

Deaths

A total of 0 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 possibility of the primary endpoints. The primary effectiveness and safety outcomes were similar by gender, cardiac surgical procedure type, and user experience (exiting 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 (0-6.6%, p=0.029). 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 (Ohora et al. Racial disparities in outcomes after cardiac surgery: the role of hospital quality. *Curr Cardiol Rep* 2015, May; 17(5):29). It is 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. (JEF - Wu et al. *Circulation* 2012 April 9; 126:16-23) A risk score for predicting long-term mortality following coronary artery bypass graft surgery*doi.org/10.1161/CIRCULATIONAHA.111.055939L | Burnsfield et al. *JACC* 2002 Nov 19; 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)0465-3*; [Lacuz 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**		Longstanding Persistent AF**		p-value**
	# of Events	% (n/N) of Subjects with Event	# of Events	% (n/N) of Subjects with Event	
Primary Safety:††					
Serious Device or Procedure Related Adverse Event (excluding pacemaker implantation) within 30 days	3	1.5% (3/207)	1	6.6% (1/157)	0.6737
Investigational Device	0	0.0% (0/207)	0	0.0% (0/157)	
All Procedures	3	1.5% (3/207)	1	6.6% (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†††		5.0% (7/146)		13.7% (29/86)	
Failure by both AAD and Holter/Pacemaker Interrogation		4.8% (7/146)		1.2% (1/86)	

** Persistent AF is defined as AF which is sustained beyond seven days or lasting less than seven days but necessitating pharmacologic or electrical cardioversion.
 †† Longstanding persistent AF is defined as continuous AF of greater than one year duration.
 ††† As Adjusted.
 †††† Pacemaker status using Fisher's Exact Test.
 ††††† 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†

Parameter	In Hospital N=365		Cumulative to 30 days N=365		All Events across All Visits N=365	
	# of Events	% (n/N) of Subjects with Event	# of Events	% (n/N) of Subjects with Event	# of Events	% (n/N) of Subjects with Event
All Adverse Events	153	42.2%	153	42.2%	153	42.2%
Device Related	14	3.8%	14	3.8%	14	3.8%
All Procedure-Related	14	3.8%	14	3.8%	14	3.8%
Other (Surgical) Procedure	14	3.8%	14	3.8%	14	3.8%
Other (Medical) Procedure	14	3.8%	14	3.8%	14	3.8%
Other Adverse Event	139	38.4%	139	38.4%	139	38.4%
AF Recurrence	140	38.4%	140	38.4%	140	38.4%
AF Recurrence	140	38.4%	140	38.4%	140	38.4%
Concomitant Surgical Procedure	140	38.4%	140	38.4%	140	38.4%
Other (Medical) Procedure	140	38.4%	140	38.4%	140	38.4%
Other (Medical) Procedure	140	38.4%	140	38.4%	140	38.4%

† 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		Cumulative to 30 days N=365		All Pacemaker Implantation** N=365	
	# of Events	% (n/N)	# of Events	% (n/N)	# of Events	% (n/N)
Need for procedure	15	4.1%	15	4.1%	15	4.1%
Need for permanent Pacemaker Implantation	15	4.1%	15	4.1%	15	4.1%
Other (Medical) Procedure	15	4.1%	15	4.1%	15	4.1%
Other (Medical) Procedure	15	4.1%	15	4.1%	15	4.1%

** 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 (0.8% 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 (Gillman 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 (AS3 and ASE3) 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
	Sterilized by Ethylene Oxide		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		Not made with Natural Rubber Latex
	Lot Number		Do Not Resterilize
	Do Not Use if the package is damaged		Manufacturer