DE NOVO CLASSIFICATION REQUEST FOR ESOLUTION® ESOPHAGEAL RETRACTOR

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Mechanical deviation device for esophageal protection during cardiac ablation procedures. This device is placed in the lumen of the esophagus to reduce the likelihood of injury or a specific adverse event during cardiac ablation procedures. The device uses mechanical means to deviate the esophagus away from the source of ablation energy.

NEW REGULATION NUMBER: 21 CFR 870.5710

CLASSIFICATION: Class II

PRODUCT CODE: QXU

BACKGROUND

DEVICE NAME: esolution® Esophageal Retractor

SUBMISSION NUMBER: DEN230006

DATE DE NOVO RECEIVED: 01/24/2023

SPONSOR INFORMATION:

S4 Medical Corp.
34 South Main St. Suite 200
Chagrin Falls, Ohio 44022

INDICATIONS FOR USE

The esolution® Esophageal Retractor is indicated as follows:

The esolution® Esophageal Retractor is indicated for use in patients undergoing percutaneous cardiac catheter ablation of atrial fibrillation to deviate the esophagus away from the ablation energy source and to reduce the risk of ablation-related esophageal injury.

LIMITATIONS

The sale, distribution, and use of the esolution® Esophageal Retractor are restricted to prescription use in accordance with 21 CFR 801.109.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The esolution® Esophageal Retractor is a catheter-based device designed to displace the esophagus away from the source of ablation energy during percutaneous cardiac catheter ablation procedures and to reduce the risk of ablation energy-induced esophageal injury. The esolution® Esophageal Retractor uses both mechanical force and vacuum suction to grasp the esophagus and deflect it away from the posterior wall of the left atrium in both left and right directions. The device comprises three components: (1) outer sheath, (2) inner mechanical displacement plates, and (3) handle and control knob. The distal end of the outer sheath features two eyelets for attaching a temperature probe (a temperature probe is not required for use of the esolution® Esophageal Retractor). Additional third-party components required for use of the esolution® Esophageal Retractor include:

- Intubation introducer (15 Fr x 70 cm, any manufacturer).
- Vacuum line with inner diameter ¼ in., wall thickness 1/16 in., connected to wall vacuum port (any manufacturer).
- Lubricants: viscous lidocaine and medical lubricant (any manufacturer).

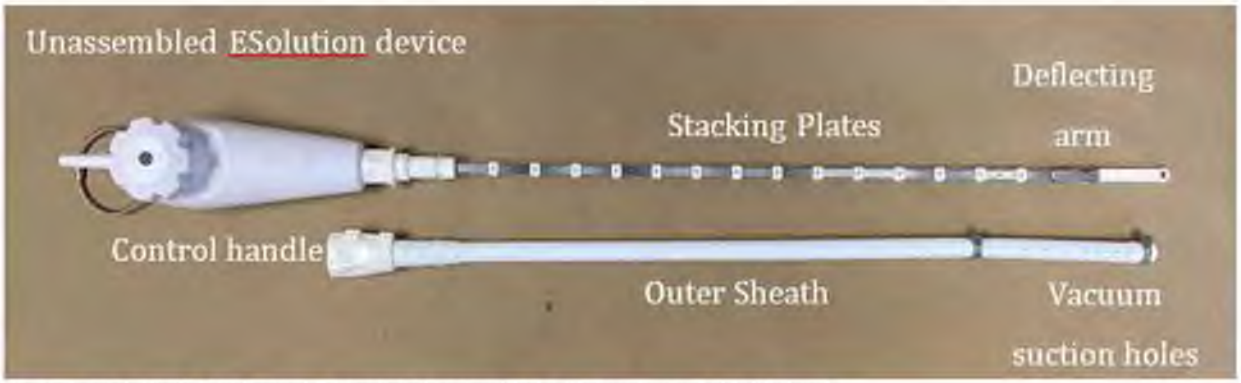


Figure 1: esolution® Esophageal Retractor disassembled with components highlighted.

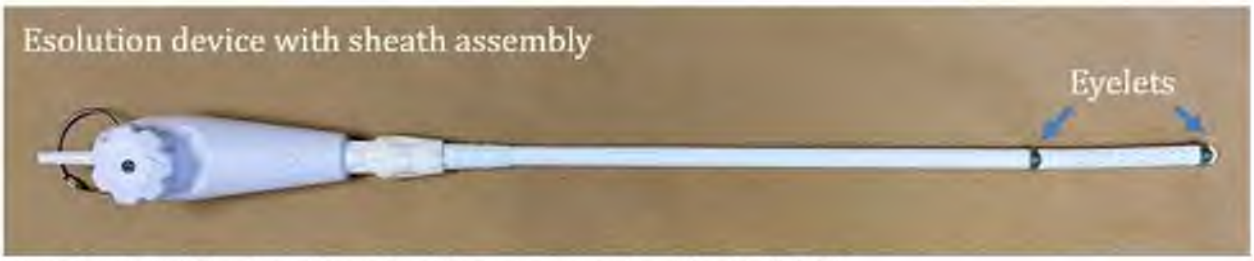


Figure 2: esolution® Esophageal Retractor with temperature probe eyelets highlighted.

Figure 3: esolution® Esophageal Retractor with distal portion deflected to the left.

Figure 4: esolution® Esophageal Retractor with distal portion deflected to the right.

To use, after lubrication of the device and attachment of the vacuum line and temperature probe (optional), the introducer is shaped and inserted into the outer sheath. The outer sheath is inserted into the esophagus via the mouth and visualized, if needed, under fluoroscopy. The device is moved to ensure proper positioning of the outer sheath relative to the cardiac anatomy. The introducer is removed and replaced with the inner mechanical displacement plates. Placement is confirmed under fluoroscopy. When desired, the esophagus is deviated by turning the Control Knob in the intended direction. Please refer to the labeling for the complete directions for use.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The esolution® Esophageal Retractor is a surface device that contacts the mucosal membrane with limited exposure (≤ 24 hours). To assess the biocompatibility, the patient contact areas of the device were tested, including the Inner Deflection Arm Assembly and the Outer Cannula. EO sterilized devices were cut into pieces and extracted in appropriate media for the specific biocompatibility tests.

Biocompatibility evaluation has been completed according to FDA Guidance, Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" (https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM348890.pdf). The test articles were found non-cytotoxic per ISO 10993-5. The test articles were found to be non-sensitizing in tests for skin sensitization per ISO 10993-10. The test articles were found to be non-irritating in tests for irritation per ISO 10993-10.

SHELF LIFE/STERILITY

The esolution® Esophageal Retractor is a sterile, single-use device.

The shelf-life for esolution® Esophageal Retractor has been established at 1 year based on an accelerated aging study per ASTM F1980-16, Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices. To support the 1-year shelf life, the sponsor conducted package integrity testing and functional testing.

Package integrity testing consisted of the following:

- Label inspection (per Resolution Medical, LLC specifications and DDL, Inc., WI # 6560-01)
- Visual inspection (per ASTM F1886/F1886M-16: Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection)
- Bubble leak (ASTM F2096-11(2019), Standard Test Method for Detecting Gross Leaks in Packaging by Internal Pressurization (Bubble Test))
- Seal strength (ASTM F88/F88M-15, Standard Test Method for Seal Strength of Flexible Barrier Materials)

Non-clinical performance testing of the accelerated aged samples was used to assess the performance shelf life. The results demonstrate that esolution® Esophageal Retractor has acceptable package integrity and functional performance over the duration of its 1-year shelf life.

MAGNETIC RESONANCE (MR) COMPATIBILITY

The device is MR Unsafe.

PERFORMANCE TESTING - BENCH

The esolution® Esophageal Retractor underwent the following bench performance tests:

- Visual Inspection. The acceptance criteria were:
  - No visible Foreign Material or manufacturing residues by inspection at Standard Viewing Conditions
  - No nicks gouges, scratches, short shots at 2X Magnification
  - No visible/exposed sharp edges and cannula tip is rounded
  - All test results met acceptance criteria
- Dimensional Verification. The acceptance criteria were:
  - Outer cannula gap length
  - OD of the cannula
  - OD of the cannula at the eyelets
  - Hole Pattern Position
  - Number of holes and numbers of holes in each ring
  - Holes Diameters
  - Distance between the centers of the holes in the [redacted] distal rows and [redacted] proximal rows
  - Length of the articulation arm of the retractor

    - Working length of the retractor
    - ID of the hook
    - All test results met acceptance criteria
- Intubation fit. The acceptance criteria were: The device is compatible with 15 F x 70 cm intubation tool. All test results met acceptance criteria.
- Immobilization. The acceptance criterion was: Device can be hung from an IV Pole for 30 minutes. All test results met acceptance criteria.
- Device Insertion and Withdrawal. The acceptance criterion was: Device can be inserted and withdrawn from the Cannula. All test results met acceptance criteria.
- Deflection. The acceptance criteria were:
    - Deflection without weights
    - Deflection with (b)(4) weights attached
    - All test results met acceptance criteria.
- Vacuum Leak/Decay Test. The acceptance criteria were: Maintain at least (b)(4) (b)(4) Vacuum when (b)(4) is applied. All test results met acceptance criteria.
- Torque Test. The acceptance criteria were: Once engaged to the Inner Deflection Device, the outer cannula shall not separate from the deflection device when subjected to a rotational torque of 1in-lb at the hub. All test results met acceptance criteria.
- Tensile Test. The acceptance criteria were: The bonds listed below have a minimum strength of (b)(4):
    - Cannula to retractor
    - Barb Connection to Cannula
    - Distal Temperature Probe Eyelet to Cannula
    - Proximal Temperature Probe Eyelet to Cannula
    - Distal Tip to Cannula
    - Vacuum Supply Fitting to Vacuum Hose
    - Hook to Handle
    - Carbon Clips to Blade Blades
    - Cable 1 to Hinge
    - Cable 2 to Hinge
    - Deflection Tip to Hinge Housing
    - Stack Mount to inner vacuum Tube
    - Barb to Inner Vacuum Tube
    - All test results met acceptance criteria

PERFORMANCE TESTING - ANIMAL

The following preclinical animal testing was performed:

- Ease and Safety of Insertion and Positioning: Testing of the final 2-piece intubation design was completed in an open chest study in 2 porcine animals on April 23 and 25, 2018. The goal of these studies was to assess ease of insertion of the outer extrusion using a bougie introducer, followed by introduction of the

inner stacking plates. The results showed that the esolution® Esophageal Retractor can successfully deviate the esophagus in the right and left direction.

- Bilateral and Controlled Degrees of Deviation: Testing of esophageal deviation to the right and to the left as well as to full and partial degrees of deflection and to confirm successful gear-locking of ProtectE deflection. Please note that the ProtectE is the first version of the esolution® Esophageal Retractor. The changes made did not introduce the need for new animal studies. The deviation mechanism design was finalized late 2018 and tested in two separate porcine studies (November 13,2018 and January 22, 2019), and confirmed with a canine ablation study, January 22, 2019. The esolution® Esophageal Retractor deviation design successfully deviated the esophagus to full or partial deflection, right or left, without injury.
- Effect of Suction Upon Esophageal Deviation: Testing of suction adherence of the esophagus to the outer extrusion and to evaluate for suction to eliminate / minimize the trailing edge of the esophagus during deviation to the right and to the left. The esolution® Esophageal Retractor suction study confirmed that 93% of deviations were not associated with any detectable trailing edge and there was a significant reduction in the trailing edge with the use of vacuum suction.
- Effect of Suction Upon Esophageal Cellular Architecture: Utilizing the same deviation and suction protocol and suction port distribution as defined above, the goal of 2 pig studies and 1 canine study was to assess the impact of prolonged maximum deviation and maximum suction during full anticoagulation upon the gross and microscopic architecture of the esophagus. The first two studies completed suction for 60 minutes and the last study applied suction for 150 minutes (2.5 hours). Mild changes with 60min and 150min suction were seen without disruption of the epithelium and were considered clinically insignificant.
- Impact of Esophageal Deviation Upon Luminal Esophageal Temperature During Ablation: Utilizing the same deviation and suction protocol and suction port distribution as defined above, the goal of this canine study was to assess the impact of esophageal deviation upon changes to LET. The results showed that without esophageal deflection, the LET increased markedly with RF ablation in a PV.
- Impact of ProtectE Upon Accurate Measurement of Luminal Esophageal Temperature: The goal of this canine study was to assess if the ProtectE catheter shielded or inhibited LET monitoring by a commercially available temperature probe. To test for this possible interaction, LET was measured in an open chest model of ablation with ProtectE and suction and the temperature probe placed in the esophagus in comparison to LET measured by insertion of only a temperature probe (i.e., LET measurement during RF ablation with a temperature probe with vs without concomitant use of ProtectE). The results confirmed that the esolution® Esophageal Retractor did not interfere with accurate luminal esophageal temperature measurement.
- Impact of esolution® Esophageal Retractor upon Electroanatomic Mapping Systems (no animal involved): The goal is to assess for any interference of the electroanatomic mapping system with the use of esolution® Esophageal Retractor. The device is tested in an experimental model of a CARTO mapping system. This

model is a fluid – filled container with CARTO-compatible mapping patches placed with the CARTO electromagnetic fields (X-, Y-, Z-axis). Within this fluid-filled bath, an electroanatomic sensor was positioned to confirm proper function of the CARTO system. Once confirmed, esolution® Esophageal Retractor is introduced into the bath container and placed in direct contact with the electroanatomic sensor. Through the CARTO system, proper function is then tested as well as an assessment of interference and artifact. The results confirmed that the esolution® Esophageal Retractor did not alter the normal function of electroanatomic mapping systems, even when in intimate contact with the tracking sensor.

SUMMARY OF CLINICAL INFORMATION

The sponsor conducted a small pilot OUS clinical trial and a pivotal IDE trial (EASY AF study, G200264) to support the clinical performance of the esolution® Esophageal Retractor.

The EASY AF Study is a prospective, randomized, controlled, single-blinded multicenter study of a catheter-based device designed to displace the esophagus away from the source of ablation energy during ablation of atrial fibrillation (AF) and to minimize the risk of esophageal injury.

The goal of esolution® Esophageal Retractor is that through the combination of mechanical displacement and vacuum suction, an entire segment of the esophagus can be easily and safely deviated away from the source of ablative energy and thus reduce the risk of esophageal injury during left atrial ablation of AF. The study was designed to assess a reduction of esophageal lesions attributable to radiofrequency (RF) ablation with use of the esolution® Esophageal Retractor in comparison to conventional therapy (no use of an esophageal retractor). The randomization is with a 1:1 randomization scheme assigning consecutive patients who meet inclusion and exclusion criteria to either: placement of a luminal esophageal temperature probe (LET) (control group); or, to placement of a LET and insertion esolution® Esophageal Retractor (intervention group). In the control group, there was no deviation of the esophagus and in the intervention group, esolution® Esophageal Retractor was utilized to deviate the esophagus during RF catheter ablation.

The primary study endpoint was the incidence of ablation related esophageal lesions noted on post ablation esophageal endoscopy completed at least $\geq$ 15 hours to $\leq$ 72 hours of the ablation procedure. The study took place at 12 medical centers and enrolled 120 subjects; at which time the first planned interim analysis took place. The interim analyses were performed to assess whether the trial should be stopped early for success, continue enrollment to the next interim analysis, or stopped for futility.

The interim analysis results met the criteria for early stopping for efficacy. Of the 53 esolution/intervention and 65 control subjects with endoscopy results, 3 esolution subjects and 23 Control subjects had ablation lesions (5.7% and 35.4%, respectively, $p < 0.0001$). The primary analysis included the Intent-to-Treat (ITT) population (N=129 randomized subjects), with missing data imputed using multiple imputation per the statistical analysis plan (SAP). Of the 129 randomized subjects, there were 9 subjects (8 esolution, 1 Control) who were withdrawn

prior to or during the ablation procedure. These subjects did not participate in any part of the study beyond consent and randomization. No aspect of the procedure protocol was performed for these subjects, no data from the procedure protocol was collected, and none received an EGD. Thus, there were 120 randomized subjects who received a study treatment. Of these, two patients (one assigned to esolution, and one assigned to Control) did not receive the endoscopy. The per-protocol population includes the subset of the ITT population who received a study treatment and an endoscopy (N=118, 65 Control and 53 esolution). Fishers Exact one-sided p-values were less than the interim success boundary (0.0027648) for all imputations, leading to the rejection of the null hypothesis and a conclusion that the proportion of esolution subjects with one or more ablation lesions is significantly lower than the proportion of Control subjects with one or more ablation lesions. This conclusion was supported by sensitivity analyses of the primary effectiveness endpoint.

There were no reports of deaths, unexpected adverse device effects (UADEs), or device-related adverse events. Nine subjects in the Control group reported one or more serious adverse events (SAEs), including 14 total events. Three subjects in the esolution group experienced SAEs, including 6 total events. Fourteen subjects in the Control group reported one or more non-serious AEs, including 16 total events. Nine subjects in the esolution group experienced one or more nonserious AEs, including 10 total events.

Subject Demographics

The mean age of subjects is 61.6 years in the esolution group and 65.3 years in the Control group. The mean BMI of subjects is 34.5 in the esolution group and 30.4 in the Control group. The mean CHADS-VASc Score of subjects is 2.2 in the esolution group and 2.6 in the Control group. The mean number of PVs is 4.0 in the esolution group and 4.0 in the Control group. The esolution group is made up of 24.1% female and 75.9% male subjects, and the Control group is made up of 36.4% female and 63.6% male subjects. The numbers and proportions of subjects with each type of atrial fibrillation (longstanding persistent, paroxysmal, or persistent) are similar for the esolution and control groups.

Overall, the demographic and baseline characteristics of subjects in the esolution and Control groups demonstrate that patients randomized to esolution device were (on average) slightly younger, had a higher BMI and less frequent history of GERD.

Parameter	Statistic	*esolution*	Control	P-value
Gender	Female, n (%)	13 (24.1%)	24 (36.4%)	
	Male, n (%)	41 (75.9%)	42 (63.6%)	0.1681
Age (Years)	N	54	66	
	MEAN (STD)	61.6 (9.22)	65.3 (10.46)	
	STANDARD ERROR	1.25	1.29	
	95% CI	59.1, 64.2	62.8, 67.9	
	MINIMUM	38.0	33.0	
	MAXIMUM	79.0	79.0	0.0443
BMI	N	54	66	
	MEAN (STD)	34.5 (8.55)	30.4 (5.29)	
	STANDARD ERROR	1.16	0.65	
	95% CI	32.2, 36.8	29.1, 31.7	
	MINIMUM	23.0	21.2	
	MAXIMUM	57.6	47.5	0.0027
CHADS-VASc Score	N	54	66	
	MEAN (STD)	2.2 (1.47)	2.6 (1.54)	
	STANDARD ERROR	0.20	0.19	
	95% CI	1.8, 2.6	2.2, 3.0	
	MINIMUM	0.0	0.0	
	MAXIMUM	6.0	7.0	0.1887
Number of PVs	N	54	66	
	MEAN (STD)	4.0 (0.27)	4.0 (0.41)	
	STANDARD ERROR	0.04	0.05	
	95% CI	4.0, 4.1	3.9, 4.1	
	MINIMUM	3.0	3.0	

Parameter	Statistic	*esolution*	Control	P-value
	MAXIMUM	5.0	5.0	0.7277
Type of atrial fibrillation	Longstanding Persistent, n (%)	2 (3.7%)	3 (4.5%)	
	Paroxysmal, n (%)	32 (59.3%)	42 (63.6%)	
	Persistent, n (%)	20 (37.0%)	21 (31.8%)	0.8955
CHADS-VASc Score	0, n (%)	6 (11.1%)	5 (7.6%)	
	1, n (%)	12 (22.2%)	11 (16.7%)	
	2, n (%)	15 (27.8%)	17 (25.8%)	
	3, n (%)	10 (18.5%)	15 (22.7%)	
	4, n (%)	7 (13.0%)	12 (18.2%)	
	5, n (%)	3 (5.6%)	3 (4.5%)	
	6, n (%)	1 (1.9%)	2 (3.0%)	
	7, n (%)	0 (0.0%)	1 (1.5%)	0.9455
Number of PVs	3, n (%)	1 (1.9%)	5 (7.6%)	
	4, n (%)	50 (92.6%)	55 (83.3%)	
	5, n (%)	3 (5.6%)	6 (9.1%)	0.2552
Left ventricular ejection fraction (%)	N	53	64	
	MEAN (STD)	53.5 (10.87)	55.7 (9.40)	
	STANDARD ERROR	1.49	1.18	
	95% CI	50.5, 56.5	53.3, 58.0	
	MINIMUM	25.0	20.0	
	MAXIMUM	72.0	75.0	0.2437
Heart Failure	No, n (%)	43 (79.6%)	57 (86.4%)	
	Yes, n (%)	11 (20.4%)	9 (13.6%)	0.3380
NYHA Class	I, n (%)	1 (9.1%)	2 (22.2%)	

Parameter	Statistic	esolution	Control	P-value
	II, n (%)	7 (63.6%)	3 (33.3%)	
	III, n (%)	2 (18.2%)	1 (11.1%)	
	Unknown, n (%)	1 (9.1%)	3 (33.3%)	0.4483
Prior Heart Surgery	No, n (%)	48 (88.9%)	57 (86.4%)	
	Yes, n (%)	6 (11.1%)	9 (13.6%)	0.7650
Pericardial Disease	No, n (%)	54 (100.0%)	66 (100.0%)	1.0000
Pulmonary disease	No, n (%)	49 (90.7%)	61 (92.4%)	
	Yes, n (%)	5 (9.3%)	5 (7.6%)	0.7524
Kidney disease	No, n (%)	50 (92.6%)	60 (90.9%)	
	Yes, n (%)	4 (7.4%)	6 (9.1%)	1.0000
Liver disease	No, n (%)	54 (100.0%)	65 (98.5%)	
	Yes, n (%)	0 (0.0%)	1 (1.5%)	1.0000
Diabetes	No, n (%)	42 (77.8%)	57 (86.4%)	
	Yes, n (%)	12 (22.2%)	9 (13.6%)	0.2369
HTN	No, n (%)	13 (24.1%)	15 (22.7%)	
	Yes, n (%)	41 (75.9%)	51 (77.3%)	1.0000
Prior stroke or TIA	No, n (%)	49 (90.7%)	61 (92.4%)	
	Yes, n (%)	5 (9.3%)	5 (7.6%)	0.7524
Vascular disease	No, n (%)	41 (75.9%)	51 (77.3%)	
	Yes, n (%)	13 (24.1%)	15 (22.7%)	1.0000
Sleep apnea	No, n (%)	31 (57.4%)	46 (69.7%)	
	Yes, n (%)	23 (42.6%)	20 (30.3%)	0.1839
Parameter	Statistic	esolution	Control	P-value
GERD	No, n (%)	46 (85.2%)	44 (66.7%)	
	Yes, n (%)	8 (14.8%)	22 (33.3%)	0.0214

Procedure Details:

The ablation strategies and additional arrhythmia mechanisms approached did not differ between the groups. In the control group, RF energy application was more likely to be stopped due to an increase in esophageal temperature (26 (55%) vs. 5 (9.4%), $p < 0.001$).

	Outcome	Control	*esolution*	Fishers Exact p-value
Ablation of focal atrial tachycardia	No, n (%)	62 (95.4%)	53 (100.0%)	
	Yes, n (%)	3 (4.6%)	0 (0.0%)	0.2514
Ablation within coronary sinus	No, n (%)	59 (90.8%)	51 (96.2%)	
	Yes, n (%)	6 (9.2%)	2 (3.8%)	0.2931
Atypical LA flutter	No, n (%)	62 (95.4%)	53 (100.0%)	
	Yes, n (%)	3 (4.6%)	0 (0.0%)	0.2514
Complex fractionated atrial electrograms in left atrium	No, n (%)	62 (95.4%)	52 (98.1%)	
	Yes, n (%)	3 (4.6%)	1 (1.9%)	0.6265
Complex fractionated atrial electrograms in right atrium	No, n (%)	63 (96.9%)	53 (100.0%)	
	Yes, n (%)	2 (3.1%)	0 (0.0%)	0.5009
Linear ablation – anterior left atrium	No, n (%)	64 (98.5%)	53 (100.0%)	
	Yes, n (%)	1 (1.5%)	0 (0.0%)	1.0000

	Outcome	Control	*esolution*	Fishers Exact p-value
Linear ablation – mitral valve isthmus left atrium	No, n (%)	63 (96.9%)	53 (100.0%)	
	Yes, n (%)	2 (3.1%)	0 (0.0%)	0.5009
Linear ablation – posterior/floor left atrium	No, n (%)	52 (80.0%)	43 (81.1%)	
	Yes, n (%)	13 (20.0%)	10 (18.9%)	1.0000
Linear ablation – roof left atrium	No, n (%)	54 (83.1%)	39 (73.6%)	
	Yes, n (%)	11 (16.9%)	14 (26.4%)	0.2594
Linear ablation – septal left atrium	No, n (%)	63 (96.9%)	53 (100.0%)	
	Yes, n (%)	2 (3.1%)	0 (0.0%)	0.5009
Primary ablation approach used on the posterior wall	High power/short duration, n (%)	22 (33.8%)	17 (32.1%)	
	All Other, n (%)	43 (66.2%)	36 (67.9%)	1.0000
SVC isolation	No, n (%)	64 (98.5%)	53 (100.0%)	
	Yes, n (%)	1 (1.5%)	0 (0.0%)	1.0000
Typical RA flutter – cavo-tricuspid isthmus	No, n (%)	36 (55.4%)	34 (64.2%)	
	Yes, n (%)	29 (44.6%)	19 (35.8%)	0.3531
Was RF energy stopped for increase in esophagus temperature	N, n (%)	29 (44.6%)	48 (90.6%)	
	Y, n (%)	36 (55.4%)	5 (9.4%)	<.0001
Wide area circumferential ablation encircling the ipsilateral pulmonary veins	Yes, n (%)	65 (100.0%)	53 (100.0%)	NA

RF ablation time: Control group (26.5 ± 22.37 minutes) versus Deviation group (21.8 ± 11.9 minutes, p = 0.14). When used, the mean ablation index (AI) for the posterior left atrial wall for Deviation group (n=17) was 375.8 ± 55.6 and was not statistically significantly different for Control group (n=21), 370.1 ± 32.6, p = 0.54. The use of high power/short duration (HP/SD) RF ablation (40-50W for 7-12 seconds) was another commonly used ablation technique and was not significantly different between the two groups: 23 patients in the Control group (34.8%) and 17 patients in the Deviation group (31.5%, p = 0.70). The mean RF energy settings for the posterior LA wall was high for both groups. For the Deviation group, the mean RF energy setting for the posterior LA wall was 40.83 ± 8.82 watts and was not significantly different in comparison to the Control group, which was also a high value, 41.32 ± 8.10 watts, p = 0.30.

	Outcome	*esolution*_N (%)
Did Deviated esophagus move? (In RAO projection) N (%)	Anterior	1 (1.9%)
	Neutral From Starting Position	30 (57.7%)
	Posterior	21 (40.4%)
Is trailing edge present with deviation? N (%)	No	49 (92.5%)
	Yes	4 (7.5%)
Total number of deviations	Mean+/-SD (Min,Max) N	6.69+/- 3.00 (2, 15) N= 54
Total number of deviations to the left	Mean+/-SD (Min,Max) N	3.26+/- 1.56 (1, 7) N= 54
Total number of deviations to the right	Mean+/-SD (Min,Max) N	3.43+/- 1.86 (1, 10) N= 54

Endoscopy Findings:

A subject interview for GI symptoms (heartburn, regurgitation, emesis, dysphagia, nausea, cough, hematemesis, hoarseness, odynophagia) was conducted, which included identifying if symptoms predated the ablation, and if they had worsened. Prevalence ranged from 0-35% (cough, hoarseness) and did not differ between groups.

Endoscopy Findings (> 15 and < 72 hours after ablation)

- Ablation lesion (graded with KCC), device lesion > 4 mm, benign suction < 3 mm, other.
- Images reviewed by EAC.
- 2 subjects (one in each arm) did not undergo endoscopy due to clinical concerns.

EAC Adjudicated Endoscopy Results				
	Outcome	Control	*esolution*	Fisher's Exact p-value
Normal Endoscopy	N, n (%)	30 (46.2%)	17 (32.1%)	
	Y, n (%)	35 (53.8%)	36 (67.9%)	0.1343
Ablation Lesion	N, n (%)	42 (64.6%)	50 (94.3%)	
Primary Study Endpoint	Y, n (%)	23 (35.4%)	3 (5.7%)	<.0001
Ablation Lesion - Type 1	N, n (%)	60 (92.3%)	53 (100.0%)	
	Y, n (%)	5 (7.7%)	0 (0.0%)	0.0636
Ablation Lesion - Type 2a	N, n (%)	46 (70.8%)	50 (94.3%)	
	Y, n (%)	19 (29.2%)	3 (5.7%)	0.0015
Device Related Lesion ≥ 4mm	N, n (%)	64 (98.5%)	53 (100.0%)	
	Y, n (%)	1 (1.5%)	0 (0.0%)	1.0000
Other Etiology	N, n (%)	54 (83.1%)	47 (88.7%)	
	Y, n (%)	11 (16.9%)	6 (11.3%)	0.4396
Benign Suction Marks	N, n (%)	65 (100.0%)	44 (83.0%)	
	Y, n (%)	0 (0.0%)	9 (17.0%)	0.0005

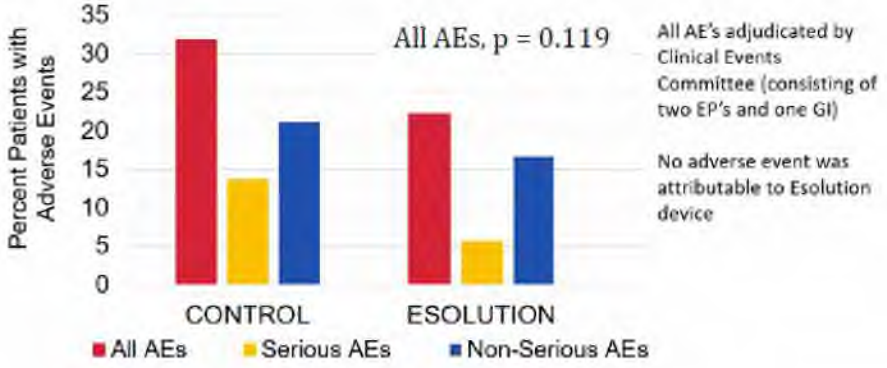
- The primary endpoint of reduction in thermal lesions was met (23/65 (35%) vs. 3/52 (6%) p< 0.0001).
- The number of thermal lesions per patient seen in the control group was larger than in the intervention group (0.7 +/- 0.96, range 0-4 vs. 0.4 +/- 0.63, range 0-2).
- Type 2a lesions were more likely in the control group (29% vs. 6%, p = 0.0015).
- Suction marks were more likely in the intervention group.
- No mechanical lesions (> 4 mm) were seen in the device group.

Reduction in ablation lesions (particularly type 2a) without concomitant increase in device related lesions is noted. No type 2b or 3 lesions were seen in either group.

Adverse events:

Serious and non-serious adverse events did not differ between groups. There were no unexpected device adverse events, device related adverse events, or deaths. In addition to the overall findings of no difference between the groups, the individual adverse events did not appear to have a pattern of harm in the intervention group.

	Control N (%) Subjects	*esolution* N (%) Subjects	Chi-Square P-value
All AE	21 / 66 (31.8%)	12 / 54 (22.2%)	0.119
Serious AE	9 / 66 (13.6%)	3 / 54 (5.6%)	0.0932
Non-Serious AE	14 / 66 (21.2%)	9 / 54 (16.7%)	0.3443



Primary Effectiveness Endpoints:

The primary endpoint of this study is the occurrence of esophageal injury attributable to radiofrequency ablation energy as noted on post ablation endoscopy. Per definition of published literature, esophageal lesions related to injury from RF ablation energy are acute lesions that occur on the anterior wall of the mid-segment of the esophagus. For this study, each esophageal ablation lesion will be characterized using the Kansas City Classification.

In addition to showing superiority over the Control treatment with respect to esophageal injury attributable to RF ablation energy, the observed rate of esophageal injury attributable to RF ablation energy in patients randomized to the esolution device was required to be $\leq 15\%$.

The interim analysis results met the criteria for early stopping for efficacy. Of the 53 esolution and 65 control subjects with endoscopy results, 3 esolution subjects and 23 Control subjects had ablation lesions (5.7% and 35.4%, respectively). Analysis results supported the rejection of the null hypothesis and a conclusion that the proportion of esolution subjects with an ablation lesion is significantly lower than the proportion of Control subjects with an ablation lesion.

Table 19. Primary Analysis – Presence of Ablation Lesion (ITT)

Imputation Number	Risk Difference, C-E (Ablation Lesion=Yes)	ASE	Lower 95% Confidence Limit	Upper 95% Confidence Limit	Fishers Exact P-value
1	0.295	0.0641	0.1693	0.4205	0.00002
4	0.295	0.0641	0.1693	0.4205	0.00002
2	0.279	0.0659	0.1497	0.4079	0.00007
3	0.279	0.0659	0.1497	0.4079	0.00007
5	0.279	0.0659	0.1497	0.4079	0.00007
N Nonmissing = 53 *esolution* and 65 Control					
N Imputed= 9 *esolution* and 2 Control					

- All Fishers Exact one-sided p values are < 0.0027648 (interim success boundary at N=120), leading to the rejection of the null hypothesis.
- Study success was based on the rejection of the null and finding that the observed rate of thermal injury was < 15%.
- Sensitivity analyses and mITT with one worst case also had one sided p values of < 0.0027648.
- A per protocol analysis including the subset of the ITT population who received a study treatment and an endoscopy (N=118, 65 Control and 53 esolution) was performed and the Fishers Exact one-sided p-value is <0.0027648.
- A tipping point analysis indicted up to 3 device subjects could be imputed with failed outcomes to reject H0.

Secondary Analyses:
There were 6 sequenced planned secondary effectiveness tests.

Secondary analysis #1 was to compare the incidence of mechanical/device related esophageal injury with a historically derived performance goal of 20%, derived from the observational RADIANCE trial of a different esophageal deviation device. No subjects had an esophageal injury.

Parameter	Frequency	Percent	95% Lower Conf Limit	95% Upper Conf Limit	P-value
Incidence of injury to the esophagus directly related to the use of the device	0/53	0.00	0.0000	0.0672	0.0003

Secondary analysis #2 was to compare achievement of esophageal deviation to a performance goal of 20 mm based on prior studies in > 65% of subjects, and did not meet that goal. Additional details were provided to demonstrate that the distance of 20mm is not consistent with RF biophysics, and does not apply to the design of esolution. The pre-clinical animal studies, clinical studies, and bench testings show that the esolution can retract an esophageal segment away from the left atrial posterior wall effectively and safely.

Parameter	Frequency	Percent	95% Lower Conf Limit	95% Upper Conf Limit	P-value
Deviation of > 20mm in any direction	34/53	64.15	0.4980	0.7686	0.8969

Secondary analysis #3 was that the proportion of subjects with PVI would be greater in the esolution group. Both groups had 100% PVI achieved.

Parameter	Statistic	eSolution	Control	P-value
Was Pulmonary vein entrance block achieved for all veins	Yes, n (%)	53 (100.0%)	65 (100.0%)	NA

Secondary analysis #4 was to test if the proportion of subjects with gastric hypomotility would be less in the esolution group. The percentages were similar in the two group.

Parameter	Statistic	eSolution	Control	P-value
Gastroparesis present	No, n (%)	32 (60.4%)	42 (64.6%)	0.7035
	Yes, n (%)	21 (39.6%)	23 (35.4%)	

Secondary analysis #5 was to compare procedure duration between groups.

Parameter	Statistic	eSolution	Control	Difference (Control – Esolution)
Total Procedure time (minutes)	N	53	65	
	MEAN (STD)	99.9 (53.85)	101.3 (58.91)	1.33
	STANDARD ERROR	7.40	7.31	10.49
	95% CI	85.1, 114.8	86.7, 115.9	-19.45, 22.12
	MINIMUM	36.0	28.0	
	MAXIMUM	278.0	280.0	

Secondary analysis #6 was to assess the proportion of subjects with KCC type 2b or 3 lesions between groups. No subjects had a type 2b or 3 lesion in either group.

Parameter	Statistic	eSolution	Control	P-value
Incidence of KCC Type 2b and Type 3 lesions	N, n (%)	0/53 (0.0%)	0/65 (0.0%)	NA

Other exploratory analyses:

- Esophageal temperature change – peak LET and change in temperature from baseline was reduced in the device group.
- There was no significant difference in mean RF ablation parameters between the groups
- The device was in the esophagus for a mean of 99.9 minutes with suction on for an average of 23.5 minutes.
- There was an average of 6.7 deviations per patient, 3.26 to the left and 3.43 to the right.
- RF energy application was stopped/reduced in 55% of the control and 9.4% of the device group ($p < 0.001$).

- There was no significant difference in fluoroscopy time between groups.
- There was no significant difference in the proportion of subjects with adverse events prior to discharge, or at 30 days.
- There was a significant reduction in overall, type 1 and type 2a ablation lesions in the device group.
- There was a significant increase in suction marks in the device group.

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

LABELING

The labeling consists of the following: device description, indications for use, instructions for use including methodology of use during AF ablation, the use of vacuum suction and temperature probe, principles of device operation, identification of device materials, contraindications, warnings, precautions, a list of potential adverse effects, and special populations that the use of esolution® Esophageal Retractor has not been studied in. Furthermore, the labeling includes sterile packaging information. The labeling meets the requirements of 21 CFR 801.109 for prescription devices.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of mechanical deviation device for esophageal protection during cardiac ablation procedures and the measures necessary to mitigate these risks.

Risks to Health	Mitigation Measures
Failure to protect the esophagus during ablation leading to esophageal perforating complications	Clinical performance testing Animal performance testing Non-clinical performance testing Labeling
Device malfunction leading to esophageal injury	Non-clinical performance testing Shelf life and packaging testing
Adverse tissue reaction	Biocompatibility evaluation
Infection	Sterilization validation Shelf life and packaging testing Labeling
Mechanical injury to esophageal or oral structures	Clinical performance testing Animal performance testing Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the mechanical deviation device for esophageal protection during cardiac ablation procedures is subject to the following special controls:

(1) Clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use and include the following:
   (i) Evaluation of reduction of the incidence of esophageal injury during cardiac ablation procedures; and
   (ii) Evaluation of any esophageal or oral injury from use of the device.

(2) Animal performance testing must demonstrate that the device performs as intended under the anticipated conditions of use and include the following:
   (i) Evaluation of the device's capability to adequately deviate the esophagus, including its trailing edge, away from the source of ablation energy; and
   (ii) Evaluation of any esophageal injury from use of the device.

(3) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use and include the following:
   (i) Mechanical integrity testing using clinically relevant forces; and
   (ii) Compatibility testing with accessory devices.

(4) Performance data must demonstrate the sterility of any device components intended to be provided sterile.

(5) The patient-contacting components of the device must be demonstrated to be biocompatible.

(6) Performance data must support the shelf life of the device by demonstrating package integrity and device functionality over the identified shelf life.

(7) Labeling must include the following:
   (i) A summary of clinical performance testing with the device; and
   (ii) A shelf life.

BENEFIT-RISK DETERMINATION

The probable risks associated with esolution® Esophageal Retractor include complications related to instrumentation, deviation, and suction in esophagus

- Minor risks associated with esolution® Esophageal Retractor device include:
  - Sore throat
  - Self-limiting odynophagia with eating
  - Dental injury
  - Benign suction lesions
  - Pharyngeal abrasion
- Major risks associated with esolution® Esophageal Retractor include:

- Laceration or perforation of oropharynx or esophagus requiring intervention
  Death related to esophageal injury

In animal studies, first in man study and in the EASY AF IDE, there were no changes in blood pressure or heart rate with use of esolution® Esophageal Retractor and no injury to the esophagus despite prolonged suction and multiple bilateral deviations.

Additionally, it is important to note that in the EASY AF study, the Clinical Events Committee, who blindly adjudicated each adverse event, did not assign any adverse event to use of the esolution® Esophageal Retractor. The risk of adverse event with the esolution® Esophageal Retractor thus is low likelihood.

Subjects in the esolution group had a significantly lower rate of ablation-related esophageal lesions, and there were no unexpected safety findings. Thus, the benefits of esolution® Esophageal Retractor, when used to displace the esophagus away from the source of ablation energy during ablation of AF and to minimize the risk of esophageal injury, outweigh the risks.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, for the following indication statement:

> The esolution® Esophageal Retractor is indicated for use in patients undergoing percutaneous cardiac catheter ablation of atrial fibrillation to deviate the esophagus away from the ablation energy source and to reduce the risk of ablation-related esophageal injury.

The probable benefits outweigh the probable risks for the esolution® Esophageal Retractor. The device provides benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the esolution® Esophageal Retractor is granted and the device is classified as follows:

> Product Code: QXU
> Device Type: Mechanical deviation device for esophageal protection during cardiac ablation procedures
> Regulation Number: 21 CFR 870.5710
> Class: II