Dipole Density Right (and left) Atrial Mapping and Assessment of Therapy In Complex Supraventricular Tachycardia (DDRAMATIC-SVT)

Protocol: CL-SVT-005, Revision 05
Date: 10 March 2016

Sponsor:
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Investigational device - exclusively for use in a clinical investigation.

CONFIDENTIALITY STATEMENT

Protocol: CL-SVT-005

I have read this protocol and agree to conduct the study as outlined herein.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure they are fully informed regarding the device and the conduct of the study.

_____

Principal Investigator's Signature Date

_____

Name of Principal Investigator (Typed or Printed)

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1.0 REVISION HISTORY

Revision #	*Date*	*Description*
01	06-Feb-2014	Initial release
02	28-May-2014	Limited use of the system to offline analysis
03	17-Apr-2015	Add additional patients and update the AcQMap System schematic diagram. Add the OTW AcQMap Catheter and AcQGuide Steerable Sheath. Also update previous clinical experience.
04	21-Apr-2015	Removed limitation to guide therapy, updated enrollment duration and formatting/grammatical errors.
05	10-Mar-2016	Increased sample size, clarified portions of the left atrial procedure, and revised reason for early termination of the study.

2.0 SYNOPSIS

Study Objective	To demonstrate safety and performance of the AcQMap™ High Resolution Imaging and Mapping System (AcQMap System) in gathering data to create right and/or left atrial dipole density activation maps in subjects with supraventricular tachycardias (SVTs).
Study Device	The AcQMap System consists of a diagnostic recording catheter with intracardiac ultrasound and electrical mapping components advanced through a steerable sheath and accessories that are connected to a computerized medical instrument.
Study Design	A prospective, non-randomized, open-label study.
Sample Size	A total of 50 subjects will be enrolled
Study Duration	Enrollment is anticipated to take approximately 3-6 months. Follow-up is 7-10 days for non-AF patients and 1 year for AF patients following the procedure for each patient.
Primary Endpoints	• The primary effectiveness endpoint of the study is the construction of pre- and post-treatment activation maps with the AcQMap System. • The primary safety endpoint is the incidence of device-and procedure-related adverse events through 7 days post-procedure.
Inclusion Criteria Subjects must:	1. Be aged 18 to 75 years 2. Be scheduled for ablation of a supraventricular tachycardia due to the arrhythmia being recurrent, poorly tolerated and/or unable to be controlled with antiarrhythmic drug therapy 3. Be able and willing to give informed consent

Exclusion Criteria Subjects must not:	1. Have any of the following: a. Patients with implanted prosthetic, artificial, or repaired cardiac valves in the chamber being mapped. b. Patients with permanent pacemaker or ICD leads in the chamber being mapped. c. Patients with hypercoagulopathy or an inability to tolerate anticoagulation therapy during an electrophysiology procedure. 2. Have had a myocardial infarction within the prior two months 3. Have had cardiac surgery within the prior three months 4. Have an intracardiac thrombus 5. Have clinically significant tricuspid and/or mitral valve regurgitation or stenosis 6. Have had any cerebral ischemic event (including transient ischemic attacks) in the prior six months 7. Be pregnant or nursing 8. Be currently enrolled in any other clinical investigation
Data Collection	**Screening** *a.* Demographics (e.g., age, sex, race) *b.* Documentation of disease-related characteristics *c.* Presence/History of arrhythmia *d.* Previous and current treatments for arrhythmias *e.* Review of all inclusion/exclusion criteria to confirm subject eligibility *f.* Adverse events g. Transesophageal Echocardiography (TEE) or similar scan to rule out thrombus. **Procedure** a. Map of the heart chamber anatomy using standard tools and the AcQMap System *b.* Confirmation of arrhythmia with c. Recording of the following (if present or performed) with the AcQMap System: • Pre-ablation: sinus rhythm, arrhythmia induction pacing, any induced or spontaneously occurring arrhythmia, and any pacing maneuvers, including entrainment pacing. • Post-ablation: sinus rhythm, arrhythmia induction pacing, any induced or spontaneously occurring arrhythmia, and any pacing maneuvers, including entrainment pacing and therapy assessment. d. Delivery of therapy using standard techniques. *e.* Confirmation of therapy treatment (post-ablation) *f.* Device- and procedure-related safety events **Follow-up visit(s)** *a.* Device- and procedure-related safety events *b.* Recurrence monitoring for AF patients

3.0 INTRODUCTION

3.1 Background

A supraventricular tachycardia (SVT) is an abnormally fast rhythm, greater than 100 beats per minute that originates superior to the ventricles. SVT refers to a range of conditions in which atrial tissue or the atrioventricular node is essential for sustaining an arrhythmia.[21]

The incidence of SVT is about 35 cases per 100 000 population per year, with a prevalence of 2.25 cases per 1000 population. SVT usually manifests as recurrent paroxysms of tachycardia. It is generally well tolerated but can produce uncomfortable symptoms that lead to acute presentation.[21]

Some of the most common forms of SVTs are: atrial flutter, atrial fibrillation, AV nodal reentrant tachycardia (AVNRT), and atrial tachycardia.

Atrial Flutter

Atrial Flutter (AFL) is the second most common supraventricular tachyarrhythmia, following atrial fibrillation (AF). It can result in significant patient symptoms and hospital visits. AFL has an overall incidence rate of 88/100,000 person-years. Incidence rates increase with age, and range from 5/100,000 in patients less than 50 years of age to 587/100,000 in patients over 80 years old. The incidence of atrial flutter for men is twice that of women. The incidence of atrial flutter in the United States is estimated at 200,000 new cases per year.[1]

The most common atrial flutter is typical cavotricuspid isthmus (CTI)-dependent flutter. Non-typical atrial flutters (NTAFLs) are less common and vary in mechanistic cause. However, their symptoms are similar to typical atrial flutter most commonly presenting with an atrial rate of about 300 beats per minute (bpm) and 2:1 conduction to the ventricle resulting in a ventricular rate of about 150 bpm. NTAFLs can be present in the right or left atrium. Non-typical atrial flutter may cause significant symptoms including palpitations, shortness of breath, chest-pain, lightheadedness, fatigue, and low blood pressure.[2] Patients are also often anticoagulated to reduce thromboembolic risk.

Atrial Fibrillation

Atrial fibrillation (AF) is among the most prevalent arrhythmias in the world today affecting approximately 1.5-2% of the general population. The age of patients with AF is steadily rising and now averages between 75 and 85 years of age. AF is associated with a five-fold risk of stroke, a three-fold incidence of congestive heart failure, and higher mortality[7].

Symptoms arise from the rapid, irregular rhythm as well as the loss of cardiac pump function related to uncoordinated atrial contractions. These uncoordinated contractions

also allow blood to pool in the atria and may ultimately lead to thromboembolism and stroke.

AF is characterized by a chaotic contraction of the atrium in which an electrocardiogram (ECG) recording is necessary to diagnose the arrhythmia. Any arrhythmia that has the ECG characteristics of AF and lasts sufficiently long for a 12-lead ECG to be recorded, or at least 30 seconds on a rhythm strip, should be considered an AF episode.[8,9]

The diagnosis requires an ECG or rhythm strip demonstrating: (1) Irregular RR intervals (in the absence of complete AV block), (2) no distinct P waves on the surface ECG, and (3) an atrial cycle length (when visible) that is usually variable and less than 200 milliseconds.[9]

AF can be characterized into 4 classifications[23]. Paroxysmal AF (PAF) is defined as recurrent AF (≥two episodes) that terminates spontaneously within seven days. Persistent AF is defined as recurrent AF that is sustained for, seven days. In addition, patients with continuous AF who undergo cardioversion within seven days should be classified as having paroxysmal AF if the cardioversion is performed within 48 hours of AF onset, and persistent AF if the cardioversion is performed more than 48 hours after AF onset. A third category of AF is "longstanding persistent AF" that is defined as continuous AF of greater than one year's duration. The term permanent AF is defined as AF in which the presence of the AF is accepted by the patient (and physician). Within the context of any rhythm control strategy, including catheter ablation, the term permanent AF is not meaningful. The term permanent AF represents a joint decision by the patient and a physician to cease further attempts to restore and/or maintain sinus rhythm at a particular point in time.[9]

For many years, three major schools of thought competed to explain the mechanism(s) of AF: multiple random propagating wavelets, focal electrical discharges, and localized reentrant activity with fibrillatory conduction.[10-14]

Significant progress has been made in defining the mechanisms of initiation and perpetuation of AF.[14-17] One of the most important breakthroughs was the recognition that, in a subset of patients, AF was triggered by a rapidly firing focus and could be "cured" with a localized catheter ablation procedure.[17, 18] This landmark observation caused the EP community to refocus its attention on the pulmonary veins (PVs) and the posterior wall of the left atrium (LA), as well as the autonomic innervation in that region. It also reinforced the concept that the development of AF requires a "trigger" and an anatomic or functional substrate capable of both initiation and perpetuation of AF.[7]

Sustained high rates in the atrium and/or the presence of heart disease are associated with structural remodeling of the atria and can alter the substrate even further and help to perpetuate AF.[19] AF can also be the result of preexisting atrial disease. Although much has been learned about the mechanisms of AF, they remain incompletely understood. Because of this, it is not yet possible to precisely tailor an ablation strategy to a particular AF mechanism in the great majority of AF patients.[7]

3D Mapping

Three-dimensional (3D) electroanatomical contact and noncontact mapping systems have been reported to facilitate ablation of SVTs by identifying anatomical structures and highlighting the precise location of ablated sites. This can guide the initial ablation and help identify existing gaps in an incomplete lesion set.[10, 11] Additionally, electromagnetic navigation systems have been shown to substantially reduce the fluoroscopy time required for SVT.[12-15]

Electrogram reconstruction using noncontact mapping for SVT has been validated in the right atrium.[16] Noncontact mapping has also been shown to be useful in identifying the tachycardia mechanism of different forms of SVT.[17]

The AcQMap™ High Resolution Imaging and Mapping System

The AcQMap High Resolution Imaging and Mapping System (AcQMap System) has been designed to provide information on cardiac dipole densities as a function of time and project that information on an image of a cardiac chamber. In this study, the System will be used to collect data from the AcQMap 3D Imaging and Mapping Catheter (AcQMap Catheter or AcQMap OTW Catheter) and create Dipole Density maps. The evaluation of these maps will include assessing anatomical data, the source and progression of cardiac electrical activation, and evaluation of therapy.

This study will evaluate the safety and potential effectiveness of the AcQMap System in supraventricular tachycardia's (SVTs). Previous studies evaluated the System in typical atrial flutter, which is a better-understood arrhythmia.

The System also includes the AcQMap Workstation with a software interface for online control of recording waveforms that are acquired from the AcQMap Catheter. The interface also enables graphical display of acquired AcQMap Catheter signals for the purpose of assessing signal quality before storing them on the workstation hard drive.

3.2 Alternative Treatments and Methods

Acute treatments that can be used to convert or control SVTs include electrical cardioversion, pharmacologic therapy with rate-lowering or antiarrhythmic drugs, and rapid atrial pacing to interrupt the arrhythmia. Curative therapy involves catheter ablation where catheters are typically advanced from the femoral vein into the right or left atrium. After electrogram-guided verification of the focal source or reentrant circuit, the ablation catheter is used to deliver radiofrequency energy to generate electrically unexcitable tissue (or scar) at a localized area and/or to block activation through tissue critical to a circuit. Procedural success is most commonly assessed by a return to sinus rhythm and the inability to re-induce the arrhythmia with aggressive pacing maneuvers.[3-6]

Additionally, three non-fluoroscopic advanced mapping systems are currently in use for SVTs, one of which may be used during the procedure as is standard of care:

3.2.1 The CARTO mapping System (manufactured by Biosense Webster, CA) incorporates the use of low energy magnetic fields and a specific mapping/ablation catheter with a magnetic sensor to locate the catheter in space and reconstruct a 3D geometry of the heart. Color-coded electrical activation or voltage maps are obtained on a point-by-point basis and superimposed on the geometry for analysis and to guide ablation.

3.2.2 The EnSite System (manufactured by St. Jude, MN) can also be used to similarly create 3D geometry with corresponding activation and voltage maps. It also utilizes contact mapping (NavX mode) using an ablation catheter and three low energy currents through orthogonally-located skin patches allowing localization of any intra-cardiac catheter. The EnSite System is also capable of noncontact mapping (EnSite Array mode) via the EnSite Array, which is a basket mesh catheter with 64 electrodes capable of measuring electrical activity within a chamber without contacting the heart wall. In this mode, single-beat mapping of an arrhythmia is possible.

3.2.3 The Polar Constellation Advanced Mapping Catheter System (manufactured by Boston Scientific, MA) is a multielectrode basket catheter with 64 electrodes on 8 splines. Once deployed, each electrode is automatically traced. The information enables a 3D model of the basket catheter to be computed. Color-coded activation maps are reconstructed online and displayed on a monitor. By using this catheter, a precise electrical map of the atrium can be obtained in several heartbeats.

3.3 Rationale for the AcQMap System

SVTs may cause significant symptoms, including palpitations, shortness of breath, chest pain, lightheadedness, fatigue, and low blood pressure. Some patients with may be at risk of stroke if certain other risk factors are present. Some patients may exhibit no symptoms at all. The potentially curative solution for SVT is catheter ablation.[22]

The AcQMap System is designed to provide automatic and instantaneous 3D displays of the chamber surface, so placement of the AcQMap Catheter is similar to other noncontact catheter-based navigation systems. In this study, the AcQMap Catheter will be placed in the right or left atrium. Online display of AcQMap Catheter signals may be performed during the procedure.

3.4 Previous Clinical Experience

The AcQMap System has been the subject of two previous similar clinical trials resulting in the System being used in 15 total patients; twelve (12) patients with typical atrial flutter, and three (3) with atrial fibrillation. Additional details regarding this experience can be found in the Investigator Brochure.

4.0 STUDY OVERVIEW

4.1 Study Design

The study is a prospective, non-randomized, open-label study conducted at Na Homolce Hospital, Prague, Czech Republic. Up to fifty (50) subjects will be enrolled to create high quality activation maps. Enrollment is anticipated to take approximately 3-6 months with follow-up expected to take 7-10 days following the procedure for non-AF patients and 1 year for AF patients. Each patient's participation in the study will be approximately 10-20 days for non-AF patients and approximately 1 year and 1 week for AF patients. It is anticipated that 1-2 AcQMap Catheters may be used per patient. A single Console with a corresponding Workstation is anticipated to be used at the site.

4.2 Study Objectives

The primary objective of the study is to demonstrate safety of the AcQMap System during data collection in subjects with SVT.

4.2.1 Primary Endpoints

The primary effectiveness endpoint is the collection of data adequate to construct pre- and post-treatment activation maps. The purpose of this endpoint is to determine if the System is capable of obtaining data sufficient enough to produce the electrophysiology maps it is designed to generate.

The primary safety endpoint is the incidence of device- and procedure-related adverse events through 7 days post-procedure. This endpoint was chosen to determine if there are any device- or procedure-specific complications that can be identified in the short-term following the procedure. It may be more difficult to determine the cause of longer-term complications relative to the investigational device compared to the ablation procedure itself.

5.0 STUDY POPULATION

5.1 General Considerations

Subjects will undergo baseline evaluation to determine eligibility for the study. Subjects who do not meet the entry criteria are considered screen failures. Case report forms do not need to be completed for screen failures.

The investigator and/or designated study personnel are responsible for screening all potential candidates and selecting those who are appropriate study candidates as defined by the study inclusion and exclusion criteria.

Signed informed consent will be obtained from the patient before any specific study procedures are undertaken. The patient will be provided with a copy of the signed consent form. The study requirements should be discussed with the patient with ample time provided for the consent review. All required parties should sign and date on the same consent as the patient. Patients will be considered enrolled once the AcQMap Catheter is introduced into the patient. In the event that the patient is not able to give consent, the patient will not be enrolled in the trial. Vulnerable patient populations are not included in this trial.

Acutus Medical reserves the right to discontinue the study at any stage, with suitable written notice to the Investigator and the appropriate government regulatory agencies. Such decisions will be based on advice from the Scientific Advisory Board or Clinical Events Committee. Similarly, Investigators may withdraw from the study, subject to providing written notification to the Sponsor within 30 days of their intent to withdraw. However, the Sponsor and Investigators will be bound by their obligation to complete the follow-up of subjects already enrolled into the trial.

If a safety concern arises that would affect the rights, safety, or welfare of a patient, the study shall be immediately halted until that safety concern can be adequately addressed. If the safety concern cannot be adequately addressed, then the study will be terminated.

Enrollment at the site may be halted or terminated due to non-compliance issues as determined by the Sponsor. In this case, enrollment at the site would not continue until the compliance issue(s) has been fully addressed and documented.

In any case of halting or terminating a study, any outstanding patient follow-up will be completed unless doing so would contribute to or exacerbate the reason for halting or terminating the study or would affect the patient's rights, safety, or welfare. In such a case, the patient would return to the care of their primary physician and the patient would be considered withdrawn from the study. In all other cases, all required patient follow-up will be completed through the enrolling site.

Individual patients may withdraw their consent to participate in the trial at any time. Also, an Investigator may discontinue a patient's participation in the trial at any time to protect the safety, rights, or welfare of the patient. Attempts to contact patients will consist of telephone, e-mail, and mailed letter before a patient is considered lost to follow-up.

5.2 Inclusion Criteria

Subjects must:

1. Be aged 18 to 75 years
2. Be scheduled for ablation of a supraventricular tachycardia due to the arrhythmia being symptomatic, recurrent, poorly tolerated and/or unable to be controlled with antiarrhythmic drug therapy:
3. Be able and willing to give informed consent

5.3 Exclusion Criteria

Potential subjects must not:

1. Have any of the following:
    a. Patients with implanted prosthetic, artificial, or repaired cardiac valves in the chamber being mapped.
    b. Patients with permanent pacemaker or ICD leads in the chamber being mapped.

c. Patients with hypercoagulopathy or an inability to tolerate anticoagulation therapy during an electrophysiology procedure.

2. Have had a myocardial infarction within the prior two months
3. Have had cardiac surgery within the prior three months
4. Have an intracardiac thrombus (by transesophageal echocardiography)
5. Have clinically significant tricuspid and/or mitral valve regurgitation or stenosis
6. Have had any cerebral ischemic event (including transient ischemic attacks) in the prior six months
7. Be pregnant or nursing
8. Be currently enrolled in any other clinical investigation

6.0 DEVICE DESCRIPTION

6.1 General Description

The AcQMap System consists of a diagnostic recording catheter (non-OTW or OTW) with ultrasound and electrical mapping components (which is advanced through a steerable sheath) and accessories that are connected to a computerized medical instrument. The System is designed to create a 3D image of a chamber's endocardial surface as well as a chamber-wide electrical activation map for percutaneous procedures. The AcQMap System should only be used by physicians thoroughly trained in electrophysiology procedures and trained on the use of the System in the DDRAMATIC-SVT protocol.

6.2 Intended Use

The AcQMap System is intended to be used to record and map right and left atrial electrical impulses. During the DDRAMATIC-SVT trial, this will be performed during the course of procedures in which patients will be treated for supraventricular tachycardia (SVT).

6.3 The AcQMap 3D Imaging and Mapping Catheter and AcQGuide Steerable Sheath Description

The AcQMap 3D Imaging and Mapping Catheter (AcQMap Catheter) has deployable splines formed in the shape of a spheroid at the distal end where an array of 48 electrodes and 48 ultrasound transducers are spatially distributed. A catheter sheath is placed within the desired chamber and the array of the AcQMap Catheter is introduced. There is no requirement for the array electrodes or transducers to be in contact with the heart wall. The AcQMap Catheter is capable of endovascular delivery and contains a flexible distal segment that allows it to be directed via a compatible catheter sheath to various locations of interest within the heart.

6.4 Hardware Description

The Acutus Medical hardware consists of a Console and a Workstation. The Console contains all electronics for interfacing with patient-contacting devices such as the Catheter, localization surface patches and ECG surface electrodes. The Console also provides patient isolation, signal filtering, signal digitization, transmission of ultrasound and localization signals, and processors for algorithm execution. The Workstation is the primary user interface and in this study, will consist of a computer running Windows 7 or later software. The Workstation will also be running custom software developed by Acutus Medical.

6.5 Clinical Procedure

Preparation and Access

The following supplies are not provided with the devices and need to be available and prepped per laboratory standard operating procedures prior to use of the AcQMap Catheter:

- Introducers
- Guiding sheath for lab supplied diagnostic catheter(s) and/or transeptal needle
- Angiographic imaging supplies (i.e. radiopaque contrast, manifold, tubing, etc.)
- Heparinized normal saline
- Guidewire for sheath insertion
- Other supplies as needed to complete the established laboratory protocol

Perform the procedure using general anesthesia or conscious sedation with Propofol, or combination of Benzodiazepines and Opioids as previously reported.[18] Insert three (3) 7-8F sheaths into the left or right groin (the lab staff will decide which will be in the left femoral vein and which will be in the right femoral vein) to allow placement of: a positional reference catheter (6-7F), an electrical reference catheter used for the AcQMap System unipolar reference and analog ground (7-8F), and positioning of the irrigated mapping/ablation catheter (8F). Insert one 16-18F introducer into the left or right femoral vein to accommodate a compatible sheath through which the AcQMap Catheter is inserted. Irrigate the compatible sheath with heparinized saline through its use. Administer a single bolus of heparin after sheath placement.

Right Atrial Access

In accordance with the AcQMap Catheters Instructions for Use:

1. Advance a guidewire into the superior vena cava (SVC) approximately 5 cm past the right atrium.
2. Over the guidewire, advance a compatible sheath to the SVC-right atrial junction per manufacturer's instructions

Left Atrial Access

1. Using standard practice, obtain left atrial access via transseptal puncture.
2. Advance a compatible sheath into the left atrium per manufacturer's instructions.

NOTE: Monitor the saline drip to ensure a constant flow throughout the procedure

Introduce AcQMap Catheter

1. Connect the sheath to a pressurized drip of heparinized saline to ensure a constant flow through the sheath.
2. Remove any guidewire used in sheath placement
3. Insert the distal end of the Catheter into the sheath with the introducer device covering the distal array.
4. While holding on to the proximal portion of the introducer device, advance the Catheter into the sheath.
5. Retract the introducer device from the sheath to the proximal section of the catheter.
6. Advance the distal array of the Catheter through the distal sheath.
7. Under fluoroscopic guidance, simultaneously advance the Catheter and retract the sheath to allow the Catheter splines to deploy within the approximate center of the atrium.

7.0 STUDY EVALUATIONS

7.1 Overview

The visit schedule and procedures required by this protocol are summarized below:

Table 1: Patient Visit Schedule (non-AF)

Event	**Screening**	**Visit 1**	**Visit 2**	**Visit 3**
Timing	*≤ 30 Days Pre-Procedure*		*Day 0*	*Day 7 (+3/-0 days)*
Medical History Review	X			
Sign Informed Consent		X		
Physical Exam		X		X
Mapping – AcQMap System			X	
Confirmation of SVT			X	
Confirmation of therapy			X	
Device- & procedure-related safety data		X	X	X

Table 2: Patient Visit Schedule (AF)

Event	**Screening**	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4,5,6**
Timing	*≤ 30 Days Pre-Procedure*		*Day 0*	*Day 7 (+3/-0 days)*	*3,6,12 Month (+1/-0 months)*
Medical History Review	X				
Sign Informed Consent		X			
Physical Exam		X		X	X
Mapping – AcQMap System			X		
Confirmation of AF			X		
Confirmation of therapy			X		
Device- & procedure-related safety data		X	X	X	X

7.2 Screening

The following tests and activities must be performed to verify eligibility and/or document baseline status:

a. Documentation of demographic information (e.g., age, sex, race);
b. Documentation of disease-related characteristics
c. Medical history review;
d. Previous treatments for arrhythmias;
e. Current treatments for arrhythmias;
f. Review of all inclusion/exclusion criteria to confirm subject eligibility.
g. Adverse events
h. Transesophageal Echocardiography (TEE) or similar scan to rule out thrombus.

7.3 Procedure

a. Map of the heart chamber anatomy using standard tools and the AcQMap System
b. Confirmation of arrhythmia
c. Recording of the following (if applicable) with the AcQMap System:
    - Pre-ablation: sinus rhythm, arrhythmia induction pacing, any induced or spontaneously occurring arrhythmia, and any pacing maneuvers, including entrainment pacing.
    - Post-ablation: sinus rhythm, arrhythmia induction pacing, any induced or spontaneously occurring arrhythmia, and any pacing maneuvers, including entrainment pacing and therapy assessment.
d. Delivery of therapy using standard techniques.
e. Confirmation of therapy treatment (post-ablation)
f. Device- and procedure-related safety events

7.4 Follow-up Visit for Non-AF Patients (7 Days, +3/-0)

a. Adverse events, including device- and procedure-related safety data
b. No patients will be replaced if they are lost to follow-up

7.5 Follow-up Visit for AF Patients (7 Days, +3/-0 and 3, 6&12 months +1/-0 months)

c. Adverse events, including device- and procedure-related safety data
d. No patients will be replaced if they are lost to follow-up

7.6 Patient Care Following the Investigation

Following the patient's involvement in the clinical investigation, there will be no special care provided. Patient care following the investigation will be exactly the same as it would be following a non-investigational procedure for the ablation of their arrhythmia. For patients with non-AF SVT, there will be no further patient follow-up or care unless the patient experiences symptoms or complications or a recurrence in which case the patient will need to see their primary physician and/or return to the hospital for care. For patients with atrial fibrillation, the institutional standard practice of monitoring the patient's need for anticoagulation therapy and/or recurrence of the arrhythmia will be followed.

8.0 STATISTICAL METHODS

8.1 Sample Size Determination

Because this is an early-stage use of the AcQMap System in humans, the sample size has been established as up to 50 subjects for an initial assessment of the System's ability to create high quality anatomies and procedural activation maps in this patient population. No statistical determination of sample size is required as this study is simply to determine the feasibility of the System to generate and collect data in a limited sample.

8.2 Data Analyses

8.2.1 Statistical Methods

Tabulation of summary statistics, graphical presentations, and analyses will be performed. No formal hypotheses will be used in this study.

8.2.2 Demographic and Baseline Characteristics

Demographic characteristics, patient history, and baseline patient data will be tabulated.

8.2.3 Safety Analysis

The safety population is comprised of all subjects enrolled in the study. The number of subjects with at least one adverse event will be tabulated. The number of subjects and the number of adverse events will be tabulated by severity and causality.

8.2.4 Effectiveness Analysis

The primary measure for effectiveness of this clinical study is the creation of pre- and post-ablation activation maps of the atrium. The percentage of patients in which this is accomplished will be calculated.

8.2.5 Claims and Intended Performance Verification

The intended performance of the AcQMap System is that it is capable of generating three-dimensional images and corresponding electrophysiology maps of the right and left atrium. The only claim to be made from the DDRAMATIC-SVT trial is that the System can obtain the data for creating these maps safely.

8.2.6 Number of Devices

It is anticipated that one Console and one Workstation will be used at the site. A backup will be available in case of a malfunction. It is also anticipated that one AcQMap Catheter will be used for each patient enrolled. A backup Catheter will be available for each procedure in case of a malfunction.

9.0 RISK ANALYSIS

9.1 Summary of Expected Benefits

The potential benefit of the AcQMap System is providing automatic and instantaneous 3D displays of the chamber surface. This has the potential to improve ablation efficiency and potentially shorten procedure time. This may also prove to be more effective at verifying an appropriate endpoint to the ablation. This could provide the investigator with an intuitive tool to rapidly identify and guide treatment of clinically-relevant sites within the chamber wall. There is, however, no guarantee that this will happen. Through the subject's participation in this study the information gathered will add to the understanding of the Dipole Density Mapping. This knowledge may advance medical science and may benefit future patients as well as society at large.

9.2 Summary of Potential Risks

The following adverse events are associated with catheterization and/or cardiac ablation:

- Adult Respiratory Distress Syndrome
- Air embolism
- Anemia
- Anesthesia reaction
- Arrhythmias
- AV fistula
- Cardiac perforation/tamponade
- Cardiac thromboembolism
- Cerebrovascular accident
- Chest pain/discomfort
- Complete heart block
- Congestive heart failure
- Coronary artery spasm
- Death
- Endocarditis
- Expressive aphasia
- Heart Failure
- Hemothorax
- Increased phosphokinase level
- Infections
- Laceration
- Leakage of air or blood into the lungs or other organs due to perforation
- Local hematomas/ecchymosis
- Myocardial infarction
- Obstruction or perforation or damage to vascular system
- Pericardial effusion
- Pericarditis
- Phrenic nerve damage
- Pleural effusion
- Pneumonia
- Pneumothorax
- Pseudoaneurysm
- Pulmonary edema
- Pulmonary embolism
- Radiation injury
- Respiratory Depression
- Seizure
- Skin burns
- Temporary complete heart block
- Thrombi
- Thromboembolism
- Transient ischemic attack
- Unintended (in)complete AV, sinus node block or other heart block or damage
- Valvular damage/insufficiency
- Vascular bleeding
- Vasovagal reactions
- Ventricular tachycardia
- Worsening chronic obstructive pulmonary disease

The use of the AcQMap System is not expected to incrementally or significantly impact the severity or occurrence of any of these risks.

9.3 Justification of Clinical Trial Design

Because this is an early-stage use of the AcQMap System, limited clinical data on fifteen (15) patients are available on the use of the System as mentioned above. Therefore, care has been taken to ensure the safety of the System prior to clinical use. The System is

similar in concept to other 3D mapping systems that have been safely and effectively used for many years.[4-11,18.19]. These mapping systems have become the gold standard of electrophysiology procedures with superior clinical results and a significant reduction in the amount of fluoroscopy used during procedures.

In addition, several separate animal studies have been conducted to test the safety of the AcQMap Catheters and AcQGuide Sheath and applicable bench and biological testing has been performed to test the basic function, construction, and biocompatibility of the Catheter and Sheath. The Investigator Brochure provides additional details on this testing. The results of this testing demonstrates that the System is safe to be used for initial clinical evaluation. The DDRAMATIC-SVT trial has been designed to perform this evaluation in a manner that exposes the fewest possible number of patients to the new device while still generating sufficient data to provide an adequate assessment of the initial safety and technical feasibility of the System. The data from this trial will be used to support additional, larger trials in the future that will focus on the effectiveness of the System in treating more complex arrhythmias.

10.0 ADVERSE EVENTS

It is not anticipated that the use of the AcQMap System will result in an incremental risk above those normally encountered during a SVT ablation procedure. Therefore, the endpoint of this study is the incidence of device- and procedure-related adverse events through 7 days post-procedure to track any complications that are related to the use of the new System or the procedure.

10.1 Definitions

Adverse Event: Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in patients, users or other persons, whether or not related to the investigational device.

Adverse Device Effect: An adverse event related to the use of the investigational device

Serious Adverse Event: An adverse event that:

- Led to death
- Led to serious deterioration in the health of the patient that resulted in:
    - A life-threatening illness or injury
    - A permanent impairment of a body function
    - In-patient or prolonged hospitalization
    - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to body structure or a body function
- Led to fetal distress, fetal death, or congenital abnormality or birth defect

Serious Adverse Device Effect: An adverse device effect resulting in any of the consequences characteristic of a serious adverse event.

Unanticipated Serious Adverse Device Effect: 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.

10.2 Categories

The following categories of adverse device events severity are to be used:

Mild	Easily tolerated by the patient, caused minimal discomfort, and did not interfere with everyday activities;
Moderate	Sufficiently discomforting to interfere with everyday activities;
Severe	Prevents everyday activities.

The following categories of adverse device events causality are to be used: definitely related, possibly related, probably unrelated, or unrelated to device.

10.3 Reporting Timeline

Adverse events are to be reported on case report forms, typically within two weeks of the event. Serious adverse events must be reported immediately to the Sponsor Vigilance Responsible Person. Serious adverse events must also be reported to the Ethics Committee according to the Ethics Committee guidelines. In addition serious adverse events must be reported by both the Sponsor and the Investigator to competent authorities according to their guidelines. In Germany this must be performed according to § 3 (5) and § 5 of the Ordinance on Medical Devices Vigilance (MPSV) using the appropriate report form.

11.0 ETHICS

11.1 Sponsor Statement of Compliance

The Sponsor will conduct the clinical study in accordance with the clinical investigational plan, the ethical practices with their origin in Declaration of Helsinki, the principles of ISO 14155 - Good Clinical Practices (GCP), and applicable regulatory requirements. This trial will not commence until a favorable opinion has been obtained by an appropriate ethics committee, including any conditions imposed by the committee. Insurance will be provided by the Sponsor as required by applicable laws in the countries in which the study is being conducted.

11.2 Investigator Responsibilities

The investigator is responsible for ensuring that the clinical study is performed in accordance with the protocol, the Declaration of Helsinki, the principles of Good Clinical Practice (GCP), applicable regulatory requirements, and institutional procedures.

11.3 Ethics Committee (EC)

The investigator will undertake the study after full approval of the protocol and adjunctive materials (e.g., informed consent form) has been obtained from a local EC and a copy of this approval has been received by the Sponsor.

During the conduct of the study, investigators must submit progress reports to the EC as required and request re-review and approval of the study at least once a year. After the study is concluded, the investigator should notify the EC of this status and prepare a final report for EC review.

12.0 MONITORING RESPONSIBILITIES & PLAN

Acutus Medical (ACM) will serve as the Sponsor of this clinical investigation. It is the responsibility of ACM as the Sponsor of the study to ensure proper monitoring of the investigation and to see that all the clinical requirements are met.

All information and data sent to ACM concerning subjects and their participation in this investigation will be considered confidential. Only authorized ACM personnel, ACM representatives, and regulatory agencies will have access to these confidential files. All data used in the analyses and reporting of this investigation will be coded without identifiable reference to the subject. Any data obtained by ACM that is not de-identified will either be destroyed or de-identified upon receipt.

12.1 Source Documentation

Source documents are original records, or certified copies of original records, that contain clinical findings, observations or other activities in a clinical trial (e.g., hospital records, clinical and office charts, laboratory notes, subject diaries, or evaluation checklists) necessary for the documentation and evaluation of the clinical trial.

Source document worksheets may be used to supplement other medical records, but should not be reviewed as the only source. Worksheets must be treated as medical records, that is, signed and dated by the person performing the evaluation.

Photocopies of source documents are acceptable for review only if the original document can be provided upon request.

The monitor will check the case report form (CRF) data points against the source document data points during a monitoring visit.

12.2 Monitors

Field and monitoring personnel contact information is as follows:

Acutus Medical, Inc.
2210 Faraday Avenue, Suite 100
Carlsbad, CA 92008

12.3 Monitoring Visits

Prior to beginning the study, ACM personnel will contact each investigator to discuss the investigational plan and to review the data requirements in detail. The monitor will visit the investigator periodically during the study to monitor progress, verify that all study requirements are completed and answer any questions that may arise. During these visits, the monitor may review the subject records to verify that all records and files are current and to assure compliance with all requirements of this investigational plan.

The monitoring plan will consist of a study initiation visit to train the site on the CIP and case report forms. After the index procedure, a monitoring visit will take place to review the pre-procedure and index procedure forms. A final monitoring visit will take place to review any outstanding items from the previous visit and any follow-up visit forms. This last monitoring visit may or may not be combined with a study close-out visit.

12.4 Publication Policy

The right of individual Investigators to publish trial results with regard to educational and scientific purposes shall not be infringed. Investigators will submit drafts of all manuscripts to the Sponsor prior to submission to ensure accuracy of technical details regarding the AcQMap System. Publication of individual results will await the publication of the multicenter study results, however, if the multicenter results are not published within 1 year, individual site data may be published.

13.0 DATA MANAGEMENT

Data will be collected using an electronic data capture database (eClinical OS) that allows direct data entry by the clinical site. This database will undergo both system and database-specific validation prior to the entry of clinical data. Data will be entered and monitored from any computer directly into the online database. Embedded edit checks will aid data entry by reducing the number of entry errors due to missing data, incorrect data format, and/or improper data type. In addition, some limited logistical data checks will also be employed to verify certain data fields. Once the data points are entered, further edit checks will generate queries that will be forwarded to the site for clarification and/or correction. All data entry and/or edits will be tracked by user in the database to ensure data integrity. Once all queries are answered and all data is entered, the online database will be closed.

13.1 Data Retention

Once the online database is closed, data will be exported from the online database into offline files for data analysis. This original export will be maintained according to applicable regulatory requirements. In Germany, record retention is required for 10 years after completion or termination of the trial.

14.0 CLINICAL INVESTIGATIONAL PLAN (CIP)

14.1 Deviations

Deviations from the CIP, GCP, applicable regulatory requirements, or institutional procedures should be documented. In general deviations are not allowed except to

protect the rights, safety or well-being of a patient. Deviations to maintain the scientific integrity of the trial are also allowed with prior approval from the Sponsor. In all cases, the deviations will be reported to the Sponsor as soon as possible if not reported prior to the deviation taking place but no later than 10 days after the deviation has taken place.

Subject non-compliance, which is not within the control of the Investigator and is a subject's right, does not need to be reported unless it impacts study data. Non-compliance issues include, but are not limited to, informed consent not obtained, inclusion or exclusion criteria not met, missed visits due to site oversight, protocol visits conducted outside the defined time period, required testing not completed.

Under emergency circumstances, deviations from the CIP to protect the rights, safety and well-being of patients are allowed without prior approval of the Sponsor but shall be documented and reported to the Sponsor and the Ethics Committee as soon as possible but no later than 5 days after the deviation has taken place and/or according to Ethics Committee policy. All deviations will be recorded by the Sponsor and reported to ethics committees according to their reporting requirements.

14.2 Modifications

Due to the small nature of this trial, modification of the CIP and related documents is not anticipated but in the event it is necessary, the Sponsor will consult with the Investigators to revise the plan or related documents. A record of the revision will be maintained within the plan or other document that will include the revision letter, the date of the revision and a summary of the revision(s). All modifications will be reported to ethics committees and competent authorities as required.

14.3 Final Report

At the conclusion of the trial, or in the event of premature trial termination, a final report of the study results will be generated by the Sponsor. This report will be submitted to all participating sites and competent authorities within the timeline required by applicable regulations.

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