electrode-tissue interface and lacks online data regarding intramyocardial changes during energy delivery.

This study demonstrated that in the RA smooth muscle, energy titration based on electrogram attenuation was safe and resulted in chronic contiguous and transmural lesions. The rational behind this method is that a single application results in a transmural lesion whose area is just larger than the catheter tip, consequently leading to a marked reduction of local electrogram amplitude. As in our study, Nakagawa et al.17 using the canine isolated heart model, found that an 80% decrease in the unipolar atrial electrogram was associated with the creation of an acute continuous and transmural atrial lesion.

Electrophysiological Evidence of Lesion Continuity
Using the SVC-IVC linear ablation as a model, we were able to study the endocardial electrophysiological parameters associated with a continuous lesion.
Presence of Conduction Block in the Activation Maps

Conduction block was confirmed in all cases and correlated well with the findings of continuous lesions in pathology. The location of the pacing electrode and the orientation of the activation wave front relative to the lesion may be of importance because conduction in the normal atrium is relatively fast using several possible pathways. The ability to assess block was facilitated here by the use of an activation wave front, which originated in close proximity and was perpendicular to the line. The rationale behind this setting was to shorten conduction time to the proximal side of the lesion and to lengthen conduction time to its distal part. This resulted in opposite orientation of the activation wave front and maximal time delay (52.0 ± 16.0 ms) between opposite sides of the lesion.

Spatial Distribution of Double Potentials

The appearance of double-spike electrograms has been shown to occur under a variety of conditions, including slow conduction, tissue anisotropy, conduction block, atrial anatomic barriers, and collision of activation waves. Our results demonstrate a tight spatial correlation between the distribution of double potentials and the presence of the linear lesion. Thus, double potentials spanning the gap in activation times between opposite sides of the lesion were recorded along its entire length.

Examining the spatial distribution of all double potentials, we noted that they could be divided into 3 groups: (1) double potentials located along the lesion displayed the longest interspike interval (52.3 ± 17.1 ms) and were related to the activation time difference between the 2 sides of the lesion; (2) double potentials located at the edges of the ablation line were characterized by intermediate interspike intervals (37.1 ± 10.5 ms); and (3) double potentials recorded at sites not related to the lesion were associated with the shortest interval between the 2 deflections (23.4 ± 8.3 ms) and may...
Low Electrogram Amplitude Along the Lesion

The association of low-amplitude electrograms with successful ablation sites was confirmed during 3 different stages: (1) initially, during RF application when the reduction in the amplitude of the local electrogram was used as an end point for delivery of energy; (2) after deployment of the lesion, when the catheter was navigated along the lesion to ensure that no viable electrograms remained; and (3) in the chronic stage, when the lesions could be delineated by the voltage map.

Although all 3 criteria were met in the chronic maps, we did not use activation mapping in the acute state to determine...
lesion continuity. Hence, the presence of “nonviable” (low-amplitude) electrograms and double potentials along the entire path of the lesion was enough to ensure lesion continuity. Activation mapping, however, besides providing additional evidence for the presence of conduction block, may also provide additional information regarding the different routes of ingress of atrial activation after lesion deployment.

Clinical Significance
The results of the present study may possess important clinical consequences. For a linear ablation to be effective, several steps have to be taken. First, one must select the desired site for ablation and then navigate the catheter to this area. Next, energy application must result in the generation of a continuous lesion. This can be achieved only if sites at which RF energy was delivered were continuous and RF application resulted in transmural necrosis. Finally, one must establish whether the lesion achieved the desired electrophysiological effect. The unique abilities of the technique presented here may possess several advantages for each of these stages, as follows.

Developing Ablation Strategy
The ability to determine the location of the mapping catheter superimposed on the 3D map and to relocate the catheter back to predefined sites allows dissociation between the mapping and ablation procedures. Hence, one may first generate a detailed 3D electroanatomic map; next, develop the ablation strategy; and finally, using the reconstruction as a “road map,” navigate the catheter back to the desired path for delivery of RF energy.

Generation of the Lesions
The combination of the ability to navigate the catheter precisely to predefined sites, to estimate the effects of RF energy (by monitoring electrogram changes during energy delivery), and to tag ablated sites ensured the generation of chronic continuous and transmural lesions. Aside from ensuring lesion continuity, these qualities may also minimize ablation burden and allow the usage of a number of different catheters or sheaths for the generation of a single lesion.

Assessment of Lesion Continuity
Our results demonstrate that a continuous lesion is associated with the presence of conduction block and spatial association of double potentials and low-amplitude electrograms along its path. Recent complementary work has shown that these criteria can be used to accurately determine the position of gaps within such lesions and that the catheter could then be re navigated to these sites for completion of the lesion.23–25

Figure 8. Microscopic examination of the lesion (trichrome staining) showing that the lesion is continuous and transmural (green-blue stain represents collagen deposition; purple, viable myocytes). Top, Tissue cut along long axis of lesion. Bottom, Transverse section of lesion, showing well-demarcated lesion.
Despite the growing number of atrial arrhythmias treated by application of linear lesions, the early and late recurrence rate is still significant. These recurrences may result from (1) generation of an incomplete lesion; (2) healing and remodeling of the initial lesion, resulting in the appearance of discontinuities. Previous studies have shown that the acute lesion is characterized by a central zone of coagulation necrosis and a peripheral zone of hemorrhage and edema and that the chronic lesion contracts significantly in volume. It can thus be speculated that healing of this transitional zone may account for the late electrophysiological recovery after an apparently successful ablation; and (3) lesion application in an area not critical for the perpetuation of the arrhythmia.

This study demonstrated that initial generation of continuous lesions resulted in chronic conduction block. Thus, with the limitation of the model studied, we can speculate that precise deployment and assessment of the initial lesion might prevent recurrences related to the first 2 mechanisms.

Limitations
The implications of the present study may be restricted to the smooth-RA animal model in which they were acquired. Thus, further studies will be necessary to define the parameters associated with the generation and assessment of such lesions in trabeculated parts of the atrium, in the left atrium, and in humans.

In addition, the precise location of the lesion in the chronic maps is not known directly. However, its position could be approximated rather accurately by anatomic correlation of the 2 maps and by the tight spatial correlation between the 3 electrophysiological parameters assessed.

A further limitation of the present study is the interpolation of the reconstructed geometry and the electrophysiological information between acquired sites. This may generate difficulties in the correct interpretation of the activation sequence and increase the chance of missing gaps. By sampling a large number of sites specifically in the area of the lesion, we were able to partially compensate for this limitation.

Conclusions
This study demonstrated that the generation of long atrial lesions by combining sequential point ablations guided by 3D magnetic navigation and by electrogram attenuation during RF ablation results in short- and long-term conduction block as well as pathological evidence of continuous and transmural lesions. We have also shown that a continuous lesion is associated with conduction block in the activation maps and the presence of double potentials and low-amplitude electrograms along the line.

References
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