

# Minimally invasive pulmonary vein isolation and partial autonomic denervation for surgical treatment of atrial fibrillation

James R. Edgerton · Warren M. Jackman ·  
Michael J. Mack

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## Abstract

**Objective** It was our goal to determine the efficacy of a minimally invasive surgical approach to the treatment of atrial fibrillation that combines pulmonary vein antral isolation with targeted partial autonomic denervation.

**Methods** Eighty-three patients underwent video-assisted bilateral pulmonary vein antral electrical isolation with confirmation of block and partial autonomic denervation. Sixty-two (41 paroxysmal, 21 persistent/long-standing persistent) patients had a follow-up of 6 months or greater. Fifty-seven of these patients had a long-term rhythm monitor at 6 months (39 paroxysmal, 18 persistent/long-standing persistent).

**Results** Success was defined as no episodes of atrial fibrillation greater than 15 s duration on long-term monitoring. Treatment was successful in 32 of 39 (82.1%) patients with paroxysmal atrial fibrillation and 10 of 18 (55.6%) with persistent/long-standing persistent atrial fibrillation.

**Conclusion** Early data suggest that pulmonary vein electrical isolation combined with targeted partial autonomic denervation is a safe and efficacious approach for the treatment of paroxysmal atrial fibrillation. Techniques are being developed for the minimally invasive surgical treat-

ment of persistent and long-standing persistent atrial fibrillation from an epicardial approach.

**Keywords** Atrial fibrillation · Surgical ablation · Pulmonary vein isolation · Ganglionated plexi

## 1 Background

The relatively recent development of enabling technologies with alternative energy sources has allowed many lesions of the Cox-Maze III procedure to be performed and facilitated in a less invasive manner [1–3]. Given the multiple theories for pathophysiologic and electrophysiologic mechanisms of atrial fibrillation [4–7], it is not surprising that there continues to be considerable discussion as to what lesion set is necessary. Though most attention now focuses on the left atrium, various approaches have been developed after taking lessons from the catheter-based literature.

The pathophysiology of atrial fibrillation involves the complex interplay between triggers and a changing left atrial substrate. Joining the pulmonary veins to the left atrial body are clusters of autonomic ganglia located in fat pads overlying the junction of the pulmonary veins and the left atrium [8, 9]. These are part of a complex network of interconnecting nerves forming the intrinsic cardiac autonomic nervous system. The composition of neurons in the ganglia is sympathetic and parasympathetic afferent, efferent, and interconnecting fibers that join together in clusters. These clusters are referred to as ganglionated plexi (GPs) by Armour et al. [9]. There is a long trail of evidence implicating these GPs in the pathogenesis of atrial fibrillation [10–17].

The parasympathetic neurotransmitter is acetylcholine, and an increase in parasympathetic tone shortens the atrial effective refractory period and increases the vulnerability to

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J. R. Edgerton · M. J. Mack  
Cardiopulmonary Research Science and Technology Institute  
(CRSTI),  
Dallas, TX, USA

W. M. Jackman  
University of Oklahoma Health Sciences Center,  
Oklahoma City, OK, USA

J. R. Edgerton (✉)  
4708 Alliance Blvd., Suite 700,  
Plano, TX 75093, USA  
e-mail: edgertonjr@aol.com

atrial fibrillation. It may also increase the absolute rate of premature atrial depolarization [18–20]. The sympathetic neurotransmitter is norepinephrine. This leads to increased calcium loading and early after-depolarizations, which may lead to triggered firing [21, 22]. Together, these sympathetic and parasympathetic activities facilitate onset and maintenance of atrial fibrillation. The location of these GPs can be mapped. Vincenzi and West described the technique of subthreshold high-frequency electrical stimulation that permits selective excitation of autonomic fibers without stimulating mechanical action of cardiac cells [23]. There is clinical evidence for successful elimination of atrial fibrillation by ablating areas of the autonomic ganglia, which strongly suggests they play a critical role in the initiation and maintenance of atrial fibrillation in the human [24–29].

## 2 Patients and methods

### 2.1 Surgical technique

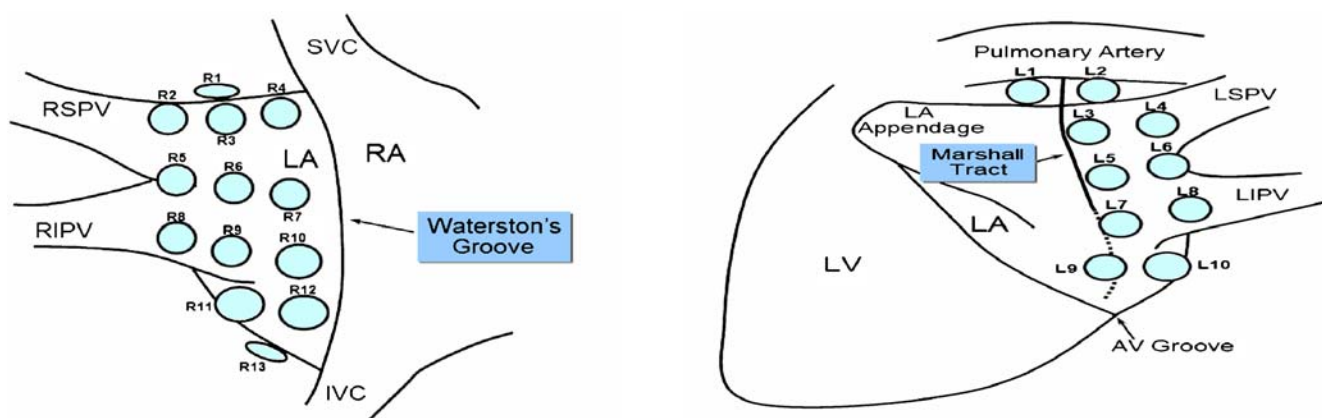
Based on the above findings, we began performing a standardized procedure for minimally invasive surgical ablation of lone atrial fibrillation, which consists of bilateral pulmonary vein antral electrical isolation and targeted autonomic denervation of the left atrium with selective left-atrial appendectomy. The feasibility of minimally invasive pulmonary vein isolation has been previously described [30]. This procedure is accomplished in two stages. With the patient in a left lateral decubitus position, the right-sided pulmonary veins are approached through a small thoracotomy in the right chest. The patient is then repositioned and redraped in the right lateral decubitus position to allow approach to the left pulmonary veins through a limited left thoracotomy. This thoracotomy is a 5.0- to 6.0-cm incision in the third or fourth intercostal space without rib spreading. It is used mainly for access to

pass instruments into the chest while visualization is accomplished by video imaging with a 5.0-mm, 30° endoscope placed in the middle to posterior axillary line in the sixth or seventh intercostal space.

On the right side, the pericardium is opened widely, with 2.0 cm anterior to the phrenic nerve. Pericardial retraction sutures are used to aid in visualization. The pulmonary veins are mapped to record the location of pulmonary vein potentials (pulmonary vein myocardial sleeve). Then, GPs are located by high-frequency stimulation [23] using a vagal response to locate them (Fig. 1). After dissecting around the pulmonary veins, a bipolar radiofrequency device is introduced and placed around the pulmonary vein antrum well up onto the left atrium, as far as possible away from the pulmonary vein bifurcation. Three to five ablation lines are placed in slightly different positions to ensure electrical isolation. Following this, mapping is repeated on the pulmonary veins and adjacent left atrium to confirm entrance block from the left atrium, indicating a transmural lesion and electrical isolation. The ablation is repeated as necessary until entrance block is demonstrated. High-frequency burst pacing is again done in areas where GPs were initially identified. If any positive responses remain, these areas are further locally ablated until the response to high-frequency stimulation is considered negative, as defined by no significant increase in the R-to-R interval during stimulation.

A 19-French silastic drain is placed through the scope site, the working port incisions are closed, the wounds are dressed, and the patient is then positioned in the right lateral decubitus position to allow approach to the left-sided pulmonary veins.

Similar exposure is obtained on the left side. The pericardium is opened posterior to the phrenic nerve, which aids in visualization of the left pulmonary veins, the ligament of Marshall, and the base of the left atrial appendage. Again, preablation mapping is done of the



**Fig. 1** Map of Pulmonary Veins and Ganglionated Plexi on the left and right sides

**Table 1** Percentage of patients off of antiarrhythmic drugs

	Paroxysmal atrial fibrillation patients <i>n</i> =41		Persistent/long-standing persistent atrial fibrillation patients <i>n</i> =21	
	ECG <i>n</i> =40	Holter/PM interrogation/event monitor <i>n</i> =39	ECG <i>n</i> =21	Holter/PM interrogation/event monitor <i>n</i> =18
Follow-up	NSR	NSR	NSR	NSR
6 Months	40 (100.0%)	32 (82.1%)	16 (76.2%)	10 (55.6%)
6 Months off AAD	34 (85.0%)	29 (74.4%)	13 (61.9%)	7 (38.9%)

AAD antiarrhythmic drugs, ECG electrocardiogram, NSR normal sinus rhythm, PM pacemaker

pulmonary veins, as well as high-frequency stimulation for localization of GPs. Electrical isolation of the left pulmonary vein antrum is accomplished again with a bipolar radiofrequency clamp after identifying and dividing the ligament of Marshall. Conduction block is again confirmed by sensing for entrance block in the pulmonary veins. High-frequency stimulation is repeated to ensure that there are no remaining GPs, as measured by the absence of a vagal response during high-frequency stimulation. The trabeculated portion of the left atrial appendage is then excised using a stapling device, the pericardium is closed, a drain is placed, and the wounds are closed and dressed. The patient is then awakened, extubated in the operating room, and transferred to the intensive care unit for observational care.

## 2.2 Patient demographics

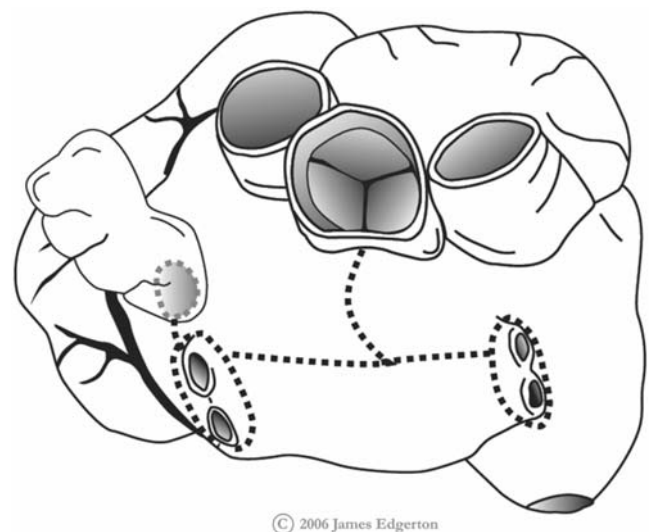
Eighty-three patients underwent minimally invasive surgical ablation of atrial fibrillation with the techniques described above. The mean age was 60 (range 38–80) years. Sixty-one were men (73.5%), and 22 were women (26.5%). In 81 patients, atrial fibrillation duration was known. Duration was greater than 12 months in 73 (90.1%), 6–12 months in five (6.2%), and less than 6 months in three (3.7%). Sixty-seven (80.7%) were on antiarrhythmics drugs at time of operation. Twenty-one (25.3%) had undergone previous catheter ablation. Mean left atrial size was 5.2 cm. Sixty-two (41 paroxysmal, 21 persistent/long-standing persistent) were more than 6 months from procedure at the time of this writing.

## 2.3 Patient follow-up

Rhythm was monitored by office electrocardiogram (ECG) at 1, 3, and 6 months. At the 6-month follow-up, 61 of 62 (98.4%) patients had an ECG. Patients were asked their perception of what rhythm they were in, and this was compared with ECG findings for accuracy of patient perception of rhythm. At 6 months the patient's rhythm was assessed by a 14- to 21-day autotriggered event monitor. When patient circumstances dictated, a 24-h Holter monitor was substituted for the 21-day event monitor.

Fifty-seven of the 62 patients had long-term monitoring at 6 months. In nine patients (14.5%), this was done with pacemaker interrogation, in 24 (42.1%) with 14- to 21-day event monitors, and in 24 (42.1%) with the 24-h Holter. Thirty-nine of these 57 patients (68.4%) were paroxysmal (six pacer interrogation, 14 event monitor, 19 Holter). Eighteen of the 57 patients (31.6%) with long-term monitors were persistent/permanent (three pacer interrogation, ten event monitor, five Holter). When atrial fibrillation was detected by an irregular rhythm, a single 15 seconds rhythm strip was recorded. Another rhythm strip was not recorded during that episode. Accordingly, we were able to count the number of episodes of atrial fibrillation, but it was not possible to determine episode duration longer than 15 seconds or the true burden of atrial fibrillation.

Although patients did not keep a date and time diary, at the 6-month evaluation, they were asked if they had any symptoms of atrial fibrillation during the preceding 3 months. For those who had symptoms, the long-term recordings were examined to determine whether there were any episodes of atrial fibrillation present that could possibly have caused the patient's symptoms.



**Fig. 2** Extended Lesion Set diagram showing isolation of the pulmonary veins with connecting lesion across the dome of the atrium, extending down to the mitral valve annulus

### 3 Results

#### 3.1 Complications

Three patients suffered complications. There was one patient with a clotted hemothorax, which required thoracoscopic drainage. One patient had renal insufficiency without the need for dialysis (transient rise in creatinine), and one patient had transient brachial plexopathy, likely related to positioning on the operating table. Very early in our experience, there was one death related to tearing of the base of the left atrial appendage.

#### 3.2 Rhythm

Success was defined as no episodes of atrial fibrillation greater than 15 seconds on monitoring at 6 months post-operatively. For the group of patients who had ECG at 6 months, 56 of 61 (91.8%) had sinus rhythm only on ECG. Of the 57 patients who had long-term monitors at 6 months, 42 (73.7%) had no detectable atrial fibrillation (longer than 15 s). Those patients with paroxysmal atrial fibrillation fared better. By longer-term monitoring, 32 of 39 (82.1%) patients had successful ablation. In patients with persistent or long-standing persistent atrial fibrillation, 16 of 21 (76.2%) had sinus rhythm by the 6-month ECG, and 10 of 18 (55.6%) had successful ablation by longer-term monitoring (Table 1). The percentage of patients off antiarrhythmic drugs is listed in Table 1. However, it should be noted that very often, the decision to discontinue antiarrhythmic drugs was not made until after the 6-month office visit.

#### 3.3 Perception of rhythm

Fifty-six patients were asked to predict their rhythm at the 6-month ECG. Forty-eight of them (86%) felt they were in sinus rhythm, seven (13%) felt they were in atrial fibrillation, and one (2%) could not assess his rhythm. Of those who felt they were in sinus rhythm, 85% were correct. Of those who felt they were in atrial fibrillation, 100% were correct. Paroxysmal patients were correct 88% of the time in predicting their rhythm, and 80% of persistent/long-standing persistent patients were correct.

#### 3.4 Symptoms

Seven patients (13%) reported that they had symptoms of atrial fibrillation. Two of these were paroxysmal, and five were persistent/long-standing persistent. Long-term monitoring of these patients revealed that every one had at least

one episode of atrial fibrillation that could possibly have been responsible for their symptoms. Among all patients who were known to be in atrial fibrillation ( $n=15$ ), only 47% reported having symptoms.

### 4 Future directions

Our success rate for patients with paroxysmal atrial fibrillation compares favorably to the published literature. However, success rates for persistent and permanent atrial fibrillation of 76% by ECG and 56% by longer-term monitoring leave room for improvement. One might expect that pulmonary vein antral isolation and partial autonomic denervation would not be adequate treatment for a patient in persistent and long-standing persistent atrial fibrillation because of the associated changes in the left atrial substrate that occur in these conditions [31, 32]. Hence, a more extensive lesion set similar to the left-sided Cox-Maze III may be necessary.

To accomplish the left-sided Cox Maze III lesion set, a connecting lesion would need to be added between the left- and right-sided pulmonary veins, a connecting lesion to the base of the atrial appendage, and a connecting lesion to the mitral valve annulus. In the minimally invasive approach, we can obtain excellent visualization through the transverse sinus behind the aorta and the pulmonary artery. Therefore, we have begun placing connecting lesions on the dome of the atrium (Fig. 2). We have early studies underway to confirm transmuralty of these lesions with conduction block and efficacy in suppression of long-standing persistent atrial fibrillation.

In summary, techniques have been developed for both epicardial pulmonary vein electrical isolation and targeted partial autonomic denervation in the treatment of atrial fibrillation. These techniques can be combined in a minimally invasive surgical approach. Early data suggest this is a safe and efficacious approach for the treatment of paroxysmal atrial fibrillation. In the future, it may be possible to add additional left-atrial lesions to improve the efficacy of minimally invasive surgical treatment of long-standing persistent atrial fibrillation from an epicardial approach.

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