Pulmonary vein isolation by duty-cycled bipolar and unipolar radiofrequency energy with a multielectrode ablation catheter

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BACKGROUND Pulmonary vein (PV) isolation for ablation of atrial fibrillation (AF) remains a complex and lengthy procedure.

OBJECTIVE The purpose of this study was to evaluate the feasibility and safety of a novel multielectrode catheter that delivers duty-cycled bipolar and unipolar radiofrequency (RF) energy.

METHODS Patients eligible for catheter ablation of paroxysmal AF after screening with magnetic resonance imaging and transesophageal echocardiography were included in the study. A decapolar (3-mm electrode, 3-mm spacing, 25-mm diameter), circular, over-the-wire mapping and ablation catheter was deployed in the antrum of each PV. Ablation was performed with 60-second, 60°C applications of duty-cycled bipolar/unipolar RF in a 4:1 ratio simultaneously at all selected electrode pairs until local activity was no longer observed. At 6 months, 7-day Holter monitoring was performed to determine freedom from AF without use of antiarrhythmic drugs.

RESULTS In 98 patients (mean age 59 ± 9 years), the PV ablation catheter was used for ablation of 369 veins (20 common left antra). All targeted veins (100%) were isolated as confirmed by the absence of potentials in the ostium either by PV ablation catheter or Lasso mapping. Mean number of RF applications was 27 ± 7, total procedural time 84 ± 29 minutes, and fluoroscopy time 18 ± 8 minutes. Follow-up after 6 months without antiarrhythmic drugs showed freedom from AF in 83% of patients. No procedure-related complications were observed.

CONCLUSION PV isolation by duty-cycled bipolar/unipolar low-power RF energy through a circular, decapolar catheter can be achieved safely and efficiently, with good efficacy at 6 months.

KEYWORDS Arrhythmia; Atrial fibrillation; Catheter ablation; Pulmonary vein isolation

Introduction

Radiofrequency (RF) catheter ablation has become first-line therapy for patients with drug-refractory atrial fibrillation (AF).1,2 An early ablation strategy consisted of focal ablation of triggers inside the pulmonary veins (PVs).3 To prevent complications of PV stenosis, this method was modified to electrical isolation of the PV by segmental isolation at the ostium.4,5 Strategies evolved to include wide area encircling of the PV antrum using sophisticated three-dimensional mapping systems that could reconstruct atrial anatomy for guiding ablation and limiting fluoroscopy time.6,7 In complex cases of persistent or permanent AF, additional ablation lines can be added, or complex fractionated electrograms can be targeted for ablation.8–10 The evolution in ablation strategies led to increasingly complex and lengthy procedures and the need for high-technology equipment. Intracardiac echocardiography, computed tomography/magnetic resonance imaging (MRI) integration, and robotic steering have been proposed as new tools for facilitating the procedure. However, the availability of imaging, mapping, and steering options has not necessarily led to better outcomes for patients, and a wide range of success rates is reported in the literature.11

Little progress has been made in the development of new ablation catheters. Traditional catheter ablation is performed in a single-tip, point-by-point ablation process. This technique requires a high degree of operator skill and procedures are lengthy, often more than 4 hours. In addition, creating reliable contiguous transmural lesions with a single-point catheter is difficult. Therefore, there is a need for specialized RF ablation catheters specifically designed for AF ablation. Alternative energy sources currently under investigation may offer advantages over conventional unipolar RF ablation. Here we describe a novel technique for isolation of the PVs by ablation using an over-the-wire multielectrode catheter delivering duty-cycled bipolar and unipolar RF energy at relatively low power.12–16
Methods
Patients and procedure
The study consisted of 98 consecutive patients with paroxysmal or persistent AF seen at the St. Antonius Hospital, Nieuwegein, The Netherlands, between April 2007 and June 2008. Patients were referred by outside cardiologists and were eligible for ablation if they had documented evidence of recurring symptomatic AF refractory to two or more antiarrhythmic drugs within the past 6 months. The study was approved by the St. Antonius Hospital review board, and all patients gave informed consent to undergo ablation. Preprocedural screening consisted of transthoracic and transesophageal echocardiography and cardiac MRI to exclude contraindications for ablation. None of the patients had significant structural heart disease, left atrial appendage thrombus, atrial enlargement greater than 45 mm, or mitral insufficiency higher than grade 1. The international normalized ratio of patients was < 2.5 on the day of the procedure.

Electrophysiologic procedures were performed with patients in a drug-free state. Mapping with the pulmonary vein ablation catheter (PVAC; Ablation Frontiers, Inc., Carlsbad, CA, USA) was performed with an electrophysiologic recording system (Prucka, GE Medical, Waukesha, WI, USA) using filter settings of 100 to 500 kHz and signal amplification set at 5,000. No additional nonfluoroscopic guiding or steering systems were used.

A 7Fr sheath was introduced through the right femoral vein under local anesthesia. A quadripolar catheter was introduced in the coronary sinus (CS) for pacing purposes. A standard transseptal puncture was performed using a Brockenbrough needle with either a 10Fr nonsteerable sheath (SL1, St. Jude Medical, Inc., Minnetonka, MN, USA) or a 12.5Fr steerable sheath (Channel, Bard, Lowell, MA, USA). Both sheaths have a 9.5Fr or larger inner lumen diameter to accommodate the PVAC. Angiography via the sheath was performed to delineate the PVs. A single heparin
bolus of 5,000 international units was administered IV through the sheath and repeated every 90 minutes after transseptal puncture when necessary without activated clotting time measurements. In 19 patients, a diagnostic, 15-mm diameter, decapolar, ring-shaped catheter (Lasso, Biosense Webster, Diamond Bar, CA, USA; or AFocus, Irvine Biomedical, Inc., Irvine, CA, USA) was introduced into the left atrium, and local PV potentials were recorded proximal to the ostium in each vein before and after ablation with the PVAC. Postprocedural management included 4 hours of bedrest with a compression bandage and 24 hours of hospitalization. Antiarrhythmic drugs were continued for the first 3 months, with all patients taking oral anticoagulants. After 3 months, anticoagulation was continued as guided by the CHADS2 score.

Catheter
The PVAC is a 9Fr, over-the-wire, circular, decapolar mapping and ablation catheter with a 25-mm-diameter array at the distal tip (Figure 1). The handle has two control knobs, which allows bidirectional deflection of the shaft and extension of the distal tip to form a spiral configuration (Figure 2). The platinum electrodes (3 mm long, 1.5-mm outer diameter, 3-mm spacing) have a thermocouple under the surface on the anterior side. Mapping was performed by five bipolar recordings through adjacent electrode pairs. The diameter of the electrode array can be effectively altered by engaging the antrum and then rotating the catheter shaft. Thus, clockwise rotation decreases the diameter to allow distal PV positions, whereas counterclockwise rotation increases the diameter of the array, facilitating ablation around larger veins. Catheter placement and stability around the PVs was facilitated by use of a 0.032-inch guidewire, selectively positioned into different side-branches to modify the tissue–electrode interface around the PV circumference.

Generator
The GENius multichannel, duty-cycled RF generator (Ablation Frontiers, Inc.) is capable of independently delivering energy to 12 electrodes. AC power can be delivered in either unipolar or bipolar current with a fixed duty-cycle by a phase difference between the channels. Unipolar energy consists of current flowing from the electrodes at the catheter tip to the dispersive electrodes on the patient’s back. Bipolar energy consists of current flowing between adjacent selected pairs of electrodes on the catheter tip. Bipolar current can be applied simultaneously with unipolar current or it can be field sequential. No bipolar current flows between electrodes 1 and 10. The generator has five preset energy settings: bipolar, unipolar, and three ratios of bipolar/unipolar energy: 4:1, 2:1, and 1:1. During RF application, energy delivery to individual electrodes is temperature controlled by a software algorithm that modulates power to reach the user-defined target temperature, avoiding overshoot, but limits power to a maximum of 8 W per electrode when using the PVAC in a 4:1 power setting or 10 W in all other settings. Lesion depth and fill between electrodes are controlled by varying the energy settings on the generator, with depth achievable up to 7 mm. Figure 3 shows a cross-section view in vivo ablation created with the PVAC using a 4:1 setting on the generator in a porcine thigh muscle preparation. One contiguous lesion approximately 80 mm long and 3 to 4 mm wide can be created with a 60-second RF application by delivering energy to all electrodes. The generator displays in real time the tem-
perature and power for each electrode, as well as the number of seconds each electrode was within 5°C of the target temperature during the ablation (Figure 1). The standard energy setting for use of the PVAC in the PV antrum is a 4:1 ratio of bipolar/unipolar energy to achieve transmurality in the PV antrum and reduce damage beyond the atrial wall.

**Ablation protocol**

The PVAC was deployed in the left atrium over a 0.032-inch guidewire inside the PV and advanced until it was wedged within the antrum proximal to the ostium. Figure 4 shows a representative image in the right inferior PV. The position of the PVAC relative to the angiogram of the ostium was confirmed by biplane fluoroscopy before each application. An optimal position was based on electrograms, aiming to find and ablate local potentials on as many electrodes as possible for each application. RF energy was never delivered via electrodes that were observed to be inside the PV. To achieve optimal tissue apposition, positional changes of the PVAC were accomplished by rotating the array, manipulating the steerable sheath, changing the curve of the PVAC shaft, counterclockwise opening or clockwise closing of the PVAC electrode array, or extending the spiral array tip into the PV. Common ostia were isolated by inserting the guidewire into different side-branches and ablationing subsequent segments of the PV. Energy was delivered through selected electrode pairs with local potentials as well as adjacent electrode pairs, allowing bipolar current to flow to the target electrode(s) from both sides. Each application lasted for 60 seconds, and the generator was set to adjust power to achieve a target temperature of 60°C for each electrode in the selected pairs. When the temperature did not rise above 50°C within 15 seconds, the application was discontinued to improve position. In most cases, all electrodes pairs were activated during the first applications to create overlapping lesion rings. For residual potentials on isolated electrode pairs, ablation was only targeted on that and adjacent pairs to facilitate reaching target temperature. This approach was repeated for all PVs until all local potentials were abolished. In 19 patients, the decapolar ring mapping catheter subsequently was reintroduced postablation to confirm isolation during sinus rhythm and coronary sinus pacing. For all other procedures, the PVAC was placed inside the ostium to verify PV isolation. In case of residual potentials, additional selective applications with the PVAC were performed until isolation was complete and reconfirmed.

**Follow-up**

Patients were seen in an outpatient clinic at 3 and 6 months after the procedure. Antiarrhythmic drugs were discontinued after a blanking period of 3 months, whereas amiodarone was discontinued immediately after the procedure. Patients were requested to call or visit the hospital for ECG, Holter, or event monitoring if they experienced palpitations or other symptoms after 3 months. Seven-day Holter monitor recording was performed off antiarrhythmic drugs at 6 months after the procedure. Freedom from AF was defined as the absence of AF/flutter lasting more than 30 seconds. Adverse events such as cerebrovascular accident, tamponade, hematoma, phrenic nerve lesions, or gastrointestinal and pulmonary events were also scored.

**Results**

The characteristics of the study group are given in Table 1. Among the 98 patients undergoing the ablation procedure, 23 were female. Mean patient age was 59 ± 9 years (range 34–76 years). Slight left atrial enlargement (40–45 mm) was seen in 18% of patients, and mild (less than grade 2) mitral insufficiency was seen in 12% of patients. The number of antiarrhythmic drugs used prior to ablation was 2 ± 1; only eight patients were taking amiodarone at inclusion into the study. In this patient population, 28% had a history of either chemical or DC cardioversion for AF usually within 48 hours. On MRI, all patients had normal PV anatomy, except for 20 patients with a common left PV. Mean dimensions of the separate PVs ranged from 15 to 19 mm and for the left common antra was 28 mm (Table 2).

### Table 1  Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of patients</th>
<th>Age (years)</th>
<th>Male/female</th>
<th>Left atrium, mild enlargement</th>
<th>Mitral insufficiency grade 1–2</th>
<th>Chemical/electrical cardioversion</th>
<th>Antiarrhythmic drugs</th>
<th>Amiodarone</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>98</td>
<td>59 ± 9 (34–76)</td>
<td>75/23</td>
<td>18%</td>
<td>12%</td>
<td>28%</td>
<td>2 ± 1</td>
<td>8</td>
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### Table 2  Characteristics of pulmonary vein anatomy and ablation

<table>
<thead>
<tr>
<th>N</th>
<th>Size (mm)</th>
<th>RF applications</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedures</td>
<td>98</td>
<td>27 ± 7</td>
<td>16–54</td>
</tr>
<tr>
<td>Left superior PV</td>
<td>78</td>
<td>17 ± 3</td>
<td>8 ± 3</td>
</tr>
<tr>
<td>Left inferior PV</td>
<td>77</td>
<td>15 ± 3</td>
<td>6 ± 3</td>
</tr>
<tr>
<td>Left common PV</td>
<td>20 (20%)</td>
<td>28 ± 3</td>
<td>13 ± 5</td>
</tr>
<tr>
<td>Right superior PV</td>
<td>97</td>
<td>19 ± 3</td>
<td>7 ± 3</td>
</tr>
<tr>
<td>Right inferior PV</td>
<td>97</td>
<td>17 ± 2</td>
<td>7 ± 3</td>
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PV = pulmonary vein; RF = radiofrequency.
Figure 5 shows examples of potentials recorded during sinus rhythm by a decapolar ring catheter inside the right superior PV (panel A) and the PVAC proximal to the ostium (panel B). The bipolar PVAC recordings show clear local potentials with a sharp deflection and good amplitude, similar to the Lasso recordings. Figure 6 shows examples of the PVAC potentials before (panel A) and after ablation inside the left inferior PV antrum (panels B and C). During RF application, ablation channels cannot be visualized because the duty-cycled RF energy creates noise that cannot be filtered. All the local potentials inside the antrum proximal to the ostium of all PVs were ablated according to protocol. Isolation was verified by positioning the PVAC distal to the lesion and inside the ostium to demonstrate absence of PV potentials. Figure 6, panel B, shows that the large local potential is no longer present on the PVAC recordings and all that remains is a small potential due to far-field sensing of left atrial activation. In 19 patients the decapolar ring catheter was reintroduced into the left atrium and positioned in all PVs to further confirm electrical isolation. Figure 6, panel C, shows far-field left atrial potentials on the ring catheter without a local component during coronary sinus pacing.

Procedural results

In 98 patients, 369 PVs, including 20 left common PV, were targeted for ablation. In three patients, two right superior PV antra and one left inferior PV antrum did not exhibit clear local electrical activity and thus were not targeted for ablation. The results of single procedure treatment are summarized in Table 2. The number of applications per vein was 8 ± 3 for the left superior PV, 6 ± 3 for the left inferior PV, 7 ± 3 for the right superior PV, and 7 ± 3 for the right inferior PV (P = NS). Usually, when applications were first performed inside an upper antrum, the lower needed fewer applications and vice versa due to the electrode array overlapping previously applied lesions. In left common PV antra, the mean number of applications was about double that of a separate antrum (14 ± 5, range 8–26). The mean number of applications per patient was 27 ± 7 (range 16–44). In a substudy of 19 patients, the ability of the PVAC to isolate the PV ostium was verified using a standard decapolar ring catheter as a gold standard. After PVAC antrum ablation, the decapolar ring catheter showed some residual ostial signals in two left inferior PVs, three right inferior PVs, and one left common PV. The PVAC was
reintroduced to abolish the remaining activity, and isolation was confirmed by the decapolar catheter. In the other patient group, the PVAC itself was advanced as a mapping catheter to confirm the absence of ostial potentials or to perform an additional application if necessary. There was no difference in the number of applications between the two groups. In 98 patients, all 369 targeted veins (100%) were completely isolated using the PVAC without the need for either a conventional catheter or three-dimensional mapping equipment.

Total procedural time was 84 ± 29 minutes (range 45–180 minutes); fluoroscopy time was 18 ± 8 minutes (range 9–45 minutes; Table 3). After completion of the ablation protocol, the PVAC catheter was visually inspected, and no char or thrombus was observed in any case. No procedure-related complications, such as groin hematomas, occurred during the procedure or through 7-day follow-up. All patients left the hospital in sinus rhythm the day after the procedure. Subsequent follow-up revealed no procedure-related adverse events. Postprocedural MRI or angiography protocol, the PVAC catheter was visually inspected, and no late recurrences were observed beyond 6 months. In three patients with AF recurrence, a second procedure was performed showing PV potentials in one or more veins.

**Freedom from AF**

Median follow-up was 7 months (range 0-16) in 98 patients. Currently, 80 (82%) patients are more than 3 months off antiarrhythmic drugs, 53 (54%) patients more than 6 months, 35 (36%) patients more than 9 months, and 13 (13%) patients more than 12 months. Seven-day Holter recording 6 months after ablation showed freedom from AF in 44 (83%) of 53 patients. Beyond 3 months, 14 (18%) of 80 patients had a documented recurrence of AF on ECG, event recorder, or 7-day Holter monitoring. No episodes of AF were asymptomatic. No late recurrences were observed beyond 6 months. In three patients with AF recurrence, a second procedure was performed showing PV potentials in one or more veins.

**Discussion**

This study reports the first clinical results of a new decapolar catheter that delivers bipolar/unipolar RF energy and can be used for both mapping and ablation of AF, with no need for three-dimensional imaging or remote navigation.

**Acute success**

The results of the study show that duty-cycled RF energy applied by the PVAC can successfully create lesions to ablate the antrum of the PVs. Isolation was achieved in every vein using only the PVAC, regardless of whether a steerable or a nonsteerable guiding sheath was used. The steerable sheath facilitated selective PV angiography and isolation of the left and right inferior PVs, but there was no significant difference in procedural times when the steerable sheath was used. Mapping with the ring catheter before and after ablation served as a comparison for electrogram interpretation but is not required for the procedure and is not necessary as routine practice.

The acute efficacy of PVAC equals or exceeds that of conventional-tip catheters for PV isolation, as described by Cheema et al19 (75%), Hocini et al20 (100%), and Verma et al21 (100%). The technique compares favorably to other novel antrum ablation techniques such as balloon catheters delivering RF, ultrasound, and cryoablation energies. A preclinical report using an RF thermal balloon indicated that 83% of 18 targeted PVs were successfully isolated.22 Natale et al23 used an ultrasound balloon for PV antrum ablation in 15 patients, but evidence for isolation was not presented, and the right inferior PV was targeted in only one patient. Van Belle et al24 investigated a cryoablation balloon (Arctic Front, Montreal, Quebec, Canada), and more than 40% (24/57) of patients required use of an additional single electrode catheter to complete isolation. Two studies using a high-intensity focused ultrasound (HIFU) balloon catheter targeted 75% (78/104) and 100% (46/46) of PVs, resulting in antral PV isolation in 87% (68/78) and 89% (41/46).25,26

**Procedural times**

The total procedural time from femoral vein access to complete catheter withdrawal was 84 ± 29 minutes (mean fluoroscopy time 18 ± 8 minutes). With conventional single-tip catheters, a wide range of procedural and fluoroscopy times have been reported for complete PV isolation: 70 ± 21 minutes procedural time with 44 ± 24 minutes fluoroscopy by Hocini et al,20 156 ± 85 minutes procedural time with 50 ± 17 minutes fluoroscopy by Oral et al,8 216 ± 28 minutes procedural time with 72 ± 17 minutes fluoroscopy by Cheema et al,19 and 256 ± 72 minutes procedural time with 72 ± 26 minutes fluoroscopy by Karch et al.27 In all of these studies, additional three-dimensional mapping techniques were described as methods for guiding ablation strategy.

In the cryoablation balloon study, procedures that were successful using only the balloon catheter had a mean fluoroscopy time of 52 ± 36 minutes, with total procedural time 211 ± 108 minutes; hybrid procedures trended toward additional fluoroscopy and procedural times (P = .06).24 In their initial experience using the HIFU balloon catheter in 15 patients, Schmidt et al25 reported procedural time of 354 ± 91 minutes and fluoroscopy time of 75 ± 18 minutes. Thus, the PVAC isolation technique compares favorably to these conventional and investigational techniques, with significantly shorter procedural times and no requirement for additional three-dimensional mapping.

<table>
<thead>
<tr>
<th>Table 3 Procedural times, safety, and efficacy</th>
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<tr>
<td>Procedural time</td>
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<td>Fluoroscopy time (min)</td>
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<td>Complications</td>
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<td>Follow-up</td>
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<td>Drug-free</td>
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<td>AF/AT recurrence</td>
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<td>Freedom from AF</td>
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AF = atrial fibrillation; AT = atrial tachycardia.
Safety
In this study of 98 patients, no short-term complications, including groin problems, stroke, gastrointestinal complaints, PV stenosis, or phrenic nerve damage, were reported. A worldwide survey on the methods and safety of conventional catheter ablation for AF published in 2005 reported an incidence of major complications of 6%. Compared with other published data on novel approaches, the cryoballoon and HIFU balloon studies each reported patients with phrenic nerve injury. Van Belle et al reported phrenic nerve paralysis events in 4 (7%) of 57 patients; two resolved during the procedure, one recovered 3 months postprocedure, and one persisted after 6-month follow-up. Schmidt et al reported 2 (17%) of 12 patients with phrenic nerve palsy at 12-month follow-up despite screening by phrenic nerve pacing and exclusion when capture occurred within 1 cm of the right superior PV ostium (3/15 patients excluded). Borchert et al reported a case of atrio-esophageal fistula after HIFU balloon ablation.

Unipolar-only RF energy may be associated with wider but nontransmural lesions, which may impair myocardial contractility. With this new technique, RF energy is bipolar 80% of the time, which should optimize lesion formation. In a study on unipolar-only, multielectrode ablation with power up to 30 W, transient ST-segment elevation was observed during ablation. In our study, such complications were not seen. By using alternating bipolar/unipolar RF energy with a power maximum of 8 W, the lesions penetrated approximately 2 to 4 mm into the myocardium, minimizing the risk of collateral damage to the phrenic nerve and esophagus. The low power and reduced convective heating of the blood pool also may minimize the risk of thromboembolic complications. In 11 of 98 patients in this study, MRI at 6 months or PV angiography at redo did not show PV stenosis. MRI follow-up data at 6 months from another study incorporating PVAC ablation in 53 chronic AF patients did not show evidence of PV stenosis despite the fact that half of the patients underwent a redo procedure. However, additional experience with a larger number of patients is needed to confirm the safety of PVAC ablation.

Study limitations
Although the current efficacy of 83% is encouraging, freedom from AF at 6 months and longer must be evaluated with Holter monitoring in the drug-free state for all treated patients to show consistency with the early results. In addition, arrhythmia detection after ablation using this new technique should be performed at 12 months and possibly longer to assess its final value against other techniques because the effect of catheter ablation in general is known to decline over time. Although patients with long-standing persistent and permanent AF were excluded from this study, we did not have detailed information on the number and duration of AF episodes and time to cardioversion prior to ablation for every patient. Therefore, we supplied the number of patients with a history of cardioversion as an alternative to persistent AF. Although care was taken to avoid RF application inside the PV, the demonstration of the absence of PV stenosis during longer-term follow-up currently is limited to 11 of 98 patients and remains to be assessed in greater detail. Data from other studies in which PVAC was used for PV isolation do not show evidence of PV stenosis at MRI follow-up. A larger study cohort with long-term follow-up is required to evaluate both the acute and the long-term safety and efficacy of this technique.

Conclusion
PV isolation by antrum ablation with a circular, multielectrode catheter using duty-cycled bipolar and unipolar RF energy appears to be feasible and safe, with promising efficacy at 6 months. The fluoroscopy and procedural times appear to be shorter than those associated with current AF ablation techniques, without the need for sophisticated mapping and/or steering modalities.

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References


