



ADULT CARDIAC SURGERY:

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The ABLATE Trial: Safety and Efficacy of Cox Maze-IV Using a Bipolar Radiofrequency Ablation System

Jonathan M. Philpott, MD, Christian W. Zemlin, PhD, James L. Cox, MD, Mack Stirling, MD, Michael Mack, MD, Robert L. Hooker, MD, Allen Morris, MD, David A. Heimansohn, MD, James Longoria, MD, Divyakant B. Gandhi, MD, and Patrick M. McCarthy, MD

Department of Surgery, Eastern Virginia Medical School, Mid-Atlantic Thoracic Surgeons, Sentara Heart Hospital, and Department of Electrical and Computer Engineering and Center for Bioelectronics, Old Dominion University, Norfolk, Virginia; Washington University School of Medicine, Barnes-Jewish Hospital, St Louis, Missouri; Munson Medical Center, Traverse City, Michigan; Baylor Heart Hospital, Plano, Texas; Spectrum Health, Butterworth Hospital, Grand Rapids, Michigan; Mercy Heart Institute, Sacramento, California; Heart Center of Indiana, Indianapolis, Indiana; Sutter Heart Institute, Sacramento, California; McLaren Greater Lansing, Lansing, Michigan; and Northwestern University, Chicago, Illinois

Background. The Cox Maze-IV procedure (CMP-IV) has replaced the Cox Maze-III procedure as the most common approach for the surgical treatment of atrial fibrillation (AF). The Food and Drug Administration-regulated AtriCure Bipolar Radiofrequency Ablation of Permanent Atrial Fibrillation (ABLATE) trial sought to demonstrate the safety and efficacy of the CMP-IV performed with the Synergy ablation system (AtriCure, Inc, Cincinnati, OH).

Methods. Fifty-five patients (aged 70.5 ± 9.3 years), 92.7% of whom had nonparoxysmal AF, underwent CMP-IV to terminate AF during a concomitant cardiac surgical procedure. Lesions were created using the AtriCure Synergy bipolar radiofrequency ablation system. All patients were seen for follow-up visits after 30 days, 3 months, and 6 months, with 24-hour Holter monitoring at 6 months. Late evaluation was performed by 48-hour Holter monitoring at an average of 21 months.

Results. The primary efficacy endpoint, absence of AF (30 seconds or less) at 6-month follow-up off

antiarrhythmic medications (Heart Rhythm Society definition), indicated 76% (38 of 50) were AF free (95% confidence interval: 62.6% to 85.7%). The primary safety endpoint, the rate of major adverse events within 30 days, was 9.1% (5 of 55; 95% confidence interval: 3.9% to 19.6%), with 3.6% mortality (2 of 55). Secondary efficacy endpoints included being AF free with antiarrhythmic drugs (6 months, 84%; 21 months, 75%), successful pulmonary vein isolation (100%), and AF burden at 6 and 21 months. The results, together with those for the secondary safety endpoint (6-month major adverse events), demonstrated that the Synergy system performs comparably to the cut-and-sew Cox Maze-III procedure.

Conclusions. The CMP-IV using the AtriCure Synergy system was safe and effective for cardiac surgical patients who had persistent and longstanding persistent AF.

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The Cox Maze procedure, developed in 1987, provided the first surgical treatment of atrial fibrillation (AF) [1]. After several refinements to its lesion set, the resulting Cox Maze-III procedure (CMP-III) became the standard

surgical treatment of AF. Large clinical studies of CMP-III report high success rates for both lone and concomitant AF, with low rates of complications [2]. To simplify and shorten the CMP-III, alternatives to its “cut-and-sew” creation of transmural lesions were tested, in particular radiofrequency (RF) ablation and cryoablation [3, 4]. These approaches are now collectively called the Cox

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Address correspondence to Dr Zemlin, Center for Bioelectronics, Old Dominion University, 4211 Monarch Way, Norfolk, VA 23508; e-mail: czemlin@odu.edu.

Drs Philpott, Zemlin, Cox, Longoria, and Gandhi disclose a financial relationship with AtriCure.

Maze-IV procedure (CMP-IV) and have reduced cross-clamp times while preserving the high success rates of the CMP-III [5]. Recent guidelines state that for patients undergoing cardiac surgery with concomitant AF [6], the evidence is in favor of surgical ablation in most cases, but adoption has been limited by a lack of standardization and systematic training.

The new bipolar RF ablation system, Synergy (AtriCure, Inc, Cincinnati, OH), uses two pairs of RF electrodes to produce wider and more reliable lesions than in the past. It has been shown to reliably create permanent transmural lesions in a porcine model [7]. Here, we report the results of the AtriCure Bipolar Radiofrequency Ablation of Permanent Atrial Fibrillation (ABLATE) clinical trial, an Food and Drug Administration Investigational Device Exemption study designed to evaluate the Synergy ablation system to achieve an approved labeling for AF.

Patients and Methods

Patients

The ABLATE trial was designed as a multicenter study to prove or disprove prespecified safety and efficacy performance goals for the Maze IV procedure using the Synergy ablation system. The Bayesian statistical method was used to detect when the performance goals had been achieved with the desired confidence; at that point, enrollment was terminated (see Statistics). To be eligible, patients had to have a history of permanent AF as defined by 2006 American College of Cardiology/American Heart Association/European Society of Cardiology guidelines and be scheduled for elective cardiac surgical procedures to be performed on cardiopulmonary bypass. Table 1 lists the full eligibility criteria. This study was approved by the Institutional Review Board/Ethics Committee of each hospital. All patients provided written informed consent for the procedure and data collection according to the policy of each hospital.

AtriCure Synergy Description

The AtriCure Synergy bipolar ablation system consists of a clamp with two left curved jaws (Fig 1) and an ablation

and sensing unit. The clamps resemble standard surgical clamps and are always under direct control of the surgeon. The curved jaws come in two sizes to accommodate the variability in the size of the atria. Each jaw contains two linear electrodes for RF delivery, and once the jaws are closed, the electrodes form two adjacent pairs (pair A and pair B) that lie exactly opposite to each other. The ablation and sensing unit delivers bipolar RF energy through both pairs of electrodes in an alternating fashion: if RF energy is delivered through pair A, pair B is not active, and vice versa. Switching between pair A and pair B is done periodically at a frequency of 267 Hz to decrease impedance directly in front of each electrode. This approach leads to wider lesions than bipolar ablation with a single pair of electrodes [7].

Surgical Strategy

Investigators were required to perform a near-complete CMP-IV [4] lesion set concomitant with an open chest structural heart procedure. The lesion set included bilateral pulmonary vein isolation, roof and floor lesions, a lesion to the left atrial appendage, the mitral isthmus lesion, right intercaval lesion, right appendage lesion, right medial wall lesion to the tricuspid annulus, and right free-wall lesion to the tricuspid annulus. No lesion was required on the coronary sinus. The Synergy clamp was the primary tool for lesion creation except for the completion of three lesions that terminate onto the mitral valve and tricuspid valve annuli. For these, the bipolar Isolator pen (AtriCure) or a cryoablation probe were prescribed to complete the lesion for anatomic and physiologic reasons. The lesion set is illustrated in Figure 2.

Study Endpoints

The primary efficacy endpoint was defined as the fraction of patients who were free of AF 6 months after the procedure while not receiving antiarrhythmic drugs (AADs [class I or III]). The decision to continue or discontinue AADs was made by the treating physician (no protocol prescription). Absence of AF was verified by Holter monitor assessment (24 hours) or pacemaker

Table 1. Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
Aged ≥ 18 years	Previous cardiac ablation (catheter or surgical)
History of permanent AF	Stand-alone AF without indication for CABG/valve surgery
Schedule for elective cardiac surgery on cardiopulmonary bypass	Class IV NYHA heart failure symptoms
Left ventricular ejection fraction $\geq 30\%$	Cerebrovascular accident within 6 months or any time if residual neurologic deficit
Life expectancy ≥ 1 year	Documented MI within 6 weeks before enrollment
Willing to provide consent and commit to return for follow-up	Need for emergent cardiac surgery
	Left atrium size ≥ 8 cm
	Carotid artery stenosis $\geq 80\%$
	Chemotherapy, systemic infection, renal failure, drug/alcohol addiction, mental impairment, pregnancy, desire to become pregnant, thoracic radiation therapy, long-term steroid treatment, connective tissue disorder

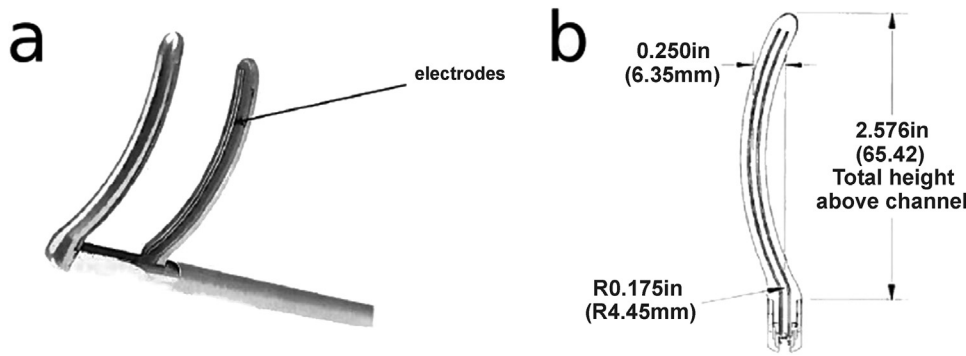


Fig 1. AtriCure Synergy clamp (a) and jaw geometry (b). Dimensions shown are for large jaws; small jaws have lower height (2.098 inches = 53.29 mm) and otherwise identical dimensions.

interrogation. All Holter and pacemaker data were evaluated in a common core laboratory.

The primary safety endpoint was the rate of major adverse events (MAEs) occurring within the initial 30 days after the procedure or up to discharge (whichever was later). Major adverse events included death, excessive bleeding, stroke, transient ischemic attack, and myocardial infarction.

The secondary efficacy endpoints were the fraction of patients who were free of AF 6 months after the procedure (episodes less than 30 seconds on 24-hour Holter monitoring); effectiveness of pulmonary vein ablation to create acute conduction block; and reduction of overall AF burden. During the preparation for the Food and Drug Administration (FDA) panel meeting, the FDA recommended an additional long-term rhythm assessment to evaluate the durability of the lesions. This assessment was performed 1 year after the procedure or later (range, 365 to 952 days; mean 640). It determined the fraction of patients free of AF with 48-hour Holter monitoring or pacemaker interrogation (40 of 48 patients); in 8 patients, Holter monitoring could not be obtained and electrocardiogram evaluation was used instead. The reduction of overall AF burden was determined for the 40 patients for whom Holter or pacemaker data were available. A secondary safety endpoint was the composite 6-month post-procedure MAE rate.

Statistics

The Bayesian statistical method was used to determine statistical significance of actual outcomes versus

prespecified performance criteria that were developed in collaboration with the FDA. The Bayesian method provides for adaptive enrollment so that if actual results achieve statistical significance, enrollment may be terminated. In this case, the desired performance criteria were achieved after 55 patients were enrolled. Continuous variables are presented as mean \pm SD. Confidence intervals (CI) for endpoint rates were determined using the Wilson score method [8]. Confidence intervals were determined for 95% confidence.

Results

Baseline Characteristics

A total of 1,047 patients who presented for open heart surgery and had a history of AF were screened for study inclusion; 55 of those patients were enrolled in nine centers (Table 2). At 55 subjects, enrollment was terminated because the performance criteria of the Bayesian model had been met (see Statistics). The baseline characteristics are summarized in Table 3. The mean patient age was 70.5 ± 9.3 years; 58% were male and 42% were female. A sex analysis did not reveal significant differences in the primary safety and efficacy endpoints.

All patients had a documented nonparoxysmal form of AF according to the 2006 guidelines in effect during enrollment, but 4 patients were subsequently reclassified as paroxysmal AF using the stricter 2012 Heart Rhythm Society guidelines for AF classification [6]. Still, an overwhelming majority of patients (92.7%) had a documented

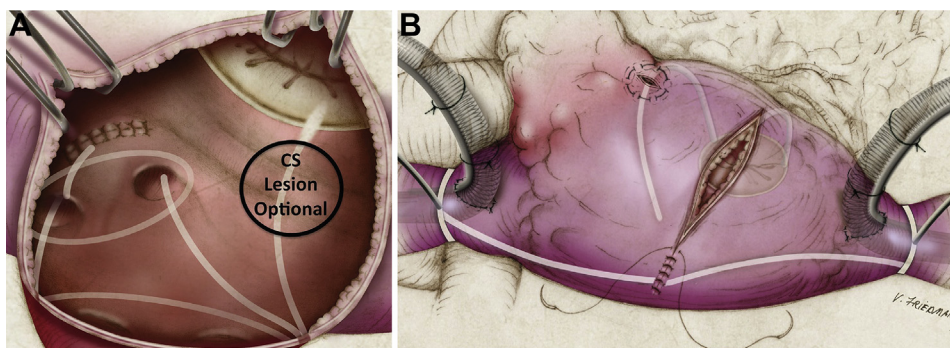


Fig 2. Lesion set specified by the AtriCure Bipolar Radiofrequency Ablation of Permanent Atrial Fibrillation (ABLATE) protocol: (A) left atrial lesions; (B) right atrial lesions. (CS = coronary sinus.)

Table 2. Participating Sites

Site Name	Patients Enrolled	Percent of Total (n = 55)
Baylor Heart Hospital	10	18.2 (10)
Munson Medical Center	10	18.2 (10)
Sentara Norfolk Heart Hospital	9	16.4 (9)
Heart Center of Indiana	7	12.7 (7)
Spectrum Health	7	12.7 (7)
Mercy Heart Institute	4	7.3 (4)
Sutter Heart Institute	4	7.3 (4)
Inova Fairfax	3	5.5 (3)
Ingham Regional Medical Center	1	1.8 (1)

nonparoxysmal form of AF, and 85% of patients had a history of AF exceeding 1 year with a mean time since AF onset of 61 ± 49 months. The average size of the left atrium was 5.93 ± 0.97 cm. The CHADS₂ score, a measure for the risk of stroke of AF patients, was 0 (low risk) for 18.2% of patients, 1 (medium) for 27.3% of patients, and 2 or more (high) for 54.5% of patients. The concomitant procedures included coronary artery bypass graft surgery, single or double valve repair, or a combination of coronary artery bypass graft surgery and valve repair (Table 4).

Surgery Implementation

The lesion set required by the protocol was completed in 87.3% of all patients (the execution of the optional coronary sinus lesion was not tracked). Omission of a

Table 3. Baseline Characteristics of Entire Cohort

Baseline Characteristics	Values (n = 55)
Age, years	70.5 \pm 9.3 (55)
Male	58.2 (32)
Left atrium size, cm	5.93 \pm 0.97 (53)
AF duration, months	61.2 \pm 49.5 (55)
Paroxysmal AF ^a	7.3 (4)
Persistent AF ^b	27.3 (15)
Longstanding persistent AF ^c	65.5 (36)
NYHA III or IV	41.8 (23) ^d
LVEF, %	50.0 \pm 10.3 (54)
Preoperative pacemaker	12.7 (7)
CHADS ₂	
0	18.2
1	27.3
2	54.5

^a Based on HRS guidelines [6] paroxysmal atrial fibrillation (AF) is defined as recurrent AF (≥ 2 episodes) that terminates spontaneously within 7 days. ^b Persistent AF is defined as AF that is sustained beyond 7 days, or lasting less than 7 days but necessitating pharmacologic or electrical cardioversion. ^c Longstanding persistent AF is defined as continuous AF lasting longer than 1 year. ^d One New York Heart Association (NYHA) class IV patient was included in a deviation from the eligibility criteria.

Values are mean \pm SD (n), % (n), or %. CHADS₂ is a measure for the risk of stroke of AF patients (higher score indicates higher risk).

LVEF = left ventricular ejection fraction.

Table 4. Concomitant Surgical Procedures

Concomitant Procedures	Values (n = 55)
CABG only	18.2 (10)
Valve surgery	40.0 (22)
Mitral valve replacement	18.2 (10)
Aortic valve replacement	21.8 (12)
Double valve surgery	16.4 (9)
Aortic + mitral	7.3 (4)
Mitral + tricuspid	9.1 (5)
CABG + valve surgery	16.4 (9)
CABG + mitral valve	10.9 (6)
CABG + aortic	5.5 (3)
CABG + double valve	9.1 (5)
Aortic + mitral	5.5 (3)
Mitral + tricuspid	3.6 (2)

Values are % (n).

CABG = coronary artery bypass graft surgery.

required lesion or failure to use the appropriate study device to complete a lesion was recorded as a protocol deviation and included in the outcomes analysis on an intention to treat basis (Table 5). In 1 case, the physician performed only pulmonary vein isolation.

Safety Endpoints

The primary safety endpoint, MAEs during the first 30 days, resulted in a 9.1% rate (5 of 55; 95% CI: 3.9% to 19.6%); the secondary safety endpoint, cumulative MAEs during the first 6 months, resulted in a 10.9% rate (6 of 55; 95% CI: 5.1% to 21.8%).

Efficacy Endpoints

Figure 3 illustrates the success rates in eliminating AF with or without AADs at 6 and 21 months. At 6 months, 84.0% (42 of 50 patients) were AF free with AADs (95% CI: 71.5 to 91.7) and 76.0% (38 of 50) were AF free without AADs (95% CI: 62.6% to 85.7%), and there was no statistically significant difference in the success rates of the participating sites. At 21 months, these numbers had fallen to 75.0% (36 of 48; 95% CI: 61.2% to 85.1%) with AADs and 62.5% (30 of 48; 95% CI: 48.4% to 74.8%) without AADs. Acute pulmonary vein isolation was assessed if sinus rhythm was achieved during the procedure (in 41.8% of patients), either by testing for exit block or entrance block. Pulmonary vein isolation was confirmed in all patients in whom it could be assessed. At 6 months, there was no residual AF burden in 82.0% of the patients; in 4% it was between 5 minutes and 1 hour; and in 14%, it was more than 1 hour. At 21 months, patients had either no AF burden, with no AF, atrial tachycardia, or atrial flutter episodes longer than 30 seconds (77.5%), or a high AF burden of at least 1 hour (22.5%). Postprocedure iatrogenic flutter was observed in 1 patient.

Pacemaker implantation was necessary in 11 patients (22.9%); 7 of these patients (12.7%) had sinus node dysfunction, 4 (7.3%) from dysfunction of the

Table 5. Lesion Statistics (n = 55)

Variables	Values (n = 55)	Success [% (n/N)] ^a
Complete Cox Maze-IV procedure	87.3 (48)	77.2 (34/44)
Incomplete procedures		
Missing right atrial lesions	7.3 (4)	66.7 (2/3)
Missing right anterior freewall appendage lesion	7.3 (4)	66.7 (2/3)
Missing lesion from right atrial appendage to tricuspid annulus	1.8 (1)	N/A (0/0)
Missing left atrial lesions	3.6 (2)	100 (2/2)
Missing completion lesion to mitral valve annulus	3.6 (2)	100 (2/2)

^a "Success" is defined as the fraction of patients in each subgroup that are free of AF without drugs after 6 months.

atrioventricular node. At the final assessment (18 months or later), there was a substantial recovery of both the sinus node and the atrioventricular node, with 6 of 11 patients in sinus rhythm (not paced), 3 of 11 continuously paced, 1 of 11 intermittently paced, and 1 of 11 in AF.

Adverse Events

Five MAEs (9.1%) were reported at 30 days: 2 deaths, 2 cases of excessive bleeding, and 1 stroke, which occurred immediately after complicated aortic valve replacement. Two more patients died between the 30-day and the 6-month assessment (one was the patient who had a stroke in the first 30 days), and then 2 more between the 6-month assessment and the 21-month assessment. None of these MAEs was related to the CMP-IV, as determined by an independent physician adjudicator. Furthermore, the Data Safety Monitoring Board raised no safety concerns for the duration of the study.

Comment

The CMP-IV has largely replaced the CMP-III as the definitive surgical treatment of choice for persistent and longstanding persistent AF [9-11]. A variety of ablation modalities have been used to create lesions [9, 12], and there is great interest in refining these modalities to ensure that they reliably create chronic lesions that are permanently contiguous and transmural. Bipolar RF ablation is the most common modality used today because clamping the tissue between electrodes allows good definition of the ablated tissue. The clamp electrodes can also be used to measure impedance of the clamped tissue, which provides immediate feedback to determine whether the lesions are transmural or not. The AtriCure Synergy bipolar RF system used in this study has two parallel pairs of bipolar ablation electrodes to increase lesion width and enhance the likelihood of permanent transmural. A previous porcine study has documented the contiguity and transmural of the lesion it creates [7].

The results for the primary efficacy endpoints of the ABLATE trial are similar to those of the most well-established and accepted studies to date. In particular,

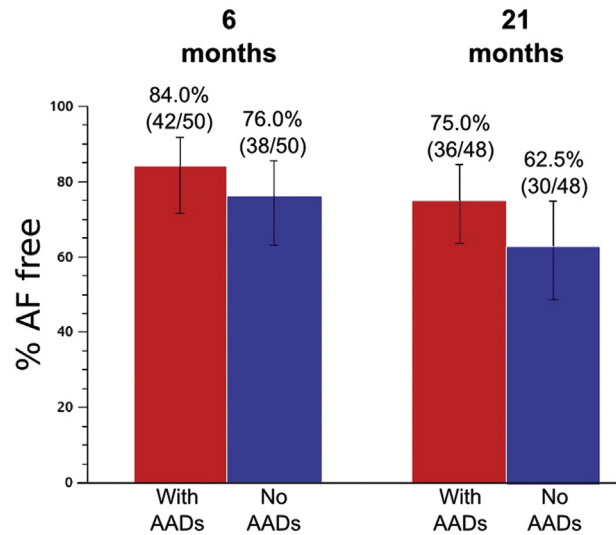


Fig 3. Efficacy endpoint results. Error bars indicate 95% confidence interval as computed by the Wilson score method. (AAD = antiarrhythmia drug; AF = atrial fibrillation.)

the primary efficacy endpoint, freedom from AF after 6 months without AADs, was achieved in 76% of cases (95% CI: 62.6% to 85.7%). This value is similar to that of major recent CMP-IV clinical trials such as that of Damiano and colleagues [13] (282 patients, 79%) and Saint and associates [14] (100 concomitant CMP-IV patients, 77%).

Secondary efficacy endpoint results are also comparable to those of previous trials. For example, freedom from AF at 6 months with AADs is 84.0% (95% CI: 71.5% to 91.7%). This is lower than, but not significantly different from, Saint and associates [14] (100 concomitant CMP-IV patients, 91%, *p* = 0.204 with a two-proportion z-test), but significantly different from Damiano and associates [13] (93%, *p* = 0.037 with a two-proportion z-test). Freedom from AF at 21 months was reached by 75% with AADs and by 62.5% without AADs. A recent review reports that these rates typically range from 65% to 85% with AADs and 55% to 75% without AADs [15].

The patient population treated in this study was particularly challenging, as the baseline characteristics show. A large majority of patients (92.7%) had nonparoxysmal AF; most other studies have far lower rates of nonparoxysmal AF [2, 3, 5, 10, 13, 14]. Duration of AF (more than 5 years, average 61.2 months) and the size of the left atrium (average 5.9 cm) were also unusually large. It is reasonable to assume that the efficacy outcomes in the present study would have been better had the patient population been more similar to that of the above-mentioned studies.

A study that is particularly comparable to the present one in terms of patient population is The Concomitant Utilization of Radio Frequency Energy for Atrial Fibrillation (CURE-AF) trial [16], which evaluated the efficacy and safety of the Medtronic Cardio-plate surgical ablation system. Its fractions of paroxysmal, persistent, and long-standing persistent AF were similar to those of the ABLATE trial, and the

concomitant surgical procedures similarly complex. The CURE-AF trial reported 66% patients AF free with AADs and 53% free without AADs after 6 to 9 months, significantly lower rates than the present study (84% with AADs and 76% without AADs after 6 months, $p < 0.01$ a with two-proportion z-test in both cases).

Interestingly, the atrial flutter rate reported was very low (1 of 55 patients at 21 months), even without a required coronary sinus lesion. It would be interesting to know how the efficacy results would be affected if the coronary sinus lesion was included. It is remarkable that at 6 months, all patients were either in sinus rhythm or had a high AF burden of 1 hour or more during a 24-hour Holter; intermediate AF burdens were never observed.

The rate of MAEs (5 of 55, or 9.1%) was within expected norms based on the complexity of the concomitant cardiac procedures, and an independent physician adjudicator determined that none of these adverse events was related to the CMP-IV procedure itself. Therefore, the current rate of MAEs was consistent with the challenging patient population and was not a result of the CMP-IV procedure.

The ABLATE investigators are a representative sample of clinical practices across the country and are not restricted to high-volume, experienced CMP-IV surgeons or large academic centers. The fact that the ABLATE results were still favorable and similar across the participating centers suggests that it will be possible to reproduce the CMP-IV results reported in this study.

We conclude that CMP-IV performed with the AtriCure Synergy system yields similar results, in regard to both efficacy and safety, as competing implementations of CMP-IV, even in light of a particularly challenging patient population, in which almost all patients had persistent or longstanding persistent AF with an average duration of more than 5 years and a left atrial size averaging 5.9 cm.

A limitation of the current study is that the ablation of the coronary sinus at the mitral annulus was not mandatory; the patients in whom this ablation is omitted have a higher risk of developing reentry around the mitral annulus, and that may have reduced efficacy. Also, the number of RF/cryoablation applications was not recorded, and omission that will be rectified in the ABLATE Post Approval Study (PAS). Moreover, the high rate of pacemaker implantations may in part be a consequence of AADs (especially amiodarone) administered before surgery. Of the 11 surviving patients who received a pacemaker, only 4 exhibited any pacemaker activity on their latest Holter monitor. Finally, the relatively small number of patients ($n = 55$) and deviations from the prescribed lesion set resulted in large 95% confidence intervals for several study endpoints. The confidence intervals will narrow in the final report of the PAS which, as of this writing, has enrolled more than 350 patients at more than 50 enrolling centers.

The results of this midterm evaluation were reviewed by an FDA expert panel, which approved the AtriCure Synergy system for treatment of AF with concomitant

surgical procedures. As part of the approval, the FDA required a large postapproval study with mandatory training of all operators in the use of the Synergy system.

The ABLATE trial was sponsored by AtriCure, Inc.

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DISCUSSION

DR CRAIG SELZMAN (Salt Lake City, UT): In the spirit of the late-breaking clinical trial, and I understand that this is a company that is trying to go through a Food and Drug Administration (FDA) process, but it kind of begs a couple of issues. One is, for this trial, there is selection bias that is just inbred into this. So how did you decide how many patients were screened to get to your 55 patients?

DR PHILPOTT: There were 1,047 subjects screened for potential enrollment. In my own institution (and we were one of the lead enrollers) we were very aggressive about screening all patients with any possible history of atrial fibrillation—so I doubt any biases as we were looking for all comers. In fact, we wanted to push the envelop in terms of enrolling complex high-risk patients—and the population studied reflects this. Our screening pattern seems to be reflected in the other institutions that participated in the trial. We were basically looking for anybody who had nonparoxysmal atrial fibrillation and trying to enroll them if they could meet the study inclusion/exclusion criteria.

DR SELZMAN: So basically 5% of the patients who were screened actually went onto the—I mean, 50 of 1,000 or so?

DR PHILPOTT: Yes, that is correct.

DR SELZMAN: Did any of the screened patients get followed?

DR PHILPOTT: No.

DR SELZMAN: In other words, I am trying to head to some kind of control group—20% of patients getting a pacemaker is a significant thing. If they were to get a coronary artery bypass graft, that may or may not alter their natural history of their overall process. So is there any kind of historical control group that is being used with these data?

DR PHILPOTT: No. I agree that would be helpful but many of the screened patients were found to have paroxysmal atrial fibrillation and thus would not make a good control group. Second, the purpose of this study was to meet the FDA requirements for safety and efficacy to earn a labeling indication. It was not designed to answer many of questions that you and I both want to know. Each variable studied adds complexity and costs. Accordingly, for this study there is no control group that we can compare it to.

However, when we look at the other studies, the 20% pacemaker rate seems to be quite consistent among the other papers, two of which were presented today. All of us are concerned about the pacemaker implantation rate, and I suspect it is multifactorial. Antiarrhythmic drugs, lesions near the sinus node, denervation of the heart, all likely play a part in delayed sinus node recovery. I concur we all want to understand that better.

DR SELZMAN: Did you have any protocolization of the method of drug utilization after the procedure?

DR PHILPOTT: Yes. At that time, the accepted practice pattern was that amiodarone was used immediately postoperatively to quell postoperative atrial fibrillation.

DR SELZMAN: Excuse me, was that prophylactic?

DR PHILPOTT: Yes—that is correct. Again, that was the practice pattern at the time.

DR SELZMAN: Yes.

DR PHILPOTT: The idea behind the prophylactic use of amiodarone was that once patients underwent a Maze, they were going to have high rates of postoperative atrial fibrillation for the first several weeks to months due to the irritation related to the ablations—the amiodarone was used in an effort to blunt or minimize this. However, in my own experience, with the passage of time and as I have gotten better with the Maze procedure, I am seeing much less postoperative atrial fibrillation and instead, delayed sinus node recovery.

So, at least in Norfolk, we have stopped prophylactic amiodarone not only immediately postoperatively but also for patients scheduled to undergo a Maze for 2 weeks preoperatively. Once they regain sinus node function, or if they do have postoperative atrial fibrillation, then we start it. In terms of how long to hold it, we do not know the right amount of time. However, again, the purpose is to foster an earlier return of sinus node function after the Maze by limiting antiarrhythmic drug suppression of the sinoatrial node.

DR SELZMAN: Okay.

DR RICHARD SHEMIN (Los Angeles, CA): Okay, I have a few questions to keep the discussion going. So you looked at Holter monitors at 6 months and 12 months. Were there any episodes of atrial fibrillation in someone who was in sinus rhythm at 6 months and at the 12-month interval but had atrial fibrillation in between? So in other words, if you did a Kaplan-Meier analysis of atrial fibrillation, if they had some episodes in between, they would be a failure. But since you are actually just looking at two timepoints, 6 and 12 months, they would be considered successes.

DR PHILPOTT: Given that there was no event monitoring between the 6-month and year-plus timepoints, we did not detect interim failures. However, at the 12-month and later timepoint we could analyze the failure. The part that I found fascinating was how they failed. Everybody in the atrial fibrillation community has been appropriately focused on detecting short, breakthrough episodes of postoperative atrial fibrillation, and a 2-week event monitor is recommended to look for these short episodes of silent atrial fibrillation. We were able to analyze burden in 40 of the patients, and interestingly, there were no short episodes. When a patient failed, they presented with continuous atrial fibrillation. There were no recorded events of atrial fibrillation less than 1 minute or 5 minutes, and so forth. The failures began at the hour or longer window—basically they were pretty much in continuous atrial fibrillation, which goes counter against some of the initial concerns about short burst of postoperative atrial fibrillation lasting longer than 30 seconds.

DR SHEMIN: Did you record indications for pacemakers?

DR PHILPOTT: We did. It was 7.3% for an atrioventricular node conduction problem, and then 12.7% was for sinus node dysfunction.

DR SHEMIN: In patients receiving pacemakers, you know how many patients were not pacing at later up? So often, we rush to get patients out of the hospital, sometimes prematurely place a pacemaker.

DR PHILPOTT: The study was not designed to look at that specifically, and thus the data on this subject was incomplete. However, what we do know is that at the last evaluation, the 11 surviving patients implanted with pacemakers, only 4 had shown any device pacing activity suggesting delayed sinus node recovery. In my personal experience in Norfolk when we looked at it, the delayed mechanical pacing was also remarkably low. To me, this suggests that what we are seeing is not typical sinus node dysfunction as much as delayed sinus recovery.

DR SELZMAN: Lastly, was it protocolized what to do with the left atrial appendage?

DR PHILPOTT: Yes.

DR SELZMAN: Since it was sponsored by a company, did you put a company thing on there, or how was that dealt with?

DR PHILPOTT: So the patients stopped enrolling in 2009, and the vast majority of them had the appendage removed.

DR SELZMAN: So it was oversewn? Cut—

DR PHILPOTT: Yes, that is correct. At the conclusion of this ABLATE study, the FDA did approve the labeling for synergy bipolar clamp for ablation for atrial fibrillation during concomitant surgery. But as part of that approval, the company had to do a large postapproval trial. In addition to amputating it and oversewing the base, the AtriClip was approved by the FDA for use in the ABLATE postapproval study; however, the choice on how to remove or exclude the appendage was up to the operating surgeon.

The ABLATE postapproval study has accrued more than 360 patients at this point. The data are actually fairly mature. So hopefully within the next year to year and a half, we can start to see some of these questions that were very, very interesting addressed. The final requirement that the FDA mandated with the labeling approval was that the company go out and formally train surgeons using the ablation devices. At this point, more than 1,500 surgeons have been trained as a result.

DR SELZMAN: Very good. Thank you so much.