Pulmonary vein (PV) isolation is the mainstay of catheter ablative therapy for patients with paroxysmal atrial fibrillation (AF). Although conceptually straightforward to consider placing a series of point-by-point ablation lesions to circumferentially isolate the PVs, in practice, these procedures are technically challenging to perform. Accordingly, there has been a tremendous amount of development work in designing various one-size-fits-all ablation catheters to facilitate PV isolation. For such devices to be practical, they need to be able to isolate PVs: (1) reproducibly using only a single catheter despite the intrapatient and interpatient variabilities in PV size, shape, and orientation, (2) without requiring the use of ancillary catheters for touch-up energy delivery, (3) without a high rate of complications, (4) with reasonable procedure times and without excessive fluoroscopy exposure, and (5) with good clinical efficacy.

Background—Because of the technical difficulty with achieving pulmonary vein (PV) isolation in the treatment of patients with paroxysmal atrial fibrillation, novel catheter designs to facilitate the procedure are in development. A visually guided laser ablation (VGLA) catheter was designed to allow the operator to directly visualize target tissue for ablation and then deliver laser energy to perform point-to-point circumferential ablation. Single-center studies have demonstrated favorable safety and efficacy. We sought to determine the multicenter feasibility, efficacy, and safety of performing PV isolation using the VGLA catheter.

Methods and Results—This study includes the first 200 paroxysmal atrial fibrillation patients treated with the VGLA catheter (33 operators, 15 centers). After transseptal puncture, the VGLA catheter was used to perform PV isolation. Electric isolation was assessed using a circular mapping catheter. Using the VGLA catheter, 98.8% (95% confidence interval, 97.8%–99.5%) of targeted PVs were isolated using a mean of 1.07 catheters per patient. Fluoroscopy and procedure times were 31±21 (mean±SD) and 200±54 minutes, respectively, and improved with operator experience. There were no instances of stroke, transient ischemic attack, atrioesophageal fistulas, or significant PV stenosis. There was a 2% incidence of cardiac tamponade and a 2.5% incidence of phrenic nerve palsy. At 12 months, the drug-free rate of freedom from atrial arrhythmias after 1 or 2 procedures was 60.2% (95% confidence interval, 52.7%–67.4%).

Conclusions—In this multicenter experience of the first 200 patients treated with the VGLA catheter, PV isolation can be achieved in virtually all patients using a single VGLA catheter with an efficacy similar to radiofrequency ablation. (Circ Arrhythm Electrophysiol. 2013;6:467-472.)

Key Words: atrial fibrillation ● catheter ablation ● lasers ● pulmonary vein isolation ● visual guidance

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Drug Administration investigational trials in the United States. In this article, we report on the international multicenter experience of the first 200 paroxysmal AF patients treated with this VGLA catheter.

Methods

The study consists of 200 patients (out of a consecutive series of 204 patients) enrolled in 1 US study (9 clinical sites) and 3 European studies (6 clinical sites). Of note, 4 additional patients who underwent ablation near the end of the 200-patient series were excluded as baseline demographics, and procedural data were not available at the time of data analysis: however, none of these excluded patients experienced any procedural complications. All of the studies were approved by institutional review committees at the participating institutions, and all subjects gave informed consent. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agreed with the article as written.

Patient Selection and Study Design

All 4 clinical studies were open label, nonrandomized studies of patients with symptomatic, recurrent, paroxysmal AF. There were only minimal differences in the inclusion criteria between the studies. Key inclusion criteria were age 18 to 75 years and recurrent paroxysmal AF that was refractory to ≥1 antiarrhythmic drug (Class I–IV). All patients were otherwise deemed to be candidates for catheter ablation. Key exclusion criteria included: a left ventricular ejection fraction <30%, left atrial (LA) diameter >5 cm, PV diameters >32 mm (for oval PVs, the mean values of the major and minor dimensions were used), the presence of an intracardiac thrombus, previous cardiac ablation, myocardial infarction or cardiac surgery within the previous 3 months, moderate or severe valvular heart disease, or a stroke/transient ischemic attack within previous 6 months. Preprocedural computed tomography (CT) or MRI scans were performed to assess LA and PV anatomy and size.

After the procedure, patients were discharged on oral anticoagulation (warfarin) and, at times, low molecular weight heparin until the international normalized ratio was ≥2.0. After the procedure, antiarrhythmic medications were typically continued for 1 to 3 months after which they were completely discontinued. There was a 3-month blanking period after ablation. Follow-up methods were variable between the 4 studies and included clinic visits at 3- or 6-month intervals, and either Holter or transtelephonic monitoring at variable intervals. Recurrence was defined as any atrial arrhythmia, whether symptomatic or not of a duration exceeding 60 s. In a subset of patients, a repeat CT or MRI scan was performed at 3 months to assess for PV stenosis.

One study required that all patients return at 3 months for PV re-mapping procedures, regardless of symptomatology. These patients underwent reisolation of reconnect PVs with radiofrequency energy. The results of the PV remapping and 1-year clinical follow-up in 52 of these patients have been previously reported. A single-center experience in an additional 40 of these patients with 1-year follow-up was also previously reported.

The Balloon-Based VGLA Catheter

The components of VGLA catheter (CardioFocus, Inc, Marlborough, MA) were previously described in detail. The VGLA catheter is a variable diameter, compliant balloon that is delivered through a deflectable 12-Fr sheath. Within the central shaft of the balloon is a 2-Fr endoscope that provides real-time visualization of the face of the balloon: both the tissue and blood in contact with the balloon. Additionally, within the central shaft are additional lumens for circulating D2O to cool the balloon, and a maneuverable optical fiber that generates a 30° arc/spot of both visible and near-infrared ablative light energy. The tip of the VGLA catheter is designed to be flexible to cause minimal trauma.

The deflectable sheath was positioned at the PV ostium and the VGLA catheter advanced and inflated to provide good tissue contact. Under endoscopic visualization, the area of tissue-ballooning contact appears white and blood appears red. The endoscopic field of view is partially obscured in the region behind the central shaft. This partially obscured region is located 180° directly opposite a radiopaque marker located on the catheter shaft. The location/orientation of the radiopaque marker on fluoroscopy is then correlated to the endoscopic image thus defining superior, inferior, anterior, and posterior directions. The 30° arc of light includes a visible aiming beam and can be advanced/retracted and rotated to any location on the face of the balloon. Once an appropriate site for ablation is identified, diode laser energy (980 nm) is delivered through the same optical fiber that generates the aiming beam to ablate tissue. Ablation lesions are placed in a contiguous and overlapping manner to achieve electric isolation of the PV.

PV Isolation Procedure

Procedures were performed using either conscious sedation or under general anesthesia per the clinical practice of the institution. Right and left femoral vein access was obtained. The transeptal puncture was performed in standard fashion with an 8-Fr sheath and a Brockenbrough needle under fluoroscopic guidance, and at some centers with adjunctive intracardiac echo guidance. The 8-Fr sheath was then exchanged for a 12-Fr deflectable sheath over a 0.035” or 0.038” guide wire. Per the operator preference, a second transeptal puncture with a standard 8-Fr sheath was placed for a diagnostic mapping catheter. At baseline, a multielectrode circular mapping catheter was used to assess electrograms of all PVs. Throughout the procedure, intravenous heparin was administered as boluses and as a continuous infusion to maintain an international normalized ratio (INR) of 2.0. After the procedure, antiarrhythmic medications were typically continued for 1 to 3 months after which they were completely discontinued. For situations when entrance block was not routinely assessed. For situations when entrance block was not routinely assessed. For situations when entrance block was not routinely assessed. For situations when entrance block was not routinely assessed. For situations when entrance block was not routinely assessed. For situations when entrance block was not routinely assessed.

The dose of laser energy used was 5.5 Watts × 30 s or 8 to 14 Watts × 20 s per lesion. When the area of balloon/tissue contact was not adequate enough to allow energy delivery to atrial tissue alone, the laser energy dose (5.5 Watts/30 s) was used to simultaneously ablate on tissue and blood that was located at the periphery of the target tissue. Blood located at the periphery of the target tissue is continually refreshed (not trapped by the balloon), and ablation at these sites with the lowest energy dose minimizes the risk of thrombus formation.

Statistics

Categorical variables were compared using Fisher exact test. Continuous variables were first tested for normality using the Shapiro–Wilk test for normality to determine whether the data were normally distributed. All tested continuous variables were determined to have a normal distribution. Comparisons between groups were tested using Student 2-sample t test (pooled). Continuous data are presented as mean and SD (mean±SD). Continuous data with skewed distribution
are represented as median with interquartile ranges. Point estimates (ie, percentage of PVs isolated and percentage of patients free of AF at 12 months) are represented with 95% confidence intervals (95% CI). A 2-sided α level of 0.05 was used for all superiority testing. Statistical analyses were performed using SAS version 9.2.

Results
Patient Demographics
The baseline demographics of the 200 patients are shown in Table 1. The mean age of the cohort was 57.0±9.9 years (limits 25–75), and 60% of the patients were men. The median duration of symptoms consistent with paroxysmal AF was 3.0 years (1.0–7.0, Q1–Q3). A total of 187 (93.5%) patients failed ≥1 antiarrhythmic medication. Transthoracic echocardiograms were performed in 178 patients and demonstrated a mean LA diameter of 4.1±0.5 cm and mean left ventricular ejection fraction of 63±8%. No patients were excluded because of inappropriate PV anatomy (ie, a PV with average diameter >32 mm). These 200 patients were treated by a total of 33 primary operators at 15 centers.

Procedural Characteristics
A total of 770 PVs were targeted in 200 patients (Tables 2 and 3). Acute electric isolation was achieved in 78.4% (95% CI, 75.4%–81.3%) of all PVs after placement of the initial encircling lesion set and ultimately in 98.8% (95% CI, 97.8%–99.5%) of PVs after an average of 1.3 attempts per vein. Of the various PVs, the left common PVs and left superior PVs were the least likely to be isolated after the first encircling lesion set (Table 3); that is, although 100% of left common PVs and 98.3% of left superior PVs were ultimately isolated, only 58.6% and 69.9% of PVs were isolated after the first encircling lesion set, respectively. Overall, the PVs were isolated using an average of only 1.07 catheters per patient. Two catheters were required in 13 (6.5%) patients; all attributable to catheter damage during use rather than PV/balloon size mismatch. No additional catheters were used to provide touch-up energy delivery.

The mean procedure and fluoroscopy times were 200±54 minutes and 31±21 minutes, respectively. As shown in the Figure, these parameters improved with operator experience. With increased operator experience (first 15 cases performed by an operator versus cases beyond the first 15), procedure times decreased by 30±55 minutes (P=0.0005), ablation times decreased by 18±36 minutes (P=0.001), and fluoroscopy times decreased by 18±19 minutes (P<0.0001). Four of the 33 operators performed >15 procedures. Interestingly, the ability to electrically isolate a PV after placement of the initial encircling lesion set did not significantly change with operator experience. That is, for operators performing ≤15 procedures, 77% of PVs were isolated after the first encircling lesion set and, for those performing >15 procedures, 82% of PVs were isolated (P=0.462).

Clinical Outcomes and Safety
Of the 200 patients, 181 patients completed 12 months of follow-up. Of these, 60.2% (95% CI, 52.7%–67.4%) of patients were free from AF and were off antiarrhythmic drugs (class I or III). After a single procedure, 72 of 123 (58.5%) patients were free of atrial arrhythmias and off antiarrhythmic drugs (95% CI, 49.3%–67.4%), and after 2 procedures 37 of 58 (63.8%) patients were free of atrial arrhythmias and off antiarrhythmic drugs (95% CI, 50.1%–76.0%). Of the 19 patients with no outcome data, 7 patients were lost to follow-up, 6 withdrew from study, and 6 patients had not yet achieved 12 months of follow-up.

There was no clinical evidence of PV stenosis in any of the patients. In addition, baseline and 3-month CT or MRI scans were available for 116 patients (Table 4). At 3 months, the mean decrease in PV diameter was 3.5%. Mild PV narrowing (1%–25% decrease in diameter) was present in 44% of PVs, and moderate PV narrowing (26%–50% decrease) in 6% of PVs. There was no significant PV stenosis (>50% decrease). A variable degree of mild-to-moderate PV diameter increase was also noted.

Phrenic nerve injury related to the VGLA occurred in 2 patients, 1 of which remained unresolved at 12 months of follow-up (Table 5). Pericardial effusions were reported in 6 patients, 4 of whom developed hemodynamic compromise/cardiac tamponade. All of these tamponades occurred during the procedure and were successfully drained. One patient with cardiac tamponade underwent pericardiocentesis and was ultimately discharged in good condition on the fourth hospital day. Two days after discharge from the hospital, he experienced sudden death. Autopsy demonstrated no pericardial effusion, cardiac perforation, atrioesophageal

<table>
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<th>Table 1. Patient Demographics (N=200)</th>
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<tr>
<td>Age, mean±SD (limits)</td>
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<td>Sex, M/F (%)</td>
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<tr>
<td>Duration of atrial fibrillation, median years (Q1–Q3)</td>
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<tr>
<td>Coronary artery disease, n (%)</td>
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<td>Hypertension, n (%)</td>
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<tr>
<td>Ejection fraction, mean±SD (limits)*</td>
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<tr>
<td>Left atrial diameter, mean±SD (limits)*</td>
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<tr>
<td>Antiarrhythmic medications†</td>
</tr>
<tr>
<td>Class I</td>
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<tr>
<td>Class II</td>
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<tr>
<td>Class III</td>
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<td>Other</td>
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*Available from 178 patients.†One hundred eighty seven patients failed a total of 309 antiarrhythmic medications.
fistula, or pulmonary embolization. However, the patient was found to have unrecognized, critical triple vessel coronary artery disease (a preprocedure stress test had revealed only a mild reversible apical defect and was thought not to be clinically significant). Accordingly, although the stress of the AF ablation procedure may have contributed to this death, an independent Data Safety and Monitoring Board adjudicated that this event was not related specifically to the laser ablation catheter. The presumed cause of death was felt to be arrhythmic. There were no patients who manifested transient ischemic attacks, strokes, or atrioesophageal fistulas.

**Discussion**

In this article, we report the international multicenter experience of the first 200 patients treated with this novel VGLA catheter. In procedures performed by 33 operators at 15 centers, the compliant, variable diameter VGLA catheter was capable of achieving PV isolation in 99% of targeted veins using (in the majority of cases) only 1 balloon catheter, irrespective of PV size and anatomy. With visual guidance alone, 78% of PVs were isolated after placing the first encircling lesion set. The mean procedure time was relatively long (200±54 minutes) but did improve with operator experience, as one would expect with new technology. At 12 months, the drug-free rate of freedom from atrial arrhythmias was 60%. These results were obtained without any instances of significant PV stenosis, stroke/transient ischemic attack, or atrioesophageal fistula. However, there was a 2% incidence of pericardial tamponade and a 3% incidence of phrenic nerve injury.

**Efficacy of the VGLA Catheter**

Although acute PV isolation was achieved in virtually all targeted PVs, the observed clinical efficacy was similar to that seen with radiofrequency energy and cryoballoon ablation. As with other technologies, it would seem to reason that clinical efficacy is limited by chronic PV reconnections. However, in a subset of these patients, we previously showed that a high rate of acute PV isolation translated to 62% of patients having persistent PV isolation of all veins at 3 months. In that study, reconnected PVs were reisolated with radiofrequency energy, but still resulted in AF recurrence in 29% of patients at 1 year. Therefore, PV reconnections alone are unlikely to account for the 40% recurrence at 1 year in this study. Other possibilities include the presence of non-PV triggers and an ostial level of electric isolation that largely excludes areas in the antrum that may be responsible for the initiation and perpetuation of AF. We previously have shown that the level of electric isolation with the first generation VGLA catheter is at the PV ostium. The level of isolation with the current generation VGLA catheter has not been systematically evaluated. However, limited data from cases, where electroanatomical mapping was performed with VGLA, suggest that the level of electric isolation maybe near the PV ostia. Further improvement in chronic PV isolation rates and clinical efficacy with VGLA may depend on the use of high-energy ablation, particularly in areas of increased tissue thickness, such as the left atrial appendage ridge, where PV reconnections commonly occur with VGLA.

**Safety of the VGLA**

There were 2 important safety issues that were observed in this 200-patient experience, albeit at a low event rate. The first of these was a 2% rate of pericardial tamponade. This is possibly attributable, in part, to the inability to use an over-the-wire technique when positioning the VGLA catheter. This is still a manageable rate given the uncensored nature of the data. That is, it is likely that this tamponade rate will decrease.
Table 4. Pulmonary Vein Diameter Change on 3 Months Postablation Computed Tomography Scans

<table>
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<tr>
<th>PV diameter change</th>
<th>Pulmonary Veins N (%)</th>
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<tbody>
<tr>
<td>PV diameter decrease</td>
<td></td>
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<tr>
<td>1% to 25%</td>
<td>168 (43.9)</td>
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<tr>
<td>26% to 50%</td>
<td>24 (6.3)</td>
</tr>
<tr>
<td>&gt;50%</td>
<td>0 (0)</td>
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<tr>
<td>PV diameter increase</td>
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<tr>
<td>0% to 25%</td>
<td>180 (47.0)</td>
</tr>
<tr>
<td>26% to 50%</td>
<td>9 (2.3)</td>
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<tr>
<td>&gt;50%</td>
<td>2 (0.5)</td>
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PV indicates pulmonary vein.

Conclusions

In this multicenter evaluation of the first 200 patients treated with the compliant, variable diameter, visually guided laser balloon catheter, acute PV isolation was achieved in 99% of targeted veins with a single balloon catheter. The catheter also proved to be reasonably safe, with no instances of embolic stroke/transient ischemic attack, PV stenosis, or atrioesophageal fistula. However, there remains a low rate of pericardial tamponade and phrenic nerve injury. The clinical efficacy was similar to other AF ablation technologies. This favorable experience sets the stage for truly comparative long-term efficacy and safety studies (versus radiofrequency ablation).

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Disclosures

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References


**CLINICAL PERSPECTIVE**

Balloon ablation catheters have been introduced to facilitate pulmonary vein isolation in the treatment of patients with atrial fibrillation. One such example is the visually guided laser ablation catheter (VGLA). This catheter consists of a compliant balloon that has the capability of real-time endoscopic visualization of target tissue during point-by-point laser energy ablation. Preclinical studies have demonstrated the potential of the VGLA to deliver contiguous and transmural lesions during pulmonary vein isolation. However, clinical data establishing feasibility, safety, and efficacy are limited. In this article, we report on the multicenter experience (15 centers, 33 operators) of the first 200 paroxysmal atrial fibrillation patients treated with the VGLA. Using the VGLA, acute isolation was achieved in 99% of targeted pulmonary veins using only 1 catheter per patient in virtually all cases. Similar to the experience with other new technologies, the mean procedure and fluoroscopy times were long but did improve with operator experience. Overall complications were few, with a 2% incidence of cardiac tamponade and a 2.5% incidence of phrenic nerve palsy. No transient ischemic attacks, strokes, atrioesophageal fistulas, or clinically significant pulmonary vein stenosis were observed. At 12 months, 60% of patients were free of atrial fibrillation without antiarrhythmic medications: a clinical efficacy similar to that observed with radiofrequency ablation. Although the findings of this study are favorable, future multicenter, randomized, comparative studies are needed to truly assess the safety and efficacy of the VGLA.
Pulmonary Vein Isolation Using a Visually Guided Laser Balloon Catheter: The First 200-Patient Multicenter Clinical Experience

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