AtriCure

Instructions for Use

EPi-Sense ST® Guided Coagulation System

 # EPiST

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Rx ONLY

⚠Caution: Federal law (US) restricts this device to sale by or on the order of a physician.

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DEVICE SETUP

Product Description

Components of the Guided Coagulation System:

1. **EPiST** 3cm EPi-Sense Guided Coagulation System Device (sterile, for single-use only)

ACCESSORIES **PROVIDED SEPARATELY**:

2. **CS-3000** nContact RF Generator plus accessories, Non-Sterile, Reusable (under separate IFU) OR **MAG** RF Generator, Non-Sterile, Reusable (under separate IFU)
3. **CSK-2030** nContact Sensing Cable, Non-Sterile, Reusable (under separate IFU)
4. **CSK-2060** nContact RF Cable, Sterile, Single Use (under separate IFU)
5. **CSK-6130, CSK 6131** – nContact Cannula– Sterile, Single Use (under separate IFU)
6. Indifferent Patient Return Electrode (Ground Pad)

The EPi-Sense ST Guided Coagulation Device is not made with natural rubber latex and is PVC-free.

Product Features

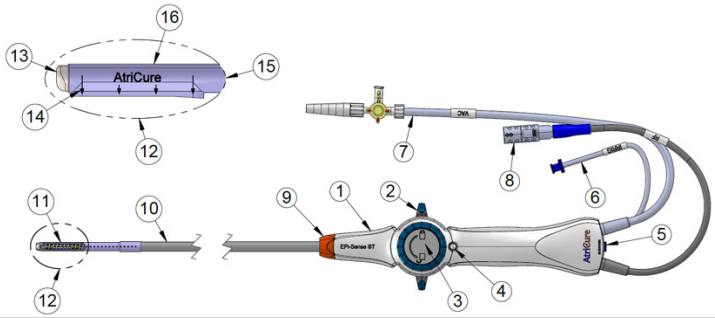


FIG. 1. GENERAL COAGULATION DEVICE KEY FEATURES

[1] Handle
[2] Steering Lever
[3] Tension Control Knob
[4] Indicator Light
[5] Guidewire Port
[6] Perfusion Tubing with Luer Connection (IRRIG)
[7] Vacuum Tube Connector (VAC)
[8] CSK-2060 RF Cable Connector
[9] Nose Cone
[10] Main Shaft
[11] Distal Shell
[12] Coagulation Ablation Electrode and Sensing Electrodes
[13] Guide Tube Opening
[14] Locator Arrows (1cm spacing)
[15] Vacuum Lumen
[16] Insulative Covering

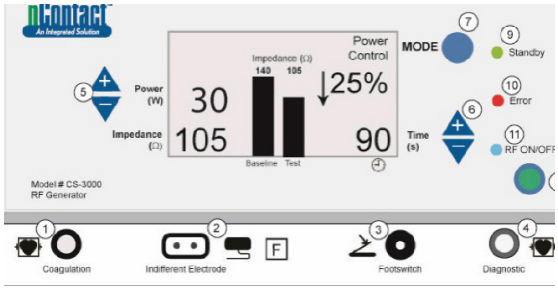


FIG. 2.A GENERAL COAGULATION DEVICE KEY FEATURES

[1] CSK-2060 RF Cable Connection
[2] Indifferent, Dispersive Electrode (Ground Pad) Connection
[3] Footswitch Connection
[4] Diagnostic Device Connection
[5] Power Adjustment
[6] Time Adjustments
[7] Mode button
[8] RF ON/OFF Button
[9] Standby Mode LED
[10] Error LED
[11] RF LED

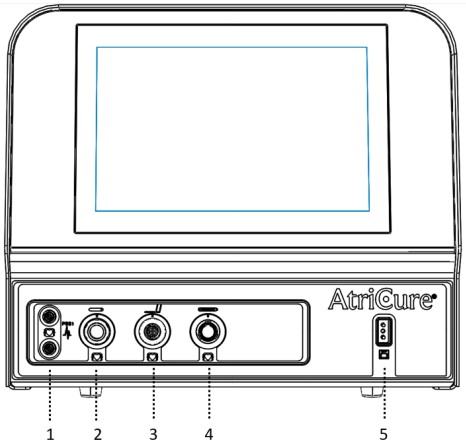


FIG. 2.B GENERAL COAGULATION DEVICE KEY FEATURES

[1] Sense-Pace Input (MLP)
[2] Pens Receptacle
[3] Clamp Receptacle
[4] EPi-Sense Receptacle
[5] Return Electrode Receptacle

Indications:

The EPi-Sense ST Coagulation Device is intended for the treatment of symptomatic long-standing persistent atrial fibrillation (continuous atrial fibrillation greater than 12 months duration) when augmented in a hybrid procedure with an endocardial catheter listed in the instructions for use, in patients:

- who are refractory or intolerant to at least one Class I and/or III antiarrhythmic drug (AAD); and,
- in whom the expected benefit from rhythm control outweighs the potential known risks associated with a hybrid procedure such as delayed post-procedure inflammatory pericardial effusions.

Contraindications:

The EPi-Sense ST Coagulation Device is contraindicated for use in:

- Patients with presence of left atrial thrombus, a systemic infection, active endocarditis, or another infection local to the surgical site at the time of surgery.
- Patients with Barrett's Esophagitis.

⚠ WARNINGS ⚠

Physicians should consider post-operative anti-inflammatory medication to decrease the potential for post-operative pericarditis and/or delayed post-procedure inflammatory pericardial effusions

Physicians should obtain post-procedural imaging (i.e. 1-3 weeks post-procedure) for detection of post-procedure inflammatory pericardial effusions.

The coagulation device utilizes preset power and time settings; adjustment of these settings may result in excess or inadequate energy transmission.

Physicians should consider post-operative proton pump inhibitors (PPIs) to decrease the potential for post-operative esophageal irritations.

The EPi-Sense ST Coagulation Device should only be used under direct visualization. Care should be taken to visualize the devices and/or guidewire components when in the body, during introduction and/or removal from the Cannula. Always fully retract devices and components prior to insertion and removal in order to avoid inadvertent tissue damage with the devices and or guidewire.

When inserting or retracting cannula from body, ablation device and standard 0.035" guidewire should NOT be extended beyond tip of cannula.

Before advancing device out of the cannula, ensure deployment path is large enough to avoid tissue damage.

⚠ WARNINGS ⚠

Excessive flexing and/or improper manipulation of the EPi-Sense ST Coagulation Device with surgical tools can result in damage to the device.

Care should be taken to ensure that the device is not in contact with tissue that is not going to be ablated (e.g. vascular and nerve tissue), in order to avoid inadvertent tissue damage.

To avoid unintentional ablation, always ensure the device or device combined with optional guidewire is oriented toward the desired ablation location.

Avoid contact with other surgical instruments, scopes, staples, or other objects while coagulating. Inadvertent contact with objects while coagulating could lead to conduction of RF energy or heat and unintentional ablation of tissues in contact with those objects.

The device is provided sterile and is intended for single patient use only. Do not reprocess or reuse. Reuse can cause damage to device, patient injury, and/or the communication of infectious disease(s) from one patient to another.

Do not scrape or scratch off the gold surface of the sensing electrodes when cleaning the RF ablation electrode to avoid an adverse reaction due to copper exposure to the patient.

To avoid unintentional ablation, care should be taken to ensure overlapping structures are separated and thermally isolated when anatomy allows.

Inspect all devices and packaging prior to use. If any breach of the packaging is found the sterility of the product cannot be ensured which poses a risk of patient injury. Do not use product if breach is found.

The risk of igniting flammable gases or other materials is inherent in the application of RF energy. Precautions must be taken to restrict flammable materials from the area where tissue ablation is performed.

Care should be taken to ensure device is not moved during RF power delivery. Device movement may cause loss of suction and tissue tear and/or unintentional ablation.

Ensure overlapping structures are separated and thermally isolated when anatomy allows. If the overlapping structures cannot be separated and thermally isolated, ablation should not be performed.

Care should be taken to ensure no vessels (or other structures) are restricted during device manipulation. Vessel restriction could cause hemodynamic instabilities or patient harm.

Care should be taken to confirm device placement before power application to avoid collateral tissue damage.

Care should be taken to fill distal end of cannula within the pericardial space with room temperature saline during ablation to avoid collateral tissue damage.

Care should be taken to ensure device is perfused during ablation to avoid unintentional tissue damage.

Physicians should implement a comprehensive anti-coagulation protocol including pre-operative, intra-operative and post-operative anticoagulation management to prevent potential thromboemboli.

Physicians should use esophageal temperature monitoring as was conducted during the clinical investigation of the device to monitor for potential collateral tissue damage. Throughout the procedure ensure the probe is located directly behind the ablation probe to ensure an accurate reading.

Reuse of the ground pad utilized in the epicardial portion of the procedure for the endocardial portion may result in patient harm.

Incorrect application of the ground pad during the procedure may result in lack of effectiveness.

Simultaneous epicardial and endocardial mapping or ablation may result in cardiac injury.

Additional warnings and precautions can be found in the Coagulation System Radiofrequency (RF) Generator Unit Model CS-3000 or MAG Operators Manual).

⚠ CAUTIONS:

- Precautionary measures should be taken prior to considering treatment of patients:
  - Deemed to be high risk and who may not tolerate a potential delayed post-procedure inflammatory pericardial effusion.
  - Who may not be compliant with needed follow-ups to identify potential safety risks.
- To ensure patients undergoing treatment with the EPi-Sense ST Coagulation Device device are well informed, the benefits, potential risks and procedural outcomes associated with the EPi-Sense ST Coagulation Device Hybrid Convergent procedure should be discussed with the patient. Physicians should document accordingly in the medical record.
- Qualified operators are physicians authorized by their institution to perform surgical sub-xyphoid pericardial access.
- Operators should complete training on the use of EPi-Sense ST Coagulation Device device before performing the procedure.
- The coil on the distal end of the device must be kept clean of coagulum during surgery to avoid loss of power. Do not clean coagulum off the electrode of the device with an abrasive cleaner or electrosurgical tip cleaner. The electrodes could be damaged resulting in device failure.
- Implantable cardioverter/defibrillators can be adversely affected by RF signals.
- Interference produced by the operation of high-frequency surgical equipment may adversely affect the operation of other electronic medical equipment such as monitors and imaging systems. Rearrange monitoring device cables so they do not overlap the Coagulation System cables.
- The use and proper placement of a ground pad is a key element in the safe and effective use of electrosurgery, particularly in the prevention of patient burns. Ensure entire area of electrode is reliably attached to the patient's body.
- While the distal portion of the device is designed to conform to the anatomy of the area to be ablated, excessive manipulation, torqueing, rough shaping, or forcing the movement of the device may damage or deform the distal end and cause potential patient harm. This may also cause the sensing electrodes to become detached and or break off the device.
- Care should be taken when handling the distal end of the device near the electrode with surgical instruments – do not squeeze or clamp the electrode. Do not cut or tear silicone.
- The coagulation device is only compatible with the AtriCure RF generators, cables, and accessories. Use of another manufacturer's accessories may cause damage to the device and/or injury to the patient.
- Coagulation devices have pre-set power and time settings for optimal ablation. Changing these settings may cause ablation dimension to vary from the values given in this document.
- Care should be taken to ensure the path to position the device is large enough to advance the device easily – forcing the device may damage the device, cause tissue damage or patient harm.
- Care should be taken to ensure device is not twisted or over manipulated during procedure. Twisting/torqueing/over manipulating device can cause damage to the device, the lumen to collapse, fracture of electrodes or vacuum lumen spring, separation of electrodes from device, kinking of PEEK guide tube, loss of suction, disconnection of perfusion/IV tubing, kinked perfusion/IV tubing, or patient harm.
- Care should be taken to assure the ablation electrode is oriented towards the heart and away from the pericardium using visual cues, i.e. Reference Dots, Locator Arrows, and white stripe.
- Connection of multiple devices to one vacuum unit may reduce vacuum functionality.
- Care should be taken to ensure optional guidewire stays in the sterile field during manipulation.
- Before ablation of tissue, ensure guidewire and/or scope are not between tissue and ablation device electrode.

⚠CAUTIONS:

- If a guidewire is used with guided device, ensure that insulative covering is intact along the exposed guidewire.
- The coagulation device should be used by physicians trained in the techniques of minimally invasive endoscopic surgical procedures and in the specific approach to be used.
- If using a TEE probe, care should be taken to withdraw the TEE probe prior to ablation to avoid compressing the esophagus against the left atrium during ablation.
- If the coagulation device is used near a pacemaker/AICD, a potential hazard exists due to possible interference with the action of the pacemaker and potential damage to the pacemaker. Consider placing a magnet on the pacemaker/AICD or programming the pacemaker/AICD per the manufacturer's instructions for use before applying RF energy.
- Low battery will trigger the indicator light on the handle to Yellow and stop the application of RF energy. Reference troubleshooting table in IFU.
- High temperature of distal pod will trigger the indicator light on the handle to Red and stop the application of RF energy. Reference troubleshooting table in IFU.
- Safety and effectiveness of concomitant left atrial appendage closure was not evaluated in the CONVERGE study.

Additional warnings and precautions can be found in the Coagulation System Radiofrequency (RF) Generator Unit Model CS-3000 or MAG Operators Manual.

Potential Complications of the Coagulation Procedure

- Infection
- Cardiac tamponade/perforation
- Pulmonary vein stenosis
- Vessel injury
- Pericardial effusion
- Tissue perforation
- Excessive bleeding
- Phrenic nerve injury
- Left atrial rupture/perforation
- Mediastinitis
- Pulmonary edema
- Vascular access complication
- Stroke/TIA
- Incisional herniation
- Esophageal injury
- Pleural effusion
- Atrio-Esophageal Fistula
- Cardiac arrest/Myocardial infarction
- New arrhythmias
- Thromboembolic complication
- Neurologic complication
- Death
- Complete heart block requiring permanent pacemaker implantation
- Pericarditis
- Serious skin burn
- Transdiaphragmatic herniation
- Damage (e.g., burn, puncture) to other adjacent structures

Additional Equipment/Supplies

- Only Use 0.9% Normal Room Temperature Saline Solution (250 mL bag recommended)
- Sterile Perfusion/IV Tubing Set (10 Drops/mL)
- Sterile Vacuum Tubing Set
- Vacuum regulated to -400 mmHg (-533 mbar; -15.75 inHg; -40 cmHg; -7.73 psi; -400 torr; -53 kPa)
- 0.035" Guidewire 100cm
- 5mm Endoscope
- Temporary external electrogram recording device that meets the following specifications: Complies with IEC 60601-1 and system accepts shielded 2mm pin connectors

Device Set Up

1. Place the ground pad on patient, per Fig. 3, and connect cable to front of generator (Figure 2.A, #2 and Figure 2.B, #5). Ensure entire area of electrode is reliably attached to the patient's body.

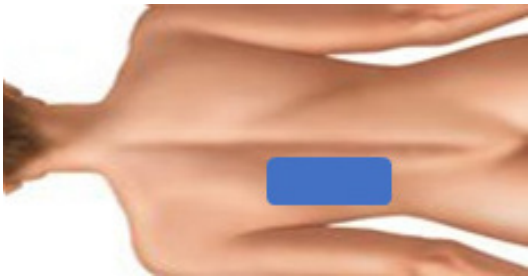


FIG. 3. PLACEMENT OF GROUND PAD

2. Place generator footswitch near the surgeon and connect the footswitch cable to front of generator. Refer to Figure 2.A #3 or Figure 8.B #7.
3. Inspect all trays, pouches, cartons, and packaging to ensure there has been no package damage which may result in product contamination. If package damage is discovered, do not use – replace the product.

a) Outside the sterile field:

i) Remove the device and cable from cartons.

ii) Remove the patient post-procedure handout from the packaging. Complete the handout and provide to patient post procedure

b) Remove the device and cable from their pouches and transfer to the sterile field.

c) Inside the sterile field, remove device from the tray by releasing the snaps and place near patient. Refer to Fig 4, #3.

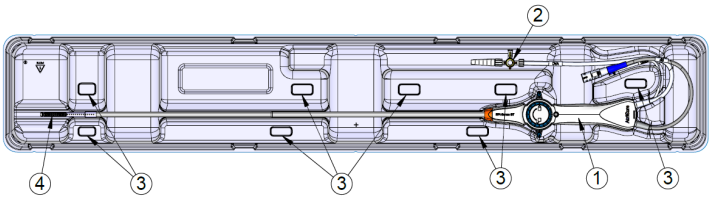


FIG. 4. COAGULATION DEVICE IN TRAY

[1] Handle;
[2] Stopcock;
[3] Snaps;
[4] Distal End

⚠**CAUTION:** Using excess force to remove the device from the tray may result in damage to the device.

4. Prepare the Vacuum

a) Attach one end of the sterile vacuum tubing to the graduated fitting indicated on device handle vacuum tube connector ('VAC') and the other to the vacuum trap (Fig 5,#1). Use the stopcock to apply and release the vacuum to the distal assembly.

b) Ensure the vacuum unit pressure is set to -400 mmHg.

⚠**CAUTION:** Do not exceed -550 mmHg for vacuum use – exceeding this pressure may reduce suction capabilities, reduce tissue contact, or cause tissue damage.

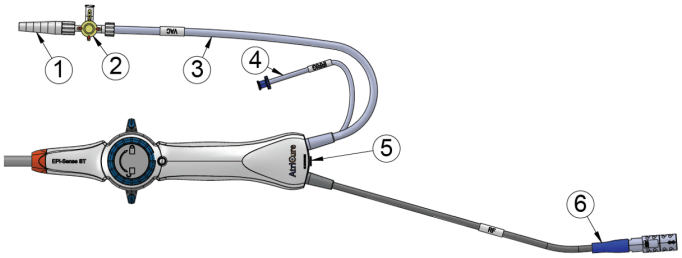


FIG. 5. COAGULATION DEVICE SETUP

[1] Graduated Fitting to Vacuum Tubing

[2] Stopcock

[3] Vacuum Tube Connector (VAC)

[4] Perfusion Tubing with Luer Connector (IRRIG)

[5] Guidewire Port

[6] CSK-2060 RF Cable Connector (RF)

5. Prepare the 0.9% Normal Saline Bag

a) Place **unpressurized** saline IV bag at patient height or above.

b) Connect perfusion tubing to the perfusion tubing with luer connector on the device handle indicated by the 'IRRIG' symbol, Fig. 5, #4. Verify IV line is fully open.

c) Insert IV tubing set into 0.9% normal saline bag.

d) Turn on vacuum pressure and prime device by engaging the suction with a sterile surface (gloved hand).

i) Ensure perfusion flow is functioning by observing drops in IV tubing drip chamber. Make sure the device is primed by observing perfusion at distal end of coagulation device before starting operation of device. Ensure IV line is fully open.

⚠CAUTIONS:

- Verify that IV line is fully open. Do not pressurize saline bag; that is, do not use an infusion pump for delivery or a pressure bag. Pressurizing saline or partially open perfusion tubing can vary perfusion rate causing loss of suction and the ablation dimensions to vary from values listed, and cause tissue perforations from excess heating.
- Ensure device is primed prior to first RF power delivery.
- Use ONLY 0.9% normal saline.
- Ensure perfusion/IV tubing is connected to perfusion tubing with luer connector (IRRIG) – do not connect perfusion tubing to stopcock or "Guidewire Port".

6. Connect RF cable CSK-2060 to RF cable connection on the device handle indicated by the 'RF' symbol - blue connection to blue connection, Fig. 5, #6 & Fig.6, #4.

⚠**CAUTION:** Ensure arrows on cable and handle are aligned and cable is completely connected. Device will not register on generator if cable is incorrectly connected.

⚠**CAUTION:** Cables to surgical electrodes should be positioned to prevent contact with patient or other leads

a) If using the CSK-2030 Sensing Cable, connect the black end of the Sensing Cable CSK-2030 to the generator front panel connector (Fig 2, & Fig 6, #1).

b) Connect the black end of the RF cable CSK-2060 to the black receptacle of the Sensing Cable CSK-2030 per the Fig. 6, #3.

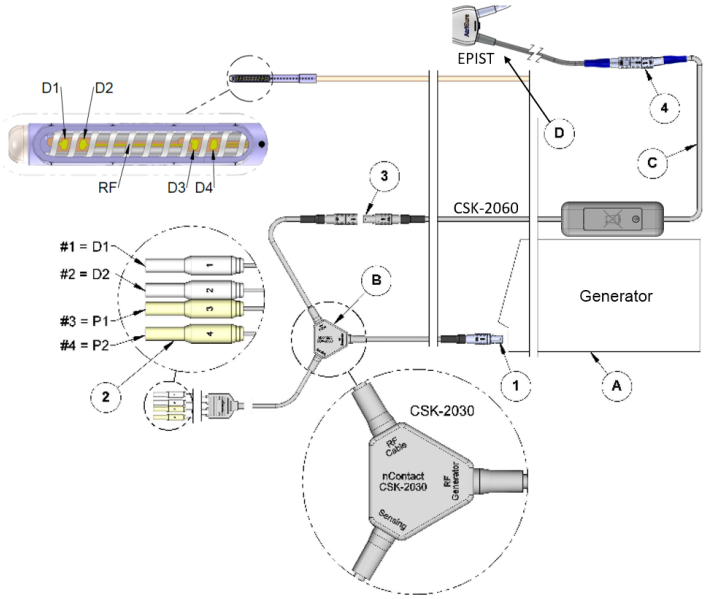


FIG. 6. SENSING SYSTEM CONNECTION USING CSK-2030

Equipment	Connections
(A) RF Generator;	(1) CSK-2030 to Generator
(B) Sensing Cable CSK-2030;	(2) CSK-2030 to Sensing
(C) RF Cable CSK-2060;	(3) CSK-2060 to CSK-2030
(D) Device EPiST	(4) CSK-2060 to EPiST

7. When connecting the shrouded pins from Cable CSK-2030 (Fig 6, #2) to the ECG recorder equipment refer to Fig 7 below.

a) Sensing electrodes provide the option to transmit signal directly from the probe to a commercially available electrogram recording system. This provides the option to pace, sense, and record directly from the device to aid in lesion assessment.

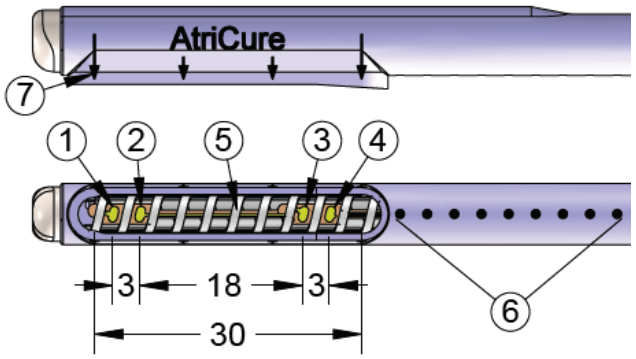


FIG. 7. SENSING ELECTRODE LOCATIONS AND SPACING (MM)

[1] **Distal #1** Sensing Electrode = CSK-2030 Shrouded Pin **#1**

[2] **Distal #2** Sensing Electrode = CSK-2030 Shrouded Pin **#2**

[3] **Proximal #1** Sensing Electrode = CSK-2030 Shrouded Pin **#3**

[4] **Proximal #2** Sensing Electrode = CSK-2030 Shrouded Pin **#4**

[5] Coagulation Electrode

[6] Reference Dots

[7] Locator Arrows

⚠**CAUTION:** Ensure inputs from the ECG recorder are isolated from earth ground, if not, there is an increased possibility of fibrillation.

8. Connect power cord to generator back panel connector (Fig. 8.A, #2 or Fig 8.B #8)

then power on the generator via the Power ON/OFF rocker switch (Fig. 8.A, #1 or Fig 8.B #8). Refer to the Operator Manual for complete generator instructions

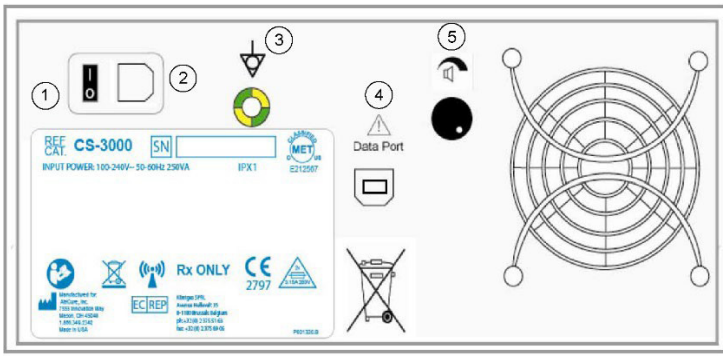


FIG. 8.A GENERATOR BACK PANEL KEY FEATURES

[1] Power Switch;
[2] AC Power connector;
[3] Grounding Stud;
[4] Serial Data connector
[5] Alarm Volume Control

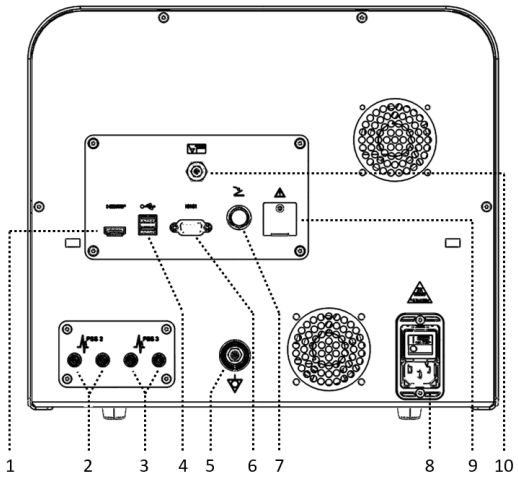


FIG. 8.B GENERATOR BACK PANEL KEY FEATURES

[1] HDMI port
[2] PSS pass-through
[3] PSS pass-through
[4] USB ports
[5] Equipotential Connector
[6] Serial Port
[7] Footswitch Connector
[8] Power Switch
[9] Service Port - AtriCure Only
[10] Vacuum Port

OPERATIONAL INSTRUCTIONS

1. **Manipulation of Guided Coagulation Device Over Cannula Guidewire – Optional**

FIG. 9. DISTAL END CONFIGURATION

2. If using cannula guidewire, place cannula guidewire in desired coagulation location.
3. If attached, remove torquer from end of guidewire.
4. Carefully feed one end of the guidewire into the guide tube in the distal end of guided coagulation device (Fig. 9, #1).
5. Slide guided coagulation device until guidewire protrudes from handle of guided coagulation device. If available, attach torquer to the end of guidewire protruding from handle of device.
6. Advance the guided coagulation device along the guidewire until positioned at desired coagulation location using guidewire to assist in placement.

Endoscopic Epicardial Access via Subxiphoid Approach

1. Utilizing instructions below, access the epicardial space utilizing subxiphoid approach.

Subxiphoid Access

1. Standard surgical subxiphoid access of the pericardial space should be performed by a physician authorized by his/her hospital to perform such surgical techniques.
2. Using standard surgical techniques for creating a pericardial window superior to the diaphragm, obtaining access to the posterior surface of the heart.
3. Create an incision immediately inferior to the xiphoid process. Direct visualization of the pericardium superior to the diaphragm can be achieved through the incision. The xiphoid process may be removed, dependent on patient anatomy.
4. A 2 cm incision should be made in the pericardium to allow access for the cannula. The cannula provides direct access to the posterior surface of the heart and is sized to create space between the epicardium and the pericardium to visualize cardiac structures and manipulate the coagulation device alongside an endoscope, so all device manipulations are performed under direct visualization.
5. After obtaining subxiphoid access, the EPi-Sense ST Coagulation Device Guided Coagulation Device, cannula, scope and surgical instruments are used to create the epicardial lesion pattern.

Cannula Placement and Manipulation

1. The cannula should be positioned through the incision and into the pericardial space. As the cannula is advanced into the pericardial space, it should be directed towards the left of the patient, away from the IVC, as shown in Figure 10.

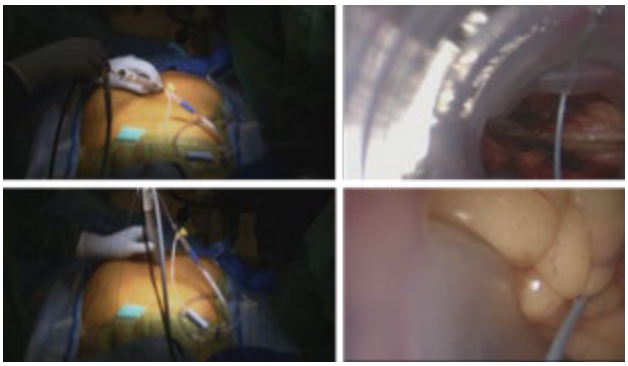


FIG. 10. CANNULA PLACEMENT AND MANIPULATION

Endoscopic Visualization

1. Use the cannula to create space so that an endoscope can provide direct visualization of the posterior left atria. When the pericardium is intact and free of adhesions, the cannula will gently separate the heart from the pericardium and create a cavity into which the device may be advanced under endoscopic visualization.

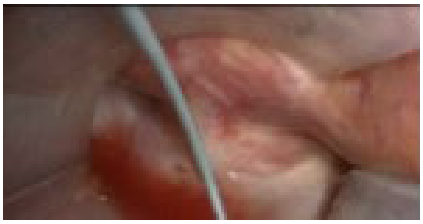


FIG. 11. POSTERIOR VIEW OF INFERIOR NEAR LPV

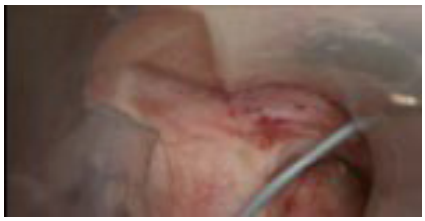


FIG. 12. POSTERIOR VIEW OF INFERIOR NEAR RPV

2. The cannula may be manipulated along the posterior heart surface to visualize the left pulmonary veins (LPV) (Figure 11), the right pulmonary veins (RPV) (Figure 12), the inferior vena cava (IVC), the coronary sinus (CS), and the posterior left ventricle (LV). To manipulate the cannula, use the bevel end to lift the heart. Rotate the cannula during manipulations to separate the heart from the pericardium and facilitate delineation of anatomic structures. Use the cleft to visualize tissue structures and assist in creating space. It is best to have the tip of the cannula against the pericardium as opposed to the heart surface.

Cardiac Coagulation

1. Esophageal temperature monitoring should be utilized during epicardial and endocardial ablation. If esophageal temperature increases more than 0.5 °C during each ablation or above an absolute maximum of 38.0 °C, RF energy should be terminated until temperature reduces to baseline or under 37 °C.
2. Ensure all steps of device set-up are performed.
3. Prior to inserting the device into the cannula, check the steering feature by articulating the steering lever on the device handle. (Fig. 13)

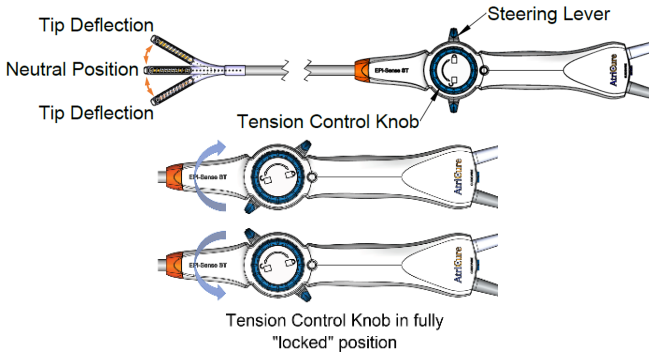


FIG. 13. STEERING AND TENSION CONTROL FEATURE

4. Use the steering lever to deflect the tip (Fig. 13). When the lever is pulled back from neutral position, the tip will deflect proportionately in one direction depending upon the amount of curve option selected. When the lever is pushed forward, the tip will deflect in the opposite direction. To straighten the tip, return the steering lever to neutral position.
5. The handle has an adjustable tension control knob (Fig 13) that allows the operator to adjust the friction to where the steering lever and tip curve can be locked in place when the desired device placement is achieved. The amount of tension increases as the tension control knob is rotated clockwise until it reaches the full 'locked" position. Counter rotation from the "locked" position decreases the friction.
6. Ensure the device is in a neutral position prior to insertion or retraction within the cannula.
7. Select the power mode of operation on the generator
8. If not using the guidewire, advance the device through the cannula to desired location by direct visualization using the steering lever as needed.
9. Engage vacuum by turning the stopcock.
10. Ensure contact between the electrode and cardiac tissue by;

   a) Using locator arrows (Fig 7, #2) to visualize the direction and location of the coagulation electrode

   b) Reference dots (Fig 7, #6) designate the exposed ablative area of the coagulation coil.

   c) Direct visualization of the device against cardiac tissue after initiation of vacuum;

   d) Visual observation of saline perfusion from the unpressurized saline bag at a rate of approximately 1 drop per second (4-6 ml/min) through the drip chamber while vacuum is initiated.

11. Use the sensing electrodes as a secondary aid to confirm contact with cardiac tissue.

   a) Pre-Coagulation with the vacuum engaged: check ECG recorder to visualize cardiac tissue waveforms.

12. Fill cannula with approximately 10 to 20 mL of room temperature saline. Saline may be administered via the cannula stopcock or directly through the cannula. See Cannula IFU for stopcock set-up.
13. Initiate power by pressing and releasing the footswitch or RF ON/OFF button on generator front panel. An audible signal will sound at the beginning of the RF cycle.
14. Ablate tissue for pre-determined cycle.

			Average Lesion Dimensions			
Device Code and Size	Power Watts	Time Sec	Depth mm	Length mm	Width Mm	Volume mm^3
EPiST	30*	90*	7	35	10	1691

*Automatic cycles have been pre-determined for optimal tissue coagulation.

15. When the generator completes a cycle, RF energy turns off automatically, and an audible completion beep sounds for 1 second.
16. In the event RF energy shuts down during the cycle:

   a) Refer to RF Generator for error message and consult troubleshooting matrix within this IFU.

   b) And the indicator light (Fig. 1, #4) on the handle is Red or Yellow, see troubleshooting matrix within this IFU.

17. Suction saline from pericardial space using cannula suction to improve visibility. Reference Cannula IFU for suction set-up.
18. After the cycle is complete, disengage vacuum from the distal end of the device by turning the stopcock lever.
19. Remove the distal end of coagulation device from tissue and observe completeness of lesion.
20. Place device electrode in next desired location.

   a) After reactivating the vacuum, ensure perfusion flow is functioning by observing drops in IV tubing drip chamber.

21. Repeat steps 8-18 from above as needed until desired lesions have been completed.
22. At completion of procedure, remove device from tissue and through the Cannula in a neutral position, disconnect all cables and tubes and discard device, tubing sets, and CSK-2060 RF cable following the local governing ordinances and recycling plans for disposal or recycling of device components.

   a) Remove the Lithium battery on **CSK-2060** RF cable prior to discarding. The battery may be discarded by removing the battery door screw (Fig 14), opening the door and disconnecting the battery. Dispose of the battery in an appropriate manner.

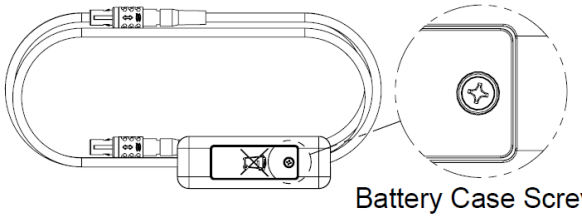


FIG. 14 CSK-2060 RF CABLE

b) CSK-2030 Sensing Cable is a reusable cable; see the cable IFU for instructions on cleaning and reuse.

23. Insert a pericardial drain through the pericardial window and into the pericardial space. Close the incisions leaving the drain to remove fluid from the pericardial space.

⚠CAUTIONS:

- Positioning and manipulation of the coagulation device without a guide wire inserted into the guide tube may cause the guide tube to kink.
- To avoid interruption of vacuum or perfusion flow, do not leave device tubing clamped during coagulation of tissue.
- Large blood clots and tissue particles may clog vacuum lumen and impair suction.
- To avoid tissue damage: Do not move the device if vacuum is engaged.
- Bending device without guidewire in guide tube may kink the guide tube. Avoid inserting guidewire into a kinked guide tube.
- Do not torque guided coagulation device if distal end is curved as damage to device may occur and the electrodes may separate and/or break off from the device.
- Visualize the distal end of the device, to ensure it is not pinching/entrapping tissue with other devices, such as the Cannula.
- Care should be taken when handling the distal end of the device near the electrode with surgical instruments – do not squeeze or clamp the electrode. Do not use tools on the electrode coil, place tools on silicone only as the electrodes may separate and/or break off from the device.
- Ensure device is properly connected – switching connections may cause inadequate tissue contact and reduced functionality.
- Temporarily unused active electrodes should be stored in a location isolated from the patient.

Epicardial Lesion Creation

1. Prior to creating any lesions, retract the TEE probe (if used) and the NG/OG tube (if used) to the upper third of the esophagus; between 18 – 23 cm from the incisors. At a minimum, retract the TEE probe relative to the esophagus, so that the probe is not near the atrium.
2. The upper alarm limit of the temperature probe should be set to 38.0°C. The preset power and time settings for ablation with the coagulation device are based on extensive testing; changing the settings may cause excessive heating and tissue damage.
3. Prior to ablation, connect a stopcock in-line between the vacuum port and the tapered adaptor to control vacuum through the cannula.
4. During ablation, room temperature saline should be administered through the cannula to cool and hydrate the pericardium and underlying anatomy. Before injecting the saline, turn the cannula vacuum off by closing the in-line stopcock.

⚠**CAUTION:** Esophageal temperature monitoring should be utilized during epicardial and endocardial ablation. If esophageal temperature increases more than 0.5 ºC during each ablation or above an absolute maximum of 38.0 ºC, RF energy should be terminated until temperature reduces to baseline or under 37 ºC.

***Note:** Baseline temperature should be taken prior to any lesion creation.

Lesion Location

1. Access the recommended anatomical locations endoscopically and create the epicardial lesions (see clinical study section for lesion map) based on patient anatomy and physician discretion.

- Left Antral Posterior Pulmonary Vein Orifice Lesion
- Right Antral Posterior Pulmonary Vein Orifice Lesion
- Posterior Parallel Vertical Connecting Lesions
- Left Antral Anterior Pulmonary Vein Orifice Lesion
- Right Antral Anterior Pulmonary Vein Orifice Lesion

2. Completion of each lesion may require multiple device placements and applications of energy delivery.

Posterior Left Atrial Lesions

1. To create lesions along the posterior left atrium, medial to the RPVs or the LPVs, position the cannula under the left atrium. Once in the proper location, use the cannula to separate the pericardium to create space and allow visualization of the posterior anatomy. This is achieved with the tip of the cannula facing the pericardium (cleft facing the heart, shown in Figure 15). This maneuver will create a space for the device. Once the cannula is at the desired location, advance the device such that the ablating coil is in the appropriate location, with coils facing the heart.

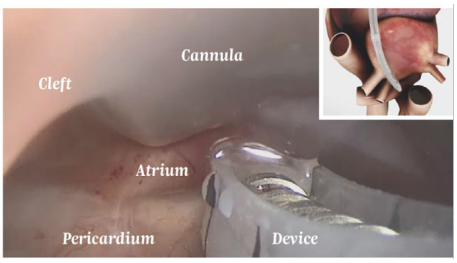


FIG. 15. DEVICE ORIENTATION

2. Retract the cannula until the sensing and coagulation electrodes are distal to the cannula tip and in contact with the left atrium. This will allow the heart to better sit against the device. Always ensure proper orientation of the exposed ablation coil electrode under endoscopic visualization, utilizing the directional arrows and white stripe stripe on back of device to confirm contact with atrial tissue only.
3. Continue to manipulate cannula and device such that lesions on the posterior LA are adjacent to one another. Repeat lesions until ablation of posterior LA is complete.
4. To avoid deformation of the pericardial reflections or the coagulation device and the misdirection of RF energy delivery, do not use excessive force when advancing the device against the reflections. Retract the cannula until the sensing and coagulation electrodes are distal to the cannula tip and in contact with the LA. Multiple applications of RF energy may be required to create the desired posterior left atrial lesion, with the 3 cm device. Always confirm that the location. Arrows are directed toward the heart, away from the pericardium.
5. Epicardial lesions are visible and connection of discrete lesions provides confirmation of lesion continuity. Use the endoscope to facilitate manipulation of the cannula when confirming that the lesions intersect.

Left Antral Lesions

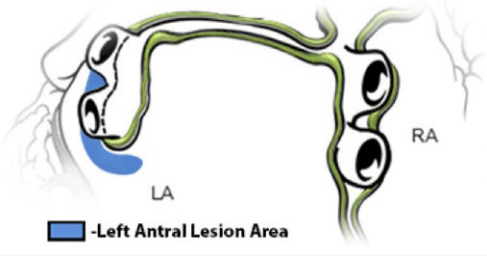


FIG. 16. LEFT ANTRAL LESIONS

To position the device along the antral aspect of the left pulmonary vein, (Figure 16), endoscopically identify the LPVs. Once in position, gently rotate the cannula clockwise to create space between the left atrium and the pericardium with the cleft toward the PVs and the tip toward the pericardium. When the desired cannula location is obtained, advance the device such that it passes anterior to the superior LPV and the exposed side of the RF coil (arrows pointing towards the left atrium, Figure 17), faces the left atrium.

Remember that in most cases, the superior LPV is anterior to the inferior LPV. Use caution when advancing the device, to not exert excessive force. Engage the vacuum and retract the cannula until the sensing and coagulation electrodes are distal to the cannula tip and in contact with the left atrium.

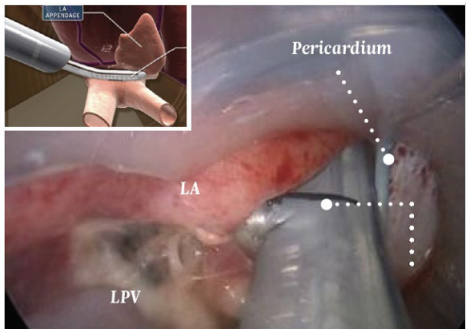


FIG. 17. DEVICE ORIENTATION TO THE SUPERIOR LPV

Right Antral Lesions

FIG. 18. RIGHT ANTRAL LESIONS

The anterior right atrium (Figure 18) can be accessed by rotating the cannula anterior to the IVC. To position the cannula anterior to the IVC, endoscopically identify the IVC and position the cannula adjacent to the IVC from the posterior left atrium. After visual conformation of the IVC, right atrium and pericardium, the cannula is rotated counterclockwise to position the cannula between the right atrium and pericardium with the cleft of the cannula directed toward the IVC and tip of the cannula toward the pericardium

With the cannula positioned over the IVC, the coagulation device may be advanced such that the ablation electrode is located along the anterior orifice, between the RPV antrum and the right atrium (Figure 19). The cannula may be used to create space between the pericardium and the atria, allowing the ablation electrode to seat against tissue . The cannula also helps separate the pericardium (and phrenic nerve) from the atrium, permitting the coagulation device to be positioned along the Waterston's groove region that defines the interatrial junction. A lesion may be created at the left orifice to the RPV antrum.

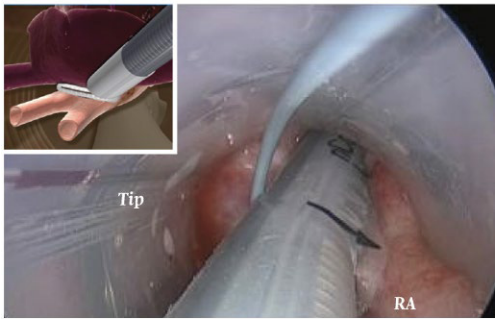


FIG. 19. DEVICE LOCATION FOR RIGHT ANTRAL LESIONS

Transseptal Access and Conventional Endocardial Catheter Ablation – (Refer to Catheter manufacturer's Instructions for Use):

1. Transseptal access and conventional endocardial catheter ablation should be performed by a physician authorized at his/her hospital to perform such procedures.
2. Obtain venous vascular access using appropriate introducers to insert diagnostic and ablation catheters into the right and left atria.
3. Use appropriate technique to obtain transseptal access to the left atrium after completion of the epicardial lesions. The patient should be heparinized before or after transseptal access is obtained to maintain a target ACT between 300 and 400 seconds to prevent thrombus formation.

⚠**CAUTION:** Esophageal temperature monitoring should be utilized during endocardial ablation. If esophageal temperature increases more than 0.5 °C during each ablation or above an absolute maximum of 38.0 °C, RF energy should be terminated until temperature reduces to baseline or under 37 °C.

The esophageal temperature probe should be positioned under fluoroscopic guidance directly posterior to the LAat the same level as the tip of the ablation catheter during endocardial ablation.

4. Using standard mapping techniques and diagnostic catheters, the locations of breakthrough between discrete epicardial lesions are detected. The Ablation Catheter is then used to ablate these locations. If additional locations of breakthrough along an epicardial lesion are suspected the endocardial ablation catheter may be used to ensure lesion completeness. Complete the following as indicated by breakthrough locations;
   - Right Superior Pulmonary Vein Lesions
   - Right Inferior Pulmonary Vein Lesions
   - Left Superior Pulmonary Vein Ridge Lesions
   - Cavotricuspid Isthmus (Typical Atrial Flutter) Lesions
5. Once all endocardial lesions are created and confirmation of lesion completeness is achieved, including pulmonary vein isolation and bi-directional block, all catheters and sheaths are removed and vascular access sites closed using standard technique.

POST OPERATIVE CARE

Postoperative mitigations for Pericarditis and/or Inflammatory Pericardial Effusions

1. To mitigate the potential of pericarditis, pericardial effusion or delayed onset cardiac tamponade, the following postoperative care is recommended:
   - Drain management: Leave pericardial drain in the pericardial space (until drainage is less than 50 mL over at least 12 hours is preferable)
   - Prophylactic anti-inflammatory agents (e.g. NSAIDs or Colchicine). A three (3) week duration is recommended.
   - Use of diuretics as needed
   - Echocardiogram should be performed between 1-3 weeks post-procedure and whenever there are suggestive symptoms or signs to screen for late onset pericardial effusion
   - Patient education regarding symptoms of pericarditis, pericardial effusion and cardiac tamponade. Patients should be closely monitored for suspected symptoms, which should be further evaluated with appropriate imaging tests.
2. Follow-up should be conducted at approximately 30 days post- procedure to monitor for signs of delayed onset pericarditis or pericardial effusion.

Anticoagulation and Anti-arrhythmic therapy management

1. Anticoagulation management should be followed per the 2017 HRS Expert Consensus on Catheter and Surgical Ablation of Atrial Fibrillation, including:
   - Systemic anticoagulation therapy should be initiated for all patients post procedure through at least two months following the ablation procedure.
   - Decisions regarding the use of systemic anticoagulation more than two months following ablation should be based on the patient's risk factors for stroke and not on the presence or type of AF.
2. Anti-arrhythmic drug management post ablation should be per physician judgement.

TRAINING RECOMMENDATIONS

Training plan for new operators

New operators are defined as de novo operators or those who have completed fewer than 5 cases with the EPi-Sense ST Coagulation Device device. New operators should complete the following training:

1. Participate in a training and education module on the Instructions For Use and best practices with emphasis on the indication and risk mitigation strategies related to pericardial effusion, atrioesophageal fistula (AEF) and stroke.
2. Peer-to-peer education (in-person or online) with focus on the above areas.
3. Pre-lab didactic review covering the salient points from (1) followed by cadaver or comparable simulated models training with the EPi-Sense ST Coagulation Device device.
4. Proctoring by a trained physician and /or a certified AtriCure training specialist for first 5 clinical (human) cases.

Training plan for current EPi-Sense operators

1. Current EPi-Sense operators will be provided a training and education module on the instruction for use and best practices with emphasis on the indication and risk mitigation strategies related to pericardial effusion, atrioesophageal fistula (AEF) and stroke.
2. Supplemental in-person training course, including case presentation and hands-on training, will also be available for current users .

MAINTENANCE AND TROUBLESHOOTING

(See Coagulation System Radiofrequency (RF) Generator Unit Model CS-3000 or MAG Operators Manual for additional system maintenance and troubleshooting)

Troubleshooting	
Situation	**Action(s)**
Device is not receiving perfusion flow	Check perfusion connections on device handle Check perfusion line connection at IV saline bag Ensure perfusion line is fully open Ensure saline bag is not empty Ensure that device perfusion line/IV tubing are not clamped/obstructed/kinked
Device is connected but does not register pre-set power and time	Check all connections to the generator and to Cables CSK-2060 and CSK-2030 Check the connection of the ground pad to the patient Check the CSK-2060 cable connection at the handle of the device; the arrows on the cable should be aligned with the arrow on the handle. If both arrows are not aligned, disconnect cable and rotate blue end 180° until aligned then reconnect Check that LED on device handle is not alight.
Device does not engage with tissue	Check vacuum connections on device handle Ensure stopcock lever is in correct position Check vacuum line connection at trap and vacuum unit and ensure other lines are not open Check vacuum pressure – should be approximately -400mmHg Ensure that device and vacuum unit lines are not clamped/obstructed/kinked Check that perfusion set-up is per IFU
Generator RF output shuts down during cycle due to high impedance (High impedance warning will be indicated on Generator)	Check that device is still engaged with tissue (see above if not) Check for excessive material on ablation electrode, remove material as required Check all cable connections including ground pad connection Check that LED on device handle is not alight. Re-start ablation
Generator RF output shuts down during cycle due to Red indicator light on device handle.	Check that device is still engaged with tissue (see above if not) Check for coagulum on the ablation electrode, remove material as required Check all cable connections including ground pad connection Withdraw the device and ensure the perfusion lines are not blocked prior to reuse. When the Red indicator light turns off, re-start ablation If Red light does not turn off, replace with new coagulation device
Generator RF output shuts down during cycle due to Yellow indicator light on device handle.	Remove existing CSK-2060 RF cable and replace with a new CSK-2060 RF Cable Verify yellow light is not on and re-start ablation
No signals are registering on sensing equipment monitors	Check all cable connections. Ensure the cables and shrouded pins are connected per Figures 6 and 7. Ensure the shrouded pin numbers match the sensing electrodes on the sensing equipment.
Unable to remove device from guidewire	Remove torquer from end of guidewire Flush guidewire port on the handle with saline
Generator does not activate cycle (High impedance warning will be indicated on Generator as "OC" which means Open Circuit)	Ensure generator is plugged in and turned on Check all cable connections; check ground pad connection for correct position and it is adhered to the patient Ensure device electrode is in direct contact with desired tissue Check for material on ablation electrode, remove material as required Verify Red indicator light is not illuminated on device handle Check footswitch connection Ensure that generator is in "Power Control Mode" Ensure that Time is not set to "zero" Refer to generator Operator Manual
Guidewire will not insert into device	Ensure guidewire is being inserted into guide tube opening at distal end of device Ensure recommended guidewire is being used Ensure guide tube opening is not blocked Ensure device is not kinked
Device will not advance along Guidewire or through nContact Cannula	Ensure guide tube is not kinked Flush guidewire port on the handle with saline Lubricate lumen of Cannula with sterile saline

SUMMARY OF CLINICAL STUDIES CONDUCTED FOR ATRIAL FIBRILLATION TREATMENT INDICATION

The CONVERGE study was a prospective, open-label 2:1 randomized controlled (convergent procedure versus standalone endocardial catheter ablation) multi-center pivotal study to evaluate the safety and effectiveness of the EPi-Sense® Guided Coagulation System for the treatment of symptomatic persistent Atrial Fibrillation (AF) in subjects who are refractory or intolerant to at least one Class I and/or III AAD as compared to a standalone endocardial catheter ablation.

The primary effectiveness endpoint was met for the overall study population. The proportion of subjects who were AF/AT/AFL-free absent class I and III AADs except for a previously failed or intolerant class I or III AAD with no increase in dosage following the 3-month blanking period through the 12-months post-procedure follow-up visit was higher in the EPi-Sense group compared to those in the standalone endocardial catheter ablation group.

The CONVERGE study included patients whose AF was sustained beyond 7 days and imposed no upper limit on duration of continuous AF. In a post hoc analysis assessing the impact of hybrid ablation as AF progresses, patients were sub-classified into persistent (>7 days and ≤12 months of continuous AF) and long-standing persistent AF (> 12 months of continuous AF) sub-groups.

The post hoc analysis based on AF classification (persistent AF or longstanding persistent AF) showed evidence of treatment heterogeneity with a larger treatment effect in the longstanding persistent AF sub-population. The benefit-risk profile of hybrid ablation appeared to be more pronounced in longstanding persistent AF patients given the unmet clinical need in this patient population. For completeness, results are presented for the pre-specified all enrolled and treated subjects (N = 153) and the two sub-groups. Because the results for the persistent AF and longstanding persistent AF sub-populations are post-hoc, they should be interpreted with caution, and the reported confidence intervals are not adjusted for multiplicity.

58% (88/153) of all subjects were classified as having Persistent AF (> 7 days to 12 months): 63% (64/102) in the EPi-Sense group compared to 47% (24/51) in the Catheter Ablation group. 42% (65/153) were classified as longstanding persistent (AF > 12 months): 37% (38/102) in the EPi-Sense group and 53% (27/51) in the Catheter Ablation group.

CONVERGE Study Design

Patients were treated between 1/8/2014 and 8/21/2018. The database for this report reflected data collected through August 2019 and included one hundred fifty-three (153) subjects treated from twenty-five (25) sites in the US and two (2) sites in the UK.

CONVERGE was a prospective, open-label, 2:1 randomized, controlled, multi-center pivotal clinical study. Subjects were randomized in a 2:1 ratio to treatment with either a convergent procedure utilizing the EPi-Sense Guided Coagulation System or a standalone endocardial catheter ablation procedure.

An independent Data Safety Monitoring Board (DSMB) reviewed all safety data throughout the course of the study. A Clinical Events Committee (CEC) adjudicated all Major Adverse Events (MAEs).

Inclusion and Exclusion Data

Enrollment in the CONVERGE trial was limited to patients who met the following inclusion criteria:

- Age > 18 years; < 80 years
- Left atrium < 6.0 cm (Trans Thoracic Echo - TTE – parasternal 4 chamber view)
- Refractory or intolerant to one AAD (class I and/or III)
- Documentation of persistent AF
- Provided written informed consent

Patients were not permitted to enroll in the CONVERGE study if they met any of the following exclusion criteria:

- Patients requiring concomitant surgery such as valvular repair or replacement, coronary artery bypass graft (CABG) surgery and atrial septal defect closure.
- Left ventricular ejection fraction < 40%
- Pregnant or planning to become pregnant during study
- Co-morbid medical conditions that limit one-year life expectancy
- Previous cardiac surgery
- History of pericarditis
- Previous cerebrovascular accident (CVA), excluding fully resolved TIA
- Patients who have active infection or sepsis
- Patients with esophageal ulcers strictures and varices
- Patients with renal dysfunction who are not on dialysis (defined as GFR ≤ 40)
- Patients who are contraindicated for anticoagulants such as heparin and coumadin
- Patients who are being treated for ventricular arrhythmias
- Patients who have had a previous left atrial catheter ablation for AF (does not include ablation for AFL or other supraventricular arrhythmias)
- Patients with existing ICDs.
- • Current participation in another clinical investigation of a medical device or a drug, or recent participation in such a study within 30 days prior to study enrollment
- Not competent to legally represent him or herself (e.g., requires a guardian or caretaker as a legal representative).

Prior to initiating the study convergent procedure or the standalone endocardial catheter ablation procedure, subjects were excluded if any of the following intra-operative exclusions were met:

1. Presence of left atrial thrombi per immediate pre-operative transesophageal echocardiograph (TEE) for the convergent procedure, and per TEE or intra- cardiac echo (ICE) for the standalone endocardial catheter ablation procedure.
2. Presence of adhesions that would prevent epicardial access to the pericardial space or the creation of the study recommended complete lesion pattern. (Convergent procedure arm only).

Convergent Procedure

Patients in the EPi-Sense arm underwent the investigational convergent procedure that included epicardial ablation with the EPi-Sense device followed shortly by an endocardial procedure using a permitted endocardial ablation catheter to complete the lesion set (Figure 1).

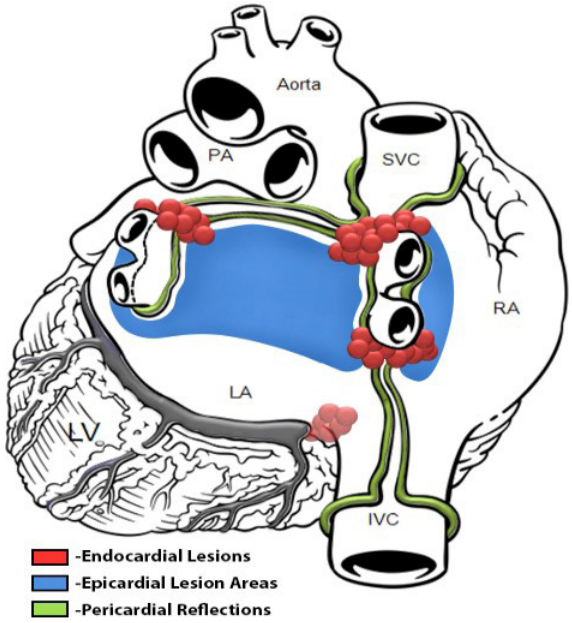


FIGURE 1: CONVERGENT EPICARDIAL AND ENDOCARDIAL LESION PATTERN

Follow-up Schedule

All patients were scheduled for follow-up examinations postoperatively at 7-days, 1-month, 3-, 6-, 12-, 18-months, and long-term phone follow- up at 2-, 3-, 4-, 5-years. Adverse events and complications were recorded at all visits. Table 1 summarizes study follow-up visits and required data collection.

TABLE 1: STUDY FOLLOW UP AND REQUIRED DATA COLLECTION

	Baseline	Pre-procedure	Procedure	7 Days	1 month	3 months	6 months	12 months
Informed Consent for Study Participation	✓							
Inclusion/Exclusion Criteria	✓	✓	✓					
Medical History	✓							
Spiral CT or MRI	✓						✓	
Procedure			✓					
ECG	✓		✓		✓	✓	✓	✓
ECHO (TTE)	✓			✓			✓	
ECHO (TEE)		✓						
24 hour Holter monitor	✓						✓	✓
Documentation of any AF treatments					✓	✓	✓	✓
Medication status Class I and III AADs, cardiac and Anticoagulants	✓		✓	✓	✓	✓	✓	✓
Evaluation of Adverse Events			✓	✓	✓	✓	✓	✓
Six minute walk test	✓							✓
Quality of Life Assessment (QOL)	✓							✓

Study Endpoints

Primary Effectiveness Endpoint

The primary effectiveness endpoint was defined as success or failure to be AF/AT/AFL free absent class I and III AADs except for a previously failed or intolerant class I or III AAD with no increase in dosage following the 3-month blanking period through the 12-months post procedure follow-up visit.

Rhythm monitoring following the 3-month blanking period consisted of ECG at 3-, 6-, 12- months visits and 24-hour Holter at 6- and 12- months. These data were evaluated by an independent reviewer.

Subjects were considered primary effectiveness failures if any of the following conditions were observed:

- Any electrocardiographically documented AF/AFL/AT episode of 30 sec duration or longer by Holter, event monitor or rhythm strip; or for the full 10 second recording of a standard 12 lead ECG following the 3-month blanking period through the 12 months post procedure follow- up visit.
- The use of a new or an increase in the dose of a previously failed class I or class III AAD following the 3-month blanking period through the 12 months post procedure follow-up visit.
- DC cardioversion for AF/AFL/AT following the 3-month blanking period through the 12 months post procedure follow-up visit.
- Subsequent left-sided catheter ablation for AF/AFL/AT at any time during the 12 months post procedure follow-up visit.
- Catheter ablation for right-sided typical atrial flutter following the 3-month blanking period through the 12 months post procedure follow-up visit.

The primary effectiveness hypothesis for this study was to demonstrate a superiority success rate of the EPi-Sense group over the Catheter Ablation group. The following primary effectiveness hypothesis was evaluated using a chi-square test at a two-sided significance level of 5% to determine if superiority of the treatment arm was attained:

$$H_0: P_T = P_C \quad \text{vs} \quad H_a: P_T \neq P_C$$

where P = the true percentage of subjects failing to achieve AF/AFL/AT freedom, PT is the true failure rate for the treatment arm and PC for the control arm.

Secondary Effectiveness Endpoints

- Success or failure to achieve a 90% reduction from baseline AF burden and off all Class I and III AADs at 12-months post procedure
- Success or failure to achieve a 90% reduction from baseline AF burden regardless of their Class I and III AAD status at 12-months post procedure
- Change in QOL measures at 12-months post procedure from baseline values
- Change in 6-minute walk test score from baseline score
- Success or failure to be AF free and off all Class I and III AADs except a previously failed or intolerant Class I or III AAD with no increase in dosage following the 3-month blanking period through the 12-months post procedure follow-up visit
- Success or failure to be AF free regardless of Class I and III AAD status following the 3-month blanking period through the 12-months post procedure follow-up visit.

AF burden percentage was captured directly on the Zio patch report and was based on the total time the subject was in AF over the time the subject wore the Zio patch, after artifact removal. A ≥90% change from baseline is based on comparing the post-procedure AF burden percentage to the baseline AF burden percentage recorded on the Holter Monitor.

Primary Safety Endpoint

The primary safety endpoint for the study was defined as the incidence of major adverse events (MAEs) occurring within 30-days post-procedure that are listed below, for subjects undergoing the convergent procedure.

All MAEs were adjudicated by the Clinical Events Committee (CEC):

- Cardiac tamponade: significant pericardial effusion resulting in hemodynamic compromise, requires elective or urgent pericardiocentesis, and results in a 1 cm or more pericardial effusion as documented by echocardiography.
- Severe Pulmonary Vein Stenosis (≥ 70% occlusion)
- Excessive bleeding requiring transfusion or > 20% drop in HCT.
- Myocardial infarction
- Stroke
- Transient Ischemic Attacks (TIA)
- Atrioesophageal fistula
- Phrenic nerve injury
- Death

No formal hypothesis testing was pre-specified in the study protocol. Instead, the protocol pre-specified an acceptable MAE rate of 12%. The primary safety endpoint would be considered met if the true incidence rate for MAEs in this study population was no more than 12% with a 95% one-sided upper bound of MAEs being less than 20%.

Secondary Safety Endpoint

The secondary safety endpoint for the study was the incidence of serious adverse events (SAEs) in the study through the 12-months post procedure visit, in each arm of the study.

Exploratory Endpoints

- Success or failure to achieve a 90% reduction from baseline AF burden with and without Class I and III AADs at 18 months post procedure
- Change in left ventricular ejection fraction
- Atrial remodeling assessed by a decrease in left atrial size
- Health Economics Data

Subject Accountability

At the time of the database lock (November 6, 2019), of 153 patients enrolled in the CONVERGE PMA study 96.7% (148/153) patients are available for analysis at the 12-months post-operative visit. Study exit reasons for randomized subjects included enrollment closure, no insurance coverage, patient withdrew consent, pericardial adhesion, severe liver disease, lung cancer, severe tricuspid regurgitation, severe mitral regurgitation. Figure 2 presents the patient accountability.

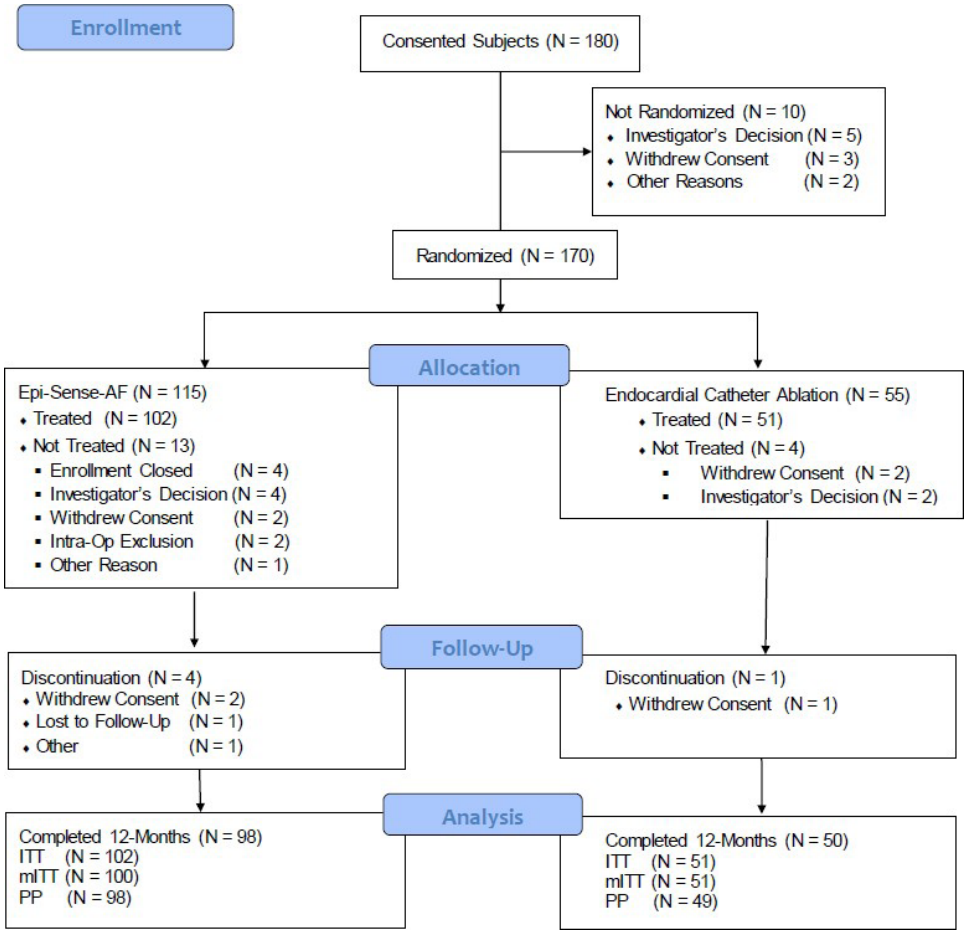


FIGURE 2: SUBJECT ACCOUNTABILITY

Subject Demographics and Baseline Characteristics

A summary of the demographic and baseline characteristics is presented in Table 2 for the all treated population (persistent and longstanding persistent AF subjects) and the longstanding persistent AF sub-population. Baseline cardiovascular comorbidities are summarized in Table 3. Additional baseline and ablation procedure data are summarized in Table 4.

The demographics of the study population are typical for an atrial fibrillation ablation study performed in the US and the UK. As detailed below, except for gender, the treatment groups were comparable with respect to demographic and baseline characteristics.

As detailed below, the major comorbidities were comparable between the EPi-Sense and Catheter Ablation groups. Most subjects 75.2% (115/153) had hypertension: 75.5% (77/102) in the EPi-Sense Sense group and 74.5% (38/51) in the Catheter Ablation group. Most subjects had some type of valvular heart disease: 57.5% (88/153) with mitral valve regurgitation and 56.2% (86/153) with tricuspid valve regurgitation.

Table 2: Demographics and Baseline Characteristics

	All Treated Subjects (N = 153)		Longstanding Persistent AF Subjects (N = 65)	
Parameter	**EPi-Sense (N = 102)**	**Catheter Ablation (N = 51)**	**EPi-Sense (N = 38)**	**Catheter Ablation (N = 27)**
Age (years), Mean ± SD	63.7 ± 9.64	65.1 ± 6.66	61.5 ± 10.27	65.2 ± 7.26
Male	78% (80/102)	53% (27/51)	82% (31/38)	56% (15/27)
Caucasian	94% (96/102)	98% (50/51)	95% (36/38)	96% (26/27)
Height (cm), Mean ± SD	177.7 ± 8.43	173.9 ± 11.64	178.5 ± 9.05	172.7 ± 8.95
Weight (kg), Mean ± SD	104.3 ± 19.98	106.3 ± 23.90	104.3 ± 20.56	105.3 ± 23.10
Body mass index (kg/m^2), Mean ± SD	33.0 ± 5.86	35.1 ± 7.13	32.7 ± 5.97	35.4 ± 7.88
Number of years in atrial fibrillation [a]	4.4 ± 4.8	4.5 ± 4.7	6.0 ± 6.4	5.8 ± 5.5
Type of atrial fibrillation				
Persistent	63% (64/102)	47% (24/51)	0% (0/35)	0% (0/27)
Longstanding Persistent	37% (38/102)	53% (27/51)	100% (35/35)	100% (27/27)

[a] The number of years since persistent AF diagnosis.

Table 3: Baseline Cardiovascular Comorbidities

	All Treated Subjects (N = 153)		Longstanding Persistent AF Subjects (N = 65)	
Parameter	**EPi-Sense (N = 102)**	**Catheter Ablation (N = 51)**	**EPi-Sense (N = 38)**	**Catheter Ablation (N = 27)**
1st Degree AV Block	5.9% (6/102)	3.9% (2/51)	2.6% (1/38)	3.7% (1/27)
Acute MI	4.9% (5/102)	2.0% (1/51)	5.3% (2/38)	0.0% (0/27)
Aortic Atherosclerosis	4.9% (5/102)	2.0% (1/51)	5.3% (2/38)	0.0% (0/27)
Aortic Valve Regurgitation	18.6% (19/102)	13.7% (7/51)	10.5% (4/38)	11.1% (3/27)
Atrial Flutter	9.8% (10/102)	15.7% (8/51)	13.2% (5/38)	14.8% (4/27)
Bradycardia	8.8% (9/102)	11.8% (6/51)	5.3% (2/38)	11.1% (3/27)
Cardiomyopathy	14.7% (15/102)	7.8% (4/51)	26.3% (10/38)	11.1% (3/27)
Congestive Heart Failure (CHF)	17.6% (18/102)	27.5% (14/51)	2.6% (1/38)	25.9% (7/27)
Coronary Artery Disease (CAD)	19.6% (20/102)	19.6% (10/51)	26.3% (10/38)	18.5% (5/27)
Hypertension	75.5% (77/102)	74.5% (38/51)	73.7% (28/38)	77.8% (21/27)
Left Ventricular Dysfunction	3.9% (4/102)	2.0% (1/51)	0% (0/38)	3.7% (1/27)
Mitral Valve Prolapse	2.0% (2/102)	5.9% (3/51)	0% (0/38)	3.7% (1/27)
Mitral Valve Regurgitation	53.9% (55/102)	64.7% (33/51)	50.0% (19/38)	55.6% (15/27)
Peripheral Vascular Disease	2.0% (2/102)	7.8% (4/51)	2.6% (1/38)	7.4% (2/27)
Pulmonary Valve Incompetence	2.9% (3/102)	3.9% (2/51)	2.6% (1/38)	0.0% (0/27)

	All Treated Subjects (N = 153)		Longstanding Persistent AF Subjects (N = 65)	
Parameter	**EPi-Sense (N = 102)**	**Catheter Ablation (N = 51)**	**EPi-Sense (N = 38)**	**Catheter Ablation (N = 27)**
Sick Sinus Syndrome	4.9% (5/102)	2.0% (1/51)	2.6% (1/38)	0.0% (0/27)
Tachycardia	2.9% (3/102)	3.9% (2/51)	7.9% (3/38)	3.7% (1/27)
Tricuspid Valve Regurgitation	52.9% (54/102)	62.7% (32/51)	50.0% (19/38)	51.9% (14/27)

Table 4: Additional Baseline and Ablation Procedure Data

	All Treated Subjects (N = 153)		Longstanding Persistent AF Subjects (N = 65)	
Parameter	**EPi-Sense (N = 102)**	**Catheter Ablation (N = 51)**	**EPi-Sense (N = 38)**	**Catheter Ablation (N = 27)**
Ablation Procedure Time (Minutes)				
Total Convergent Procedure Time [a]	293.9 ± 80.4	Not Applicable	301.9 ± 60.4	Not Applicable
Total Epicardial Procedure Time [b]	115.8 ± 35.5	Not Applicable	116.1 ± 27.7	Not Applicable
Total Epicardial Ablation Procedure Time [c]	69.5 ± 21.2	Not Applicable	77.3 ± 19.9	Not Applicable
Total Epicardial RF Time [d]	42.9 ± 13.7	Not Applicable	45.0 ± 13.3	Not Applicable
Total Endocardial Ablation Procedure Time [e]	135.8 ± 49.9	171.4 ± 59.7	139.6 ± 44.1	180.7 ± 64.1
Total Time to Create Endocardial Lesion [c]	82.6 ± 42.6	113.3 ± 48.5	83.6 ± 35.5	110.9 ± 54.6
Total Endocardial RF Time [d]	40.0 ± 22.1	61.3 ± 25.7	43.0 ± 18.1	65.0 ± 26.6
Left Atrial Diameter (cm)	4.4 ± 0.62	4.3 ± 0.56	4.5 ± 0.68	4.3 ± 0.56
Left ventricular ejection fraction (%)	55.3 ± 7.79	55.7 ± 6.13	54.4 ± 7.50	54.7 ± 6.22

Note: Data are presented as Mean ± SD.

[a] Abdominal incision to removal of catheters-not sheath pull.

[b] Abdominal incision to abdominal access site closure.

[c] Time from first lesion to last lesion.

[d] Cumulative time of RF energy delivery.

[e] Groin access to removal of catheters.

Primary Safety Results

The primary safety endpoint was defined as the incidence of MAEs for subjects undergoing the convergent procedure for the procedural to 30- day post-procedure time period. A summary of MAEs during is provided in Table 5 below.

In comparison to the EPi-Sense group, no MAEs occurred in the 51 Catheter Ablation subjects. Eight subjects (7.8% (8/102) [95% UCL: 13.7%]) in the EPi-Sense group experienced nine MAEs. One subject experienced a tamponade and an excessive bleeding event. The most commonly reported MAE was a delayed pericardial effusion, occurring in 3.9% (4/102) of subjects. Per the protocol, the observed MAE rate of 7.8% (95% UCL: 13.7%) in this study population was no more than 12% with a 95% one-sided upper bound of MAEs being less than 20%. A total of 3 of 8 MAEs occurred within 7 days post-procedure: excessive bleeding, cardiac tamponade, and stroke.

As per the protocol definition, only those pericardial effusions that had tamponade physiology on echocardiogram and resulted in an intervention for pericardial fluid drainage counted towards the primary safety endpoint. Other than the 4 primary safety endpoint events of tamponade, two additional EPi-Sense subjects experienced pericardial effusion of greater than 1 cm but without tamponade physiology on echocardiogram within 30 days of the procedure. Both subjects were treated with invasive procedure for pericardial drainage. Overall, 6 subjects had pericardial effusion that were drained within 30 days of the procedure. These pericardial effusion events were delayed and likely due to inflammatory response to pericardiotomy and extensive epicardial ablation. In one subject, delayed recognition of symptomatic pericardial effusion/tamponade despite repeated clinical encounters led to cardiac arrest. Subsequently the patient had acute multi-organ dysfunction syndrome and anoxic brain injury.

The results for the persistent AF and longstanding persistent AF sub-populations are considered post-hoc and should be interpreted with caution since the confidence intervals are presented without adjustment for multiplicity.

Table 5: Primary Safety Endpoint

Major Adverse Event (MAE)	Protocol Definition	
	All Treated (N = 102)	Longstanding Persistent (N = 38)
Death	0% (0/102)	0% (0/38)
Atrioesophageal Fistula	0% (0/102)	0% (0/38)
Cardiac Tamponade	3.9% (4/102)	2.6% (1/38)
Excessive Bleeding (requiring transfusion)	1% (1/102)	0% (0/38)
Transient Ischemic Attack	1% (1/102)	0% (0/38)
Stroke	1% (1/102)	2.6% (1/38)
Phrenic Nerve Injury	1% (1/102)	2.6% (1/38)
Safety Event (MAE) Rate	7.8% (8/102)† [13.7% UCL]	7.9% (3/38) [19.2% UCL] [a]

[a]: Confidence intervals are not adjusted for multiplicity.

†One experienced a tamponade and an excessive bleeding event. The subject is included once in the tamponade event.
Note: No Severe Pulmonary Vein Stenosis; Myocardial Infarction were reported in the trial.
No protocol pre-specified MAEs were observed in the Catheter Ablation arm.
All events resolved without sequelae, except for one patient with the strokes who continues with slightly slower left facial movement and one with unknown recovery due to subject withdrawal.

Primary Effectiveness Results

The primary effectiveness endpoint was defined as the proportion of subjects who were AF/AT/AFL-free (that is, no episodes > 30 seconds by Holter; or for full 10 second recording on standard 12 lead ECG) absent Class I and III AADs except for a previously failed or intolerant Class I or III AAD with no increase in dosage following the 3-month blanking period through the 12-months post procedure follow up visit. The primary effectiveness endpoint analysis is presented for the ITT (with imputation), ITT (without imputation), mITT and Per-Protocol populations in Table 6.1 below.

In the full all treated patient population, the primary effectiveness endpoint of superiority of the EPi-Sense compared to Catheter Ablation was met. Freedom from AF/AFL/AT was achieved in 65.7% (67/102) [95% CI: 56.5%, 74.9%] subjects in the EPi-Sense treatment group compared to 49.0% (25/51) [95% CI: 35.3%, 62.7%] subjects in the Catheter Ablation group. The observed success rate difference of 16.7% [95% CI: 0.1%, 33.2%] is statistically significant (Chi-Squared p-value = 0.0472) in favor of the EPi-Sense treatment group. The success rate difference for the ITT population, without imputation for missing data was 17.7% [95% CI: 1.0%, 34.3%] which is statistically significant (Chi-Squared p-value = 0.0360) in favor of the EPi-Sense treatment group. The result was sustained across the mITT and Per-Protocol populations.

Table 6.1: Primary Effectiveness Endpoint (All Treated Subjects)

	All Treated Subjects (N = 153)		
Primary Effectiveness	**EPi-Sense (N = 102)**	**Catheter Ablation (N = 51)**	**Treatment Difference [c][d]**
ITT Population [a]	65.7% (67/102)	49.0% (25/51)	16.7% (p=0.0472)
95% Confidence Interval	56.5 - 74.9%	35.3 – 62.7%	0.1 - 33.2%
ITT Population [b]	67.7% (67/99)	50.0% (25/50)	17.7% (p=0.0360)
95% Confidence Interval	58.5 - 76.9%	36.1 – 63.9%	1.0 - 34.3%
mITT Population [a]	67.0% (67/100)	49.0% (25/51)	18.0% (p=0.0322)
95% Confidence Interval	57.8 – 76.2%	35.3 – 62.7%	1.5 – 34.5%
PP Population [b]	68.0% (66/97)	51.0% (25/49)	17.0% (p=0.0450)
95% Confidence Interval	58.8 – 77.3%	37.0 – 65.0%	0.2 – 33.8%

Note: The ITT population consists of all subjects who received a randomized study procedure.

The mITT population consists of all subjects who received a randomized study procedure and have at least one post-treatment follow-up visit after the 3-month blanking period with non-missing efficacy results.

The PP population consists of all subjects who received a randomized study procedure, have non-missing efficacy results at the 6-month visit, and have at least four of the five first year visits (e.g., at least 4 of the 7 day, 1 month, 3 month 6 month and 12 month visits are completed) and who have no major protocol violations or deviations.

[a] Subjects with indeterminate results are classified as failures.

[b] Indeterminate (missing) data are not imputed.

[c] Confidence intervals calculated using the Wald asymptotic method.

[d] Difference between treatment arms evaluated using Chi-Squared test.

The results for the longstanding persistent AF sub-population are considered post-hoc and should be interpreted with caution since the confidence intervals are presented without adjustment for multiplicity.

Further analysis revealed evidence of heterogeneity of the treatment effect based on AF class (interaction p-value = 0.1469), primary effectiveness success driven by the longstanding persistent AF sub-population.

Persistent AF Subjects

Freedom from AF/AFL/AT was achieved in 65.6% (42/64) [95% CI: 54.0%, 77.3%] subjects in the EPi-Sense treatment group compared to 62.5% (15/24) [95% CI: 43.1%, 81.9%] subjects in the Catheter Ablation group. The observed success rate difference was 3.1% [95% CI: - 19.5%, 25.7%].

Longstanding Persistent AF Subjects

Freedom from AF/AFL/AT was achieved in 65.8% (25/38) [95% CI: 50.7%, 80.9%] subjects in the EPi-Sense treatment group compared to 37.0% (10/27) [95% CI:18.8%, 55.3%] subjects in the Catheter Ablation group. The observed success rate difference was 28.8% [95% CI: 5.1%, 52.4%]. The success rate difference for the Per-Protocol population was 27.3% [95% CI: 3.3%, 51.4%].

Table 6.2: Post-Hoc Primary Effectiveness Endpoint (Persistent and Longstanding Persistent AF Sub-Populations)

	Persistent AF Subjects (N = 88)			Longstanding Persistent AF Subjects (N = 65)		
Primary Effectiveness	**EPi-Sense (N = 64)**	**Catheter Ablation (N = 24)**	**Treatment Difference [c]**	**EPi-Sense (N = 38)**	**Catheter Ablation (N = 27)**	**Treatment Difference [c]**
ITT Population [a]	65.6% (42/64)	62.5% (15/24)	3.1%	65.8% (25/38)	37.0% (10/27)	28.8%
95% Confidence Interval	54.0 - 77.3%	43.1 - 81.9%	-19.5 - 25.7%	50.7 - 80.9%	18.8 - 55.3%	5.1 - 52.4%
ITT Population [b]	68.8% (42/61)	65.2% (15/23)	3.6%	65.8% (25/38)	37.0% (10/27)	28.8%
95% Confidence Interval	57.2 - 80.5%	45.8 - 84.7%	-19.0 - 26.3%	50.7 - 80.9%	18.8 - 55.3%	5.1 - 52.4%
mITT Population [a]	67.7% (42/62)	62.5% (15/24)	5.2%	65.8% (25/38)	37.0% (10/27)	28.8%
95% Confidence Interval	56.1 - 79.4%	43.1 - 81.9%	-17.4 - 27.8%	50.7 - 80.9%	18.8 - 55.3%	5.1 - 52.4%
PP Population [b]	69.5% (41/59)	65.2% (15/23)	4.3%	65.8% (25/38)	38.5% (10/26)	27.3%
95% Confidence Interval	57.7 - 81.2%	45.8 - 84.7%	-18.5 - 27.0%	50.7 - 80.9%	19.8 - 57.2%	3.3 - 51.4%

Note: Refer to footnotes on Table 6.1. Confidence intervals are not adjusted for multiplicity.

Secondary Safety and Effectiveness Results

Secondary Safety (Serious Adverse Events within 12 months)

The secondary safety endpoint for the study was the incidence of serious adverse events (SAEs) in the study through the 12-months post- procedure, in each treatment arm of the study. A summary of SAEs that occurred through the 12-months post-procedure is provided in the tables below.

SAEs occurring within the 12-months post-procedure period were reported in 32.4% (33/102) subjects in the EPi-Sense group compared to 35.3% (18/51) subjects in the Catheter Ablation group. The most commonly reported SAEs through the 12-months post-procedure period included: cardiac failure congestive (4.9% and 2% of subjects in the EPi-Sense AF and Catheter Ablation groups, respectively); cardiac tamponade (3.9% of subjects in EPi-Sense AF group); pericardial effusion (3.9% of subjects in EPi-Sense AF group); pericarditis (2.9% of subjects in EPi-Sense group); and pneumonia (2.9% and 7.8% of subjects in EPi-Sense and Catheter Ablation groups, respectively). Sinus node dysfunction was reported in 3.9% (2/51) subjects in the Catheter Ablation group.

Table 7.1: Summary of Serious Adverse Events within 12 months (All Treated Subjects)

All Treated Subjects (N = 153)				
	EPi-Sense (N = 102)		**Catheter Ablation (N = 51)**	
System Organ Class MedDRA Preferred Term	Subjects n (%)	Events n	Subjects n (%)	Events n
ANY SERIOUS ADVERSE EVENT	33 (32.4%)	58	18 (35.3%)	22
CARDIAC DISORDERS				
ATRIOVENTRICULAR BLOCK COMPLETE	1 (1.0%)	1	0 (0%)	0
CARDIAC FAILURE CONGESTIVE	5 (4.9%)	5	1 (2.0%)	1
CARDIAC TAMPONADE	4 (3.9%)	4	0 (0%)	0
PERICARDIAL EFFUSION	4 (3.9%)	4	0 (0%)	0
PERICARDITIS	3 (2.9%)	3	0 (0%)	0
SINUS NODE DYSFUNCTION	0 (0%)	0	2 (3.9%)	2
OVERALL INCIDENCE	15 (14.7%)	17	3 (5.9%)	3
ENDOCRINE DISORDERS				
HYPERTHYROIDISM	1 (1.0%)	1	0 (0%)	0
OVERALL INCIDENCE	1 (1.0%)	1	0 (0%)	0
GASTROINTESTINAL DISORDERS				
DIVERTICULAR PERFORATION	1 (1.0%)	1	0 (0%)	0
GASTROINTESTINAL HAEMORRHAGE	1 (1.0%)	1	1 (2.0%)	1
GASTROINTESTINAL ULCER HAEMORRHAGE	1 (1.0%)	1	0 (0%)	0
HAEMORRHOIDAL HAEMORRHAGE	0 (0%)	0	1 (2.0%)	1
INTESTINAL OBSTRUCTION	1 (1.0%)	1	0 (0%)	0
NAUSEA	1 (1.0%)	1	0 (0%)	0
OVERALL INCIDENCE	5 (4.9%)	5	2 (3.9%)	2
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
CHEST PAIN	3 (2.9%)	3	0 (0%)	0
MULTI-ORGAN DISORDER	1 (1.0%)	1	0 (0%)	0
OVERALL INCIDENCE	4 (3.9%)	4	0 (0%)	0
INFECTIONS AND INFESTATIONS				
CELLULITIS	0 (0%)	0	1 (2.0%)	1
CHOLECYSTITIS INFECTIVE	1 (1.0%)	1	0 (0%)	0
DIVERTICULITIS	0 (0%)	0	1 (2.0%)	1
ERYSIPELAS	1 (1.0%)	1	0 (0%)	0
INFECTION	0 (0%)	0	1 (2.0%)	1
LOWER RESPIRATORY TRACT INFECTION	1 (1.0%)	1	0 (0%)	0
PNEUMONIA	3 (2.9%)	3	4 (7.8%)	4
UPPER RESPIRATORY TRACT INFECTION	0 (0%)	0	1 (2.0%)	1
URINARY TRACT INFECTION	0 (0%)	0	1 (2.0%)	1
OVERALL INCIDENCE	6 (5.9%)	6	9 (17.6%)	9
INJURY, POISONING AND PROCEDURAL COMPLICATIONS				
INCISIONAL HERNIA	1 (1.0%)	1	0 (0%)	0

LOWER LIMB FRACTURE	0 (0%)	0	1 (2.0%)	1
NERVE INJURY	1 (1.0%)	1	0 (0%)	0
POST PROCEDURAL HAEMORRHAGE	1 (1.0%)	1	0 (0%)	0
OVERALL INCIDENCE	3 (2.9%)	3	1 (2.0%)	1
METABOLISM AND NUTRITION DISORDERS				
FLUID OVERLOAD	2 (2.0%)	2	0 (0%)	0
HYPONATRAEMIA	1 (1.0%)	1	0 (0%)	0
OVERALL INCIDENCE	3 (2.9%)	3	0 (0%)	0
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS				
CERVICAL SPINAL STENOSIS	1 (1.0%)	1	0 (0%)	0
MUSCULAR WEAKNESS	1 (1.0%)	1	0 (0%)	0
OVERALL INCIDENCE	2 (2.0%)	2	0 (0%)	0
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)				
BREAST CANCER RECURRENT	0 (0%)	0	1 (2.0%)	1
GLIOBLASTOMA	1 (1.0%)	1	0 (0%)	0
INVASIVE DUCTAL BREAST CARCINOMA	1 (1.0%)	1	0 (0%)	0
KAPOSI'S SARCOMA	0 (0%)	0	1 (2.0%)	1
OVERALL INCIDENCE	2 (2.0%)	2	2 (3.9%)	2
NERVOUS SYSTEM DISORDERS				
CEREBROVASCULAR ACCIDENT	1 (1.0%)	1	0 (0%)	0
TRANSIENT ISCHAEMIC ATTACK	1 (1.0%)	1	0 (0%)	0
OVERALL INCIDENCE	2 (2.0%)	2	0 (0%)	0
RENAL AND URINARY DISORDERS				
ACUTE KIDNEY INJURY	1 (1.0%)	1	0 (0%)	0
CHRONIC KIDNEY DISEASE	1 (1.0%)	1	0 (0%)	0
OVERALL INCIDENCE	2 (2.0%)	2	0 (0%)	0
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS				
ACUTE RESPIRATORY FAILURE	1 (1.0%)	1	0 (0%)	0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	1 (1.0%)	1	0 (0%)	0
CHRONIC RESPIRATORY FAILURE	1 (1.0%)	1	0 (0%)	0
HAEMOPTYSIS	0 (0%)	0	1 (2.0%)	1
ORGANISING PNEUMONIA	0 (0%)	0	1 (2.0%)	1
PLEURAL EFFUSION	2 (2.0%)	2	1 (2.0%)	1
PLEURITIC PAIN	1 (1.0%)	1	0 (0%)	0
PULMONARY OEDEMA	3 (2.9%)	3	0 (0%)	0
OVERALL INCIDENCE	8 (7.8%)	9	3 (5.9%)	3
SURGICAL AND MEDICAL PROCEDURES				
COLOSTOMY CLOSURE	1 (1.0%)	1	0 (0%)	0
OVERALL INCIDENCE	1 (1.0%)	1	0 (0%)	0
VASCULAR DISORDERS				
HAEMATOMA	0 (0%)	0	1 (2.0%)	1
HYPERTENSIVE EMERGENCY	0 (0%)	0	1 (2.0%)	1
JUGULAR VEIN THROMBOSIS	1 (1.0%)	1	0 (0%)	0
OVERALL INCIDENCE	1 (1.0%)	1	2 (3.9%)	2

Table 7.2: Summary of Serious Adverse Events within 12 months

(Persistent and Longstanding Persistent AF Sub-Populations)

	Persistent AF Subjects (N = 88)		Long-standing Persistent AF Subjects (N = 65)					
	EPi-Sense (N = 64)		Catheter Ablation (N = 24)		EPi-Sense (N = 38)		Catheter Ablation (N = 27)	
System Organ Class MedDRA Preferred Term	Subjects n (%)	Events n	Subjects n (%)	Events n	Subjects n (%)	Events n	Subjects n (%)	Events n
ANY SERIOUS ADVERSE EVENT	23 (35.9%)	37	9 (37.5%)	12	10 (26.3%)	21	9 (33.3%)	10
CARDIAC DISORDERS								
ATRIOVENTRICULAR BLOCK COMPLETE	1 (1.6%)	1	0 (0%)	0	0 (0%)	0	0 (0%)	0
CARDIAC FAILURE CONGESTIVE	3 (4.7%)	3	1 (4.2%)	1	2 (5.3%)	2	0 (0%)	0
CARDIAC TAMPONADE	3 (4.7%)	3	0 (0%)	0	1 (2.6%)	1	0 (0%)	0
PERICARDIAL EFFUSION	3 (4.7%)	3	0 (0%)	0	1 (2.6%)	1	0 (0%)	0
PERICARDITIS	1 (1.6%)	1	0 (0%)	0	2 (5.3%)	2	0 (0%)	0
SINUS NODE DYSFUNCTION	0 (0%)	0	0 (0%)	0	0 (0%)	0	2 (7.4%)	2
OVERALL INCIDENCE	11 (17.2%)	11	1 (4.2%)	1	4 (10.5%)	6	2 (7.4%)	2
ENDOCRINE DISORDERS								
HYPERTHYROIDISM	1 (1.6%)	1	0 (0%)	0	0 (0%)	0	0 (0%)	0
OVERALL INCIDENCE	1 (1.6%)	1	0 (0%)	0	0 (0%)	0	0 (0%)	0
GASTROINTESTINAL DISORDERS								
DIVERTICULAR PERFORATION	1 (1.6%)	1	0 (0%)	0	0 (0%)	0	0 (0%)	0
GASTROINTESTINAL HAEMORRHAGE	1 (1.6%)	1	1 (4.2%)	1	0 (0%)	0	0 (0%)	0
GASTROINTESTINAL ULCER HAEMORRHAGE	1 (1.6%)	1	0 (0%)	0	0 (0%)	0	0 (0%)	0
HAEMORRHOIDAL HAEMORRHAGE	0 (0%)	0	0 (0%)	0	0 (0%)	0	1 (3.7%)	1
INTESTINAL OBSTRUCTION	1 (1.6%)	1	0 (0%)	0	0 (0%)	0	0 (0%)	0
NAUSEA	0 (0%)	0	0 (0%)	0	1 (2.6%)	1	0 (0%)	0
OVERALL INCIDENCE	4 (6.3%)	4	1 (4.2%)	1	1 (2.6%)	1	1 (3.7%)	1
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS								
CHEST PAIN	1 (1.6%)	1	0 (0%)	0	2 (5.3%)	2	0 (0%)	0
MULTI-ORGAN DISORDER	1 (1.6%)	1	0 (0%)	0	0 (0%)	0	0 (0%)	0
OVERALL INCIDENCE	2 (3.1%)	2	0 (0%)	0	2 (5.3%)	2	0 (0%)	0
INFECTIONS AND INFESTATIONS								
CELLULITIS	0 (0%)	0	0 (0%)	0	0 (0%)	0	1 (3.7%)	1
CHOLECYSTITIS INFECTIVE	1 (1.6%)	1	0 (0%)	0	0 (0%)	0	0 (0%)	0
DIVERTICULITIS	0 (0%)	0	1 (4.2%)	1	0 (0%)	0	0 (0%)	0
ERYSIPELAS	0 (0%)	0	0 (0%)	0	1 (2.6%)	1	0 (0%)	0
INFECTION	0 (0%)	0	0 (0%)	0	0 (0%)	0	1 (3.7%)	1
LOWER RESPIRATORY TRACT INFECTION	0 (0%)	0	0 (0%)	0	1 (2.6%)	1	0 (0%)	0
PNEUMONIA	3 (4.7%)	3	3 (12.5%)	3	0 (0%)	0	1 (3.7%)	1
UPPER RESPIRATORY TRACT INFECTION	0 (0%)	0	0 (0%)	0	0 (0%)	0	1 (3.7%)	1
URINARY TRACT INFECTION	0 (0%)	0	0 (0%)	0	0 (0%)	0	1 (3.7%)	1
OVERALL INCIDENCE	4 (6.3%)	4	4 (16.7%)	4	2 (5.3%)	2	5 (18.5%)	5
INJURY, POISONING AND PROCEDURAL COMPLICATIONS								
INCISIONAL HERNIA	0 (0%)	0	0 (0%)	0	1 (2.6%)	1	0 (0%)	0
LOWER LIMB FRACTURE	0 (0%)	0	1 (4.2%)	1	0 (0%)	0	0 (0%)	0
NERVE INJURY	0 (0%)	0	0 (0%)	0	1 (2.6%)	1	0 (0%)	0
POST PROCEDURAL HAEMORRHAGE	1 (1.6%)	1	0 (0%)	0	0 (0%)	0	0 (0%)	0
OVERALL INCIDENCE	1 (1.6%)	1	1 (4.2%)	1	2 (5.3%)	2	0 (0%)	0
METABOLISM AND NUTRITION DISORDERS								
FLUID OVERLOAD	0 (0%)	0	0 (0%)	0	2 (5.3%)	2	0 (0%)	0
HYPONATRAEMIA	1 (1.6%)	1	0 (0%)	0	0 (0%)	0	0 (0%)	0
OVERALL INCIDENCE	1 (1.6%)	1	0 (0%)	0	2 (5.3%)	2	0 (0%)	0

Table 8: SAEs Related to device and/or procedure through 12 months post-procedure

	All Treated Subjects (N = 153)		Longstanding Persistent AF Subjects (N = 65)	
Parameter	**EPi-Sense (N = 102)**	**Catheter Ablation (N = 51)**	**EPi-Sense (N = 38)**	**Catheter Ablation (N = 27)**
Number of subjects with events	19.6% (20/102)	9.8% (5/51)	18.4% (7/38)	7.4% (2/27)
Cardiac Events	13.7% (14/102)	2.0% (1/51)	15.7% (6/38)	0.0% (0/27)
Cardiac Tamponade* [a]	3.9% (4/102)	0.0% (0/51)	2.6% (1/38)	0.0% (0/27)
Chest pain	1.0% (1/102)	0.0% (0/51)	2.6% (1/38)	0.0% (0/27)
Congestive Heart Failure	2.0% (2/102)	0.0% (0/51)	2.6% (1/38)	0.0% (0/27)
Hypertensive Emergency	0.0% (0/102)	2.0% (1/51)	0.0% (0/38)	0.0% (0/27)
Pericardial Effusion [b]	3.9% (4/102)	0.0% (0/51)	2.6% (1/38)	0.0% (0/27)
Pericarditis	2.9% (3/102)	0.0% (0/51)	5.3% (2/38)	0.0% (0/27)
Respiratory Events	4.9% (5/102)	3.9% (2/51)	5.3% (2/38)	3.7% (1/27)
Acute Respiratory Failure	1.0% (1/102)	0.0% (0/51)	2.6% (1/38)	0.0% (0/27)
Pneumonia	1.0% (1/102)	2.0% (1/51)	0.0% (0/38)	0.0% (0/27)
Pleural Effusion	2.0% (2/102)	0.0% (0/51)	2.6% (1/38)	0.0% (0/27)
Upper Respiratory Infection	0.0% (0/102)	2.0% (1/51)	0.0% (0/38)	3.7% (1/27)
Pulmonary Edema	1.0% (1/102)	0.0% (0/51)	0.0% (0/38)	0.0% (0/27)
Excessive Bleeding*	2.0% (2/102)	0.0% (0/51)	2.6% (1/38)	0.0% (0/27)
Phrenic Nerve Injury*	1.0% (1/102)	0.0% (0/51)	2.6% (1/38)	0.0% (0/27)
Stroke*	1.0% (1/102)	0.0% (0/51)	2.6% (1/38)	0.0% (0/27)
Volume overload	2.0% (2/102)	0.0% (0/51)	5.3% (2/38)	0.0% (0/27)
Transient Ischemic Attack*	1.0% (1/102)	0.0% (0/51)	0.0% (0/38)	0.0% (0/27)

* Event also classified as MAE in previous Tables.

[a] Pericardial effusions with tamponade physiology.

[b] Pericardial effusions (intervention or medical management).

In addition to those listed in Table 8, the following other events were reported in 5.9% (6/102) unique subjects in the all treated subjects EPi- Sense group: Acute kidney injury; abdominal hernia; jugular vein thrombosis; hyponatremia; multi-organ dysfunction; and nausea. Hemoptysis and urinary tract infection was reported in 3.9% (2/51) unique subjects in the Catheter Ablation group. For longstanding persistent AF subjects, other events were reported in 7.9% (3/38) unique subjects in the EPi-Sense group: acute kidney injury; abdominal hernia; and nausea. Urinary tract infection was reported in 3.7% (1/27) of subjects in the Catheter Ablation group.

Secondary Effectiveness Results

The fixed-sequence procedure proposed, was prospectively specified in the SAP to evaluate the key secondary endpoints. Each of these tests were performed at the same two-sided significance level (α=0.05) in this predetermined order. Each endpoint was only tested if the prior endpoint was successful ($p \leq 0.05$). This procedure maintained the Type I error rate as no further testing was performed once an endpoint in the sequence failed to show significance ($p > 0.05$).

The fixed-sequential resulted in two statistically significant secondary endpoints:

1. Proportion of subjects achieving >=90% reduction from baseline AF burden and off Class I and III AADs, except for previously failed or intolerant Class I and III AADs with no increase in dosage at 12-months post-procedure.
2. Proportion of subjects free of AF and off Class I and III AADs except for previously failed or intolerant Class I and III AADs with no increase in dosage following the 3-months blanking period through the 12-months post-procedure visit.

Analyses of these two statistically significant endpoints are presented in Tables 9.1 and 9.2. The other secondary effectiveness endpoints are descriptively summarized in Table 10.

The results for the persistent AF and longstanding persistent AF sub-populations are considered post-hoc and should be interpreted with caution since the confidence intervals are presented without adjustment for multiplicity.

AF Burden Reduction of at Least 90% at 12-Months Compared to Baseline:

AF burden percentage was captured directly on the Zio patch report and was based on the total time the subject was in AF over the time the subject wore the Zio patch, after artifact removal. A ≥90% change from baseline is based on comparing the post-procedure AF burden percentage to the baseline AF burden percentage recorded on the Holter Monitor.

All Treated Subjects

The proportion of subjects achieving at least 90% reduction in AF burden, absent of an increased dose or new Class I/III AADs, at 12-months compared to baseline was 80% (60/75) [95% CI: 70.9%, 89.1%] in the EPi-Sense treatment group, compared to 56.8% (25/44) [95% CI: 42.2%, 71.5%] in the Catheter Ablation group. The success rate difference of 23.2% [95% CI: 6.0%, 40.4%] is statistically significant (Chi-Squared p- value = 0.0069) in favor of the EPi-Sense treatment group.

The superiority of the EPi-Sense group over the Catheter Ablation group in achieving at least 90% reduction in AF burden at 12-months relative to baseline, absent of an increased dose or new Class I/III AADs, was achieved based on the ITT analysis. These results were supported by the mITT (produced identical results as the ITT population) and PP population analyses.

Persistent AF Subjects

The proportion of subjects achieving at least 90% reduction in AF burden, absent of an increased dose or new Class I/III AADs, at 12-months compared to baseline was 81.1% (30/37) [95% CI: 64.8%, 92.0%] subjects in the EPi-Sense treatment group compared to 72.2% (13/18) [95% CI: 46.5%, 90.3%] subjects in the Catheter Ablation group. The success rate difference was 8.9%.

Longstanding Persistent AF Subjects

The proportion of subjects achieving at least 90% reduction in AF burden, absent of an increased dose or new Class I/III AADs, at 12-months compared to baseline was 78.9% (30/38) [95% CI: 66.0%, 91.9%] in the EPi-Sense treatment group, compared to 46.2% (12/26) [95% CI: 27.0%, 65.3%] in the Catheter Ablation group. The success rate difference was 32.8% [95% CI: 9.7%, 55.9%] in favor of EPi-Sense.

AF Freedom Through 12-Months, Absent Class I/III AADs:

All Treated Subjects

The proportion of subjects achieving AF freedom through 12-Months, absent of an increased dose or new Class I/III AADs was 70.6% (72/102) [95% CI: 61.7%, 79.4%] in the EPi-Sense treatment group, compared to 51.0% (26/51) [95% CI: 37.3%, 64.7%] in the Catheter Ablation group. The difference in success rate of 19.6% [95% CI: 3.3%, 35.9%] is statistically significant (Chi-Squared p-value = 0.0172) in favor of the EPi- Sense treatment group. The superiority of the EPi-Sense group over the Catheter Ablation group in achieving at AF freedom through 12-months, absent of an increased dose or new Class I/III AADs, was achieved based on the ITT analysis. These results were supported by the mITT and PP population analyses.

Persistent AF Subjects

The proportion of subjects achieving AF freedom through 12-Months, absent of an increased dose or new Class I/III AADs was 70.3% (45/64) [95% CI: 59.1%, 81.5%] in the EPi-Sense treatment group, compared to 66.7% (16/24) [95% CI: 47.8%, 85.5%] in the Catheter Ablation group. The difference in success rate was 3.6%.

Longstanding Persistent AF Subjects

The proportion of subjects achieving AF freedom through 12-Months, absent of an increased dose or new Class I/III AADs was 71.1% (27/38) [95% CI: 56.6%, 85.5%] in the EPi-Sense treatment group, compared to 37.0% (10/27) [95% CI: 18.8%, 55.3%] in the Catheter Ablation group. The difference in success rate was 34.0% [95% CI: 10.8%, 57.3%] in favor of EPi-Sense.

Table 9.1: Secondary Effectiveness Endpoints (Burden Reduction and Freedom from AF) – All Treated Subjects

All Treated Subjects (N = 153)			
Secondary Effectiveness Endpoint	**EPi-Sense (N = 102)**	**Catheter Ablation (N = 51)**	**p-value[b]**
Achieved ≥90% Burden Reduction at 12 Months, without New/Increased Class I/III AADs: 95% Confidence Interval [a]	80.0% (60/75) 70.9 – 89.1%	56.8% (25/44) 42.2 – 71.5%	0.0069*
AF Free at 12 Months, without New/Increased Class I/III AADs: 95% Confidence Interval [a]	70.6% (72/102) 61.7 – 79.4%	51.0% (26/51) 37.3 – 64.7%	0.0172*

*P-values that are statistically significant based on the fixed sequential testing specified in the SAP.

[a] Confidence intervals based on Wald asymptotic or Clopper-Pearson (Exact) method.

[b] Difference in change from baseline between treatment arms evaluated using an ANCOVA model with treatment arm and baseline score as covariates. Difference in percent of binary endpoints between treatment arms evaluated using Chi-Squared or Fisher's Exact test.

Table 9.2: Secondary Effectiveness Endpoints (Burden Reduction and Freedom from AF) by AF type (Post-Hoc)

Persistent and Longstanding Persistent AF Sub-Populations

	Persistent AF Subjects (N = 88)		**Longstanding Persistent AF Subjects (N = 65)**	
Secondary Effectiveness Endpoints	**EPi-Sense (N = 64)**	**Catheter Ablation (N = 24)**	**EPi-Sense (N = 38)**	**Catheter Ablation (N = 27)**
Achieved ≥90% Burden Reduction at 12 Months, without New/Increased Class I/III AADs: 95% Confidence Interval [a]	81.1% (30/37) 64.8 – 92.0%	72.2% (13/18) 46.5 – 90.3%	78.9% (30/38) 66.0 – 91.9%	46.2% (12/26) 27.0 – 65.3%
AF Free at 12 Months, without New/Increased Class I/III AADs: 95% Confidence Interval [a]	70.3% (45/64) 59.1 – 81.5%	66.7% (16/24) 47.8 – 85.5%	71.1% (27/38) 56.6 – 85.5%	37.0% (10/27) 18.8 – 55.3%

Note: Refer to footnotes on Table 9.1. Confidence intervals are not adjusted for multiplicity.

Table 10: Additional Effectiveness Endpoints (All Treated Subjects)

All Treated Subjects (N = 153)		
	EPi-Sense (N = 102)	**Catheter Ablation (N = 51)**
Achieved ≥90% Burden Reduction at 12 Months, Regardless of AADs: n (%)	96.0% (72/75)	88.6% (39/44)
AF Free at 12 Months, Regardless of AADs: n (%)	81.4% (83/102)	62.7% (32/51)
Change in AFSS Composite Score at 12 Months: n, Mean ± SD	60, -11.7 ± 7.71	37, -10.3 ± 7.16
Change in SF-36 Physical Health Composite Score at 12 Months: n, Mean ± SD	97, 7.3 ± 10.67	50, 5.7 ± 10.49
Change in SF-36 Mental Health Composite Score at 12 Months: n, Mean ± SD	97, 5.7 ± 10.51	50, 7.7 ± 12.78
Change in 6-Minute Walk Score at 12 Months: n, Mean ± SD	94, 9.2 ± 120.59	48, -12.4 ± 190.09
Change in LVEF at 6 Months, n, Mean ± SD	99, 3.5 ± 9.25	51, 1.9 ± 6.68
Change in Left Atrial Diameter at 6 Months: n, Mean ± SD	99, -0.1 ± 0.62	51, -0.2 ± 0.60
Burden of ≤ 12% at 12 Months, without New/Increased Class I/III AADs: n (%)	79.4% (77/97)	60.0% (30/50)
Burden of ≤ 12% at 12 Months, Regardless of AADs: n (%)	93.8% (91/97)	90.0% (45/50)

Achieved ≥90% Burden Reduction at 18 Months, Regardless of AADs: n (%)	88.9% (64/72)	88.1 (37/42)

Subgroup Analysis Results

The primary effectiveness endpoint was summarized and analyzed by the following subgroups of interest as shown on Figure 3.

Subgroup	Epi-Sense Events/N (%)		Catheter Ablation Events/N (%)		Delta (95% CI)
Overall	67/102	(65.7)	25/51	(49.0)	16.70 (0.10, 33.2)
Geographic Location					
United States	57/90	(63.3)	23/45	(51.1)	12.20 (-5.50, 29.9)
United Kingdom	10/12	(83.3)	2/6	(33.3)	50.00 (-3.00, 88.2)
Sex					
Female	14/22	(63.6)	11/24	(45.8)	17.80 (-10.5, 46.1)
Male	53/80	(66.3)	14/27	(51.9)	14.40 (-7.10, 35.9)
Age (Years)					
< 65	36/46	(78.3)	12/23	(52.2)	26.10 (2.40, 49.7)
≥ 65	31/56	(55.4)	13/28	(46.4)	8.90 (-13.7, 31.5)
Body Mass Index					
< 30	22/31	(71.0)	4/10	(40.0)	31.00 (-6.00, 65.2)
≥ 30	45/71	(63.4)	21/41	(51.2)	12.20 (-6.80, 31.1)
Left Atrium Size (cm)					
< Median (4.4)	33/47	(70.2)	11/23	(47.8)	22.40 (-1.90, 46.6)
≥ Median (4.4)	34/55	(61.8)	14/28	(50.0)	11.80 (-10.7, 34.4)
Left Atrium Size (cm)					
< 5	51/80	(63.8)	21/44	(47.7)	16.00 (-2.10, 34.2)
≥ 5	16/22	(72.7)	4/7	(57.1)	15.60 (-27.6, 57.9)
Left Atrial Volume (ml)					
< Median (137)	21/28	(75.0)	8/18	(44.4)	30.60 (2.60, 58.6)
≥ Median (137)	23/34	(67.6)	7/14	(50.0)	17.60 (-12.9, 48.2)
AF Classification					
Persistent AF	42/64	(65.6)	15/24	(62.5)	3.10 (-19.5, 25.7)
Longstanding Persistent	25/38	(65.8)	10/27	(37.0)	28.80 (5.10, 52.4)
Catheter Type					
Biosense Webster	46/68	(67.6)	17/34	(50.0)	17.60 (-2.50, 37.8)
TactiCath	17/28	(60.7)	8/13	(61.5)	-0.80 (-32.9, 31.2)
Other	4/6	(66.7)	0/4	(0.0)	66.70 (-0.50, 95.7)
Region					
United Kingdom	10/12	(83.3)	2/6	(33.3)	50.00 (-3.00, 88.2)
Midwest	7/12	(58.3)	3/6	(50.0)	8.30 (-42.6, 56.5)
Northeast	7/9	(77.8)	4/6	(66.7)	11.10 (-41.4, 59.3)
South	42/66	(63.6)	16/31	(51.6)	12.00 (-9.10, 33.1)
West	1/3	(33.3)	0/2	(0.0)	33.30 (-60.4, 90.6)

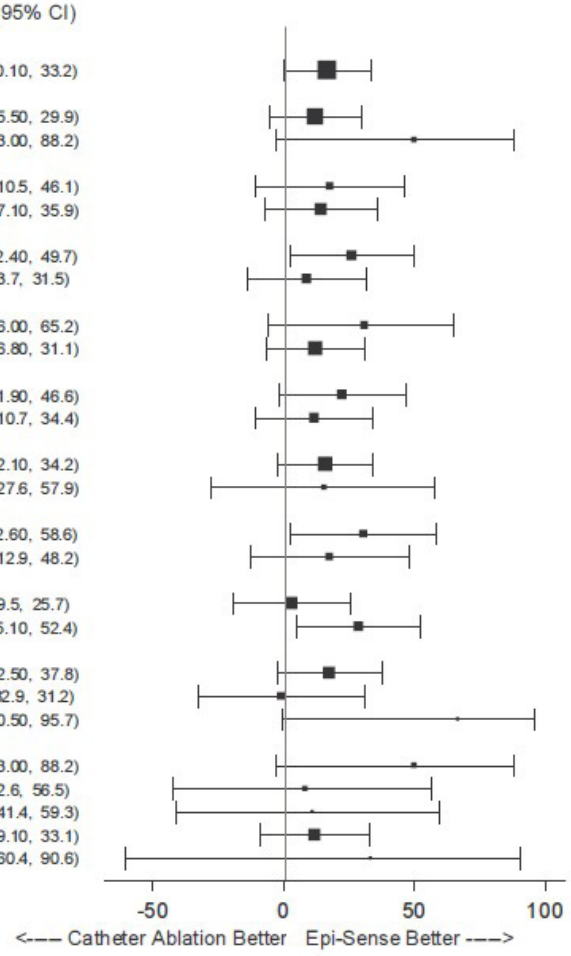


FIGURE 3: FOREST PLOT OF PRIMARY EFFECTIVENESS ENDPOINTS FOR SUBGROUP ANALYSES (ALL TREATED SUBJECTS)

Quality of Life (SF-36 and AFSS) Results

Composite and scale scores for SF-36 and AFSS are summarized in Tables 11 and 12. These summary results are considered post-hoc and should be interpreted with caution. Subjects with missing data were excluded from the analyses.

Table 11: Post-Hoc Quality of Life – SF-36

	All Treated Subjects (N = 153)		Longstanding Persistent AF Subjects (N = 65)	
SF-36 Scores	**EPi-Sense (N = 102) N, Mean ± SD**	**Catheter Ablation (N = 51) N, Mean ± SD**	**EPi-Sense (N = 38) N, Mean ± SD**	**Catheter Ablation (N = 27) N, Mean ± SD**
Physical Component Score	97, 7.3 ± 10.67	50, 5.7 ± 10.49	38, 7.9 ± 9.27	27, 3.0 ± 10.40
Physical Functioning	97, 17.6 ± 27.30	50, 17.1 ± 27.41	38, 19.9 ± 26.72	27, 14.1 ± 27.56
Role Physical	97, 26.1 ± 31.50	50, 26.4 ± 31.27	38, 28.0 ± 28.43	27, 19.7 ± 31.62
Bodily Pain	97, 5.5 ± 25.08	50, 4.3 ± 21.28	38, 8.7 ± 20.68	27, 0.8 ± 23.65
General Health	97, 13.1 ± 9.36	50, 9.6 ± 22.92	38, 11.4 ± 18.50	27, 2.3 ± 22.75
Mental Component Score	97, 5.7 ± 10.51	50, 7.7 ± 12.78	38, 5.6 ± 13.49	27, 6.5 ± 14.61
Vitality	97, 21.8 ± 25.60	50, 19.4 ± 28.86	38, 19.1 ± 28.02	27, 12.0 ± 28.90
Social Functioning Score	97, 16.5 ± 27.04	50, 17.8 ± 33.22	38, 18.8 ± 29.03	27, 11.6 ± 36.35
Role Emotional	97, 10.4 ± 24.80	50, 17.5 ± 30.92	38, 11.8 ± 29.55	27, 16.0 ± 33.96
Mental Health	97, 8.6 ± 17.50	50, 10.9 ± 18.29	38, 9.1 ± 22.75	27, 10.6 ± 19.43

Note: SF-36 values range from 0 to 100 and higher values represent better quality of life.

Table 12: Post-Hoc Symptom Relief – AFSS

	All Treated Subjects (N = 153)		Longstanding Persistent AF Subjects (N = 65)	
AFSS Scores	**EPi-Sense (N = 102) N, Mean ± SD**	**Catheter Ablation (N = 51) N, Mean ± SD**	**EPi-Sense (N = 38) N, Mean ± SD**	**Catheter Ablation (N = 27) N, Mean ± SD**
AFSS Composite Score [a]	60, -11.7 ± 7.71	37, -10.3 ± 7.16	23, -12.9 ± 7.79	22, -9.8 ± 7.93
AFSS Overall Symptom [b]	97, -10.1 ± 7.82	50, -9.2 ± 8.35	38, -9.8 ± 7.55	27, -8.0 ± 7.75
Overall Subject-Perceived Severity Score [c]	95, -1.1 ± 2.84	50, -0.8 ± 2.91	37, -1.0 ± 2.84	27, -0.1 ± 2.57
Global Well-Being [d]	96, 1.1 ± 1.97	50, 1.3 ± 2.45	38, 1.2 ± 2.02	27, 0.6 ± 2.15
Atrial Fibrillation Frequency [e]	69, 7.0 ± 3.71	40, 6.2 ± 3.91	25, 7.5 ± 3.58	23, 6.4 ± 3.91
Atrial Fibrillation Duration [f]	62, 3.5 ± 3.54	37, 3.3 ± 3.17	24, 3.9 ± 3.78	22, 3.0 ± 3.67

[a] Scores from 3 to 30 and higher values represent greater burden.

[b] Scored as 1 = less severe to 35 = more severe.

[c] Scored as 1 = not at all severe to 10 = extremely severe.

[d] Scored as 1 = worst possible life to 10 = best possible life.

[e] Scored as 1 = continuously to 11 = less than once a year.

[f] Scored as 1 = continuously to 8 = a few minutes.

Symptom Relief Results

Symptom relief assessments based on the AFSS are presented in Figures 4.1 and 4.2 for the all treated and the longstanding persistent AF sub- population for the EPi-Sense subjects. These summary results are considered post-hoc and should be interpreted with caution. Subjects with missing data were excluded from the analyses.

Figure 4.1: Symptom Reduction from Baseline to 12-Months in EPi-Sense Group (All Treated Subjects)

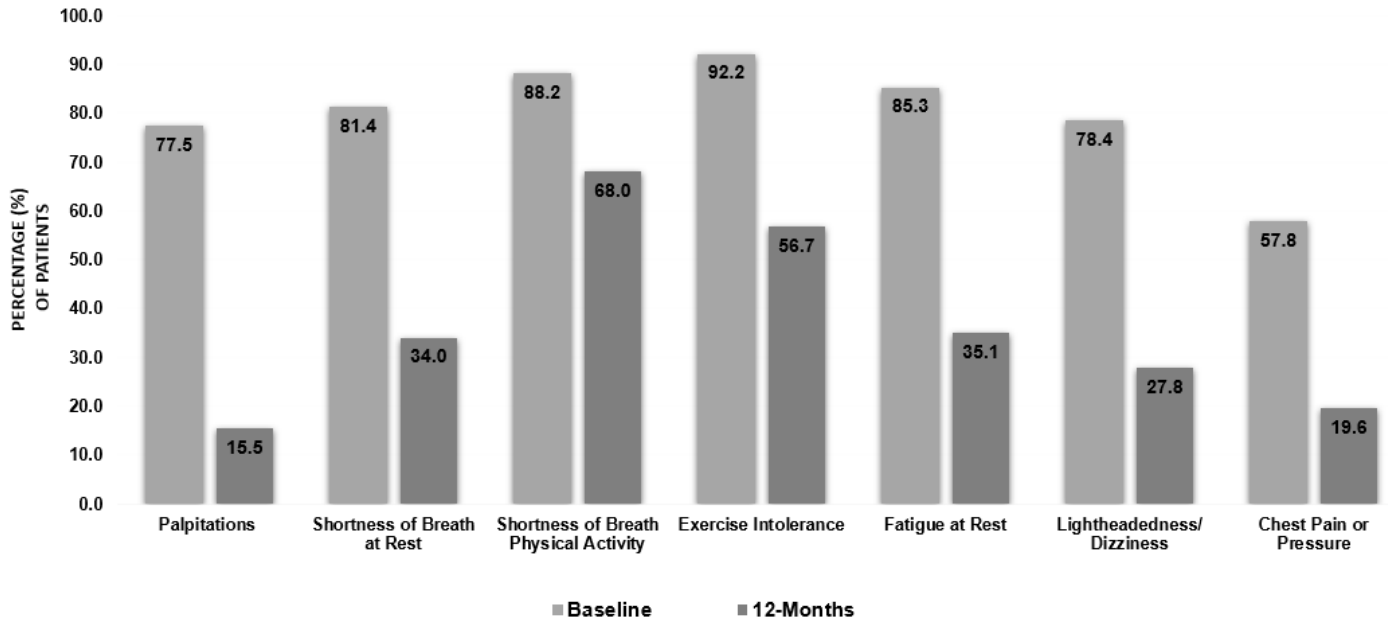
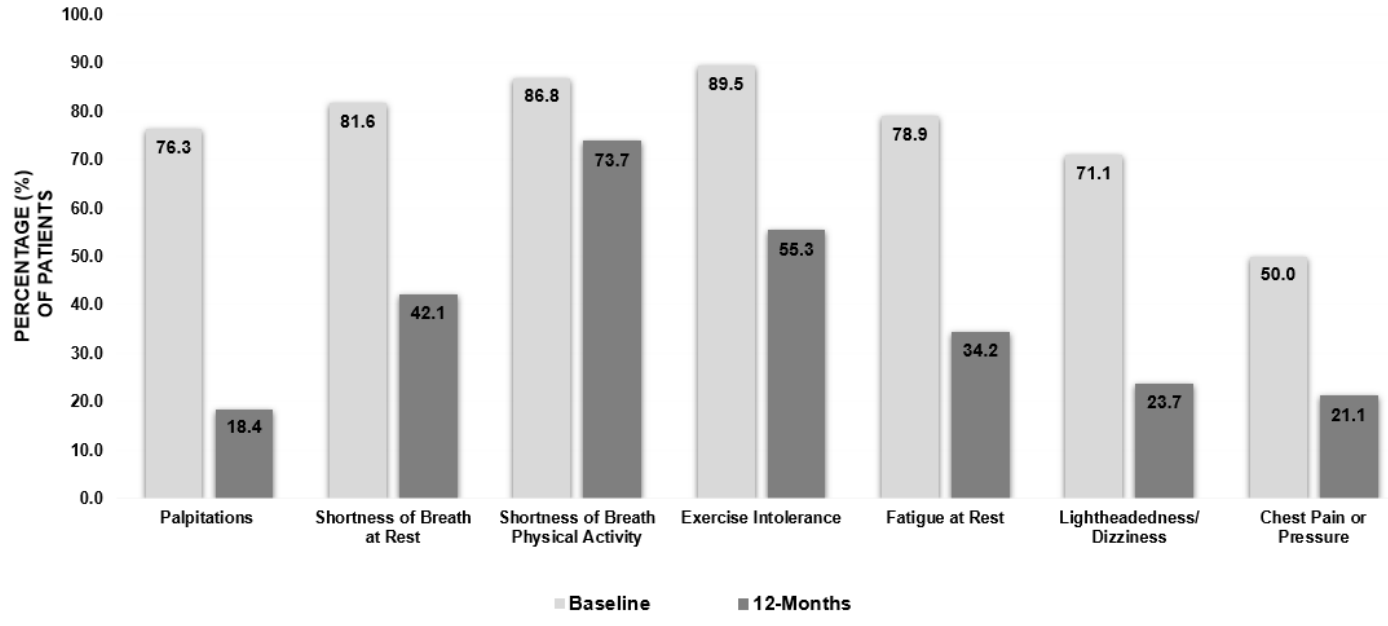


Figure 4.2: Post-Hoc Symptom Reduction from Baseline to 12-Months in EPi-Sense Group (Long-Standing Persistent AF Patients)



Additional Data Analysis

Additional analysis was performed based alternative HRS definitions of treatment success:

- Freedom from atrial arrythmias from the 3-month blanking period through 12- and 18-months, after removal from antiarrhythmic drug therapy.
- Freedom from atrial arrythmias from the 3-month blanking period through 12- and 18-months, regardless of antiarrhythmic drug therapy.

The results presented for all treated patients (N = 153) and the longstanding persistent AF sub-population are considered post-hoc and should be interpreted with caution since the confidence intervals are presented without adjustment for multiplicity. The confidence intervals calculated using the Wald asymptotic method and are presented only for descriptive purpose and are neither adjusted for multiplicity nor related to any prospectively defined hypothesis.

The summary of the analysis is provided in Tables 13.

Table 13: Post-Hoc Additional Effectiveness Endpoints

(Freedom from AF/AFL/AT Absent Class I/III AADs and Freedom from AF/AFL/AT Regardless of Class I/III AADs)

	All Treated Subjects (N = 153)			Longstanding Persistent AF Subjects (N = 65		
Effectiveness Endpoint	**EPi-Sense (N = 102)**	**Catheter Ablation (N = 51)**	**Treatment Difference 95% CI [c]**	**EPi-Sense (N = 38)**	**Catheter Ablation (N = 27)**	**Treatment Difference 95% CI [c]**
Effectiveness from 3-Months Post-Blanking Period through 12-Months						
Freedom from Arrhythmia off AADs [a]	52.0% (53/102)	31.4 (16/51)	20.6% (4.6 – 362.6%)	52.6% (20/38)	25.9% (7/27)	26.7% 3.8 – 49.6%
Freedom from Arrhythmia Regardless of AADs [b]	74.5% (76/102)	58.8% (30/51)	15.7% (-0.25 – 31.6%)	73.7% (28/38)	44.4% (12/27)	29.2% 5.8 – 52.6%
Effectiveness from 3-Months Post-Blanking Period through 18-Months						
Freedom from Arrhythmia off AADs [a]	43.1% (44/102)	23.5% (12/51)	19.6% (4.5 – 34.7%)	47.4% (18/38)	22.2% (6/27)	25.2% 2.8 – 47.5%
Freedom from Arrhythmia Regardless of AADs [b]	63.7% (65/102)	47.1% (24/51)	16.7% (0.0 – 33.2%)	68.4% (26/38)	33.3% (9/27)	35.1% 12.0 – 58.2%

[a] Freedom from arrythmia after removal of Class I or III antiarrhythmic drug therapy.

[b] Freedom from arrythmia regardless of Class I or III antiarrhythmic drug therapy.

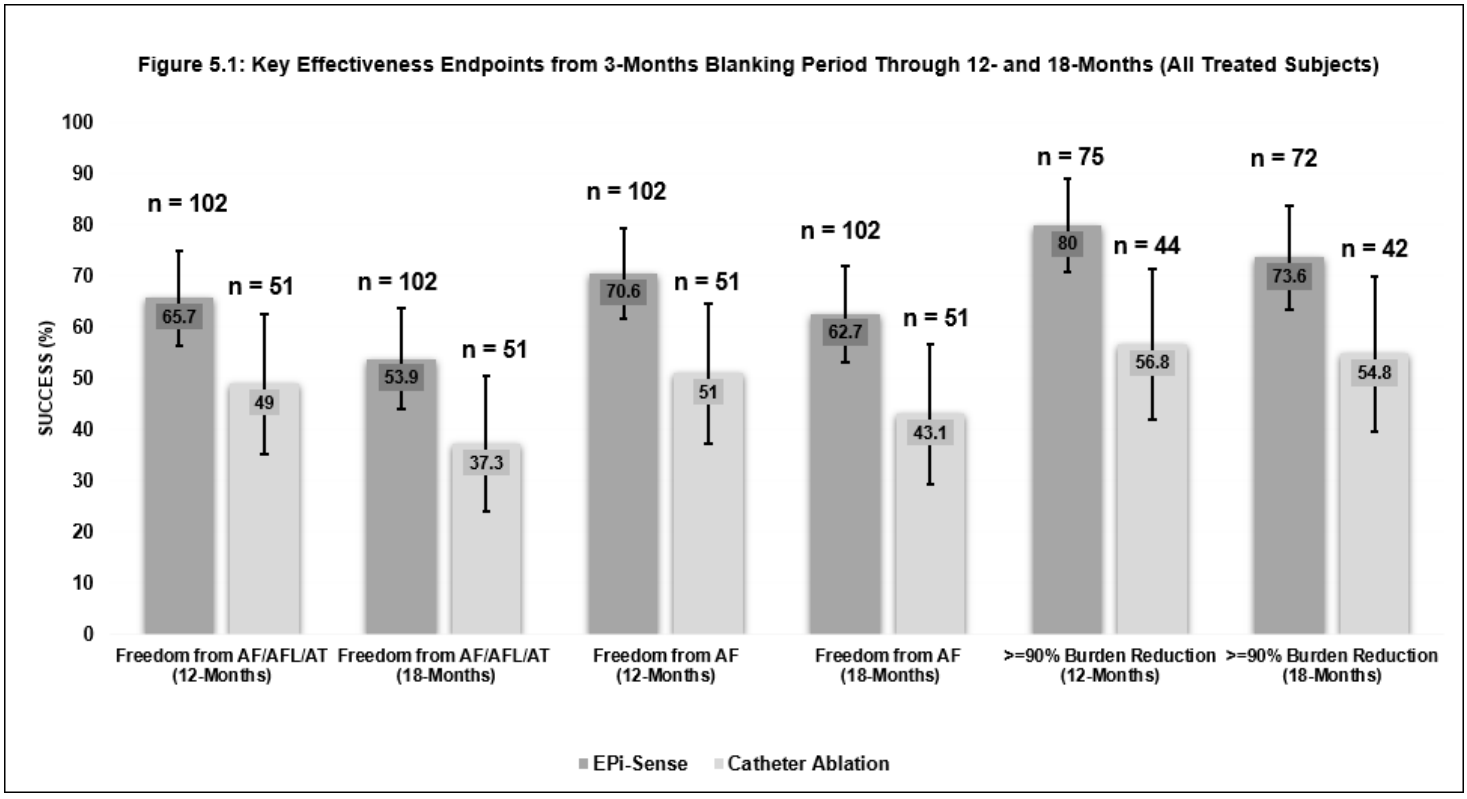
[c] Confidence intervals are not adjusted for multiplicity.

Key Effectiveness Endpoints from 3-Months Blanking Period Through 18-Months

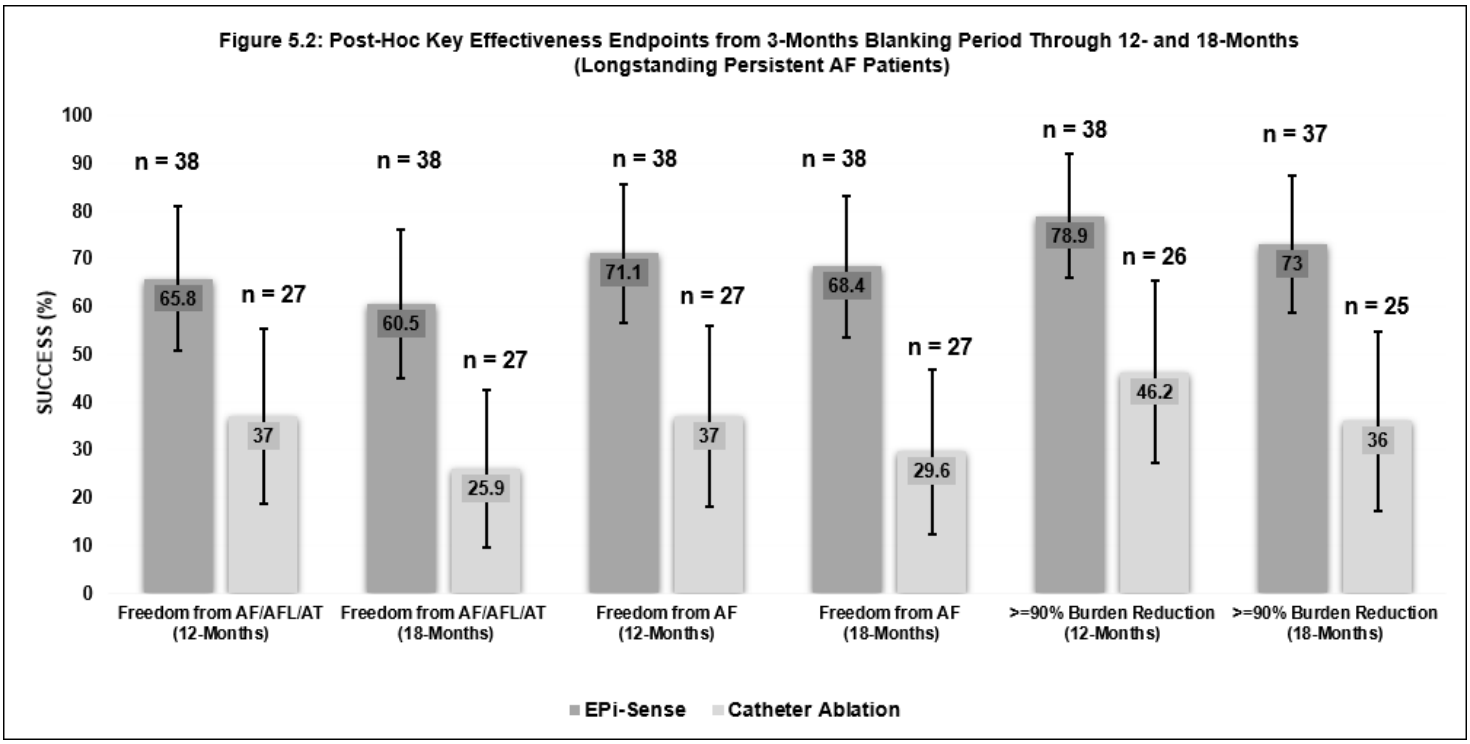
The primary effectiveness endpoint and the key secondary effectiveness endpoints of burden reduction and freedom from AF were summarized from the 3-months blanking period through 18-months. The results are presented in Figures 5.1 and 5.2.

The 18-months effectiveness analyses for the all treated subjects, and the longstanding persistent AF sub-population are considered post-hoc and should be interpreted with caution since the confidence intervals are presented without adjustment for multiplicity.

For the "All Treated" population, missing arrhythmia endpoints data were imputed as treatment failures. Missing burden data were not imputed. For the longstanding persistent AF sub-population, there were no missing arrhythmia data. Missing burden data were not imputed for this sub- population.



Note: Confidence intervals for the 18-months analyses are not adjusted for multiplicity.



Note: Confidence intervals are not adjusted for multiplicity.

Included Endocardial Irrigated Catheters

The following endocardial irrigated catheters were used during the Converge study:

Table 14: Endocardial Irrigated Catheters Used in the CONVERGE Study

No	Description of Endocardial Irrigated Ablation Catheter	Manufacturer
1	CELSIUS® THERMOCOOL® Catheter	Biosense Webster, Inc
2	EZ STEER® THERMOCOOL® Catheter	Biosense Webster, Inc
3	FlexAbility™ Irrigated Ablation Catheter	Abbott Laboratories
4	IntellaNav™ Open-Irrigated Ablation Catheter	Boston Scientific Corporation
5	Safire BLU™ Duo Irrigated Ablation Catheter	Abbott Laboratories*
6	TactiCath™ Quartz Contact Force Ablation Catheter	Abbott Laboratories*
7	Therapy™ Cool Path™ Duo Irrigated Ablation Catheter	Abbott Laboratories*
8	Therapy™ Cool Path™ Irrigated Ablation Catheter	Abbott Laboratories*
9	THERMOCOOL® SF Catheter	Biosense Webster, Inc
10	THERMOCOOL® SF NAV Catheter	Biosense Webster, Inc
11	THERMOCOOL SMARTTOUCH® Catheter	Biosense Webster, Inc
12	THERMOCOOL SMARTTOUCH® SF Catheter	Biosense Webster, Inc
*Abbott Laboratories (formerly, St. Jude Medical, Inc.)		

Conclusions

Effectiveness Conclusions

The effectiveness outcomes of the CONVERGE study demonstrate that the hybrid convergent procedure with EPi-Sense® Guided Coagulation System is effective for the treatment of symptomatic drug refractory recurrent persistent atrial fibrillation. Freedom from AF/AT/AFL absent Class I and III AADs except for a previously failed or intolerant Class I or III AAD with no increase in dosage following the 3-month blanking period through the 12-months post procedure follow up visit was achieved in 65.7% (67/102) [95% CI: 56.5%, 74.9%] subjects in the EPi-Sense treatment group compared to 49.0% (25/51) [95% CI: 35.3%, 62.7%] subjects in the Catheter Ablation group. The observed success rate difference of 16.7% [95% CI: 0.1%, 33.2%] is statistically significant (Chi-Squared p-value = 0.0472).

Post-hoc subgroup analysis showed that the difference in the primary effectiveness endpoint success was driven primarily by the substantial treatment effect difference in the long-standing persistent AF sub-population. In patients with a history of continuous AF > one year, the primary effectiveness success rate difference was 28.8% (95% CI: 5.1%, 52.4%) through 12 months in favor of EPi-Sense. The effectiveness results in the longstanding persistent AF sub-population are consistent and clinically significant regardless of the duration of evaluation (i.e., 12- or 18- months).

Safety Conclusions

The primary safety event rate was 7.84% (8/102) [95% UCL: 13.7%]. No deaths occurred within 30-days of the procedure and no AEFs or cardiac perforations were reported. The events reported included: pericardial effusions; excessive bleeding; phrenic nerve injury; TIA; and stroke. Almost all of these safety events resolved without sequelae. There were no deaths attributable to the EPi-Sense Guided Coagulation System or hybrid Convergent procedure.

The rate of pericardial effusion requiring percutaneous and/or surgical drainage was 5.9%. These events were delayed onset and likely represent inflammatory response to pericardiotomy and the pericardial ablation procedure with the device. They occurred 1-3 weeks post-ablation, and were treated successfully with timely recognition.

Overall Conclusions

The totality of evidence from the randomized CONVERGE clinical trial and real-world clinical experience demonstrates there is a reasonable assurance of safety and effectiveness to support the use of the EPi-Sense device to treat patients presenting with symptomatic drug refractory longstanding persistent atrial fibrillation.

GLOSSARY OF TERMS

Electrocoagulation	Surgical procedures in which high-frequency electric current is used to coagulate tissues.
Coagulation Electrode	The metal conductor in the coagulation device used to transmit radiofrequency energy to tissue.
Sensing Electrodes	Metal conductors between the coagulation electrode used to sense cardiac voltages from the heart.
Indifferent, Dispersive Electrode	Commonly referred to as the "return electrode" or "patient electrode" or "ground pad." Large surface area indifferent ground used to complete the circuit of the electrical current. Usually placed on the patient's back or thigh, the indifferent, dispersive electrode is connected to the generator at the Indifferent Connector.

Abbreviations

RF	Radiofrequency	IFU	Instructions for Use
VAC	Vacuum	LT	Label
OC	Open Circuit	s	Seconds
W	Watts		

Symbols

	Manufacturer	Rx ONLY	Caution: Federal law (US) restricts this device to sale by or on the order of a physician.
REF	Catalog Number	LOT	Lot Number
#	Model Number		Use-By Date
	Follow instructions for use		Caution
	Single Use Only	STERILIZE	Do Not Resterilize
	Do Not Use if Package is Damaged		Waste Electrical and Electronic Equipment
LATEX	Not made with Natural Rubber Latex or Dry Natural Rubber		Non-pyrogenic
	Defibrillation Proof Type CF Applied Part	STERILE EO	Sterile by ethylene oxide
	Caution: Electrical Shock Hazard		Non-ionizing Radiation
	Indifferent, Dispersive Electrode		Footswitch Connection
	Equipotential		Perfusion
	Time	Ω	Ohms
85% % 30%	Transit Humidity Range	60°C 140°F -20°C -4°F	Transit Temperature Range

Limited Warranty

AtriCure warrants that reasonable care has been used in the design and manufacture of this instrument. This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether expressed or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for a particular use. AtriCure's sole obligation under this warranty is limited to the repair or replacement of this instrument. AtriCure neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this instrument

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