Pulmonary Vein Isolation for Atrial Fibrillation

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Nonpharmacological treatment for atrial fibrillation (AF) has evolved dramatically over the past 20 years. Pulmonary vein isolation, a catheter ablation technique developed in the last decade, prevents focal triggers in the pulmonary veins from initiating episodes of AF. Although the procedure initially involved focal ablation with a catheter directly in the pulmonary veins, investigators subsequently found that isolating the pulmonary veins by applying ablation energy at their junction with the left atrium is more effective. After the procedure is performed once or twice, it is 70% to 80% successful in preventing recurrence of AF episodes in the first year of follow-up. The pulmonary vein isolation procedure is most suitable for patients whose recurring symptomatic episodes of AF have not been suppressed by antiarrhythmic drugs or who do not wish to take long-term antiarrhythmic or anticoagulation medications. The procedure is more successful in patients with intermittent (paroxysmal) AF than in those with long-standing, continuous (chronic) AF.
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Key words: Atrial fibrillation • Catheter ablation • Pulmonary vein isolation • Arrhythmia

Introduction

Nonpharmacological therapy for patients with atrial fibrillation (AF) has evolved dramatically over the past two decades. The initial surgical approach, the maze procedure, was developed by Dr. James Cox, based on the large body of basic pathophysiologic data suggesting that persistence of AF was related to multiple re-entrant wavelets. Thus, the surgical procedure compartmentalized the atria to prevent maintenance of re-entry. It is noteworthy that a significant part of this procedure is to isolate all four pulmonary veins from the rest of the left atrium. The maze procedure has been successful for many patients but has not been widely applied in clinical practice.

Initial catheter ablation approaches to AF were developed to create complete heart block with implantation of a pacemaker rather than as a primary cure of the arrhythmia. Subsequent curative techniques tried to mimic the surgical maze procedure without much success and with significant complications. In the mid-1990s Haïssaguerre and colleagues made a seminal discovery regarding the pathophysiologic mechanism of AF in humans. They observed rapidly firing atrial foci in the pulmonary veins, which revolutionized the approach to radiofrequency catheter ablation to cure patients with AF.[1] This clinical observation has sent many basic scientists back to the laboratory to re-evaluate the pathophysiologic mechanisms of AF in various animal models.

Catheter ablation to cure AF has become the prime focus of research for many electrophysiologists around the world. Much has been learned regarding both mechanisms and techniques to cure patients with AF, but more research is needed to better define which techniques and patients will derive the most benefit from catheter ablation. In addition, newer ablation techniques ranging from "fire to ice" have been used in the search for the cure of AF. Keane and Ruskin's review of pulmonary vein catheter ablation isolation techniques is both timely and well done. Not only have these authors given their important perspective on this area, but they provide the reader with a glimpse into potential future methods and energy sources that might be used in ablation of AF. I hope the reader will enjoy this article as much as I have.
[Eric N. Prystowsky, MD]

The complex mechanisms underlying AF have, up until recently, made catheter ablation a challenging task. It was initially thought that AF would not be amenable to a curative catheter ablation procedure. Therefore, a palliative procedure, atrioventricular (AV)-node or His-bundle ablation, was developed in 1981 to prevent the ventricles from beating rapidly. The limitations of this procedure include not only that it gives the patient a new condition (ie, lifelong pacemaker dependency), but also that the patient's AF continues and may therefore necessitate lifelong anticoagulation. For patients with paroxysmal AF, AV-node ablation and pacing appear to accelerate the progression to persistent AF. For these and other reasons, AV-node ablation and pacemaker implantation are now less frequently performed in patients who are active or under 70 years of age.[2]

Atrial fibrillation is maintained by the coexistence of multiple activation wavefronts that spread randomly over the atria.

While the multiple coexistent excitation waves maintaining AF are difficult to interrupt and organize by catheter techniques, the focal triggers initiating episodes of AF are more consistent in their origin and offer a more standardized target for catheter ablation. Two catheter ablation approaches were developed in the last decade for the treatment of AF:

- the *catheter maze procedure*, which creates lines of conduction block to interrupt the maintenance of AF;
- the *pulmonary vein isolation procedure*, which prevents focal triggers in the pulmonary veins from initiating episodes of fibrillation in the atria.

The catheter maze procedure was originally developed as a method to treat patients with chronic AF, whereas the pulmonary vein isolation procedure was developed to treat patients with paroxysmal AF. The indications for each of these procedures have more recently evolved to include both AF patterns. Furthermore, the pulmonary vein isolation procedure can be combined with either a limited catheter maze procedure for patients with chronic AF or with regional periostial catheter ablation in the left atrium in the region surrounding the pulmonary veins (where it is felt that excitation waves may serve as drivers for the maintenance of AF).

Percutaneous Catheter Maze

In contrast to normal sinus rhythm, in which the atria are activated by a single organized wave of excitation (activation wavefront), in AF the atrial rhythm is disorganized and almost chaotic. Atrial fibrillation is maintained by the coexistence of multiple activation wavefronts that spread randomly over the atria. The wavefronts continuously merge to form mother wavefronts and diverge to form daughter wavelets in an almost chaotic fashion. The wavefronts can occasionally be extinguished when they collide or confront the anatomical boundaries of the atria. When a critical number of wavefronts are extinguished simultaneously, AF terminates and normal sinus rhythm resumes. The detection of rotors with marked periodicity in the left atrium suggests that they may serve as drivers in the maintenance of fibrillation in some patients.

The catheter maze procedure (Figure 1), modeled on the surgical maze operation, is intended to create lines of conduction block (Figure 2) to interrupt the multiple wavefronts

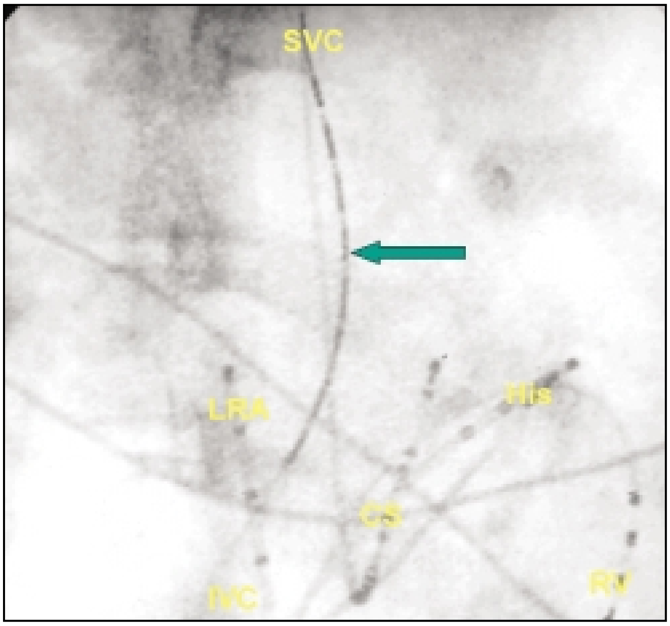


Figure 1. *Fluoroscopic view of a patient undergoing a right-atrial catheter maze procedure. The catheter maze procedure involves the creation of linear lesions in the atria. Lesion sets in the right atrium typically involve a septal line being drawn from the superior vena cava to the inferior vena cava. The ablation catheter is a flexible octapolar microcatheter (green arrow) that is aligned along the right atrial septum. The distal electrode of the microcatheter is in the superior vena cava (SVC), where atrial myocardium is known to extend. Other catheters are placed in the heart to pace and record at different locations: LRA indicates low lateral right atrium; His, His catheter; IVC, inferior vena cava; CS, coronary sinus; RV, right ventricle.*

maintaining AF.[1,3,4] The original surgical maze operation involved the creation of incisions during open heart surgery that effectively divided the atria into channels and compartments. The surgical maze operation involves general anesthesia and conventionally has required both open thoracotomy and cardiopulmonary bypass. It is therefore associated with a risk of surgical complications and is most appropriate in patients undergoing concomitant heart surgery for valve replacement or coronary artery bypass grafting. More recently the operative maze procedure has evolved towards a shorter and less invasive procedure. The lines of conduction block are now being created in the operating room by ablation tools with microwave, laser, cryothermy, and ultrasound; and minimally invasive epicardial surgical approaches through 1-cm port access incisions are currently undergoing clinical evaluation.

In contrast to the surgical maze operation, the catheter maze procedure is performed percutaneously via the femoral veins and trans-septal access. Lines of conduction block were created originally by dragging an ablating catheter tip along the atria[1,3] and subsequently by the use of multielectrode linear array–ablating catheters that are aligned in contact with the atrial endocardium.[4] When performed on the left atrium, the catheter maze procedure is more efficacious but carries a significant risk of stroke when conventional ablation technology is used. To improve the efficacy of the procedure, alternative energy sources and catheter designs, including linear cryothermy,[5] diode laser,[6] and irrigated radiofrequency[7] ablation, are under research and development (Figures 3 and 4). When limited to the right atrium, the catheter maze procedure is safer but is associated with a lower probability of success.[2–4] Overall, clinical results for the right-atrial catheter maze procedure show a significant reduction in the number of symptomatic episodes of AF, but few patients are cured, and most patients continue to have some episodes of AF and require long-term antiarrhythmic drug therapy.

Pulmonary Vein Isolation

More recently, it has been found that catheter approaches addressing the triggers that initiate AF may be more effective than those attempting to interrupt the maintenance of AF. Specifically, clinical investigators in Bordeaux, France, found that triggers for paroxysmal AF often arise from the pulmonary veins and that ablation of such ectopic foci within the pulmonary veins may eliminate AF recurrences in some patients.[8,9] When the pulmonary veins are developing

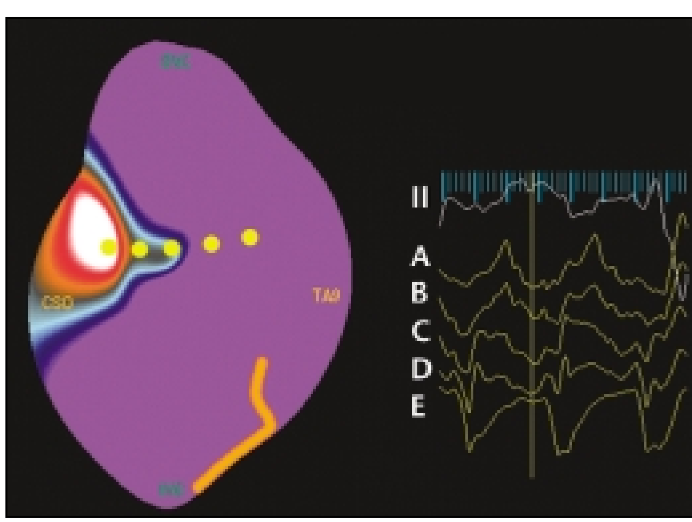


Figure 2. *Reverse gap conduction during atrial fibrillation. Noncontact mapping of the atria can be used to guide the catheter maze procedure and to detect any break in a line of conduction block as indicated by the activation pattern. SVC indicates superior vena cava; IVC, inferior vena cava; CSO, coronary sinus ostium; and TA9, crista catheter.*

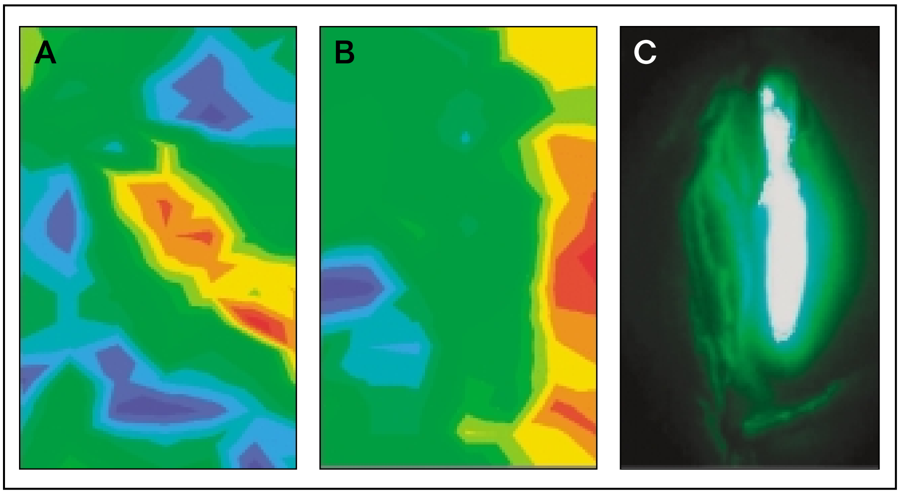


Figure 3. *Linear catheter maze procedure with a diode laser. Mapping of the atrial activation (red indicates early activation; blue indicates late activation) preablation* **(A)** *and postablation* **(B)** *shows that linear conduction block has been achieved by transvenous linear laser ablation* **(C)**. *Reproduced from Keane D, Ruskin J.*[6]

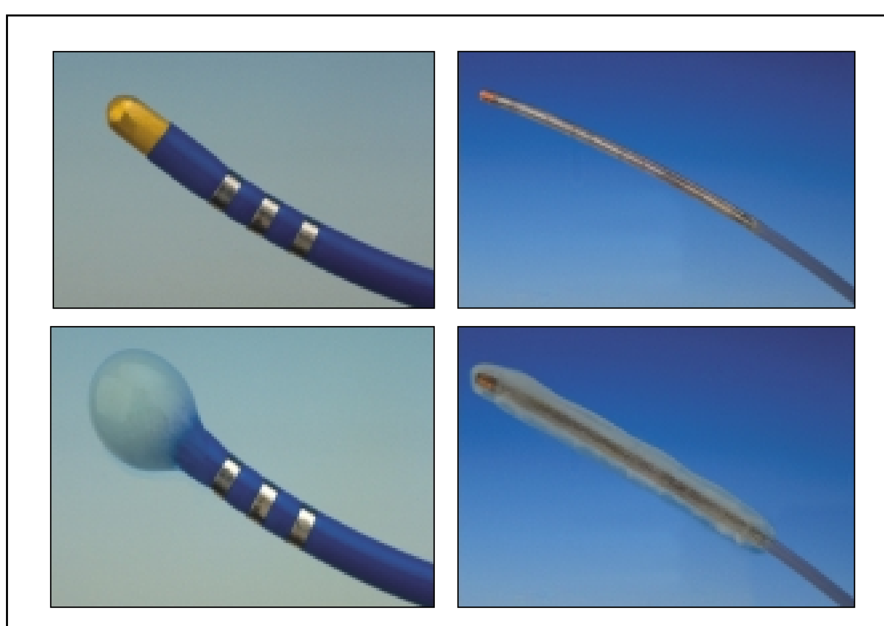
in utero, they receive a sleeve of atrial muscle as they bud out from the heart to the lungs. This sleeve of atrial muscle in the proximal pulmonary veins may become active and show spontaneous, rapid discharge[10] in later life, triggering episodes of AF.

Initially, patients underwent focal ablation with a catheter directly in the pulmonary veins. However, the recurrence rate following this focal ablation procedure was relatively high (>60%). The recurrences arose from the involvement of multiple veins and their branches, and if one or two foci were ablated on one day, other active foci would be found when the patient was brought back to the electrophysiology laboratory for recurrent AF on another day.

Subsequently, the investigators in Bordeaux found that isolating the pulmonary veins by applying ablation energy at their junction with the left atrium was more effective.[11,12] This procedure, which is more empiric and standardized, avoids the need for detailed mapping of foci within the veins. It also avoids the need to apply energy within the branches of the pulmonary veins and reduces the risk of pulmonary vein stenosis. Approximately half of the patients who undergo the procedure need to come back for a repeat, "touch-up" procedure. While a 50% recurrence rate after the first procedure appears high, this rate arises from the use of lower power settings for the ablation energy source. By limiting the power and temperature settings of the catheter ablation procedures, the procedural risks can be reduced.[13] After one or two procedures in the electrophysiology laboratory there is an overall success rate of 70% to 80% in eliminating AF episodes in the first year of follow-up.

In addition to recovery of the muscular connections bridging the left atrium and pulmonary veins, reasons patients experience recurrence after such a procedure include the existence of ectopic foci outside of the pulmonary veins (including the left and right atria, coronary sinus, superior vena cava,[14] and ligament of Marshall) as well as slim cuffs of surviving muscle proximal to the site of ablation at the pulmonary vein ostia. The existence of ectopic sites at the os of the pulmonary vein

Figure 4. *Cryothermal ablation catheters. Catheter cryoablation can be applied to produce point lesions (left panels) or a line of conduction block for the catheter maze procedure (right panels). For each pair of images, the lower image shows ice formation on the active element of the catheter. Cryoablation has been found to be safe over decades of use by cardiac surgeons treating ventricular tachycardia and accessory atrioventricular pathways.*



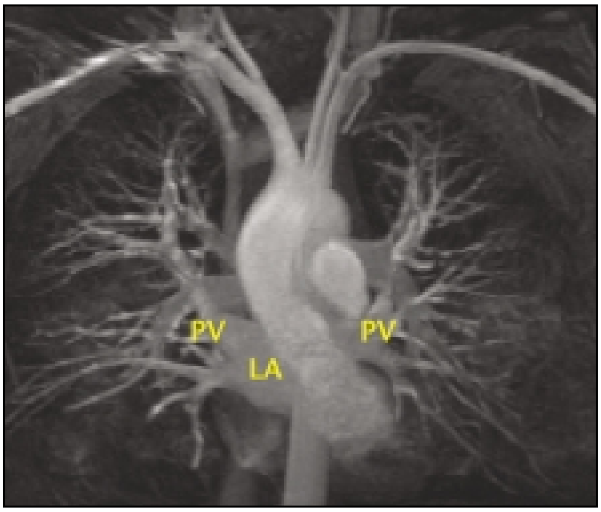


Figure 5. *Magnetic resonance imaging (MRI) of the pulmonary veins (PV) and left atrium (LA) in a patient with atrial fibrillation. The variation in size, angulation, and proximal branching pattern of the pulmonary veins is revealed by MRI. Custom slices for each pulmonary vein can be selected to guide the circumferential ablation of each vein and determine when ipsilateral veins have a common ostium.*

has given rise to the pursuit of periostial ablation approaches in the left atrium (see Figures 8 and 9).

Segmental Versus Circumferential Ablation Approaches

It was originally envisaged that isolation (conduction block) of a pulmonary vein from the left atrium would require a full (360°) circumferential ablation around the pulmonary vein os. To this end, a number of balloon-based systems have been developed that are designed to deliver ablative energy in a uniform distribution around the atrio-venous junction. However, Haïssaguerre and his colleagues in Bordeaux have demonstrated that the myocardial connections between the pulmonary veins and atria are generally not fully circumferential around the venous os (Figures 6 and 7).[8,9] Instead, the connections appear in most patients to be limited to two quadrants or segments. Point ablation of these quadrants with a conventional catheter tip electrode results in effective isolation of the pulmonary veins.

Identification of the individual quadrants or arcs containing myocardial connections at the atrio-venous junction is based on the recording of either fusion (connection) or splitting of the atrial and pulmonary vein (spike) potentials during paced or sinus rhythm (Figure 7). These data can be obtained sequentially by the exploring catheter tip electrode used for ablation and/or by a multi-electrode circumferential recording catheter. Target quadrants can alternatively be identified with contact or noncontact isochronal electroanatomical mapping. Advantages of segmental or quadrant ablation include 1) that in patients with thick muscular connections, higher energy (> 25 watts) can be effectively delivered at the points necessary, and 2) that much of the venous os will not receive ablative energy, which should reduce the risk of concentric stenosis.

In contrast, an ablative system that delivers energy uniformly over the entire (360°) circumference of the atrio-venous junction may be

Figure 6. *Circumferential pulmonary vein mapping catheter. Circumferential mapping catheters have been developed to define in detail the junction of the pulmonary vein and left atrium. The connecting muscular bridges between the pulmonary veins and left atrium are thereby identified and ablated at their junction by a separate ablating catheter.*

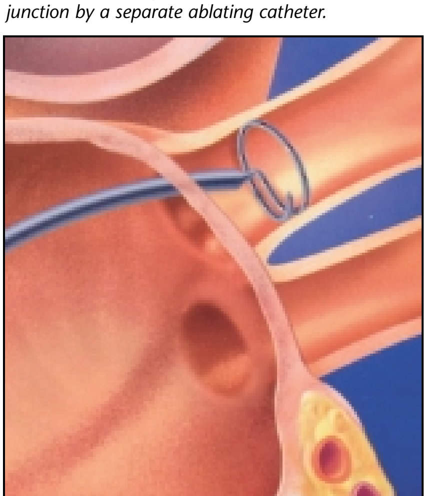
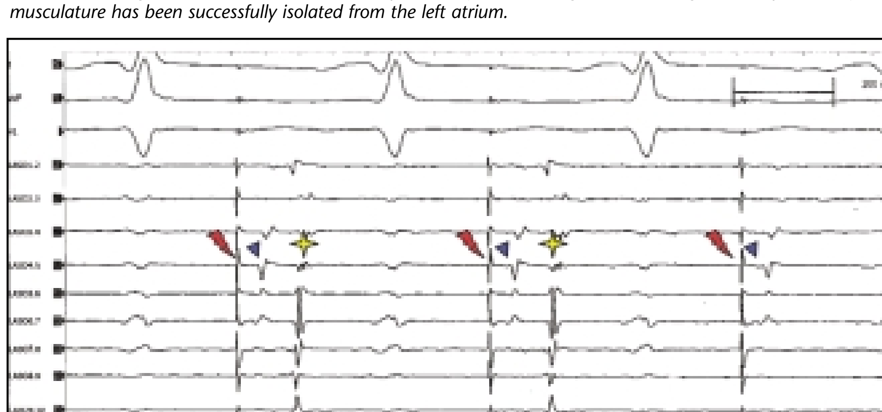


Figure 7. *Electrogram recordings from a circumferential mapping catheter in the pulmonary vein during radiofrequency ablation. The top three signals are the surface electrocardiogram. Three consecutive paced beats are shown. The left atrium is being paced from the coronary sinus. For the first two beats a pacing spike (red mark) is seen followed by an electrogram from the left atrium (blue triangle), followed after some delay by an electrogram from the pulmonary vein (yellow star). For the last beat on the right, a pacing spike is again seen followed by a left-atrial electrogram; however, now there is no pulmonary vein electrogram, indicating that the pulmonary vein musculature has been successfully isolated from the left atrium.*



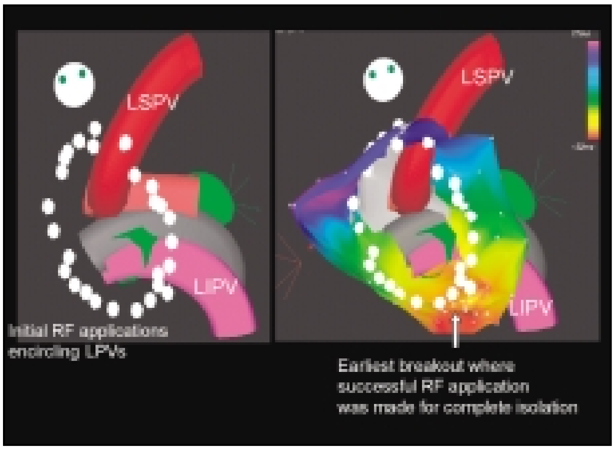


Figure 8. *Three-dimensional electroanatomical guidance of pulmonary vein isolation in a patient with atrial fibrillation. The colored cylinders in this right inferior oblique view are the different branches of the left pulmonary veins. The white spots mark the points at which radiofrequency (RF) applications were made, encircling the left pulmonary veins. On the right, the colorized (isochronal) activation map of the lateral left atrium during pacing from the left superior pulmonary vein (LSPV) indicates where conduction persists (red = early, blue = late) and where a final RF application was required before complete isolation of the left pulmonary veins was achieved. LIPV, left inferior pulmonary vein.*

unable to deliver sufficient energy to points at which the atrio-venous myocardial connections are deep, and deliver redundant energy to the quadrants without direct atrio-venous myocardial connections. Circumferential balloon-based ablation systems may be further restricted by anatomical variabilities such as an ostial carina or bifurcation.[15] Balloon-based systems are also subject to mismatch between the balloon and pulmonary vein diameters. Balloon-based systems can also be difficult to align in the precise longitudinal axis of the proximal pulmonary vein, and the ablative ring lesion may therefore be oblique and ineffective. On the other hand, once balloon-sizing and orientation issues can be overcome, circumferential (anatomical-based) systems, such as balloon-based ablation systems, offer the potential advantages of reducing procedure time and obviating the requirement for detailed local mapping other than to confirm conduction block following ablation. One strategy to overcome problems of mismatch between the balloon and vein sizes is to use a forward-ablating balloon with which circumferential ablation is performed on the left atrial wall proximal to the pulmonary vein os (Figure 9). Thus, at this early stage of clinical evaluation, both segmental and circumferential ablation approaches offer potential advantages. Randomized clinical trials comparing the safety and efficacy of the two approaches will be required.

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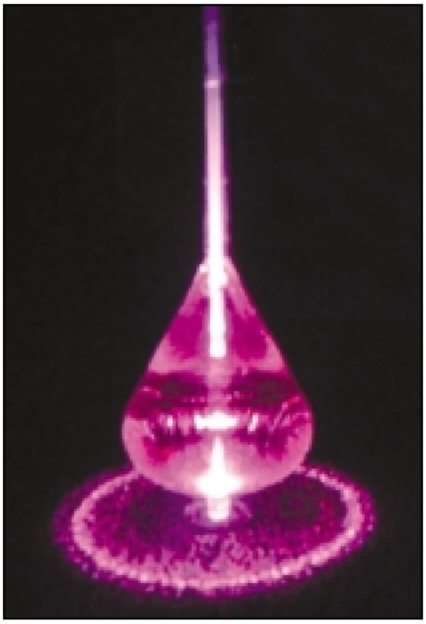
Figure 9. *Forward-projecting diode laser balloon catheter designed to isolate the pulmonary veins by ablation outside the vein rather than at the os or junction of the vein itself.*



Periostial Regional Atrial Ablation at Sites of High Frequency and Periodicity

In addition to pulmonary vein isolation alone, periostial ablation (Figures 10 and 11) in the vicinity of the pulmonary veins may play an added role in the prevention of AF recurrence.[16,17] It has been proposed that high frequency and periodicity of activation in these regions (Figures 11, 12, and 13) may play a role in the maintenance of AF via possible rotors or drivers.[18] Comparative clinical studies are required to determine the added clinical benefit, beyond pulmonary vein isolation alone, of periostial regional ablation in the left

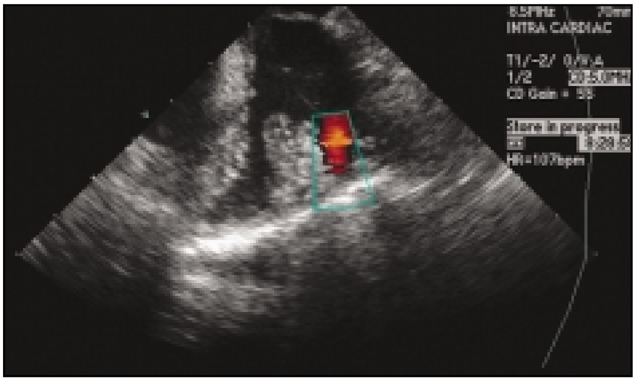


Figure 10. *Intracardiac echo can be used to image the orifice and flow from the pulmonary veins and to guide catheter ablation. It can also be used to guide balloon sizing and assess balloon orientation.*

atrium at sites of high frequency and periodicity (Figures 11, 12, and 13).

Preprocedural Patient Evaluation
Prior to catheter ablation, patients undergo clinical evaluation and any basic tests that are clinically indicated (eg, to exclude hyperthyroidism or a procoagulant state). A transthoracic echo is routinely performed to detect any congenital or acquired structural heart disease.

Patients' pulmonary veins vary extensively in their anatomical course and dimensions, and therefore preprocedural imaging is often performed. One option is to perform outpatient magnetic resonance imaging (MRI) with three-dimensional reconstruction of the pulmonary veins (see Figure 5) prior to admission for the catheter ablation procedure. The advantages of MRI over computed tomography (CT) imaging include the avoidance with MRI of exposure to ionizing radiation. However, in patients with a pacemaker or other contraindication to MRI, a CT scan is obtained. While not absolutely essential for the performance of the procedure, the detailed, high-resolution imaging by MRI or CT of the pulmonary veins provides a roadmap for catheter ablation. It reveals the presence of additional pulmonary veins (some patients have five instead of four), shows common orifices when an upper and lower pulmonary vein join the left atrium as a common trunk, and detects any small proximal side-branch that may be predisposed to stenosis. It also detects anomalies that may not have been identified on routine transthoracic echo, such as persistence of a left superior vena cava. It can further help preprocedural planning by sizing the origin of the veins so that appropriately sized catheters may be selected for the procedure.

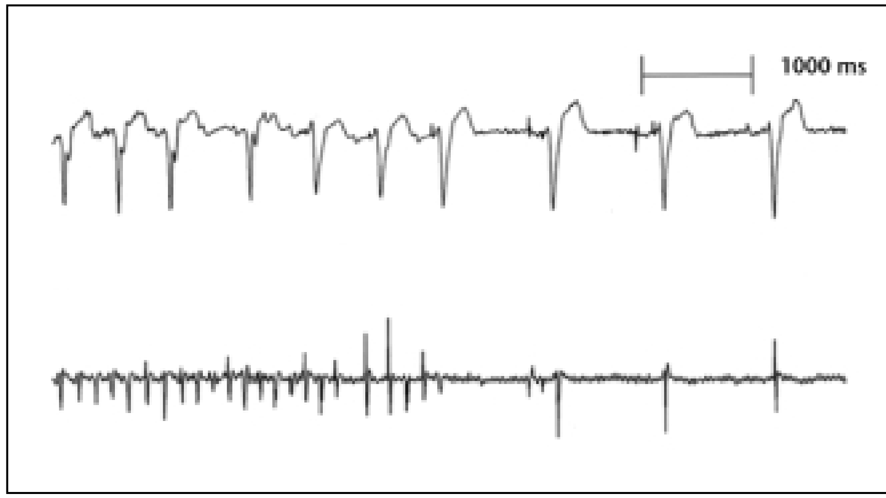


Figure 11. *Electrocardiogram showing termination of atrial fibrillation (AF) during regional periostial ablation. The top tracing is from the surface, and the lower tracing is from the left atrium. Halfway through the recording of the ablation, the rapid, irregular activity of AF can be seen to terminate, and regular rhythm resumes. This patient had a previous dual-chamber pacemaker implantation for sinus node disease (sick sinus syndrome).*

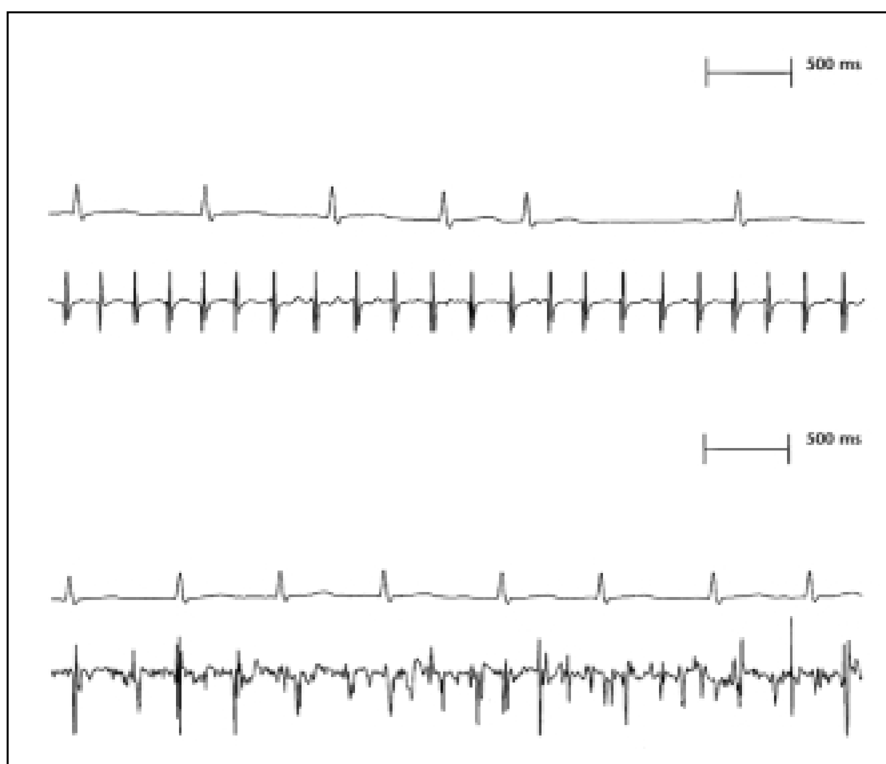


Figure 12. *Electrogram recordings from a patient in atrial fibrillation (AF). The electrograms in the upper and lower panels were recorded from sites within 1 cm of the left superior pulmonary vein. In the upper panel, electrical activity remained constant and organized over time. In the lower panel, activity remained chaotic and disorganized over time. These recordings are consistent with the concept that not all parts of the atria are of equal importance in the maintenance of AF. Regions of left atrial myocardium in proximity to the pulmonary veins may function as rotors or drivers in the maintenance of AF. This possibility has given rise to the concept of additional regional periostial catheter ablation beyond pulmonary vein isolation alone.*

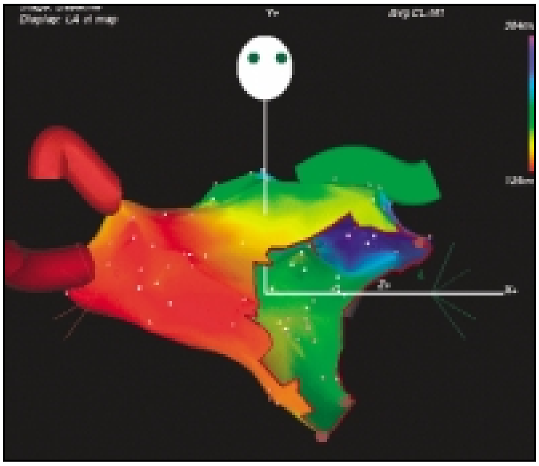


Figure 13. *Left-atrial color map seen from a right anterior oblique angle showing the distribution of frequency of activation during atrial fibrillation (AF). The area of highest frequency is shown in red and, in this particular patient, lies in the septum below the right pulmonary veins.*

Procedure

Pulmonary vein isolation is performed in the cardiac electrophysiology laboratory and typically takes between 3 and 5 hours. The procedure is performed under conscious sedation and local anesthesia. At the beginning of the procedure, a transesophageal echo is usually performed to exclude a thrombus in the left atrial appendage. Multiple catheters are then introduced into the heart via the femoral veins and positioned under fluoroscopic guidance. One or two catheters are introduced into the left atrium by transseptal puncture and other catheters are placed in the coronary sinus and right side of the heart. A custom circumferential loop catheter may be used to map the junction of the pulmonary veins with the left atrium and guide where ostial lesions should be applied (Figures 6 and 7). The ablating catheter may also be localized in three-dimensional space by triangulation of external electromagnetic fields or a similar technique. A number of investigational systems to isolate the pulmonary veins have entered clinical trials, including an ultrasound balloon, a laser balloon (Figure 9), and a cryoablating loop catheter.

After pulmonary vein isolation has been achieved by ablation of the muscle fibers connecting the left atrium and pulmonary veins, a drug may be given to stimulate the heart, and pacing maneuvers may be performed in an attempt to elicit any other focus of activity that may lie outside of the pulmonary veins. A final check is then performed to ensure that the pulmonary veins remain isolated at the end of the procedure. The patient is then transferred to the arrhythmia unit for inpatient monitoring and antithrombotic medications, which may include combinations of clopidogrel, aspirin, subcutaneous low molecular weight heparin, or warfarin.

Risks Associated with Catheter Ablation

Cardiac catheterization and ablation carry a risk of complications that may occur either during or after the procedure. The risks of catheter ablation depend in part on whether the procedure is limited to the right side of the heart (right atrial catheter maze procedure, ablation of typical atrial flutter, or AV-node ablation procedure) or left side (pulmonary vein isolation, left atrial periostial ablation, or left atrial catheter maze ablation). The risks include cardiac tamponade, stroke, pulmonary vein stenosis, phrenic nerve injury, peripheral vascular injury, or death. In experienced electrophysiology laboratories the risk of a major complication appears to be 1% to 2%.

Main Points

- The multiple coexistent excitation waves maintaining atrial fibrillation (AF) are difficult to interrupt and organize by catheter techniques; however, the focal triggers initiating episodes of AF are more consistent in their origin and offer a more standardized target for catheter ablation.
- The catheter maze procedure creates lines of conduction block to interrupt the maintenance of AF, whereas the pulmonary vein isolation procedure prevents focal triggers in the pulmonary veins from initiating episodes of AF.
- Pulmonary vein isolation is achieved by ablation of the muscle fibers connecting the left atrium and pulmonary veins.
- After one or two procedures, the overall success rate is 70% to 80% in preventing recurrence of AF episodes in the first year of follow-up.
- The procedure is more successful in patients with paroxysmal AF than in those with chronic AF.
- The risks and benefits of a catheter ablation approach must be weighed against the risks and impact on the patient's quality of life of AF and long-term drug therapy.

In making a fully informed choice of treatment, patients need to thoroughly understand the risks involved and need to compare them to the risks of alternative treatment options. For example, the risks of long-term anticoagulation treatment with warfarin include excessive bleeding (which may be fatal) or intracranial hemorrhage. The risk of serious bleeding on warfarin is 0.5% to 1% per year. Antiarrhythmic drugs can carry a small risk of sudden death from torsades de pointes ventricular tachycardia. Risks also exist that are specific to particular antiarrhythmic agents, such as potentially fatal blood dyscrasias on propafenone or permanent visual loss from optic neuritis on amiodarone. Pacemakers carry acute procedural risks at the time of implantation (including perforation of the heart and death) as well as longer-term complications such as infection.

Which Patients with Recurrent AF Are Appropriate Candidates for a Pulmonary Vein Isolation Procedure?

The pulmonary vein isolation procedure is most suitable for patients whose recurring symptomatic episodes of AF have not been suppressed by antiarrhythmic drugs or who do not wish to take long-term antiarrhythmic or anticoagulation medications. Each patient must consider the risks and merits of a catheter ablation approach relative to the impact of AF and long-term drug therapy on his or her quality of life. The success of the procedure is lower in patients with long-standing, continuous (chronic) AF than in patients with intermittent (paroxysmal) AF.

An ongoing, multicenter study in Europe and the United States is comparing clinical outcome (freedom from AF recurrence and risks) of antiarrhythmic drug therapy versus pulmonary vein isolation in patients with paroxysmal AF. Until the results of such studies become available, the comparative efficacies, limitations, and risks of antiarrhythmic drug therapy versus catheter ablation as first-line therapy will remain unclear. Thus, at present, most patients fail treatment with at least one antiarrhythmic drug before undergoing an invasive procedure such as pulmonary vein isolation. ■

In experienced electrophysiology laboratories the risk of a major complication appears to be about 1% to 2%.

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