Evaluating Active Esophageal Cooling during Cardiac Ablation Procedures

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1 PROTOCOL SYNOPSIS

Sponsor:	Advanced Cooling Therapy d/b/a Attune Medical, 3440 S. Dearborn St #215-S, Chicago, IL, 60616, USA
Version:	1.0
Protocol ID	201904751
PI/Site:	
Objective:	This pilot study will evaluate the efficiency impact of conducting active temperature management during cardiac ablation procedures.
Patient Population:	This study is intended for patients undergoing left atrial ablation including pulmonary vein isolation for the treatment of atrial fibrillation.
Study Design:	Prospective, single center pilot study
Study Conduct:	This prospective interventional pilot study will use the FDA cleared Attune Medical esophageal heat transfer device (ensoETM) to actively cool the esophagus when RF ablations are performed on the posterior atrial wall and to actively warm the patient at all other times to minimize perioperative hypothermia. In consented participants, following induction of anesthesia and intubation, the ensoETM will be placed into the esophagus according to the device Instructions and maintained at 40-42°C. Active cooling will be initiated approximately 15 minutes prior to any ablations placed on the posterior left atrium. The ensoETM will continuously circulate 4-6°C water inside the device during all ablations directed at the posterior wall of the atrium. Once all ablations to the posterior wall of the atrium are complete, the water set-point will be returned to nominal until the conclusion of the procedure. Total procedure time from trans-septal puncture to pulmonary vein isolation (PVI) will be recorded. All patients will be followed up in total for 6 weeks (Long Term FU visit) after the procedure to document any clinical complication related to thermal esophageal injuries if applicable.
Study Duration:	The study duration is projected to be approximately 145 days (estimated 3-month enrollment and a 6-week long term follow-up window).
Inclusion Criteria:	1. Adult patients (age over 18 years)

2. Undergoing first left atrial ablation for the treatment of atrial fibrillation including pulmonary vein isolation
3. Undergoing catheter-based ablation procedure using radiofrequency energy
4. Patients must be able to understand and critically review the informed consent form.
5. Subjects must understand and agree to study requirements and sign a written informed consent

Exclusion Criteria:

1. Patients who are unable to provide informed consent.
2. History of prior AF ablation procedures with ablation in the left atrium.
3. Significant co-morbidities that preclude standard ablation procedure.
4. Patients with <40 kg of body mass
5. Patients with relevant esophageal pathology (e.g. esophageal cancer, esophageal varices)

Primary Endpoint:

Total time of active ablation procedure, measured from trans-septal puncture to achievement of PVI.

Sample Size:

Up to 20 participants will be enrolled in the study.

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3 INTRODUCTION

3.1 Background

Left atrial catheter ablation including pulmonary vein isolation is a standard therapy in the management of symptomatic atrial fibrillation; however thermal esophageal injury is a known potential consequence of this procedure.[1-4] Delivery of radiofrequency (RF) energy necessary to perform left atrial ablation has the potential to cause injury to the nearby esophagus including ulceration, hematoma, spasm, esophageal motility disorders, and, in the most extreme case, atrial-esophageal fistula.[1,2] Esophageal mucosal lesions are the likely precursor to AEF, and esophageal mucosal lesions have been detected on post-ablation endoscopy after pulmonary vein isolation with an incidence ranging from 3% to 60%.[5-8]

Active esophageal cooling during RF ablation as a means of esophageal injury prevention has been investigated through mathematical models, pre-clinical studies, and in clinical trials. Existing data support the efficacy of this approach, but the practice has not been widely adopted due to lack of a commercially available device. [9-16]

A new esophageal heat transfer device (ensoETM, Attune Medical, Chicago, IL, USA) was recently commercialized for a variety of patient temperature management needs.[17-22] This device provides a closed-circuit water flow through a multi-channel cylindrical silicone tube placed in the esophagus analogously to a standard orogastric tube. Warming or cooling a patient is accomplished through conductive heat transfer across the esophagus and convective heat transfer through the device.[20,23]

Esophageal heat exchange is designed to take advantage of the favorable heat exchange environment created by proximity to the heart and great vessels. The device includes an independent lumen to decompress the stomach and avoid distention of the esophagus away from the device, which ensures good contact with the esophageal mucosa, thus maximizing heat transfer between the device and the patient. The esophageal heat transfer device is made of standard medical-grade silicone and is generally similar in shape and size to gastric tubes currently used and other devices routinely placed in the esophagus (esophagogastroduodenoscopy scopes, transesophageal echocardiography scopes, Ewald tubes, etc.).

Clinical studies in a variety of scenarios have shown strong support for the efficacy and safety of the esophageal heat transfer device in critical care and OR settings.[20,24-34] Specifically, the device has demonstrated effectiveness in the intentional reduction of patient body temperature below normal for conditions such as cardiac arrest,[19,24,27] the reduction of patient temperature from hyperthermic levels to normal range, [35] the prevention of inadvertent perioperative hypothermia, [22,36] and the reduction of elevated intracranial pressure.[25]

A number of studies of the device have been completed, or are in progress, evaluating feasibility, safety, and effect size of esophageal protection during both RF ablation and cryoablation, including pre-clinical models and formal randomized clinical trials.[37-42] Because the impact on procedural time has not yet been evaluated, the purpose of this study is to determine the impact on procedural efficiency of ablation procedures performed using esophageal heat transfer with the ensoETM.

3.2 Study Objective, Hypothesis and Rationale

The objective of this study is to evaluate the impact on procedural efficiency of ablation procedures performed using esophageal heat transfer to cool the esophagus during left atrial RF ablation. This study is designed to measure procedural time of RF ablation to obtain pulmonary vein isolation (PVI) and serve as a pilot to compare to historical controls and enable adequate determination of sample size requirements for a subsequent larger study. The hypothesis is that active esophageal cooling will show a reduced procedural time when compared to standard of care using esophageal temperature monitoring.

3.3 Primary Endpoint

Procedural time, from trans-septal puncture to attainment of successful PVI. Ablation will be performed as standard procedure with pre-specified ablation technology on the posterior left atrial wall using standard ablation settings.

4 STUDY PROTOCOL

4.1 Study Design

This study is a prospective, pilot study using the Attune Medical ensoETM esophageal heat transfer device to actively cool the esophagus during RF ablation procedures. This design is appropriate to gather the data needed regarding overall procedural time, compare this to historical controls, and estimate a sample size for a larger study powered for statistical significance.

Once patient consent is obtained, the subject will undergo preparation and anesthesia procedures following standard practice. Once the patient is intubated, the esophageal heat transfer device will be placed into the esophagus according to the IFU. The device will remain in place until the ablation procedure is completed and will be removed before extubation. Posterior left atrial wall ablation using standard parameters will only be performed when the ensoETM has reached a temperature of 4-6°C for at least 2 minutes. The device will be set to neutral or warming temperature (37-42°C) during other aspects of the procedure (such as mapping and anterior wall ablations).

4.2 Study Device Description and Intended Use

The ensoETM is a non-sterile multi-lumen silicone tube placed in the esophagus for the purpose of cooling or warming a patient while simultaneously allowing gastric decompression and drainage. Modulation and control of the patient's temperature is achieved by connecting the ensoETM to an external heat exchanger. Two lumens connect to the external heat exchanger, while a third central lumen provides stomach access for connection to a fluid collection device with low intermittent suction

for gastric decompression (Figure 1). The ensoETM is made of standard medical-grade silicone. It is a single-use, disposable, non-implantable device with an intended duration of use of 72 hours or less. Distilled water circulates inside the ensoETM, water does not come into contact with the patient.

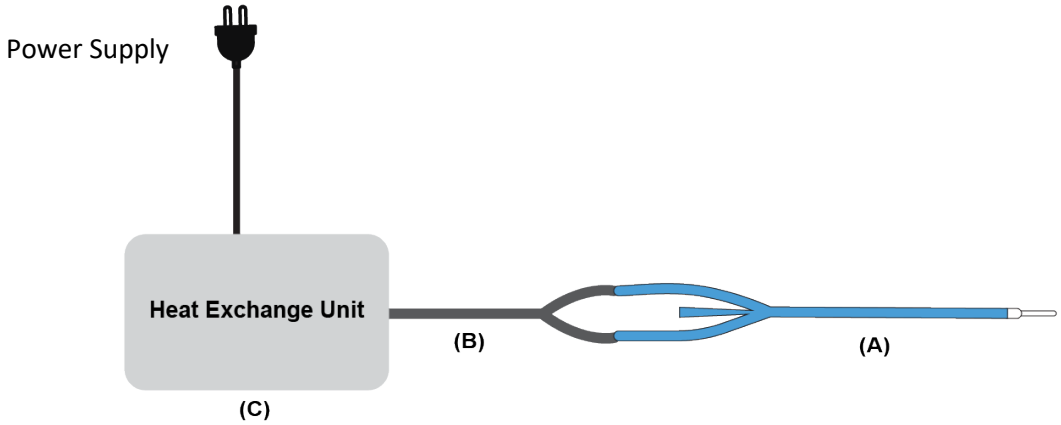

Figure 1. ensoETM System

Table 1: ensoETM System Components

Diagram Letter	Name	Description
A	ensoETM	ensoETM (ECD-01B or ECD-02B)
B	Tube set connector	Stryker Model 8001-064-035 Insulated Clik-Tite Hose or Cincinnati Sub-Zero connector hose (CSZ P/N 286)
C	Heat exchanger	Stryker Altrix Model 8001 Precision Temperature Management System or Cincinnati Sub-Zero Blanketrol III Hyper-Hypothermia System

The ensoETM has received FDA clearance and its intended use is as a thermal regulating device intended to connect to an external heat exchanger in order to modulate and control patient temperature in the operating room, recovery room, emergency room, or intensive care unit.

4.3 Installation Use and Storage of the Device

Detailed operation of the system is included in the IFU. The ensoETM device should be stored in a dry and clean place and handled according to the IFU. The research team will ensure that the heat exchange unit will be operated in accordance with the appropriate IFU.

The Company will provide on-site support for training and operation of the ensoETM according to the IFU. As the insertion procedure is similar to placing a standard orogastric tube, it is expected that insertion of the probe and operation of the ensoETM will require limited training and ongoing support, however, the Company will support cases as requested.

4.4 Subject Study Population

Subjects that are indicated for first catheter-based ablation of AF using radiofrequency ablation treatment will be eligible for the study.

4.5 General Inclusion Criteria

Participants must meet all of the following general inclusion criteria:

1. Adult patients (age over 18 years)
2. Undergoing first left atrial ablation for the treatment of atrial fibrillation including pulmonary vein isolation
3. Undergoing catheter-based ablation procedure using radiofrequency energy
4. Patients must be able to understand and critically review the informed consent form.
5. Subjects must understand and agree to study requirements and sign a written informed consent.

4.6 General Exclusion Criteria

Subjects must meet none of the following general exclusion criteria:

1. Patients who are unable to provide informed consent.
2. History of prior AF ablation procedures.
3. Significant co-morbidities that preclude standard ablation procedure.
4. Patients with <40 kg of body mass
5. Patients with relevant esophageal pathology (e.g. esophageal cancer)

5 DATA COLLECTION AND MANAGEMENT

5.1 Confidentiality

All parties involved, at all times throughout the clinical investigation shall observe confidentiality of data. All data shall be secured against unauthorized access, and the privacy of each subject and confidentiality of his/her information shall be preserved in reports and when publishing any data. Study subject identification will remain confidential by the assignment and use of study specific identification numbers. All study documentation and/or medical records collected and used for study purposes will be pseudonymizised so that an individual subject will not identified outside the study. Data safety applies to the standard and patient data safety is secured throughout the study. All patients will give informed consent on data safety issues.

5.2 Informed Consent

This study will require subjects to have the ensoETM inserted intra-orally prior to the ablation procedure. As the ensoETM is not routinely used at this Center, detailed information regarding risks are included in the Informed Consent Form presented to subjects enrolling in the study.

This study will require that the operating physician carry out the standard of care for AF ablation. Ultimately, the number and location of ablation lesions and determination of whether to end the procedure will be at the discretion of the operating physician and will be based on the Center´s standards as used in recent years. Subjects will be required to sign an Informed Consent Form detailing the potential risks and benefits of their study participation. A study subject can withdraw consent at any time, and for any reason. All patients included will also sign a separate informed consent for AF ablation procedure as standard in the Center.

5.3 Data De-Identification

Except where required by law, information shared with persons and organizations outside of the investigational site will not identify the subject by name, government identification number, address, telephone number, or any other direct personal identifier. To ensure that subject identification is kept confidential, a subject's unique identification number will be employed. At the investigational site, a confidential file of informed consent forms and anonymization code numbers will be retained, accessible to the Principal Investigator and/or designee and other authorized personnel. The subject's unique identification number will be employed on all source documentation that is used for data review and analysis.

5.4 Data Management

Data entry and development of the primary database of the study will be performed by PI or his designee(s). Data inserted into the database will be reviewed after 10 cases, based on original patient documentation. In case of data queries, PI will resolve based on original patient documentation.

The database is password secured and has an audit trail. Changes to the database can only be made by the delegated study group. Verification of data will be done after 10 cases based on original patient documentation. PI or designee will also be responsible for auditing the database and confirming the overall integrity of the database.

5.4.1 Case Report Forms

The Center will perform primary data collection based on source-documented hospital chart reviews and data transcribed or exported from the mapping and navigation system. Temperature set point and timing will be transcribed and annotated into the mapping software.

Deviations from the study protocol or adverse events will be recorded on the appropriate forms (Deviation / Adverse Event Report). Deviations will be documented, and patients will be excluded from

final analysis although deviations will be documented and summarized in final reports. Any deviations that concern patient safety and/or the rights of a study subject will be reported to IRB within 24 hours.

5.4.2 Monitoring Plan

The investigator and research team will allocate adequate time for monitoring activities and monitoring of all data will be performed on a regular basis throughout the study. For monitoring access to all the above noted study-related documents and study related facilities (e.g. clinical EP laboratories) will be granted. Monitoring will be performed by a committee not involved in the study conduct.

5.4.3 Protocol Deviations and Modifications

Any changes to the approved clinical study must originate from Sponsor in the form of a protocol amendment that must be submitted to the relevant IRB contact. Protocol deviations should be avoided by the PI and site supporting staff. Any deviation from the protocol should be reported to the Sponsor. Any deviation to the clinical study will be reported to the ethical committee in accordance with local requirements. In the situation where deviating from the protocol is in order to protect the life or physical wellbeing of the subjects, which are considered emergency deviations, these should be reported to the Sponsor and Ethical Committee per their local guidelines.

A deviation is any variance from the Investigational Plan requirements (e.g., failure to obtain informed consent, failure to meet inclusion/ exclusion, etc.).

5.4.4 Data Analysis and Acceptance

All analyses will be performed using validated statistical software. In general, the study endpoints will be assessed relative to the study objectives. Patient data listings and tabular and graphical presentations of baseline and operative characteristics and outcome results will be created.

5.4.4.1 Sample Size Determination

As a pilot study, the data obtained will provide information necessary for a formal sample size estimate for a subsequent larger study. A sample size of 20 patients is estimated to be sufficient to provide a 95% confidence interval of +/- 15 minutes around mean procedure duration, assuming a procedure duration of 95 minutes with a standard deviation of 20 minutes.

5.4.4.2 Analysis Populations

Safety Population

All enrolled subjects who underwent a catheter ablation of persistent and paroxysmal atrial fibrillation procedure will be included in the safety population.

Evaluable Population

All enrolled subjects who have received catheter ablation of persistent and paroxysmal atrial fibrillation with complete ablation data and procedural timing will be included in the evaluable population.

Primary Endpoint Analysis

The primary endpoint of this study will be the total time of active ablation procedure, measured from trans-septal puncture to achievement of PVI. All ablations at posterior left atrial wall during AF ablation are performed under standardized conditions including predefined sets of ablation parameters as per standard of care.

Secondary Endpoint Analysis

Secondary endpoints include:

1. Total procedure time (from patient entry to EP lab until discharge to PACU)
2. Number of procedural pauses during left atrial instrumentation

5.4.4.3 Safety Analysis

All safety-related issues related to the usage of the device will be recorded and documented as **device-related AEs (ADE)**. All safety analyses will be performed on the safety population. No imputation of missing observations will be performed. The Medical Dictionary for Regulatory Activities (MedDRA) version 13.0 or later will be used to code all AEs to a system organ class (SOC) and a preferred term (PT) within the SOC.

The incidence and frequency of AEs will be summarized by system organ class and preferred term for all AEs, device-related AEs (with relationship to study devices and/or study-device-related procedure), serious device-related AEs and device-related AEs leading to study withdrawal and death. The incidence of ADEs will also be tabulated by seriousness, severity, and relationship to study devices and/or procedure.

No AEs will be recorded for study purposes that are not specifically device-related (e.g. arrhythmia recurrences) as this is not within the scope of the study.

6 STUDY PROCEDURE AND ASSESSMENTS

Table 2: Schedule of Assessments and Procedures

Assessment/ Evaluation	Baseline (-14 days)	Day 0 (pre-admission)	Index Procedure	Discharge (+1d)
Pre-screening for Inclusion/ Exclusion Criteria	X			

Medical History	X			
Demographics	X			
Informed Consent		X		
Randomization	N/A			
Device-related Adverse Events			X	X

6.1 Pre-Procedure Subject Preparation/Baseline

Prior to subject participation the following steps will be completed and documented in the CRF:

1. Signed informed consent is obtained.
2. Confirmation that all inclusion criteria are met.
3. Confirmation that no exclusion criteria are present.
4. All subjects enrolled into this study will undergo and have documented the following evaluations (within two weeks prior to study unless otherwise noted) as standard of care in the Center but not related to the study:
    a. Medical history and physical examination
    b. Pregnancy test in female of childbearing potential
    c. Standard of care AF ablation pre-procedure testing (CT or/and TEE)

Informed consent will be obtained by the study investigators after discussion with the patient. The study investigators will provide additional information required and requested by the patient. Any information needed for fulfilling the study requirements will be gathered prior to inclusion. Enrollment begins when the informed consent form has been executed.

6.2 Index Procedure

Cardiac Ablation

Only participants who are scheduled for a pulmonary vein isolation are eligible for participation in the trial. Cardiac ablation will be performed using irrigated contact-force radiofrequency ablation catheters with a maximum power of 50W when ablating at the posterior wall. Ablation will be performed to electrically isolate the pulmonary veins from the left atrial myocardium. The location of the catheter in relation to the posterior left atrial wall is continuously determined in real-time electroanatomic maps of the left atrium.

Active Esophageal Cooling

In consented patients, the ensoETM esophageal heat transfer device will be inserted according to standard protocol during preparation for the ablation procedure, following intubation. The ensoETM is a

non-sterile multi-lumen silicone tube placed in the esophagus much like a standard orogastric tube. The ensoETM holds FDA clearance and is intended for use as a thermal regulating device intended to connect to an external heat exchanger in order to modulate and control patient temperature. The device will remain in place until the ablation procedure is completed. Patients will undergo posterior wall ablation when the ensoETM device has reached a temperature of 4-6°C for at least 2 minutes. The device will be set to neutral body temperature (no cooling) during other aspects of the procedure.

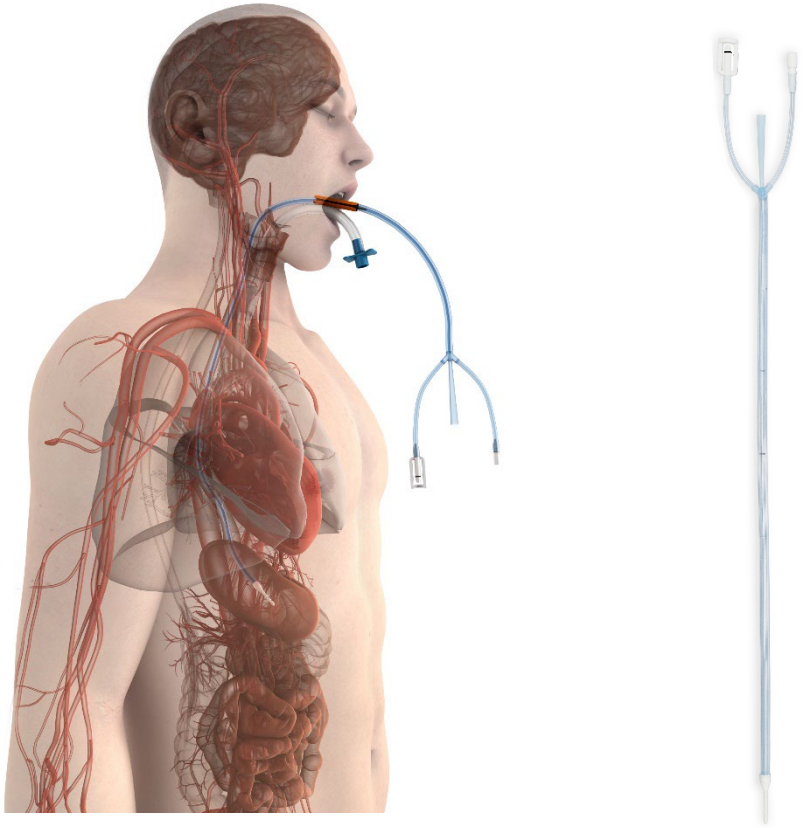

Figure 2: The esophageal heat transfer device is constructed from medical grade silicone with an outer diameter of ~12mm (36 Fr), length of 758mm, and circulating water volume of 55mL. The device is placed similarly to an orogastric tube. Distilled water circulates inside the tube (never entering the patient), directly cooling the esophageal tissue.

6.3 Data Collection During AF Ablation Procedure

In this study the study team will collect ablation data from the ablation system.

6.4 Hospital Discharge

Patients discharged from the hospital following the procedure will follow post procedural standard of care for AF Ablation procedures.

6.5 Study Duration and Early Termination

Study duration is expected to be minimum of 3 months. The IRB may suspend or prematurely terminate the clinical study at the investigation site. If suspension or premature termination occurs, the terminating party shall justify its decision in writing and promptly inform the other parties involved. If, for any reason, the Sponsor suspends or prematurely terminates the investigation the Sponsor shall inform the responsible regulatory authority and Ethics Committee as appropriate.

6.6 Protocol Deviations

Except for an emergency situation in which proper care for the protection, safety, and well-being of the study subjects requires medical treatment, the study will be conducted as described in the approved protocol, and in accordance with GCP and regulatory requirements. The investigator will not deviate from the protocol for any reason without prior written approval, except in cases of medical emergencies, when the deviation is necessary to eliminate an apparent immediate hazard to the subject. In that event, the investigator will notify the Sponsor or designee immediately by phone, and confirm notification to the Sponsor or designee in writing.

Any deviation(s) from the protocol will be recorded and presented in the final clinical study report.

6.7 Adverse Event (AE) Reporting Requirements

All ADEs will be documented according to institutional standards. All ADEs must be monitored until they are adequately resolved or explained.

SAEs where causal relationship to device and procedure can be excluded will be added to a summary table and reported quarterly. At the end of the study an evaluation report of all SAEs will be provided to the Ethics Committee if required.

Definitions regarding adverse events can be found in Section 9.

7 RISK MANAGEMENT

7.1 RISK ANALYSIS

Risk analysis associated with the ensoETM device has been performed in accordance with ISO 14971: Application of Risk Management to Medical Devices.

Risk Management activities include

- Identification of intended use
- Identification of Hazards – Biological, Environmental, Radiation
- Estimation of Risk

- Risk Evaluation
- Risk Control
- Evaluation of overall residual risk
- Risk Management Report

The Attune Medical ensoETM has received CE Marking and FDA 510(k) clearance, and its intended use is as a thermal regulating device intended to connect to an external heat exchanger in order to modulate and control patient temperature. The ensoETM is constructed from medical grade silicone with an outer diameter of 12mm (36 Fr), length of 758mm, and circulating water volume of 55mL. Distilled water circulates inside the tube (never entering the patient), directly cooling the esophageal tissue. The device is placed similarly to an orogastric tube. Risks associated with ensoETM use are similar to those of standard orogastric tubes.

The overall risks associated with this study are the same risks associated with standard catheter ablation, including standard esophageal temperature monitoring.

7.1.1 Risk Analysis of esophageal damage related to AF ablation

Esophageal injury is a well-established risk associated with AF ablation procedures. Current strategies to minimize injury risk include reducing energy and force while ablating the left posterior atrial wall and luminal esophageal temperature (LET) monitoring. Neither strategy actively prevents esophageal injury, as esophageal thermal damage related to AF ablation procedures can be detected in up to 60% of asymptomatic patients undergoing post-ablation endoscopy.

However, early studies of active esophageal cooling have demonstrated various levels of protection. These studies encompass many devices (primarily with various balloon configurations) and have been investigated with mathematical modeling, preclinical models, and in clinical trials. The preponderance of data shows the effectiveness of the approach, especially among high flow rate devices, but the applications were limitations by the implementations investigated (early prototypes were complicated to use or deformed the atria from ballooning of the device).

The ensoETM accommodates high flow rate without causing esophageal deformity. The device has been used safely in thousands of critical care patients. We expect there to be no incremental risk associated with the use of the ensoETM during compared to the existing approach. Unlike temperature monitoring strategies that prompt reactive strategies (such as pausing ablation) this approach may actively reduce tissue damage while improving procedural efficiency and reducing the time under anesthesia.

7.1.2 Risk Benefit Summary

During this pilot study, the ensoETM will be inserted into the esophagus intra-orally while patients are under general anesthesia. The risks to the patient are expected to be similar or the same as those associated with the introduction of any standard orogastric tube.

Only personnel with knowledge of and experience in placing gastric tubes will be involved in the study. Patients will be continuously monitored throughout the procedure.

All patients will be treated with standard of care technology and ablation settings. All procedures performed during the study are part of the standard approach to AF ablation patients at the Center.

Subjects might not directly benefit from participation in the trial, but the findings of the current study will improve the knowledge of esophageal thermal lesion prevention strategies. Information gained in the current study will be applied to larger patient cohorts in the future, in an effort to reduce esophageal thermal injury and make AF ablation safer and more efficient.

AF ablations will be monitored in this study with the safest technology currently available and patients will receive optimized treatments using standard of care technology. All patients will be closely monitored and receive optimum diagnostic and therapeutic management.

8 ADVERSE EVENT DEFINITIONS AND CLASSIFICATIONS

8.1 ADVERSE EVENTS

Adverse events are categorized as defined in ISO 14155:

Adverse event (AE): Any untoward medical occurrence in a subject

Note: this definition does not imply that there is a relationship between the AE and the device under investigation

Adverse device event (ADE): Any untoward and unintended response to a medical device.

Note 1: this definition includes any event resulting from insufficiencies or inadequacies in the instructions for use or the deployment of the device.

Note 2: this definition includes any event that is a result of a user error

Serious adverse event (SAE): Adverse event that:

1. Lead to a death
2. Lead to a serious deterioration in the health of the subject:
   - resulted in a life-threatening illness or injury
   - resulted in a permanent impairment of a body structure or a body function
   - required in-patient hospitalization or prolongation of existing hospitalization
   - Resulted in medical or surgical intervention to prevent permanent impairment to body structure or a body function
3. Lead to fetal distress, fetal death or a congenital abnormality or birth defect

Serious adverse device event (SADE): Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less opportune.

Note: The Investigator is responsible for any reporting requirements to the local government or Ethics Committee.

Unanticipated serious adverse device event (USADE): is a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report

Note: Anticipated serious device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.

Emergency contact details for reporting SAEs and SADEs 24/7 are listed below:

8.2 ANTICIPATED ADVERSE EVENTS AND DEVICE EFFECTS

Acute Adverse Events that may possibly be caused by or associated with the use of the device or the related procedures in this clinical trial are anticipated and characterized in the device insert.

8.3 DURATION OF FOLLOW-UP POST ADVERSE EVENTS

All adverse events related to the device procedure (ADE) must be followed until resolution or until stable clinical endpoint is reached. All required treatments and outcomes of the adverse events must be recorded per reporting requirements defined in Section 5.

8.4 DEVICE FAILURES AND MALFUNCTIONS

All device failures and malfunctions will be documented on the CRF and reported to the Company within 24 hours. Devices that fail or malfunction will be returned to Attune Medical for analysis as soon as practicable. Attune Medical will follow its internal procedure (QSP 8.2-1 Customer Inquiries and Complaints) to determine the course of testing, further reporting and any corrective action, if required.

Device Failure:

A device has failed if it does not perform according to labeling and negatively impacts the treatment while used according to the labeling.

Device Malfunction:

A device malfunction is an unexpected change to the device that is contradictory to the labeling and may or may not affect device performance.

All malfunctioning devices must be returned to Attune Medical after appropriate decontamination per hospital guidelines. Attune Medical will follow its internal procedure (QSP 8.2-1 Customer Inquiries and Complaints) to determine the course of testing, Medical Device Reporting and any corrective action, if required.

9 DEVICE ACCOUNTABILITY

The Company's devices will be identified by Lot Number. The site must maintain device accountability records documenting study device usage. This form must be maintained and reviewed by the study monitor.

The manufacturer will provide the Center with devices, sufficient to provide the Center with approximately 10% additional devices to accommodate demonstration or replacement, to ensure that the maximum number of patients may be enrolled in this study.

10 ISO 14155 COMPLIANCE

This Clinical Trial has been designed and will be conducted in compliance with the Clinical Investigation Plan, ISO 14155:2011, Declaration of Helsinki, ICH Guidelines for Good Clinical Practice (GCP) and applicable local and national regulatory requirements.

11 PUBLICATION POLICY

Results of this investigation will be published in peer-reviewed scientific journals, and/or presented at scientific symposia. Company agrees to review and comment on manuscript/ presentation within sixty (60) days of receipt.

12 ACRONYMS

AE: Adverse event

AEF: Atrio-esophageal fistula

AF: Atrial Fibrillation

EMR: Electronic Medical Record

LET: luminal esophageal temperature

RF: Radiofrequency

SAE: Serious adverse event

SOC: Standard of care

UP: Unanticipated Problem

13 REFERENCES

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