

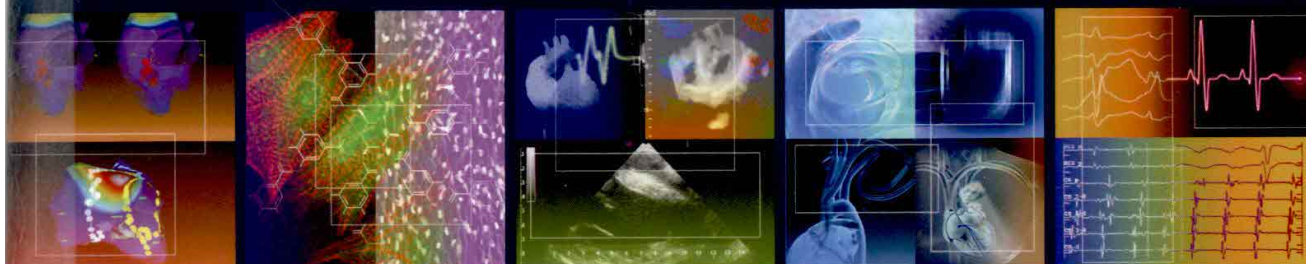
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INTERVENTIONAL CARDIAC ELECTROPHYSIOLOGY

An International Journal of Cardiac Arrhythmias and Rhythm Management



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Pulmonary vein isolation using a compliant endoscopic laser balloon ablation system in a swine model

Edward P. Gerstenfeld · John Michele

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Abstract

Introduction The incidence of pulmonary vein reconnection and recurrent atrial fibrillation after a single catheter ablation procedure is unacceptably high. We studied the ability of a novel endoscopic laser balloon ablation system (EAS) to achieve acute and chronic pulmonary vein (PV) isolation in a swine model.

Methods Eight swine underwent EAS ablation and two underwent standard radiofrequency ablation for comparison. In the EAS arm, laser energy was delivered under visual guidance around the PV antrum in overlapping 30-degree arcs. In the standard ablation arm, radiofrequency energy was delivered via a 4-mm-tip catheter. PV isolation was confirmed acutely after 30 min, and reassessed after 4–6 weeks. Animals were then sacrificed for histopathologic analysis of the PVs.

Results For the EAS animals, 44 ± 10 overlapping lesions were required to achieve acute RSPV isolation. Chronic PV isolation was documented with the circular mapping catheter a mean of 28 ± 9 days after ablation in 7/8 animals (83%). In the standard ablation arm, 30 ± 3 RF lesions were delivered to achieve acute PV isolation. There was evidence of PV reconnection in both animals during the chronic study. Histologically, completely transmural circumferential

lesions were found in 7/8 EAS animals, with 99% circumferentiality in the remaining animal. Both control RF animals had evidence of gaps, with isolation of 90% and 75% of the targeted PV segments, respectively.

Conclusion Visually guided laser ablation using light energy via a compliant balloon catheter is feasible and achieved chronic isolation in 83% of targeted PVs.

Keywords Pulmonary vein · Atrial fibrillation · Ablation · Laser · Swine

1 Introduction

Pulmonary vein (PV) isolation has become an accepted treatment for atrial fibrillation (AF). The standard ablation approach is to use a radiofrequency ablation catheter and widely encircle the PVs with radiofrequency energy lesions in a connect-the-dots approach, using electrical entrance block into the PVs as the endpoint. Yet the Achilles' heel of AF ablation continues to be recurrent AF due to reconnection of the PVs after ablation [1–4]. The mechanism of PV reconnection is unknown but likely occurs because of gaps between lesions and incomplete transmurality due to catheter sliding during energy delivery. Various modalities have been suggested to detect incomplete PV isolation during the ablation procedure, including a waiting period after PV isolation [5], use of isoproterenol [6], or use of adenosine [7]. However, the problem of chronic PV reconnection continues to exist.

Because of this limitation of focal radiofrequency energy, alternative ablation technologies need to be considered. One such technology is the endoscopic laser balloon ablation system (EAS). The EAS has several attractive advantages compared to standard catheter ablation. First,

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the inflated balloon maintains stable contact with the PV, allowing the light energy to create a consistent lesion depth because there is no catheter sliding during respiration and the cardiac cycle. Second, the EAS contains an endoscopic fiber that allows direct visualization of the tissue being ablated. Visual recognition of lesion formation can lead to feedback to prevent gaps and minimize ablation related complications. Third, because lesions are delivered under direct visualization, no fluoroscopy or electroanatomic mapping systems are required during ablation. This preclinical study tested the ability of the EAS to achieve acute and chronic PV isolation in a swine model. We also monitored for complications and performed histopathologic analysis.

2 Methods

Eight swine underwent EAS ablation and two swine underwent standard radiofrequency ablation for comparison. Because the anatomy of the right superior pulmonary vein (RSPV) in swine is closest to humans, we only assessed isolation of the RSPV. All procedures were performed in compliance with the American Heart Association guidelines for animal research protocol and were approved by the Institutional Animal Care and Use Committee (IACUC) of the University of Pennsylvania.

General anesthesia was induced with ketamine 10 mg/kg IV and maintained with inhaled isoflurane 2–4% administered throughout the procedure. Animals were ventilated with 100% oxygen and a warming blanket was used to maintain body temperature $>37^{\circ}\text{C}$. Venous access was obtained by femoral arterial and venous cutdowns; hemostatic sheaths were placed to allow for catheter insertion and monitoring of arterial pressure. An esophageal temper-

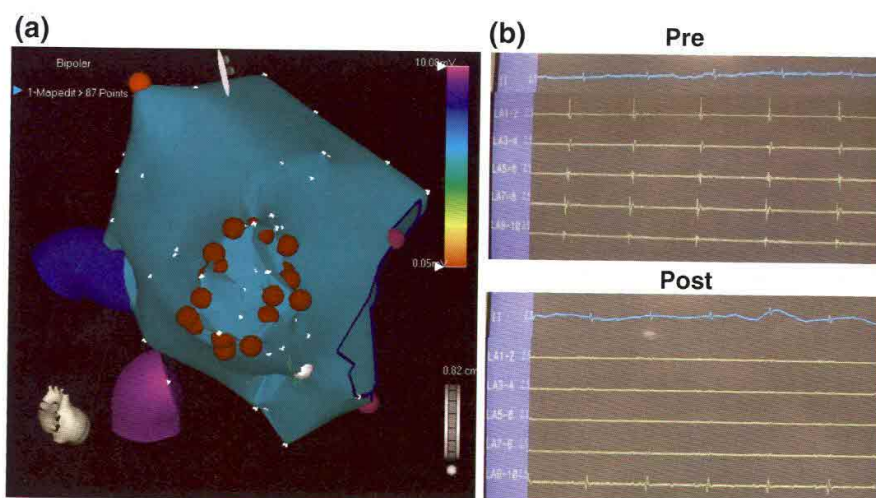
ature probe was inserted for monitoring temperature during ablation—the probe was moved under fluoroscopy to be nearest the PV being ablated. A heparin bolus was administered prior to transseptal puncture, and ACT was monitored (istat) every 30 min with additional boluses given to maintain the $\text{ACT} > 300$ s.

A phased-array diagnostic intracardiac ultrasound catheter (ICE, AcuNav, Siemens Medical, Mountain View, CA, USA) was positioned in the right atrium to guide mapping and transseptal puncture; the left atrial (LA) size was measured from the mid septum to the posterior LA wall at the level of the mitral annulus. The RSPV diameter was measured at the junction of the RSPV with the LA septum and posterior wall. One transseptal puncture was performed using a preface sheath. The sheath was advanced to the RSPV and a baseline venogram was performed. A 15-mm 10-pole circular mapping catheter (Lasso, Biosense Webster, Diamond Bar, CA, USA) was advanced to the RSPV and baseline PV potentials were recorded.

In the standard ablation arm, a 4-mm-tip ablation catheter (Navistar, Biosense Webster) was exchanged for the mapping catheter and used together with an electroanatomic mapping system to guide antral circumferential ablation around the RSPV in a connect-the-dots fashion (Fig. 1). Radiofrequency energy was delivered in the temperature controlled mode, with a maximum temperature of 50 degrees, power of 60 W, and lesion duration of 50 s. After circumferential PV ablation, the ablator was switched for the circular mapping catheter and the RSPV was interrogated. Further RF lesions were delivered until PV entry block was achieved and persisted for 30 min.

The EAS (CardioFocus, Marlborough, MA, USA) consists of a compliant balloon filled with deuterium oxide to allow transmission of the 980-nm laser energy. The compliant balloon is mounted on a 12-F catheter shaft and

Fig. 1 (a) Electroanatomic map depicting the location of radiofrequency lesions placed in a circumferential manner around the RSPV in a control animal. (b) Recordings from a circular mapping catheter before (top) and after (bottom) PV isolation using the standard catheter. The electrograms on poles L9–10 are far-field ventricular signals



is delivered to the LA via a custom 15-F steerable sheath. The balloon can be varied in diameter by varying the inflation pressure (Fig. 2). The central lumen of the catheter contains a fiberoptic endoscope and lesion generator and has been described previously [8]. The reusable 500- μ m diameter endoscope has a 110° field of view and allows direct visualization of the intravascular cardiac anatomy when the balloon is inflated. The lesion generator (arc) consists of an optical fiber located within the central shaft, which projects an arc of light onto the tissue in contact with the balloon. This arc can be advanced/retracted and rotated, positioning the energy beam from the distal tip of the balloon to the proximal point of maximal balloon diameter. The aiming beam of green light determines the location where the laser energy (980 nm) will be delivered. The lesion generator delivers a 30-degree arc of laser energy which can be varied from 5.5 to 16 W for 20–30 s. Based on prior work, the lesion duration was 30 s for 5.5 and 7 W lesions and 20 s for lesions > 7 W. Power was titrated based on balloon contact, distance of the aiming beam from the center of the shaft, and lesion visualization. Power was always limited to 5.5 W when any portion of the aiming beam was in contact with blood, based on prior work demonstrating lack of thrombus formation at this dose. Because the size of the beam (30 degrees, which is smaller closer to the center of the balloon) is smaller at the center shaft of the laser balloon, a lower power will result in a more intense lesion. Further out towards the balloon equator, the energy is dispersed over a wider region and higher power may be needed. The power was titrated down if the beam was located near the center of the balloon shaft

or a brisk visual lesion developed, and upwards if the laser was positioned further towards the equator of the balloon and a clear visual lesion did not develop.

In the EAS arm, the EAS was advanced to the RSPV and inflated. The balloon was positioned in order to achieve maximal 360 degree proximal endocardial contact without incorporating pockets of stagnant blood. Laser energy was then delivered in a circular fashion of overlapping 30-degree arcs guided by direct visualization of lesion formation and online tracking of lesion delivery location (Fig. 3, Video 1 10 $\times$ speed). Energy dose ranged from 5.5 W when the laser arc was in contact with moving blood, to 8–10 W more distally toward the PV ostium, to 12–16 W at the proximal PV. Once lesions were delivered around the PV circumference, additional lesions were delivered to fill in any visualized gaps. The EAS was then exchanged for the circular mapping catheter. If the PV remained connected, the EAS was moved back into the PV and additional laser energy deliveries were made until PV disconnection was confirmed. This may have involved filling in gaps if the same catheter orientation could be obtained, or another circumferential PV isolation if the catheter was not coaxial with the prior lesions. The RSPV was reinterrogated with the circular mapping catheter after a 30-min waiting period to ensure persistent isolation (Fig. 4).

After ablation, animals were recovered and survived for 4–6 weeks. At the time of the repeat study, animals were intubated, placed under general anesthesia, and repeat femoral access and a single trans-septal puncture was performed. The circular mapping catheter was advanced to the RSPV to determine if PV conduction was present (Fig. 4). Pacing was performed from the right atrium to

Fig. 2 (a) Schematic of the endoscopic laser balloon catheter. (b) Photographs of the compliant balloon at 3 PSI (left) and 6 PSI (right) showing the change in size of the balloon with increasing pressure

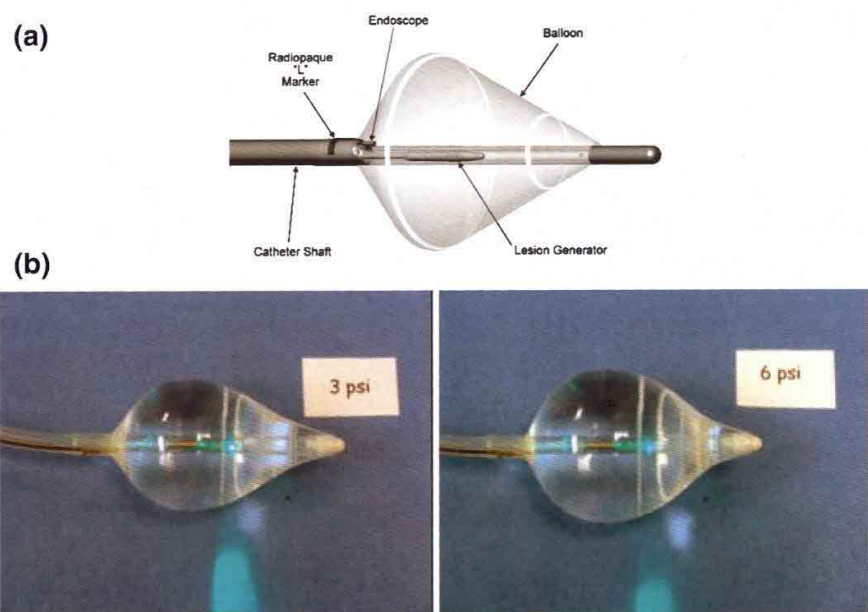
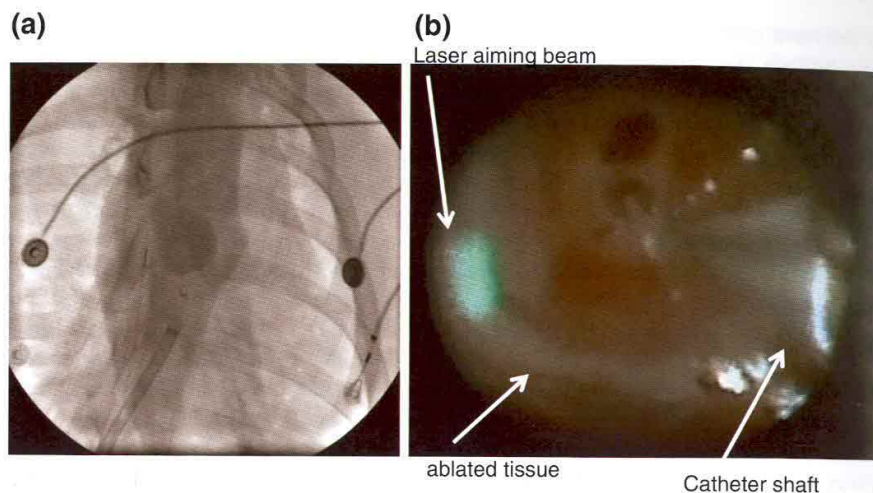


Fig. 3 *Left panel:* Fluoroscopy view in the anteroposterior projection of the laser balloon positioned inside the RSPV. *Right panel:* Still image of the endoscopic view through the laser balloon showing the 30-degree laser arc aiming light (green) and visualization of ablated and nonablated antral PV tissue. See supplemental video



distinguish PV potentials from far-field atrial potentials. Animals were then euthanized. The heart was excised and subjected to gross visual inspection and histopathology. For histology evaluation, the entire specimen is circumferentially and longitudinally (parallel to the blood flow) sectioned. The blocks were submitted for paraffin processing. The paraffin blocks were cut on a rotary microtome at 4–5 μm , mounted on charged slides and stained with hematoxylin–eosin (H&E), Movat pentachrome and Masson's trichrome stains. The slides were examined by light

microscopy (Olympia BX41) and evaluated for thermal injury, inflammation, hemorrhage, thrombus, and necrosis. A semi-quantitative score from 0 to 4 was used to grade the histological changes observed: 0 = absent; 1 = minimal, 2 = mild, 3 = moderate, 4 = marked/severe. Histology slides were measured using digital planimetry with an NIST calibrated microscope system (IP Lab software, Rockville, MD, USA). The atrial wall thickness was measured in the region of injury (atrial wall thickness) and the injury thickness was measured at the deepest extent of injury (either within the atrial tissue, depth

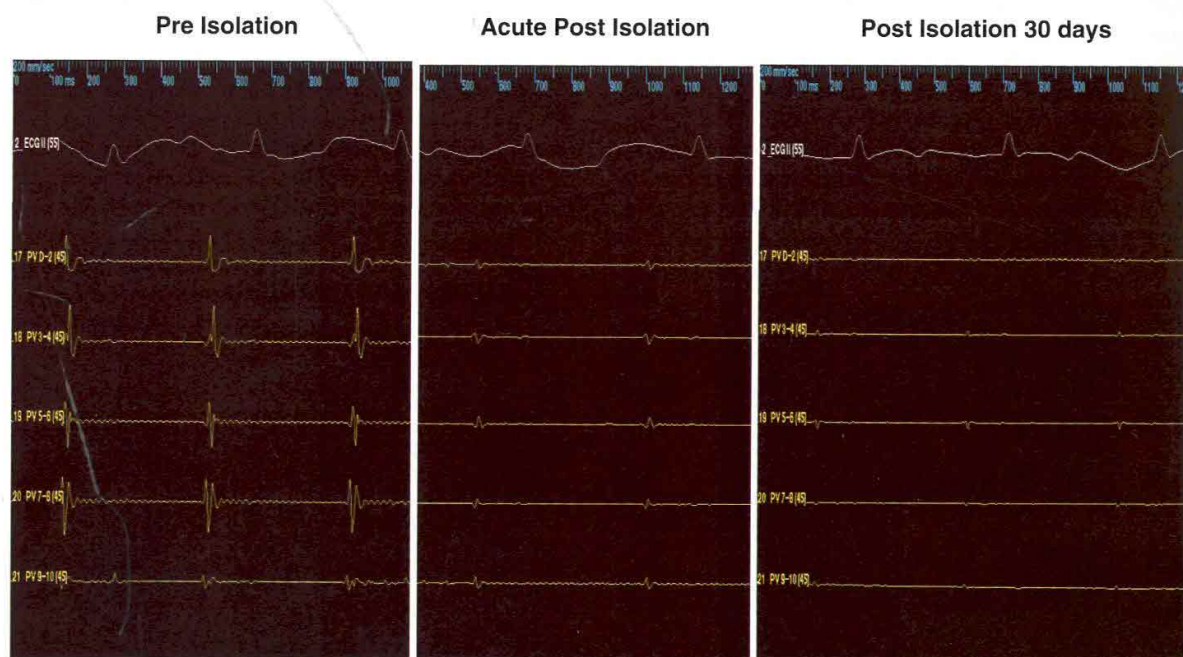


Fig. 4 Recordings from a circular mapping catheter at the RSPV ostium before (*left*), 30 min after (*middle panel*), and 30 days after (*right panel*) PV isolation using the laser balloon. Isolation persisted at

30 days by demonstration of electrical entry block and histopathologic demonstration of continuous circumferential lesions. PV pulmonary vein

of injury within atrial wall, or beyond the atrial tissue, maximum depth of injury). The percent of wall thickness injury was calculated as: depth of injury within the atrial wall/atrial wall thickness $\times$ 100.

3 Results

3.1 Acute PV Isolation

Eight animals underwent PV isolation with the EAS system and two using standard radiofrequency energy. Among the 10 animals, the baseline weight was 55.8 ± 6.5 kg and the baseline LA size was 39 ± 7 mm. The RSPV ostial diameter measured on ICE was 16 ± 5 mm.

For the eight EAS animals, 44 ± 10 overlapping lesions were required to achieve RSPV isolation. RSPV isolation was achieved with the first circumferential lesion attempt in three animals; additional lesions were required to achieve isolation in the remaining five animals. Overall, low power ($5.5 \text{ W} \times 30 \text{ s}$) was delivered in 15% of the lesions because of proximity to moving blood and the remaining 85% of lesions were delivered with higher power ($8\text{--}16 \text{ W}$, 20 s). The time from trans-septal access to achieve PV isolation averaged 55 ± 15 min, and decreased significantly throughout the experience, from 75 min for the first animal to 30 min for the last animal. There was no significant increase in PV flow velocity measured with ICE after ablation (pre vs post; 0.56 ± 0.15 vs 0.58 ± 0.13 m/s; $p=0.44$). PV isolation was achieved in 8/8 animals and persisted for 30 min after isolation in animals without requiring further lesions. In one animal, delivery of a 16-W lesion led to tissue darkening and power was immediately turned off; however, loss of balloon inflation pressure resulted. When the balloon was removed, a pinhole was noted in the balloon, requiring replacement with a new catheter and balloon. There were no obvious acute or chronic adverse sequelae noted in this animal. There was no evidence of PV stenosis in any animal. There were no esophageal temperature rises during ablation in any animal.

In the 4-mm standard ablation control arm, 30 ± 3 RF lesions were delivered for 40 s each at 60 W power in the temperature control mode with a temperature cutoff of 60 degrees Celsius. There was one audible steam pop with no adverse sequelae. Acute RSPV isolation was achieved in both animals and persisted for 30 min. There was also no significant increase in PV flow by ICE in this small group (0.57 ± 0.18 vs 0.71 ± 0.16 ; $p=0.5$).

3.2 Chronic study

EAS animals were restudied a mean of 28 ± 9 days after ablation. There was a trend toward a small decrease in PV

flow from the survival study to the chronic study (0.58 ± 0.12 vs 0.52 ± 0.18 ; $p=0.08$). Chronic PV isolation was documented with the circular mapping catheter by confirmed entry and exit block in 7/8 animals (83%). In one of these animals, there was some atrial activity noted on the circular mapping catheter that appeared far-field when pacing from the superior vena cava—subsequent gross analysis demonstrated that the RSPV in this animal was smaller than the size of the circular mapping catheter, and histology confirmed 100% transmural isolation of the PV. In one animal, a clear gap was noted at the superior-septal RSPV with conduction both into and out of the PV (Fig. 5).

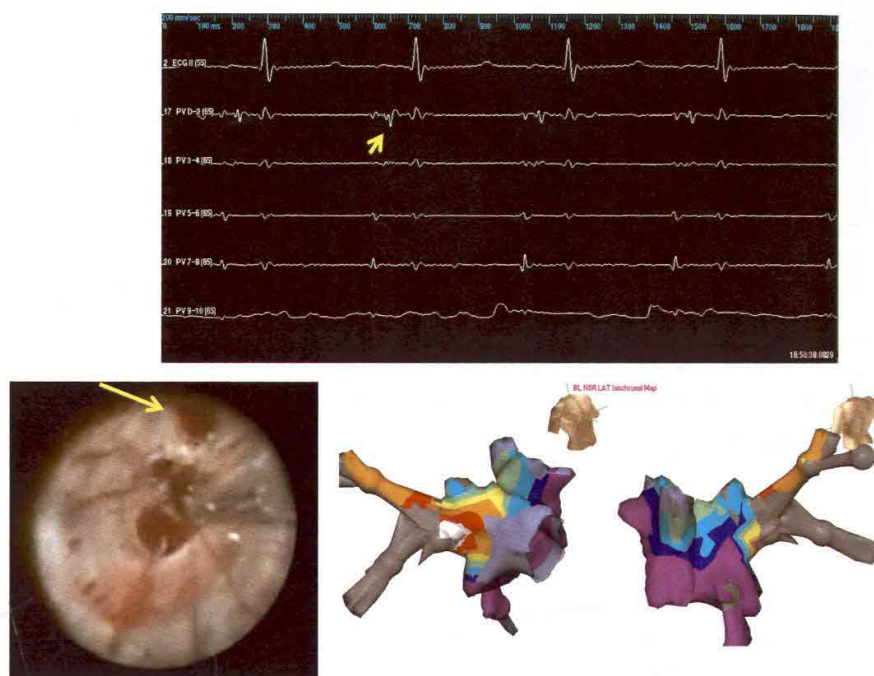
Animals in the 4-mm-tip ablation arm were studied a mean of 33 days after ablation. There was no difference in PV flow from the survival study to the terminal study (0.71 ± 0.16 vs 0.66 ± 0.17 ; $p=0.17$). Both control animals had evidence of chronic PV reconnection recorded with the circular mapping catheter.

3.2.1 Histopathology

The EAS animals (Fig. 6) showed resolving thermal injury that was circumferential and transmural, with the exception of one animal (9/10 slices showed transmural injury). In general, the thermal injury was located in a band-like distribution on the atrial side of the veno-atrial junction. The injury was identified at gross examination as a pale scar and was corroborated by histology. The histological changes induced by the ablation device are consistent with typical tissue thermal injury effects that are observed at 30 days, including organizing granulation tissue with persistent chronic inflammation, fibrosis, calcification, residual myocyte necrosis, and focal hemorrhage. There was a mean maximum depth of 5.00 ± 1.21 mm through the atrial wall (mean atrial wall thickness of 5.01 ± 1.21 mm) and the injury focally extended past the atrial wall into the pulmonary artery and/or aorta in eight laser ablation animals (Fig. 6). A second area of injury distal to the PV ostium was also identified in the majority of the animals characterized by granulation tissue, focal necrosis, and hemorrhages and most likely represents a continuation of the primary lesion. All eight animals also showed evidence of a small area of focal transmural injury to the underlying pulmonary artery epicardial to the ablation lesions. Several animals demonstrated platelet thrombus around the foramen ovale consistent with trans-septal puncture site. There was no gross or histologic evidence of esophageal injury in any animal. There was no gross evidence of injury to the overlying lung in any animal (see Table 1).

For the two radiofrequency control ablations (Fig. 7), quantitative histologic analysis demonstrated that the lesion was circumferential but not transmural in all sections. In the first animal, 9/12 (75%) histologic slices demonstrated

Fig. 5 The *top panel* shows recordings from the circular mapping catheter in one animal 30 days after laser ablation. There is evidence of reconnection of the RSPV at poles 1–2, which corresponded to the superior aspect of the PV (*arrow*). *Bottom left panel*: endoscopic view of the left superior PV showing a small collection of blood at the superior aspect of the vein (*arrow*). This led to lower power delivery in this region and likely the lack of lesion transmural. The *lower right panel* shows an anterior (AP) and posterior (PA) view of an activation map of the RSPV demonstrating entry into the PV at the superior aspect



transmural injury and in the second animal 9/10 (90%) slices demonstrated transmural injury. Overall, the histological changes induced by the radiofrequency device were similar to those observed in the pivotal laser ablations and showed organizing granulation tissue with focally persistent

chronic inflammation, fibrosis, calcification, residual myocyte necrosis, and focal hemorrhage. There was evidence of lesion extension to the epicardial pulmonary artery in both animals. There was no gross or histologic evidence of esophageal injury in any animal.

Fig. 6 *Left panel*: gross appearance of the RSPV 30 days after ablation. Note the smooth white appearance of the lesions located at the PV antrum (*black arrows*). The transseptal puncture can also be noted inferiorly. *Right panel*: histology using Movat Pentachrome stain (1.25× power) demonstrating a transmural lesion with replacement of the normal cellular architecture with fibrotic tissue. The *lower panel* shows penetration of a transmural lesion focally to the pulmonary artery epicardial to the PV (*white arrow*)

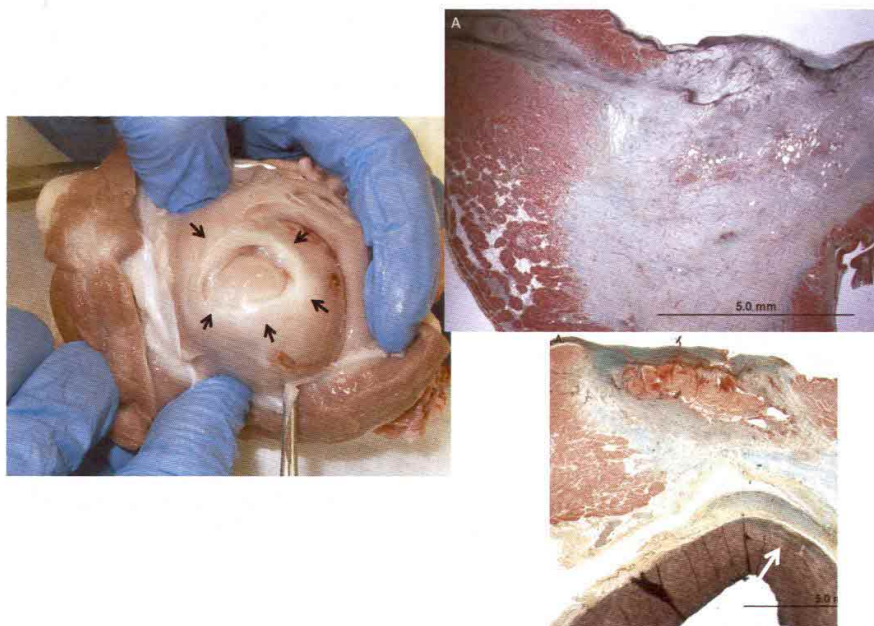


Table 1 Histopathologic analysis in the eight EAS animals and two control animals

Treatment	Number of slices around PV	Number of 100% transmural slices	Percent circumferentiality	% circumferential and transmural
Chronic laser	11	11	100	100
Chronic laser	10	9	100	99.18
Chronic laser	10	10	100	100
Chronic laser	11	11	100	100
Chronic laser	12	12	100	100
Chronic laser	9	9	100	100
Chronic laser	13	13	100	100
Chronic laser	11	11	100	100
RF control	10	9	100	93.73
RF control	12	9	100	92.37

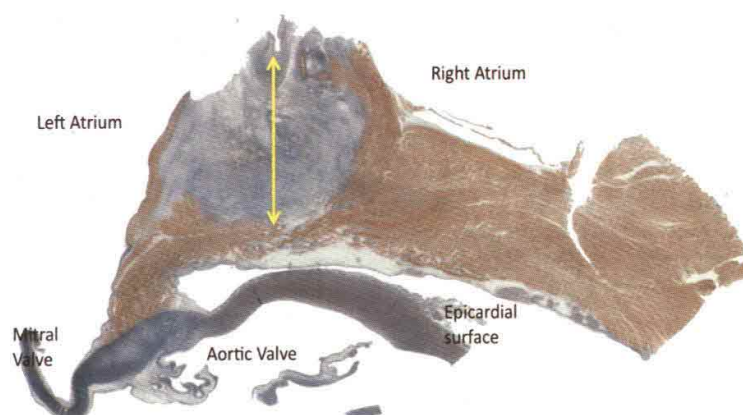
4 Discussion

Despite the hope that ablation would offer a “cure” for AF, both early and late AF recurrences after ablation remain quite common, with success rates ranging from 28–85% [9] depending on the center and patient population. Several studies have demonstrated that nearly all patients with recurrent AF have evidence of PV reconnection [1, 2]. Use of irrigated tip catheters may have improved the safety of ablation, but do not seem to have improved the success rate. In a recent multicenter clinical trial involving centers with recognized expertise in AF ablation, the 6-month freedom from AF in paroxysmal AF patients was 63%. The most likely etiology of PV reconnection is gaps in the connect-the-dot lesions patterns due to edema between lesions or lack of lesions transmural. If a reconnected PV segment was the site of an AF trigger, early AF recurrence may result. If the reconnected segment was not an AF trigger, then continued structural atrial changes due to hypertension, fibrosis, sleep apnea, or other comorbidities may lead these segments to develop AF triggers that lead to a late AF

recurrence. It is unlikely that larger or more powerful catheters will solve this problem. Excessive power and use of ablation on the posterior wall has already led to reports of LA-esophageal fistula [10], a life-threatening complication of ablation.

We found that the EAS system was able to achieve circumferential contact and acute isolation in 83% of the RSPVs in all animals studied. Although a large number of overlapping lesions were required to achieve PV isolation (mean 44), the procedure duration and number of lesions significantly decreased as more cases were performed. The major reason for the large number of lesions required for PV isolation in some animals was that if PV isolation was not achieved with the first circumferential attempt at ablation, a change in angle of the balloon after repositioning often necessitated delivery of a second set of circumferential lesions. This was also noted on histopathology when two sets of lesions at different depths were seen in some PVs. With further experience, we learned to spend additional time up front to achieve optimal balloon positioning and contact around the circumference of the

Fig. 7 Low power view of a lesion (yellow arrow) near the septum of the RSPV delivered using the standard ablation catheter. The lesion demonstrates fibrosis with organizing granulation tissue, but has a surviving layer of epicardial muscle that allowed recovery of PV conduction. The yellow arrow denotes the depth measured for assessing transmural of the lesion (Movat pentachrome stain, 1× power)



balloon, so that the initial circumferential ablation more often led to acute PV isolation. Chronically, 7/8 RSPVs showed persistent PV isolation, and this was confirmed histologically with 100% transmural and circumferential lesions in these seven animals. The lesion characteristics histologically were encouraging, showing little endocardial disruption, no adherent thrombus, and contiguous transmural lesions characterized by replacement of the atrial wall with fibrotic tissue. It is interesting that in both control RF ablation animals there was evidence of PV reconnection, with only 75% and 90% circumferential and transmural lesions, respectively. This is consistent with the high degree of PV reconnection seen with standard RF ablation.

4.1 Prior work

Reddy and colleagues [8] described the results of preclinical and clinical ablation using an earlier version of the EAS system, which used a noncompliant balloon of various diameters and 90- or 150-degree laser energy arc. In the preclinical phase, 9/10 PVs isolated remained isolated 4–7 weeks after the ablation procedure; however, PV stenosis was noted in 25% of PVs. In the human clinical phase ablation was performed in 30 patients with paroxysmal AF; the 12-month freedom from AF was 60%. Despite use of the 90-degree arc, procedures were quite long, with a total procedure time of 334 ± 112 min. PV narrowing was noted in up to 13% of cases. Experience with the prior balloon demonstrated several limitations, including: (1) the need to use multiple size balloons for each case depending on PV diameter, (2) the tendency for ablation lesions to be at or just inside the PV ostium because the noncompliant balloon needed to inflate just inside the PV, and (3) difficulty with positioning the 90 degree arc so that it was not partly in the blood pool when the PV ostium was not circular or was off-axis in relation to the balloon shaft. This led to redesigning the current version noncompliant balloon, which can sit much more proximally at the PV antrum and has an adjustable diameter depending on the inflation pressure. Although the smaller 30-degree arc seems counterintuitive, it actually facilitates ablation by allowing the user to target any area within the visualized field of view without concern about the larger arc overlying stagnant blood, and then to “stitch” together lesions in any configuration to achieve PV isolation. The antral level of PV isolation and lack of any evidence of PV stenosis in the current study represents an improvement over the prior balloon design.

Although we observed no esophageal temperature rises in any animal, there was histologic evidence of lesions extending to the epicardial pulmonary artery in all EAS and one RF animal. In our opinion, these findings are the price of achieving transmural lesions. Certainly any energy source capable of creating transmural lesions has the potential for

damage to collateral structures such as the lung and esophagus, and the EAS does not eliminate this possibility. Delivery of lower power lesions along the posterior LA wall and esophageal temperature monitoring is therefore still a requirement during clinical ablations using this system.

4.2 Limitations

Due to cost considerations, the sample size and control group were small. Only the RSPV was targeted for ablation. This is because the anatomy of RSPV is most similar to the human PVs. The left superior PV in the swine is often quite small with proximal branching and the lower PVs have an acute angulation that has made the balloon catheter placement challenging in the normal swine atrium. Prior experience has also found that creating a technology ideal for isolating the small swine PVs often does not translate well to humans with large atria and may require significant redesign to allow clinical effectiveness. Therefore, we tested the catheter in the PV that we felt would most closely replicate the human condition.

The swine model may not be ideal for testing the lack of esophageal injury, as the esophagus is located further from the posterior LA than in humans and is often insulated by fat.

5 Conclusions

The EAS represents a new paradigm in PV isolation, visually guided ablation using light energy via a balloon catheter. The compliant balloon allowed proximal circumferential contact and achieved acute PV isolation in all targeted PVs and chronic isolation in 83% targeted PVs with histologic confirmation of 100% circumferential transmural lesions in these animals. Recurrent PV conduction and incomplete isolation were noted in the control animals targeted with radiofrequency energy. Clinical trials of the EAS system in humans with AF are warranted.

References

1. Gerstenfeld, E. P., Callans, D. J., Dixit, S., Zado, E., & Marchlinski, F. E. (2003). Incidence and location of focal atrial fibrillation triggers in patients undergoing repeat pulmonary vein isolation: implications for ablation strategies. *Journal of Cardiovascular Electrophysiology*, 14, 685–690.
2. Callans, D. J., Gerstenfeld, E. P., Dixit, S., Zado, E., Vanderhoff, M., Ren, J. F., et al. (2004). Efficacy of repeat pulmonary vein isolation procedures in patients with recurrent atrial fibrillation. *Journal of Cardiovascular Electrophysiology*, 15, 1050–1055.
3. Mainigi, S. K., Sauer, W. H., Cooper, J. M., Dixit, S., Gerstenfeld, E. P., Callans, D. J., et al. (2007). Incidence and predictors of very

- late recurrence of atrial fibrillation after ablation. *Journal of Cardiovascular Electrophysiology*, 18, 69–74.
4. Lemola, K., Hall, B., Cheung, P., Good, E., Han, J., Tamirisa, K., et al. (2004). Mechanisms of recurrent atrial fibrillation after pulmonary vein isolation by segmental ostial ablation. *Heart Rhythm*, 1, 197–202.
 5. Cheema, A., Dong, J., Dalal, D., Marine, J. E., Henrikson, C. A., Spragg, D., et al. (2007). Incidence and time course of early recovery of pulmonary vein conduction after catheter ablation of atrial fibrillation. *Journal of Cardiovascular Electrophysiology*, 18, 387–391.
 6. Marchlinski, F. E., Callans, D., Dixit, S., Gerstenfeld, E. P., Rho, R., Ren, J. F., et al. (2003). Efficacy and safety of targeted focal ablation versus PV isolation assisted by magnetic electroanatomic mapping. *Journal of Cardiovascular Electrophysiology*, 14, 358–365.
 7. Arentz, T., Macle, L., Kalusche, D., Hocini, M., Jais, P., Shah, D., et al. (2004). "Dormant" pulmonary vein conduction revealed by adenosine after ostial radiofrequency catheter ablation. *Journal of Cardiovascular Electrophysiology*, 15, 1041–1047.
 8. Reddy, V. Y., Neuzil, P., Themistoclakis, S., Danik, S. B., Bonso, A., Rossillo, A., et al. (2009). Visually-guided balloon catheter ablation of atrial fibrillation: experimental feasibility and first-in-human multicenter clinical outcome. *Circulation*, 120, 12–20.
 9. Cheema, A., Vasamreddy, C. R., Dalal, D., Marine, J. E., Dong, J., Henrikson, C. A., et al. (2006). Long-term single procedure efficacy of catheter ablation of atrial fibrillation. *Journal of Interventional Cardiac Electrophysiology*, 15, 145–155.
 10. Pappone, C., Oral, H., Santinelli, V., Vicedomini, G., Lang, C. C., Manguso, F., et al. (2004). Atrio-esophageal fistula as a complication of percutaneous transcatheter ablation of atrial fibrillation. *Circulation*, 109, 2724–2726.