AtriCure®

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AtriCure® Synergy Ablation System Instructions for Use

DESCRIPTION

The AtriCure Synergy Ablation System is comprised of the Ablation and Sensing Unit (ASU) and an AtriCure Switch Box (ASB3), or the Multifunctional Ablation Generator (MAG), an AtriCure Synergy Ablation Clamp, and a footswitch. The AtriCure Synergy Ablation Clamp is a single patient use electrosurgical instrument designed for use only with the ASU or MAG. The Synergy Ablation Clamp is intended to ablate cardiac tissue for the treatment of patients with persistent or longstanding persistent atrial fibrillation who are undergoing open concomitant coronary artery bypass grafting (CABG) and/or valve replacement or repair. When activated, the ASU or MAG delivers radiofrequency (RF) energy to the linear electrodes on the insulated jaws of the Synergy Ablation Clamp. The Operator controls the application of this RF energy by pressing the Footswitch.

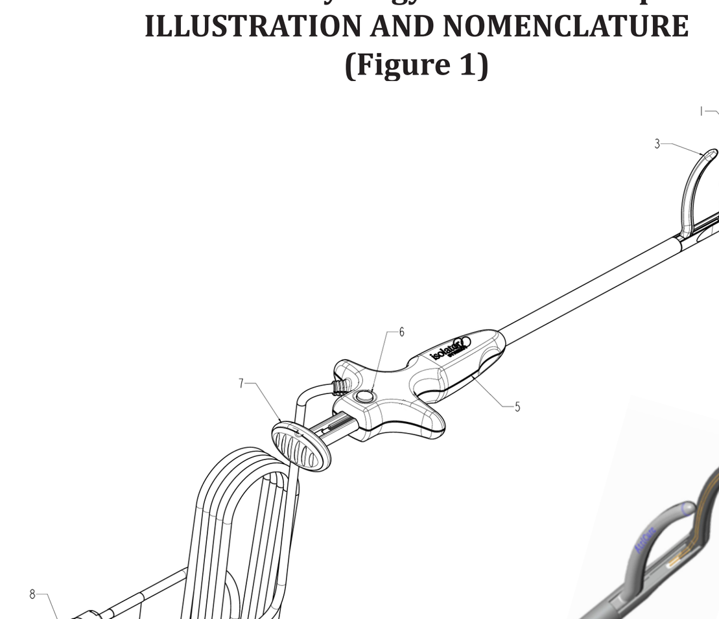
The Synergy™ Ablation (See Figure 1) Clamps feature two pairs of opposing dual electrodes, an in-line handle with syringe-type actuation and button release mechanisms. The Synergy Ablation Clamp requires the use of the AtriCure Switch Box (ASB3) and Ablation Sensing Unit (ASU or MAG).

NOTE:

- The AtriCure Synergy Ablation System has not been studied in the reoperative setting, so safe and effective use cannot be assured.
- The full Maze IV procedure cannot be completed with the AtriCure Synergy Ablation System alone. See Table 1 for a description of the devices used in the ABLATE Clinical study.

NOTE: Please refer to the AtriCure ASU/ASB3 or MAG Instructions for Use for information specific to the ASU/ASB3 or MAG.

AtriCure Synergy Ablation Clamp ILLUSTRATION AND NOMENCLATURE (Figure 1)



(AtriCure SYNERGY ABLATION CLAMP)	
1. Distal Jaw	6. Release Mechanism
2. Electrodes	7. Closure Lever
3. Proximal Jaw	8. Connector
4 Jaw Heel	9. Connector Alignment Arrow
5. Handle	

INDICATION FOR USE

The AtriCure Synergy Ablation System is intended to ablate cardiac tissue for the treatment of persistent atrial fibrillation (sustained beyond seven days or lasting less than seven days but necessitating pharmacologic or electrical cardioversion) or longstanding persistent atrial fibrillation (continuous atrial fibrillation of greater than one year duration) in patients who are undergoing open concomitant coronary artery bypass grafting and/or valve replacement or repair.

CONTRAINDICATIONS

The AtriCure Synergy Ablation System should not be used for contraceptive coagulation of the fallopian tubes. The device is not designed for safe and effective use for that purpose.

⚠ WARNINGS

- Any tissue within the RF energy field may experience heating and/or tissue damage. Ensure that non-target tissue is adequately separated from the RF field. Ensure non-target tissue is protected from the RF field by carefully placing and orienting the electrodes. Refer to Potential Complications list.
- Inspect the product packaging prior to opening to ensure that the sterility barrier is not breached. If the sterility barrier is breached, do not use the Synergy Ablation Clamp to avoid the risk of patient infection.
- Electrosurgery should be used with caution in the presence of internal or external pacemakers and/or internal cardiac defibrillators (ICD). Interference produced with the use of electrosurgical devices can cause devices such as a pacemaker and/or ICD to enter an asynchronous mode, block pacemaker conduction, or deliver inappropriate shock therapy. Consult the pacemaker manufacturer or hospital Cardiology department for further information when use of electrosurgical appliances is planned in patients with cardiac pacemakers and/or ICD.
- Do not re-sterilize or reuse the Synergy Ablation Clamp as this could damage the device or result in infection

Read all instructions carefully for the AtriCure Synergy Ablation System, prior to using the device. Failure to properly follow instructions may lead to electrical or thermal injury and may result in improper functioning of the device.

Potential Complications

The AtriCure Synergy Ablation System is indicated for use as a concomitant procedure with open coronary artery bypass grafting and/or valve replacement or repair. Below is a list of potential adverse effects (e.g., complications) that are associated with this combined procedure:

- Death,
- Excessive bleeding that may require re-intervention,
- Cardiac tamponade,
- Pulmonary vein stenosis,
- Restrictive or constrictive pericarditis,
- Infection that may result in sepsis or endocarditis,
- Myocardial infarction (MI),
- Stroke or transient ischemic attack (TIA),
- Thromboembolism,
- Diaphragmatic (phrenic nerve) paralysis,
- Esophageal-left atrial fistula or esophageal rupture,
- Atrial perforation or rupture,
- Ventricular perforation or rupture,
- Atelectasis,
- Pneumonia,
- Congestive heart failure,
- Cardiac valve injury,
- Persistent pneumothorax,
- Excessive pain and discomfort,
- Deep sternal wound infection (mediastinitis),
- Perioperative atrial or ventricular rhythm/conduction disturbance,
- Pericardial effusion,
- Damage to adjacent nerve and/or blood vessels
- Injury to unintended surrounding tissues, including tears and punctures,
- Extension of cardiopulmonary bypass time or aortic cross clamp time.

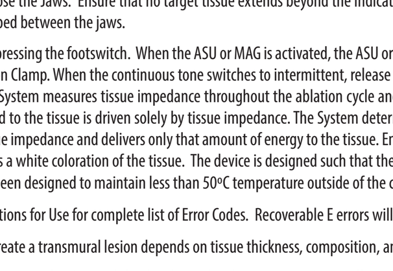
⚠ PRECAUTIONS

- Do not drop the Synergy Ablation Clamp as this may damage the device. If the Synergy Ablation Clamp is dropped, do not use. Replace with a new Synergy Ablation Clamp.
- Do not use the Synergy Ablation Clamp with another manufacturer's generator to avoid damage to the device, which may result in patient injury. The Synergy Ablation Clamp is only compatible with the AtriCure ASU or MAG and ASB.
- Do not ablate tissue greater than 10 mm thick with the Synergy Ablation Clamp. Tissues greater than 10 mm thick may not be fully ablated.
- The use of the AtriCure Synergy Ablation System is limited to physicians with specific training on the procedure and the product.
- Inspect the area between the jaws of the Synergy Ablation Clamp for foreign matter before activating the ASU or MAG or ASB. Foreign matter captured between the jaws will adversely affect the ablation.
- Do not insert excessive tissue into the jaw heel as it may result in poor ablation at the jaw heel.
- Do not ablate in a pool of blood or other fluids as this may extend the ablation time. Users should suction excess fluids away from the jaws prior to ablation. Immersion of any part of the Synergy Ablation Clamp in fluids may also damage the device.
- Do not attempt to use a Synergy Ablation Clamp that has reached its time limit expiration. The Synergy Ablation Clamp has an 8-hour useful life that is tracked by the ASU or MAG. The Synergy Ablation Clamp will no longer function after 8 hours of use and the ASU or MAG will display a message indicating that the Synergy Ablation Clamp must be replaced.
- WHEN THE ASU OR MAG (RF GENERATOR) AND SYNERGY ABLATION CLAMP ARE USED ON A PATIENT SIMULTANEOUSLY WITH PHYSIOLOGICAL MONITORING EQUIPMENT, ENSURE THAT THE MONITORING ELECTRODES ARE PLACED AS FAR AS POSSIBLE FROM THE SURGICAL ELECTRODES. BE SURE TO POSITION THE SYNERGY ABLATION CLAMP CABLES SO THAT THEY DO NOT COME IN CONTACT WITH THE PATIENT OR THE OTHER LEADS.
- Monitoring systems that incorporate high frequency RF filtering devices are recommended for use with the ASU or MAG (RF generator) and Synergy Ablation Clamp.
- When the ASU or MAG (RF generator) is activated in conjunction with the Synergy Ablation Clamp, the conducted and radiated electrical fields may interfere with other electrical medical equipment. Refer to the ASU or MAG IFU for more information regarding potential electromagnetic or other interference, and advice regarding avoidance of such interference.
- Do not use the Synergy Ablation Clamp if there is any sign of damage as it may adversely affect ablation performance.
- Do not connect the Synergy Ablation Clamp to the ASB if the connector pins are bent.
- Do not use abrasive cleaners or electrosurgical tip cleaners to clean debris from the Jaws. Use of abrasive cleaners or electrosurgical tip cleaners can damage the electrodes and result in device failure. Use saline-soaked gauze to clean debris off the electrodes.
- Do not touch the electrodes of the Synergy Ablation Clamp while activating the ASU or MAG. Touching the Synergy Ablation Clamp electrodes during ASU or MAG activation could result in burn to the operator.
- Do not touch the electrodes of the Synergy Ablation Clamp to metal staples or clips, or to sutures while activating the ASU or MAG.
- Do not use this device in the presence of flammable anesthetics; other flammable gases; near flammable fluids such as skin prepping agents and tinctures; flammable objects; or with oxidizing agents. Observe appropriate fire precautions at all times.

INSTRUCTIONS FOR USE

SET UP

1. Examine the packaging of the device to ensure the sterility of the product has not been breached. Remove the sterilized instrument from its package per standard sterile technique.
2. With the Connector Alignment Arrow symbol in the 12 o'clock position, push the connector into the appropriate Synergy Ablation Clamp receptacle on the front of the ASB3. Each Synergy Ablation Clamp has a unique receptacle on the ASB3. To ensure device performance, verify proper connections to the ASB3 by consulting the ASB3 package insert. Verify that the connections between the Synergy Ablation Clamp and the ASB3 are secure. If the connections are loose, do not use the Synergy Ablation Clamp. Inspect the cable and do not use the Synergy Ablation Clamp if the cable is frayed or the insulation is damaged.



ABLATION

3. Place the targeted tissue between the distal and proximal jaws of the Synergy Ablation Clamp.
4. Depress the Closure Lever to close the Jaws. Ensure that no target tissue extends beyond the Indicator Line on either the distal or proximal jaws or into the jaw heel and that the target tissue is firmly clamped between the jaws.
5. Activate the ASU or MAG by depressing the footswitch. When the ASU or MAG is activated, the ASU or MAG will emit an audible tone indicating that current is flowing between the jaws of the Synergy Ablation Clamp. When the continuous tone switches to intermittent, release the footswitch.
6. The AtriCure Synergy Ablation System measures tissue impedance throughout the ablation cycle and uses this information to control the application of energy to the tissue. The amount of energy delivered to the tissue is driven solely by tissue impedance. The System determines the minimum energy delivery required to create a transmural (full thickness) lesion based on tissue impedance and delivers only that amount of energy to the tissue. Energy delivery changes throughout the ablation cycle as tissue impedance changes. The lesion is visible as a white coloration of the tissue. The device is designed such that the lesions will not spread beyond the jaw width.
   Note: All of the clamps have been designed to maintain less than 50ºC temperature outside of the clamped region.
   Note: See ASU or MAG Instructions for Use for complete list of Error Codes. Recoverable E errors will remain on the display until the footswitch is pressed again.
   Note: The time necessary to create a transmural lesion depends on tissue thickness, composition, and the length of tissue captured between the electrodes.
7. To open the jaws, press the Release Mechanism and slowly release the Closure Lever. Do not allow the jaws to spring back. Be aware of any surrounding tissues that could be damaged as the jaws open.
8. Inspect the surgical area to ensure adequate ablation.
9. Between ablations, wipe the jaws clean with a saline-soaked gauze pad. Important: For optimal performance, keep the Synergy Ablation Clamp electrodes clear of coagulum. To ensure the electrodes are clear of coagulum:
   Use a saline soaked gauze pad to clean the electrodes after each ablation. If coagulum is present, it is much easier to remove within the first several seconds after ablation. In a brief period of time, the coagulum could dry out making removal more difficult.
   Check both electrodes before each ablation to ensure that the gold of the electrode is visible, and coagulum is removed.
   If the Synergy Ablation Clamp is idle between ablations, clamp the jaws onto a saline soaked gauze pad to prevent any coagulum on the electrodes from drying.
10. Repeat the ablation process as necessary.

REMOVAL AND DISPOSAL

11. Discard the Synergy Ablation Clamp after use. Follow local governing ordinances and recycling plans regarding disposal or recycling of device components.

SUMMARY OF CLINICAL STUDIES CONDUCTED FOR ATRIAL FIBRILLATION TREATMENT INDICATION

The ABLATE (AtriCure Synergy Bipolar RF Energy Lesions for Permanent Atrial Fibrillation Treatment during Concomitant On-Pump Endo/Epicardial Cardiac Surgery) clinical study has been performed in demonstration of the AtriCure Synergy Ablation System's safety and effectiveness for the treatment of persistent or longstanding persistent atrial fibrillation (AF) in patients undergoing concomitant coronary artery bypass grafting and/or valve replacement or repair.

A continued registry study (ABLATE AF) was established following ABLATE. The ABLATE AF study had identical inclusion and exclusion criteria as ABLATE, except that ABLATE enrolled patients with "permanent AF" (per 2006 ACC/AHA/ESC Guidelines) and ABLATE AF enrolls patients with "persistent or longstanding persistent AF" (per the 2007 HRS Consensus Statement). Results of both studies are presented.

The Post-Approval Study (ABLATE PAS) was initiated to evaluate clinical outcomes though 36 months postoperatively in a newly enrolled cohort of patients treated during commercial use of the AtriCure Synergy Ablation System by physicians performing the MAZE IV procedure. A sample of 365 subjects was enrolled across 50 U.S. sites. The results of the PAS are presented.

ABLATE and ABLATE AF

Study Design

ABLATE was a multi-center, prospective, non-randomized study based on a Bayesian adaptive design that provides high probability of demonstrating safety and effectiveness of the AtriCure Synergy Ablation System for the treatment of permanent atrial fibrillation. The safety and effectiveness of the device was compared to performance goals derived from historical information. The Bayesian adaptive clinical design incorporated interim analyses of the data to determine the point of completion of trial enrollment. Enrollment was targeted to be between 50 and 100 subjects at 20 sites. The study was designed to have an initial assessment of results at the point that 50 subjects were enrolled with a minimum of 20 subjects completing their six-month follow-up visit. Nine investigational sites enrolled 55 subjects.

In the Bayesian setting probabilistic statements are made about parameters given observed data (as compared to the frequentist setting where probabilistic statements are made about the data given an assumed parameter value, e.g. a p-value). Two such Bayesian constructs are the posterior probability and credible interval. A posterior probability conveys the probability that the true but unknown effectiveness rate or MAE rate lies above (effectiveness) or below (safety) the stated threshold. For example, "There is a 97.9% chance that the true but unknown effectiveness rate is greater than or equal to 60% in this patient population." Similarly, a Bayesian credible interval gives a range for the likely values: a 95% credible interval conveys there is a 95% chance that the true but unknown parameter lies between the interval's lower and upper bounds. For example, "given the results of the trial, there is a 95% probability that the chance of success ranges from 60.4% to 82.5%". A narrower interval conveys greater precision in the estimate.

Inclusion and Exclusion criteria

Key Inclusion Criteria included:

- ≥ 18 years of age
- History of permanent AF in which cardioversion (electrical and/or pharmacologic) has failed or has not been attempted (as defined by the 2006 ACC/AHA/ESC Guidelines).
- Scheduled to undergo elective cardiac surgical procedure(s) to be performed on cardiopulmonary bypass
- Left Ventricular Ejection Fraction ≥ 30%

Key Exclusion Criteria included:

- Class IV NYHA heart failure symptoms
- Preoperative need for intra-aortic balloon pump or intravenous inotropes
- Left atrial size ≥ 8cm
- Cerebrovascular accident within the prior 6 months
- Myocardial Infarction within the prior 6 weeks
- Need for emergent cardiac surgery
- Renal failure requiring dialysis or hepatic failure
- Repeat (re-do) cardiac surgical procedure

Maze IV Procedure

Figure 1 and Table 1 below summarize the lesions specified by the ABLATE protocol for completion of the Maze IV lesion set, as well as which lesions were to be performed using the AtriCure Synergy Ablation System or other devices.

Figure 1: Maze IV Procedure Lesion Set

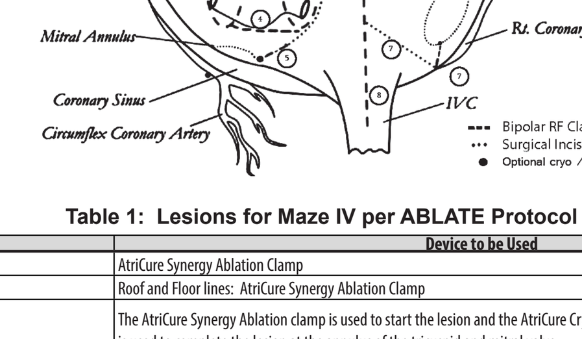


Table 1: Lesions for Maze IV per ABLATE Protocol

Lesion	Device to be Used
Pulmonary Vein Lesions	AtriCure Synergy Ablation Clamp
Box Lesion	Roof and Floor lines: AtriCure Synergy Ablation Clamp
Mitral Valve Annulus Lesion	The AtriCure Synergy Ablation clamp is used to start the lesion and the AtriCure Cryoablation System, or the AtriCure Bipolar Pen is used to complete the lesion at the annulus of the tricuspid and mitral valve.
LA Appendage Lesion	AtriCure Synergy Ablation Clamp
Tricuspid Valve Lesion	AtriCure Cryoablation System, or the AtriCure Bipolar Pen is used to complete the lesion at the annulus.
SVC to IVC Lesion	AtriCure Synergy Ablation Clamp
Right Atrial Free Wall Appendage Lesion	AtriCure Synergy Ablation Clamp
Right Atrial Appendage to Tricuspid Annulus Lesion	The AtriCure Synergy Ablation clamp is used to start the lesion and the AtriCure Cryoablation System, or the AtriCure Bipolar Pen is used to complete the lesion at the annulus.

Study Endpoints

The Primary Effectiveness endpoint is the rate of subjects free of AF without the need for Class I and III antiarrhythmic drugs six months after treatment with the system. Freedom from AF is defined as no events of AF longer than 5 minutes and combined events of AF do not exceed 1 hour per 24-hour period assessed by a 24-hour Holter that was reviewed by an independent core laboratory. The effectiveness performance goal was extrapolated from literature to be 60% AF Free and off any AADs at six months.

The Primary Safety endpoint is a composite rate of acute major adverse events within 30 days post procedure or hospital discharge, whichever is later. This composite safety endpoint includes death, stroke (resulting in significant permanent disability), TIA, myocardial infarction, and excessive bleeding (requiring >2 units of blood replacement and surgical intervention). It also included deaths after 30 days if the death was procedure related. The safety performance goal was extrapolated from literature to be 18.95%.

Subject Accountability

Table 2 demonstrates the accountability of subjects enrolled in the ABLATE and ABLATE AF studies.

Table 2: Subject Accountability

Parameter	ABLATE N=55	ABLATE Non-Paroxysmal N=51	ABLATE + ABLATE AF N=69	ABLATE + ABLATE AF Non-Paroxysmal N=64
Patients Enrolled [n] [1]	55	51	69	64
Procedure and Follow-up visit data available [% (n/N)]	N=55	N=51	N=69	N=64
Procedure	100.0% (55/55)	100.0% (51/51)	100.0% (69/69)	100.0% (64/64)
Discharge	96.4% (53/55)	96.1% (49/51)	97.1% (67/69)	96.9% (62/64)
30 Day [2]	96.4% (53/55)	96.1% (49/51)	97.1% (67/69)	96.9% (62/64)
3 Month [3]	87.3% (48/55)	86.3% (44/51)	88.4% (61/69)	87.5% (56/64)
6 Month [4]	90.9% (50/55)	90.2% (46/51)	89.9% (62/69)	89.1% (57/64)
12 Months or later [5]	87.3% (48/55)	88.2% (45/51)		
Follow-up Time in Study (Days) [6]				
Mean +/- SD (N)	555.6 +/- 208.1 (55)	555.8 +/- 208.0 (51)	491.9 +/- 227.9 (69)	492.5 +/- 227.5 (64)
Median	554.0	554.0	547.0	547.0
Min, Max	4.0, 743.0	4.0, 743.0	4.0, 743.0	4.0, 743.0

[1] All subjects treated with Ablation procedure.
[2] Two ABLATE subjects expired prior to 30 days. One subject discharged at 35 days. Assessment performed on that day included in both discharge and 30 days summaries.
[3] One ABLATE subject withdrew prior to 3-month assessment, three ABLATE subjects missed the 3-month visit, and one ABLATE subject expired prior to the 3-month assessment.
[4] One ABLATE subject expired prior to 6 months. Subjects in ABLATE AF are shown with completed assessment at 6 months or later. Two ABLATE AF subjects were not evaluated at 6 months or later at the time of this analysis.
[5] Subjects are shown with completed assessment at 12 months or later. Two ABLATE subjects expired between the 6 month and long-term follow-up assessments.
[6] Study entry to last scheduled follow-up assessment or study exit.

Table 3 demonstrates the population of subjects represented in this dataset. The data are presented for all treated subjects and for the indicated (longstanding persistent and persistent) subjects. In the ABLATE population, there were 4 subjects with paroxysmal AF and 51 subjects with persistent or long-standing persistent AF (hereafter referred to as non-paroxysmal AF). When also including the ABLATE AF registry subjects, there were 5 subjects with paroxysmal AF and 64 subjects with non-paroxysmal AF.

Table 3: AF Classification

	ABLATE	ABLATE AF	ABLATE + ABLATE AF
AF Classification			
Paroxysmal	4	1	5
Persistent	22	2	24
Longstanding Persistent	29	11	40
Indicated Population	**51**	**13**	**64**

Subject Demographics

Table 4 demonstrates subject demographics for all groups.

Table 4: Subject Demographics

Parameter	ABLATE N=55	ABLATE Non-Paroxysmal N=51	ABLATE + ABLATE AF N=69	ABLATE + ABLATE AF Non-Paroxysmal N=64
Age [years]				
Mean +/- SD (N)	70.5 +/- 9.3 (55)	70.8 +/- 9.6 (51)	70.4 +/- 9.0 (69)	70.8 +/- 9.2 (64)
Median	72.0	73.0	72.0	72.5
Min, Max	45.0, 88.0	45.0, 88.0	45.0, 88.0	45.0, 88.0
Gender [% (n/N)]				
Male	58.2% (32/55)	60.8% (31/51)	62.3% (43/69)	64.1% (41/64)
Female	41.8% (23/55)	39.2% (20/51)	37.7% (26/69)	35.9% (23/64)
Time since AF onset (months)				
Mean +/- SD (N)	61.2 +/- 49.5 (55)	61.7 +/- 51.1 (51)	67.3 +/- 55.6 (69)	68.4 +/- 57.3 (64)
Median	48.6	48.6	54.8	55.8
Percentile: 25th, 75th	20.1, 96.1	19.5, 98.4	20.5, 98.4	19.8, 99.9
Min, Max	1.78, 188.39	1.78, 188.39	1.78, 247.17	1.78, 247.17
Left Atrial Size (cm)				
Mean +/- SD (N)	5.9 +/- 1.0 (50)	6.0 +/- 1.0 (46)	5.8 +/- 1.1 (64)	5.9 +/- 1.1 (59)
Median	6.0	6.0	5.7	5.8
Min, Max	3.9, 7.7	3.9, 7.7	3.0, 7.7	3.0, 7.7
>= 5 cm	86.0% (43/50)	87.0% (40/46)	81.3% (52/64)	81.4% (48/59)
Surgical Procedure Type(s)				
CABG only	18.2% (10/55)	19.6% (10/51)	21.7% (15/69)	23.4% (15/64)
Valve Surgery	40.0% (22/55)	37.3% (19/51)	34.8% (24/69)	32.8% (21/64)
Mitral Valve Repair/Replacement	18.2% (10/55)	17.6% (9/51)	15.9% (11/69)	15.6% (10/64)
Aortic Valve Repair/Replacement	21.8% (12/55)	19.6% (10/51)	18.8% (13/69)	17.2% (11/64)
Double Valve Surgery	16.4% (9/55)	17.6% (9/51)	14.5% (10/69)	15.6% (10/64)
Aortic & Mitral	7.3% (4/55)	7.8% (4/51)	5.8% (4/69)	6.3% (4/64)
Mitral & Tricuspid	9.1% (5/55)	9.8% (5/51)	8.7% (6/69)	9.4% (6/64)
CABG and Valve Surgery	16.4% (9/55)	15.7% (8/51)	21.7% (15/69)	20.3% (13/64)
CABG + Mitral Valve Repair/Replacement	10.9% (6/55)	9.8% (5/51)	11.6% (8/69)	10.9% (7/64)
CABG + Aortic Valve Repair/Replacement	5.5% (3/55)	5.9% (3/51)	10.1% (7/69)	9.4% (6/64)
CABG + Double Valve Surgery	9.1% (5/55)	9.8% (5/51)	7.2% (5/69)	7.8% (5/64)
Aortic & Mitral	5.5% (3/55)	5.9% (3/51)	4.3% (3/69)	4.7% (3/64)
Mitral & Tricuspid	3.6% (2/55)	3.9% (2/51)	2.9% (2/69)	3.1% (2/64)
Any Mitral Valve Surgery	54.5% (30/55)	54.9% (28/51)	49.3% (34/69)	50.0% (32/64)

Primary Safety Results

The Primary Safety Endpoint for ABLATE has been evaluated in both the treated population and the non-paroxysmal AF study population that were enrolled and treated with the AtriCure Synergy Ablation System. A clinic visit was performed at 30 days to fully assess the patient for potential adverse events. An evaluation of all subjects was available to assess this primary safety endpoint. There were five safety failures in the cohort including two deaths, two excessive bleeds and one stroke, as outlined in Table 5. When tested against the objective performance goal, the upper bound of the Bayesian Credible Interval fell below 0.1895 for the full ABLATE population, but above 0.1895 for the non-paroxysmal subpopulation.

Table 5: Primary Safety Endpoint

Primary Safety Endpoint	ABLATE N=55	ABLATE Non-paroxysmal N=51	ABLATE + ABLATE AF N=69	ABLATE + ABLATE AF Non-paroxysmal N=64
Primary Safety Endpoint	% (n/N) [BCI] [1] PP [2]	% (n/N) [BCI] [1] PP [2]	% (n/N)	% (n/N)
Primary Endpoint (Acute MAE within 30 days post procedure)	9.1% (5/55) [0.00, 0.179] PP = 0.967	9.8% (5/51) [0.00, 0.192] PP = 0.946	7.2% (5/69)	7.8% (5/64)
Death	3.6% (2/55)	3.9% (2/51)	2.9% (2/69)	3.1% (2/64)
<=30 days	3.6% (2/55)	3.9% (2/51)	2.9% (2/69)	3.1% (2/64)
>30 days, procedure related	0.0% (0/55)	0.0% (0/51)	0.0% (0/69)	0.0% (0/64)
Stroke/TIA	1.8% (1/55)	2.0% (1/51)	1.4% (1/69)	1.6% (1/64)
Stroke (with significant permanent disability)	1.8% (1/55)	2.0% (1/51)	1.4% (1/69)	1.6% (1/64)
TIA	0.0% (0/55)	0.0% (0/51)	0.0% (0/69)	0.0% (0/64)
MI	0.0% (0/55)	0.0% (0/51)	0.0% (0/69)	0.0% (0/64)
Excessive Bleeding (>2 units blood and surgical intervention)	3.6% (2/55)	3.9% (2/51)	2.9% (2/69)	3.1% (2/64)

[1] "BCI" is the 95% one-sided Bayesian Credible Interval. Beta (1,1) prior in accordance with the statistical plan.
[2] "PP" is the posterior probability the safety rate is less than 0.1895, Pr (qT < 0.1895 | Trial Results).

Primary Effectiveness Results

The primary effectiveness endpoint was defined as the rate of subjects that achieved successful obliteration of atrial fibrillation while off of any antiarrhythmic medication (Class I or III) evaluated at six months post procedure via 24 hour Holter monitor assessment (or permanent pacemaker interrogation in the case of those subjects who had a pacemaker implanted). The effectiveness results are presented in Table 6. When tested against the objective performance goal, the lower bound of the Bayesian Credible Interval exceeded 0.60 for the full ABLATE population but was below 0.60 in the non-paroxysmal subpopulation. The results for pulmonary vein isolation are presented in Table 7.

Table 6: Primary Effectiveness Endpoint

Summary of Effectiveness Endpoints	ABLATE % (n/N) [BCI] [1] PP [2]	ABLATE Non-paroxysmal % (n/N) [BCI] [1] PP [2]	ABLATE + ABLATE AF % (n/N)	ABLATE + ABLATE AF Non-paroxysmal % (n/N)
Effectiveness Evaluable at 6-month Follow-up	N=50	N=46	N=62	N=57
Free of AF and off AAD	74.0% (37/50) [0.604, 1.00] PP = 0.978	73.9% (34/46) [0.597, 1.00] PP = 0.972	75.8% (47/62)	75.4% (43/57)
Free of AF	84.0% (42/50)	82.6% (38/46)	85.5% (53/62)	84.2% (48/57)

[1] "BCI" is the 97.5% one-sided Bayesian Credible Interval. Beta (1,1) prior in accordance with the statistical plan.
[2] "PP" is the posterior probability that the effectiveness rate exceeds 0.60, Pr (pT > 0.60 | Trial Results).

Table 7: Pulmonary Vein Isolation Summary

Parameter	ABLATE N=55 % (n/N)	ABLATE Non-paroxysmal N=51 % (n/N)	ABLATE + ABLATE AF N=69 % (n/N)	ABLATE + ABLATE AF Non-paroxysmal N=64 % (n/N)
Both Right & Left Pulmonary Vein Isolation Evaluated [1]	41.8% (23/55)	43.1% (22/51)	47.8% (33/69)	48.4% (31/64)
Both Right & Left Pulmonary Vein Isolation Confirmed [2]	100.0% (23/23)	100.0% (22/22)	100.0% (33/33)	100.0% (31/31)

[1] Includes subjects evaluable on both sides.
[2] Successful pulmonary vein isolation on both left and right side.

Secondary Safety and Effectiveness Results

Table 8 demonstrates primary and secondary effectiveness endpoints, including long-term effectiveness. ABLATE AF subjects had not reached the 12-month follow-up at the time of review.

Table 8: Primary and Secondary Effectiveness Endpoints

Summary of Effectiveness Endpoints	ABLATE % (n/N) [BCI] [1] PP [2]	ABLATE Non-paroxysmal % (n/N) [BCI] [1] PP [2]	ABLATE + ABLATE AF % (n/N)	ABLATE + ABLATE AF Non-paroxysmal % (n/N)
Effectiveness Evaluable at 6-month Follow-up	N=50	N=46	N=62	N=57
Free of AF and off AAD	74.0% (37/50) [0.604, 1.00] PP = 0.978	73.9% (34/46) [0.597, 1.00] PP = 0.972	75.8% (47/62)	75.4% (43/57)
Free of AF	84.0% (42/50)	82.6% (38/46)	85.5% (53/62)	84.2% (48/57)
AF Burden [3]				
= 0 min	82.0% (41/50)	82.6% (38/46)	83.9% (52/62)	84.2% (48/57)
<= 5 min	2.0% (1/50)	0.0% (0/46)	1.6% (1/62)	0.0% (0/57)
> 5 min - 1 hr.	2.0% (1/50)	2.2% (1/46)	1.6% (1/62)	1.8% (1/57)
> 1 hr.	14.0% (7/50)	15.2% (7/46)	12.9% (8/62)	14.0% (8/57)
Effectiveness Evaluable at 12-month Follow-up or greater	N=48	N=45		
Time to Evaluation (days)				
Mean +/- SD (N)	640.9 +/- 147.3	641.7 +/- 151.7		
Min, Max	365.0, 952.0	365.0, 952.0		
Method of Evaluation				
Holter	81.3% (39/48)	82.2% (37/45)		
Pacemaker Interrogation (PMI)	2.1% (1/48)	2.2% (1/45)		
ECG	6.3% (3/48)	4.4% (2/45)		
Other/Telephone Assessment	10.4% (5/48)	11.1% (5/45)		
Free of AF and off AAD (12-month follow-up or greater)	62.5% (30/48)	62.2% (28/45)		
Free of AF (12-month follow-up or greater)	75.0% (36/48)	73.3% (33/45)		
AF Burden (initial 24 hrs. or >24 - 48 hrs.) [3] [4]				
= 0 min	77.5% (31/40)	76.3% (29/38)		
<= 5 min	0.0% (0/40)	0.0% (0/38)		
> 5 min - 1 hr.	0.0% (0/40)	0.0% (0/38)		
> 1 hr.	22.5% (9/40)	23.7% (9/38)		

[1] "BCI" is the 97.5% one-sided Bayesian Credible Interval. Beta (1,1) prior in accordance with the statistical plan.
[2] "PP" is the posterior probability that the effectiveness rate exceeds 0.60, Pr (pT > 0.60 | Trial Results).
[3] Patients with Pacemaker Interrogation (PMI) included as 0 min if no Atrial Fibrillation (AFib) on PMI, otherwise included based on equivalent proportion of AFib burden per total pacemaker interrogation period.
[4] Evaluable only in patients with a Holter or Pacemaker Interrogation (PMI)

Table 9 demonstrates the pacemaker implantation rate through 30 days.

Table 9: Pacemaker Implantation Through 30 days

	ABLATE N=55 % [n/N]	ABLATE Non-paroxysmal N=51 % [n/N]	ABLATE + ABLATE AF N=69 % [n/N]	ABLATE + ABLATE AF Non-paroxysmal N=64 % [n/N]
Pacemaker Pre-procedure	12.7% (7/55)	9.8% (5/51)	14.5% (10/69)	12.5% (8/64)
Post Procedure				
Permanent Pacemaker Implantation, as Adjudicated [1] [2]	25.0% (12/48)	26.1% (12/46)	20.3% (12/59)	21.4% (12/56)
AV node dysfunction	8.3% (4/48)	8.7% (4/46)	6.8% (4/59)	7.1% (4/56)
Sinus node dysfunction	16.7% (8/48)	17.4% (8/46)	13.6% (8/59)	14.3% (8/56)

[1] One subject has both an AV Nodal Block and a Bradycardia event leading to permanent pacemaker implant.
[2] One subject had a single chamber pacemaker present at baseline which was upgraded to dual chamber at follow-up.

The rate of serious device- and ablation procedure-related adverse events through 6 months is demonstrated in Table 10. Table 11 lists the observed serious device- or ablation procedure-related adverse events. There were four subjects with AV node dysfunction who received pacemakers. Using the most conservative approach, these were attributed to the MAZE procedure. However, the need for a pacemaker could be attributed to the primary procedure. Three events occurred during surgical access. They included one case of a pulmonary vein tear when dissecting the vein to place the clamp, one torn IVC during cannulation and one left atrial tear which occurred when lifting the heart for surgical access. The final case of akinesis caused by ischemia was associated with possible coronary injury from an ancillary ablation pen. The event was successfully treated with two bypass grafts.

Table 10: Serious Device- and Ablation Procedure-Related Adverse Events Through 6 Months

Parameter [1] [2]	ABLATE N=55 # of Evts	ABLATE N=55 % (n/N) of Pts with Event	ABLATE Non-Paroxysmal N=51 # of Evts	ABLATE Non-Paroxysmal N=51 % (n/N) of Pts with Event	ABLATE+ABLATE AF N=69 # of Evts	ABLATE+ABLATE AF N=69 % (n/N) of Pts with Event	ABLATE+ABLATE AF Non-paroxysmal N=64 # of Evts	ABLATE+ABLATE AF Non-paroxysmal N=64 % (n/N) of Pts with Event
Investigational Device	0	0.0% (0/55)	0	0.0% (0/51)	0	0.0% (0/69)	0	0.0% (0/64)
AF Procedure	7	12.7% (7/55)	7	13.7% (7/51)	7	10.1% (7/69)	7	10.9% (7/64)
Ancillary Device	1	1.8% (1/55)	1	2.0% (1/51)	1	1.4% (1/69)	1	1.6% (1/64)

[1] As Adjudicated or site reported if not yet adjudicated.
[2] Relationship presented hierarchically as listed in table.

Table 11: Listing of Observed Serious Device- or Ablation Procedure-Related Serious Adverse Events

Event Name	Relationship	Description
A-V Node Dysfunction	AF Ablation Procedure	AV-Node dysfunction requiring permanent pacemaker implantation. Conservatively attributed to the MAZE procedure, however the need for a pacemaker could be attributed to the primary procedure.
A-V Node Dysfunction	AF Ablation Procedure	AV-Node dysfunction requiring permanent pacemaker implantation. Conservatively attributed to the MAZE procedure, however the need for a pacemaker could be attributed to the primary procedure.
A-V Node Dysfunction	AF Ablation Procedure	AV-Node dysfunction requiring permanent pacemaker implantation. Conservatively attributed to the MAZE procedure, however the need for a pacemaker could be attributed to the primary procedure.
A-V Node Dysfunction	AF Ablation Procedure	AV-Node dysfunction requiring permanent pacemaker implantation. Conservatively attributed to the MAZE procedure, however the need for a pacemaker could be attributed to the primary procedure.
Cardiac Akinesis	Ancillary Device Related	Cardiac akinesis caused by ischemia was associated with possible coronary injury from an ancillary ablation pen. The event was successfully treated with two bypass grafts.
Pulmonary Vein Tear (LPV)	AF Ablation Procedure	Pulmonary vein tear during surgical access when dissecting the vein to place the clamp. The event was successfully treated with a suture to repair the tear.
Torn IVC Cannulation Site	AF Ablation Procedure	During surgical access, the IVC was torn during cannulation. The event was successfully treated with a patch to repair the tear.
Left Atrial Tear	AF Ablation Procedure	A left atrial tear which occurred when lifting the heart for surgical access, prior to use of the AtriCure Synergy Ablation System. The event was successfully treated with epicardial and endocardial sutures.

Table 12 demonstrates a summary of adverse events through 6 months for the ABLATE populations.

Table 12: Summary of Adverse Events by Attribution through 6 Months

Parameter [1] [2]	ABLATE N=55 # of Evts	ABLATE N=55 % (n/N) of Pts with Event	ABLATE Non-paroxysmal N=51 # of Evts	ABLATE Non-paroxysmal N=51 % (n/N) of Pts with Event
Any Adverse Event	198	90.9% (50/55)	188	94.1% (48/51)
Investigational Device	0	0.0% (0/55)	0	0.0% (0/51)
AF Procedure	8	14.5% (8/55)	8	15.7% (8/51)
Ancillary Device	1	1.8% (1/55)	1	2.0% (1/51)
General Surgical Procedure	144	87.3% (48/55)	138	90.2% (46/51)
Other Relationship	45	41.8% (23/55)	41	43.1% (22/51)
Serious Adverse Event	106	74.5% (41/55)	99	76.5% (39/51)
Investigational Device	0	0.0% (0/55)	0	0.0% (0/51)
AF Procedure	7	12.7% (7/55)	7	13.7% (7/51)
Ancillary Device	1	1.8% (1/55)	1	2.0% (1/51)
General Surgical Procedure	70	61.8% (34/55)	66	62.7% (32/51)
Other Relationship	28	32.7% (18/55)	25	33.3% (17/51)

[1] As Adjudicated or site reported if not yet adjudicated.
[2] Relationship presented hierarchically as listed in table.

Table 13 through Table 17 demonstrate the rates of device use for the Maze IV procedure per subject and per lesion.

Table 13: Ablation Procedure Summary

Parameter	ABLATE N=55 % (n/N)	ABLATE Non-paroxysmal N=51 % (n/N)	ABLATE + ABLATE AF N=69 % (n/N)	ABLATE + ABLATE AF Non-Paroxysmal N=64 % (n/N)
Ablation Procedure Summary				
Complete MAZE Procedure [1]	90.9% (50/55)	92.2% (47/51)	92.8% (64/69)	93.8% (60/64)
Lesion Set Deviations				
Incomplete Lesion Set				
Pulmonary Vein Isolation Only	1.8% (1/55)	0.0% (0/51)	1.4% (1/69)	0.0% (0/64)
Incomplete Right Atrial Ablation Lesion Set	7.3% (4/55)	7.8% (4/51)	5.8% (4/69)	6.3% (4/64)
Right Anterior freewall appendage lesion not done	7.3% (4/55)	7.8% (4/51)	5.8% (4/69)	6.3% (4/64)
Lesion from right atrial appendage to tricuspid annulus not done	1.8% (1/55)	2.0% (1/51)	1.4% (1/69)	1.6% (1/64)
Incomplete Left Atrial Ablation Lesion Set	0.0% (0/55)	0.0% (0/51)	0.0% (0/69)	0.0% (0/64)
Required Lesion Completed with Method other than Synergy Ablation Clamp				
Floor Lesion [2]	12.7% (7/55)	13.7% (7/51)	13.0% (9/69)	14.1% (9/64)
LA Appendage [2]	3.6% (2/55)	3.9% (2/51)	2.9% (2/69)	3.1% (2/64)
Roof [2]	1.8% (1/55)	2.0% (1/51)	1.4% (1/69)	1.6% (1/64)
Mitral Annulus [2]	1.8% (1/55)	2.0% (1/51)	1.4% (1/69)	1.6% (1/64)

[1] Complete MAZE IV procedure includes subjects in which required lesions were performed using methods not specified in the protocol.
[2] Alternative methods for ABLATE include Cut & Sew (6 Floor lesions), Cryoablation (2 LA appendage lesions and 1 mitral annulus lesion), and RF pen (One Floor lesion and one roof lesion). Alternative methods for ABLATE AF include Cut & Sew (2 floor lesions).

Table 14: Biatrial Lesion Details - Left Atrial Lesions

Parameter	ABLATE N=55 % (n/N)	ABLATE Non-paroxysmal N=51 % (n/N)	ABLATE + ABLATE AF N=69 % (n/N)	ABLATE + ABLATE AF Non-paroxysmal N=64 % (n/N)
Left Sided Lesions [1]				
I. Mitral Valve Connecting Lesion [2]	100.0% (54/54)	100.0% (51/51)	100.0% (68/68)	100.0% (64/64)
AtriCure Clamp	33.3% (18/54)	29.4% (15/51)	35.3% (24/68)	32.8% (21/64)
Cryo	1.9% (1/54)	2.0% (1/51)	22.1% (15/68)	23.4% (15/64)
AtriCure Clamp and AtriCure Pen	27.8% (15/54)	29.4% (15/51)	32.4% (22/68)	32.8% (21/64)
AtriCure Clamp and Cryo	29.6% (16/54)	31.4% (16/51)	8.8% (6/68)	9.4% (6/64)
AtriCure Clamp and Surgical (cut and sew)	7.4% (4/54)	7.8% (4/51)	1.5% (1/68)	1.6% (1/64)
II. Floor Line Lesion	100.0% (54/54)	100.0% (51/51)	100.0% (68/68)	100.0% (64/64)
AtriCure Clamp	87.0% (47/54)	86.3% (44/51)	86.8% (59/68)	85.9% (55/64)
AtriCure Pen	1.9% (1/54)	2.0% (1/51)	1.5% (1/68)	1.6% (1/64)
Surgical (cut and sew)	11.1% (6/54)	11.8% (6/51)	11.8% (8/68)	12.5% (8/64)
III. Roof Line Lesion	100.0% (54/54)	100.0% (51/51)	100.0% (68/68)	100.0% (64/64)
AtriCure Clamp	98.1% (53/54)	98.0% (50/51)	98.5% (67/68)	98.4% (63/64)
AtriCure Pen	1.9% (1/54)	2.0% (1/51)	1.5% (1/68)	1.6% (1/64)
IV. LAA Appendage to Pulmonary Vein	100.0% (54/54)	100.0% (51/51)	100.0% (68/68)	100.0% (64/64)
AtriCure Clamp	96.3% (52/54)	96.1% (49/51)	97.1% (66/68)	96.9% (62/64)
Cryo	3.7% (2/54)	3.9% (2/51)	2.9% (2/68)	3.1% (2/64)

[1] One subject did not undergo the Maze IV procedure.
[2] Mitral valve connecting lesion includes the full complement of the mitral valve annular lesion (lesion taken from the atriotomy to the mitral valve annulus and lesion completed on the posterior mitral valve annulus).

Table 15: Biatrial Lesion Details - Right Atrial Lesions

Parameter	ABLATE N=55 % [n/N]	ABLATE Non-paroxysmal N=51 % (n/N)	ABLATE + ABLATE AF N=69 % [n/N]	ABLATE + ABLATE AF Non-paroxysmal N=64 % (n/N)
Right Sided Lesions [1]				
I. Tricuspid Valve Annulus lesion	100.0% (54/54)	100.0% (51/51)	100.0% (68/68)	100.0% (64/64)
AtriCure Clamp	46.3% (25/54)	43.1% (22/51)	50.0% (34/68)	46.9% (30/64)
AtriCure Pen	14.8% (8/54)	15.7% (8/51)	13.2% (9/68)	14.1% (9/64)
Surgical (cut and sew)	1.9% (1/54)	2.0% (1/51)	1.5% (1/68)	1.6% (1/64)
Cryo	14.8% (8/54)	15.7% (8/51)	17.6% (12/68)	18.8% (12/64)
AtriCure Clamp and AtriCure Pen	9.3% (5/54)	9.8% (5/51)	7.4% (5/68)	7.8% (5/64)
AtriCure Clamp and Cryo	11.1% (6/54)	11.8% (6/51)	8.8% (6/68)	9.4% (6/64)
AtriCure Clamp and Surgical (cut and sew)	1.9% (1/54)	2.0% (1/51)	1.5% (1/68)	1.6% (1/64)
II. Ablation of SVC / IVC	100.0% (54/54)	100.0% (51/51)	100.0% (68/68)	100.0% (64/64)
AtriCure Clamp	100.0% (54/54)	100.0% (51/51)	100.0% (68/68)	100.0% (64/64)
III. Freewall Appendage Lesion	92.6% (50/54)	92.2% (47/51)	94.1% (64/68)	93.8% (60/64)
AtriCure Clamp	100.0% (50/50)	100.0% (47/47)	100.0% (64/64)	100.0% (60/60)
IV. Right Atrial Appendage Lesion	98.1% (53/54)	98.0% (50/51)	98.5% (67/68)	98.4% (63/64)
AtriCure Clamp	54.7% (29/53)	52.0% (26/50)	52.2% (35/67)	50.8% (32/63)
AtriCure Pen	9.4% (5/53)	10.0% (5/50)	9.0% (6/67)	9.5% (6/63)
Cryo	18.9% (10/53)	20.0% (10/50)	22.4% (15/67)	22.2% (14/63)
AtriCure Clamp and AtriCure Pen	7.5% (4/53)	8.0% (4/50)	7.5% (5/67)	7.9% (5/63)
AtriCure Clamp and Cryo	5.7% (3/53)	6.0% (3/50)	6.0% (4/67)	6.3% (4/63)
AtriCure Clamp and Surgical (cut and sew)	1.9% (1/53)	2.0% (1/50)	1.5% (1/67)	1.6% (1/63)
Surgical (cut and sew) and Cryo	1.9% (1/53)	2.0% (1/50)	1.5% (1/67)	1.6% (1/63)

[1] One subject did not undergo the Maze IV procedure.

Table 16: Biatrial Lesion Details - Optional Procedures

Parameter	ABLATE N=55 % (n/N)	ABLATE Non-paroxysmal N=51 % (n/N)	ABLATE + ABLATE AF N=69 % (n/N)	ABLATE + ABLATE AF Non-paroxysmal N=64 % (n/N)
Right atrial appendage removal [1]	1.9% (1/54)	2.0% (1/51)	1.5% (1/68)	1.6% (1/64)
Surgical (cut and sew)	100.0% (1/1)	100.0% (1/1)	100.0% (1/1)	100.0% (1/1)
Septal lesion [1]	20.4% (11/54)	21.6% (11/51)	17.6% (12/68)	18.8% (12/64)
AtriCure Clamp	63.6% (7/11)	63.6% (7/11)	66.7% (8/12)	66.7% (8/12)
Cryo	36.4% (4/11)	36.4% (4/11)	33.3% (4/12)	33.3% (4/12)

[1] One subject did not undergo the Maze IV procedure.

Table 17: Left Atrial Appendage Exclusion

Parameter	ABLATE N=55 % (n/N)	ABLATE Non-paroxysmal N=51 % (n/N)	ABLATE + ABLATE AF N=69 % (n/N)	ABLATE + ABLATE AF Non-paroxysmal N=64 % (n/N)
Left Atrial Appendage [1]				
Excised	88.9% (48/54)	88.2% (45/51)	91.2% (62/68)	90.6% (58/64)
Excluded Only	11.1% (6/54)	11.8% (6/51)	8.8% (6/68)	9.4% (6/64)

[1] One subject did not undergo the Maze IV procedure.

Additional Data Analysis

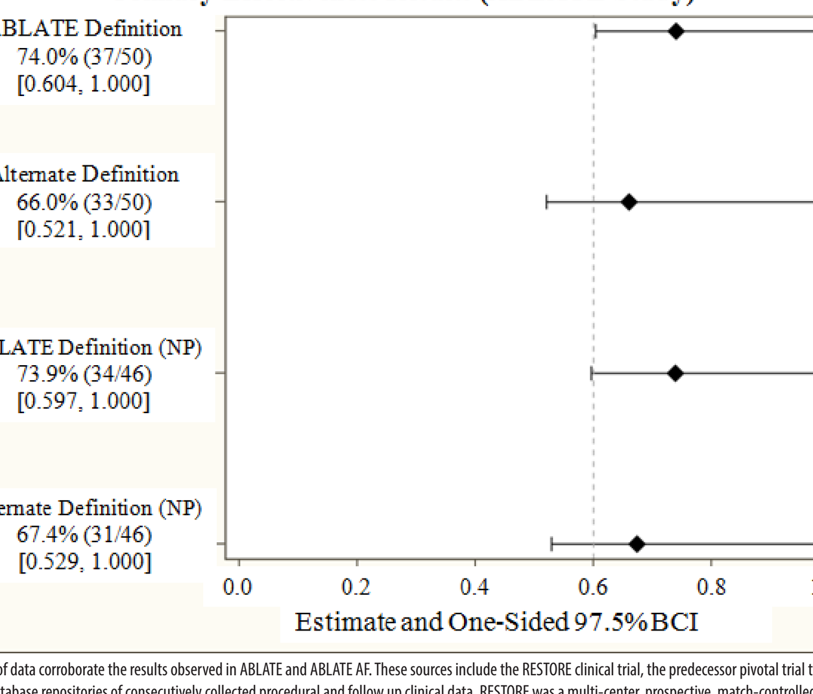
Table 18 and Figure 2 present results considering the following factors that affect interpretation of the effectiveness results. First, current definitions for freedom from atrial fibrillation would categorize subjects having any episode of AF, atrial flutter or atrial tachycardia > 30 seconds and/or subjects that were cardioverted after a 3-month blanking period as treatment failures. In addition, one subject had not completed the AAD washout at their 6-month effectiveness evaluation but was considered to be an effectiveness success based on freedom from AF at later timepoints.

Table 18: Summary of Effectiveness Endpoints for New Definition

Primary Effectiveness through 6 Months	ABLATE N=55 % (n/N) [BCI] [1]	ABLATE Non-paroxysmal N=51 % (n/N) [BCI] [1]	ABLATE + ABLATE AF N=69 % (n/N)	ABLATE + ABLATE AF Non-paroxysmal N=64 % (n/N)
Effectiveness Evaluable at 6-month Follow-up	N=50	N=46	N=62	N=57
ABLATE Definition (AF Free and Off AADs)	74.0% (37/50) [0.604, 1.00]	73.9% (34/46) [0.597, 1.00]	75.8% (47/62)	75.4% (43/57)
Alternate Definition [2]	66.0% (33/50) [0.521, 1.00]	67.4% (31/46) [0.529, 1.00]	64.5% (40/62)	64.9% (37/57)
Primary Effectiveness Failures by Alternate Definition [3]				
Failure by Rhythm	11	10	13	12
Atrial Fibrillation	(9)	(8)	(10)	(9)
Atrial Flutter	(2)	(2)	(2)	(2)
Atrial Tachycardia	(0)	(0)	(1)	(1)
Failure by AAD	6	5	9	8
Inadequate drug washout	(3)	(3)	(5)	(5)
Failure by CV between 3 and 6 Months	4	4	4	4

[1] 97.5% one-sided Bayesian Credible Interval. Beta (1,1) prior in accordance with the statistical plan.
[2] Alternate definition defined as AF free and off AADs with no Atrial fibrillation, Atrial flutter, or Atrial tachycardia > 30 seconds, AADs washed out and no cardioversion after 3 months.
[3] Overall rate cannot be computed by simple summation of counts for individual failure modes as several subjects failed by more than one mode: Late CV and AAD (1); Rhythm (AFL) and AAD (1); Late CV and Rhythm (AF) (2).

Figure 2: Forest Plot, Primary Effectiveness Success



Additional sources of data corroborate the results observed in ABLATE and ABLATE AF. These sources include the RESTORE clinical trial, the predecessor pivotal trial to ABLATE, and institutional database repositories of consecutively collected procedural and follow up clinical data. RESTORE was a multi-center, prospective, match-controlled clinical trial to evaluate the safety and effectiveness of the AtriCure Ablation System. The Washington University Institutional Database was a prospective single center registry of baseline, procedure, and follow-up data from a repository of information on all AF treated subjects at the institution. The Baylor Plano Institutional Database was a prospective single center registry of baseline, procedure, and follow-up data from a repository of information on all AF treated subjects at the institution. Table 19 and Table 20 demonstrate the data for the non-paroxysmal subjects from these sources.

Table 19: Primary Safety Endpoint, Additional Sources of Data

	ABLATE Non-Paroxysmal (N=51)	ABLATE+ ABLATE AF Non-Paroxysmal (N=64)	RESTORE (N=36)	Wash U. (N=56)	Baylor (N=8)
Primary Safety Endpoint (Acute MAE within 30 days post procedure) Frequentist Observed % (n/N	9.8% (5/51)	7.8% (5/64)	8.3% (3/36)	14.3% (8/56)	25.0% (2/8)
Death (<= 30 days or > 30 days procedure related)	3.9% (2/51)	3.1% (2/64)	5.6% (2/36)	3.6% (2/56)	12.5% (1/8)
Stroke/TIA	2.0% (1/51)	1.6% (1/64)	0.0% (0/36)	1.8% (1/56)	0.0% (0/8)
MI	0.0% (0/51)	0.0% (0/64)	0.0% (0/36)	0.0% (0/56)	0.0% (0/8)
Excessive Bleeding (>2 units blood and surgical intervention)	3.9% (2/51)	3.1% (2/64)	8.3% (3/36)	8.9% (5/56)	25.0% (2/8)

Table 20: Effectiveness Endpoints

	ABLATE Non-Paroxysmal	ABLATE+ ABLATE AF Non-Paroxysmal	RESTORE	Wash U.	Baylor
6 Month Follow-Up Assessment	N = 46	N = 57	N = 33 [1]	N = 47	N = 2
Primary Effectiveness Endpoint 6 mo. AF Free and off AADs Frequentist Observed % (n/N)	73.9% (34/46)	75.4% (43/57)	64.3% (18/28)	74.5% (35/47)	0% (0/2)
6 mo. AF Free Frequentist Observed % (n/N)	82.6% (38/46)	84.2% (48/57)	81.8% (27/33)	91.5% (43/47)	50.0% (1/2)
12 Month or Greater Follow-Up Assessment	N = 45		N = 24	N = 46	N = 3
12 mo. (or greater) AF Free and off AADs Frequentist Observed % (n/N)	62.2% (28/45)		45.8% (11/24)	84.8% (39/46)	0% (0/3)
12 mo. (or greater) AF Free Frequentist Observed % (n/N)	73.3% (33/45)		66.7% (16/24)	91.3% (42/46)	0% (0/3)

[1] Subjects off AAD's at 6 months and AF Free but not through the wash-out period are not evaluable.

Conclusions:

The results demonstrate that there is a reasonable assurance of safety and effectiveness to support the use of the AtriCure Synergy Ablation System for the treatment of persistent or longstanding persistent atrial fibrillation in patients who are undergoing open concomitant coronary artery bypass grafting and/or valve replacement or repair.

Post-Approval Study

A. Objective

The primary objective for the ABLATE Post-Approval Study (or "ABLATE PAS") was to evaluate clinical outcomes in a cohort of patients receiving treatment with the AtriCure Synergy Ablation System in performing the Maze IV procedure.

B. Study Design

The ABLATE PAS Study was a multi-center, prospective, observational study designed to evaluate the AtriCure Synergy Ablation System for continued safety and effectiveness during commercial use in a real-world setting, in patients with non-paroxysmal forms of AF who are undergoing surgical AF ablation during a concomitant open, on-pump cardiac surgery. All patients underwent a clinical assessment prior to hospital discharge and at 30 days, 4, 12, 24, and 36 months post procedure. Rhythm surveillance was obtained at 12, 24 and 36 months using a 48-hour Holter monitor (or equivalent). The use of post-operative anti-arrhythmic drugs was at the discretion of the investigators.

Key Study Endpoints

Primary Effectiveness: The proportion of patients free from AF (i.e. no episodes lasting > 30 continuous seconds duration of either Atrial Fibrillation, Atrial Flutter or Atrial Tachycardia) while off Class I and III antiarrhythmics (at least 12 weeks for amiodarone and at least 4 weeks for other class I/III AADs), at a minimum of 12, 24, and 36 months postoperatively. The study protocol had a pre-defined performance goal of 47.8% established based on the results of the ABLATE study for the evaluation of the primary effectiveness outcome at 36 months post procedure. Electrocardiographic data from 48-hour Holter, Zio Patch or PPM interrogation performed at follow-up (12, 24, and 36 months post procedure) was reviewed by an independent core lab.

Secondary Effectiveness: The proportion of patients free from AF, regardless of AAD usage at a minimum of 12, 24, and 36 months postoperatively.

Primary Safety: The proportion of patients with any serious device or ablation procedure-related adverse event within 30 days post-procedure or hospital discharge (whichever is later), excluding pacemaker implantation. The study protocol had a pre-defined performance goal of 10% derived from the combined results of the ABLATE and ABLATE AF trials for the evaluation of the primary safety outcome. All device/procedure related serious adverse events that occurred within 30 days post procedure were adjudicated by an independent Clinical Events committee.

Secondary Safety: Composite major adverse event: Serious adverse events occurring post-operatively within 30 days of procedure or hospital discharge (whichever is later) including: Death (includes deaths after 30 days or hospital discharge if death is procedure related), stroke (resulting in significant permanent disability), TIA, Myocardial infarction, and excessive bleeding (requiring >2 units of blood replacement and surgical intervention).

C. Study Population

The ABLATE PAS protocol was conducted at 50 North American centers. Of the 50 sites, 40 sites enrolled at least one subject. Participating sites were split into three categories: ABLATE AF Registry Centers (N=20), New Users (N=7), and Existing users (N=23). All participating sites successfully participated in AtriCure's training/certification program. Existing/ Current Users were users of the AtriCure Synergy Ablation System but did not participate in the ABLATE AF Registry. The intent of the ABLATE AF Registry was to provide further supportive data on the concomitant MAZE procedure with the AtriCure Synergy Ablation System. The FDA approved the transfer of the ABLATE AF Registry subjects into the ABLATE PAS protocol. New Users were defined as centers that had not performed the MAZE IV procedure or had not performed the procedure with the AtriCure Synergy Ablation System. The ABLATE PAS protocol included 7 new user centers.

The following tables represent the population enrolled in the ABLATE PAS Study. The study population included subjects who had non-paroxysmal forms of AF and were scheduled to undergo a primary open cardiac surgical procedure requiring cardiopulmonary bypass including valve surgery and/or CABG.

Patient Accountability

Table 21 documents the accountability and disposition of enrolled subjects.

Table 21 Patient Accountability

Patients Status	Total [1]
Patients Consented [n]	365
Patients Enrolled [n]	365
Patients Treated with Ablation Procedure [1]	363
Study Exit Timing	
<=30 days (or hospital discharge)	6.3% (23/365)
> 30 days, < 4 months	3.8% (14/365)
>= 4 months, < 12 months	6.8% (25/365)
>= 12 months, < 24 months	10.7% (39/365)
>= 24 months	72.3% (264/365)
Time to Study Exit (days)	
Mean +/- SD (N)	846.8 +/- 406.5 (365)
Median	1073.0
Min, Max	0.0, 1346.0
Reason for Early Study Exit	
Deceased	62
Lost to follow-up	13
Refused additional follow-up	36
Other	4

[1] One procedure aborted. One patient exited day of procedure due to Exclusion #3 (Preoperative need for an intra-aortic balloon pump or intravenous inotropes).

Atrial Fibrillation Classification

Table 22 summarizes data on the types of AF the study subjects had at baseline. The data are presented for all enrolled subjects and for the indicated (longstanding persistent and persistent) subjects. In the ABLATE PAS population, there was 1 subject with paroxysmal AF and 364 subjects with persistent or long-standing persistent AF.

Table 22: Atrial Fibrillation Classification [1]

Parameter	Total N=365
Study Entry AF Status [1]	
Type of AF [% (n/N)]	
Paroxysmal [2]	0.3% (1/365)
Persistent (7 days continuous) [3]	56.7% (207/365)
Longstanding Persistent (1 year continuous) [4]	43.0% (157/365)

[1] Based on Heart Rhythm Society AF ablation consensus statement. Calkins, H., et al., HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation Europace, 2007. 9(6): p. 335-79.
[2] Paroxysmal AF is defined as recurrent AF (>=2 episodes) that terminates spontaneously within 7 days.
[3] Persistent AF is defined as AF which is sustained beyond seven days or lasting less than seven days but necessitating pharmacologic or electrical cardioversion.
[4] Longstanding persistent AF is defined as continuous AF of greater than one-year duration.

Baseline Characteristics

Table 23 summarizes the demographics and other baseline characteristics of the subjects enrolled in the study.

Table 23: Baseline Characteristics

Parameter	Total N=365 (%)
Age (years)	69.8 ± 9.3
Male	217 (59.5)
Caucasian	331 (90.7)
New York Heart Association functional class III or IV	146 (40.0)
Prior cardiac surgery (reoperation)	47 (12.9)
Renal failure	44 (12.1)
Chronic Obstructive Pulmonary Disease	72 (19.7)
Diabetes	113 (31.0)
Body mass index (kg/m^2)	30.5 ± 6.4
Preoperative pacemaker	36 (9.9)
CHADS$_2$ Score Risk Category	
Low Risk (score=0)	0
Medium Risk (score=1)	22 (6.1)
High Risk (score>=2)	340 (93.9)
Not Assessed	3 (0.8)
Prior CVA/Stroke	41(11.2)

Atrial Fibrillation History

Table 24 summarized the atrial fibrillation history of the subjects enrolled in the study

Table 24: Atrial Fibrillation History

Parameter	Total N=365
History of AF > 12 months	63.8% (233/365)
Time since AF onset (months)	
Mean +/- SD (N)	60.0 +/- 84.2 (361)
Median	28.7
Percentile: 25th, 75th	4.5, 82.9
Min, Max	0.10, 846.81
Current AF Status at Time of Surgery	
in AF	87.9% (321/365)
Cardioversion Attempted prior to bypass in OR	16.2% (59/365)
Cardioversion Successful [1]	55.9% (33/59)

[1] Based on number of subjects with attempted Cardioversion.

D. Surgical Procedure

Table 25 summarizes the surgical procedure by procedure type.

Table 25: Surgical Procedure - Procedure Type

Parameter	Total N=363 % (n/N)
Surgical Procedure Type(s)	
CABG only	17.9% (65/363)
Valve Surgery	35.8% (130/363)
Mitral Valve Repair/Replacement	24.5% (89/363)
Aortic Valve Repair/Replacement	9.9% (36/363)
Tricuspid Valve Repair/Replacement	1.4% (5/363)
Double Valve Surgery	23.4% (85/363)
Aortic & Mitral	3.3% (12/363)
Mitral & Tricuspid	15.7% (57/363)
Aortic & Tricuspid	4.4% (16/363)
CABG and Valve Surgery	16.3% (59/363)
CABG + Mitral Valve Repair/Replacement	10.2% (37/363)
CABG + Aortic Valve Repair/Replacement	5.5% (20/363)
CABG + Tricuspid Valve Repair/Replacement	0.6% (2/363)
CABG + Double Valve Surgery	6.6% (24/363)
Aortic & Mitral	0.6% (2/363)
Mitral & Tricuspid	5.2% (19/363)
Aortic & Tricuspid	0.8% (3/363)
Any Mitral Valve Surgery	63.4% (230/363)

Table 26 summarizes the lesion sets and energy source.

Table 26 Lesion Set and Energy Source

Lesion	Devices Used	ABLATE PAS: Number of Applications (mean+/-SD)	ABLATE PAS: Sample Size [1]
Pulmonary Vein Isolation	AtriCure Synergy Ablation Clamp	Left Pulmonary Veins: Synergy Activations: 4 ± 2	356
		Right Pulmonary Veins: Synergy Activations: 4 ± 2	354
Box Lesion (Roof and Floor Lines)	AtriCure Synergy Ablation Clamp	Roof: Synergy Activations: 3 ± 1	300
		Floor: Synergy Activations: 3 ± 1	310
Mitral Valve Annulus Lesion [2]	AtriCure Synergy Ablation Clamp	Synergy Clamp	277
	AtriCure CryoAblation System	Cryoprobe	282
	AtriCure Bipolar Pen	Bipolar Pen	10
Left Atrial Appendage Lesion	AtriCure Synergy Ablation Clamp	Synergy Activations: 2 ± 1	92
Tricuspid Valve Lesion [2]	AtriCure Cryoablation System, or the AtriCure Bipolar Pen is used to complete the lesion at the annulus.	Synergy Clamp	143
		Cryoprobe	253
		Bipolar Pen	10
Superior Vena Cava to Inferior Vena Cava Lesion	AtriCure Synergy Ablation Clamp	SVC: Synergy Activations: 2 ± 1	300
		IVC: Synergy Activations: 2 ± 1	302
Right Atrial Free Wall Appendage Lesion	AtriCure Synergy Ablation Clamp	Synergy Activations: 2 ± 1	245
Right Atrial Appendage to Tricuspid Annulus Lesion [2]	AtriCure Synergy Ablation Clamp	Synergy Clamp	111
	AtriCure CryoAblation System	Cryoprobe	186
	AtriCure Bipolar Pen	Bipolar Pen	7

[1] Sample size represents the number of subjects out of the 363 total subjects that used the clamp for each lesion location.
[2] Number of Synergy Activations and Cryo Freezes were not recorded separately in the PAS study

E. Rhythm Surveillance Monitoring during follow-up

The presence or absence of AF was assessed in each treatment subject pre-discharge (not more than 48 hours prior to discharge), at the 30 day, and 4 months follow-up using a 12 lead ECG. Rhythm status was further evaluated at 12, 24, and 36 months post-operative using a 48-hour Holter Monitor, Zio Patch, or Pacemaker Interrogation. Compliance to study-required rhythm monitoring at the 12-month, 24-month and 36-month visits was 97.5% (271/278), 98.8% (242/245), and 98.3% (228/232), respectively, in the subjects who received treatment and were still enrolled in the study at the visit when subject's rhythm status was evaluated.

F. Results

Primary Effectiveness

The primary effectiveness outcome of the study was the proportion of patients free from AF (i.e. no episodes lasting > 30 continuous seconds duration of either Atrial Fibrillation, Atrial Flutter or Atrial Tachycardia) while off Class I and III antiarrhythmic at a minimum of 12, 24 and 36 months postoperatively. Per study protocol, the primary effectiveness outcome was analyzed on the evaluable population that consisted of all subjects who received treatment and were still enrolled in the study at the visit when the outcome was evaluated.

Table 27 summarizes Primary effectiveness outcomes. The primary effectiveness success was achieved in 62.9% of the evaluable population at 36 months with a lower 95% confidence interval of 56.4%, which was greater than the pre-defined performance goal of 47.8%. Therefore, the primary effectiveness endpoint was met.

Table 27: Primary Effectiveness Outcomes

	12 months % (n/N) [1]	24 months % (n/N) [1]	36 months % (n/N) [1]	p-value [5]
Primary Success [2]	66.2% (184/278)	64.9% (159/245)	62.9% (146/232)	<0.0001
90% CI [3]	(61.2, 70.9)	(59.6, 70.0)	(57.4, 68.2)	
95% CI [4]	(60.3, 71.7)	(58.6, 70.9)	(56.4, 69.2)	
Failure by AAD	14.0% (39/278)	12.7% (31/245)	11.2% (26/232)	
90% CI [3]	(10.7, 17.9)	(9.3, 16.7)	(8.0, 15.2)	
Failure by Holter/Pacemaker Interrogation	16.5% (46/278)	19.6% (48/245)	22.4% (52/232)	
90% CI [3]	(13.0, 20.7)	(15.5, 24.2)	(18.0, 27.4)	
Type of Arrhythmia [6]				
Atrial Fibrillation	12.9% (36/278)	11.4% (28/245)	15.5% (36/232)	
Atrial Flutter	2.9% (8/278)	6.1% (15/245)	5.6% (13/232)	
Atrial Tachycardia	0.7% (2/278)	2.0% (5/245)	1.3% (3/232)	
Failure by both AAD and Holter/Pacemaker Interrogation	3.2% (9/278)	2.9% (7/245)	3.4% (8/232)	
90% CI [3]	(1.7, 5.6)	(1.4, 5.3)	(1.7, 6.1)	
Type of Arrhythmia [6]				
Atrial Fibrillation	2.5% (7/278)	2.4% (6/245)	0.9% (2/232)	
Atrial Flutter	0.7% (2/278)	0.4% (1/245)	1.3% (3/232)	
Atrial Tachycardia	0.0% (0/278)	0.0% (0/245)	1.3% (3/232)	

Primary Safety Outcome

The primary safety outcome of the study was the proportion of patients with any serious device or ablation procedure-related adverse event within 30 days post-procedure or hospital discharge (whichever is later). Per study protocol, the primary safety analysis population consisted of all subjects who had received the AtriCure Synergy Ablation System for treatment of non-paroxysmal AF in the setting of a concomitant cardiac surgical procedure. Subjects were considered to have received treatment once a device was opened, regardless of whether or not the opened device passed the skin.

Table 28 summarizes the safety outcomes. The primary safety event rate was 1.1% (4/365) with an upper 95% confidence interval of 2.8%, which was smaller than the pre-defined performance goal of 10%. Therefore, the primary safety endpoint was met.

Table 28: Primary Safety Outcome [1]

Parameter	# of Events	% (n/N) of Subjects with Event	95% CI [2]	p-value [3]
Serious Device or Procedure Related Adverse Event (excluding pacemaker implantation) within 30 days	4	1.1% (4/365)	(0.3, 2.8)	<0.0001
AtriCure Device	0	0.0% (0/365)	-	
AF Procedure	4	1.1% (4/365)	(0.3, 2.8)	

[1] As Adjudicated.
[2] 95% confidence interval calculated using the Clopper-Pearson method.
[3] P-value calculated using an exact binomial test at the one-sided alpha=0.05 level against the null hypothesis $\pi \geq 10.0\%$.

The four safety events include the following:

- Post-procedure ventricular tachycardia with hypotension requiring cardioversion.
- Sinus node dysfunction and asystole post-procedure requiring new pacemaker implant.
- Left posterior pulmonary vein tear occurring during procedure requiring surgical correction.
- Significant blood loss during procedure requiring intra-aortic balloon pump placement and replacement of blood products.

Secondary Effectiveness Endpoint

Per study protocol, the secondary effectiveness endpoint was defined as freedom from AF regardless of antiarrhythmic drug usage. The secondary success was 79.7% (216/271) [95% CI: 74.4%, 84.3%] at 12-months, 77.3% (187/242) [95% CI: 75.1%, 82.4%] at 24-months and 73.7% (168/228) [95% CI: 67.5%, 79.3%] at 36-months.

Table 29 summarizes the secondary effectiveness outcome.

Table 29 Secondary Effectiveness Outcome

Secondary Effectiveness Outcomes	12 months % (n/N) [1]	24 months % (n/N) [1]	36 months % (n/N) [1]
Free from AF on or off AADs	79.7% (216/271)	77.3% (187/242)	73.7% (168/228)
95% CI [2]	(74.4, 84.3)	(75.1, 82.4)	(67.5, 79.3)
Free from AF off AADs	67.9% (184/271)	65.7% (159/242)	64.0% (146/228)
95% CI [2]	(62.0, 73.4)	(59.4, 71.7)	(57.4, 70.3)
Free from AF on AADs	11.8% (32/271)	11.6% (28/242)	9.6% (22/228)
95% CI [2]	(8.2, 16.3)	(7.8, 16.3)	(6.2, 14.2)

[1] Denominators are subjects who are evaluable for effectiveness outcome.
[2] 95% confidence interval calculated using the Clopper-Pearson method.

Secondary Safety Endpoint

The secondary safety outcome was a composite of Major Adverse Events (MAE): serious adverse events occurring postoperatively within 30 days post-procedure or hospital discharge (whichever is later) including; Death (include deaths after 30 days or hospital discharge if the death is procedure related), Stroke (resulting in significant permanent disability), TIA, Myocardial infarction and Excessive bleeding (requiring >2 units of blood replacement and surgical intervention)

Table 30 shows the composite secondary safety outcomes. A total of 36 secondary safety outcome events occurred in 32 (8.8%) subjects. Death was the most common, in 5.5% (20/365) subjects, all occurring <= 30 days (or prior to discharge), followed by excessive bleeding in 1.9% (7/365) subjects and stroke in 1.6% (6/365) subjects. Myocardial infarction occurred in less than 1% of subjects. These events are well known complications of cardiac surgery and the rates observed are consistent with what would be expected in this study population.

Table 30 Secondary Safety Outcome [1]

Parameter	# of Events	% (n/N) of Subjects with Event	95% CI [2]
Secondary Safety Events (Acute MAE within 30 days post procedure)	36	8.8% (32/365)	(6.1, 12.2)
Death	20	5.5% (20/365)	(3.4, 8.3)
=<30 days (or prior to discharge)	20	5.5% (20/365)	(3.4, 8.3)
>30 days, procedure related	0	0.0% (0/365)	-
Stroke/TIA	6	1.6% (6/365)	(0.6, 3.5)
Stroke (with significant permanent disability)	6	1.6% (6/365)	(0.6, 3.5)
TIA	0	0.0% (0/365)	-
MI	3	0.8% (3/365)	(0.2, 2.4)
Excessive Bleeding (>2 units blood and surgical intervention)	7	1.9% (7/365)	(0.8, 3.9)

[1] As Adjudicated if available, else as reported by the site.
[2] 95% confidence interval calculated using the Clopper-Pearson method.

Deaths

A total of 62 subjects died during follow-up. None of the deaths were attributed to the study device or ablation procedure.

Subgroup Analysis

Several subgroup analyses were performed per the study protocol to evaluate the poolability of the primary endpoints. The primary effectiveness and safety outcomes were similar by gender, cardiac surgical procedure type, and user experience (existing users vs new users). Subjects with persistent AF had a greater effectiveness success at 36 months compared to subjects with longstanding persistent AF (Table 31). Additionally, the rate of device related and procedure related SAEs did not vary across cardiac surgery type. Race showed statistically significantly different results, likely due to small numbers of non-Caucasian subjects. Black subjects had a higher rate of serious device or procedure related AEs within 30 days (11.8% of subjects) as compared to subjects of other races (0-0.6%, p=0.039). Given that only 17 black subjects were treated in the study and there were 2 primary safety events, cautious interpretation of this finding is warranted. However, higher mortality rates post cardiac surgery in blacks and minorities have been observed (Khera et al. Racial disparities in outcomes after cardiac surgery: the role of hospital quality. Curr Cardiol Rep 2015; May;17(5):29), likely associated with differences in biology, comorbid health conditions, socioeconomic background, and quality of hospital care. When adjusting for these factors, race was frequently not identified to be independently predictive. (REF- [Wu et al. Circulation 2012 April "A risk score for predicting long-term mortality following coronary artery bypass graft surgery".doi.org/10.1161/CIRCULATIONAHA.111.055939]; [Rumsfeld et al. JACC 2002 Nov Vol 40, Issue 10 "The impact of ethnicity on outcomes following coronary artery bypass graft surgery in the Veterans Health Administration". DOI: 10.1016/S0735-1097(02)02485-3]; [Lucas et al. "Race and surgical mortality in the United States". Ann Surg. 2006;243(2):281-286]).

Table 31 summarizes the primary safety and effectiveness outcomes by AF type.

Table 31

Primary Safety and Effectiveness Outcomes by AF Type

Outcome	Persistent AF [1] # of Events	Persistent AF [1] % (n/N) of Subjs with Event	Longstanding Persistent [2] # of Events	Longstanding Persistent [2] % (n/N) of Subjs with Event	p-value [4]
Primary Safety: [3]					
Serious Device or Procedure Related Adverse Event (excluding pacemaker implantation) within 30 days	3	1.5% (3/207)	1	0.6% (1/157)	0.6737
Investigational Device	0	0.0% (0/207)	0	0.0% (0/157)	
AF Procedure	3	1.5% (3/207)	1	0.6% (1/157)	
Primary Effectiveness:					
Primary Success: Free from AF while off AADs at 36 months		69.9% (102/146)		51.2% (44/86)	0.005
Failure by AAD		9.6% (14/146)		14.0% (12/86)	
Failure by Holter/Pacemaker Interrogation [3] 15.8% (23/146)				33.7% (29/86)	
Failure by both AAD and Holter/Pacemaker Interrogation		4.8% (7/146)		1.2% (1/86)	

[1] Persistent AF is defined as AF which is sustained beyond seven days or lasting less than seven days but necessitating pharmacologic or electrical cardioversion.
[2] Longstanding persistent AF is defined as continuous AF of greater than one-year duration.
[3] As Adjudicated.
[4] P-value calculated using Fisher's Exact test.
[5] Rhythm surveillance was obtained at 12, 24- and 36- months using a 48-hour Holter monitor (or equivalent).

Adverse Events

An adverse event was any untoward medical occurrence (signs, symptoms, abnormal laboratory findings) in a patient regardless of relationship to the device or procedure. Each adverse event was evaluated to be either anticipated or unanticipated as described below. The sites reported all adverse events that occurred in the study.

Table 32 summarizes all the adverse events that occurred on the study.

Table 32: Summary of Adverse Events – Cumulative[1]

Parameter	In Hospital N=365 # of Events	In Hospital N=365 % (n/N) of Subjects with Event	Cumulative to 30 days N=365 # of Events	Cumulative to 30 days N=365 % (n/N) of Subjects with Event	All Events across All Visits N=365 # of Events	All Events across All Visits N=365 % (n/N) of Subjects with Event
Any Adverse Event	928	75.1% (274/365)	1108	83.3% (304/365)	2352	95.1% (347/365)
AtriCure Device	2	0.5% (2/365)	2	0.5% (2/365)	2	0.5% (2/365)
AF Procedure [2]	20	4.9% (18/365)	22	5.5% (20/365)	24	5.8% (21/365)
Concomitant Surgical Procedure	568	62.7% (229/365)	626	66.6% (243/365)	670	67.9% (248/365)
Other Relationship	348	45.8% (167/365)	469	58.4% (213/365)	1668	87.1% (318/365)
Serious Adverse Event	287	41.4% (151/365)	372	53.7% (196/365)	916	79.2% (289/365)
AtriCure Device	0	0.0% (0/365)	0	0.0% (0/365)	0	0.0% (0/365)
AF Procedure [2]	6	1.6% (6/365)	6	1.6% (6/365)	8	2.2% (8/365)
Concomitant Surgical Procedure	168	26.8% (98/365)	200	32.6% (119/365)	222	35.6% (130/365)
Other Relationship	133	20.3% (74/365)	166	30.4% (111/365)	687	66.3% (242/365)

[1] As Adjudicated if available, else as reported by the site. Note: Site reported events may be counted in more than one relationship category.
[2] Includes AF procedure related events requiring permanent pacemaker implantation which are not primary safety outcome events.

Pacemaker Implantation

Table 33 demonstrates the pacemaker implantations across all visits.

Table 33: Pacemaker Implantation Across Visits

Parameter	In Hospital N=365 % (n/N)	Cumulative to 30 days N=365 % (n/N)	All Pacemaker Implantation [1] N=365 % (n/N)
Pacemaker Pre-procedure	9.9% (36/365)	9.9% (36/365)	9.9% (36/365)
Post Procedure Permanent Pacemaker Implantation	14.6% (48/329)	15.2% (50/329)	23.7% (78/329)
Does not meet requirements for adjudication	0.0% (0/329)	0.0% (0/329)	8.5% (28/329)
Causes for Post-Procedure Pacemaker Implantation			
AV Conductional Abnormality	4.9% (16/329)	4.9% (16/329)	4.9% (16/329)
Sino Atrial Node Abnormality	7.3% (24/329)	7.9% (26/329)	7.9% (26/329)
Combination of AV Conductional Abnormality and Sinal Atrial Node Abnormality	2.4% (8/329)	2.4% (8/329)	2.4% (8/329)

[1] Includes pacemaker implantation where actual date of implant is unknown.

G. Study Strengths and Weaknesses:

Study Strengths

- This large, prospective, multi-center study was conducted in a less selected patient population with non-paroxysmal AF treated at sites with and without prior experience in the use of the study device to perform a Maze procedure. Therefore, the results of the study represented more closely the outcomes of concomitant surgical ablation of non-paroxysmal AF using the AtriCure Synergy Ablation System in the real world compared to previous controlled studies.
- The study had sufficient statistical power to test the primary safety and effectiveness hypotheses.
- The study provided long term (3-year) safety and effectiveness data of concomitant surgical ablation of non-paroxysmal AF.
- The primary safety events were adjudicated by an independent committee and thus increased the rigor for detecting acute serious device or ablation procedure-related adverse events.
- Rhythm surveillance monitoring data collected during follow-up were reviewed by a core lab.

Study Weaknesses

- This was a single arm study comparing primary endpoints to pre-specified performance goals. There was no control group in which patients received no surgical ablation for AF in addition to their concomitant cardiac surgeries. Therefore, the treatment effect attributable to the concomitant surgical ablation could not be ascertained.
- This study did not employ continuous rhythm monitoring but mainly relied on periodic Holter monitoring for the detection of AF recurrence. Also, effectiveness success at 12, 24, and 36 months post procedure was determined based only on subject's anti-arrhythmic drug use and rhythm status at the time of each follow-up visit. Moreover, the study protocol did not require discontinuation of class I/III anti-arrhythmic drugs post procedure As a result, the success rates of concomitant surgical AF ablation reported in the study may be overestimated due to the likelihood of missing episodes of AF occurring outside of the monitoring periods and the potential confounding effect of Class I/III anti-arrhythmic drugs on effectiveness outcomes.

H. Conclusions

- The 3-year effectiveness success, defined as freedom of AF recurrence off class I/III anti-arrhythmic drugs at the 36-month follow-up visit, was achieved in 62.9% of the evaluable population with a lower 95% confidence interval of 56.4%, and thus met the pre-defined effectiveness performance goal of 47.8%.
- The primary safety endpoint of 30-day serious device or ablation procedure-related adverse event rate was 1.1% (4/365) with an upper 95% confidence interval of 2.8%, and thus met the pre-defined safety performance goal of 10%.
- There were no device-related serious adverse events or device malfunctions.
- The secondary safety endpoint of 30-day major adverse events rate and 30-day mortality (8.8% and 5.5%, respectively) were comparable to that observed in the ABLATE IDE study.
- The 30-day pacemaker implantation rate of 15.2% observed in this study compared favorably to that observed in the ABLATE IDE study and was similar to that reported in a recent randomized controlled trial (Gillinov AM et al. Surgical Ablation of AF during mitral-valve surgery. NEJM 2015; 372: 1399-409) in which the addition of surgical AF ablation to mitral-valve surgery was associated with a significant increase in the need for implantation of a permanent pacemaker.

HOW SUPPLIED

The Synergy Ablation System is supplied as a STERILE clamp and is for single patient use only. Sterility is guaranteed unless the package is opened or damaged. Do not resterilize. The other components (ASU, MAG, and ASB3) are not sterile and may be reused

RETURN OF USED PRODUCT

If for any reason these products must be returned to AtriCure, a return goods authorization (RGA) number is required from AtriCure prior to shipping.

If the products have been in contact with blood or body fluids, they must be thoroughly cleaned and disinfected before packing. They should be shipped in either the original carton or an equivalent carton, to prevent damage during shipment; and they should be properly labeled with an RGA number and an indication of the biologically hazardous nature of the contents of shipment.

Instructions for cleaning and materials, including appropriate shipping containers, proper labeling, and an RGA number may be obtained from AtriCure, Inc.

CAUTION: It is the responsibility of the health care institution to adequately prepare and identify the products for shipment.

DISCLAIMER STATEMENTS

Users assume responsibility for approving the acceptable condition of this product before it is used, and for ensuring that the product is only used in the manner described in these instructions for use, including, but not limited to, ensuring that the product is not re-used.

Under no circumstances will AtriCure, Inc. be responsible for any incidental, special or consequential loss, damage, or expense, which is the result of the deliberate misuse or re-use of this product, including any loss, damage, or expense which is related to personal injury or damage to property.

This Instruction for Use describes the procedures for proper use of the products. Any deviation from these procedures, which may compromise the function of the products, is the responsibility of the user.

Glossary of Symbols Used in the Product Labeling:

	Non-Pyrogenic		Caution
STERILE EO	Sterilized by Ethylene Oxide	Rx ONLY	Caution: Federal Law (US) restricts this device to sale by or on the order of a physician
	Single Use Only		Follow instructions for use
	Use by Date	LATEX	Not made with Natural Rubber Latex
LOT	Lot Number		Do Not Resterilize
	Do Not Use if the package is damaged		Manufacturer

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