Visual Balloon-Guided Point-By-Point Ablation:
Reliable, Reproducible, and Persistent Pulmonary Vein Isolation

Dukkipati et al.: Visually-Guided AF Ablation

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ABSTRACT

Background — While conceptually straightforward, placing point-to-point contiguous radiofrequency lesions to achieve pulmonary vein isolation (PVI) is technically challenging in patients with paroxysmal atrial fibrillation (PAF). Furthermore, chronic efficacy is limited by late PV reconnections. A novel compliant balloon ablation catheter (BAC) able to deliver visually-guided short arcs/spots of laser energy was tested in initial pre-clinical and clinical cases to determine if visual guidance could predict reliable and persistent PVI.

Methods and Results — This study consisted of i) an experimental porcine phase with both acute (n=15 pigs) and 4-week chronic (n=10) data, and ii) a single-center clinical feasibility phase (n=27 PAF patients), again with acute and 3-month chronic data. Under endoscopic guidance, point-by-point peri-venous ablation was performed in a contiguous and overlapping manner. Each porcine PV was longitudinally sectioned for detailed histological analysis. At 3-months post-ablation, patients underwent a pre-specified remapping procedure regardless of symptomatology. In the acute and chronic animals, 29/30 (97%) PVs were electrically isolated after placing the initial circumferential lesion set. For the 4-week chronic animals, 80% of PVs remained isolated; lesions were histologically circumferential in 120/120 (100%) PV sections, and transmural in 116/120 (96.7%) PV sections (average transmurality = 99.0±5.5%). In patients, 100% of the PVs were isolated after 1.3 attempts/PV – 84% of them (85/101) isolated after the initial visually-guided lesion set. At 3 months, 61/68 (90%) PVs continued to be electrically isolated.

Conclusions — Using a visually-guided, compliant balloon ablation catheter with point-by-point ablative capability, PV isolation can be achieved in a reliable, reproducible, and persistent manner.

Key words: Atrial Fibrillation, Catheter Ablation, Laser, Pulmonary Veins, Visual Guidance
INTRODUCTION

Pulmonary vein (PV) isolation is the mainstay of catheter based therapy for atrial fibrillation (AF).\textsuperscript{1-11} However, achieving electrical PV isolation with point-by-point ablation is technically challenging. Recently, balloon catheters utilizing multiple energy sources have been utilized to facilitate PV isolation.\textsuperscript{12-17} While many of these balloons share similar characteristics, the laser balloon is unique in its ability to provide real-time endoscopic visualization and to deliver laser energy at operator-determined locations around the PV-left atrial junction.\textsuperscript{17}

Although clinically promising, the first generation laser balloon ablation catheter (BAC) was limited in its ability to deliver optimal lesions due to balloon noncompliance and the large 90° – 120° ablative arc. This translated to suboptimal balloon contact and difficulty in delivering sufficient energy along the large ablative arc due to risk of thrombus formation from ablation at areas with overlapping blood. Accordingly, the rate of acute PV isolation in the clinical series was only 91% with an AF recurrence rate of 60%. Because of these limitations, the balloon was redesigned to 1) maximize balloon-tissue contact by making a balloon of adjustable diameter and compliance, and 2) allow the delivery of spot laser lesions. This second generation balloon was evaluated in a two-phase study. The pre-clinical phase involved electrophysiological and histological assessment of the lesions delivered by the balloon in a series of acute and chronic porcine experiments. The clinical phase involved a single center evaluation in patients undergoing catheter ablation for paroxysmal atrial fibrillation with a prespecified PV remapping procedure at ~3 months regardless of intervening symptomatology. Thus, in addition to the acute procedural performance of this BAC, we are also able to report on the 3-month permanency of electrical PV isolation.

METHODS

The pre-clinical experiments were approved by the Institutional Animal Care and Use Committees. The clinical phase was approved by the human ethics committee at Homolka
Hospital. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Endoscopic Ablation System with Adaptive Contact (EASAC): The EASAC (CardioFocus, Inc., Marlborough, Massachusetts) consists of the following major components: (i) delivery sheath, (ii) balloon ablation catheter (BAC), (iii) endoscope, (iv) lesion generator, and (v) cooling console. The delivery sheath is a deflectable 12-Fr ID sheath with the capability of 180° deflection. The BAC (Figure 1) is a variable diameter, compliant balloon with a flexible tip (to minimize the possibility of mechanical trauma). Contained within the balloon are multiple lumens within the central shaft for the endoscope, lesion generator, and cooling conduits. The balloon is constantly cooled with circulating D₂O.

The BAC is positioned at the PV ostium and inflated (Figure 2A&B) to provide good contact. A 2-Fr endoscope is located at the proximal portion of the balloon and provides real-time visualization of the face of the balloon (Figure 2C). Regions of the balloon in contact with blood appear red, and regions in contact with tissue blanch white. The field of view is partially obscured in the area behind the central shaft. This partially obscured view is located 180° opposite the radiopaque “L” marker on the balloon catheter shaft and allows positional correlation between the fluoroscopic and the endoscopic images. The lesion generator consists of an optical fiber within the central shaft that generates a 30° arc of light that is projected onto regions of balloon contact. This arc serves as an aiming beam for laser delivery, and can be easily advanced/retracted and rotated along the balloon face with endoscopic visualization. Once an appropriate location is selected, laser energy (980 nm) is delivered through the same optical fiber to ablate the target tissue. Multiple lesions are delivered in an overlapping manner to achieve circumferential ablation (Figure 2D).

Pre-Clinical Phase – Ablation Procedure: After an overnight fast, 25 pigs (15 acute, 10 chronic) were induced with 1.4 mg/kg Telazol, 1.1 mg/kg acetylpromazine, and 0.05 mg/kg IM
atropine. The animals were intubated and ventilated with oxygen and 1.5-2.5% Isoflurane. Femoral venous access was obtained and transseptal puncture was performed using a Brockenbrough needle under fluoroscopic guidance. The deflectable 12-Fr sheath was advanced into the LA over a 0.035” or 0.038” guidewire. Intravenous heparin was given as a continuous infusion and boluses to maintain an ACT>300 sec. The deflectable sheath was positioned at the ostium of the target PV. Contrast was injected through the sheath to assess PV anatomy and diameter. A circular mapping catheter (Biosense-Webster, Inc., Diamond Bar, California) was placed in the PV to evaluate electrograms at baseline and post-ablation to assess for electrical isolation.

The BAC was delivered through the deflectable sheath and inflated at the ostium of the target PV. The right superior (RSPV), and sometimes the left superior (LSPV), were targeted for ablation; the decision to target a PV was based on the presence of baseline PV electrograms. The porcine right inferior (RIPV) and left inferior (LIPV) were not targeted as PV electrograms are rarely, if ever, present. Additionally in pigs, the esophagus is located much more posteriorly to the LA than seen in humans, and esophageal injury is never seen. However, the course of the right phrenic nerve is similar to humans and injury is possible during ablation. Therefore, during ablation around the RSPV, phrenic nerve pacing was performed with a catheter placed in the superior vena cava. Using endoscopic visualization, the aiming beam was manipulated around the PV and laser energy was delivered in a contiguous, overlapping, and circumferential manner to achieve PV isolation.

The dose of laser energy available for use ranged between 5.5 – 16 Watts/cm at 20-30 sec duration per lesion. When ablation in regions with overlapping blood was required, the lowest energy of 5.5 Watts/cm for 30 sec per lesion was used (this is based upon pre-clinical data indicating safety despite blood overlap at this dose). To ablate the tissue located at the partially distorted region behind the central shaft, the BAC was partially deflated, rotated, and then reinflated to allow full visualization of this obscured region. Following circumferential ablation PV isolation was assessed with the circular mapping catheter. If electrical breakthrough was
observed, the BAC was repositioned in the PV ostium to ablate in the region of breakthrough and achieve PV isolation. At \( \geq 30 \) min post-ablation, PV isolation was confirmed again and PV angiography was repeated to again assess PV diameters.

The acute animals were sacrificed and pathological examination was performed. The chronic animals were recovered and brought back for a repeat procedure at \( \sim 4 \) weeks to assess PV diameters and electrical isolation by the methods described above. For these chronic experiments, at the time of the second procedure, the animals were sacrificed and pathological examination was performed.

**Pre-Clinical Phase – Pathological Examination:** The explanted heart and surrounding tissue, were subjected to gross examination. In all animals, the LA and PVs were examined to assess location and circumferentiality of the lesions. The LA and PVs, as well as any abnormal tissue were fixed with 10% formalin for histological examination. The PVs were opened longitudinally at the superior-most aspect (12 o’clock position) and sectioned (8-15 slices/PV) in a circumferentially longitudinal pattern parallel to blood flow. The sections underwent paraffin processing and were stained with either hematoxylin-eosin (H&E), Movat pentachrome, or Masson’s trichrome stains. The slides were examined by light microscopy and evaluated for thermal injury and necrosis.

**Clinical Phase – Study Design.** The clinical phase was a prospective, open label, non-randomized, single center study of patients with symptomatic, recurrent, paroxysmal AF. The inclusion criteria were: age 18-75 years, and recurrent paroxysmal atrial fibrillation that was refractory to at least one antiarrhythmic drug (Class I – IV). All patients were otherwise deemed to be candidates for radiofrequency catheter ablation. Key exclusion criteria included: a prior PV isolation procedure, presence of intracardiac thrombus or spontaneous echo contrast, myocardial infarction or cardiac surgery in the prior 3 months, moderate to severe valvular disease, left ventricular ejection fraction <30%, LA diameter >5 cm, PV diameter >30 mm (for
oval PVs, the mean of the PV major and minor dimension was used), or stroke/transient ischemic attack in previous 6 months. Pre-procedural CT scans were performed to assess LA and PV anatomy and size.

A total of 27 patients underwent ablation with the BAC. Following the procedure, all patients were discharged on warfarin, and at times, low molecular weight heparin until the international normalized ratio was ≥2.0. Following the procedure, antiarrhythmic medications were either discontinued or reduced in dosage for 1 month after which they were completely discontinued. There was a 1 month blanking period following ablation. All patients were discharged with an event monitor for weekly transmissions and for recurrence of AF symptoms. Post-procedure clinic visits were performed at 1 and 3 months. A repeat CT scan was performed at 3 months to assess for PV stenosis. At ~3 months after the index procedure, patients were brought back for a repeat procedure to assess for the permanency of PV isolation. This second procedure was performed regardless of the intervening symptomatology.

Clinical Phase – Ablation and Remapping Procedures: The ablation and remapping procedures were performed in a modified manner to the methods described for the preclinical experiments. All procedures were performed under conscious sedation. Two transseptal punctures were performed; one for the deflectable sheath and BAC, and the second for the circular mapping catheter. Intracardiac echocardiography was used during the procedures to facilitate transseptal puncture and BAC positioning. During ablation of the RSPV, pacing from the superior vena cava was performed to minimize risk of phrenic nerve palsy. In all patients, an esophageal temperature probe was placed to monitor esophageal heating and ablation was stopped when the temperature reached 38.5°C. After inflation of the BAC, laser energy was delivered around the PV ostium in a contiguous, overlapping, and circumferential manner. After completion of a single circumferential lesion set, PV electrical isolation was assessed with the circular mapping catheter. If breakthrough was present, further ablation with the BAC was
performed at sites of electrical breakthrough. After PV isolation was achieved, it was reassessed at 30 min post-ablation.

The remapping procedures were also performed under conscious sedation. After a transseptal puncture, PV isolation was assessed with a circular mapping catheter. If electrical breakthrough was identified, a second transseptal puncture was performed. Then ablation was performed with a externally-irrigated radiofrequency ablation catheter (Celsius or Navistar ThermoCool, Biosense-Webster, Inc., Diamond Bar, CA). All data are expressed as mean ± standard deviation.

RESULTS

Pre-Clinical Phase – Acute Porcine Experiments: Among 15 pigs, a total of 20 PVs (15 RSPV, 5 LSPV) were targeted for ablation. The BAC conformed well to the PV ostia and antra and provided adequate contact and visualization (Figure 2). With the initial visually-guided placement of an overlapping circumferential ablation lesion set, 19/20 (95%) PVs were electrically isolated. After identifying the area of electrical breakthrough using a circular mapping catheter, the remaining PV was isolated with additional balloon laser lesions. The mean number of ablation lesions needed to isolate each PV was 31.0±14.1 with a mean ablation time of 24.7±11.9 min. All PVs (100%) remained electrically isolated after ≥30 minutes post-ablation. The mean PV diameter change was -2.5±7.7% (limits -22.2 to +8.3%).

Gross pathological examination of the PVs revealed well-demarcated circumferential and contiguous lesions. Interestingly, grossly visual gaps were identified in 7/20 (35%) PVs (Figure 3) despite the fact that all PVs were electrically isolated. Histological examination was performed in 13/15 pigs (12 RSPV, 5 LSPV). The histological lesion characteristics observed are shown in Table 1. On a per vein basis, histological acute lesion transmurality was 80.8±16.2% (limits 57.0-100%). When assessed by histological sections (n=187), the mean
transmurality was 84.6±27.8% (limits 0.0-100%). Of the PV sections, 122/187 (65.2%) had completely transmural lesions while only 8/187 (4.3%) had no lesion. The maximal lesion depth observed was 12.7 mm which represented a completely transmural lesion. On histological examination, all injury was confined to the PV antra without extension into the PVs. One animal had a lung lesion in a location directly adjacent to the PV antrum. There was no phrenic nerve injury or thrombi seen on either the BAC or atrial tissue.

**Pre-Clinical Phase – Chronic Experiments:** In 10 pigs, 10 PVs (all RSPV) were targeted for ablation. All PVs (100%) were electrically isolated on first attempt and remained isolated ≥30 minutes post-ablation. Based on the finding of visual gaps in the acute animal experiments, more overlapping lesions (30-50% overlap) were delivered in the chronic series. When remapped after 4 weeks, 8/10 PVs (80%) were still electrically isolated. On gross pathological examination, the lesions appeared contiguous and circumferential although they were more difficult to discern because they had a whiter, less intense appearance than those observed acutely (Figure 4A). On a per vein basis, the chronic mean lesion transmurality was 98.8±2.1% (limits 94.6-100%). When analyzed by histological PV sections (n=120), the mean lesion transmurality was 99.0±5.5% (limits 93.8-100%). Complete lesion transmurality was present in 96.7% of PV sections with lesion depths of up to 12.0 mm. The lesions were completely circumferential without any gaps by histology. In the two animals with recovered electrical conduction, the circular mapping catheter identified breakthrough in the anterior/inferior portion of the RSPV. One animal was ablated using low-dose energy (5.5 W/30 sec) in this region and had a 59.8% transmural lesion (total wall thickness = 10.5 mm) in this region by histology. The second animal had showed 100% transmural lesions in the sampled PV sections; presumably, the area of chronic conduction gap was between the sampled slices.
In all 10 animals, ablation lesions extended beyond the atrial wall onto the adjacent pulmonary artery (Figure 4B) and in 6 animals there was extension of thermal injury into the PV. Lung injury was seen in 3 animals and there was no phrenic injury seen. The mean change in chronic PV diameters was -2.6±19.0% (limits -33.9 to +21.7%).

Clinical Phase – Patient Demographics: The baseline patient demographics are shown in Table 2. The mean age of the cohort was 52.7±12.6 years (limits 25-66). All patients had paroxysmal AF with a mean duration of symptoms of 6.7±7.1 years, and 77.8% (21/27 patients) failed ≥1 class I or III antiarrhythmic drug. Nine patients (33.3%) were taking warfarin, 1 (3.7%) aspirin, and 6 (22.2%) low molecular weight heparin just prior to the procedure.

Clinical Phase – Visually-Guided Ablation: There were a total of 101 PVs in 27 patients – all PVs were targeted for ablation. The variable diameter and compliant nature of the balloon provided adequate contact for visualization (Figure 5) and made it amenable for use with diverse PV anatomies (Supplemental Table 1, Figures 6 & Supplemental Figure 1). With visual guidance, 84.2% (85/101) PVs were isolated with the initial visually-guided circumferential placement of contiguous point-by-point lesions. By using the circular mapping catheter to identify the point of electrical breakthrough, the remaining PVs were isolated; thus, 100% of PVs were ultimately isolated. The average number of attempts to isolate each vein was 1.3. All PVs remained isolated after a minimum of 30 minutes post-ablation. The mean fluoroscopy time per patient was 17.3±6.3 minutes, mean ablation time was 110.9±29.6 minutes, and total laser energy delivery time was 65.9±14.9 minutes.

Nine patients had esophageal temperature rises >38.5°C prompting cessation of energy delivery. The temperature rises occurred posterior to the: LIPV in 4 patients, LCV in 3, at the junction of the LSPV/LIPV in 1, and LSPV and LIPV in 1. There were no significant
temperature rises >38.5°C with ablation near the right sided PVs seen. There were no instances of loss of phrenic nerve capture during ablation of the right sided veins. No major adverse events were seen including cardiac tamponade, strokes or transient ischemic attacks, or bleeding.

**Clinical Phase – PV Remapping and Follow-Up.** Of the 27 patients, 23 were at least 3 months post-ablation. Of these 23, 18 agreed to undergo PV remapping at a mean of 11.1±0.9 weeks post-ablation. In these patients, persistent electrical isolation was present in 61/68 PVs (89.7%). *In toto,* resumption of electrical conductivity was observed in 6 patients and 7 veins – 5 patients had one reconnection each, while the remaining patient had two PV reconnections (*Supplemental Table 2*). All PVs were completely isolated in 12/18 (66.7%) patients. Each of the reconnected PVs had a single area of focal reconnection. An analysis of the location of these gaps is shown in *Supplemental Figure 2.* The distribution of reconnections observed on a per vein basis was: 2 in the LSPV, 2 in the RSPV, and 3 in the RIPV. There were no reconnections involving the LIPV, left or right common PVs. On a per vein basis, the success of chronic PV isolation was 86.7% (13/15) for the LSPV, 100% (15/15) for the LIPV, 88.2% (15/17) for the RSPV, and 82.4% (14/17) for the RIPV. There was 100% chronic PV isolation in the 3 left common and 1 right common PVs.

At 3 months, 4/23 patients had recurrent AF symptoms with documentation of the episodes in 3. All of the patients with recurrence were remapped and 2 of 4 had PV reconnections (*Supplemental Table 2*). The remaining 2 patient had documented recurrence of AF, however, all PVs were electrically isolated suggesting a non-PV trigger for the AF. These 2 were the only patients still on a Class I or III antiarrhythmic drug. There was no significant PV stenosis >30% as assessed by CT scans at 3 months. There was also no evidence of other
complications: including phrenic damage, atrial esophageal fistula, gastric dysmotility, and thromboembolism/stroke.

**DISCUSSION**

In patients with paroxysmal AF, the goal of catheter based therapy is to achieve permanent PV electrical isolation.\(^1\)\(^-\)\(^\text{11}\) Despite, a high rate of acute isolation, the incidence of recurrent AF related to PV reconnections is substantial.\(^1\)\(^8\)\(^-\)\(^\text{20}\) In the present study, we have shown that with visual-guidance, 100% of targeted PVs could be isolated using the variable diameter, compliant balloon with the capability of real-time endoscopic visualization during point-by-point ablation using laser energy. Furthermore, with adequate lesion overlap, a high degree of lesion circumferentiality and transmurality could be achieved. In the chronic preclinical experiments, lesions were 100% circumferential and 99% transmural in the sampled PV histological sections. This likely translated to the high rate of chronic PV isolation seen at remapping (80% in the preclinical experiments, 90% in patients). These favorable results were achieved safely without any major adverse events.

**Feasibility of PV Isolation.** In patients with paroxysmal AF, visually-guided PV isolation using a balloon ablation catheter utilizing laser energy delivery was previously shown to be possible.\(^1\)\(^7\) Although clinically promising, acute PV isolation was feasible in only 91% of PVs and there was a high rate of clinical recurrence, with only 60% of patients remaining free of AF without antiarrhythmic drugs at 12 months. These results could be explained in-part by the suboptimal area of balloon/tissue contact and a large 90°-120° ablative arc which often necessitated low energy delivery due to overlapping blood and concern for thrombus formation. In the present study, a compliant balloon with a variable diameter and a point-by-point ablative capability was used. These changes translated in the ability to isolate 100% of targeted PVs acutely in both the preclinical and clinical experiments.

With visual guidance alone, 97% of PVs in pigs and 84% of PVs in humans were isolated after placement of the *initial* encircling lesion set. In pigs, acute lesions created with laser
energy were more readily identifiable with endoscopic visualization, than in humans. The acute lesions in humans appeared paler and less intense than in pigs, and were frequency difficult to discern. Additionally, the area of balloon/tissue contact was also better in pigs. These factors likely account for the observed difference.

**Lesion Characteristics.** Although all PVs were isolated, visual gaps in the ablation line were observed in 35% of PVs in the acute preclinical series, highlighting the fact that isolation can often be achieved in the absence of a completely circumferential lesion set. Whether these PVs would have been chronically reconnected, or whether there might have been lesion progression is unanswered in these experiments. Based on these observations, in the subsequent chronic preclinical and clinical experiments, there was an attempt to achieve a 40-50% lesion overlap. Thus in the chronic pigs, no gaps were identified either visually or by histology. Complete lesion transmurality was seen in 65% of sampled PV sections in the acute pigs, and 97% of PV sections in the chronic pigs. While more lesion overlap may partially account for this difference, it is more likely that the full extent of injury is more readily appreciated following lesion maturation. The chronic pig experiments highlight that it is possible to achieve complete lesion circumferentiality and tranmurality using the visually-guided BAC.

**Efficacy & Safety.** At ~3 months, 90% of PVs remained electrically isolated and 83% of patients were free of AF. All PVs were isolated in 67% of remapped patients. These favorable results are likely due to improved balloon characteristics as previously described. These findings also compare favorably to the other available balloon ablation technologies, particularly the cryoballoon.12,13 Unlike with the visually-guided BAC, often more than one cryoballoon was used in conjunction with another catheter for “spot ablation”, to achieve isolation of all the PVs. The most common reported adverse event with the cryoballoon is reversible right phrenic nerve palsy. In the present study, one balloon was often enough to isolate all PVs and there were no major adverse events, including phrenic nerve injury.

**Limitations.** In animals, the ablation lesions are more readily visible and balloon/tissue contact is better than in humans. Therefore, with visual-guidance alone, a high proportion of
veins were isolated. While a similar trend was seen in humans, notable differences included
difficulty in visually discerning the lesion; thus overlap was often based more on overlap of each
laser spot with the subsequent laser spot. In patients, although the endpoint was persistent PV
isolation at ~3 month remapping, the procedures were done in a single center with 27 patients.
Therefore, more experience with this particular balloon ablation catheter in multiple centers is
needed to more accurately determine the long-term efficacy and safety. Also, the 3 month
timepoint was chosen as a reasonably late after the initial procedure; however, we cannot rule
out the possibility that more reconnections might be seen at later timepoints. Finally, while only
18, and not all, patients presented for the remapping study, it should be noted that any potential
bias is more likely to be against the device. That is, it is more likely that symptomatic patients
would show up for the second procedure; thereby artificially decreasing the true chronic isolation
rate on an intention-to-treat basis.

CONCLUSIONS

Using a compliant, variable diameter, visually-guided laser balloon with point-by-point
ablative capability, acute PV isolation can be safely achieved in all PVs. The properties of the
balloon make it amenable to address diverse PV sizes and anatomies. With visual-guidance and
placement of overlapping and contiguous lesions, circumferential and transmural lesions can be
reproducibly achieved which translates to persistent electrical isolation in ~90% of PVs.

FUNDING SOURCES

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DISCLOSURES

Vivek Y. Reddy, Petr Neuzil, and Shephal K. Doshi: Research grant support from CardioFocus, Inc.
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Table 1. Histological Lesion Characteristics in the Pre-Clinical Acute and Chronic Porcine Experiments.

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Chronic</th>
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<tr>
<td><strong>Pulmonary Veins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td># of PVs</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>Mean Lesion Depth, mm</td>
<td>2.4±0.8</td>
<td>5.0±0.9</td>
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<tr>
<td>Mean Atrial Wall Thickness, mm</td>
<td>3.0±1.0</td>
<td>5.1±0.9</td>
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<tr>
<td>Mean Lesion Transmurality, %</td>
<td>80.8±16.2</td>
<td>98.8±2.1</td>
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<tr>
<td><strong>Histological Sections</strong></td>
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<td># of Sections</td>
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<td>120</td>
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<tr>
<td>Mean Lesion Depth, mm</td>
<td>2.4±2.0</td>
<td>5.0±2.6</td>
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<tr>
<td>Mean Atrial Wall Thickness, mm</td>
<td>3.1±2.5</td>
<td>5.1±2.7</td>
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<tr>
<td>Mean Lesion Transmurality, %</td>
<td>84.6±27.8</td>
<td>99.0±5.5</td>
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Values are mean±standard deviation
Table 2. Clinical Phase – Patient Demographics.

<table>
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<th>Patient Data (N = 27)</th>
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<tbody>
<tr>
<td>Age, mean ± SD (limits)</td>
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<tr>
<td>Gender, M/F</td>
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<td>Duration of AF, mean ± SD yrs (limits)</td>
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<tr>
<td>Coronary Artery Disease, n (%)</td>
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<td>Hypertension, n (%)</td>
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<td>Congestive Heart Failure, n (%)</td>
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<td>Stroke, n (%)</td>
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<tr>
<td>Structural Heart Disease, n (%)</td>
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<tr>
<td>Ejection Fraction, mean ± SD (limits)</td>
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<td>LA Diameter, mean ± SD (limits)</td>
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<td>History of Atrial Flutter, n (%)</td>
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Antiarrhythmic Medications

<table>
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<th>Class</th>
<th>n (%)</th>
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<tbody>
<tr>
<td>Class I</td>
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<tr>
<td>Class II</td>
<td>14 (51.9%)</td>
</tr>
<tr>
<td>Class III</td>
<td>6 (22.2%)</td>
</tr>
<tr>
<td>Class IV</td>
<td>4 (14.9%)</td>
</tr>
</tbody>
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* LA diameter (N=20, ejection fraction (N=22). One patient had a LA diameter of 5.6 cm and represented a protocol deviation.
FIGURE LEGENDS

Figure 1. *The Visually-Guided Laser Balloon Ablation Catheter.* A schematic representation of the catheter is shown in (A). Within the central shaft are the 2F endoscope, lesion generator, and cooling conduits for circulating D$_2$O. The radiopaque “L” marker is located 180° opposite to the partially obscured view location seen on endoscopic visualization. The balloon catheter is shown in (B). The catheter also consists of a variable diameter and compliant balloon, and an atraumatic and flexible tip. The adjustable aiming point is also shown in a view from the tip of the catheter (C). This aiming point can be manipulated in a circumferential and longitudinal manner to control the site of laser energy delivery.

Figure 2. *Positioning of the Balloon Ablation Catheter and Endoscopic Views.* (A) The deflectable sheath and circular mapping catheter is situated at the ostium of the LSPV of a pig. The anatomy of the PV is identified with injection of dye through the sheath. (B) The balloon ablation catheter is shown situated at the ostium of the LSPV and conforms well to the shape of the PV ostium and antrum (arrow). Endoscopic views from a different animal with the balloon in the LSPV are shown in (C) and (D). The area of good balloon contact around the vein is pale and the area with blood is red. The partially obscured view due to the central shaft is also shown (white, dashed lines). The aiming point is manipulated around the ostium of the PV and determines site of laser energy delivery. The ablation lesions are also visualized.

Figure 3. *Gross Examination of the Pulmonary Veins Following Laser Ablation Using the Balloon Ablation Catheter.* The explanted left atrium of a pig following laser balloon ablation of the RSPV and LSPV is shown in (A). The left atrium is inverted to display the endocardial surface. The ablation lesions are seen around the PVs and appear to be contiguous and circumferential. However, on closer examination a visual gap in the ablation line was identified (B) and (C). While this was not fully appreciated during the procedure, careful retrospective
review of the endoscopic films identified the gap which occurred due to insufficient lesion overlap in the area. Interestingly, despite the visible gap, the PV was electrically isolated.

**Figure 4. Gross and Histological Assessment of Chronic Lesions.** (A) Circumferential and contiguous lesions around the pulmonary vein (PV) of a pig are shown 4 weeks post-ablation. The lesions are paler and less intense than those seen acutely. (B) A histological section (Masson’s trichrome stain) showing a transmural lesion adjacent to the PV ostium is shown (arrow). The lesion extends into the adjacent lung and pulmonary artery.

**Figure 5. Balloon Contact and Visualization.** A 3D CTA reconstruction of the left atrium of a patient who underwent ablation is shown in the right anterior oblique (A) and posteroanterior (B) projections. The RIPV of the patient has multiple proximal branches (1-4). The compliant balloon catheter was placed in the RIPV and conformed well to the size and shape of the PV ostium (C). An endoscopic view through the balloon catheter showed not only good contact with the area around the PV ostium, but was also able to delineate the numerous branches of the RIPV (D).

**Figure 6. A Single Balloon Catheter Conforming to Multiple PVS.** (A) The baseline 3D CTA reconstruction of the left atrium of a patient who underwent ablation is shown in the posteroanterior projection is shown. This patient had an LSPV (yellow dashed line), LIPV, and a single RCV (white dashed line). The variable radius and compliant nature of the balloon was able to conform to the different size and shapes of the LSPV (B) and RCV (C) allowing for successful pulmonary vein isolation. (D) The post-ablation electroanatomical map in the posteroanterior view of the left atrium of the same patient is shown. Superimposed on the 3D CTA is a bipolar voltage map following electrical isolation of all veins. The color range of the voltage map spans from 0.1mV (gray) to 1.0mV (purple) and delineates the level of electrical isolation.
A B C

Balloon
Adjustable
Aiming Point
Flexible
Tip

A

Balloon
Flexible
Tip
Adjustable
Aiming Point

C

Adjustable
Aiming Point
Ablation Lesions
Visual Balloon-Guided Point-By-Point Ablation: Reliable, Reproducible, and Persistent Pulmonary Vein Isolation
Srinivas R. Dukkipati, Petr Neuzil, Jan Skoda, Jan Petru, Andre d'Avila, Shephal K. Doshi and Vivek Y. Reddy

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SUPPLEMENTAL MATERIAL
**Supplemental Table 1.** Number and Type of PVs Targeted for Ablation

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**Supplemental Table 2.** Chronic PV Isolation in Patients with Remapping Procedures.

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Supplemental Figure 2
SUPPLEMENTAL FIGURE & VIDEO LEGENDS

Supplemental Figure 1. 3D CTA Reconstructions of the Left Atria Illustrating the Different PV Anatomies that were Targeted. These posteroanterior views of the left atrium show typical PV variants that were successfully targeted with the balloon ablation catheter. There were patients with separate ostia for all 4 PVs (upper left), a right common vein (upper right), a left common vein (bottom left), and a small left middle vein (arrow, bottom right).

Supplemental Figure 2. An Illustration Highlighting Areas of Chronic PV Reconnection. An anteroposterior illustration of the left atrium and pulmonary veins showing the areas of chronic PV reconnections that were seen in 6 of 18 patients during the remapping procedures. There were no reconnections involving the right or left common veins, or the LIPV.

Movie 1. Endoscopic Visualization of PV Branches. The endoscopic view of the branches of the right inferior PV described in Figure 5 are seen.

Movie 2. Endoscopic Visualization During Point-by-Point Ablation. The balloon catheter is at the ostium of the right superior PV; shown are the fluoroscopic image (top left), an intracardiac ultrasound image (bottom left), and the endoscopic view (right). The laser ablation lesions are shown being created (from ~1 o’clock to ~5 o’clock); in the interests of time, the video is shown at accelerated speed.