In patients with a pulmonary vein (PV) source for atrial fibrillation (AF), we sought the use of intracardiac echocardiography (ICE) to evaluate PV anatomy, guide radiofrequency (RF) ablation and monitor for acute PV stenosis during ablation.

BACKGROUND
A focal source for AF may be found in the proximal component of the PVs and can be effectively treated by ablative techniques. However, the procedure may be challenging due to the complex anatomy of the left atrium and PVs, uncertain catheter positioning within the PVs and difficulties in mapping atrial extrasystoles, which may be rare or repeatedly induce AF and require cardioversion.

METHODS
Sixty-four patients were referred for RF ablation of a focal source of AF, and 56 were identified as having AF triggers in ≥1 PV. Using ICE guidance, RF lesions were applied around the circumference of the vein near the ostium until there was electrical isolation.

RESULTS
Lesions were placed in 82 veins (36 right superior PV, 33 left superior PV, 9 left inferior PV, 4 right inferior PV); 24 ± 12 lesions per vein were necessary to create electrical isolation with a mean of 11 ± 4 min and a mean of 22% reduction in luminal area. After a follow-up of 13 ± 7 months, 66% of patients remained free of AF, and another 13% responded better to medications.

CONCLUSIONS
We describe an anatomic approach to PV electrical isolation in which ICE is used to define the anatomy, guide RF ablation and monitor for acute PV changes.

From the Cardiovascular Division, Department of Internal Medicine, University of Virginia Health System, Charlottesville, Virginia.

For many patients with paroxysmal atrial fibrillation (PAF), an atrial ectopic focus may serve as the initiating event (1,2). These sources of focal activity are frequently located in a sleeve of myocardial tissue that may extend up to 4 cm outside the adventitia of a proximal pulmonary vein (PV) (3,4). Locating and mapping these foci may be difficult owing to the complex and variable left atrial/pulmonary venous anatomy (5), difficulties manipulating the catheters within the PVs, and difficulties in mapping atrial extrasystoles, which may be rare or repeatedly induce atrial fibrillation (AF) and require cardioversion. For these reasons, electrical isolation of the PV, rather than limited ablation of the discrete arrhythmogenic focus, has become a favored ablation approach. Another concern is that symptomatic PV stenosis has been reported after extensive radiofrequency (RF) lesions in the left atrium (LA) and PVs, and increased pulmonary venous flow velocity has been demonstrated in up to 42% of patients with RF lesions localized to the PVs (6–8). Nevertheless, RF catheter ablation or isolation of these foci can significantly reduce or eliminate PAF episodes or improve the effectiveness of suppressive antiarrhythmic therapy (1,2,8–11).

One imaging modality, intracardiac echocardiography (ICE), continues to develop and has become an important adjunct to fluoroscopy for both focal and linear RF ablations (12–16). Some noted advantages of ICE include anatomic evaluation, precise localization of the ablation catheter, guidance of tissue contact and ablation, evaluation of tissue immediately after ablation, and immediate identification of complications such as clot formation or pericardial effusions (17).

We hypothesized that ICE could facilitate focal AF ablations by defining the PV anatomy, guiding radiofrequency ablation and monitoring anatomic changes during ablation to prevent PV stenosis.

METHODS

Patient selection. All patients had a history of PAF and were referred to the electrophysiology lab at the University of Virginia for AF ablation of presumed focal origin. They had either failed or refused one or more antiarrhythmic medications for AF suppression. Patients were classified into one of four categories based upon AF frequency: daily, weekly, monthly or fewer than once a month. A 24-h Holter monitoring or 30-day event recorder was not required but was obtained in 45% of patients. These demonstrated either frequent premature atrial contractions (PACs) or short periods of AF preceded by atrial tachycardia and/or PACs.

Strategies to prevent thromboembolism. Before the electrophysiology procedure, a transesophageal echocardiograph (TEE) was performed to exclude left atrial thrombi. These were performed with an ATL HDI 5000CV imaging.
**Abbreviations and Acronyms**

ACT = activated clotting times
AF = atrial fibrillation
EP = electrophysiology
ICE = intracardiac echocardiography
LA = left atrium
LSPV = left superior pulmonary vein
PAC = premature atrial contraction
PAF = paroxysmal atrial fibrillation
PV = pulmonary vein
PVP = pulmonary vein potential
RF = radiofrequency
RSVP = right superior pulmonary vein
TEE = transesophageal echocardiography

system (Philips Medical Systems, N.A., Bothell, Washington). Benzocaine 20% was used for local anesthesia, and intravenous midazolam was used for sedation. If a thrombus was present, no electrophysiology (EP) procedure was attempted.

During the EP procedure, 7,500 to 10,000 U of heparin was administered immediately after the double transeptal puncture. Activated clotting times (ACTs) were monitored every 30 min with additional boluses of heparin administered in order to maintain the ACT ≥300.

At the end of the procedure, intravenous protamine (30 to 40 mg) was given to facilitate sheath removal. Patients were hospitalized overnight for observation and discharged the next day. Each patient received three days of subcutaneous enoxaparin (1 mg/kg twice daily) during initiation of warfarin therapy and was maintained on warfarin for at least one month after the procedure.

**Catheter placement.** Each patient received conscious sedation using intravenous midazolam and fentanyl. Venous access was obtained in the right and left femoral veins and left subclavian vein. A Fischer Tangent V fluoroscopic imaging system (Fischer Imaging Corp., Denver, Colorado) with pulsed imaging at 7 frames/s was used throughout all studies. Two soft-tipped, 60-cm sheaths with 120° and 55° distal curves (EP Technologies, San Jose, California) were introduced through the right and left femoral veins, respectively, and advanced to the right atrium. A double transeptal catheterization was then performed using a Brockenbrough needle under ICE-guidance (as described in the following text) with a 9F, 9 MHz catheter and ClearView imaging system (Boston Scientific, San Jose, California) (10,18). The 120° sheath was positioned in the right superior PV (RSPV) and the 55° sheath in the left superior PV (LSPV). Quadripolar mapping/ablation catheters (EP Technologies) were positioned through the sheaths to record PV potentials (PVP).

Additional mapping catheter placement included a 20-pole deflectable Halo catheter (Cordis Webster) positioned in the right atrium, a decapolar catheter (Daig, Minnetonka, Minnesota) positioned in the coronary sinus and a quadripolar catheter (Cordis Webster, Baldwin Park, California) positioned in the right ventricle.

**Intracardiac echocardiography.** A 9F 9 MHz ICE catheter with the ClearView imaging system (Boston Scientific) was used to aid in the transeptal puncture. Initially, the ICE catheter was placed in a 55° curve sheath with the tip of the catheter placed at the fossa ovalis. Under ICE guidance, along with hemodynamic and fluoroscopic monitoring, a transeptal puncture was performed with a Brockenbrough needle through a 120° curve sheath. After successfully crossing the septum, the ICE catheter and the Brockenbrough needle with dilator were exchanged. With the ICE catheter inserted in the 120° sheath, placed at the fossa ovalis with imaging through the sheath, a second transeptal puncture was performed with the 55° sheath.

The sheaths were placed in the superior PVs. By exchanging the ICE catheter through each sheath, the location could be confirmed and local PV anatomy examined. Variability in PV anatomy was defined as “early branching” if secondary venous branches were noted within 5 mm of the ostium, “common ostium” if superior and inferior veins shared same ostium and “additional ostia” if more than four noted.

Intracardiac echocardiography was used to guide circumferential RF ablation of PV (see the following text) and to monitor for PV stenosis. Before any RF application, planimetry of the PV was performed and repeated immediately after electrical isolation of the vein.

**Mapping.** Multipolar electrode catheters were placed in each superior PV. Bipolar electrode signals were filtered at 40 to 500 MHz and displayed on a Bard Duo recording system (Bard Electrophysiology, Lowell, Massachusetts). During sinus rhythm, PVPs were identified by a sharp deflection preceded by a low amplitude potential. Mapping was performed during sinus rhythm looking for either isolated PACs originating from a PV or PV PACs initiating episodes of AF. If PACs were absent or rare, provocative maneuvers using isoproterenol infusion (0.5 to 4.0 μg/min), intravenous adenosine (6 to 12 mg), programmed electrical stimulation and high-rate atrial pacing were used. A target vein was defined as having ectopy in which the PVP preceded all other atrial electrograms and surface P waves with a distal to proximal activation sequence on the multipolar catheter positioned in the PV (Fig. 1). If ectopy originated from other sites in the LA or in the inferior veins, the mapping catheters were repositioned and location determined by activation sequence mapping. If patients developed AF that persisted for >10 min, external direct cardioversion was used for conversion to sinus rhythm. After cardioversion, early ectopy was sought.

**RF ablation technique.** Once the target vein was identified, the ICE catheter was advanced into the targeted PV through the soft-tip sheath (Fig. 2). This provided direct visualization of the position of the ablation catheter tip and guided placement of the catheter tip during RF energy
Circumferential ablation was performed under ICE guidance to the proximal component of the vein, near the os, which was free of branches and had a diameter of >1.0 cm. Radiofrequency energy was delivered using EPT-1000TC generator (EP Technologies) with target temperatures of 50°C to 60°C (operator’s discretion) and power limited to 25 to 30 W. Each RF lesion placed lasted 20 to 30 s. If target temperature was not reached, the power was kept constant; rather the ablation catheter was repositioned using ICE to obtain better tissue contact. The pre-ablation pacing threshold of the PV at 5 mm distal to the line of ablation was determined and repeated after completion of RF ablation. Electrical isolation of PV was identified by bidirectional conduction block, that is, loss of PVP during sinus rhythm and inability to conduct out of the vein towards the LA when pacing distal to the ablation line at high outputs (>20 mA) (Fig. 4). With an axial view from the ICE, initially 12 lesions were applied (at 1 o’clock to 12 o’clock positions). If the PV was not electrically isolated, additional lesions were applied to areas on the circumferential line with sharp potentials. If loss of PVP was noted during the initial 12 lesions and there was loss in ability to
conduct out of the vein to the LA, then no further lesions were given.

Patients with a history of atrial flutter or right atrial flutter observed during procedure and confirmed with entrainment mapping also received a tricuspid annulus/inferior vena cava linear lesion(s) until bidirectional conduction block across the isthmus was demonstrated. Additionally, ectopy-initiating AF that was outside the

Figure 2. Intracardiac echocardiography (ICE) placed in left superior pulmonary vein (LSPV). An ablation catheter and ICE catheter are placed within the LSPV to guide radiofrequency ablation. (A) Fluoroscopic image of intracardiac catheters: duodecapolar catheter in right atrium with ICE and ablation catheter in LSPV. (B) Concomitant image from ICE visualizing the ablation catheter within the LSPV lumen.

Figure 3. Positioning of the ablation catheter in the pulmonary vein. Intracardiac echocardiography (ICE) catheter is placed in the left superior pulmonary vein along with a 4-mm tip Blazer radiofrequency ablation catheter. The catheter can be seen within the lumen of the vein. The tip of the ablation catheter casts an echogenic shadow and allows precise location and apposition along the vessel wall. (A to D) Demonstrating catheter movement to the 12, 3, 6 and 9 o’clock positions.
PVs was mapped with activation sequence mapping and the foci ablated.

Follow-up. All patients were seen initially in the electrophysiology clinic or referring physicians clinic within six to eight weeks after procedure or sooner if patients developed symptoms. During each visit, an electrocardiogram was obtained, and the patient was questioned as to the recurrence of symptoms. Further clinic follow-up was performed on at least an annual basis. Additionally, all patients were contacted by telephone and were questioned about recurrence of symptoms. If patients had symptoms of palpitations, Holter monitoring or event recorders were performed. If AF recurrence was identified, antiarrhythmic medication was started and a repeat PV isolation procedure or enrollment in a linear ablation research protocol was offered to the patient.

Ablation success was defined as absence of symptomatic AF episodes without antiarrhythmic medications. Partial ablation success was defined as a reduction in AF frequency by one category (daily, weekly, monthly, or less than monthly) with or without a previously failed antiarrhythmic medication.

Figure 4. Electrical isolation of pulmonary vein (PV). Pacing threshold from within the PV was determined before ablation. After the intracardiac echocardiography (ICE)-guided circumferential lesions were created, pacing thresholds were again determined. Electrical isolation was defined by dissociation of an ectopic focus from within the vein or loss of PV potentials with pacing threshold distal to the ablation line exceeding 20 mA. (A) An ectopic focus is noted within the vein but does not conduct into the atria and is dissociated from the sinus rhythm. (B) Pacing from within the vein distal to the ablation line at 20 mA fails to conduct to the atria. DCS = distal coronary sinus; HALO = duodecapolar catheter in right atrium; MAP D = distal bipolar of mapping catheter; MAP P = proximal bipolar of mapping catheter; MCS = middle coronary sinus; PCS = proximal coronary sinus.
Table 1. Baseline Patient Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>52 ± 12</td>
<td></td>
</tr>
<tr>
<td>Male/Female</td>
<td>40/16</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>5</td>
<td>9%</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>16</td>
<td>29%</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>3</td>
<td>5%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4</td>
<td>7%</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>AF frequency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>30</td>
<td>54%</td>
</tr>
<tr>
<td>Weekly</td>
<td>15</td>
<td>27%</td>
</tr>
<tr>
<td>Monthly</td>
<td>7</td>
<td>13%</td>
</tr>
<tr>
<td>Fewer than once a month</td>
<td>4</td>
<td>7%</td>
</tr>
<tr>
<td>History of cardioversion</td>
<td>19</td>
<td>34%</td>
</tr>
<tr>
<td>Antiarrhythmic drug failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>11</td>
<td>20%</td>
</tr>
<tr>
<td>1</td>
<td>18</td>
<td>32%</td>
</tr>
<tr>
<td>2</td>
<td>19</td>
<td>34%</td>
</tr>
<tr>
<td>≥3</td>
<td>8</td>
<td>14%</td>
</tr>
</tbody>
</table>

AF = atrial fibrillation.

Data analysis. Statistical analysis was performed using Excel 5.0. Data is presented as mean with SD. Comparisons of PV luminal area were performed using a two-tailed Student t test. Significance was defined as p < 0.05.

RESULTS

Patients. A total of 64 patients (42 males, 22 females) were referred for “focal AF ablation” (Table 1). The mean age of our study population was 52 ± 12 years (range: 24 to 73), and the average duration of PAF before the ablation procedure was 5 ± 5 years. A total of 81% of patients had failed at least one class I or class III antiarrhythmic medication.

TEE. Transesophageal echocardiography was performed in 61/64 patients. The first patient in our series did not have a TEE; and two additional patients were unable to undergo TEE, because of significant esophageal pathology. A left atrial appendage thrombus was identified in one patient; therefore, no ablation procedure was performed.

Mapping and ICE-guided RF ablation. Only PVs that were the site of origin for PACs underwent the electrical isolation technique. Pulmonary vein PACs were absent in 7/63 patients; therefore, PV isolation was not performed in these patients. In these patients, ectopy initiating AF were either located in the right atrium (4), LA, (2) or no AF trigger could be identified (1).

Intracardiac echocardiography was employed to define regional PV anatomy. Variability in PV anatomy was seen in 20 patients (36%); 11 patients had a common os between the upper/lower veins, seven patients had very early branching of a PV, and two patients had additional ostia.

Demonstration of PV PACs initiating an episode of AF was observed in 40/56 patients. The other patients demonstrated PV ectopy without AF initiation. Mapping was performed with provocative maneuvers in 60 of 63 patients. Isoproterenol infusion was given alone in 41%, and isoproterenol with additional provocative means that included programmed electrical stimulation, rapid atrial pacing, adenosine bolus and intentional induction of AF followed with cardioversion and looking for early recurrence of AF was used in 55% of the patients.

A total of 82 veins were targeted for isolation. A total of 84% of target veins were superior (36 RSPV, 33 LSPV). A total of 61% of patients had one culprit PV, 32% of patients had two PVs and 7% of patients had three PVs. Complete electrical isolation with bidirectional conduction block was achieved in 81 veins. An additional focal right or left atrial source was noted in three patients and atrial flutter in 13 patients.

A mean of 24 ± 12 lesions (10.8 ± 8.8 min of RF energy) were required to electrically isolate each PV. Four PVs were electrically isolated during the initial lesion set of 12 lesions (4, 6, 9, and 9 lesions). After RF ablations were delivered, increased echogenicity could be seen (Fig. 5). Planimetry at the ablation site revealed a mean acute reduction in crosssectional luminal area by 22 ± 10% (p < 0.001), which corresponds to a 12% decrease in luminal diameter. In four patients, circumferential ablation was terminated prematurely because of a >50% reduction in luminal area. However, electrical isolation was still achieved in three of the four veins.

The mean procedural time was 243 ± 75 min with a mean fluoroscopy time of 11 ± 4 min. The estimated “fluoroscopic pedal time” is approximately 48.6 min.

Follow-up. After mean follow-up of 13 ± 7 months, 37/56 patients (66%) remain free from symptomatic AF after the initial procedure (34/56) or after a second procedure (3/6). A total of seven patients returned for repeat procedure due to AF recurrence (six focal and one linear ablation protocol). Four of those patients had PV ectopy from other veins not isolated on the original procedure. Seven of the remaining 15 patients have a reduction in AF frequency with or without previously failed antiarrhythmic medication. No symptomatic PV stenosis has been observed.

Complications. Two minor (pericarditis) and six major complications occurred (one esophageal perforation, one Mallory-Weiss esophageal tear, one cardiac tamponade, three cerebrovascular events). The esophageal perforation was a complication of the TEE. The patient had no history of esophageal pathology. The Mallory-Weiss tear was due to severe nausea/vomiting after the procedure, possibly related to pharmacologic agents used for sedation/analgesia. All cerebrovascular events occurred during the first year of performing focal AF ablations, and all occurred in patients >60 years old. Two patients had a prior history of transient ischemic attacks. The first patient did not receive a preprocedure TEE; the other two patients had preprocedure TEEs that were negative for LA thrombi. All patients had clinical presentation and post-event neurologic imaging that
was consistent with embolism. Neurologic deficits have persisted in one patient.

**DISCUSSION**

The PVs are well recognized as a source for focal triggers in patients with paroxysmal AF and structurally normal hearts. Methods of intracardiac mapping and ablation of these sites continue to evolve. In this paper we have described a method of identifying a “target vein” by PV PACs and directly placing an ICE catheter across the intra-atrial septum within the PV in order to evaluate the LA/PV anatomy, guide RF delivery at the PV ostia and monitor for acute tissue changes.

**PV imaging.** Significant variability in LA/PV anatomy is known (5). In this series of patients, 36% had either more than four PV ostia, common PV ostium or early branching. We have found that fluoroscopy guidance alone is inadequate to determine the anatomy and for the subtle catheter manipulations required to circumferentially ablate a PV, particularly at the LA/PV junction.

The use of phased-array ICE placed within the right
atrium to identify and guide lesions at the PV os has been described in an animal model (16). Although the LA and PV junction can be seen well, exact catheter positioning within the vein is difficult to determine with this imaging. Intracardiac echocardiography placed within the PV and containing a single rotating transducer provides a 360° field of view and allows exact positioning of the ablation catheter.

An additional potential advantage of this technique is reduction in fluoroscopic time as most catheter manipulation within the vein and monitoring for catheter stability during RF delivery can be achieved with ICE-guidance alone. However, comparisons with fluoroscopic times from other studies are difficult as different systems are used with different pulsed compression algorithms (5,10,11).

**Comparison with other techniques.** This ICE-guided technique differs from initial ablation methods described in five ways (11,19–23). First, only PVs from which PACs originate are targeted for ablation. Second, initiation of AF by these PACs was not required. Third, advanced mapping in the LA or within the PV is not required. Fourth, adjunctive imaging (ICE) is used to directly visualize catheter positioning, tissue contact and lesion formation. Fifth, bidirectional conduction block is used as the end point. Presently, investigators are employing PV isolation procedures that are map-guided using fluoroscopic or electroanatomic imaging of ablation catheter positioning (11,24). It is unknown whether the primarily anatomically guided procedure described in the present paper is superior to the map-guided techniques, but the success rates are similar with the two techniques.

**Complications.** Pulmonary vein stenosis is a known, but fortunately rare, complication following PV RF ablation. Strategies to minimize this complication include: 1) reducing power; 2) setting lower target temperature; and 3) limiting the number of RF ablations. In this series we reduced the set power and temperature but did not limit the number of ablations unless significant narrowing of the PV was seen (four veins). We saw an acute reduction in luminal area but have not had any symptomatic PV stenosis. The acute effects probably represents edema or PV spasms. The acute effects of RF lesions at the superior vena cava/right atrial junction has been well described, and, in a series of patients with inappropriate sinus tachycardia, a reduction in the orifice diameter of 24% was seen (25,26). However, in three patients who required a second procedure, no persistent swelling was observed (25).

The experience of three cerebrovascular events in our series of patients raises our concern that there may be neurologic complications associated with catheter ablation of “focal” AF. A review of thromboembolic complications with all RF ablation in the left heart reveals a stroke risk of 2% to 2.8% (27). This risk may certainly be increased with longer procedures and more extensive lesions in the LA. Three modifications to our protocol were made since these complications that occurred during the first year of performing this procedure. A higher saline flow through the 8.5F soft-tipped sheaths was employed to reduce blood stasis within the sheaths during RF ablation, ICE imaging and catheter exchanges; patients were given aspirin on the morning of the elective procedure for antiplatelet effect; and patients >60 years are dissuaded from pursuing focal AF ablation, particularly if they had a history of prior transient ischemic attacks. All of the cerebrovascular events occurred during the first 12 months of performing this procedure. Although speculative, we believe that the cause was likely related to technical problems during catheter manipulations or changes. Since the institution of the three measures noted above, no further cerebrovascular events have occurred at our center over the last 20 months.

**Study limitations.** We restricted our population to patients with paroxysmal AF. Therefore, the effects of this technique on more persistent forms of AF are unknown. We demonstrated an acute reduction in luminal area of 22% after RF ablation, but we do not know the long-term effects or the incidence of asymptomatic PV stenosis in these patients. Additionally, success was defined on clinical grounds; therefore, we cannot exclude occurrence of asymptomatic PAF.

**Conclusions.** In summary, we conclude that, in a heterogeneous population with paroxysmal AF, ICE-guided electrical isolation of arrhythmogenic PVs can be an effective treatment and a possible cure. The primary advantages of this approach are the ability to obtain a detailed evaluation of the PV anatomy, guide RF ablation and monitor for acute changes in the vessel.

**Reprint requests and correspondence:** Dr. James Michael Mangrum, University of Virginia Health System, Cardiology Division, Electrophysiology Laboratory, Box 800158, Charlottesville, Virginia 22908. E-mail: mmangrum@virginia.edu.

**REFERENCES**