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Off-Pump Epicardial Atrial Fibrillation Surgery Utilizing a Novel Bipolar Radiofrequency System

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ABSTRACT

Background. Over the past several years, pulmonary vein isolation for the treatment of atrial fibrillation has gained significant popularity. This study was undertaken to evaluate a novel radiofrequency (RF)-enabled clamp system designed to create transmural lesions epicardially on the beating heart using bipolar RF.

Methods. A set of differently shaped clamps modified to deliver bipolar RF energy were used to create a series of lesions in a beating heart canine model. The pulmonary veins and atrial appendages of 6 dogs were electrically isolated using bipolar RF energy. The right and left atrial appendages served as controls for the right and left pulmonary veins, respectively. Temperature-controlled RF energy was delivered to maintain a tissue temperature of 80°C for 15 seconds. Electrical isolation was assessed acutely and after 4 weeks by a bipolar pacing protocol.

Results. A total of 24 circumferential lesions were created. By pacing analysis, 100% (24/24) of these lesions were electrically isolated acutely and 95% (19/20) were still isolated 4 weeks later. At 4 weeks, 92% (22/24) of lesions were transmural by histologic analysis, and 96% (23/24) demonstrated endocardial continuity. One animal experienced a fatal cardiac arrhythmia during initiation of the post-survival procedure, prior to electrophysiologic evaluation, accounting for the reduced number of potential electrically isolated lesions.

Conclusion. Bipolar RF ablation utilizing a novel bipolar RF clamp device results in electrical isolation and histologic transmurality in an off-pump epicardial model.

INTRODUCTION

Atrial fibrillation (AF) has been clinically recognized as the most common sustained supraventricular tachyarrhythmia confronting physicians in the United States [Scherlag 2002; Lonnerholm 2002]. It affects at least 5% to 10% of the population over the age of 65, and accounts for approximately 345,000 new cases annually [Cox 1996]. AF is also the predominant cause of hospitalization for cardiac arrhythmias, and because of the dilemmas it poses—with regards to the need for anticoagulation, antiarrhythmic therapy, heart rate control, cardioversion, and additional evaluations of underlying cardiac pathology—AF often results in prolonged hospital stays [Zimmer 2003]. Current medical management of AF has not demonstrated a clear benefit for patients in clinical trials receiving only rate control therapies [Wyse 2002]. A more aggressive approach to treating AF may change this dynamic.

Moe et al hypothesized and demonstrated that AF was the result of multiple random atrial reentrant circuits [Moe 1959, 1964]. Their work was later substantiated by multiple clinical and experimental studies performed by Allessie et al [1985]. More recent clinical and animal investigations have suggested that the origin of paroxysmal AF centers around locations within or juxtaposed to the pulmonary veins (PVs) [Haissaguerre 1998]. Other investigators have suggested that microreentry circuits anchored near the PVs induce fibrillatory conduction and thereby cause AF [Jalife 1998].

James Cox et al, during the early 1980s, designed the Maze procedure, a surgical technique developed to treat AF [Cox 1991a, 1991b, 1991c, 1991d]. This technique involved incising and suturing the atria, thereby interrupting the conduction of reentrant circuits [Cox 1996]. The Cox- Maze III procedure has afforded more than 95% of its recipients freedom from AF. However, the procedure is not widely applied because of the invasiveness associated with a traditional "cut and sew" approach. Of particular concern are the risks of postoperative bleeding from suture line, prolonged cardiopulmonary bypass time, and the high incidence of permanent pacemaker implantation.

Previous animal studies conducted by Prasad et al have demonstrated success in performing off-pump epicardial bipolar radiofrequency (RF) ablation of atrial tissue [Prasad 2002]. We evaluated a simple clamping device that delivers bipolar RF energy to treat AF. Additionally, this device allows for a completely off-pump, epicardial beating heart approach. The objective of this study was to assess the ability of a RF bipolar device to rapidly create electrically insulating and histologically transmural myocardial lesions.

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MATERIALS AND METHODS

All animals involved in this study received humane care according to federal, state, and local laws and Columbia University policies governing animal research. This study also conformed to the guidelines established by the "Guide for the Care and Use of Laboratory Animals," published by the National Institutes of Health (National Institutes of Health publication no. 85-23, revised 1985).

In vitro data were gathered using fresh bovine cardiac tissue. In preparation for ablation, the bovine myocardium was sectioned into 6-cm long blocks with depths of 3 mm, 6 mm, 9 mm, and 10 mm. Prior to ablation, the fresh bovine cardiac tissue blocks were immersed into a 37°C saline bath for 5 minutes and were ablated as described below. At each temperature-time setting, 6 ablations were performed with the resulting mean lesion depths and standard deviations illustrated in Table 1. All temperature-time settings evaluated from the in vitro study created transmural lesions. These data were utilized to identify a conservative temperature-time setting for the survival study.

Six adult dogs, 4 females and 2 males, each weighing 25 to 28 kg, were used for this study. Prior to any procedure, the animals were allowed an acclimation period of 48 to 72 hours in their new environment. Sedation was initially achieved with intravenous thiopental (15 mg/kg), followed by orotracheal intubation and general anesthesia with 1% inhaled isoflurane. Access for continuous arterial pressure monitoring was achieved through percutaneous puncture and cannulation of the femoral artery. The external jugular vein was percutaneously accessed for fluid infusion. An epidural catheter was also inserted preoperatively to provide adequate postoperative pain control. The cardiac rhythm was continuously monitored via transcutaneous electrocardiographic leads.

Each dog underwent a partial median sternotomy. The pericardium was incised, and a pericardial cradle created. The interatrial groove was dissected, mobilizing the right atrium medially. A vessel loop was placed around the confluence of the right PVs. The left PVs were then dissected and a vessel loop was also placed around their confluence at the left atrium.

Pre-ablation pacing analyses were performed utilizing PowerLab software (ADInstruments, Colorado Springs, CO, USA). This software filtered electrical signals using a combination of low-pass and high-pass filtering options. Data were collected in the low-pass and high-pass filter modes at 200 Hz and 10 Hz, respectively. To record the cardiac rhythm and rate, a bipolar electrode was placed at the base of the left atrial appendage (LAA), and a second bipolar electrode was placed onto the extrapericardial left superior PV. Pacing electrodes were placed onto the extrapericardial middle PV, and a pacer stimulator was activated to document the baseline threshold for capturing the electrical activity of the atrium. The PV recorder and the pacing electrodes were then transferred to the tip of the LAA. Again, the heart rate and rhythm were recorded, and pacing analyses were performed to document a baseline threshold. The above steps were repeated on the right side utilizing the right superior PV, middle PV, and the right atrial appendage (RAA).

Table 1. In Vitro Radiofrequency Bipolar Coagulation Data

Time, sec	Depth of Tissue Necrosis, mm		
	70°C	80°C	90°C
20, n = 18	3 ± 0	3 ± 0	3 ± 0
30, n = 18	6 ± 0	6 ± 0	6 ± 0
45, n = 18	9 ± 0	9 ± 0	9 ± 0
60, n = 18	10 ± 0	10 ± 0	10 ± 0

A set of differently shaped clamps (Figure 1), modified to deliver bipolar RF energy (Boston Scientific/EP Technologies, San Jose, CA, USA), was used to create a series of lesions. Temperature-controlled RF energy was delivered from the RF generator (Boston Scientific/EP Technologies) to maintain a tissue temperature of 80°C for 15 seconds. These settings were based on previous bench-top feasibility studies (Table 1).

Four circumferential lesions were created on each animal. Two lesions encircled the right and left PVs at their confluences, and 2 other lesions encircled the distal aspects of the LAA and RAA. Lesions were defined as electrically insulating when a bipolar recorder placed on a nonisolated atrial segment was unable to sense pacing signals from the PVs or distal atrial appendage that were greater than 3 times the baseline threshold (mA).

After 28 days, the animals were returned to the operating room. At the post-survival procedure, each animal underwent a second sternotomy and pacing analyses were repeated. Electrical isolation was defined as above. The atria, PV, and atrial appendages were grossly evaluated for stricture and thrombus formation. The hearts were excised and histologi-

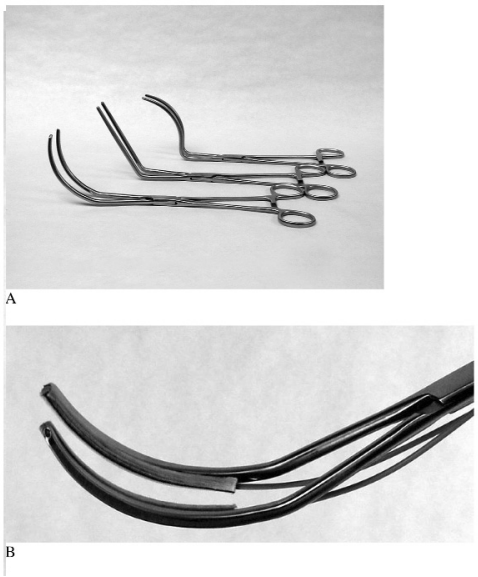

Figure 1. A, Set of 3 differently shaped clamps without ablative inserts. This set of clamps affords easy access to the pulmonary veins with minimal trauma while positioning the device. B, A curve clamp with the bipolar ablative elements in place.

Table 2. Ablation Summary*

Lesion Location	No. of Lesions	Pre-Ablation Threshold (mA)	Early Post-Ablation Threshold (mA)	Late Post-Ablation Threshold (mA)	Acute Isolation	Chronic Isolation	Transmurality
Right pulmonary vein	6	1.25 ± 0.82 (0.5-2)	18.83 ± 2.86 (13-20)	20 ± 0	6/6 100%	5/5 100%	6/6 100%
Left pulmonary vein	6	1.33 ± 0.61 (0.5-2)	20 ± 0	20 ± 0	6/6 100%	5/5 100%	6/6 100%
Right atrial appendage	6	0.68 ± 0.23 (0.5-1)	16.92 ± 7.55 (1.5-20)	20 ± 0	6/6 100%	5/5 100%	5/6 83%
Left atrial appendage	6	0.58 ± 0.20 (0.5-1.5)	16.88 ± 7.63 (1.8-20)	15.25 ± 9.5 (1-20)	6/6 100%	4/5 80%	5/6 83%
Overall	24	0.97 ± 0.62 (0.5-2)	18.16 ± 5.35 (1.5-20)	19.10 ± 4.15 (1-20)	24/24 100%	19/20 95%	22/24 92%

*Data are presented as ± standard deviation (range).

cal staining was performed with Masson Trichome to assess lesion characteristics. The microscopic analysis following Masson Trichrome staining provided information pertaining to lesion transmurality, but could not provide accurate measurements for lesion depth and width due to the fixation process that removed water from the tissue. Thus, complete tissue and lesion depths were evaluated using a tissue viability dye, triphenyl-tetrazolium chloride (TTC). For the TTC staining process, a portion of the lesion with surrounding normal tissue was excised and placed into TTC solution for 45 minutes. This process resulted in nonviable tissue appearing white, and viable tissue was stained a dark red hue. Transmurality via gross inspection was determined by the presence of a thin white linear scar traversing the entire depth of the ablated tissue from the epicardial surface to the endocardial surface.

RESULTS

Operative Results

One animal died during the induction of anesthesia for the post-survival surgery, and post-survival electrophysiologic studies were not performed on this animal. There were neither intraoperative nor postoperative complications directly related to the surgical procedure. The animals left the operative suite in sinus rhythm and were still in sinus rhythm when they were returned to the operative suite 28 days later.

Pacing Analysis

Twenty-four circumferential epicardial lesions were created on the right PV, left PV, LAA, and RAA. Pre-ablation pacing studies of all 24 target sites revealed a mean baseline threshold of 0.99 ± 0.59 mA (see Table 2). One hour after ablation, all lesions were electrically insulated to a mean pacer stimulator output of 18.36 ± 5.07 mA. Twenty-eight days later, repeat pacing analyses were performed. The recorders and pacer stimulator were once again placed in their previously documented positions immediately following creation of PV-encircling lesions. Post-survival pacing analyses revealed that 95% (19/20) of the lesions had retained their electrically insulating properties with a mean threshold of 19.17 ± 3.96 mA. The single lesion that failed to demonstrate post-survival isolation was located on an atrial appendage.

Histology

Upon harvesting of the cardiac tissue, a pair of samples was taken from each of the 4 lesion sites. One of these tissue samples was immersed in formalin, sent to the histology laboratory for Trichrome staining, and mounted on microscopic slides. The other sample was submerged in TTC for 45 minutes and then analyzed for tissue and lesion depths. The mean tissue depth was 2.21 ± 0.55 mm, and the mean lesion depth was 2.11 ± 0.5 mm with a corresponding mean lesion width of 2.5 ± 0.72 mm. Microscopic and gross tissue evaluation revealed an overall transmurality of 92% (Figure 2), with 96% of the lesions demonstrating endocardial continuity (Figure 3) at 28 days. There was no gross evidence of thrombus formation or PV stenosis at the time of post-survival procedures.

DISCUSSION

The treatment of AF is responsible for a significant burden on healthcare finances. According to the Health Care Finance Administration, AF was responsible for 1.4 million outpatient visits and 227,000 hospitalizations in the United States in a 1-year period [Health Care Finance Administration Report 1997; Cox 2000; Prasad 2002]. Although currently available medical therapy ameliorates the symptoms associated with AF, this approach is not curative. The Maze procedure remains the leading effective means of curing

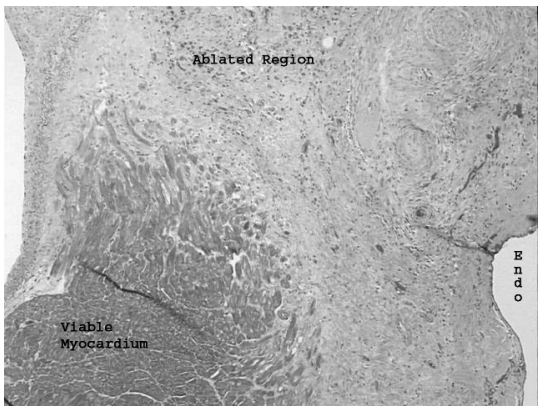

Figure 2. Masson Trichrome stain of left atrial cuff just distal to the confluence of the right pulmonary veins. Endo indicates endocardial surface.

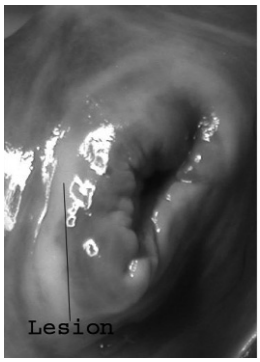

Figure 3. Circumferential lesion surrounding the confluence of the right pulmonary veins. The lesion is highlighted by a pale line encircling the ostium compared to the darker viable tissue.

medically refractory AF in selected patients with long-term follow-up [Cox 1996], but is not widely applied. An epicardial approach to performing a modified Maze procedure that will result in reproducible creation of electrically nonconducting lesions is paramount to the development of an acceptable and applicable surgical cure for AF.

The present study describes our experience with a novel bipolar RF device that reproducibly creates electrically insulating, transmural lesions on a beating heart canine model via an epicardial approach. Although the results of this study and similar work done by others [Prasad 2002] appear promising, it must be taken into account that the canine atrial myocardium is thinner than humans. This may significantly contribute to a high percentage of transmural lesions in the animal models. To compensate for this limitation, we also created lesions on both atrial appendages of each animal, which are typically thicker than the atrium. Ninety-two percent of the lesions created on the atrial appendage were histologically transmural and demonstrated electrical insulating properties. The LAA lesion that recovered excitability 4 weeks following acute isolation may be attributed to the trabeculated nature of the distal atrial appendage. Initial isolation could have been a result of myocardial stunning, which subsequently resolved without maturation into a nonconducting scar along the ablation line. Like the "cut and sew" technique of the original Cox-Maze procedure, the goal of this and other tissue ablation devices is to replace electrically conducting cardiac tissue with a linear, nonconducting scar. Although the ability of an ablative device to create transmural lesions often defines success, conduction block in both the short- and long-term follow-up, irrespective of transmurality, is the only undisputable indicator of success.

Unlike other bipolar devices currently in use, the system we tested uses a variety of differently shaped clamps, broadening the surgeon's options. In addition, the handling and locking mechanism for this device is identical to that of commonly used surgical clamps. Locking the clamp across the target tissue allows for continuous, even pressure application, and ensures that the RF bipolar energy is transmitted without gaps. The bipolar inserts can be removed from one clamp and reinserted onto another by the surgeon as needed to facilitate placement and minimize trauma to the target tissue.

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