Abbott	Clinical Investigation Plan Cover Page [redacted]

NCT Number: NCT04904809
Perclose Multi-Access DUS Trial
Assess the Safety and Performance of the Perclose ProGlide® Suture-Mediated Closure System and the Perclose Prostyle Suture-Mediated Closure and Repair System in Managing Multiple Venous Access Sites
Study Document No: [redacted]
Version [redacted]
Date: 30-March-2022

Sponsor: Abbott [redacted]

[redacted]

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[redacted]

Perclose Multi-Access DUS Trial

Assess the Safety and Performance of the Perclose ProGlide® Suture-Mediated Closure System and the Perclose Prostyle Suture-Mediated Closure and Repair System in Managing Multiple Venous Access Sites (Evaluation by Duplex Ultrasound)

Version Number	[redacted]
Date	[redacted]
Study Principal Co-Investigator:	[redacted]
Planned Number of Sites and Region(s)	2 in the US
Clinical Investigation Type	Prospective, single arm, US multi-center, descriptive clinical study
Abbott Medical Expert	[redacted] Chief Medical Officer
Sponsor	Abbott [redacted]
Electronic Data Capture Software	Oracle Clinical
Core Laboratories	[redacted]
CEC	[redacted]
Protocol Author of Current Version	[redacted]

[redacted]

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COMPLIANCE STATEMENT:

This clinical investigation will be conducted in accordance with this Clinical Investigation Plan (CIP), the Declaration of Helsinki and the applicable regulatory requirements (such as, 21 CFR Part 50, 21 CFR Part 56,21 CFR Part 812, 21 CFR Part 54, and 21 CFR Part 11). The conduct of the clinical investigation will be approved by the Food and Drug Administration (FDA) and the appropriate Institutional Review Board (IRB) of the respective investigational site.

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1.0 INTRODUCTION

1.1 Background and Rationale

1.1.1 Background

The Perclose ProGlide Suture-Mediated Closure System and the Perclose ProStyle Suture-Mediated Closure and Repair System (hereinafter referred to as Perclose SMC) is indicated for the percutaneous delivery of a suture for closing the common femoral artery and vein access sites of patients who have undergone diagnosis or interventional catheterization procedures. The devices can be used for access sites in the common femoral vein, 5F to 24 F sheaths, and the use of sheath sizes greater than 8F require at least two devices and the pre-close technique.

The vein indication was approved from the ProGlide Cohort of the Realism Clinical Trial. The prospectively planned retrospective analysis included patients in whom ProGlide SMC was used as the primary method for large bore venous access-site closure during the MitraClip procedure with a 24 F vascular sheath.

The MitraClip procedure requires single vein access with a 24 F vascular sheath. There are several interventional procedures using multiple vein access, such as atrial septal defect (ASD) closure and cardiac ablation.

The use of multiple catheters (sheaths) within the same vein is the standard practice of atrial septal defect (ASD) closure. Mahadevan et al. evaluated 65 ASD patients who underwent femoral vein closures with the ProGlide SMC and concluded that two ProGlide devices can be safely used at two different access sites in the same vein[1]. Hamid et al. reported the safety and effectiveness of vein closure, including 107 ASD closures with ProGlide [2]. Cardiac ablation is a procedure that can correct arrhythmias. Cardiac ablation uses multiple catheters for ablation, imaging (echo), and diagnosis (mapping), also pacing when appropriate. There is no standard practice in the selection of the access site of these catheters. Some prefer two access vessels (such as two sheaths from the left femoral vein and two from the right femoral vein), and some use a single vessel for all sheaths. When vein access is used for ablation (such as treatment of atrial fibrillation), manual compression is the most widely used method to achieve hemostasis after the sheath removal. However, manual compression is known to have frequent vessel complications and require more time for hemostasis and mobilization compared to vascular closure devices.

In these procedures, manual compression (MC) is the standard of care, and figure of 8 (Fo8) suturing technique is also used. Each sheath size of these procedures (4-15F) is smaller than the 24F sheath size used during the MitraClip procedure.

Abbott is aware that the current Instructions for Use contains the warning: "do not use the ProGlide SMC if there are multiple punctures since such punctures may result in a hematoma or retroperitoneal bleed". However, this warning is intended for multiple vessel punctures in a

single access site, not for multiple access sites in a single vein. Abbott believes vessel closure in multiple site access can be performed safely.

Abbott proposed to use 3 Abbott-funded real-world Investigator Sponsored Studies to evaluate the safety and effectiveness of the Perclose SMC for closure of multiple site access procedures such as cardiac ablation. The FDA accepted Abbott's proposal but also requested prospective duplex ultrasound (DUS) "sub-study" in which femoral DUS exams are performed in subjects undergoing atrial fibrillation or atrial flutter ablation procedures involving multiple femoral venous access sites per leg that are closed with the Perclose SMC to confirm the safety of the Perclose SMC in asymptomatic subjects.

1.1.2 Rationale for Conducting this Clinical Investigation

Femoral DUS is not routinely done in the standard practice of medicine and is typically in ablation procedures and other cardiovascular interventional procedures and only done when access site-related complications are visible (such as hematomas) and/or symptomatic. However, asymptomatic vascular complications are not always benign or insignificant. Therefore, this study will assess access site-related complications, including asymptomatic or non-visible, associated with multiple access site closures with the Perclose SMC by scheduled femoral DUS at discharge and at 30 days.

2.0 CLINICAL INVESTIGATION OVERVIEW

2.1 Clinical Investigation Objective

The objective of the study is to evaluate the safety of multiple access site closure in a single vein with the Perclose SMC by scheduled DUS at discharge and at 30 days (if vascular complications observed at discharge) in asymptomatic or non-visible subjects.

2.2 Devices Used in the Clinical Investigation

2.2.1 Name of the Device(s) Under Investigation

Devices used in this study are the commercially available Perclose ProGlide® Suture-Mediated Closure System and the Perclose Prostyle Suture-Mediated Closure and Repair System (Perclose SMC). The Perclose SMC is designed to deliver a single monofilament polypropylene suture to close femoral vessel access sites following diagnostic or interventional catheterization procedures.

Abbott will cover the cost of the study device/s for subjects who participate in the study. The study is an investigation using market released devices and device accountability is not required for this investigation.

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2.2.2 Indication for Use

The Perclose SMC in this study will be used for **multiple access site closures in a single vein** in the ablation procedure. Either pre-close or post-close technique can be used per the site standard practice. The number of Perclose SMC to be used per access site should also be per site standard practice.

2.2.3 Description of the Device(s) Under Investigation

The Perclose SMC is market-released. The U.S. indication for use is the percutaneous delivery of suture for closing the common femoral artery and vein access site of patients who have undergone diagnostic or interventional catheterization procedures. The devices are under evaluation in this study for **multiple access site closure in a single vein**. The closure methodology for each access site is the same with the single access site closure. Please refer the Instruction for Use for more details.

3.0 CLINICAL INVESTIGATION DESIGN

This study is the prospective, single-arm, US multi-center, descriptive study to evaluate the safety of multiple access site closure in a single vein with the Perclose SMC. A total of 35 subjects will be registered at 2 US investigational sites. All subjects must have femoral DUS at discharge and at a 30-day follow-up visit (if any access site-related vascular complications (either symptomatic/visible or asymptomatic/nonvisible), nerve injury, or infection at discharge, by either the investigator or the core laboratory). All DUS images are assessed by the independent DUS core laboratory.

3.1 Clinical Investigation Procedures and Follow-up Schedule

The study flowchart is shown in **Figure 3-1**. A subject who is planned to have an ablation procedure and satisfies the eligibility criteria will be registered in this trial. Written informed consent must be obtained prior to the registration.

The ablation procedure and access site closure should be done per the site's standard practice. If the pre-close technique is used, the subject is considered to be registered in this study at the insertion of the 1st Perclose SMC into the body (in the case that the ablation procedure is not performed after pre-close by the Perclose, then the subject will be de-registered). If only the post-close technique is used, the subject is considered to be registered in this study at the insertion of the 1st Perclose SMC into the body after the ablation procedure.

3.2 Measures Taken to Avoid and Minimize Bias

The independent DUS core laboratory is used to assess DUS-detected vascular complications to avoid inter-site bias.

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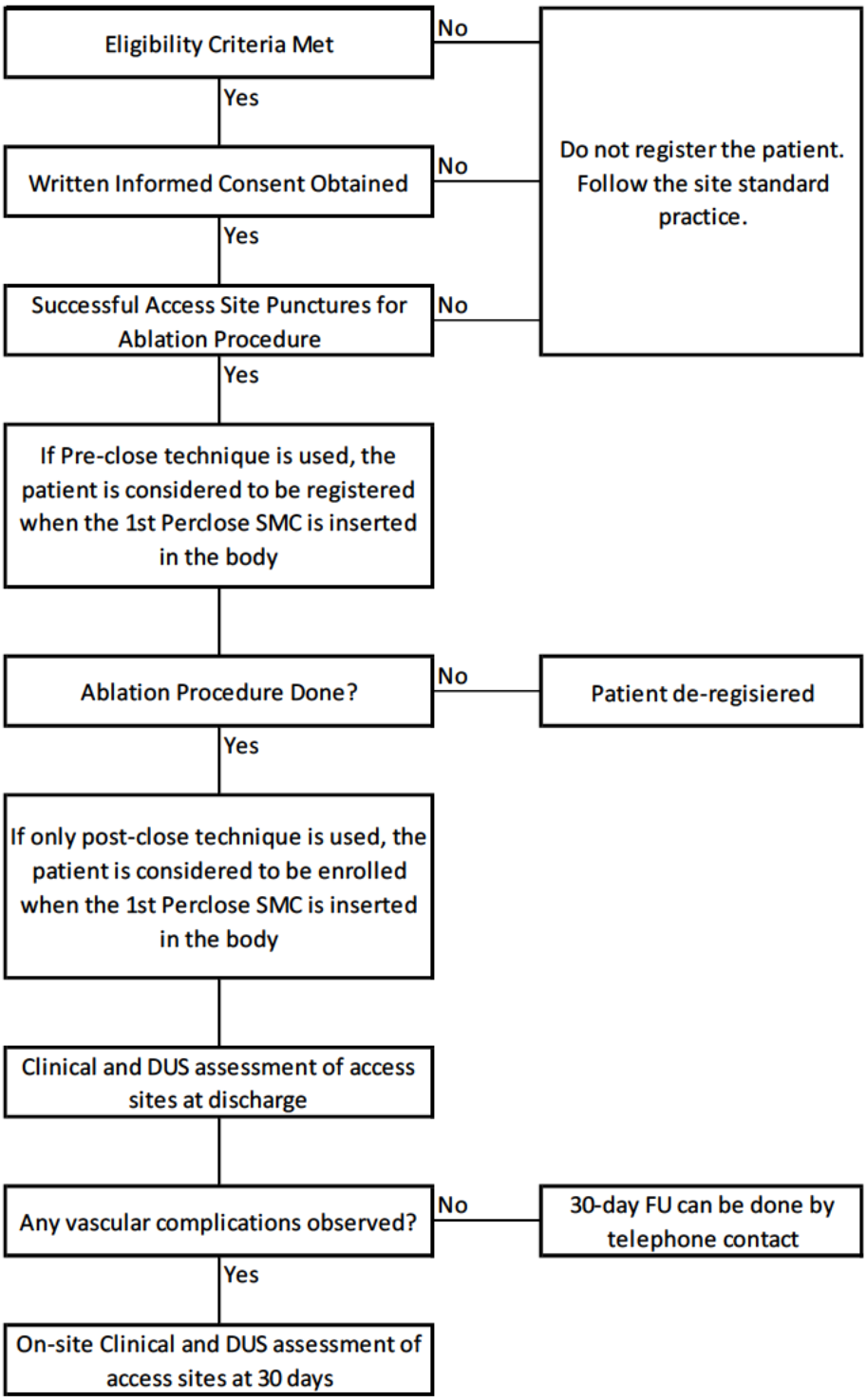

Figure 3-1: Study Flowchart

3.3 Early Termination of the Clinical Investigation

No formal statistical rule for early termination of the trial is defined. However, the Sponsor reserves the right to discontinue the study at any stage or reduce the follow-up period with suitable written notice to the investigator. Should the clinical investigation be discontinued by the Sponsor, the Principal Investigator or authorized designee will promptly inform the registered subjects at his/her site, if appropriate, and subjects will be followed per routine hospital practice.

A Principal Investigator, IRB, or regulatory authority may also suspend or prematurely terminate participation in the clinical investigation at the investigational site(s) for which they are responsible. The investigators will follow the requirements specified in the Clinical Trial Agreement.

4.0 ENDPOINTS

4.1 Primary Endpoints and Rationale

The primary endpoint of this study is:

- Vascular complications detected by scheduled DUS at discharge or 30 days in asymptomatic/non-visible complication subjects

In real-world practice, femoral DUS is not routinely done in ablation procedures and only done when access site-related complications are visible (such as hematomas) and/or symptomatic. Therefore, a scheduled femoral DUS in asymptomatic or non-visible complication subjects will support the overall safety of Perclose SMC in multiple access site closures in a single vein. Any visible and/or symptomatic access site-related complications will be also be captured but will be excluded from the primary endpoint analysis.

The primary endpoint is further categorized as major or minor. Major complications are defined as those which require surgical, interventional, or pre-specified repair and/or hospitalization. All other complications are considered to be minor complications.

Vascular access site-related complications include, but are not limited to:

- **Femoral vein stenosis (> 50%) development at the puncture site related to closure technique**
  - Requiring surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair
- **Deep vein thrombosis in the target limb**
  - Requiring surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair

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- Venous bleeding, retroperitoneal bleeding
  - Requiring surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair
- Venous access site injury including vessel laceration
  - Requiring surgical repair, angioplasty, stenting, ultrasound-guided compression, or thrombin injection (major)
  - Not requiring above
- Re-bleeding at the access site
  - Requiring treatment or re-hospitalization (major)
  - Not requiring treatment or re-hospitalization
- **Hematoma**
  - Hematoma ≥ 6 cm
  - Requiring surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair
- **Pseudoaneurysm**
  - Requiring surgical or percutaneous repair (major)
  - Requiring thrombin injection, fibrin adhesive injection, or ultrasound-guided compression (major)
  - Not requiring above
- **Arteriovenous (AV) fistula**
- **Venous tear**
  - Requing surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair
- **Venous perforation**
  - Requiring surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair
- **Arterial tear**
  - Requiring surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair
- **Arterial perforation**
  - Requiring surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair

- **Other Complications found by DUS**

DUS images will be analyzed by the independent DUS core laboratory and used for the primary endpoint analysis (**complications with bold face**). Investigators are also required to assess DUS detected complications, but the core laboratory is blinded to the site's assessment.

4.2 Descriptive Endpoints

Any vascular complications and access site complications will also be analyzed as the descriptive endpoints. Vascular complications include but are not limited to:

- Femoral vein stenosis (> 50%) development at the puncture site related to closure technique
- Deep vein thrombosis in the target limb
- Venous bleeding, retroperitoneal bleeding
- Venous access site injury including vessel laceration
- Re-bleeding at the access site
- Hematoma
- Pseudoaneurysm
- AV fistula
- Venous tear
- Venous perforation
- Arterial tear
- Arterial perforation
- Infection
  - requiring oral, intramuscular, or intravenous antibiotics, or leading to a prolonged hospitalization (major)
  - Not requring above (minor)
- Non-flow limiting suture material
- Access site-related nerve injury
  - Persisting for > 30 days (major)
  - Resolved ≤ 30 days
- Pulmonary embolism

  - Requiring surgical or endovascular intervention and/or resulting in death, to be confirmed by CT pulmonary angiography, lung ventilation/perfusion scan (VQ scan), or autopsy (major)
  - Not requring or resulting above
- Other (specify)

Procedural information listed below will also be analyzed.

- Procedure duration
- Type of Procedure (Cryo-ablation, RF ablation, etc.)
- Number of Femoral Vein Access Sites Per Subject
- Number of Femoral Vein Access Sites Per Leg
- Sheath Sizes Used
- Total Number of SMC used
- Number of SMC used per closure procedure
- Number of SMC used per access site
  - Number of SMC used for > 8F access site
- Number of SMC used per leg
- Device Success rate per access site
  - Successful hemostasis without surgical conversion, or additional non-study device (adjunctive manual compression and subcutaneous stitch are regarded as the standard of care and not included as failure)
- Anticoagulant and antiplatelet medications
- Use of protamine for heparin reversal

5.0 SUBJECT SELECTION AND WITHDRAWAL

5.1 Subject Population

This clinical study will register subjects of all genders who are planned to have elective ablation procedures requiring multiple vein access sites in a single femoral vein. Subjects must meet all eligibility criteria and provide written informed consent prior to registration in this study. Although complications are collected from all registered subjects, primary endpoint analysis is performed only in subjects with asymptomatic/non-visible complications, as the objective of this study is to understand asymptomatic/non-visible complications only observed by DUS.

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5.2 Subject Recruitment/Screening and Informed Consent

5.2.1 Subject Recruitment and Screening

Subjects admitted for an ablation procedure must be screened for the clinical study.

Subjects meeting the inclusion criteria and none of the exclusion criteria will be informed about the clinical study and asked to sign an informed consent. As the study-specific procedure is limited to femoral DUS at discharge and at 30 days, each site should follow their site standard practice for baseline information collection, the ablation procedure, and access site closures with the Perclose SMC, as well as the subject management.

5.2.2 Informed Consent

The Investigator or his/her authorized designee (if applicable) will conduct the Informed Consent process, as required by applicable regulations and the center's IRB. This process will include a verbal discussion with the patient on all aspects of the clinical investigation that are relevant to the patient's decision to participate, such as details of clinical investigation procedures, anticipated benefits, and potential risks of clinical investigation participation. Sites must inform patients about their right to withdraw from the clinical investigation at any time and for any reason without sanction, penalty, or loss of benefits to which the patient is otherwise entitled. Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the patient and will respect patient's legal rights. Financial incentives will not be given to patients. Patients may be compensated for time and travel directly related to the participation in the clinical investigation. The site shall provide the patient with the Informed Consent form (ICF) written in a language that is understandable to the patient and that has been approved by the center's IRB. The patient shall have adequate time to review, ask questions, and consider participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the patient understands the information provided. If the patient agrees to participate, they must sign and date the Informed Consent form, along with the person obtaining the consent prior to any clinical investigation-specific procedures. The site will file the signed original in the patient's hospital or research charts, and provide a copy to the patient.

Sites should report any failure to obtain informed consent from a patient to the Sponsor within 5 working days and to the reviewing center's IRB according to the IRB's reporting requirements.

If, during the clinical investigation, new information becomes available that can significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee (if applicable) will provide this information to the subject. If relevant, sites will ask the subject to confirm their continuing informed consent in writing.

In addition, sites must obtain an authorization for use and disclosure of the subject's protected health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), from the subject or their legally acceptable representative.

5.3 Eligibility Criteria

Assessment for eligibility criteria is based on medical records of the site and interview with a candidate patient. Subjects must meet ALL of the inclusion criteria to be considered for the clinical investigation. If ANY of the exclusion criteria are met, the subject is excluded from the clinical investigation and cannot be registered. If any clinical and/or laboratory tests are required for patient screening and are not included in a site's standard tests, they must be completed after written informed consent is obtained.

5.3.1 Inclusion Criteria

1. Age ≥18 years
2. Subject is planned to have an ablation procedure that requires multiple sheaths insertion in a single femoral vein
3. All the access sites are planned to be treated with Perclose SMC
4. Written informed consent is obtained prior to the procedure

5.3.2 Exclusion Criteria

Site standard exclusion criteria should be used for eligibility of ablation procedure. In addition, the exclusion criteria for Perclose SMC procedure listed below will be applied.

1. Visible vascular thrombus (angiographic or ultrasound) in the ipsilateral leg prior to the ablation procedure
2. Prior ipsilateral deep vein thrombosis within 6 months
3. International Normalized Ratio >3.5 for patients on warfarin
4. Subject who is not able to ambulate pre-procedure
5. Women who are pregnant (based on site standard pre-procedure pregnancy test)
6. Has active symptoms and/or a positive test result of COVID-19 or other rapidly spreading - infectious agent within the prior 2 months

5.4 Subject Registration

Registration is defined as the time at which, the Perclose SMC is inserted into the body. This study allows either pre-close or post-close technique. If pre-close technique is used, the subject is considered to be registered even before the ablation procedure.

5.4.1 Enrollment of Medicare Beneficiaries

This clinical investigation will enroll Medicare beneficiaries and therefore conforms to all standards of Medicare coverage requirements. The Risks and Benefits section describes how all enrolled subjects, including Medicare beneficiaries, may be affected by the device under investigation.

A portion of the subjects enrolled in the clinical investigation display characteristics consistent with the Medicare population based on age. The clinical investigation results will be analyzed by age (< 65 years and > 65 years) and compared to ensure that the outcomes are similar between the Medicare and non-Medicare populations.

5.4.2 Historically Under-Represented Demographic Subgroups

The Sponsor intends to implement FDA's guidance on sex-specific data in medical device clinical investigations to ensure adequate representation of women and other traditionally under-represented demographic subgroups in this clinical investigation. As noted in the guidance, some barriers to participation of women and ethnic minorities in clinical investigations have traditionally been:

- Lack of understanding about main obstacles to participation of such subgroups in clinical research
- Inclusion/exclusion criteria potentially not needed to define the clinical investigation population may unintentionally exclude specific subgroups
- Under diagnosis of disease etiologies and pathophysiology leading to under referral of demographic subgroups
- Avoidance of specific subgroups by investigators and Sponsors due to the perception that it takes more time and resources to recruit them
- Fear of fetal consequences (for female participants)
- Family responsibilities limiting women's ability to commit time for follow-up requirements

5.5 Subject Withdrawal and Discontinuation

Each registered subject shall remain in the clinical investigation until completion of the 30-day follow-up period; however, a subject's participation in any clinical study is voluntary and the subject has the right to withdraw at any time without penalty or loss of benefit.

however, a subject’s participation in any clinical investigation is voluntary and the subject has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but not be limited to, the following:

- Subject death
- Subject voluntary withdrawal
- Subject lost-to follow-up as described below

- Subject's follow-up is terminated according to Section 3.3, Suspension or Early Termination of the Clinical Investigation.

Sites must notify the Sponsor of the reason(s) for subject discontinuation. Investigators must also report this to their respective IRB as defined by their institution's procedure(s).

No additional follow-up is required or data recorded from subjects once withdrawn from the clinical investigation, except for the status (deceased/alive).

However, if a subject withdraws from the investigation due to problems related to the safety or performance of the device under investigation, the investigator shall ask for the subject's permission to follow his/her status/condition outside of the clinical investigation.

In case of subject withdrawal of consent, the site should make attempts to schedule the subject for a final clinical investigation visit. At this final follow-up visit, the subject will undergo the following assessments:

- Review and report adverse events in electronic case report form (eCRF)
- Review and report protocol and concomitant medications in eCRF
- Complete subject reported outcomes in eCRF

Lost-to-Follow-up

If the subject misses two consecutive scheduled follow-up time points and the attempts at contacting the subject detailed below are unsuccessful, then the subject is considered lost-to-follow-up. Site personnel shall make all reasonable efforts to locate and communicate with the subject (and document these efforts in the source documents), including the following, at each contact time point:

- A minimum of two telephone calls on different days over the specified follow-up windows to contact the subject should be recorded in the source documentation, including date, time and initials of site personnel trying to make contact.
- If these attempts are unsuccessful, the site should send a letter (certified if applicable) to the subject.
- If a subject misses one or more non-consecutive follow-up contact time points, it will be considered a missed visit. The subject may then return for subsequent visits. If the subject misses two consecutive time points and the above-mentioned attempts at communicating with the subject are unsuccessful, the subject will be considered lost-to-follow-up.

Note: Telephone contact with General Practitioner, non-clinical investigation cardiologist or relative without the presence of the subject or indirect documentation obtained via discharge letters will not be considered as subject contact.

5.6 Number of Subjects

A total of 35 subjects will be registered in the clinical study. Of these,

[redacted]

- 8 subjects will be treated with two Perclose SMC for a single access site closure > 8F.
- 12 subjects will have 3 or 4 access sites in a single vein.

5.7 Total Expected Duration of the Clinical Study

The expected duration of registration is 3 months. The expected duration of each subject's participation is 1 month, including the scheduled visits and data collection for this clinical study. Subjects will exit the trial at the end of their 1-month follow-up visit. Therefore, the total duration of the clinical investigation is expected to last 4 months, consisting of approximately 3 months of registration plus 1 month of follow-up.

6.0 TREATMENT AND EVALUATION OF ENDPOINTS

6.1 Baseline/Pre-procedure

All baseline/pre-procedure clinical, laboratory, and imaging assessments should be done per the site standard practice. Demographics and risk factors are listed below to be entered in the eCRF.

6.1.1 Baseline/Pre-procedure Assessment

Demographics

- Gender at Birth
- Birthdate
- Ethnicity
- Race

Risk Factors

- Height
- Weight
- Body Mass Index
- Hypertension
- Dyslipidemia
- Diabetes
- Coronary Artery Disease
- Chronic Kidney Disease
- Congestive Heart Failure
    - Systolic
    - Diastolic
    - Combined
- Cerebrovascular Accident

- Type of Arrhythmia
  - Paroxysmal Atrial Fibrillation (AF)
  - Persistent AF
  - Atrial Flutter

6.1.2 Chronic concomitant Medications

Chronic concomitant anticoagulants and antiplatelet medications should be recorded. These concomitant medications may be stopped several days before the procedure, and in such a case stop and restart date should be recorded in the eCRF. If the subject stops medications one day prior and resume post-procedure, it is still recorded.

Oral Anticoagulation

- Warfarin
- Apixaban
- Rivaroxaban
- Dabigatran
- Edoxaban
- Other (specify)

Oral Antiplatelet

- Aspirin
- Clopidogrel
- Prasugrel
- Ticagrelor
- Other (specify)

6.2 Ablation Procedure including Access Site Closure with Perclose SMC

6.2.1 Procedural Medication

Procedural medications, including anticoagulants, should be administered per site standard. The type of anticoagulant should be recorded in the eCRF.

Procedural Anticoagulation

- Heparin
- Bivalirudin
- Other (specify)

6.2.2 Vein access and Pre-close

Investigators should use site standard practice to obtain vein access sites for catheter insertion. Locations of the access sites (left or right femoral vein), sheath sizes must be recorded in the eCRF.

If the pre-close technique is used for the Perclose SMC, the subject is considered to be registered in this study at the point the first Perclose SMC is inserted into the body (proximal tip of the Perclose SMC crosses the distal end of the sheath).

In the case that an access site cannot be successfully obtained, a subject should be treated per the site standard practice and not be registered in this study (even though sutures are already placed using the pre-closure technique).

6.2.3 Ablation Procedure

The investigator should follow the site's standard practice for the ablation procedure. The type of ablation should be recorded in the eCRF.

Type of Ablation

- Radiofrequency
- Cryoablation

6.2.4 Vessel Closure with Perclose SMC

The investigator should follow site standard practice for the closure procedure using Perclose SMC. All access sites are planned to be treated with Perclose SMC. In the case only post-close technique is used, the subject is considered to be registered in this study at the point the first Perclose SMC is inserted into the body (proximal tip of the Perclose SMC crosses the distal end of the sheath).

The investigator should record the following information for each access site.

- Procedure start and end time
- Closure technique (pre-close or post-close)
- Number of Perclose Device used and Number of sutures deployed
    - Planned
    - Additional
        - If Perclose SMC is inserted, but suture cannot be deployed, it is still included in the number of Perclose devices used but is not included in the number of sutures deployed)
        - If such a case happens, it must be recorded as the device malfunction in the CRF, as well as reporting as a device malfunction to Abbott PPG.

- Additional hemostat procedure used
  - Manual compression
  - Tissue stitch
  - Use of other closure devices (specify)
  - Conversion to surgical cut-down
- DUS-guided closure technique
- Time to Hemostasis
  - Per access site
    - Defined as the time from the suture knotting to the time of hemostasis achieved at each access site
  - Per subject
    - Defined as the time from the first suture knotting to the time of the final hemostasis achieved of all access sites

If the investigator encounters any device malfunctions, even though prior to use, they must be recorded in the eCRF (for registered subjects) and must be reported to Abbott PPG.

6.2.5 Heparin Reversal

If heparin reversal is done, it should be recorded in the eCRF.

6.3 Post-Procedure

Post-procedure subject management to discharge should be per the site standard. The investigator should record:

- Time to mobility (time to remove leg movement restrictions while patient is in bed)
- Time to ambulation (time to move outside the bed)

6.4 Discharge (Complication Assessment)

At the time of discharge, the investigator should assess whether the subject has symptomatic or visible access site complications. In addition, femoral DUS must be done per the Corelab Guideline in the leg or legs in which access sites were closed in all subjects registered in this study to detect asymptomatic/non-visible complications if they exist. If a complication is treated, it should also be recorded in the eCRF.

DUS images should be uploaded for Corelab analysis per Abbott's specified method within 7 days from the procedure. The core laboratory will review the images and provide their assessment to investigators to determine whether 30-day DUS is required.

The investigator should record:

- Time of DUS
- Time of Discharge

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Access site complications:

- Femoral vein stenosis (> 50%) development at the puncture site related to closure technique
  - Requiring surgical or percutaneous repair
  - Not requiring surgical or percutaneous repair
- Deep vein thrombosis in the target limb
  - Requiring surgical or percutaneous repair
  - Not requiring surgical or percutaneous repair
- Venous bleeding, retroperitoneal bleeding
  - Requiring surgical or percutaneous repair
  - Not requiring surgical or percutaneous repair
- Venous access site injury including vessel laceration
  - Requiring surgical repair, angioplasty, stenting, ultrasound-guided compression or thrombin injection
  - Not requiring above
- Re-bleeding at the access site
  - Requiring treatment or re-hospitalization
  - Not requiring treatment or re-hospitalization
- Hematoma
  - Requiring surgical or percutaneous repair
  - Hematoma ≥ 6 cm but not requiring transfusion or surgical intervention
  - None of above
- Pseudoaneurysm
  - Requiring surgical or percutaneous repair
  - Requiring thrombin injection, fibrin adhesive injection, or ultrasound-guided compression
  - Not requiring above
- AV fistula
  - Requiring surgical or percutaneous repair
  - Not requiring surgical or percutaneous repair
- Venous tear
  - Requiring surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair

- Venous perforation
  - Requiring surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair
- Arterial tear
  - Requiring surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair
- Arterial perforation
  - Requiring surgical or percutaneous repair (major)
  - Not requiring surgical or percutaneous repair
- Infection
  - requiring oral, intramuscular, or intravenous antibiotics, or leading to a prolonged hospitalization (major)
  - Not requring above (minor)
- No flow-limiting suture material
- Access site-related nerve injury
  - Persisting for > 30 days
  - Resolved ≤ 30 days
- Pulmonary embolism
  - Requiring surgical or endovascular intervention and/or resulting in death, to be confirmed by CT pulmonary angiography, lung ventilation/perfusion scan (VQ scan), or autopsy
  - Not requiring or resulting above
- Other

6.5 30-day Follow-up Assessments

All subjects registered in the study must have follow-up assessments at 30 days (+/- 7 days).

If a subject has any access site-related vascular complications (either symptomatic/visible or asymptomatic/nonvisible), nerve injury, or infection at discharge, the follow-up must be done by a site visit. For those subjects who had vascular complications detected on femoral DUS at discharge, a repeat femoral DUS must be done at the 30-day visit in the leg or legs in which the vascular complication(s) was (were) found at discharge.

For a subject who does not have an access site-related vascular complication, nerve injury, or infection, 30-day follow-up can be done by telephone contact. The investigator or the designee should ask whether the subject has any signals of vascular complications. If the subject has a

susceptive signal, he/she is asked to visit the hospital for further assessment, and this site visit is regarded as the 30-day follow-up. If the telephone contact is done within the time window, it is not regarded as the deviation even though the site visit occurs outside of the window.

6.6 Unscheduled Visit

Additional visits, such as unscheduled visits (other than the protocol required visits), may occur as clinically warranted. In this case the subject should be managed per the site standard practice.

If a DUS is performed, the data should be reported on the eCRF. In the case no complications are observed at unscheduled DUS, 30-day DUS is not required.

If a medication or AE assessment is performed, the data should be reported on the eCRF.

If the unscheduled visit is done prior to the 30-day follow-up (FU) window (< 23 days), 30-day FU is still required, via either the site visit (if vascular complications are detected at discharge DUS and/or unscheduled DUS) or telephone contact.

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6.7 Scheduled Event

CIP Activity	Baseline (within 30 days prior to index procedure)	Pre-Procedure	Procedure	Discharge	30 days (± 7 days) office visit	Unscheduled visits
Subject Medical/Clinical History (Age, Sex, Risk Factors)	✓					
Subject Informed Consent	✓					
Inclusion/Exclusion Criteria	✓					
Duplex Ultrasound[1]				✓	✓[1]	✓[2]
Concomitant Medications	✓	✓		✓	✓	✓[2]
Procedure Medications			✓			
Procedure Information			✓			
Perclose Usage Information			✓			
Heparin Reversal			✓			
Adverse Events			✓	✓	✓	✓[2]

[1] 30-day DUS is only required if a complication is observed at discharge DUS. The core laboratory will review the DUS images and provide its assessment to investigators to determine whether 30-day DUS is required.

[2] Unscheduled visits are to occur per site standard of care. Data to be collected if performed. Protocol deviations will not be required if not done.

7.0 ADVERSE EVENTS

All vascular complications must be recorded as adverse events. In addition to vascular complications, serious adverse events (SAE) and device-related adverse events (adverse device effect) must be recorded in the CRF. Any Device Deficiency/Device Malfunction must also be recorded. Additional reporting criteria are listed under 7.3 Adverse event reporting.

7.1 Definitions

7.1.1 Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the medical device under investigation.

Note 1: This definition includes events related to the medical device under investigation or the comparator.
Note 2: This definition includes events related to the procedures involved.
Note 3: For users or other persons, this definition is restricted to events related to medical devices under investigation.

7.1.2 Serious Adverse Event

If the AE meets any of the criteria below, it is regarded as a serious adverse event (SAE).

a) Led to a death,
b) Led to a serious deterioration in the health of the subject, that either resulted in
    1. a life-threatening illness or injury, or
    2. a permanent impairment of a body structure or a body function, or
    3. in-subject 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.
    5. chronic disease
c) Led to fetal distress, fetal death, or a congenital abnormality or birth defect.

Note: A planned hospitalization for pre-existing conditions without a serious deterioration in health, is not considered to be an SAE.

7.1.3 Device Deficiency/Device Malfunction

Device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error, and inadequate labeling. This includes the failure of the device to meet its performance

specifications or otherwise perform as intended. Note: Performance specifications include all claims made in the labeling of the device.

A device malfunction is the failure of a device to meet its performance specifications or otherwise perform as intended when used in accordance with the instructions for use.

7.2 Device Relationship

Determination of whether there is a reasonable possibility that an investigational product or device under investigation caused or contributed to an AE is to be determined by the Investigator and recorded on the appropriate CRF form. Determination should be based on an assess temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and subject condition (pre-existing condition).

7.2.1 Unanticipated (Serious Adverse) Device Effect [U(S)ADE]

Unanticipated serious adverse device effect (USADE) refers to 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.

7.3 Adverse Event and Device Deficiency/Device Malfunction Reporting

7.3.1 Adverse Event (AE) Reporting

In this study, all vascular complications (regardless of the seriousness), all serious adverse events, procedure-related adverse events, and adverse device effects related to Perclose SMC must be reported.

Safety surveillance and reporting starts when the first Perclose SMC enters the subject's vasculature and will continue until a 30-day follow-up visit has been performed, unless the subject is deceased, or the subject withdraws from the clinical study. Adverse events will not be collected on de-registered subjects (unless specifically required by the CIP or requested by the regulatory authority). Safety surveillance and reporting will continue until sites perform the last follow-up visit, the subject is deceased, the subject concludes participation in the clinical investigation, or the subject withdraws from the clinical investigation. Sites will collect all adverse event data, including deaths and device deficiency data (if applicable), throughout the period defined above and will report these events to the Sponsor on a CRF. Sites should update additional information regarding an adverse event on the appropriate CRF.

Unchanged, chronic, non-worsening, or pre-existing conditions are not AEs and should not be reported.

The investigator must report all SAEs to the Sponsor as soon as possible but no later than outlined below.

Clinical Site	Reporting timelines
All Sites	SAEs must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined above.

The Sponsor will provide an offline form to allow the investigator to report SAEs in the event the entry cannot be made in the Electronic Data Capture (EDC). This does not replace the EDC reporting system. Sites should still enter all information in the EDC system as soon as feasible.

The date the site staff became aware the event met the criteria of an SAE must be recorded in the source document. The Investigator will further report the SAE to the local IRB according to the institution's IRB reporting requirements.

Adverse Device Effect (ADE)

An adverse event related to the use of an investigational medical device.

This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

This definition includes any event resulting from the use error or from intentional misuse of the investigational medical device.

7.3.2 Unanticipated Serious Adverse Device Effect (USADE) Reporting to Sponsor and IRB

The Sponsor requires the Investigator to report any USADE to the Sponsor within 3 calendar days of the investigator’s knowledge of the event, unless local requirements are more stringent, and to the IRB/EC per IRB/EC requirements.

7.3.3 Device Deficiency/Malfunction Reporting

All device deficiencies/malfunctions for the investigational device must be reported on the appropriate eCRF form. Device deficiencies/malfunctions must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements if the requirement is more stringent than those outlined.

The device, if not implanted or not remaining in the subject, should be returned to the Sponsor.

Device deficiencies/malfunctions should be reported to the IRB per the investigative site's local requirements.

An offline form will be made available to allow the investigator to report device deficiencies/malfunctions in the event that the entry cannot be made in the EDC system. This does not replace the EDC reporting system. All information should still be entered into the EDC system as soon as feasible.

In case a device deficiency/malfunction occurred before the subject registration or in the de-registered subject, the device deficiency should be reported through the Sponsor's standard Abbott Vascular reporting channel.

7.3.4 Adverse Event Reporting to Country Regulatory Authorities by the Sponsor

The Sponsor will report SAEs and reportable device deficiencies/malfunctions to the country regulatory authority, per local requirements.

Note: Reportable device deficiencies/malfunctions include device deficiencies/malfunctions that might have led to an SAE if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate. These are handled under the SAE reporting system.

8.0 STATISTICAL CONSIDERATIONS

8.1 Analysis Population

[redacted]

8.2 Statistical Analyses

Descriptive analyses will be performed for subject baseline characteristics, procedural characteristics, and all endpoints[redacted]

8.3 Sample Size

[redacted]

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The sample size of 35 patients [redacted]

Subjects who will be treated with 2 Perclose SMC for closure of access sites > 8F.

A minimum of 8 subjects will be enrolled. [redacted]

Subjects who will have 3 or 4 access sites per vein

[redacted] enrolling 12 subjects is expected.

8.4 Timing of Analysis

The primary analysis will be performed after database lock when all subjects have completed their 30-day follow-up visit.

8.5 Subgroup Analysis

Abbott will have a subgroup analysis by:

- Number of access site per a subject
- Number of access site per a vein
- > 8F vs ≤ 8F
- Female vs Male
- Age ≥ 65 vs < 65
- Race/Ethnicity
- Diabetes

8.6 Multiplicity

Since no hypothesis testing is planned, no adjustment will be made for multiple testing.

8.7 Success Criteria

No success criterion is applied in this clinical investigation.

8.8 Deviations from Statistical Plan

Any major changes to the statistical plan will be documented in an amendment to the statistical analysis plan. Less significant changes to the planned analyses will be documented in the final report.

8.9 Statistical Criteria for Termination

There are no statistical criteria for the termination of this clinical investigation.

9.0 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The investigator/institution will permit direct access to source data/documents for the purpose of performing clinical investigation-related monitoring, audits, IRB review, and regulatory inspections.

Subjects providing informed consent are agreeing to allow clinical investigation monitors or regulatory authorities, including foreign countries, to review, in confidence, any records identifying the subjects in this clinical investigation. This information may be shared with regulatory agencies; however, Sponsor undertakes not to otherwise release the subject's personal and private information.

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

10.1 Selection of Clinical Sites and Investigators

The Sponsor will select investigators qualified by training and experience to participate in the clinical investigation. Sites will be selected based upon a review of a recent site assessment, if applicable, and the qualifications of the investigators who will participate in the clinical investigation.

10.2 Clinical Investigation Finances and Agreements

The clinical investigation will be financed by Abbott. Investigational sites will be compensated by Abbott for participation in the clinical investigation per the conditions of agreement between the Sponsor and the Investigational site.

10.3 CIP Amendments

Approved CIP amendments will be provided to the Investigators by the Sponsor prior to implementing the amendment. The Principal Investigator is responsible for notifying the IRB or equivalent committee of the CIP amendment (administrative changes) or obtaining IRB's approval of the CIP amendment (changes in subject care or safety), according to the instructions provided by the Sponsor with the CIP amendment.

Acknowledgement/approval by the IRB of the CIP amendment must be documented in writing prior to implementation of the CIP amendment. Copies of this documentation must also be provided to the Sponsor.

10.4 Training

10.4.1 Site Training

All Investigators and clinical investigation personnel are required to attend Sponsor training sessions, which may be conducted at an Investigator's meeting, a site initiation visit, or other appropriate training sessions. Over-the-phone or self-training may take place as required. Training of Investigators and clinical investigation personnel will include but is not limited to, the CIP requirements, electronic case report form completion, and clinical investigation personnel responsibilities. All Investigators and clinical investigation personnel that are trained must sign a training log (or an equivalent) upon completion of the training.

10.5 Monitoring

Sponsor and/or designee will monitor the clinical investigation over its duration according to the CIP-specific monitoring plan, which will include the planned extent of source data verification.

Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

- The investigator understands and accepts the obligation to conduct the clinical investigation according to the protocol and applicable regulations, and has signed the Investigator Agreement.
- The Investigator and his/her staff should have sufficient time and facilities to conduct the clinical investigation and should have access to an adequate number of appropriate subjects to conduct the clinical investigation.
- Source documentation (including original medical records) must be available to substantiate proper informed consent procedures, adherence to protocol procedures, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.
- The Investigator/site will permit access to such records. A monitoring visit sign-in log will be maintained at the site. The Investigator will agree to dedicate an adequate amount of time to the monitoring process. The Investigator and/or research coordinator will be available for monitoring visits. It is expected that the Investigator will provide the monitor with a suitable working environment for review of clinical investigation-related documents.

10.6 Deviations from CIP

The Investigator should not deviate from the protocol for any reason except in cases of medical emergencies when the deviation is necessary to protect the rights, safety, and well-being of the subject or eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify Sponsor immediately by phone or in writing.

No waivers for protocol deviations will be granted by the Sponsor. All deviations must be reported to the Sponsor using the Deviation CRF. The occurrence of protocol deviations will be monitored by the Sponsor for evaluation of investigator compliance to the protocol and regulatory requirements and dealt with according to written procedures. Investigators will inform their IRB or equivalent committee of all protocol deviations in accordance with their specific IRB or equivalent committee reporting policies and procedures.

In the event of repeated non-compliance, as determined by the Sponsor, a Sponsor's monitor or company representative will attempt to secure compliance by one or more of the following (and not limited to):

- Visiting the investigator and/or delegate
- Telephoning the investigator and/or delegate
- Corresponding with the investigator and/or delegate

Repeated non-compliance with the signed agreement, the protocol, or any other conditions of the clinical investigation may result in further escalation in accordance with the Sponsor's written procedures, including securing compliance or, at its sole discretion, Sponsor may terminate the investigator's participation in the clinical investigation.

10.7 Quality Assurance Audit

A Sponsor representative or designee may request access to all clinical investigation records, including source documentation, for inspection during a Quality Assurance audit.

If an investigator is contacted by a Regulatory Agency in relation to this clinical investigation, the Investigator will notify Sponsor immediately. The Investigator and Research Coordinator must be available to respond to reasonable requests and audit queries made during the audit process. The Investigator must provide the Sponsor with copies of all correspondence that may affect the review of the current clinical investigation (e.g., Form FDA 483, Inspectional Observations, Warning Letters, Inspection Reports, etc.). The Sponsor may provide any needed assistance in responding to regulatory audits.

10.8 Clinical Events Committee (CEC)

The CEC is an independent adjudication body comprised of qualified physicians who are not participants in the clinical investigation. The CEC will review and adjudicate pre-specified vascular complications and other access site-related complications (endpoint events described in Section 4.2) reported by investigators or identified by Safety personnel for the clinical

investigation as defined in the CEC charter and according to definitions provided in this CIP and relations (closure procedure related, SMC related) will also be determined.

11.0 DATA HANDLING AND RECORD KEEPING

Sponsor and/or its affiliates will maintain documentation of the systems and procedures used in data collection for the duration of the clinical investigation.

CRF data collection will be performed through a secure web portal, and only authorized personnel will access the Electronic Data Capture (EDC) system using a unique username and password to enter, review, or correct data. Passwords and electronic signatures will be strictly confidential.

The data will be subjected to consistency and validation checks within the EDC system and supplemental review by the Sponsor.

At the conclusion of the clinical investigation, completed CRF images with the date-and-time stamped electronic audit trail indicating the user, the data entered, and any reason for change will be provided to the investigational sites.

For the duration of the clinical investigation, the Investigator will maintain complete and accurate documentation including, but not limited to, medical records, clinical investigation progress records, laboratory reports, CRFs, signed ICFs, correspondence with the IRB, and clinical investigation monitor/Sponsor, adverse event reports, and information regarding subject discontinuation or completion of the clinical investigation.

11.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical investigation.

The Sponsor implements technical and physical access controls to ensure that Personal Information is accessible only to and processed only on a 'need to know' basis, including periodic review of access rights, and revocation of access when an individual's employment is terminated or the individual transitions to a role that does not require access to Personal Information, and appropriate restrictions on physical access to premises, facilities, equipment, and records containing Personal Information.

The Sponsor requires the investigational sites to enter only pseudonymous Personal Information (key-coded) necessary to conduct the Clinical Investigation, such as the subject's medical condition, treatment, dates of treatment, etc., into Sponsor's data management systems. The Sponsor discloses as part of the clinical investigation informed consent process that some Sponsor representatives still may see Personal Information at the participating sites for technical support of the participating physicians on the device implant or procedures, monitoring, and quality control purposes. All parties will observe confidentiality of Personal

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Information always throughout the clinical investigation. All reports and data publications will preserve the privacy of each subject and confidentiality of his/her information.

The Sponsor data management systems and processes were designed, developed, and tested according to industry standards to appropriately safeguard Confidential Information (including any Personal Information) against unauthorized access and/or interference by third parties, intrusion, theft, destruction, loss, or alteration. Clinical Investigation data are encrypted in transit and at rest.

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

11.2 Data Management Plan

A Data Management Plan (DMP) will describe procedures used for data review, data cleaning, and issuing and resolving data discrepancies. If appropriate, the DMP may be updated throughout the duration of the clinical investigation. All revisions will be tracked and document controlled.

11.3 Source Documentation

Abbott requires the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. The following information should be included in the subject record at a minimum and if applicable to the clinical investigation:

- Medical history/physical condition of the subject before involvement in the clinical investigation sufficient to verify protocol entry criteria
- Dated and signed notes on the day of entry into the clinical investigation referencing the Sponsor, protocol number, subject ID number, and a statement that informed consent was obtained
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Adverse events reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, ECGs, and lab results, including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- Notes regarding medications taken during the clinical investigation (including start and stop dates)
- Subject's condition upon completion of or withdrawal from the clinical investigation
- Any other data required to substantiate data entered into the CRF

11.4 Electronic Case Report Form Completion

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the protocol and eCRF completion. The investigator will ensure accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor on the eCRFs and in all required reports. eCRF data will be collected for all subjects that are registered in the trial.

Only authorized site personnel will be permitted to enter the eCRF data through the EDC system deployed by the Sponsor. An electronic audit trail will be used to track any subsequent changes of the entered data.

11.5 Record Retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the clinical investigation as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any clinical investigation records.

12.0 ETHICAL CONSIDERATION

12.1 Institutional Review Board Approval

Institutional Review Board (IRB) approval for the protocol and ICF/other written information provided to the subject will be obtained by the Principal Investigator at each investigational site prior to consenting and registering subjects in this clinical investigation. The approval letter must be received prior to the start of this clinical investigation and a copy must be provided to the Sponsor.

Any amendments to the protocol as well as associated ICF changes will be submitted to the IRB/EC/Competent Authority and written approval obtained prior to implementation, according to each institution's IRB requirements.

No changes will be made to the protocol or ICF or other written information provided to the subject without appropriate approvals, including IRB, the Sponsor, and the regulatory agencies (if applicable).

Until the clinical investigation is completed, the Investigator will advise his/her IRB of the progress of this clinical investigation, per IRB requirements. Written approval must be obtained from the IRB yearly to continue the clinical investigation, or according to each institution's IRB requirements.

No investigative procedures other than those defined in this protocol will be undertaken on the registered subjects without the written agreement of the IRB and the Sponsor.

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13.0 CLINICAL INVESTIGATION COMPLETION

The clinical investigation will end when the last visit of the last subject registered has been completed.

The clinical investigation will be concluded when:

- All sites are closed AND
- The final report has been provided to investigators, or the Sponsor has provided formal documentation of clinical investigation closure.

The final clinical investigation report will be submitted within one year of the end of the investigation.

14.0 PUBLICATION POLICY

The data and results from the clinical investigation are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the clinical investigation. The Investigators will not use this clinical investigation-related data without the written consent of the Sponsor for any purpose other than for clinical investigation completion or for generation of publication materials, as referenced in the Clinical Trial Agreement. Single-center results are not allowed to be published or presented before the multi-center results. Any proposals for publications or presentations by the investigators must be reviewed and approved by the Sponsor in a timely manner to enable Sponsor review in compliance with the Sponsor's publication policy set forth in the Clinical Trial Agreement.

Upon receiving IDE approval from the FDA, the Sponsor will be responsible for registering this clinical investigation on the ClinicalTrials.gov website, in accordance with the International Committee of Medical Journal Editors guidelines, or any other applicable guidelines. Sponsor shall be responsible for any such registration and results posting as required by the ClinicalTrials.gov website. Institution and/or Principal Investigator(s) shall not take any action to register the clinical investigation. A full report of the pre-specified outcomes, regardless of the results, will be made public through the ClinicalTrials.gov website no later than 12 months after clinical investigation completion, as required by section 801 of the FDA Amendments Act. If this clinical investigation is terminated early, the Sponsor will make every effort to hasten the release of the pre-specified outcomes through the ClinicalTrials.gov website.

15.0 RISK ANALYSIS

This clinical study is designed to confirm the frequency of asymptomatic/non-visible vascular complication possibly related to Perclose SMC by femoral DUS at discharge and 30 days.

This study follows site standard practice of ablation and vessel closure procedures and discharge, and the 30-day DUS (if complications are observed at discharge DUS) is the only study-specific requirement.

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Although "scheduled" femoral DUS is not a routine practice after the catheterization procedure, it is used for further confirmation of symptomatic or suspected vascular complications as the standard practice. Femoral DUS is a non-invasive modality and no additional risks are expected. Therefore, this study is a non-significant risk study.

[redacted]

Clinical Investigation Plan

REFERENCES:

1. Mahadevan, V.S., et al., *Pre-closure of femoral venous access sites used for large-sized sheath insertion with the Perclose device in adults undergoing cardiac intervention.* Heart, 2008. **94**(5): p. 571-2.
2. Hamid, T., et al., *Preclosure of large-sized venous access sites in adults undergoing transcatheter structural interventions.* Catheter Cardiovasc Interv, 2013. **81**(4): p. 586-90.
3. Mohanty, S., et al., *Venous access-site closure with vascular closure device vs. manual compression in patients undergoing catheter ablation or left atrial appendage occlusion under uninterrupted anticoagulation: a multicentre experience on efficacy and complications.* Europace, 2019. **21**(7): p. 1048-1054.
4. Sekhar, A., et al., *Femoral arterial closure using ProGlide(R) is more efficacious and cost-effective when ambulating early following cardiac catheterization.* Int J Cardiol Heart Vasc, 2016. **13**: p. 6-13.

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APPENDIX I: ABBREVIATIONS AND ACRONYMS

Abbreviations	
ADE	Adverse Device Effect
AE	Adverse Event
AF	Atrial Fibrillation
ASD	Atrial Septal Defect
AV	Arteriovenous
CEC	Clinical Events Committee
CIP	Clinical Investigation Plan
COVID-19	Coronavirus Disease 2019
CT	Computer Tomography
DMP	Data Management Plan
DUS	Duplex Ultrasound
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
F	French Size
FDA	Food and Drug Administration
Fo8	Figure of 8
FU	Follow-up
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent For
IRB	Institutional Review Board
ITT	Intent-to-treat
MC	Manual Compression
PPG	Product Performance Group
SAE	Serious Adverse Event
SMC	Suture-Mediated Closure (and Repair) System
US	United States
USADE	Unanticipated Serious Adverse Device Effect

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APPENDIX II: DEFINITIONS

DUS-detected Vascular Complication Definitions

Hematoma - A collection of blood outside of the blood vessel. Characterized on ultrasound by a hypoechoic region adjacent to the blood vessel with no flow on doppler interrogation.

Pseudoaneurysm - A blood vessel abnormality resembling an aneurysm (localized abnormal dilatation of a blood vessel) but consisting of a collection of blood with persistent flow outside an artery, contained by surrounding tissue and due to a leaking hole through all layers of the arterial wall. The leaking hole is due to injury of (e.g., rupture of or trauma to) the arterial wall, and is related to the access site

DVT (Deep Venous Thrombosis) - Clot in the deep venous system. The age of the clot is categorized as Acute, Age-Indeterminate or Chronic.

Acute:
Homogenous hypoechoic thrombus.
Thrombus poorly organized.
Dilated vein wall (if occluded).
Edema surrounding vessel wall.
Age Indeterminate:
Shares characteristics of acute and chronic thrombus.
Lightly echogenic thrombus.
Less organized thrombus.
Vein wall appearing close to normal in size.
Partially compressible.
Chronic:
Hyperechoic thrombus.
Thrombus well organized with well-defined borders.
Thrombus attached to vessel walls.
Collaterals may be present.

AV (Arterio-Venous) Fistula - an abnormal narrow connection between an artery and vein. The doppler characteristics include high turbulence within the fistula and arterialized/ pulsatile flow in the vein cephalad to the fistula. The artery may demonstrate a low resistive flow cephalad to the fistula tract.

Dissection - A tear of the vessel wall that allows blood to separate the intima and media from the externa. This appears a hyperechoic line within the vessel. Doppler

flow within the dissection depends on the extent of the dissection flap. It may range from a to-and-fro pattern to complete occlusion of the involved vessel.

A complete perforation on duplex ultrasound - a visible jet of color doppler traveling through the vessel wall resulting in a non-organized anechoic or heterogenous collection outside of the vessel that is actively increasing in size.

A complete tear on duplex ultrasound - a combined dissection/perforation duplex appearance with a jet of color doppler traveling through the vessel wall resulting in a non-organized anechoic or heterogenous collection outside of the vessel actively increasing in size, as well as possible visibility of a linear echogenic structure visible within the vessel lumen.

Other Access Site Related Complications

Access site-related nerve injury - Dysfunction with a loss of movement or sensation in parts of the legs due to damage to the femoral nerve. It may be caused by direct injury (trauma), prolonged pressure on the nerve compression, stretching, or entrapment of the nerve.

Infection - The invasion and growth of germs in the body. The germs may be bacteria, viruses, yeast, fungi, or other microorganisms. Infections can begin anywhere in the body and may spread all through it. An infection can cause fever and other health problems, depending on where it occurs in the body.

Pulmonary embolism - A pulmonary embolism (PE) is a sudden blockage in a pulmonary artery by a substance that has moved from elsewhere in the body through the bloodstream. DVT is the main cause of PE.

Venous access site injury including vessel laceration - Access site injury is defined as any untoward harm associated with a therapeutic or diagnostic health care intervention. Vessel laceration is defined as a tear in tissue caused by a shearing or crushing force.

Venous bleeding, retroperitoneal bleeding - Venous bleeding is defined as a continuous blood flow from a vein. Venous bleeding is less severe than arterial bleeding, but it can still be life threatening. Retroperitoneal bleeding is defined as bleeding into the retroperitoneal space.

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APPENDIX III: SITE CONTACT INFORMATION

[redacted]

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APPENDIX IV: LABELS

The Perclose ProGlide Suture-Mediated Closure System and the Perclose ProStyle Suture-Mediated Closure and Repair System are commercially approved devices. The sites will be using commercial devices with existing labels.

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APPENDIX V: CASE REPORT FORMS

[redacted]

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APPENDIX VI: INFORMED CONSENT FORM

[redacted]

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APPENDIX VII: IRB Information

[redacted]

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APPENDIX VIII: MONITORING PLAN

[redacted]

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APPENDIX IX: REVISION HISTORY

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]