A PROSPECTIVE, MULTI-CENTER, OPEN-LABEL, SINGLE-ARM STUDY TO EVALUATE THE SAFETY AND TECHNICAL PERFORMANCE OF THE CATHVISION ECGENIUS® SYSTEM

INVESTIGATIONAL PRODUCT:	**CATHVISION ECGENIUS® SYSTEM**
PROTOCOL NUMBER:	**CP-00003-A**
DATE:	**09 DECEMBER 2021**
CLINICALTRIALS.GOV NUMBER:	**NCTXXXXXXXX**

ADMINISTRATIVE INFORMATION

CONTACTS

Medical, Clinical, and Operational Support

Sponsor Name:	CathVision ApS
Sponsor Telephone Number	+45 61 30 50 61
Manufacturer and Sponsor Address:	CathVision ApS Titangade 11 2200 Copenhagen N Denmark

AMENDMENT HISTORY:

Date	Amendment Number	Amendment Type
05 March 2020	Original	Original protocol, version 1.0
12 May 2020	Amendment 1	Revised protocol, version 2.0
09 Dec 2021	Amendment 2	Revised protocol, version 3.0

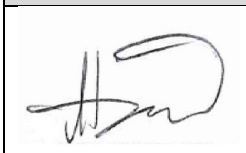
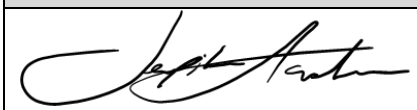
SPONSOR PROTOCOL APPROVAL

Representatives of CathVision ApS

This study will be conducted with the highest respect for the individual participants in accordance with the requirements of this clinical study protocol and in accordance with the following:

- The ethical principles that have their origin in the Declaration of Helsinki.
- International Conference on Harmonized Tripartite Guideline for Good Clinical Practice E6 (ICH GCP E6).
- All applicable laws and regulations, including, without limitation, data privacy laws and regulations.

SIGNATURES

Signature	Location	Date
	CathVision Inc	13 Dec 2021
Name: Mads Emil Matthiesen		dd-Mmm-yyyy
CEO		
	MEDIcept Inc	13 Dec 2021
Name: Adelina Paunescu, PhD		dd-Mmm-yyyy
Principal Consultant & Owner of ACMP Clinical and Regulatory Consulting LLC		
	MEDIcept Inc	13 Dec 2021
Name: Jerika Acosta		dd-Mmm-yyyy
Consultant, Director of Clinical		

INVESTIGATOR'S AGREEMENT

I have read this Clinical Trial Protocol. I will provide copies of this Clinical Trial Protocol and all pertinent information to all site personnel involved in this study. I will discuss this material with them and ensure they are fully informed regarding the study products and the conduct of the study.

I agree to conduct the study as outlined in the Clinical Trial Protocol and in accordance with the signed clinical study agreement.

I will obtain written informed consent from all participating subjects/patients in accordance with requirements as specified in ICH Guidelines for Good Clinical Practice; Section 4.8 and I will fulfill all responsibilities for submitting pertinent information to the IRB. I will use only the informed consent form approved by the sponsor and the Institutional Review Board (IRB) or it's representative.

I understand that this study will not be initiated without the approval of the appropriate Institutional Review and that all administrative requirements of the governing body of the institution will be complied with fully.

I also agree to report all information or data in accordance with the protocol and I agree to report without unjustified delay, all Adverse Events (AEs), and Serious Adverse Events (SAEs) that could have led to Unanticipated Adverse Device Events (UADEs).

I agree to provide all the information requested in the Case Report Forms presented to me by the Sponsor in a manner to assure completeness, legibility, and accuracy.

I also agree that all information provided to me by the Sponsor, including pre-clinical data, protocols, Case Report Forms, and any verbal and written information, will be kept strictly confidential and confined to the clinical personnel involved in conducting the study.

In addition, no reports or information about the study or its progress will be provided to anyone not involved in the study other than the Sponsor, the IRB, and regulatory authorities (if applicable). Any such submission will indicate that the material is confidential.

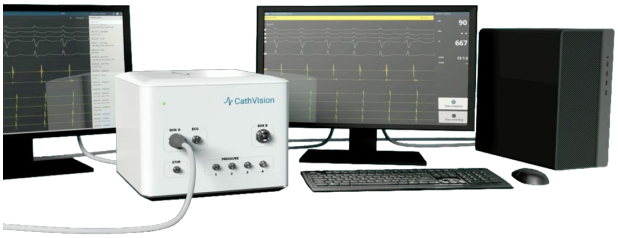
I agree to have control over all clinical supplies and the investigational product provided by CathVision. I further agree not to originate or use the name of CathVision ApS and/or ECGenius® System, or any of its employees, in any publicity, news release or other public announcements, written or oral, whether to the public, press or otherwise, relating to this protocol, to any amendment hereto, or the performance hereunder, without the prior written consent of CathVision ApS.

I herewith declare that I agree with the protocol described in detail in this document and agree to conduct the study in accordance with the protocol and compliance with Good Clinical Practice and all applicable regulatory requirements.

INVESTIGATOR SIGNATURE

Signature	**Location**	**Date**
Name: <Enter>		dd-Mmm-yyyy
<Title>		

PROTOCOL SYNOPSIS

Title	A Prospective, Multi-Center, Open-Label, Single-Arm Study to Evaluate the Safety and Technical Performance of the CathVision ECGenius® System
Investigational device	The CathVision ECGenius® System is an electrophysiology (EP) recording system to be used in EP studies as a tool to monitor, display, and record signals of the heart and cardiac arrhythmias. 
Intended Use	To acquire, amplify, digitize, stream atrial and ventricular intracardiac electrophysiology signals during cardiac electrophysiology studies and related procedures.
Objective	The primary objective is to evaluate the safety and technical performance of the CathVision ECGenius® System. The secondary objective is to benchmark the intracardiac electrogram signal quality compared to commercially available systems in patients undergoing assessment and ablation of cardiac arrhythmias.
Study Design	A prospective, multi-center, open-label, single-arm study to evaluate the safety and technical performance of the CathVision ECGenius® system. Patients who are scheduled to undergo an EP procedure and meet the inclusion/exclusion criteria will be enrolled in the study. Intracardiac signals will be passively recorded using CathVision ECGenius® System in parallel with the commercial EP recording system.
Sample size	Up to 30 subjects shall be enrolled in the study.
Investigational Sites	Up to two (2) investigational sites in the United States.
Study Duration / Follow-up Period	Study enrollment is planned for 1-3 months.

Primary Endpoint	The Primary endpoint of the study will be evaluated as the safety and technical success of CathVision ECGenius® System to collect and record intracardiac signals during EP procedures. With focus on: • To record and plot low voltage electrograms • To assess the improved signal (better signal to noise ratio) compared with the standard signal • To visualize the shape and timing of electrograms
Secondary Endpoint	The Secondary endpoint of the study will be evaluated as the technical performance of CathVision ECGenius® System during routine EP procedures. • To log time stamp for arrhythmia termination when termination is successful • To confirm compatibility of CathVision ECGenius® system with commercially available 3D mapping systems and with available intracardiac catheters. • To have no or minimal device malfunctions reported with the use of the CathVision ECGenius®
Entry Criteria	Inclusion Criteria Eligible subjects will meet ALL the following inclusion criteria: 1. Patient is scheduled for catheter ablation or diagnostic electrophysiology procedure. 2. At least 18 years of age. 3. Able and willing to provide informed consent or obtain consent from a legally authorized representative (LAR). Exclusion Criteria Eligible subjects will not meet ANY of the following exclusion criteria: 1. Patient inability to understand or refusal to sign informed consent. 2. Patient is a prisoner or under incarceration 3. Patients who in the opinion of the physician are not candidates for this study.

TABLE OF CONTENTS

ABBREVIATIONS

ADE	Adverse Device Effect
AE	Adverse Event
AF	Atrial Fibrillation
AV	Arteriovenous
β-HCG	Beta Human Chorionic Gonadotropin
CFR	Code of Federal Regulations
CPK	Creatinine Phosphokinase
CRF	Case Report Form
CRO	Contract Research Organization
CS	Clinically Significant
CVA	Cerebrovascular Accident / Stroke
EC	Ethics Committee
ECG/EKG	Electrocardiogram
EP	Electrophysiology
EPAMP	Electrophysiology Amplifier
GCP	Good Clinical Practices
GI	Gastrointestinal
HCVA	Hemorrhagic Cerebrovascular Accident
HEENT	Head, Eyes, Ear, Nose and Throat
ICD	Implantable Cardioverter-Defibrillator
ICF	Informed Consent Form
ICH	International Council for Harmonisation
ICVA	Ischemic Cerebrovascular Accident
IRB	Institutional Review Board
ISO	International Organization for Standardization
LAR	Legally Authorized Representative
NCS	Not Clinically Significant
PI	Principal Investigator
PV	Pulmonary Vein
RF	Radiofrequency
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SID	Subject Identification Number
SW	Software
TIA	Transient Ischemic Attack
TTM	Transtelephonic Monitoring
UADE	Unanticipated Adverse Device Effect
WCT	Wilson Central Terminal

1. INTRODUCTION

1.1 CARDIAC ELECTROPHYSIOLOGY

Of the total worldwide population, 1% and 2% of rural and urban areas suffer from cardiac arrhythmia, respectively. Approximately 15% of patients do not respond to drug treatment and need a device-based interventional treatment. As a result, there is a great need for cardiac arrhythmia ablation. Today, however, the exact identification of the mechanism of the arrhythmia and subsequent successful ablation treatment are challenging for physicians. The three most prevalent arrhythmias ("complex arrhythmias") for catheter ablation are atrial fibrillation, atrial tachycardia, and ventricular tachycardia.

1.2 INTRACARDIAC ELECTROPHYSIOLOGY SIGNALS DURING CARDIAC ELECTROPHYSIOLOGY STUDIES

Cardiac electrograms are generated by the potential (voltage) differences recorded at two recording electrodes during the cardiac cycle. All clinical electrogram recordings are differential recordings from one source that is connected to the anodal (positive) input of the recording amplifier and a second source that is connected to the cathodal (negative) input. Unipolar recordings are obtained by positioning the exploring electrode in the heart and the second electrode (referred to as an indifferent electrode) distant (theoretically an infinite distance) from the heart such that it has little or no cardiac signal.

Bipolar recordings are obtained by connecting two electrodes that are exploring the area of interest to the recording amplifier. At each point in time, the potential generated is the sum of the potential from the positive input and the potential at the negative input. The potential at the negative input is inverted and thus subtracted from that at the positive input. Because the far-field signal is similar at each instant in time, it is largely subtracted out, leaving the local signal. In a homogeneous sheet of tissue, the initial peak of the bipolar signal coincides with depolarization beneath the recording electrode. [2]

1.3 RATIONALE FOR THIS CLINICAL INVESTIGATION

Electrograms and their interpretation are a key tool for electrophysiologists to target ablation sites and are acquired from electrodes on intracardiac diagnostic catheters and surface Electrocardiograms (ECGs). Besides the dominant noise contributor of 50/60Hz from the main power line, there are noise contributors from stimulation, ablation, and defibrillation artifacts that disturb the clear view of electrophysiological signals. Stimulation artifacts today are a result of (poor) software filter design, whereas ablation artifacts are mostly a hardware problem from the high energy exposure on the ablation tip electrode that is also used for measurements.

Baseline noise peak-to-peak levels below 15µV in bipolar recordings and below 30µV in unipolar recordings would be considered best-in-class. Bipolar recordings between adjacent band electrodes are the most commonly used and practically they are often "derived bipolar". This means they are individual signals first amplified against a different but common reference, and then subtracted from each other. Unipolar recordings are important for advanced algorithms, such as 3D mapping

and rotor mapping for atrial fibrillation. The unipolar reference is most often Wilson Central Terminal (WCT), but it can also be a distant intracardiac electrode.

Electrograms are usually sampled at 1 to 2kHz, and bandpass filtered at 30 to 500Hz for bipolar and 0.5 to 300Hz for unipolar recordings. 64 to 160 channels are the typical capacity of recording systems today.

In the operating room, other devices and technologies are present: 3D mapping (triangulation of catheter tip position with impedance- and magnetic technology, <0.2 gauss), fluoroscopy/X-ray, Radiofrequency (RF) generator, cryo gas station, stimulator, saline coolant pump for ablation catheter RF-tip irrigation, hemodynamics, magnetic catheter steering (0.08T).

It is not unusual to defibrillate the patient to cardiovert them from an arrhythmia. It is not unusual that patients have implanted cardioverter-defibrillators (ICDs).

It is CathVision's goal to develop a new electrophysiology recording system with improved signal quality particularly of unipolar recordings, with fast pacing and defibrillation recovery times, and with minimal or reduced RF ablation artifacts. The reduction in noise and artifacts will allow for better diagnosis and delivery of advanced ablation therapy in arrhythmia patients.

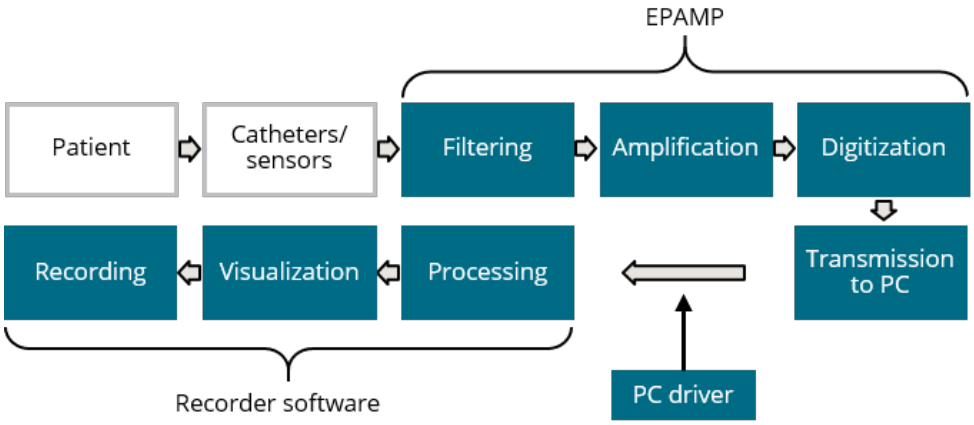
2. DEVICE DESCRIPTION

The CathVision ECGenius System is an electrophysiology (EP) recording system to be used in EP studies as a tool to monitor, display, and record signals of the heart and cardiac arrhythmias. The investigational device ECGenius System includes the following items:

- EP amplifier (EPAMP)
- Pin box cable assembly for connection of catheters
- Surface ECG cable
- Data cable to host computer
- Recording system software (RECORDER SW)
- Host computer (ECGenius PC) and monitors

2.1 SIGNAL PROCESSING OVERVIEW

The main hardware amplifier of ECGenius is the EPAMP, which acquires signals from third-party catheters and sensors connected to the patient. It then sends the signals to the ECGenius PC, which has a software program called the RECORDER SW that visualizes the signals to the user and provides the users a way to interactively analyze them. The following figure illustrates this signal pathway.



There are no parts of the tested medical device that may come into contact with the subject's body or body fluids. There are no medicinal products, human or animal tissues or their derivatives, or other biologically active substances used in the device.

Each manufacturing lot of investigational device part is assigned a unique lot number that is printed on the device package labeling, providing a means of traceability. A device accountability log will be used to track the use of devices in the study. The lot number will be recorded in each case report form.

3. RISK-BENEFIT ANALYSIS

There are no known risks to the potential subjects specifically associated with the use of the ECGenius®.

Potential risks include product failures similar to commercially available EP recording systems, with a similar likelihood of occurrence.

Risks associated with cardiac electrophysiology procedures include events reported in the literature related to catheter procedures, identified in the risk and hazard analyses, and associated with percutaneous interventions. A list of anticipated adverse events are defined in Section 6.5. Each adverse event and/or device effect will be evaluated in detail as described in Section 6 of this document.

The protocol is designed for parallel data collection during an electrophysiology study. The investigator diagnostic decisions will be guided by an approved EP recording system as per institution standard of care. Due to the protocol design and noninvasive nature of the tested medical device the rate of expected occurrence of SAEs or SADEs related to the use of the investigational device is low.

CathVision personnel will be responsible for the installation of the investigational device. During the study, the device will be operated by study trained site personnel.

As the treatment will be guided by an approved EP recording system the reduction in symptomatic arrhythmia will be similar to the benefit of currently available EP recording systems.

4. INVESTIGATIONAL PLAN

4.1 STUDY OBJECTIVES

The primary objective is to evaluate the safety and technical performance of the CathVision ECGenius® System. The secondary objective is to benchmark the intracardiac electrogram signal quality compared to commercially available systems in patients undergoing assessment and ablation of cardiac arrhythmias.

4.2 STUDY DESIGN

This is a prospective, multi-center, open-label, single arm study to evaluate the safety and technical performance of the CathVision ECGenius® system in up to 30 adult patients scheduled to undergo an EP procedure.

Intracardiac signals will be passively recorded in parallel with the commercial EP recording system. The tested device will not be used to direct clinical care decisions or therapy. The EP procedure will be guided by study site's standards of care. A summary of the schedules of evaluations and visits can be found in section 4.7.1.

4.3 STUDY DURATION

Study enrollment is planned for 1-3 months.

4.4 SUBJECT POPULATION

Up to 30 adult subjects will be enrolled in the study.

Eligible subjects must meet the inclusion and exclusion criteria described in Sections 4.4.1 and 4.4.2 to be enrolled in the study and undergo an EP procedure using the CathVision ECGenius® System.

4.4.1 INCLUSION CRITERIA

Subjects must meet all of the following inclusion criteria to be included in the study:

1. Patient scheduled for catheter ablation or diagnostic electrophysiology procedure.
2. At least 18 years of age.
3. Able and willing to provide informed consent from a legally authorized representative (LAR).

4.4.2 EXCLUSION CRITERIA

Subjects will not be eligible for the study if any of the following exclusion criteria are met:

1. Patient inability to understand or refusal to sign informed consent.
2. Current participation in another investigational drug or device study that interferes with this study
3. Patient is a prisoner or under incarceration
4. Patients who in the opinion of the physician are not candidates for this study.
5. Patients who are considered part of any vulnerable population.

4.5 STUDY OUTCOMES

4.5.1 PRIMARY OUTCOME

The Primary endpoint of the study will be evaluated as the technical success of CathVision ECGenius® System to collect and record intracardiac signals during routine EP procedures. Specifically:

- To record and plot low voltage electrograms
- To assess the improved signal (better signal to noise ratio) compared with the standard signal
- To visualize the shape and timing of electrograms

A defined evaluation scale for CathVision ECGenius signal versus the standard of care signal will be defined as 1 (best) to 5 (worse) for different areas of interest. This evaluation will be done by the institution principal investigator for both signal and mapping if available.

4.5.2 SECONDARY OUTCOME

The Secondary endpoint of the study will be evaluated as the technical performance of CathVision ECGenius® System during routine EP procedures.

- To log time stamp for arrhythmia termination when termination is successful
- To confirm compatibility of CathVision ECGenius® system with commercially available 3D mapping systems and with available intracardiac catheters.
- To have no or minimal device malfunctions reported with the use of the CathVision ECGenius

4.6 STUDY PROCEDURES

The following is a detailed list of study visits and the required procedures/tests. Specific tests/procedures are described in Section 5.

4.6.1 INFORMED CONSENT

Pre-screening, i.e., medical record review without obtaining informed consent, is allowed.

Prior to enrollment of any subjects into the study, written approval of the protocol and informed consent must be obtained from the Institutional Review Board (IRB).

Informed consent will be obtained as outlined in 21 CFR Part 50 and the Good Clinical Practice: Integrated Addendum to ICH E6 (R1) (ICH E6 (R2), 9 November 2016).

A research study member at the IRB approved study site will speak with the study candidate about the purpose of the study and investigational research. Explanation of the study background, study procedures, visits, assessments, risks, and benefits will be reviewed in detail with the potential subject.

The potential subject will be given the time they need to read through the study information and informed consent document and ask as many questions as necessary to make them comfortable with the study and the requirements. After informed consent is obtained, study assessments may begin.

After informed consent is obtained, the study eligibility criteria are checked. All patients who signed a consent form are considered study subjects. A patient is considered enrolled after the patient has signed the informed consent form and after the inclusion/exclusion criteria have been met.

The original informed consent form will be retained with the subject records. A copy of the informed consent will be provided to the subject or legal representative. The informed consent must be written in a language in which the subject or his/her legal representative is fluent. If a foreign language translation is required, a statement of certification of the translation must be issued. Regulations require that foreign language informed consent forms be submitted to the IRB for approval. The investigator must forward a copy of the consent form, the certified foreign language translation, and an IRB approval letter to the Sponsor or its designee.

4.6.2 SUBJECT IDENTIFICATION

To maintain confidentiality, the subject's name will not be recorded on any study document other than the informed consent form. Each enrolled subject will be assigned a study specific Subject Identification Number (SID) will be assigned in consecutive order in the following format: CP00003-SSYYY. CP00003 is the study number, SS is the site number, and YYY is the 3-digit sequential subject ID number starting with 001. For example, the first subject at site 01 will be assigned CP00003-01001. Subject ID numbers will not be re-used (e.g., if the subject is determined to be a screen failure).

4.7 STUDY VISITS

4.7.1 SCHEDULE OF ASSESSMENTS

	Screening	Day 0 Index Procedure
Visit Number	**1**	**2**
Informed Consent	✓	
Demographics	✓	
Cardiac History	✓	
Cardiac Anti-Arrhythmia Medications	✓	
Inclusion/Exclusion	✓	
Physical Exam	✓	
Vital Signs	✓	✓
12 lead EKG	✓	
EP procedure		✓
Adverse Events		✓
Device Malfunction		✓

4.7.2 VISIT 1: DAY –15 ± 15 (SCREENING VISIT)

Screening will be completed within 30 days of the index EP and/or ablation procedure.
Test results from routinely performed standard assessments may be used to determine eligibility. Initial screening will consist of a review of relevant cardiac history including duration and frequency of arrhythmia(s), their subsequent treatments (e.g., medications, previous ablation), and associated symptoms.

Eligibility will be assessed sequentially, starting with the least invasive and least expensive tests as follows. Results from each test or screening activity should be reviewed prior to proceeding to the next step.

- Demographics
- Baseline cardiac history
- Arrhythmia history (Type of arrhythmia, TTM, EKG, Holter, etc.)
- Baseline cardiac anti-arrhythmia medications
- Physical Examination
- Vital Signs
- 12-lead EKG

Any protocol deviations during screening will be documented per section 8.2.

4.7.3 SCREEN FAILURES

Subjects not meeting all study entry criteria will be designated as screen failures. End of study procedures will not be performed for these subjects, but their reason for ineligibility will be

recorded on the Screening Log. Screen failures after the screening visit are counted towards total study enrollment.

4.7.4 VISIT 2: DAY 0 (INDEX PROCEDURE THROUGH DISCHARGE)

During the index EP procedure, institutional standard of care is to be utilized to treat the subject.

When the subject is connected to the standard EP recording system, during manipulation of catheters or diagnostic tests, intracardiac signals will be recorded using the investigational device in parallel. The total procedure time is not expected to differ by adding the CathVision ECGenius® system to the EP system as the final comparison of data recorded from the Standard EP recording system and the tested device will occur post procedure.

Prior to discharge, the following will be documented:

- Adverse events (AE)
- CathVision ECGenius device malfunctions
- Protocol deviations

Subjects will be considered to have completed and exit the study after this visit.

4.8 STUDY COMPLETION

4.8.1 COMPLETED SUBJECTS

Subjects will be considered complete when all assessments through the Discharge have been performed in accordance with the protocol. There will be no follow up requirement for this study.

4.8.2 DISCONTINUED SUBJECTS

Subjects may withdraw consent at any time throughout the course of the trial. The investigator may discontinue a subject from the study at any time if they consider that remaining in the study compromises the subject's health or the subject is not sufficiently cooperative. In either event, reason(s) for discontinuation should be documented appropriately.

Possible reasons for study discontinuation include the following:

- Adverse events (AEs) necessitating discontinuation from the study.
- Subject decision (specify).
- Investigator decision (specify).
- Other reason (specify).

The reasons for any subject discontinuation will be documented on the study completion form of the study Case Report Form (CRF). If possible, subjects who withdraw before study completion will complete the reporting of data as best possible, at minimum AE assessment and CathVision ECGenius® system device malfunction, if applicable.

4.8.3 PREMATURE STUDY TERMINATION

The Sponsor, Investigators, Competent Authority, or Institutional Review Board have the right to suspend or terminate the study prematurely for any safety, ethical, or administrative reason at any time.

The study will be suspended or prematurely terminated if, in the opinion of the Sponsor, Investigator, Competent Authority, or reviewing IRB, the safety of patients and/or data is uncertain. The sponsor should make sure that the suspension or premature termination will be communicated to the Principle Investigator (PI) and reviewing IRB.

CathVision reserves the right to suspend/terminate the investigational site from the study for any of the following reasons:

- Failure to obtain written Informed Consent
- Investigator failure to comply with training or Instructions for Use
- Failure to report SAEs/SADEs/UADEs to Sponsor within 24 hours of knowledge
- Loss of (or unaccounted for) investigational product inventory
- Repeated protocol violations
- Repeated failure to complete case report forms prior to scheduled monitoring visits

The decision to resume study enrollment and treatment at the site will be made by the Sponsor. Additionally, the triggering of the stopping/re-activation will promptly be submitted to the involved Competent Authority and reviewing IRB for approval.

In case of study termination, patients enrolled in the study would be treated and monitored per standard of care and best clinical practices at the investigator's discretion.

4.9 INVESTIGATIONAL DEVICE ACCOUNTABILITY

Documentation of receipt, use, and return of the CathVision ECGenius® System and its parts must be maintained by the Principal Investigator (PI) or his/her designee in a device accountability log. Investigational devices are to be used only in accordance with this protocol and under supervision of the PI or a duly designated person. It is the PI's responsibility to ensure that all study devices are kept in a secure location, with access limited to individuals authorized by the investigator. A record of all study devices (by their lot or serial numbers) received, used, and returned must be maintained by the site until the conclusion of the study. Following accountability of the study devices by the Sponsor or its designee, all study devices will be returned to the Sponsor/Designee as directed in writing by the Sponsor or designee.

5. EXAMINATIONS AND EVALUATIONS

5.1 DEMOGRAPHICS

Date of birth, gender, race, ethnicity, height, and weight will be recorded.

5.2 CARDIAC HISTORY

Relevant cardiac history including duration and frequency of arrhythmia(s), their subsequent treatments (e.g., medications, previous ablation) and associated symptoms will be obtained at Screening. All positive and negative findings will be carefully documented. Any new finding discovered during the Screening evaluation and prior to the index ablation procedure will be considered to be part of the cardiac history and will not be recorded as an AE.

5.3 PHYSICAL EXAM

A physical exam will be performed at Screening. Any abnormalities, if clinically significant, should be recorded.

5.4 12 LEAD EKG

A 12-lead electrocardiogram (EKG) will be conducted. The EKG recording will be printed out and will be placed with subject records. A copy of the EKG recording, and report summary will be made available for the study and filed with the subject study records. Any clinically significant abnormalities will be documented.

5.5 CARDIAC MEDICATIONS

Cardiac anti-arrhythmia medications will be recorded at screening visit, and medications prescribed during the index procedure visit. For each medication, the following information will be collected:

- Medication trade or generic name
- Indication for which the medication was given
- Dose/strength, route, and frequency of administration
- Date started
- Date stopped (or continuation at study completion)

5.6 VITAL SIGNS

Vital signs consisting of blood pressure (while subject is sitting), temperature, weight, heart rate, and respiratory rate will be measured.

6. EVALUATION OF ADVERSE EVENTS AND DEVICE DEFICIENCIES

6.1 ADVERSE EVENTS DEFINITIONS

An **adverse event (AE)** is the development of an untoward medical occurrence or the deterioration of a pre-existing medical condition following or during exposure to an investigational medical device, whether or not considered causally related to the investigational medical device.

An untoward medical condition can be symptoms (e.g., nausea, chest pain), signs (e.g., tachycardia, enlarged liver), or clinically significant abnormal results of an investigation (e.g., laboratory findings, electrocardiogram).

A **serious adverse event (SAE)** is any untoward medical occurrence which:

- Results in death, permanent impairment of a body function or permanent damage to a body structure;
- Results in serious deterioration in the subject's health that either:
    - Is life-threatening;
    - Requires inpatient hospitalization or prolongation of hospitalization which is not specifically required by the protocol or is elective;
    - Results in permanent impairment of a body function or permanent damage to a body structure; or
    - Requires medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

Additionally, important medical events that may not result in death, be life-threatening or require hospitalization may be considered SAEs when they jeopardize the subject or require medical or surgical intervention to prevent one of the serious outcomes listed above.

Adverse device effect (ADE) is an AE related to the use of an investigational medical device. Note, this definition includes AEs resulting from insufficient or inadequate instructions for use, operation, or any malfunction of the investigational medical device. In addition, this definition includes any event resulting from use error or intentional misuse of the investigational medical device.

Serious adverse device effect (SADE) is an ADE that has resulted in any of the consequences characteristic of an SAE.

An **unanticipated adverse device effect** (UADE) is defined as any serious adverse effect on health, safety, any life-threatening problem, death caused by or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in predicate devices, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

6.2 ASSESSMENT OF ADVERSE EVENTS

The need to capture AEs is not dependent upon whether or not the clinical event is associated with the use of the study device or procedure. All AEs, regardless of severity, occurring at the index ablation through study completion visit must be recorded. Events occurring prior to the EP procedure must be listed in the cardiac history.
Any Adverse Event(s) that may occur in this study should be reported directly to the Sponsor and IRB, as applicable. Participants experiencing Adverse Events must be treated by the treating physician per standard clinical practice at the institution.

The following information should be obtained for each AE:

1. **Event description.** Every effort must be made to report the underlying condition or unifying diagnosis for the event. To avoid vague, ambiguous or colloquial expressions, the AE should be recorded in standard medical terminology rather than the subject's own words when possible. Signs and symptoms that are considered unrelated to an encountered syndrome or disease should be recorded as individual AEs on the CRF (e.g., if congestive heart failure and severe headache are observed at the same time, each event should be recorded as an individual AE).

2. **Duration:** The date of onset and date of resolution should be reported. Every effort should be made to capture the exact dates.

3. **Outcome:** The final status of the event should be reported as resolved, ongoing, or if it resulted in death. If the event is present at the final study visit, the ongoing box must be marked.

4. **Severity:** The severity of the event must be reported as mild, moderate, or severe using the following definitions:

    - **Mild:** Aware of sign or symptom, but easily tolerated
    - **Moderate:** Discomfort enough to cause interference with usual activity
    - **Severe:** Incapacitating with inability to work or do usual activity

5. **Action taken**: Treatment of the event may be reported as none, medical and/or surgical.

6. **Seriousness:** Determined by using the criteria in Section 6.1.

7. **Relationship to device (study device or ancillary device) and/or procedure.** The relationship to device and study procedure will be assessed using the following criteria.
    - **Not related:** no temporal association or the cause of the event has been identified, or the device or procedure cannot be implicated.
    - **Unlikely**: the relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
    - **Possible:** temporal association, but other etiologies are likely to be the cause; however, the involvement of the device or procedure cannot be excluded
    - **Probable**: the relationship with the use of the investigational device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.
    - **Causal:** temporal association; other etiologies are possible but unlikely.

    If any AE is considered to be "possibly related" or "related" to the use of the study device, that event will be classified as an ADE or a SADE. Any reported AEs will be assessed by the reporting investigator.

6.3 REPORTING/RECORDING OF AEs

Throughout the course of the study, all efforts will be made by the investigator to remain alert to possible AEs. The first priority will be the safety of the subject and providing appropriate medical intervention. The period of observation for collection of AEs starts at index procedure until study completion.

6.4 ADVERSE EVENTS REQUIRING EXPEDITED REPORTING

The Investigator must complete and submit SAE worksheet(s) containing all information required by local and/or regional regulations to the sponsor and Clinical Research Organization (CRO) by email immediately (within 24 hours of awareness). When medical reports (lab results, examinations, etc.) associated with AEs are submitted to the Sponsor or CRO, all personal subject information (name, address, etc.) must be removed or redacted. The redacted materials must be identified only with the subject ID number.

Sponsor Contact:	MEDIcept Inc.
	Attn: L. Adelina Paunescu, PhD
Telephone:	781-526-8152
Email:	SafetyReporting@medicept.com

Upon notification of SAEs, the Sponsor will initiate and complete a review and evaluation of the event within time frames that will maintain reporting compliance with applicable regulatory agencies. The Sponsor is responsible for classification and reporting of AEs and ongoing safety evaluation of the clinical investigation in line with EN ISO 14155:2020 and regulatory requirements. If insufficient information is available to reach a definitive diagnosis, the Sponsor may instruct the monitor responsible for the site to contact the site to request additional confirmatory information, if any.

In the event of a subject's death, the Investigator will make reasonable effort to obtain a copy of the autopsy report and/or death summary. The Investigator will determine the cause of death and its relationship to the investigational device; the Investigator will record results on the AE case report form (CRF). The Investigator will include copies of an autopsy report, if available, and/or a death summary with this form.

The Investigator is responsible for reporting all SAEs, SADEs, and device deficiencies that could have led to a SADE to the Ethics Committee (EC), according to national regulations and EC requirements. The investigator will forward a copy of this report to the Sponsor and file it in the site regulatory binder.

The Sponsor will ensure that its Authorized Representative will report all SAEs and device deficiencies that could have led to an SADE to the Competent Authorities in accordance with European Medical Devices directives and all applicable national regulations.

The SAE/SADE worksheet must be signed by a medically qualified investigator (as identified on the delegation of authority log). The signature confirms the accuracy and completeness of the SAE/SADE data as well as the investigator causality assessment including the explanation for the causality assessment.

In addition, the Investigator will report adverse events to the reviewing IRB (as applicable) according to the local reporting requirements.

Investigators must submit safety reports as required by their IRB within the required timelines. Documentation of the submission and receipt by the IRB of should be retained by the study site.

6.5 ANTICIPATED ADVERSE EVENTS

There are no anticipated Adverse Events specifically associated with the use of the CathVision ECGenius® system.

Arrythmias requiring an EP procedure that are chronic but stable, and present at screening, should not be recorded as an AE. Changes in a chronic condition or disease that are consistent with natural disease progression are NOT considered AEs and should not be recorded. These medical conditions should be adequately documented in the subject's cardiac history. However, medical conditions present at enrollment that worsen in intensity or frequency in a manner inconsistent with the natural course of the disease during the EP and/or ablation procedures and during the study should be reported and recorded as AEs.

A recurrence of an atrial tachyarrhythmia requiring hospitalization in order to administer cardioversion within the blanking period is within the scope of treatment for chronic but stable Atrial Fibrillation (AF) patients. This will not be considered an adverse event. Self-limiting pericarditis attributable to the ablation procedure, defined as pleuritic chest discomfort with or without pericardial rub and ECG changes, is not considered an adverse event.

The expected rates of occurrence of these anticipated AEs using the study device are expected to be the same as the rate experienced when using commercially available EP recording systems for the same indication. The mitigations and treatments for these AEs will follow published guidance for the same AEs occurring with other commercially available devices [1].

Anticipated AEs include associate with arrhythmia and EP procedure, but are not limited to:

- Air embolism
- Allergic reaction (including anaphylaxis)
- Anesthesia reaction
- Angina
- Aorto-right atrial fistula
- Arterial-venous fistula
- Cardiac perforation/ tamponade
- Cardiac thromboembolism
- Cardiac or respiratory arrest
- Catheter entrapment
- Cerebrovascular accident / Stroke
- Chest pain/discomfort
- Congestive heart failure
- Coronary artery dissection
- Coronary artery spasm
- Coronary artery thrombosis/occlusion
- Death

- Diaphragmatic paralysis
- Endocarditis
- Esophageal ulceration
- Gastroparesis
- Heart failure (or worsening)/pump failure
- Hemoptysis
- Hemothorax
- Hypotension
- Hospitalization (initial and prolonged)
- Increased creatinine phosphokinase (CPK) level
- Infections
- Laceration
- Leakage of air or blood into the lungs or other organs due to perforation
- Left atrial esophageal fistula
- Major bleeding, requiring surgery or transfusion
- Myocardial infarction
- Obstruction or perforation or damage to the vascular system
- Pericarditis
- Pericardial Effusion
- Phrenic nerve damage including Diaphragmatic paralysis
- Pleural Effusion
- Pneumonia
- Pneumothorax
- Pulmonary edema
- Pulmonary embolism
- Pulmonary vein dissection
- Pulmonary vein thrombus
- Pulmonary hypertension
- Respiratory depression
- Skin burns
- Severe PV stenosis or complete occlusion, even asymptomatic
- Tamponade, potentially requiring surgery
- Temperature elevation or fever
- Tissue Erosion and other tissue damage
- Transient Ischemic Attack (TIA)
- Thromboembolism
- Thrombosis
- Unintended complete or incomplete AV, Sinus node, or other heart block or damage
- Valve damage
- Vascular bleeding / local hematomas / ecchymosis
- Vasovagal reactions
- Ventricular tachyarrhythmia
- Volume overload

6.6 DEVICE MALFUNCTIONS

Device deficiency is defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance.

Note, device deficiencies include malfunctions and use errors. All device deficiencies that occur during the trial will be recorded.

Device malfunction: failure of an investigational medical device to perform per its intended purpose when used in accordance with the instructions for use.

User error: act or omission of an act that results in a different medical device response than intended by the manufacturer or expected by the user.

The Device Deficiency CRF is specific for reporting all device deficiencies, or malfunctions that occur during the trial, whether or not they were associated with an adverse event. Device Deficiency CRFs should be submitted to the Sponsor within 24 hours of the occurrence defining the device deficiency.

Anticipated device deficiencies and malfunctions with any standard of care EP system include but are not limited to:

- Catheter deflection deficiency or failure
- Malfunction of a catheter electrode
- Malfunction of a catheter temperature sensor
- Unexpected termination of ablation due to internal system error
- Failure to initiate ablation due to internal system error
- Temporary or sustained loss of catheter navigation/visualization capability/signal

Record any CathVision ECGenius® system deficiencies and malfunctions including but are not limited to:

- ECGenius® system issues (Cube® EPAMP/RecSW)
    - Not able to power on
    - Power indicators not on
    - Not able to connect to the standard of care EP system
    - Note able to retrieve signal from standard of care EP system
    - Not able to power down
    - Database issues
    - Backup data issues
    - Not possible to clear fault without reboot
- ECGenius® Recorder Software
    - Malfunction
    - Loss of power
    - Loss of wave form
    - Recording issues (interruption, stop)
    - Not able to create patient
    - Not able to save patient
    - Live Mode issues (not able to create/resume patient, etc)

    - Review Mode issues (not able to retrieve a patient)
    - SW crashes
    - SW loses connection to EPAMP
    - Limitation: Only possible to review the latest recording file, while streaming is active
    - Bug: Not possible to use the notch filter, if high-pass and low-pass is set to 'None'
- Host Computer Malfunctions
    - Not able to boot/start
- User errors
    - Not recording data

7. STATISTICAL METHODS

7.1 SAMPLE SIZE CALCULATION

This trial is intended to demonstrate the safety and performance of the device. As a result, no formal statistical hypothesis was applied to derive the sample size.

7.2 DESCRIPTIVE ANALYSES

Continuous variables will be summarized using standard quantitative statistics: number of available observations, mean, standard deviation, median, quartiles, and range (minimum and maximum observed values). The number of missing observations, if any, will also be summarized.

Categorical variables will be summarized using classical frequency statistics: number of non-missing observations and percentages by categories. Number and percent of missing data, if any, will also be summarized.

There are no predefined criteria for terminating the study based on statistical outcomes. Missing data will not be replaced or imputed.

8. STUDY CONDUCT

8.1 ETHICS COMMITTEE (EC)

Prior to the initiation of the study, the protocol, and the informed consent form will be submitted to the EC for approval. By signing the clinical trial agreement, the investigator is assuring that an EC will be responsible for the initial and continuing review of the proposed clinical study. A copy of the EC approval letter for the protocol, the informed consent, and the protocol signature page must be submitted to the Sponsor or its designee prior to release of investigational supplies to the study site. The approval letter must refer to the specific protocol and the informed consent form. Any Investigator who is also a member of the EC is not to participate in the protocol approval decision. This non-participation must be noted in the approval letter. The study site must maintain an accurate and complete record of all reports, documents and other submissions made to the EC concerning this protocol.

ANY REPORT OF WITHDRAWAL OF EC APPROVAL WILL BE SUBMITTED TO THE SPONSOR OR ITS DESIGNEE WITHIN FIVE (5) WORKING DAYS.

8.2 COMPETENT AUTHORITY

If needed, the study will be reviewed by the relevant Competent Authority as well. The Sponsor or its designee is responsible for obtaining regulatory approval for the study from the relevant Competent Authority. No subjects may be enrolled in the study until written notification of such approval has been given by the Sponsor. The Sponsor or its designee is responsible for reporting SAE and Device Deficiencies that might have led to a SADE as appropriate to the relevant Competent Authority. The Sponsor or its designee is responsible to provide the relevant Competent Authority with the study final report within 90 days of the study termination.

The study will not start without the written approval of the EC and, where needed, the Competent Authority approval and after the completion of any other local regulation requirements.

8.3 INFORMED CONSENT PROCESS

It is the responsibility of the Investigator to inform each subject or his/her legal representative, prior to the screening evaluation, of the purpose of this clinical trial, including possible risks and benefits and document the informed consent process in the subject's chart. Any changes made to the informed consent must be approved by the Sponsor or its designee, prior to submission to an EC. After approval by the Sponsor or its designee, the informed consent must be submitted to and approved by an EC. Prior to entry into the study or initiation of any study-related procedures, the subject or his/her legal representative must read, sign and date the informed consent form. The person executing the consent must also sign and date the EC-approved consent form. One original informed consent form is to be retained by the study site and a copy is to be given to the subject or his/her legal representative. The informed consent process must be documented in the subject's source/medical record.

8.4 CONFIDENTIALITY

In accordance with GCP and the national data protection laws, all information concerning the subjects in the study must be treated as strictly confidential by all persons involved in the study. Health data will be recorded and forwarded to the Sponsor or its designee, and participating IRB, for evaluation as required. Any information that is obtained in connection with this study that can be identified with the subjects will remain confidential. Any data that may be published in scientific journals will not reveal the identity of the study participants

The investigator acknowledges that all information acquired from the Sponsor or its designee or developed or acquired in connection with the study are strictly confidential. The investigator will not disclose any confidential information to any third party nor use confidential information for any purpose without first obtaining the consent of the Sponsor in writing. Such consent shall be deemed to have been given for disclosure to any person for whom the investigator is responsible at their center, but only so far as required for the study, and, in the case of disclosures to staff, only if such staff are bound by obligations of confidentiality no less strict than those set out herein.

8.5 PROTOCOL DEVIATIONS

The Investigator is not allowed to deviate from the protocol.

Under emergency circumstances, deviations from the Clinical Study Protocol to protect the rights, safety, and well-being of human subjects may proceed without prior approval of the Sponsor and the IRB. These deviations will be reported to the Sponsor and the IRB as soon as possible after detection, but no later than 24-hours from the time of the deviation, as required.

Deviations must be documented on the appropriate Protocol Deviation CRF. If a Clinical Monitor becomes aware that an Investigator is not complying with the signed Investigator's Agreement, the Clinical Study Protocol, the requirements of GCP/ICH Guidelines or other applicable regulations, or any conditions of approval imposed by the reviewing IRB, the Sponsor or designee will immediately either secure compliance or terminate the Investigator's participation in the investigation. The Investigator will be required to return all investigational components of the study device and system unless this action would jeopardize the rights, safety, or welfare of a patient.

Protocol deviations will be analyzed by the Sponsor for the impact to the overall integrity of the study. Disqualification is warranted when an Investigator has repeatedly or deliberately violated governing regulations or has repeatedly or deliberately submitted false information in any report. Where protocol deviations occur, which do not warrant disqualification from a study, the Sponsor or designee will implement appropriate corrective and preventive actions, including repeat training as deemed necessary.

8.6 STUDY TRAINING

The study device is intended for use by experienced medical personnel. The Investigator and study staff will receive Sponsor-led training on the proper use of the device to ensure the study team is familiar with its use prior to study enrollment and participation.
The study center will undergo a study initiation visit including but not limited to a review of the following:

- Study Protocol
- Study Procedures and Assessments
- Process for obtaining Informed Consent and completing Informed Consent Form
- Reporting requirements
- electronic Case Report Form (eCRF) completion and Good Documentation Practices
- Study device overview, usage, and accountability
- Protection of patient confidentiality

8.7 STUDY MONITORING AND SOURCE DOCUMENTATION

The Sponsor or its designee will meet with investigators prior to the initiation of the study at their site to review the adequacy of the subject population, facilities, equipment for the needs of the study, and to familiarize the investigator with the study protocol and the investigational device.

CathVision or designee will monitor the investigative site to ensure that the study is conducted in accordance with the protocol and following guidelines and standard: ISO 14155, the Code of Federal Regulations 21 CFR Part 812 and country specific regulations.

During monitoring visits, the monitor will review the source documents used for completion of the CRFs to verify the accuracy and completeness of the information contained in those reports in preparation for retrieval. CRFs must be completed within 48 hours of the subject visit. Source documents must contain all data entered in the CRFs. Source documents may include a subject's medical record, hospital charts, clinic charts, the Investigator's study files, the results of diagnostic tests such as laboratory tests, EKGs, 24-hour Holter monitoring, and the like. All data generated during this study and the source documents from which they originated are subject to inspection by the Sponsor or its representatives and/or regulatory agencies.

CathVision intends to monitor the investigational site at an interval consistent with the screening rate. At least 2 monitoring visits will be scheduled (based on enrollment), approximately after 15 subjects have been enrolled at the site.

To maintain subject safety, data quality and integrity, during unexpected circumstances (i.e., COVID-19), alternative approaches to on-site visits, such as; central monitoring, telephone contact with the site(s) to review study procedures, trial participant status, and study progress; or remote monitoring of individual enrolled subjects may occur.

8.8 SITE CLOSE-OUT

Upon completion of the study, the clinical monitor will conduct a final visit (close-out) at the site. At the time of the site close-out visit, the Monitor will collect all outstanding study documents, ensure that the Investigator's files are accurate and complete, review record retention requirements with the Investigator, make a final accounting of all study supplies, and ensure that all applicable requirements are met for the study. The observations and actions made at this visit will be documented in a final closeout report.

8.9 PROTOCOL AMENDMENTS

The Sponsor will document modifications to the protocol in the form of a written amendment. All protocol modifications must be approved by the IRB before implementation. In the case of a medical emergency, to remove immediate apparent hazard to subjects, a change may be made preferably after discussion with the Sponsor or its designee. In these instances, the IRB will be notified as soon as possible.

8.10 RECORD KEEPING AND RETENTION

Data generated for the study should be stored in a limited-access file area and be accessible only to representatives of the study site, the Sponsor and its representatives, and relevant health authorities/regulatory agencies. All reports and communications relating to study subjects will identify subjects only by initials and subject identification number. Complete subject

identification will be kept by the investigator. This information will be treated with strict adherence to professional standards of confidentiality.

All study-related records must be maintained for at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. The Sponsor will notify the Investigator when records are no longer needed. The Investigator will not discard any records without notifying the Sponsor. If the Investigator moves from the current investigational site, the Sponsor should be notified of the name of the person who will assume responsibility for maintenance of the records at the investigational site or the new address at which the records will be stored. The Investigator will notify the Sponsor as soon as possible in the event of accidental loss or destruction of any study documentation.

8.11 INVESTIGATOR FINAL REPORT

The investigator shall provide the IRB and the Sponsor with an accurate final report within 2 months after completion, termination, or discontinuation of the study. The final report may not precede final data submission which has not been monitored.

8.12 STUDY REPORT AND PUBLICATION

The results of the study may be submitted for publication. Upon the prior written consent of the Sponsor, the Investigator shall have the rights to publish papers related to the Study.

If written permission from the Sponsor is provided, the PI may publish and/or present the results of the study conducted at their site, provided that, prior to any such publication or presentation, the site and/or the PI shall provide the Sponsor with two (2) hard copies and one electronic copy of any materials intended for publication or presentation at least sixty (60) days prior to the submission of manuscripts. The Sponsor shall then have sixty (60) days from the receipt of such materials to review and provide the site and/or the PI with written comments.

9. REFERENCES

1. H. Calkins, G. Hindricks, R. Cappato, Y. Kim, E. Saad, L. Aguinaga, J. Akar, V. Badhwar, J. Brugada, J. Camm and P. Chen, "2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation," *Heart Rhythm,* vol. 14, no. 10, pp. e275-e444, 2017.
2. "Recording Techniques for Clinical Electrophysiology", Stevenson W. G., Soejima K. (2005). J. Cardiovasc. Electrophysiol. 16, 1017–1022.