1. TABLE OF CONTENTS

1. Table of Contents 1
2. Signatures 3
3. Template Version History (filled in by QA) 3
4. Document Version History 3
5. Protocol 5
5.1. Contact Information 6
5.2. Protocol Synopsis 7
5.3. Background 10
5.3.1. Rationale for the clinical study 12
5.4. Device Description 12
5.4.1. General 12
5.4.2. VERAFEYE Imaging Catheter 13
5.4.3. VERAFEYE Imaging System 14
5.4.4. Indications for Use/Contraindications 16
5.5. Study Objective 16
5.6. Study Endpoints 17
5.7. Study Design 17
5.8. Subject Selection 18
5.9. Subject Accountability 20
5.9.1. Point of Enrolment 20
5.9.2. Subject Classification 21
5.9.3. End of Study 22
5.9.4. Withdrawal 22
5.9.5. Lost-to-follow up 23

5.10. Study Assessments 23
5.10.1. Informed Consent 23
5.10.2. Baseline Visit 23
5.10.3. Procedure 24
5.10.4. Post-Procedure Visit 27
5.10.5. 7-Day Follow-Up 28
5.10.6. Data Collection Schedule 28
5.11. Potential Risks and Benefits 29
5.11.1. Risks associated with the Procedure 29
5.11.2. Risks associated with the Study Device 30
5.11.3. Potential Adverse Events 30
5.11.4. Risks associated with Study Participation 33
5.11.5. Benefits associated with Study Participation 33
5.12. Statistical Design and Analysis 34
5.13. Safety Reporting 34
5.13.1. Reportable Events 34
5.13.2. Reporting Requirements 36
5.13.3. Death Reporting 41
5.14. Regulatory and Ethical Aspects 41
5.14.1. Study Financing 41
5.14.2. General Duties of Sponsor and Principal Investigator 41
5.14.3. Role of LUMA Vision Representative(s) 43
5.14.4. Ethics Committee 44
5.14.5. Study Registration 44
5.14.6. Study Insurance 44
5.14.7. Patient Confidentiality 44
5.14.8. Protocol Deviations 44
5.14.9. Protocol Amendments 44
5.14.10. Early Termination 45
5.15. Study Documentation 45
5.15.1. Data Management 45

5.15.2. Source Documents 45
5.15.3. Technical Source Forms 46
5.15.4. Investigator Files/Retention of Documents 47
5.15.5. Device Accountability 47
5.15.6. Monitoring 48
5.15.7. Audits and Inspections 48
5.15.8. Confidentiality of Trial Documents And Patient Records 48
5.16. Publication Policy 48
5.17. Bibliography 49
5.18. Abbreviations and Accronyms 50

2. SIGNATURES

Signature Meaning	Name	Title	Date	Signature
Author	Elke Sommerijns	Clinical Manager	22-Nov-2024 14:16:45	**sign-p14-i161471-b20241122131645202**
Reviewer	Sean Crowe	QA Manager	22-Nov-2024 14:37:31	**sign-p14-i161471-b20241122133731358**
Approver	Marta Walker	Director Regulatory	25-Nov-2024 10:26:05	**sign-p14-i161471-b20241125092605314**

3. TEMPLATE VERSION HISTORY (FILLED IN BY QA)

OP Document Number	Version	Change Description	Change Date
T-10118	1.0	Initial release	26-Jun-2023

4. DOCUMENT VERSION HISTORY

OP Document Number	Version	Change Description	Change Date
VER-DOC-527	1.0	Initial release	30-Jun-2023
VER-DOC-527	2.0	Protocol Synopsis and Section 5.8: reworded IEC1 (removed future tense)	01-Aug-2023

OP Document Number	Version	Change Description	Change Date
		Section 5.4.3.2: Figure 4: replaced with an updated figure Section 5.10.3.4: • 12-lead ECG to be obtained at the end of the procedure • Fluoroscopy time will be measured for the entire procedure; fluoroscopy dose will be measured Throughout document: administrative corrections were made (section numbering was corrected). Section 5.15.2: section on source documents was added.	
VER-DOC-527	3.0	Section 5.4.2: Deleted size of catheter Picture of the VERAFEYE Imaging catheter removed Section 5.4.3.2: clarified that Figure 3 is an example of the room setup during a procedure Section 5.10.3.3: VERAFEYE imaging data will only be collected from the right atrium. Clarified that standard of care imaging = standard of care echocardiography imaging (intracardiac echocardiography (ICE), transesophageal echocardiography (TEE) Section 5.10.3.4: VERAFEYE imaging time replaced with time VERAFEYE imaging catheter was in the body Section 5.13.1: Reportable events were updated	18-Dec-2023
VER-DOC-527	4.0	Protocol Synopsis: number of subjects updated to 40, Georgia removed as potential country Table 1: VERAFEYE System components description restructured to improve clarity Section 5.4: Device description updated to be aligned with IFU Section 5.7: • Added that up to 4 operators per site will be allowed to perform	22-Nov-2024

OP Document Number	Version	Change Description	Change Date
		study procedures, unless written approval from LUMA Vision was obtained • Added that enrolment in this study is competitive • Added that subject procedures will follow a sequential pattern (one site after the other) • Number of subjects updated to 40 and rationale explained Section 5.9.1 and 5.9.2: Number of subjects updated to 40, Georgia removed as potential country Section 5.10.3.1: Added that up to 4 operators per site will be allowed to perform study procedures, unless written approval from LUMA Vision was obtained.	

5. PROTOCOL

Luma V**i**sio**n**'s feas**i**bility study on the VERAF**E**YE system

LUMINIzE

Clinical Investigational Plan/Clinical Study Protocol

Protocol Number	P001

Single Identification Number/CIV-ID	Not Applicable
ClinicalTrials.gov Number	NCT05931835

This protocol is a confidential document for the use of the investigator's team and other persons involved in the study only. The information contained within this document shall not be communicated to a third party without prior written approval of LUMA Vision. The protocol will be kept confidential and maintained in a secure location.

5.1. CONTACT INFORMATION

Position	Details
Sponsor	LUMA Vision Ltd. Block C, Parkview House, Beech Hill Office Campus, Beech Hill Road, Dublin 4, D04 K5D0 Ireland
Coordinating Principal Investigator	Prof. Dr. Gabor Szeplaki MD, PhD, FESC, FEHRA Mater Private Network Heart & Vascular Centre 72 Eccles Street Dublin 7 D07 RD8P

	Ireland Email: gabor.szeplaki@materprivate.ie
Clinical Manager	Elke Sommerijns +32 479 76 71 56 Elke.sommerijns@lumavision.com
Clinical Research Engineer	Alisa Komleva +44 7473 78 34 21 Alisa.komleva@lumavision.com

5.2. PROTOCOL SYNOPSIS

Study title: LUMINIzE: Luma Vision's feasibility study on the VERAFEYE system

Study Objective: The objective of the study is to collect data on the usability and integration of the VERAFEYE System in

- standard of care catheter-based ablation treatments for Typical Atrial Flutter (AFL) or Atrial Fibrillation (AF)
- standard of care left atrial appendage (LAA) closure procedures
- standard of care atrial septal defect (ASD) closure procedures

Results from this study will be used to guide development and refinement the VERAFEYE System.

Indication for Use: The VERAFEYE System is indicated for intracardiac and intraluminal ultrasound visualization of cardiac and great vessel anatomy and physiology as well as visualization of other devices in the heart and great vessels of patients.

Clinical Investigation Device: VERAFEYE System, comprising of

- **VIC** - VERAFEYE Imaging Catheter
- **CIU** - Catheter Interface Unit
- **SC** – System Console

Control Device: NA

Study Design: The LUMINIzE study is a prospective, non-randomized, single-arm feasibility study.

Planned Number of Subjects: Enrolment will be considered as complete when 40 subjects have completed the ablation, or LAA/ASD closure procedure with the VERAFEYE System as imaging system.

Planned Number of Sites/Countries: Up to 2 sites in Ireland may participate in this study.

Study Endpoints: This is a feasibility study and no formal endpoints or hypothesis testing are planned in the study. The study is not designed to collect data for product approval and as such does not have a safety or efficacy endpoint.

Inclusion Criteria:

- IC1: Subject is 18 to 80 years of age at the time of consent
- IC2: Subject is scheduled to undergo a standard of care*, de-novo
- catheter-ablation procedure to treat typical AFL or AF

or

- left atrial appendage (LAA) closure procedure

or

- atrial septal defect (ASD) closure procedure

**according to current international and local guidelines and currently approved indications*

- IC3: Subject is able to understand and willing to provide written informed consent
- IC4: Subject is able and willing to complete all study assessments

Exclusion Criteria:

- EC1: Any of the following within 6 months prior to enrolment:
  - Cardiac surgery including coronary artery bypass grafting, ventriculotomy, atriotomy
  - Thromboembolic event (stroke), transient ischemic attack (TIA) or neurological disturbances
  - Myocardial infarction
  - Any surgical or percutaneous cardiac procedure including coronary intervention and cardiac ablation
  - Dilated or hypertropic cardiomyopathy

- EC2: Any planned surgical or endovascular intervention within 30 days before or after the ablation, or LAA/ASD closure procedure.
- EC3: Any of the following cardiac conditions:
- New York Heart Association (NYHA) class IV
- Left ventricular ejection fraction (LVEF) < 30%
- Implanted with a cardiac rhythm management device (pacemaker, CRT, ICD, loop recorder)

- Presence of intramural thrombus, tumor, or other abnormality that precludes vascular access, catheter introduction, or manipulation
- Active coronary ischemia, significant valvular heart disease, or hemodynamically significant congenital cardiac abnormality
- EC4: Body mass index (BMI) > 40 kg/m2
- EC5: Body weight < 50kg
- EC6: Pregnant women or women who plan to become pregnant during the course of their participation in the study (women should either be of non- childbearing potential at the time of enrolment (as documented in the medical file) or have a negative pregnancy test within the previous 7 days prior to the ablation, or LAA/ASD closure procedure)
- EC7: Life expectancy less than 12 months
- EC8: Subjects who are currently enrolled in another study

Imaging Exclusion Criteria:

- IEC1: Subjects with a thrombus or pericardial effusion detected in the LA/LAA during standard of care imaging.

Subject Follow-Up: A study subject's participation will be considered complete when all protocol required visits have been completed. For subjects who underwent the ablation, or LAA/ASD closure procedure, subject participation in the study is concluded at 7 days follow-up.

Study Duration and Participant Duration: Enrolment in the study is expected to be completed in approximately 6 months. The follow-up for each participant is expected to be approximately 7 days, therefore the total study duration is expected to last approximately 7 months.

Statistical Methods: There are no statistical methods to be employed in this feasibility study. Analysis of study data will use descriptive statistical methods.

Procedure/Assessment	Baseline Visit	Procedure Visit	Post-Procedure Visit	7- Day Follow-Up *(office visit/phone call)*
	≤ 60 days prior to Day 0	*Day 0*	*Day 0- Day 2*	*Day 7 ± 2 days*

Procedure/Assessment	Baseline Visit	Procedure Visit	Post-Procedure Visit	7- Day Follow-Up *(office visit/phone call)*
Informed Consent Form and Process	X			
Eligibility Criteria	X			
Demographics including age and gender	X			
Medical history	X			
Physical Assessment	X	X	X	
Cardiac imaging*	X		(X)	(X)
Medication regimen	X	X	X	X
Procedural data collection		X		
Investigational Data Collection		X		
Device Performance		X		
Protocol Deviations	X	X	X	X
Adverse Events	X	X	X	X
Device Deficiencies		X		

*: per hospital standard of care

( ): optional, collect only if performed per hospital's standard of care

5.3. BACKGROUND

With an increasing number of interventional procedures performed for structural heart disease and cardiac arrhythmias each year, echocardiographic guidance is necessary for safe and efficient results[1,

[2]. Both transthoracic (TTE) and transesophageal echocardiography (TEE) are available echo options but have their limitations. Intracardiac echocardiography (ICE) provides advantages over TTE and TEE by providing imaging from within the heart, providing shorter image distances and higher resolution. Additionally, it is known that ICE has the benefit of avoiding general anesthesia, reducing procedure time and reducing x-ray exposure in comparison to other techniques. Studies have also reported that ICE may reduce periprocedural complications as compared with TEE. At the same time, the efficacy of procedures guided by ICE appear to be comparable to procedures guided by other imaging techniques. Importantly, echocardiography features as a key part of standard practice as recommended in all clinical practice guidelines referred to in this review; four of the guidelines name ICE specifically as an acceptable or standard imaging option[3-6]. The growing body of evidence finding ICE to have comparable efficacy, and perhaps superior safety and added benefits relative to TEE, gives evidence that ICE is a critical part of the state of the art for intraprocedural imaging in Atrial Fibrillation (AF), Atrial Flutter (AFL), Left Atrial Appendage Closure (LAAC) and Atrial Septal Defect Closure (ASDC).

Although transcatheter procedures for ablating tissues or closing cardiac defects are well established in standard practice, success rates and durability of those treatments have not reached satisfactory levels. AF after ablation, for example, commonly recurs in 25-50% of procedures or more[7-11]. This leaves patients at higher risk for stroke and in need of additional procedures which incur additional risk. While clinical guidelines make recommendations to mitigate these risks, and studies are assessing procedural improvements and treatment modifications such as adding additional ablation lines or substrates to improve the acute and long-term outcomes, there remains a need for additional device advancements. Factors such as catheter-tissue contact[12] and precision of tag placement[13] in PVI have been shown to relate to durability of the ablation and ultimately to better long-term outcomes. Although contact-force catheters and other imaging techniques have improved the safety outcomes, there remains a need for additional improvement in those technologies that will enable better visibility of anatomy. Future device technologies are needed to provide improved imaging resolution and expanded 3-D imaging range and field of view.

Similarly, for procedures addressing structural heart defects, ICE provides important benefits, but also suffers from disadvantages that may hinder the achievement of ideal safety and performance outcomes. For example, the mono-planar nature of its images has been suggested to limit ICE's application to procedures such as the sizing of Left Atrial Appendage (LAA) occlusion devices[14] and also other structural heart interventions generally[15].Therefore, for the improvement of safety and performance outcomes in structural heart interventions, as with ablation procedures, it will be necessary to improve the resolution, far-field imaging and 3D capabilities of ICE.

The design of the VERAFEYE System, developed by LUMA Vision, employs a catheter concept providing 360° imaging and verification all around the catheter. The system enables high-resolution real-time anatomical imaging, while the catheter allows for dynamic navigation and requires minimal repositioning within the target anatomical structure. In combination with the dedicated processing in software, the VERAFEYE System can provide an advantage over commercially available ICE catheters by providing the operator with greater anatomical information.

5.3.1. RATIONALE FOR THE CLINICAL STUDY

Numerous pre-clinical studies have demonstrated that the VERAFEYE System provides optimal visualization of anatomical structures that the Sponsor believes may lead to improved cardiac anatomical information and ultimately more effective treatment for patients undergoing electrophysiology and structural heart procedures. To further develop the VERAFEYE System, human data is required to assess the usability and integration of the VERAFEYE System in electrophysiology and structural heart workflows. Results from this study will be used to guide development and refinement the VERAFEYE System.

5.4. DEVICE DESCRIPTION

5.4.1. GENERAL

The VERAFEYE System (Figure 1) comprises of a disposable VERAFEYE Imaging Catheter (VIC) and the VERAFEYE Imaging System. The Imaging System consists of a System Console (SC) and a Catheter Interface Unit (CIU). The individual devices listed in Table 1 must be used together and it is not allowed to combine with non-investigational devices.

Figure 1: The VERAFEYE System

The VERAFEYE Imaging System will be used according to the indications for use and the inclusion/exclusion criteria specified within this protocol. A copy of the device labeling and IFU will be provided in local language as required per national regulations.

Table 1 provides an overview of the components of the VERAFEYE System, with their associated model numbers.

Table 1: VERAFEYE System

Individual Devices within the VERAFEYE System	Model Number
VERAFEYE Imaging Catheter	VF-VIC-001
VERAFEYE Imaging System	VF-VIS-001
System Console compromised of: System Console Computer 3D Tracking System Pulse Phase Module	VF-SC-001
Catheter Interface Unit	VF-CIU-001

5.4.2. VERAFEYE IMAGING CATHETER

The VERAFEYE Imaging Catheter is a disposable, sterile, single-use component containing an ultrasound transducer at the tip. It is delivered by the VERAFEYE Imaging Catheter operator through femoral venous access to the patient's heart. It has bidirectional steering at the distal end through a handle to allow the user to navigate the cardiac structures. The transducer is rotating to allow a 360° view around the tip axis. The catheter tip contains a radiopaque element. The proximal end provides a connector that is plugged into the VERAFEYE Imaging System Catheter Interface Unit.

Figure 2: VERAFEYE Imaging Catheter

5.4.3. VERAFEYE IMAGING SYSTEM

5.4.3.1. System Console

A non-sterile component for multiple use installed and used in the operational room of a hospital. The System Console is placed on a dedicated cart next to the patient bed. Consists of the following proprietary and off-the-shelf components:

- System Console Computer – the control and display unit of the VERAFEYE Imaging System which can be interacted with by the System Console operator via a keyboard and a computer mouse. It contains hardware to run the software of the VERAFEYE Imaging System (VeraApp). The software enables the hardware to control the Catheter Interface Unit, processes the data streams for visualization onto the display and provides the graphical user interface on the display to interact with the user. The System Console Computer operating hardware encompasses a central processing unit for running the operating system, graphics processing unit for processing the ultrasound data streams and displaying on the monitors. It also contains hardware for receiving Pulse Phase signals from the patient and hardware for tracking and location of the VERAFEYE Imaging Catheter tip through an electro-magnetic field.
- Monitors –components allowing for image display and manipulation to allow for image view and review for both VERAFEYE Imaging Catheter operator and System Console operator. The VERAFEYE Imaging System software on the Monitors is controlled by the users via an easy-to-

use interface using multiple methods of input including a mouse, keyboard and/or a touch screen. Monitors interface with System Console Computer and displays the VERAFEYE Imaging System data acquisitions.

- 3D Tracking System – an electromagnetic tracking system to register the VERAFEYE Imaging Catheter's position in the heart. The non-sterile, multiple use system is comprised of an 3DTSensor Interface Unit that receives analogue tracking sensor signals from reference sensors on the patient's chest and back and from the VERAFEYE Imaging Catheter sensor inside the patient's heart. The unit transmits a digital signal to a 3DT-System Control Unit that receives signals from and provides power to the 3DT field generator. The System Console operator connects the reference sensors and places the EM Field Generator close to the patient's chest to capture the sensor positions. The tracking signal will not be displayed to the VERAFEYE Imaging Catheter operator during the procedure but will be registered in the background. The System Console operator can tune the signal in the tracking's setup window in the GUI.
- Pulse Phase Module – a module that receives and transmits heartbeat signals to the System Console Computer. The Pulse Phase signal will not be displayed to the VERAFEYE Imaging Catheter operator during the procedure but will be registered in the background. The System Console operator can tune the signal in a setup window in the GUI.

5.4.3.2. Catheter Interface Unit

A non-sterile component for multiple use intended to send and receive analog signals to/from the VERAFEYE Imaging Catheter. The sterile, single-use VERAFEYE Imaging Catheter is plugged into the non-sterile Catheter Interface Unit. The Catheter Interface Unit receives signals from the VERAFEYE Imaging Catheter, converts them into digital signals and transports them through optical fibers to the System Console Computer. Furthermore, the Catheter Interface Unit contains a motor drive for rotating the transducer in the VERAFEYE Imaging Catheter. The motor and the ultrasound conversion unit are controlled by the System Console Computer. The conversion unit rotates, the power, control and data signals are transmitted through rotating joints. The Catheter Interface Unit is placed on a dedicated cart next to the patient's bed and with proximity to the System Console cart.

Figure 3 provides an example of the room setup during a procedure.

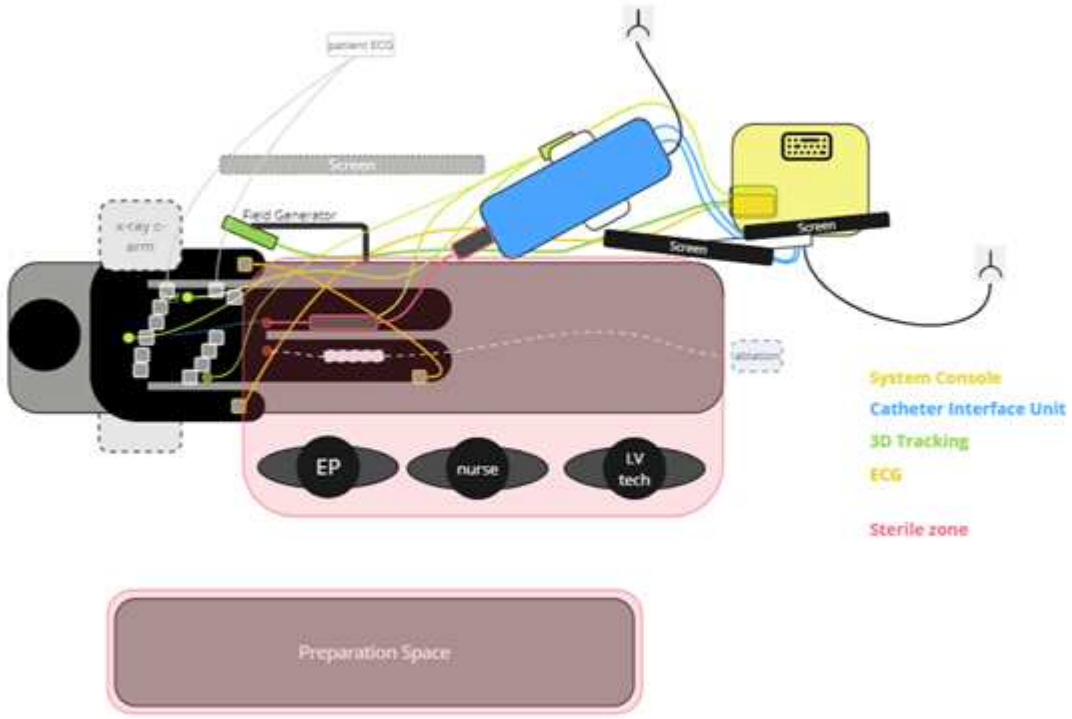

Figure 3: Room Setup During Procedure

5.4.4. INDICATIONS FOR USE/CONTRAINDICATIONS

The VERAFEYE System is intended to be used for real-time, minimally-invasive guidance of endovascular and intracardiac procedures, e.g. such as cardiac ablation, structural heart procedures, or transseptal punctures. The system provides image information of cardiovascular anatomic features, physiological information of cardiovascular structures and features, and spatial relationships of other devices within the heart and great vessels. Please refer to the IFUs for an overview of contraindications.

5.5. STUDY OBJECTIVE

The objective of the study is to collect data on the usability and integration of the VERAFEYE System in

standard of care

- catheter-based ablation treatments for Typical Atrial Flutter (AFL) or Atrial Fibrillation (AF)
- left atrial appendage closure (LAAC) procedures
- atrial septal defect (ASD) closure procedures

Results from this study will be used to guide development and refinement the VERAFEYE System.

5.6. STUDY ENDPOINTS

This is a feasibility study and no formal endpoints or hypothesis testing are planned in the study. The study is not designed to collect data for product approval and as such does not have a safety or efficacy endpoint.

5.7. STUDY DESIGN

This is a prospective, non-randomized, single-arm feasibility study. This study is a pilot stage study according to ISO/FDIS 14155: 2020 (E) - Annex I. Results from this study will be used to guide development and refinement of the VERAFEYE System.

The study is designed to assess the usability and integration of the VERAFEYE System in standard of care, catheter-based ablation treatments for Typical Atrial Flutter (AFL) or Atrial Fibrillation (AF), standard of care left atrial appendage closure (LAAC) procedures and standard of care atrial septal defect (ASD) closure procedures. Results from this study will be used to guide development and refinement the VERAFEYE System.

Intended Users of the VERAFEYE System are interventional cardiologists and electrophysiologists who are trained in percutaneous and transseptal procedures and who have completed the VERAFEYE System training. The VERAFEYE System training is offered by the Sponsor. The VERAFEYE System should only be performed by these Intended Users.

A prospective study design will ensure that identical procedures are followed for data capture and review.

Up to 4 operators per site will be allowed to perform study procedures, unless written approval from LUMA Vision was obtained.

A sample size of 40 subjects was chosen to allow for sufficient feasibility testing and data collection for the ablation, LAA and ASD closure procedures. The sample size is not statistically based but is based on a reasonable number of data sets to assess the images collected with the VERAFEYE System.

In protocol rev 4.0, the sample size was extended from 20 subjects to 40 subjects, in order to collect more clinical data for further system development and to ensure the collection of information from different operators.

Enrolment in this study is competitive, there is no limit of enrolments per site.

Subject procedures will follow a sequential pattern (one site after the other) to allow LUMA Vision field support personnel to be present during the procedures and to ensure the availability and installation of necessary equipment.

Enrolment in the study is expected to be completed in approximately 6 months. The follow-up for each participant is expected to be approximately 7 days, therefore the total study duration is expected to last approximately 7 months.

The Figure below shows the schematic of the study design.

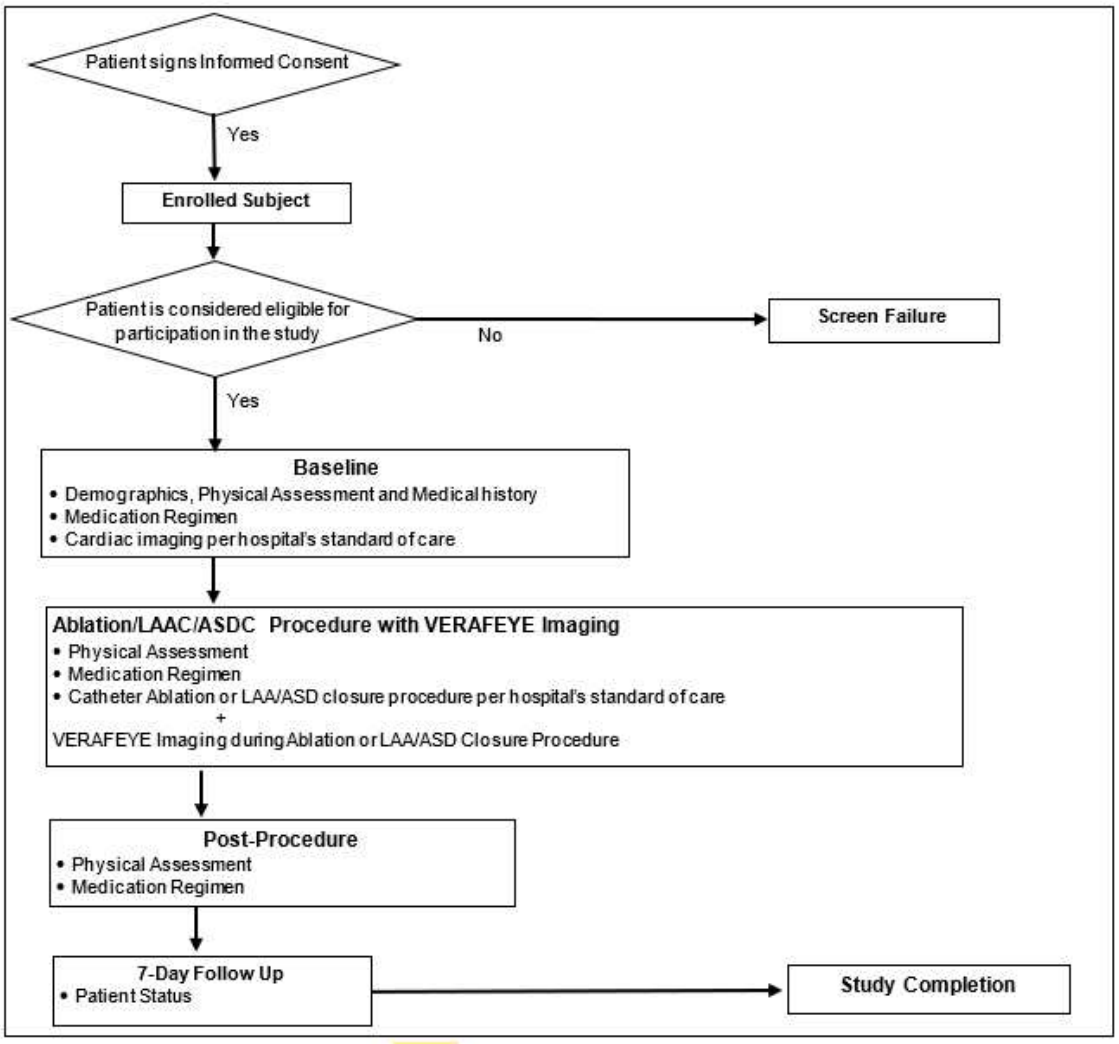

Figure 4: Schematic of the LUMINIzE Study Design

5.8. SUBJECT SELECTION

Subjects will be recruited from the investigator's general patient population. Subjects considered for participation in this study will be entitled to undergo a standard-of-care ablation, LAA or ASD closure procedure. It is the site's responsibility to verify the subject's eligibility for participation in the trial. A subject is considered as enrolled once the study-specific Informed Consent Form is signed.

An overview of the in-and exclusion criteria is listed in Table 2 below.

Table 2: In-and Exclusion Criteria for the LUMINIzE Study

Inclusion Criteria
IC1: Subject is 18 to 80 years of age at the time of consent
IC2: Subject is scheduled to undergo a standard of care*, de-novo · catheter-ablation procedure to treat typical AFL or AF or · left atrial appendage (LAA) closure procedure or · atrial septal defect (ASD) closure procedure *according to current international and local guidelines and currently approved indications
IC3: Subject is able to understand and willing to provide written informed consent
IC4: Subject is able and willing to complete all study assessments
Exclusion Criteria
EC1: Any of the following within 6 months prior to enrolment: · Cardiac surgery including coronary artery bypass grafting, ventriculotomy, atriotomy · Thromboembolic event (stroke), transient ischemic attack (TIA) or neurological disturbances · Myocardial infarction · Any surgical or percutaneous cardiac procedure including coronary intervention and cardiac ablation · Dilated or hypertropic cardiomyopathy
EC2: Any planned surgical or endovascular intervention within 30 days before or after the ablation, or LAA/ASD closure procedure.
EC3: Any of the following cardiac conditions: · New York Heart Association (NYHA) class IV

· Left ventricular ejection fraction (LVEF) < 30% · Implanted with a cardiac rhythm management device (pacemaker, CRT, ICD, loop recorder) · Presence of intramural thrombus, tumor, or other abnormality that precludes vascular access, catheter introduction, or manipulation · Active coronary ischemia, significant valvular heart disease, or hemodynamically significant congenital cardiac abnormality
EC4: Body mass index (BMI) > 40 kg/m2
EC5: Body weight < 50kg
EC6: Pregnant women or women who plan to become pregnant during the course of their participation in the study (women should either be of non- childbearing potential at the time of enrolment (as documented in the medical file) or have a negative pregnancy test within the previous 7 days prior to the ablation, or LAA/ASD closure procedure)
EC7: Life expectancy less than 12 months
EC8: Subjects who are currently enrolled in another study
Imaging Exclusion Criteria
IEC1: Subjects with a thrombus or pericardial effusion detected in the LA/LAA during standard of care imaging.

5.9. SUBJECT ACCOUNTABILITY

5.9.1. POINT OF ENROLMENT

A subject is considered as enrolled when the study-specific Informed Consent Form has been obtained.

A study subject's participation will be considered complete when all protocol required visits have been completed. For subjects who underwent the ablation, LAA or ASD closure procedure, the last protocol required follow-up is at 7 days post procedure. Therefore, subjects who underwent the procedure will be followed from enrolment through the ablation/LAA/ASD closure procedure, hospital discharge, and 7-day follow up. There are no other additional study-related visits required for participating subjects except for those additionally scheduled per physician's decision.

Study enrolment will be considered as complete when 40 procedure subjects have been enrolled (see section 'subject classification').

Enrolment in the study is expected to be completed in approximately 6 months. The follow-up for each participant is expected to be approximately 7 days, therefore the total study duration is expected to last approximately 7 months.

Up to 2 sites in Ireland may participate in the study. Enrolment in this study is competitive, there is no limit of enrolments per site.

5.9.2. SUBJECT CLASSIFICATION

- Enrolled subject- Any participant who signs the informed consent form.
- Screen Failure subject- Any participant who signs the consent form but is found to not meet eligibility criteria.
- Intent subject- Any participant who signs the consent form, met the eligibility criteria but did not have the VERAFEYE Imaging Catheter inserted into the body.
- Attempt subject- Any participant who signs the consent form, met the eligibility criteria, did have the VERAFEYE Imaging Catheter inserted into the body but did not undergo the ablation/LAA/ASD closure procedure per this study protocol.
- Procedure subject - Any participant who undergoes the ablation/LAA/ASD closure procedure with the VERAFEYE System as imaging system per this study protocol.

These subjects are followed in accordance with the Follow-Up schedule and data will be included in all study analyses.

- Withdrawn subject - A participant who chooses to or is withdrawn from the study.
- Lost-to-follow up subject - A participant who cannot be reached anymore after 3 attempts.

Enrolment will be considered as complete when 20 procedure subjects have been enrolled.

The Figure below shows the subject classifications.

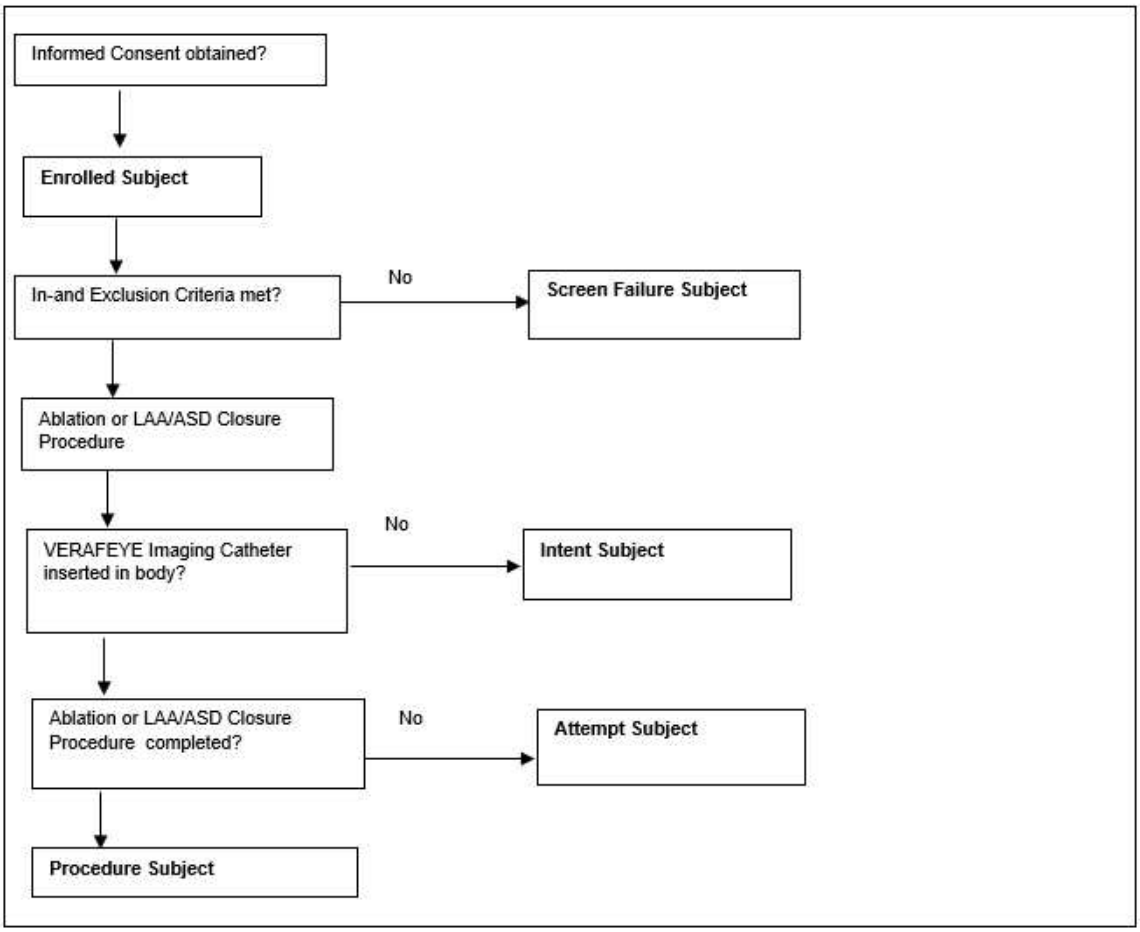

Figure 5: Subject Classifications

5.9.3. END OF STUDY

Individual study subject participation will end when the last subject follow-up visit is completed; when the subject withdrew or was withdrawn from the study or when the subject is considered as lost-to-follow up.

The study will be considered as complete when the last subject's follow up visit occurs or when subjects are no longer being considered for participation. Routine management and standard practice of care will continue for the subjects who have completed the study.

5.9.4. WITHDRAWAL

In accordance with the legal requirements and ICH-GCP guidelines, a subject can leave the study at any time without having disadvantages. The subject may be withdrawn from the study at any time at the discretion of the investigator. The reason(s) for withdrawal shall be reported. Routine management and standard practice of care will continue for such a patient. Where a patient is withdrawn or excluded, the

patient's number shall not be re-assigned to another subject. Data collected up to the point of subject withdrawal may be used but additional data may no longer be collected after the point at which a subject has been withdrawn from the study or withdraws consent.

5.9.5. LOST-TO-FOLLOW UP

Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record or study file. Should the participant continue to be unreachable, he or she will be considered as lost to follow-up.

5.10. STUDY ASSESSMENTS

5.10.1. INFORMED CONSENT

If a potential participant is found to be eligible for enrolment, the study consent form will be reviewed with the subject and the study methods and requirements will be explained. Subjects will be provided with sufficient information to make an informed decision about their participation in this study. Subjects will be given sufficient time to consider participation and ask questions if necessary.

No study-specific procedures should be conducted prior to consent. A copy of the signed consent form will be provided to the study participant and the original signed consent form will be maintained in the subject's files at the site. The consent form must be signed by the subject, and the Investigator-designated research professional obtaining the consent.

All changes to the consent form shall require EC approval; a determination will be made by the sponsor regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

The patients who have received the study patient information for consideration of participation in the study will be listed in a screening log, regardless of whether they are eligible to the study or whether they consented to participate or not. The screening log list will not include the patient identity information except for the first and the second name initials, and the date of providing the study written patient information to the patient.

5.10.2. BASELINE VISIT

The data collection requirements for the baseline visit are outlined below and will be collected prior to the procedure.

- Verification of eligibility criteria
- Documentation of informed consent process, including ICF signature date (see section 13.1.1 below)
- Subject demographics, including age, gender and race

- Medical history, including cardiac history and arrhythmia disorder history
- Physical assessment (including height, weight, blood pressure, heart rate, 12-lead ECG))
- Pre-procedural imaging per hospital's standard of care, if performed at baseline*
- Medication Regimen
- Adverse events, if applicable
- Protocol deviations, if applicable

*Pre-procedural imaging data will be saved and stored to external media, as provided by the sponsor

5.10.3. PROCEDURE

5.10.3.1. General

The procedure visit must occur within 60 calendar days of the baseline visit.

The ablation, or LAA/ASD closure procedure must be performed by investigators trained in Electrophysiology or Interventional Cardiology, trained to the LUMINIzE study protocol and authorized by LUMA Vision to handle investigational devices. Up to 4 operators per site will be allowed to perform study procedures, unless written approval from LUMA Vision was obtained.

5.10.3.2. VERAFEYE System Preparation/LUMA Vision Support

The System Console will create a record for each view attempted. In order to accurately capture information

relevant to the study, the following steps need to be followed for each procedure:

1. Start a new study. Input subject name, date of birth, gender and subject ID
2. In Graphical User Interface (GUI) main screen, select appropriate 2D and 4D configs.
3. In the Component screen,
    - Home the motor (if the button is enabled).
    - Input the VERAFEYE Imaging Catheter serial number with the format.
    - Confirm the VERAFEYE Imaging Catheter has been flushed and confirm the connection.
4. If tracking sensors are disconnected,
    - Disable tracking from the tracking tab before inserting the sensor to the control unit.
    - Enable tracking again after connecting the sensor.
5. Start imaging.
6. Navigate to intended view (see section 12.6), manipulating 3D volume and 2D plane as required.
7. Acquire clip and full data.
8. Freeze if needed for measurements / change configurations and repeat acquisition.
9. Navigate to the next intended view (see section 12.6).

10. Before finishing a study, always freeze the imaging and wait until the motor stops. Then, select the "finish" option in the dropdown with the subject name. Close the study and the data will automatically save.

LUMA Vision will ensure (a) company representative(s) is/are present during each procedure to manage the System Console and to assist the physician with the VERAFEYE Imaging Catheter preparation.

5.10.3.3. Procedure Workflows
Pre-Procedural Imaging

Pre-procedural imaging will be performed per hospital standard of care to assess the anatomy and to exclude the presence of thrombus. If an intracardiac thrombus is visualized, the procedure will be aborted and the subject will be withdrawn from the study. Pre-procedural imaging may be collected at baseline or on the day of the procedure.

Intra-Procedural Imaging

VERAFEYE imaging data from the right atrium will be obtained during the ablation, or LAA/ASD closure procedure. This procedure is to be performed using a commercially available ablation catheter or LAA/ASD closure device. The choice of the ablation catheter, or LAA/ASD closure device is at the operator's discretion. This ablation, or LAA/ASD closure procedure will be performed according to standard of care. The ablation, or LAA/ASD closure procedure will not be guided by the data collected from the VERAFEYE System, the physician is to adhere to a standard workflow and rely on standard imaging and diagnostic tools, as applicable. In order to prevent artifact between the VERAFEYE System and the standard of care echocardiography imaging (intracardiac echocardiography (ICE) transesophageal echocardiography (TEE)), the VERAFEYE imaging has to be frozen during standard of care echocardiography imaging and vice versa.

No concomitant procedures are allowed to be performed at the time of the ablation, or LAA/ASD closure procedure under this protocol. It is also not allowed to combine an ablation procedure with an LAA/ASD closure procedure or to combine an LAA closure procedure with an ASD closure procedure.

It is recommended that the following views with the VERAFEYE Imaging Catheter be obtained in order to visualize the major anatomical structures, as well as third party devices.

RA (typical AFL) Ablation

- Home view
- A variety of anatomical views from different VERAFEYE Imaging Catheter locations, at the discretion of the investigator
- View to visualize mapping* and/or ablation catheter

**If used, per hospital standard's of care*

LA (AF) Ablation

- Home view
- A variety of anatomical views from different VERAFEYE Imaging Catheter locations, at the discretion of the investigator
- Transseptal puncture view
- View to visualize mapping* and/or ablation catheters

**If used, per hospital standard's of care*

LAA Closure

- Home view
- A variety of anatomical views from different VERAFEYE Imaging Catheter locations, at the discretion of the investigator
- Transseptal puncture view
- View to visualize closure device delivery catheter

ASD Closure

- Home view
- A variety of anatomical views from different VERAFEYE Imaging Catheter locations, at the discretion of the investigator
- View to visualize closure device delivery catheter

Indications for conversion to general anesthesia are at the discretion of the treating physicians and include, but are not limited to, hemodynamic instability, inability to maintain a protected airway during the procedure and patient discomfort. Routine clinical assessment for complications will be made during the case.

The VERAFEYE Imaging Catheter is to be removed after the removal of any third party catheters.

Post-Procedural Imaging

VERAFEYE imaging data will be collected after the last ablation has been performed/after deployment of the closure device. Prior to the completion of the procedure (after removing all the devices except the VIC), additional VERAFEYE imaging of the pericardial space maybe performed at the discretion of the physician.

5.10.3.4. Procedural Data Collection

The following data *related to the procedure* will be collected:

- Date of procedure
- Pre-procedural imaging per hospital's standard of care, if performed at procedure visit*

- Intra-procedural imaging per hospital's standard of care, as applicable
- Identification of all investigational study devices
- Identification of non-study devices
- Rhythm at the beginning of the procedure (by means of a 12-lead ECG)
- Method of delivering sedation or anesthesia for the procedure
- Method of access to left atrium: single or double transseptal
- Performance of the study device
- Procedural outcome details
    - Ablation procedures: successful isolation of CTI (typical AFL) or PVs (AF)
    - LAA/ASD closure procedures: successful deployment of closure device

At the end of the procedure, the following information will be collected:

- Total procedure time, defined as time elapsed from time first access sheath insertion into the subject until the last catheter removed
- Total fluoroscopy time and dose
- Total time VERAFEYE imaging catheter was in the body, defined as time elapsed from inserting the VIC into the subject until the time of VIC removal from the subject
- Rhythm at end of case (by means of a 12-lead ECG)
- Physical assessment
- Concomitant procedures, if applicable
- Changes in Medication Regimen
- Adverse Events if applicable
- Device Deficiencies
- Protocol Deviations, if applicable
- The data collected through the System Console will be saved and stored to external media, as provided by the sponsor

*Standard of care imaging data will be saved and stored to external media, as provided by the sponsor

After the completion of the procedure, the images collected with the VERAFEYE System during the procedure may be reviewed with the physician and the physician will be asked to rate the performance of the system by means of a questionnaire.

5.10.4. POST-PROCEDURE VISIT

The Post-Procedure visit is applicable for attempt subjects and procedure subjects.

The post-procedure visit will occur per standard of care but not to exceed 2 days from the end of the study procedure. The data collection requirements of the post procedure visit are outlined below:

- Date of visit
- Physical assessment (incl. vital signs and 12-lead ECG)
- Changes in Medications Regimen

- Adverse Events, if applicable
- Protocol Deviations, if applicable

5.10.5. 7-DAY FOLLOW-UP

The 7-day follow-up is applicable for attempt subjects and procedure subjects.

If the patient was discharged prior to the day 7 follow-up, a telephone contact will occur. If the patient is still hospitalized at the time of the day 7 follow-up, the 7 days follow-up will be performed as an in-hospital visit. The data collection at the day 7 follow-up includes:

- Date of contact (visit/telephone call)
- Changes in Medication Regimen
- Adverse Events, if applicable
- Protocol Deviations, if applicable

5.10.6. DATA COLLECTION SCHEDULE

The data collection schedule for the study is shown in Table 3.

Table 3: Data Collection Schedule

Procedure/Assessment	Baseline Visit	Procedure Visit	Post-Procedure Visit	7- Days Follow-Up (office/phone call)
	≤ 60 days prior Day 0	Day 0	Day 0- Day 2	Day 7
Informed Consent Form and Process	X			
Eligibility Criteria	X			
Demographics including age and gender	X			

Procedure/Assessment	Baseline Visit	Procedure Visit	Post-Procedure Visit	7- Days Follow-Up (office/phone call)
Medical history	X			
Physical Assessment	X	X	X	
Cardiac imaging	X		(X)	(X)
Medication regimen	X	X	X	X
Procedural data collection		X		
Investigational Data Collection		X		
Protocol Deviations	X	X	X	X
Adverse Events	X	X	X	X
Device Deficiencies		X		

*: per hospital standard of care

( ): optional, collect only if performed per hospital's standard of care

5.11. POTENTIAL RISKS AND BENEFITS

5.11.1. RISKS ASSOCIATED WITH THE PROCEDURE

There are risks associated with the standard procedures that are part of the study such as exposure to radiation (e.g. because of the usage of fluoroscopy, or because of the standard of care imaging modality performed prior to/during the ablation or LAA/ASD closure procedures) or risks that are common to ablation or LAA/ASD closure procedures. These risks are not changed by the use of the VERAFEYE System.

5.11.2. RISKS ASSOCIATED WITH THE STUDY DEVICE

The risks associated with use of the VERAFEYE System are not substantially or incrementally different from commercially available and widely used ICE systems for cardiac EP or LAA/ASD closure procedures. The below list of potential adverse effects associated with the use of this device and other devices in this field is widely known and understood when considering usage of ICE in EP or LAA/ASD closure procedures.

5.11.3. POTENTIAL ADVERSE EVENTS

Subjects participating in this study are subject to the same risks shared by all patients undergoing an ablation procedure for treatment of AFL or AF; or an LAA/ASD closure procedure.

Based upon the current literature, the tables below includes an alphabetical list of the possible anticipated adverse events and possible adverse device effects associated with ablation catheters and closure devices. Occurrence of any of the listed events could lead to prolonged hospitalization for the subject.

Table 4: Potential adverse events during catheter ablation procedures

Access site complications	Headache
Allergic reaction	Heart failure
Anemia	Hematoma
Arrhythmias	Hemothorax
Bleeding/Hemorrhage	Hemodynamic instability
Blurred vision	Hypertension/Hypotension
Cardiac perforation	Inadvertent injury to adjacent structures
Cardiac/pulmonary arrest	Infection
Catheter entrapment	Myocardial infarction
Cerebrovascular accident (CVA)	Nerve weakness/palsy/injury (i.e. phrenic/ vagus)
Chest discomfort/pain or pressure	Pericarditis
Complete heart block (transient/permanent)	Pneumothorax

Complications of sedative agents/anesthesia/medications	Pseudoaneurysm
Coronary artery spasm	Pulmonary complications (i.e. edema, pulmonary hypertension, pleuritis, pneumonia)
Cough	Pulmonary vein stenosis
Death	Radiation injury/exposure
Diaphragmatic paralysis	Renal insufficiency/failure
Dizziness or lightheadedness	Respiratory Depression
Edema	Residual atrial septal defect (ASD)
Pericardial effusion/pleural effusion	Skin burns (i.e. radiation/defibrillator/ cardioverter)
Elevated cardiac enzymes	ST segment Elevation
Embolism (venous/arterial) (i.e. air, gas, thrombo, pulmonary)	Sore Throat
Endocarditis	Tamponade
Esophageal injury	Thrombus/thrombosis
Fever	Transient ischemic attack (TIA)
Exacerbation of existing conditions	Valvular damage
Fatigue	Vasospasm
Fistula (arterial-venous, atrial-esophageal)	Visual disturbances
Gastroparesis	Vasovagal reactions

Table 5: Potential adverse events during catheter closure procedures

Air embolism	Hemoptysis

Airway trauma	Hypotension
Allergic reaction to contrast media/medications or device	Hypoxia
Altered mental status	Improper wound healing
Anemia requiring transfusion	Inability to reposition, recapture, or retrieve the device
Anesthesia risks	Infection/pneuomina
Angina	Interatrial septum thrombus
Anoxic encephalopathy	Intratracheal bleeding
Arrhythmias	Major bleeding requiring transfusion
Atrial septal defect	Misplacement of the device / improper seal of the appendage / movement of device from appendage wall
AV fistula	Myocardial erosion
Bruising, hematoma or seroma	Nausea
Cardiac perforation	Oral bleeding
Chest pain/discomfort	Pericardial effusion / tamponade
Confusion post procedure	Pericarditis
Congestive heart failure	Pleural effusion
Contrast related nephropathy	Prolonged bleeding from a laceration
Cranial bleed	Pseudoaneurysm
Death	Pulmonary edema
Decreased hemoglobin	Pulmonary embolism

Deep vein thrombosis	Renal failure
Device embolism/migration	Respiratory insufficiency / failure
Device fracture	Surgical removal of the device
Device thrombosis	Systemic embolism
Edema	TEE complications (throat pain, bleeding, esophageal trauma)
Bleeding	Thrombocytopenia
Fever	Thrombosis
Groin pain	Transient ischemic attack (TIA)
Groin puncture bleed	Valvular damage
Hematuria	Vasovagal reactions

5.11.4. RISKS ASSOCIATED WITH STUDY PARTICIPATION

Subjects enrolled in the study will receive treatment with commercially-available devices and equipment per the site's standard-of-care. The investigational system will function independently from the commercially-available devices. Therefore, there is no risk that the investigational system will affect the functionality of the commercially-available devices.

Since all subjects enrolled in the study are required to undergo intracardiac echocardiography with the VERAFEYE System, the total procedure duration is likely to increase compared to a procedure without intracardiac echocardiography. Care will be taken to limit any potential increase in procedure time, and the total procedure time is expected to continue to be in line with standard of care intracardiac echocardiography cases. There is no increased risk for serious injury due to the potential increased procedure time.

5.11.5. BENEFITS ASSOCIATED WITH STUDY PARTICIPATION

The VERAFEYE System is similar in technology and indication to existing commercially available ICE systems, such as UltraICE (Boston Scientific), AcuNav and Soundstar (Biosense Webster), ViewFlex (Abbott). ICE systems provide the operator with additional means of intra-operative guidance such as orientation within the heart, and evaluating the size of the lumens. While there may be no direct benefit from participating in this study, because the VERAFEYE System provides real-time imaging, complications may potentially be detected earlier on.

The data collected in this clinical investigation will serve as critical input for VERAFEYE imaging technology improvement, as well as for the novel features development in future device releases. In this regard, the proposed clinical investigation is a pivotal step toward the development of next-generation intraoperative 4D-imaging devices, aimed to improve outcomes for future patients undergoing catheter ablation and structural heart procedures.

5.12. STATISTICAL DESIGN AND ANALYSIS

Given the nature of this feasibility study, analysis of study data will use descriptive statistical methods. The Sponsor shall use the imaging data for product development purposes only. Study data will be summarized and included in a clinical study report at the conclusion of the study enrolment.

5.13. SAFETY REPORTING

5.13.1. REPORTABLE EVENTS

The investigator is responsible for documenting and reporting any of the following events to the study Sponsor:

- All Investigational Device Deficiencies
- All Serious Adverse Events
- Unanticipated Adverse Device Effects and Unanticipated Serious Adverse Device Effects
- All Thromboembolic Events
- All Device Related Adverse Events
- All Procedure Related Adverse Events
- New findings/updates in relation to already reported events

Definitions of reportable events are included in the Table below.

Table 6: Reportable Events Definitions

Term	Definition
Adverse Event	Any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons, in the context of a clinical investigation, whether or not related to the investigational medical device and whether anticipated or unanticipated. **NOTE 1**: This includes events related to the investigational medical device or comparator. **NOTE 2**: This definition includes events related to the procedures involved.

Term	Definition
	NOTE 3: For users or other persons, this definition is restricted to events related to the investigational medical device.
Adverse Device Effect	Adverse event related to the use of an investigational medical device **NOTE 1**: This includes any adverse event resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device. **NOTE 2**: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device. **NOTE 3**: This includes 'comparator' if the comparator is a medical device.
Serious Adverse Event	Adverse event that led to any of the following: a. death, b. serious deterioration in the health of the subject, users or other persons as defined by either: 1. a life-threatening illness or injury, or 2. a permanent impairment of a body structure or a body function, including chronic diseases, or 3. in-patient hospitalization or prolongation of existing hospitalization, or 4. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function c. fetal distress, fetal death, or a congenital abnormality or birth defect including physical or mental impairment. **NOTE 1:** Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without a serious deterioration in health, is not considered a serious adverse event.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Term	Definition
Unanticipated Adverse Device Effect	Any serious adverse effect on health or safety or any life-threatening problem or 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 the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
Unanticipated Serious Adverse Device Effect	Serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current risk assessment. **NOTE 1**: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.
Serious Health Threat	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons. **NOTE 1**: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.
Device Deficiency	An inadequacy of a medical device related to its identity, quality, durability, reliability, usability, safety or performance. **NOTE 1**: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling. **NOTE 2**: This definition includes device deficiencies related to the investigational medical device [or the comparator].

5.13.2. REPORTING REQUIREMENTS

5.13.2.0.1. Investigator Reporting Requirements to Sponsor

All reportable events experienced by study participants must be reported if they occur after the point of enrolment as defined in the subject classification section. Pre-existing conditions should not be reported as adverse events unless they worsen in severity or increase in frequency.

Adverse events and device deficiencies must always be reported to the Sponsor through the CRFs. Completed CRFs are to be sent to the following email address of the sponsor:

luminize@lumavision.com

Reporting timelines are included in Table 7 below.

Table 7: Investigator Reporting Requirements

Event Classification	Communication Method	Communication Timeline pre-market studies
Unanticipated Adverse Device Effect / Unanticipated Serious Adverse Device Effect	Complete AE CRF page with all available new and updated information.	· Within 1 business day of first becoming aware of the event. · Terminating at the end of the study
	Provide all relevant source documentation (de-identified/ pseudonymized) for reported event, as requested by sponsor.	· Upon request of sponsor.
Serious Adverse Event	Complete AE CRF page with all available new and updated information.	· Within 3 calendar days of first becoming aware of the event or as per local/regional regulations. · Reporting required through the end of the study
	Provide all relevant source documentation (de-identified/ pseudonymized) for reported event.	· Upon request of sponsor

Event Classification	Communication Method	Communication Timeline pre-market studies
Serious Adverse Device Effects	Complete AE CRF page with all available new and updated information.	· Within 3 calendar days of first becoming aware of the event or as per local/regional regulations. · Reporting required through the end of the study
	Provide all relevant source documentation (de-identified/ pseudonymized) for reported event.	· When documentation is available · At sponsor request.
Device Deficiencies (including but not limited to failures, malfunctions, and product nonconformities)	Complete Device Deficiencies CRF with all available new and updated information.	· Within 3 calendar days of first becoming aware of the event. · Reporting required through the end of the study
	Provide all relevant source documentation (de-identified/ pseudonymized) for reported event.	· Upon request of sponsor
Adverse Event including Adverse Device Effects	Complete AE CRF page, which contains such information as date of AE, treatment of AE resolution, assessment of seriousness and relationship to the device.	· In a timely manner after becoming aware of the information · Reporting required through end of study · Upon sponsor request
	Provide all relevant source documentation (de-	

Event Classification	Communication Method	Communication Timeline pre-market studies
	identified/pseudonymized) for reported event, as requested by sponsor.	

All events will be assessed by the investigator for relationship to study device and the study procedure.

Table 8: Relationship Events to Procedure/Device

Classification	Description
Not Related	Relationship to the device, comparator or procedures can be excluded when: - the event has no temporal relationship with the use of the investigational device or the procedures related to the use of the investigational device; - the serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible; - the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event; - the event involves a body-site or an organ that cannot be affected by the device or procedure; - the serious event can be attributed to another cause (e.g. an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors); - the event does not depend on a false result given by the investigational device used for diagnosis, when applicable;

Classification	Description
	In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.
Possibly Related	The relationship with the use of the investigational device or comparator, or the relationship with procedures is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed or no information has been obtained should also be classified as possible.
Probably Related	The relationship with the use of the investigational device or comparator, or the relationship with procedures seems relevant and/or the event cannot be reasonably explained by another cause.
Causal Relationship	The serious event is associated with the investigational device or comparator or with procedures beyond reasonable doubt when: - the event is a known side effect of the product category the device belongs to or of similar devices and procedures; - the event has a temporal relationship with investigational device use/application or procedures; - the event involves a body-site or organ that -the investigational device or procedures are applied to; -the investigational device or procedures have an effect on; - the serious event follows a known response pattern to the medical device (if the response pattern is previously known); - the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious event (when clinically feasible); - other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out; - harm to the subject is due to error in use;

Classification	Description
	- the event depends on a false result given by the investigational device used for diagnosis, when applicable; In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious adverse event.

5.13.2.0.2. Sponsor Reporting Requirements

The sponsor is responsible for reporting adverse event information to all participating Principal Investigators, ECs and regulatory authorities, as applicable. All events will be assessed by the Sponsor for relationship to study device and study procedure.

5.13.3. DEATH REPORTING

A subject death during the study should be reported to LUMA Vision no later than 3 calendar days of site notification. A detailed narrative (death letter) that provides detailed information describing the circumstances surrounding the death and cause of death should be submitted to the sponsor. In addition, a death case report form needs to be submitted to the sponsor, including the following details:

- Date and time of death
- Primary organ cause of death
- Timing of the death in relation to the procedure
- Whether or not the death was witnessed/monitored
- Whether the death was related to the procedure, or investigational device
- Autopsy report, if applicable

5.14. REGULATORY AND ETHICAL ASPECTS

5.14.1. STUDY FINANCING

This study is financed by the Sponsor. The study site(s) shall enter into a clinical study agreement with the Sponsor that details the financing of the study as well as the rights and obligations of both the Sponsor and the site. The clinical study agreement must be executed before any participant is enrolled.

5.14.2. GENERAL DUTIES OF SPONSOR AND PRINCIPAL INVESTIGATOR

5.14.2.0.3. General Duties of Sponsor

The Sponsor’s general duties consist of submitting applications and information to appropriate regulatory authorities as required by local and national regulations, obtaining regulatory and EC approvals prior to allowing study start, selecting Investigators and ensuring proper clinical site monitoring.

5.14.2.0.4. General Duties of Principal Investigator

It is the responsibility of the Principal Investigator to ensure that the study will be conducted according to the protocol, recognized ethical principles for medical research involving humans, principles of good clinical practice, (ICH-GCP), ISO 14155:2020 Clinical Investigation of medical devices for human subjects, principles of the “Declaration of Helsinki”, any conditions of approval imposed by the reviewing EC and by the local regulation, if applicable.

The Principal Investigators will assure that all site personnel involved in the conduct of this study have completed ICH GCP Training as it pertains to this study. The protocol, informed consent form(s) and other related study materials will be submitted to the EC, and regulatory authority (as applicable) for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any additional requirements imposed by the EC or regulatory authority shall be implemented.

It is the responsibility of the Principal Investigator to ensure the following requirements are met before the start of the study:

- sign the Clinical Study Agreement, and comply with the Investigator responsibilities as described in such Agreement.
- sign the Investigator Brochure Signature Page and Protocol Signature page
- provide his/her recent curriculum vitae and that of site staff involved in the study
- insurance coverage for subjects in the study was obtained
- EC approval was obtained

It is the responsibility of the Principal Investigator to

- ensure that no deviations from this protocol occur, except if considered as needed to protect the life and physical well-being of a subject in an emergency. Any deviations that occurred during the study need to be documented, together with a rationale for the deviation.
- ensure that source documents and essential study documents throughout the clinical study are maintained and retained per requirements.
- ensure that the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports
- record, report, and assess every adverse event as applicable per the protocol and observed device deficiency.
- report to sponsor, per the protocol requirements, all reportable events
- report to the EC and regulatory authorities any SAEs and device deficiencies that could have led to a SADE and potential UADE or USADE, as required by local/regional regulations
- maintain the device accountability records and control of the devices
- ensure that adequate facilities are available to perform the study
- ensure that informed consent is obtained in accordance with applicable laws, this protocol and local EC requirements (see section 21.4)
- allow the sponsor to perform monitoring and auditing activities.

- regulatory authorities and ECs to perform auditing activities.

The Principal Investigator or his/her designee will take measures to prevent accidental or premature destruction of these documents.

5.14.2.0.4.1. Delegation of Responsibilities

The Principal Investigator may decide to delegate certain responsibilities to members of his/her site staff (Sub-Investigators, Clinical Research Coordinators and other site staff members, as applicable). These responsibilities shall then be appropriately documented prior to being performed. The Principal Investigator shall ensure his/her site staff is qualified and adequately trained prior to conducting any study-specific requirements. The Principal Investigator shall provide adequate supervision of those to whom tasks are delegated. Where there is a Sub- Investigator at a site, the Sub-Investigator cannot be delegated the primary supervisory responsibility for the site.

5.14.3. ROLE OF LUMA VISION REPRESENTATIVE(S)

LUMA Vision personnel can provide technical support to the investigator and other health care personnel (collectively HCP) as needed. Support may include HCP training, addressing HCP questions, or providing clarifications to HCPs concerning the operation of LUMA Vision's equipment/devices.

At the request of the investigator and while under investigator supervision, LUMA Vision personnel may operate equipment during the procedure, and interact with the subject to accomplish requested activities.

Typical tasks may include the following:

- Provide technical support or assist in the operation of the VERAFEYE System and other supporting equipment based on instructions provided by the HCP during the procedure.
- Be present and have some direct contact with the patients at the procedure.
- After the procedure, review how the study equipment performed, and transfer pseudonymized data to the Sponsor's study database.
- Assist and review the collection of information about the procedure and study documents for completeness and accuracy.
- Complete the Technical Source Form during the procedure, in order to assist the HCP with data collection during the procedure.

LUMA Vision personnel will not do the following.

- Practice medicine
- Provide medical diagnosis or treatment to subjects
- Discuss a subject's condition or treatment with a subject
- Independently collect study data
- Enter data in electronic data capture systems or on paper case report forms

5.14.4. ETHICS COMMITTEE

The protocol, its modifications, and the patient consent forms will be reviewed and approved in writing by an Ethics Committee (EC) prior to initiation of the study. No changes can be made to the protocol or patient consent forms without Sponsor and EC approvals. No investigative procedures other than those defined in this protocol will be undertaken on the enrolled patients without the written agreement of the EC and Sponsor. The Principal Investigator will advise their EC of the progress of this clinical study according to EC reporting requirements. The EC must operate in accordance with the current national regulations.

5.14.5. STUDY REGISTRATION

The study will be registered at the www.clinicaltrials.gov website.

5.14.6. STUDY INSURANCE

The Sponsor shall maintain clinical study insurance to provide coverage for the reasonable and necessary costs associated with the diagnosis and treatment of a research injury, defined as: “an illness or injury directly caused by the study product (drug/device) or study procedures required by the study protocol and would not have been expected from the standard treatment for a condition.”

5.14.7. PATIENT CONFIDENTIALITY

Patient confidentiality will be maintained throughout the clinical study in a manner that ensures the information can always be tracked back to the source data. For this purpose, a unique patient identification code will be used that allows identification of all data reported for each patient.

Data relating to the trial may be made available to third parties (e.g., in the case of an audit performed by a Regulatory Authority) provided the data are treated confidentially and that the patient’s privacy is guaranteed.

5.14.8. PROTOCOL DEVIATIONS

No deviations from the protocol are allowed, except to protect the rights, safety, and well-being of human subjects under emergency circumstances. In that event, the Investigator will notify Sponsor immediately in writing. The Investigator will also inform their EC of all deviations according to Institutional requirements. In the event of any deviation from the clinical protocol, a deviation CRF will be completed. The occurrence of clinical investigation plan deviations will be monitored by the Sponsor on an ongoing basis.

5.14.9. PROTOCOL AMENDMENTS

Any amendment to the protocol will require review and approval by the EC, and regulatory authority (as applicable) before the changes are implemented to the study.

5.14.10. EARLY TERMINATION

The Sponsor retains the right to terminate the study at any time after carefully weighing the benefits against any possible risks. In case of early termination of the study, the Sponsor will promptly inform the Principal Investigators, Ethics Committee and regulatory authorities, as applicable. The Sponsor shall provide the reason for early termination.

The following circumstances may justify early termination of a site:

- The investigational site fails to comply with Good Clinical Practices (GCP) standards
- The first subject fails to be recruited within a reasonable period after initiation of the investigational site
- Recruitment of subsequent subjects is unreasonably slow.

The following circumstances may justify early termination of a study:

- Occurrence of severe device-related complications in one or more subjects
- Information that is expected to be gathered by this study has already been gained by other means
- The development of the test product is discontinued by the Sponsor, or the study proves not to meet the expected goal
- Instructions from the EC or regulatory authorities to suspend or terminate the study
- Other important or unforeseen circumstances

5.15. STUDY DOCUMENTATION

5.15.1. DATA MANAGEMENT

All applicable case report forms per the protocol must be completed for every patient. On completion, each CRF shall be signed and dated by the investigator ensuring the data accurately reflects the patient's clinical results. The sponsor will put a data management plan in place, describing the mechanisms for data collection and data cleaning.

5.15.2. SOURCE DOCUMENTS

Source document is the document where the data has been recorded first. Investigators are responsible for maintaining information of the patients' medical records that contain the source data reported into

the CRFs. Source documentation includes but is not limited to those items noted in the Table below.

Table 9: Source Documentation Requirements

Requirement	Disposition
Informed consent form and documentation of ICF consenting process	Retain at site
Documentation of: • Medical history • Physical examination • Demographics • Pregnancy, if applicable • Medication Regimen and Changes	Retain at site
12-lead ECGs	Retain at site
Signed Technical Source Form	Retain at site
VERAFEYE Imaging Data	Retain at site (saved to external media, as provided by the sponsor)
VERAFEYE Export Case Data	Submit to LUMA Vision
Standard of Care Imaging Data	Retain at site Submit copy to LUMA Vision (saved to external media, as provided by the sponsor)
Printed Lab Procedure Report	Retain at Center
In the event of patient death (if available): • Death narrative • Relevant medical records • Death certificate • Autopsy report	Retain at site Submit copy to LUMA Vision

5.15.3. TECHNICAL SOURCE FORMS

A Technical Source Form (TSF) is developed by LUMA Vision to capture protocol required data elements that are not duplicated in any other source documents. This form is to be used by the study

sites as a source document. A LUMA Vision representative may complete the TSF at the request of the Investigator performing the procedure. The TSF will be reviewed and signed for approval by the Investigator who performed the procedure at the end of each procedure.

5.15.4. INVESTIGATOR FILES/RETENTION OF DOCUMENTS

The investigator must maintain accurate records for full documentation of the study and study data verification.

The Investigator's Study File will contain the signed protocol with all amendments, signed patient informed consent, CRFs, copies of the AE/SAE reports, EC and regulatory authority approvals and correspondence, correspondence with the Sponsor, staff curriculum vitae and financial/conflict disclosures for investigators physicians, Investigators Brochure, Instructions for Use and other appropriate documents.

Patient Clinical Source Documents include all records to show eligibility to participate in and date of entry into the study, patient hospital/clinic records, physician's and nurse's notes from each visit. All AEs, their resolution and supporting documentation much also be maintained. The patient’s condition upon completion of the study or withdrawal must be included.

The investigator must keep these documents on file in compliance with the applicable regulatory requirements.

Should the investigator wish to assign the study records to another party or move them to another location, the Study Sponsor must be notified.

5.15.5. DEVICE ACCOUNTABILITY

All investigational devices of the VERAFEYE System shall be documented on a Device Accountability Log.

Upon receipt of the investigational devices, the site will ensure these devices are stored in a locked cabinet and/or room, and access shall be strictly restricted to authorized users of the device, or to the site monitor. The site is responsible for keeping records of receipt, usage and return.

Records of receipt, use, and return of all investigational devices shall be maintained by the Investigator or his/her designee. Any investigational device damaged or considered unusable in shipment shall be documented in the study files and the Investigator shall notify the Sponsor.

Following accountability of the investigational devices and other hardware at the site, all used and unused devices will be returned to LUMA Vision. Used VERAFEYE Imaging Catheters shall be sanitized prior to return to the sponsor. Any discrepancies noted between the device log and unused devices will be investigated, resolved, and documented prior to return of device(s).

5.15.6. MONITORING

Contracted monitors, the Sponsor or their designee will perform site monitoring during the study to ensure compliance with the study protocol and applicable regulations, that data is collected in a timely, accurate and complete manner and that the Investigator continues to have appropriate staff and facilities to conduct the study safely and effectively.

With appropriate notice, the Investigator will allow the monitor/s access to all relevant CRFs, study binders and patient records. The Investigator and a Clinical Research Coordinator will be available for monitoring visits. It is expected that the site will provide the monitors with a suitable working environment for review of Clinical Trial-related documents.

The monitor will assess compliance to the protocol and that the CRFs submitted by the Investigator with respect to timeliness, clarity and accuracy by reviewing source documents. The monitor will also assess that the site continues to have sufficient staff to conduct the study, training records, and completeness of site-specific binders.

Patient confidentiality will be maintained in accordance with the local requirements.

The sponsor will put a monitoring plan in place, describing the monitoring activities to be performed for the study.

5.15.7. AUDITS AND INSPECTIONS

Source documents for this trial must be made available to personnel monitoring and auditing the study, and/or representatives of the Sponsor, EC, regulatory inspectors and to health authority inspectors after appropriate notification. The Case Report Forms must be made available for direct inspection by such parties and for comparison with the contents of the source documents.

5.15.8. CONFIDENTIALITY OF TRIAL DOCUMENTS AND PATIENT RECORDS

The Investigator must assure maintaining of the study participants' anonymity at all occasions. Patients should be identified using a study identification code. The Investigator must keep a separate confidential patient enrolment log showing study numbers and patient's identity codes/names.

5.16. PUBLICATION POLICY

The data and results from the Clinical Trial are the property of the Sponsor as governed by the Research Agreement. LUMA Vision requires disclosure of its involvement as a sponsor or financial supporter in any publication or presentation relating to the LUMINIzE study or its results. LUMA Vision may submit study results for publication following the conclusion or termination of the study. LUMA Vision personnel may assist authors and investigators in publication preparation provided the first and senior authors are the primary drivers of decisions regarding publication content, review, approval, and submission. The directives of the International Committee of Medical Journal Editors will be respected when considering authorship (www.icmje.org).

Study results will be made available in accordance with the legal requirements and the recognized ethical principles. A Clinical Investigation Report will be made available to the Principal Investigator, EC and regulatory authorities, as applicable in accordance local requirements. As applicable, an abbreviated Clinical Investigation Report will be made available on the www.clinicaltrials.gov website.

5.17. BIBLIOGRAPHY

1 Lung B, Vahanian A. Epidemiology of valvular heart disease in the adult. Nat Rev Cardiol. 2011;8:162–72.

2 D'Arcy JL, Prendergast BD, Chambers JB, Ray SG, Bridgewater B. Valvular heart disease: the next cardiac epidemic. Heart. 2011;97:91–3.

3 Saw J, Holmes DR, Cavalcante JL, et al. SCAI/HRS expert consensus statement on transcatheter left atrial appendage closure. Heart Rhythm. 2023;20(5):e1-e16.

4 Stout KK, Daniels CJ, Aboulhosn JA, et al. 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;73(12):e81-e192.

5 Korsholm K, Berti S, Iriart X, et al. Expert Recommendations on Cardiac Computed Tomography for Planning Transcatheter Left Atrial Appendage Occlusion. JACC Cardiovasc Interv. 2020;13(3):277-292.

6 Sperlongano S, Giordano M, Ciccarelli G, et al. Advances in Percutaneous Patent Foramen Ovale Closure: From the Procedure to the Echocardiographic Guidance. J Clin Med. 2022;11(14).

7 Kuo L, Frankel DS, Lin A, et al. PRECAF Randomized Controlled Trial. Circ Arrhythm Electrophysiol. 2021;14(1):e008993.

8 Matsubara TJ, Fujiu K, Asada K, et al. Direct left atrial ICE imaging guided ablation for atrial fibrillation without employing contrast medium. Int J Cardiol. 2016;203:733-739.

9 Kawakami T, Saito N, Yamamoto K, et al. Zero-fluoroscopy ablation for cardiac arrhythmias: A single-center experience in Japan. J Arrhythm. 2021;37(6):1488-1496.

10 Kirstein B, Morris A, Baher A, et al. Magnetic resonance imaging-guided cryoballoon ablation for left atrial substrate modification in patients with atrial fibrillation. J Cardiovasc Electrophysiol. 2020;31(7):1587-1594.

11 Reddy VY, Dukkipati SR, Neuzil P, et al. Pulsed Field Ablation of Paroxysmal Atrial Fibrillation: 1-Year Outcomes of IMPULSE, PEFCAT, and PEFCAT II. JACC Clin Electrophysiol. 2021;7(5):614-627.

12 Sulkin MS, Laughner JI, Hilbert S, et al. Novel Measure of Local Impedance Predicts Catheter-Tissue Contact and Lesion Formation. Circ Arrhythm Electrophysiol. 2018;11(4):e005831.

13 Inoue K, Tanaka N, Ikada Y, et al. Characterizing clinical outcomes and factors associated with conduction gaps in VISITAG SURPOINT-guided catheter ablation for atrial fibrillation. J Arrhythm. 2021;37(3):574-583.

14 Streb W, Mitrega K, Podolecki T, et al. Comparison of transesophageal and intracardiac echocardiography in guiding percutaneous left atrial appendage closure with an Amplatzer Amulet device. Postepy Kardiol Interwencyjnej. 2019;15(4):446-454.

15 Alkhouli M, Hijazi ZM, Holmes DR, Jr., Rihal CS, Wiegers SE. Intracardiac Echocardiography in Structural Heart Disease Interventions. JACC Cardiovasc Interv. 2018;11(21):2133-2147.

5.18. ABBREVIATIONS AND ACCRONYMS

AF	Atrial Fibrillation
AFL	Atrial Flutter
ASD	Atrial Septal Defect
CRF	Case Report Form
EC	Ethics Committee
EC (1-8)	Exclusion Criterium
EP	Electrophysiology
FIH	First In Human
GUI	Graphical Unser Interface
IC (1-4)	Inclusion Criterium
ICE	Intracardiac Echocardiography
ICF	Informed Consent Form
IEC (1)	Imaging Exclusion Criterium
LA	Left Atrium
LAAC	Left Atrial Appendage Closure
LV	Left Ventricle

RA	Right Atrium
RV	Right Ventricle

Cross-project links