# ICE-Guided Cardiac Interventional Percutaneous Procedures

## Project: “The Philips ICE Registry”

## Protocol ID: IGT_IGD_ICE Registry Study_2019_10745

## Version 2.0

## Date: 24 APR 2021

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| **Registry Sponsor:** | Philips Image Guided Therapy Devices |
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## Version History

| Version No. | Amendment No. | Version Date | Summary of Changes | Rationale |
|---|---|---|---|---|
| 1.0 | NA | 21OCT 2019 | NA | NA |
| 2.0 | 1 | 24APR 2021 | • New template conversion<br>• Updated primary and secondary analyses<br>• Increase in no. of patients and sites<br>• General formatting, grammatical updates | Align with Philips process updates<br><br>Streamlining data points for analyses |

## Sponsor Sign-Off

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## Abbreviations

| Abbreviation | Definition |
|---|---|
| AE | Adverse Event |
| ADE | Adverse Device Effect |
| ANOVA | Analysis of Variance |
| CFR | Code of Federal Regulation |
| CRF | Case Report Form |
| CRO | Contract Research Organization |
| DDE | Direct Data Entry |
| DICOM | Digital Imaging and Communications in Medicine |
| eCRF | Electronic Case Report Form |
| EDC | Electronic Data Capture |
| GCP | Good Clinical Practice |
| ICE | Intracardiac echocardiography |
| ICH | International Conference on Harmonization |
| IRB | Institutional Review Board |
| ISO | International Organization for Standardization |
| PACS | Picture Archiving and Communication System |
| SADE | Serious Adverse Device Effect |
| SAE | Serious Adverse Event |
| SAS | Statistical Analysis Software |
| UADE | Unanticipated Adverse Device Effect |
| USADE | Unanticipated Serious Adverse Device Effect |

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## Statement of Compliance

The trial will be carried out in accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP), the principles of the Declaration of Helsinki, the applicable parts of ISO 14155:2011 and the following: United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56 21 CFR Part 11).

The protocol, informed consent form(s), recruitment materials, and all subject materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any subject is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from subjects who provided consent, using a previously approved consent form.

## 1. PROTOCOL SUMMARY

| | |
|---|---|
| **Study Title & ID** | The Philips ICE Registry<br>Protocol ID: IGT_IGD_ICE Registry Study_2019_10745 |
| **Project Name** | "Philips ICE Registry" |
| **Study Description** | The purpose of this observational registry is to report real-world safety and performance of VeriSight for ultrasound guided ICE imaging in percutaneous cardiac intervention procedures when used in standard clinical practice. |
| **Study Design** | Prospective, multicenter, observational, single-arm registry |
| **Primary Analyses** | **Technical success** – defined as successful delivery of VeriSight to the target intracardiac position and sustained device operation during the procedure<br><br>**Imaging success** – Adequate image quality as determined by the investigator.<br><br>**Clinical success** – Adequacy of VeriSight imaging for visualization of major cardiac structures, and guiding procedural intervention, and ability to detect/ assess intra-procedural complications.<br><br>**Safety** – Device-related adverse events periprocedural through discharge or ≤48 hours post-procedure, whichever is earlier. |
| **Secondary Analyses** | 1. Procedural characterization when using VeriSight<br>2. Device characterization when using VeriSight<br>3. Physician survey regarding the Philips ICE system<br>4. Staff survey regarding the Philips ICE system |

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|---|---|
| **Patient Population** | Inclusion Criteria<br>• ≥18 years of age and willing to provide written, signed and dated, informed consent.<br>• Scheduled for a procedure that is within the scope of clinical indications for VeriSight, per Instructions for Use (IFU)<br><br>Exclusion Criteria<br>• Contraindicated for ICE catheter placement or patient considerations that make placement of VeriSight not technically feasible<br>• If alternate access (as needed instead of femoral) is not viable.<br>• Known contraindicated conditions include sepsis, major coagulation abnormalities, presence of any intracardiac thrombus, presence of class IV angina or heart failure, deep vein thrombosis, or significant peripheral vascular disease. |
| **Planned Enrollment** | Up to 200 patients scheduled to undergo cardiac interventional percutaneous procedures for which ICE is indicated. Interim analysis is planned after the 100$^{th}$ patient before further continuity of enrollment in the registry. |
| **Registry Sites** | Up to 10 sites in the United States with a maximum enrollment of no more than 30% patients at each participating site |
| **Registry Exit** | Either at discharge or ≤48 hours post-procedure, whichever is earlier |
| **Registry Duration** | Duration of the registry is estimated to be approximately 24 – 36 months. |
| **Statistical Methodology** | No hypothesis testing is planned. All subjects enrolled in the study will be accounted for in the study report. Descriptive statistics and 95% confidence intervals will be calculated for variables. |

# 2. INTRODUCTION

## 2.1. Device Description

Philips Image Guided Therapy Devices has recently developed and received FDA approval an intracardiac echocardiography (ICE) catheter (VeriSight/ VeriSight Pro, henceforth defined as VeriSight in this protocol) that has 2D and/or 3D imaging capabilities. These catheters are for use with Philips EPIQ series of ultrasound system. The indication for use for VeriSight is intended for intracardiac and intra-luminal visualization of cardiac and great vessel anatomy and physiology as well as visualization of other devices in the heart. The catheter is intended for imaging guidance only, not treatment delivery, during cardiac interventional percutaneous procedures. A detailed description of VeriSight can be found in the products' IFU.

The current benchmark for image guidance in percutaneous cardiac intervention procedure is transesophageal echocardiography. The major advantage of ICE over TEE is its unique imaging from within the heart, providing shorter image distances to target anatomy or device, and higher resolution. In addition, ICE can be used under conscious sedation thus avoiding the need of esophageal intubation and eliminating the risk for esophageal trauma. Further, ICE can also reduce fluoroscopy exposure to both the patient and the operator.

## 2.2. Background

ICE has been around for more than 20 years and its use has significantly increased with the advent of invasive electrophysiology (EP) and percutaneous structural heart disease (SHD) interventions. ICE is an advanced imaging modality that has become an integral part of a variety of percutaneous interventional and EP procedures, potentially improving outcomes and reducing risks[1-3].

Recent reports demonstrate that ICE utility as a primary guidance or as a supplement to transesophageal echocardiography (TEE) in various SHD and EP interventions such as left atrial appendage (LAA) closure, interatrial shunt closure, left and right heart transcatheter valve intervention, ventricular septal defect (VSD) and patent ductus arteriosus (PDA) closure[4]. There are several ultrasound imaging tools/techniques to guide cardiac interventions. Transthoracic echocardiography (TTE) was initially described to guide percutaneous interventions in 1984 by Kronzon et al. and offers a unique way to provide real time imaging[4,5]. However, TTE is limited by shadow artifact from anterior structures, lower quality images from increased distances between the probe and heart, and image distortion from bone and lung tissue. The TTE probe over the chest wall also does not offer continuous procedural guidance and may disrupt the workflow during interventional procedures. TTE use during an intervention can be also problematic due to the need for a separate operator (a sonographer) to acquire and manipulate the images. TEE unlike TTE offers superior image resolution for left heart structures, and may allow visualization of the entire picture, including catheter tips, wires, and devices[6]. Drawbacks of TEE include the requirement for esophageal intubation and potential complications such as gastrointestinal tract injury, aspiration,

and anesthetics side effects[7]. Additionally, anterior structures may be difficult to visualize on TEE secondary to far-field exposure and shadowing from adjacent structures. The probe may also obscure the interventionalists' field of view on fluoroscopy[8].

The use of ICE avoids most of those limitations. As such, ICE has become a widely used ultrasound based imaging tool in the interventional laboratory. Imaging with ICE has evolved from cross-sectional imaging using a rotating transducer, to sector-based imaging using a phased-array transducer[9]. Phased array ICE has many advantages over rotational ICE including a greater frequency range, greater depth of field, steerability, and the possibility of acquiring Doppler and color flow imaging. Phased-array catheters can be easily advanced and positioned through short sheaths and do not require long guide sheaths. The major advantage of ICE over TEE is its unique imaging from within the heart, providing shorter image distances to target anatomy or device, and higher resolution. In addition, ICE can be used under conscious sedation thus avoiding the need of esophageal intubation and eliminating the risk for esophageal trauma. Further, ICE can reduce fluoroscopy exposure to both the patient and the operator[10].

**Evidence of Prior Clinical Data with ICE Technology**

The performance and safety of the ICE imaging modality has been well established in different percutaneous interventions. Below we provide several examples of the outcomes of the utility of ICE technology in a variety of SHD and EP procedures.

Structural Heart diseases interventions

During transseptal catheterization, ICE helps provide direct visualization of the interatrial septum and is invaluable tool to guide a safe transseptal puncture. ICE delineates the anatomy of intra- and extracardiac structures not identified with fluoroscopy and simplifies correct positioning of the transseptal dilator, puncture of the fossa ovalis, and cannulation of the left atrium in a timely and uncomplicated fashion[11]. In another study, the use of AcuNav ICE catheter during left heart radiofrequency ablation and transcatheter closure procedures successfully guided transseptal catheterization, provided imaging of normal or aberrant anatomy of the right/left atrial (interatrial septum, fossa ovalis, appendages, 4 pulmonary vein ostia) and right/left ventricular (valves and papillary muscles) structures. AcuNav was crucial in providing early identification of procedure complications, including pericardial effusion (n = 2, detected before systematic hemodynamic deterioration) and thrombus formation on sheaths deployed in the right atrium (n = 9) and left atrium (n = 2, early elimination with management of the sheath)[12].

*Atrial Septal Defect Closure*

Several studies have reported the feasibility and safety of ICE for guiding transcatheter closure of Atrial Septal Defect (ASD)[3]. There was close agreement between ICE and TEE in their assessment of device position and the adequacy of septal capture before device release (98%) and in identifying

the presence of significant residual shunts. ICE detected all potentially adverse events, including four malpositions, and guided appropriate remedial action[13,14].

Left Atrial Appendage (LAA) Imaging and Closure Procedures

ICE provides adequate visualization of the LAA and can be used as an alternative to TEE in guiding LAA occlusion (LAAO) procedures[15-17]. Matsuo et al. investigated a total of 27 patients with AF receiving Watchman left atrial appendage closure under ICE guidance at a single center. All patients were successfully implanted. There were no major procedural complications. The overall procedure-related complication rate was 14.8% primarily attributed to access site hematoma[16].

Baseline clinical and procedural characteristics, and in-hospital outcomes were compared between patients in whom a Watchman was implanted with ICE vs. TEE guidance. Device implantation success rate was 100% in both groups. There were no device embolization, significant peri-device leak, tamponade, stroke, and access site bleeding reported in any patient. Total hospital stay for stand-alone LAAO was comparable between groups (2 days [2-2] vs. 2 days [2-3.3], P = 0.17, in ICE vs. TEE, respectively)[17].

The impact of ICE to guide LAAO has been established[15-18]. Reported high technical success rates range between 96.7% and 100.0%, irrespective of RA or LA ICE probe position. Korsholm et al. studied the efficacy and safety of ICE and TEE from the left atrium for procedural guidance of transcatheter LAAO. Technical success was achieved in 99% of both the TEE and ICE group. Procedural success was 94.5% in ICE-guided group. Major peri-procedural complications occurred in 4.7% of the TEE group and 1.8% of the ICE group. In addition, contrast use and procedural time were reduced with ICE[19].

Mitral Valve Procedures

ICE guidance for percutaneous catheter-based Mitral Valve (MV) repair techniques have been described. Saji et al. used ICE adjunctively with TEE for guiding percutaneous MV repair with the MitraClip system (Abbott Vascular) in patients with failed prior surgical rings. In this study, the ICE catheter was introduced transarterially into the LV and anteflexed to obtain a short-axis view of the valve. The authors state that ICE was helpful to assess the insertion of the posterior leaflet into the MitraClip's arms, particularly in this group of patients, in which TEE imaging of the MV may be shadowed by the surgical ring[20]. During the MV Valvuloplasty procedure, ICE is used to rule out LAA thrombus, guide the transseptal catheterization, confirm optimal balloon position, monitor balloon inflation, and assess the valve before and after valvuloplasty[21, 22].

Transcatheter Aortic Valve Replacement (TAVR)

ICE-guided TAVR may represent an important alternative to TEE for TAVR imaging guidance and possibly allow for less-intensive sedation or anesthesia[23]. Other advantages of ICE include

uninterrupted monitoring, no fluoroscopic interference, and precise Doppler-based assessment of pulmonary artery pressures[24].

Electrophysiology procedures

The EP procedure involves study and treatment of rhythm disorders of the heart. There are several therapeutic and surgical methods to treat many of the rhythm disturbances of the heart such as surgical implantation of pacemakers and implantable cardioverter–defibrillator.

ICE can be used in AF ablation procedures to guide transseptal puncture. ICE imaging can also be used in the following procedural steps, including (1) characterization of pulmonary vein anatomy (number of veins, diameter, anatomic variants), (2) transseptal catheterization, (3) catheter positioning and contact monitoring, (4) assessment of lesion formation, (5) prevention and early detection of procedural complications such as pericardial effusion or thrombus formation, (6) assessment of pulmonary veins physiology/flow before and after ablation, and (7) location of the esophagus in relationship to the pulmonary vein ostium[25, 26]. ICE is useful to assist ablation of the cavotricuspid isthmus (CTI) in patients with typical atrial flutter. In a randomized trial that included 102 patients with typical flutter, ICE-guided ablation of the CTI significantly shortened the procedure time radiation exposure, and time spent for ablation in comparison with fluoroscopy-only procedures. About 13% of the patients from the fluoroscopy-only group crossed over to ICE guidance because of failure to achieve CTI block and were all treated successfully[27].

ICE has an invaluable role in the mapping and ablation of ventricular arrhythmias. It provides real-time visualization of the ablation catheter in relation to a particular anatomic structure, allowing for continuous assessment of catheter–tissue contact. This is key for effective energy delivery to the targeted structure of interest, possibly increasing effectiveness and limiting collateral damage. Lesion formation is typically visualized in ventricular tissue as the development of increased echogenicity during ablation[28]. Saksena et al. studied the role of ViewFlex ICE catheter in comparison to TEE in imaging of left atrium and interatrial septal during atrial fibrillation. ICE and TEE showed concordance for LAA, IAS and SEC imaging but not for LA and LAA thrombus detection where ICE imaging was less sensitive compared to TEE for LAA thrombus identification. There were no adverse events or complications reported for ICE or TEE[29].

Transvenous Lead Extraction

Sadek et al. reported the utility of ICE during transvenous lead extraction. ICE imaging provides continuous monitoring for procedural complications. It allows for identification of lead binding sites within the heart or the SVC, which are predictive of a more complex procedure and the need for advanced extraction tools. In addition, ICE can detect the presence of lead-related echo densities, suggestive of thrombi or vegetations. Interestingly, these echo densities were found in 72% of patients, mostly in the absence of bacteremia[30].

## 2.3. Registry Rationale

Until recently, ICE has been limited to only two-dimensional (2D) imaging planes. Enabling real-time three-dimensional (3D) imaging with the Philips VeriSight combines the advantages of ICE with imaging capabilities that so far have only been available for TEE, and it has the potential to improve procedural guidance; quickly and easily locate guidewires, catheters, and devices; and provide greater anatomic information during percutaneous interventions. This novel real time 2D/3D ICE system has received US Food and Drug Administration clearance for commercial use and distribution. The purpose of this observational multi-center registry is to evaluate real-world safety and performance of VeriSight for ultrasound guided ICE imaging in percutaneous cardiac intervention procedures when used in standard clinical practice. The intended patient population are patients undergoing percutaneous cardiac intervention procedures for which VeriSight is indicated. The evidence from this post-market registry will be used for publications and to support regulatory filings outside of the US market.

## 2.4. Risk/Benefit Assessment

This will be an open-label all-comers registry. The design of the protocol is observational and there are no interventions as part of the registry. All interventions such as procedures occurring during this protocol are the standard clinical practice and their use will be directed by the investigator as part of the standard care. The Philips VeriSight ICE catheter has received 510(k) clearance from FDA allowing U.S. commercial sale. Investigators enrolling patients into the registry, will be imaged with the VeriSight catheter. Use of the product in this registry will be on label per the IFU and standard clinical practice. Patients will not be placed at additional clinical risk by participating in this registry. Although there are no added risks due to standard of care, the benefit at large will involve a better understanding of the safety profile for the ICE catheter tech within the respective intervention. Any complications associated with the VeriSight catheter and those related to the cardiac intervention procedures will be collected and reported.

# 3. REGISTRY DESIGN

## 3.1. General Description

This is a prospective, multi-center, observational, single-arm registry intended to gather real-world data to report VeriSight ICE catheter performance and safety. It will be conducted in the United States under the approval of one or more recognized institutional review boards and in compliance with GCP guidelines defined in ISO:14155;2011, the Declaration of Helsinki, and all applicable federal and local laws and regulations. Only on label uses of the VeriSight ICE catheter will be allowed. No specific claims are being validated during this registry, though data analyzed from this protocol are intended to inform of future claims regarding the performance and safety of the VeriSight catheter.

Enrolled patients will be imaged with VeriSight for various types of percutaneous cardiac interventional procedures. Enrolled subjects will be followed until discharge or ≤48 hrs post-procedure. The registry has a planned duration of approximately 24-36 months with interim analysis planned at 100 patients before further enrollment will be considered. Statistical hypotheses are not intended for this registry and descriptive analysis will be conducted. Data from all clinical sites are intended to be pooled for analysis. It is possible that sub-analyses may be conducted to demonstrate VeriSight guidance for target intervention types in structural heart and electrophysiology procedures.

## 3.2. Performance and Safety Analyses

The overall purpose of this observational multi-center registry is to report real-world performance and safety of VeriSight ultrasound guided ICE imaging in percutaneous cardiac intervention procedures when used in standard clinical practice.

Primary Analyses

The primary analyses will include the following:

a) **Technical success** – defined by successful delivery of VeriSight to the target intracardiac position and sustained device operation during the procedure
Successful device delivery is defined as ability of the VeriSight catheter to reach the target intracardiac anatomical position. Sustained operation of VeriSight is absence of technical complications or procedural delays/ disruption.

b) **Imaging success** – Adequate image quality as determined by the investigator using a Likert scale assessment.

c) **Clinical success** - Adequacy of VeriSight imaging for visualization of major cardiac structures, and guiding procedural intervention, and ability to detect/ assess intra-procedural complications.
Clinical success will be measured by ability of VeriSight to adequately guide procedural intervention using the following parameters:
   i. number of great vessels imaged, number of chambers imaged, including angle of views, axis, and modality
   ii. assessment of key cardiac structures and sizing relevant anatomy
   iii. verification of delivery and/or placement of interventional device (e.g. trans septal puncture devices, closure devices (LAAO, PFO, ASD, VSD), valves (e.g for TAVR), clip devices (e.g. mitral clip), annuloplasty devices (e.g. Cardioband), ablation devices (e.g cryoballoon, RF ablation catheter), leads (leads extraction), etc.),
   iv. assessment of procedural related complication (e.g. cardiac tamponade, pericardial effusion, thrombus) will be documented for each patient based on the procedure type.

d) **Safety** - Device related adverse events periprocedural through discharge or 48 hours post-procedure, whichever is earlier.

Secondary Analyses

Secondary analyses will include the following:

a) Procedural characterization when using VeriSight measured by
   i. type of procedure utilizing ICE imaging
   ii. total procedural room time (door-in to door-out, mins), total procedure time (skin to skin, mins)
   iii. total fluoroscopy time (mins)
   iv. total contrast volume used (cc), fluoroscopic dosage (mGy)
   v. ability to image from the right side of the heart for a left sided intervention
   vi. TEE usage rate and avoidance of TEE procedure
   vii. Other imaging modality used during the procedure
   viii. Change in management from use of VeriSight – need for high risk patient and/or procedure management
   ix. Duration and type of anesthesia
   x. Freedom from general anesthesia

b) Device characterization when using VeriSight based on a scoring scale for the physical attributes of the VeriSight catheter
c) Physician survey regarding the Philips ICE using a five-point ordinal Likert-type rating scale
d) Staff survey regarding the Philips ICE using a five-point ordinal Likert-type rating scale

### 3.3. Measures to Minimize Bias

The following measures will be taken to minimize and/or avoid bias in this registry:

a) A multi-center observational registry design is used to help ensure a representative sample of physicians performing the procedure and to provide a reasonable enrollment period.
b) Sites will have the ability to represent all-comers in various percutaneous cardiac intervention procedures.
c) Subjects will be screened to confirm study eligibility with defined inclusion/exclusion criteria prior to inclusion. Sites are required to maintain a log of all subjects screened and enrolled for the study.
d) Data collection requirements and study procedures will be standardized across all sites. All sites will follow the same version of the protocol and eCRFs.
e) Collection and archiving of image data will be managed adequately to reduce the impact of data loss and error in analysis.

f) Standardized protocol training will be developed and distributed to all participating sites to ensure data of uniform quality are obtained from all subjects
g) Regular monitoring will be conducted to verify source data and adherence to the protocol.

# 4. REGISTRY POPULATION

## 4.1. Inclusion Criteria

1. 18 years of age and willing to provide written, dated and signed, informed consent
2. Scheduled for a procedure that is within the scope of clinical indication for VeriSight per Instructions for Use (IFU)

## 4.2. Exclusion Criteria

Patients who have ANY of the following exclusion criteria are NOT eligible for participation on the registry.

1. Contraindicated for ICE catheter placement or patient considerations that make placement of VeriSight not technically feasible
2. If alternate access (as needed instead of femoral) is not viable
3. Known contraindicated conditions include sepsis, major coagulation abnormalities, presence of any intracardiac thrombus, presence of class IV angina or heart failure, deep vein thrombosis, or significant peripheral vascular disease.

## 4.3. Number of Subjects

Enrollment of up to 200 all-comers is planned with distribution across multiple case types such as structural heart disease interventions and electrophysiology procedures. Based on a sample of 100 patients, minimum representation of anticipated enrollment for each procedure type based on investigator survey is the following: minimum of 30 cases for electrophysiology, minimum of 30 cases for left atrial appendage occlusion, minimum of 20 cases for valve intervention, and 5 for ASD/PFO. Each participating registry site will be allowed a maximum enrollment of no more than 30% patients from the total planned enrollment.

## 4.4. Enrollment

Subjects who sign the informed consent form and are indicated for treatment procedure per VeriSight commercial labeling will be considered for the registry. A subject is considered enrolled in the registry when VeriSight has been placed in their vasculature and the device is switched “ON”. Participation is complete at discharge or ≤48 hours post-procedure from the registry site, whichever occurs first.

### 4.5. Screen Failures

Only consented subjects who are considered enrolled in the registry will be followed. Those who provide consent, but then are determined to be ineligible at the time of enrollment will be considered screen failures.

### 4.6. Registry Exit Definition

A subject is considered to have completed and exited the registry if he or she has completed all phases of the study including the last visit or the last scheduled procedure shown in the **Schedule of Activities (SoA)**, **Section 6.2.**

### 4.7. Subject Discontinuation/Withdrawal from the Study

Study participation is voluntary. The subject may refuse to consent or may withdraw from the study at any time without penalty or loss of benefits of quality of care to which he/she is otherwise entitled. All information regarding the subject's withdrawal must be recorded in the subject's medical record. In addition, the appropriate case report forms must be completed for the Subject and clear documentation of the subject's withdrawal must be provided to the Sponsor.

### 4.8. Lost to Follow-Up

Follow-up in this registry is limited to discharge or ≤48 hours post-procedure, whichever is earlier. All follow-up data is expected to be collected and lost to follow-up is not anticipated in this registry.

### 4.9. Registry Duration

The expected duration of the registry is estimated to be approximately 24 – 36 months.

## 5. DEVICE ACCOUNTABILITY

The Philips VeriSight catheter is a commercially approved device that will be used within their approved indication. The intended indication is for intracardiac and intra-luminal visualization of cardiac and great vessel anatomy and physiology as well as visualization of other devices in the heart. A complete description of the VeriSight catheter can be found in the product's IFU.

The Philips VeriSight catheter will be purchased by each site and will not require product packing and shipment information to be tracked. The EPIC console will be loaned to site with the latest software for use with the VeriSight ICE catheter.

## 6. REGISTRY PROCEDURES & EVALUATIONS

Subjects enrolled in this registry will have at least one visit and may have up to three visits, depending on the scheduling of their procedure at each clinical site. Individual visits and their specific procedures will consist of the events described below.

### 6.1. Schema

Patients scheduled to undergo percutaneous cardiac intervention procedures in which VeriSight will be used for imaging and are willing to participate in the registry may be enrolled. Subjects will be enrolled at up to 10 clinical sites in the United States. Patients who are indicated for the use of VeriSight per the commercial IFU will be screened for registry participation at the screening/baseline visit, and enrolled subjects will be evaluated on the day of the procedure and again within discharge or ≤48 hours post-procedure (whichever is first), as per site's standard of care. Figure 1 provides an overview of the registry procedures at each visit.

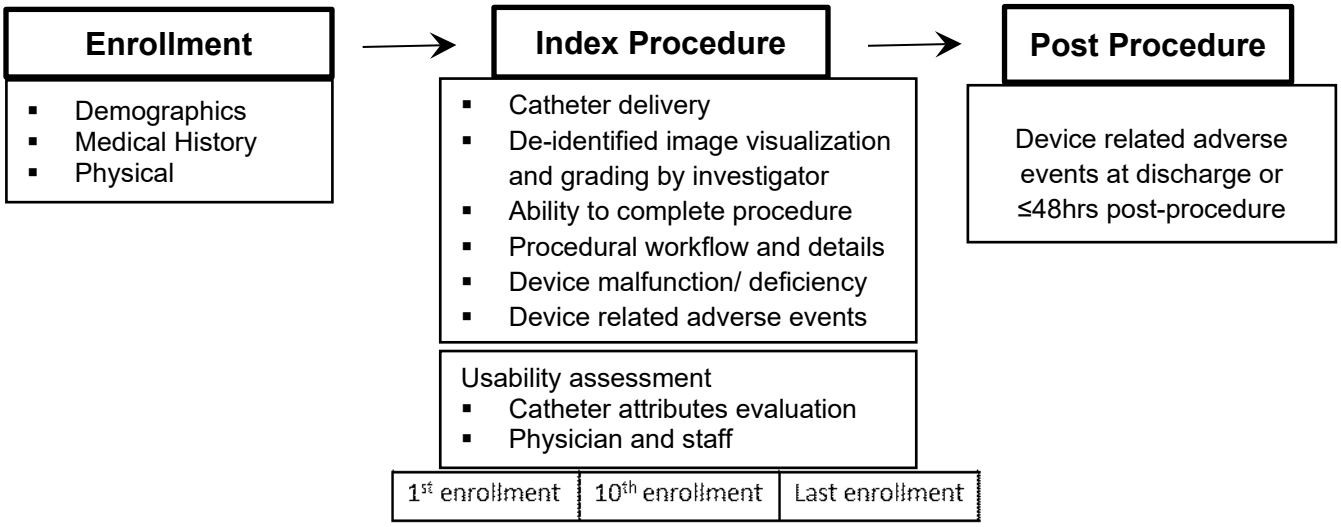


**Figure 1.** Study flow diagram

### 6.2. Schedule of Activities (SOA)

Table 1 provides an overview of registry procedures per visit.

| **Table 1.** Overview of registry procedure | | | |
|---|---|---|---|
| **Procedures** | **Screening*** | **Index procedure** | **Post-Procedure (at discharge or 48hrs)** |
| Assessment of eligibility | **X** | | |
| Informed consent | **X** | | |
| Record demographics | **X** | | |
| Medical History and Physical (H&P) | **X** | | |
| Record any baseline diagnostic imaging | | **X** | |
| ICE imaging with VeriSight | | **X** | |
| Image grading | | **X** | |
| Procedural workflow and details | | **X** | |
| Adverse device effects related to VeriSight | | **X** | **X** |
| Registry exit | | | **X** |
| **Usability assessment** | **Aggregate input** | | |
| Physical attributes of catheter | After 1st patient enrolled | After 10th patient enrolled | After last patient enrolled |
| Physician and staff survey | After 1st patient enrolled | After 10th patient enrolled | After last patient enrolled |
| *up to 30 days prior to index | | | |

Below are the brief study procedure steps.

- Subjects are evaluated for eligibility based on the inclusion and exclusion criteria
- Record demographics of subjects: age, gender, height, weight, ethnicity/race (if applicable)
- Record relevant medical and surgical histories
- The subjects will be imaged using the VeriSight device according to the routine workflows
- Relevant imaging for each procedural steps will be recorded.
- The Investigator will grade the imaging recorded
- The corresponding clinical information and information about the use of device and system, including device deficiencies and safety-related adverse device effects related to VeriSight, will be recorded by the Investigator in the CRF
- The registry examinations including all collected de-identified images will be transferred to Philips

- After the completion of the procedure, subject are dismissed from the registry after monitoring for post-procedure adverse device effects either at discharge or ≤48 hrs post-procedure, whichever is sooner.

## 6.3. Screening (up to 30 days prior to index procedure)

This visit consists of screening and enrollment activities and may also include any pre-procedural planning in accordance with standard practice and local institution protocol. Subjects will be recruited from a pool of regular patient population that are eligible for percutaneous cardiac intervention procedure. This visit will consist of the following procedures.

**Assessment of Eligibility**

The Investigator will assess the subject's eligibility for this study per the inclusion and exclusion criteria listed in **Section 4.0** and will document the outcome of the eligibility assessment. If the subject qualifies, he or she will then undergo the registry-related imaging examinations described below. The investigator shall screen the patient and deem them suitable for conducting the procedure under conscious sedation.

**Informed Consent**

Study participation is voluntary. The potential subject if deemed eligible for the study based on the known information in the medical records, will be informed about the study and asked to participate. He/she will be given the most current IRB-approved Informed Consent Form (ICF) to read. Ample time will be provided for review and an opportunity to ask questions about the study. If the subject agrees to participate, they will sign the ICF and be given a copy of the signed document for their records. All components of the consent process will be documented in source documents. A detailed description of the consent process is provided in **Section 9.2**.

**Medical History and Demographics**

Standard subject demographics (e.g. age, gender, race, ethnicity, height, weight), relevant medical and surgical histories will be recorded. The assessments will be performed following the institutions' standard protocols and the results recorded on the appropriate subject case report forms. Any pertinent diagnostic imaging as it relates to the index procedure (e.g. CT, MRI, TTE) if performed per standard institutional protocol will be documented.

**New information about the study**

As the subject will exit registry at discharge, or ≤48 hrs post-procedure, whichever is earlier, it is unlikely that any new information will influence a subject's decision to participate. However, as ultrasound technology is constantly evolving it may be necessary from time to time to update the ICF so the subject may be informed of any new information. This will be done in conjunction with IRB approval, as appropriate.

## 6.4. Index Procedure

Subjects enrolled in the registry will undergo imaging using the VeriSight catheter at the time of the index procedure. This visit will consist of the following procedures.

The indication for ICE imaging and the types of procedures that utilized VeriSight will be documented. Patient management and treatment decisions are at the discretion of the care team per routine standard clinical practice. The model of VeriSight and the venous access approach are to be per the investigator's discretion. Confirmation of the delivery of the VeriSight catheter to reach the target intracardiac anatomical position including the number of attempts depending on the procedure type will be recorded. The sustained operation of the catheter will be monitored throughout the case and recorded as part of the device technical complications including device malfunction/ deficiency and any additional procedural delays/ disruption when using VeriSight for various procedures.

Clinical data on the imaging views obtained during the procedure will be obtained. The angle of the views (0, 45, 90, 135 sweep) including axis, and the use of xPlane, iRotate, 2D or 3D, TrueVue, MultiVue modalities are left to the investigator's discretion. The anatomical landmarks for image quality assessment depend on the procedure type. Image acquisitions of cardiac structures with VeriSight shall be recorded depending on the procedure type.

The sequence of imaging for each procedure type are according to physician workflow preference. The method and access to the left atrium including transseptal puncture depending on the procedure type are to be per the investigator's discretion. For each procedure labeled screenshots and respective measurements will be documented for key procedural steps. The number of great vessels and chambers imaged will be documented. Sizing relevant anatomy for intervention or device placement and visualization, guidance and verification for delivery and/or placement of interventional device will also be noted in the case report form. Imaging with VeriSight for visualization and evaluation of intra-procedural complications and hemodynamic monitoring will be captured. Images obtained from different procedure types will be reviewed by the participating investigators at regular intervals as part of ongoing development of standard of care workflow with VeriSight ICE imaging.

The image quality will be scored by the investigator using a four point ordinal Likert-type rating scale with the following response options: excellent, good, acceptable, unacceptable, and unusable. The image quality evaluation is an overall assessment of the quality of images of each anatomical position/ utilization for the procedure types.
During the procedure, the total length of the procedure (wheels in/out time, and skin to skin time), fluoroscopy time, total contrast volume, and fluoroscopic dosage will be documented. The ability to image from the right side of the heart for a left sided intervention for certain procedure types will be noted in the case report form. Change in management (if any) including both patient and

procedural aspects as a result of information provided by imaging with VeriSight will be documented.

Any additional standard of care procedural imaging used in addition to VeriSight, or as conversion, including TTE, TEE, fluro, etc. or avoidance of TEE procedure will be collected and pertinent images maintained in the sponsor's image library. Labeled screenshots of side by side VeriSight and TEE images when utilized in the same procedure may be documented for educational purposes. The duration and type of anesthesia will be documented. Freedom from general anesthesia will be captured. Indications for conversion to general anesthesia if using conscious sedation related to patient discomfort, hemodynamic instability, inability to maintain a protected airway, or inadequate cardiac imaging with VeriSight are at the discretion of the investigators.

*Note:* The total amount of contrast administered to a subject shall be limited per the labelling recommendations of the contrast agent and at the discretion of the investigator.

*Safety Evaluation*
Device related peri-procedural complication and outcomes attributed to VeriSight will be recorded. Adverse device effects related to the VeriSight catheter during the procedure will be documented appropriately in the case report form. The subcategories are defined per ISO14155:2011, as described in **Section 7.0**.

## 6.5. Post-procedure

Patients will be followed up until discharge or until ≤48 hours post procedure whichever is earlier. Adverse device effects related with the use of the VeriSight device will be captured in the case report form during this visit as defined in **Section 7.0**.

## 6.6. Usability Assessments during Index Procedure

**Physical attributes of Catheter evaluation method**
The evaluation of the physical attributes of the catheter such as catheter handling characteristics, EPIQ system navigation, and imaging modality will be assessed at specific enrollment stages at each participating site: after first patient enrolled, 10$^{th}$ patient enrolled, and last patient enrolled. Evaluation of response will be captured via a scoring scale (poor, average, good, excellent) based on experience acquired with VeriSight in this registry.

The participating investigator will evaluate the same physical characteristics of the catheter, ultrasound system navigation, and imaging modality based on their own clinical experiences of imaging that would have been generally used during the procedure. This rating score is defined as inferior, better, superior and will be gathered at first enrollment, 10$^{th}$ enrollment, and last enrollment at each participating site.

**Physician and staff survey**

Physician and staff evaluations regarding Philips ICE will be collected at first enrollment, 10th enrollment, and last enrollment at each participating site. The survey will consist of a series of claim statements ("stimuli"), each of which will be presented alongside a five-point ordinal Likert-type rating scale that will be evaluated by the participating investigator using the knowledge and experience acquired during the registry, and additionally individual clinical experience working with other ICE products or imaging modalities (e.g., TEE).

## 7. SAFETY EVENTS: DEFINITIONS AND REPORTING

### 7.1. Definition

Adverse Event (AE) - any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects during registry participation, which does not necessarily have a causal relationship with the VeriSight device or procedures.

Serious Adverse Events (SAE) - defined as an AE that:

- Led to Death
- Are Life-threatening
- Led to Hospitalization (in-patient or prolonged)
- Resulted in Disability or Permanent Damage
- Led to Fetal Distress, Fetal Death or Congenital Anomaly/Birth Defect
- Required Intervention to Prevent Permanent Impairment or Damage

NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered an SAE.

Adverse Device Event (ADE) - an AE related to the use of a medical device. This definition includes AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the VeriSight catheter. This definition also includes any event resulting from use error or from intentional misuse of the medical device.

Serious Adverse Device Effect (SADE) - adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event

Unanticipated Serious Adverse Device Effect (USADE) - serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report

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

Device Deficiency - inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance such as malfunctions, misuse or use errors and inadequate labeling

### 7.2. Device Malfunction or Use Errors

Device malfunctions or use errors will be recorded and evaluated for possible untoward effects on the subject. For the purposes of this study, a device malfunction is defined as a failure of the device to perform its intended function when used in accordance with the Instructions for Use (IFU). If a VerSight device malfunction results in an adverse experience for the subject, this adverse experience should be considered an adverse device effect and recorded on the appropriate CRF. A device malfunction by itself should not be reported as ADE unless it leads to the new medical condition or worsening of pre-existing condition. If a VeriSight device malfunction occurs in this registry, the site should follow standard commercial procedures.

### 7.3. Reporting Requirements

Philips VeriSight catheter used in this registry for imaging during percutaneous cardiac interventional procedures is cleared for commercial use by the FDA. Therefore, the use described in this protocol constitutes a standard clinical practice use. Information related to contraindications, adverse effects, warnings and precautions are included in the device instructions for use.

Reporting for this registry will be limited to peri-procedural (at discharge or ≤ 48H) ADEs, SADEs and USADEs (per the above definition) occurring while performing the index procedure with the guidance of Philips VeriSight. VeriSight may be used in the detection/monitoring of adverse events related to the procedure (i.e., post cardiac procedure thrombus recognition) during the procedure.

Adverse device effects related to the device should also be reported to the Study Medical Monitor (see below). All adverse device effects must be reported to Philips IGTD as soon as possible after first awareness of the event; every attempt must be made to report such events to Philips IGTD within 24 hours of first awareness of the event.

Study Medical Monitor contact information for adverse device effects reporting:

**Peter Angelopoulos, M.D**
**Medical Monitor**
Philips Image Guided Therapy Devices
**Mobile:** +1 (516) 967-6261
**Email:** peter.angelopoulos@philips.com

The Investigator is responsible for reporting the adverse device event to the approving IRB as dictated by the guidelines defined by the IRB and, if applicable, regulatory authorities. The investigator is required to submit to the sponsor and to the reviewing IRB, a report of any unanticipated adverse device effects occurring during an investigation as soon as possible, but in

no event later than 10 working days after the investigator first learns of the effect. Additionally, the Investigator will report to regulatory authorities as required by national regulations.

Contact information for complaint reporting is: **IGTD.CustomerInquiry@philips.com**. The sites should follow standard commercial procedures for reporting device complaints. Device deficiencies are NOT to be reported as ADEs. However, if there is an ADE that results from a device deficiency, that specific event would be recorded on the appropriate case report form.

## 7.4. Severity of Event

The following guidelines will be used to assess event severity:

- **Mild** – Events require minimal or no treatment and do not interfere with the subjects daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a subject's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".)

## 7.5. Relationship to Study Device

Relationship to registry device administration will be determined as follows:

- Possible Relationship: An AE that follows a reasonable temporal sequence with use of the VeriSight device and follows a known response pattern to the study treatment but could have been produced by the subject's clinical state or by other therapies.
- Probable Relationship: An AE that follows a reasonable temporal sequence with use of the VeriSight device; follows a known response pattern to the study treatment; and cannot be reasonably explained by the known characteristics of the subject's clinical state or by other therapies.
- Definite Relationship: An AE that follows a plausible temporal sequence with use of the VeriSight device and follows a known response pattern to the study treatment. The reaction cannot be reasonably explained by the known characteristics of the subject's clinical state or other modes of therapy administered to the subject.
- Unknown/Impossible to Determine: Given the information available, sequence and timing of events, it is unknown or impossible to determine the relationship of the AE with the VeriSight device.

## 7.6. Expectedness

The Principal Investigator will be responsible for determining whether an adverse device event is expected or unexpected. An ADE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the device in this registry. Please refer to the instructions for use for a listing of adverse effects.

### 7.7. Time Period and Frequency for Event Assessment and Follow-Up

Only ADEs will be collected starting from the time the subject is enrolled until the time of discharge which is less than or equal to 48 hours post procedure. Events will be followed until resolution if possible.

Events will be reported via the electronic case report form and submitted to the Sponsor.

Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study device (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event.

Any medical condition that is present at the time that the subject is screened will be considered as baseline and not reported as an AE. However, if the study subject's condition deteriorates at any time during the study due to the use of the study device, it will be recorded as an ADE.

## 8. DATA ANALYSIS AND STATISTICAL CONSIDERATION

### 8.1. Sample Size Determination

The sample size of up to 200 subjects was selected based on a goal for the registry to be able to obtain performance and safety associated with use of the VeriSight catheter. This study is observational. Outcomes remain in the exploratory phase, and therefore hypotheses will not be created. Instead, the study will serve to monitor, measure, and evaluate outcomes as a basis for future research. This sample size will provide the opportunity to make proper statistical inference for hypothesis generation. Due to the various procedure types available for use with VeriSight, up to 200 subjects could be enrolled in order to analyze the secondary endpoints by case type.

### 8.2. Populations for Analyses

All subjects age 18 and older that are scheduled for and will undergo a planned cardiac interventional percutaneous procedure in which the guidance of ICE is indicated, eligible and willing to sign an informed consent without meeting any of the exclusion criteria set and meeting all the inclusion criteria set forth in the protocol will be included in the population for analyses. Those who sign consent but do not undergo a cardiac procedure utilizing the Philips ICE catheter will be excluded from the analyses (screen failures).

### 8.3. Statistical Analyses

No formal statistical hypothesis test is planned and the primary and secondary endpoints will be presented as descriptive statistics only. An interim analysis will be conducted following 100$^{th}$ patient enrollment to monitor, measure, and review performance and safety measures prior to determination of further enrollment in the registry.

Statistical analyses will be done on the real-world, all-comer population and presented as descriptive statistics and 95% confidence intervals. Subject data from all clinical sites are intended to be pooled for analysis to broaden demographic representation. However, it is possible that sub-analyses may be conducted in a population stratified by procedure characteristics and baseline characteristics.

# 9. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

## 9.1. Regulatory, Ethical, and Study Oversight Considerations

This registry will be conducted in accordance with the relevant parts of the Code of Federal Regulations (21 CFR 11, 50, 56), ISO 14155:2011, the ICH-E6 Guidelines for GCP, the Declaration of Helsinki (2013). Additional state and local regulations will be followed when applicable.

Investigators and sites are required to have the protocol, informed consent forms, and any other materials related to this study plan approved by the IRB. Any additional requirements imposed by the IRB shall be followed. Any amendments to the protocol must be reviewed and approved by the study Sponsor, and subsequently, by the designated IRB, according to the approval committee's requirements. Prior to enrollment, the Sponsor or designee will review the written approvals for completeness, including the required elements of the consent form, and the Sponsor will provide protocol and study administration training. The continued eligibility for participation by an investigator and the institution requires maintenance of all approvals (e.g. annual reviews, amendment reviews).

Each subject will provide written, informed consent as outlined in **Section 9.2** prior to any study activities taking place.

## 9.2. Informed Consent Process, Procedures, and Documentation

In obtaining and documenting informed consent, the investigator must comply with applicable regulatory requirements (e.g., 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56) and should adhere to ICH GCP. Prior to the beginning of the registry, the investigator should have the IRB's written approval for the protocol and the written informed consent form(s), ICF and any other written information to be provided to the subjects. The consent form describes in detail the study, procedures, and risks. If new information becomes available during the course of the study that is relevant to the safety or well-being of the subjects, the consent form may be updated and presented to the subjects for review and consideration of continued participation. Consent forms will be provided to subjects in their native language and will be translated from the IRB approved version.

Study participation is voluntary. Potential subjects, and/or their legal representatives if subject is unable to consent on their own behalf, are given the most current IRB-approved consent form to read. They shall be provided ample time for review and an opportunity to ask questions about the study. If they agree to participate, they shall sign the consent form and be given a copy of the signed document for their records, along with any additional subject information. Each of these

actions/steps shall be documented. Only after Informed Consent has been obtained, may the remaining study procedures begin.

Patients scheduled for percutaneous cardiac intervention procedure and not contraindicated for ICE use will be asked to provide consent to use their data. Patients who agree to study participation must sign an IRB-approved ICF. Subjects will be informed that their participation in this study is voluntary and they may refuse to participate or discontinue from the study at any time. Subjects may withdraw from the study at their own request or at the request of their legally acceptable representative. The sponsor must be informed in each withdrawal case. The reason for withdrawal must be recorded in the eCRF and in the patient medical record.

## 9.3. Registry Discontinuation and Closure

When a registry is prematurely terminated, refer to **Section 4.7**, for handling of enrolled study subjects.

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the Sponsor to the study Principal Investigators. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study subjects, the Institutional Review Board (IRB), and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to subjects
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the Sponsor, IRB and/or Food and Drug Administration (FDA).)

## 9.4. Confidentiality and Privacy

This registry protocol, its associated methodologies, study devices, study-generated data, and the data management system contain confidential and proprietary information. Subject confidentiality will be maintained according to the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Release of such information outside the scope of planned study operation is prohibited. All federal and local laws regarding protection of patient confidentiality will be followed, as well as any additional site-specific requirements that may be required. Personal Health Information (PHI) will be acquired during the consenting process of the subject and from the medical records. All data

will be de-identified at each site before being entered into EDC. Individual subjects and their research data will be identified by a unique study identification number. The protocol, documentation, data, and all other information generated will be held in strict confidence to the extent allowed by law, including PHI. At the end of the study, all study databases will be de-identified and archived by the Sponsor.

The study monitor, Sponsor and other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), or regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the subjects in this study. The clinical study site will permit access to such records.

The study subject's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or Sponsor requirements.

## 9.5. Safety Oversight

Due to the nature of this observational real world registry, a safety oversight/data safety monitoring committee is not planned for this post-market registry.

## 9.6. Clinical Monitoring

This study will be monitored using a risk-based monitoring approach, consistent with the FDA guidance Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring (2013) and Philips clinical study monitoring procedures. Registry monitoring is the responsibility of the Sponsor. The Sponsor or designee will monitor the study throughout its duration. Monitoring will ensure that documents used to originally record subject data (source documents) are maintained, and to verify that transcribed data are accurately reflected on the study electronic Case Report Forms (eCRFs). Monitoring visits will be scheduled based on the enrollment rate at each site, duration of the registry, compliance, and any known or suspected inconsistency in data that requires investigation. Monitoring visits may be conducted onsite and/or remotely (e.g., virtual visit), as necessary.

The sponsor may terminate investigator and site participation in the registry if there is evidence of an investigator's failure to maintain adequate clinical standards or evidence of an Investigator or staff's failure to comply with the protocol. Notification of suspension or termination will occur no later than 5 working days after the Sponsor makes the determination. In the event of registry suspension or termination, the Sponsor will send a report outlining the circumstances to the reviewing IRB and the appropriate regulatory agencies, and to all participating investigators.

The registry may also be suspended or discontinued early if there is an observation of serious adverse events presenting an unreasonable risk to the registry subjects or inadequate subject enrollment.

The sponsor may delegate some of the above monitoring activities to appropriately qualified contract personnel.

## 9.7. Quality Assurance and Quality Control

Each site, both clinical and laboratory, should have SOPs for quality management that describe:

- How data will be evaluated for compliance with the protocol, ethical standards, regulatory compliance, and accuracy in relation to source documents.
- The documents to be reviewed (e.g., CRFs, clinic notes, product accountability records, specimen tracking logs, questionnaires, audio or video recordings), who is responsible, and the frequency for reviews.
- Who will be responsible for addressing QA issues (e.g., correcting procedures that are not in compliance with protocol) and QC issues (e.g., correcting errors in data entry).
- Staff training methods and how such training will be tracked.
- If applicable, calibration exercises conducted prior to and during the study to train examiners and maintain acceptable intra- and inter-examiner agreement.

Regular monitoring and an independent audit, if conducted, must be performed according to ICH GCP. See also **Section 9.6.**

Each clinical site will perform internal quality management of study conduct, data collection, documentation and completion. An individualized quality management plan will be developed to describe a site's quality management.

Quality control (QC) procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

Following written Standard Operating Procedures (SOPs), the monitors will verify that the clinical trial is conducted and data are generated and biological specimens are collected, documented (recorded), and reported in compliance with the protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

The investigational site will provide direct access to all trial related source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

## 9.8. Data Collection and Management Responsibilities

This registry will use an electronic data capture system, DataTrak EDC that is a 21 CFR Part 11-compliant data capture system provided by the Sponsor. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents. Limited access will be granted to only those working directly on the study and with study subjects. It is expected that electronic case report forms be completed no later than 5 working days from the time of data collection and submitted to the Sponsor for review. This includes the eCRF along with imaging obtained as part of the study. Data queries should be resolved within a timely manner but no later than 30 days of being issued.

Access to the EDC system will be protected by login identification and password. The Sponsor will train delegated Site personnel on procedures for data entry into the web-based system. Following training, delegated staff will be provided ID codes and passwords unique to each team member's delegated study role. They will be trained on Philips guidelines for maintenance of electronic ID codes and passwords. A staff member's ID code/password will never be shared or used by another staff member, in any circumstance. If prior training has already been delivered for other Philips-sponsored studies of similar design, this training may be reinforced via teleconference prior to study commencement as appropriate.

Source data are all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the registry. Electronic source data are data initially recorded in electronic form. Hardcopies of the study visit worksheets will be provided for use as source document worksheets for recording data for each subject enrolled in the registry. Data recorded in the electronic case report form (eCRF) derived from source documents should be consistent with the data recorded on the source documents. It is acceptable to use worksheets that mirror the eCRFs as source documents. Physician surveys and imaging collection worksheets will be provided to the site to capture data that may not otherwise be found in typical source documents.

It is not acceptable for the CRF to be the only record of a subject's inclusion in the study. Registry participation should be captured in a subject's medical record. This is to ensure that anyone who would access the subject's medical record has adequate knowledge that the subject is participating in the registry.

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

## 9.9. Data Handling and Record Keeping

This study will be performed using an electronic data capture (EDC) system with password protection. The investigator and study site staff will receive training and support on the use of the EDC system and will be granted specific user privileges. All eCRF data are to be completed by the investigator, study coordinator, or other designated site personnel. The investigator will perform a final review and sign-off at designated times (e.g. registry exit).

Images acquired by the EPIQ console will be downloaded and anonymized to a removable drive or can be downloaded from PACS after anonymization, prior to transfer of images to DataTrak following appropriate privacy protections. All images will be saved in Digital Imaging and Communication in Medicine (DICOM) format and transferred to a DICOM server. For any representative images, loops and/or 3D volumes that are collected as part of the scan, subject names and identifiers will be removed. The site may provide to the Sponsor any additional de-identified baseline, procedural images that are performed as part of the index procedure (TEE, TTE, CT, MRI, fluro etc.). De-identified images, loops, and/or 3D volumes may be used for internal/external training, marketing brochures, and promotions.

Completeness of data entry will be monitored against the medical record by a monitor during the onsite and/or remote data reviews against the information in the subject's medical records. The clinical database will be a closed system, allowing for tracking all the data elements and any changes made.
Sponsor will provide the investigational site with supplies for setting up the study files. Essential documents are listed below:

- Signed Protocol and amendments;
- Signed Investigator Agreement;
- IRB Committee approval letters, consent forms and correspondence;
- Investigator and Sponsor Reports;
- Relevant correspondence between the Investigator and Sponsor;
- Signed Informed Consent Forms (site files only);
- Notification to Sponsor and IRB of Serious Adverse Events;
- Administrative Tracking Logs (Monitoring Visits, Training Logs, etc.).

## 9.10. Study Records Retention

Study documents should be retained for a minimum of 2 years after the conclusion of the study (all patients at all sites have concluded participation and the Sponsor has indicated the registry is completed/closed out) or longer if institution requirements dictate. . No records will be destroyed without the written consent of the sponsor. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

## 9.11. Protocol Deviations

A protocol deviation is defined as an event where the clinical Investigator or site personnel deviate from the registry protocol or study procedures. It is the Investigator's responsibility to ensure that there are no deviations from the protocol without prior notification and approval of the Sponsor or Sponsor's designee and in full compliance with all established procedures and conditions of the reviewing IRB.

The Investigator may deviate from the protocol without prior written approval from the Sponsor or Sponsor's designee in cases of medical emergencies, when the deviation is necessary to eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify the Sponsor or Sponsor's designee immediately by phone or electronic communication, notify the reviewing IRB, and confirm notification to the Sponsor or designee in writing. Prior deviation approval is generally not expected in situations where unforeseen circumstances are beyond the Investigator's control, for example, the subject was not available for a scheduled follow-up office visit. These events, although outside the Investigator's control, are still required to be reported on the appropriate protocol deviation form in order to ensure that all deviations from the standard subject population are adequately documented and reported. The Investigator will inform the Sponsor or Sponsor's designee of all deviations, and the reviewing IRB of all protocol deviations as per the IRB requirements for this study. The Investigator shall document all protocol deviations on the electronic case report form and submit to the Sponsor for review.

The occurrence of protocol deviations will be monitored by the Sponsor or Sponsor's designee for evaluation of Investigator compliance to the Protocol, Good Clinical Practices, and regulatory requirements.

## 9.12. Publication and Data Sharing Policy

The results of this registry may be submitted for publication to clinical or medical journals or to congresses or conferences for podium presentations. The rights for publication of results from this registry remain with Philips. The Investigator must request permission from Philips prior to initiating any publication and received in writing. Review and approval of any data, abstract or manuscript is required. Philips reserves the right to delay publication to review the presentation of study methodology, data collection, data analysis, interpretation of data, proprietary information or patented technology. A request for delay and the reason(s) shall be communicated by Philips to the Investigator in writing.

The study will be registered on ClinicalTrials.gov and the NCT number will be noted in the Sponsor study files. The registry results will be used for publications and therefore will be posted on the website.

## 9.13. Conflict of Interest Policy

The independence of this registry from any actual or perceived influence, such as by the medical device industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The Institute or Center (IC) may have established policies and procedures for all study group members to disclose all conflicts of interest and may have established a mechanism for the management of all reported dualities of interest. Each investigator participating in the research will be asked to complete a financial disclosure form, submit a copy to the Sponsor, and notify the Sponsor when there is a change in such disclosures during the course of the study and one year following investigator discontinuation of participation. Investigators should continue to follow their institutional policies regarding the reporting of conflicts of interest in addition to any Sponsor requirements.

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## 11. INVESTIGATOR'S STATEMENT

I agree to conduct the trial as outlined in this registry protocol in accordance with the Sponsor's guidelines, Good Clinical Practices, the Declaration of Helskinki, and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB. The Sponsor's guidelines include, but are not limited to:

- Provide Philips with current curriculum vitae including a statement regarding relevant experience.
- Provide accurate financial disclosure information to allow Philips to make an accurate disclosure statement as required under 21 CFR, Part 54 for the course of the investigation and for up to one year after its completion
- Provide supervision of all testing of the device involving human subjects.
- If applicable, provide Philips with information regarding past investigations or other research that was terminated, including an explanation of the circumstances that led to the termination.
- Permission to allow Philips and/or regulatory agencies to inspect study facilities and pertinent records at reasonable times and in a reasonable manner that ensures subject confidentiality. If this study is to be inspected by a regulatory agency, Philips is to be notified as soon as possible.
- Submission of the proposed clinical investigation including the protocol and the consent form to an IRB for approval and the acquisition of written approval for each subject ensuring that the requirements for obtaining informed consent are obtained prior to the use of any test articles.
- Submission of any proposed change in or significant deviation from the protocol to the IRB using a signed formal amendment document prepared by the Sponsor. Any proposed changes or deviations from the protocol require that the informed consent also reflects such changes or deviations and that the revised informed consent be approved by an IRB.
- Documentation and explanation of individual protocol deviations and violations are captured with explanations as indicated.
- Submission of reports of Adverse Events to the Sponsor and IRB as outlined in the protocol.
- Submission of timely progress reports to the IRB/EC and Sponsor at appropriate intervals on a schedule determined by the IRB or Sponsor, as indicated.
- Record keeping: the Investigator shall maintain adequate and accurate records designed to record completion of all study procedures, related observations and other key data (such as safety, compliance and product accountability) pertinent to the investigation on each subject enrolled. The investigator must maintain these records for a period as specified by Philips following completion of the study report.

I agree that all information provided to me by the Sponsor including pre-clinical data, protocols, electronic databases, CRFs, and verbal and written information shall be kept strictly confidential and confined to the clinical personnel involved in conduct of the trial. It is recognized that this information may be related in confidence to the IRB. I also understand that reports or information about the trial or its progress shall not be provided to anyone not involved in the trial other than the Sponsor or other legally constituted authority.

_____ _____

Principal Investigator's Signature Date

_____

Principal Investigator's Printed Name