Perclose™ ProStyle™

Rx ONLY

Suture-Mediated Closure and Repair System

Instructions for Use

Table of Contents

TO ENSURE PROPER DEPLOYMENT AND USE OF THIS DEVICE AND TO PREVENT INJURY TO PATIENTS, READ ALL INFORMATION CONTAINED IN THESE INSTRUCTIONS FOR USE.

Note: This IFU may be revised from time to time. Please refer to the Abbott website (www.abbottvascular.com/ifu) for the most current version at the time of the procedure.

If you have difficulties accessing this document or would like to request a paper copy at no extra cost, please contact: Abbott Customer Service at 1-800-227-9902.

1.0 CAUTION

Federal law restricts this medical device to sale by or on the order of a physician (or allied healthcare professionals, authorized by, or under the direction of, such physicians) who is trained in diagnostic and / or interventional catheterization procedures and who has been trained by an authorized representative of Abbott.

Prior to use, the operator must review the Instructions for Use and be familiar with the deployment techniques associated with the use of this device.

During closure of access sites using a procedural sheath greater than 8F, it is recommended that a vascular surgeon or a surgeon with vascular training be available in case surgical conversion to control bleeding and to repair the vessel is needed.

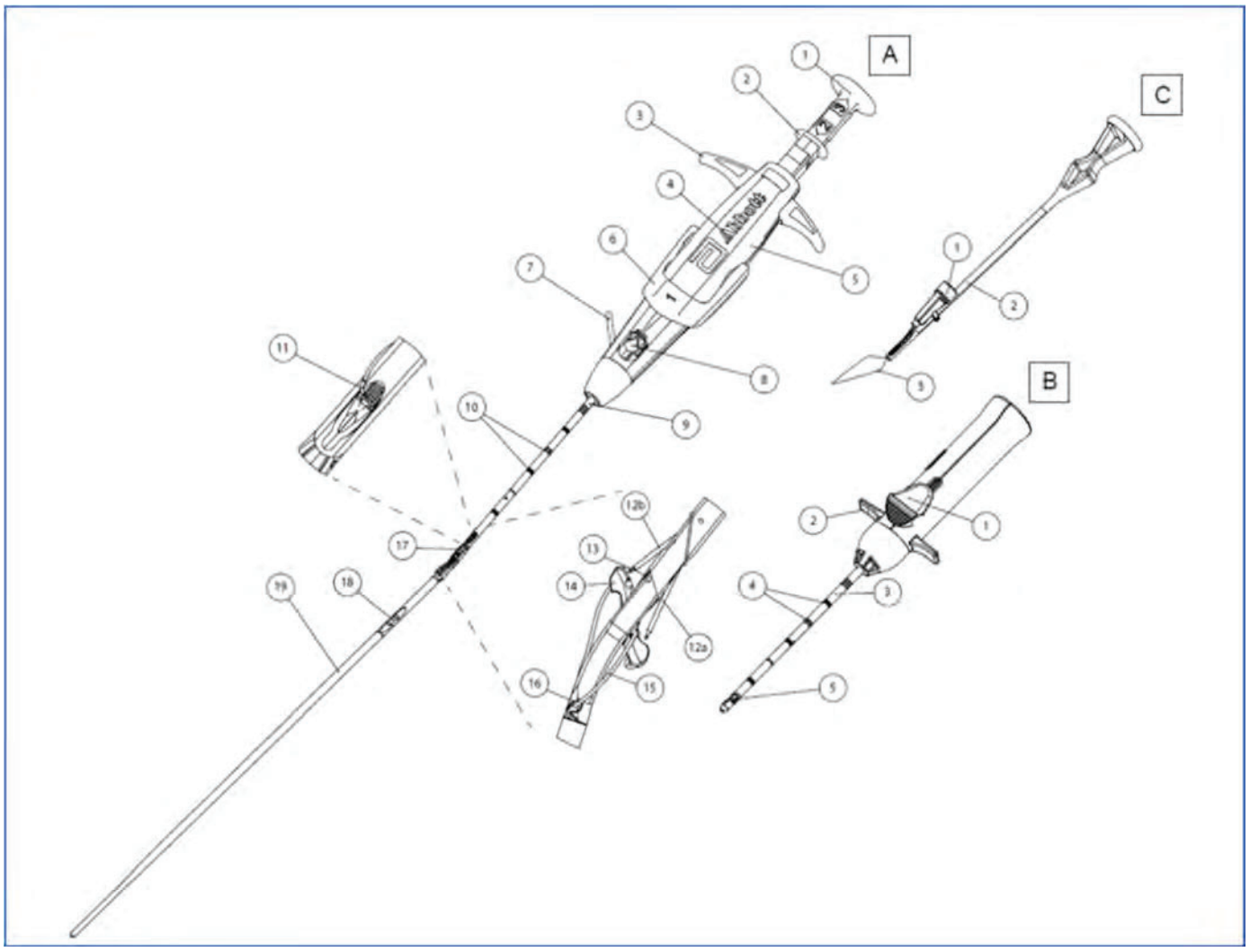
2.0 DEVICE DESCRIPTION

The Perclose™ ProStyle™ Suture-Mediated Closure and Repair (SMCR) System (Figure 2.0-1) is designed to deliver a single monofilament polypropylene suture for use in closing and repairing femoral vessel access sites following diagnostic or interventional catheterization procedures.

This Perclose ProStyle Device is composed of a plunger, handle, guide, and sheath. The Perclose ProStyle Device tracks over a standard 0.038" (0.97 mm) (or smaller) guide wire. A hemostasis valve restricts the blood flow through the sheath with or without a guide wire in place. The guide houses the anterior and posterior needles, and the foot with cuffs, and precisely controls the placement of the needles around the access site. The handle is used to stabilize the device during use. The plunger advances the needles and is used to retrieve the suture. A marker lumen is contained within the guide, with the intraluminal marker port positioned at the distal end of the guide. Proximally, the marker lumen exits from the body of the device. The marker lumen allows a pathway for back-bleeding (obtaining mark) from the femoral vessel to ensure proper device positioning.

The Perclose™ ProStyle™ Suture Trimmer and Perclose™ Snared Knot Pusher are designed to position the pre-tied suture knot to the top of the access site. The Perclose ProStyle Suture Trimmer is also designed to trim the trailing limbs of suture below the skin.

Figure 2.0-1



A. **Perclose™ ProStyle™ Device**
   1. Plunger
   2. Collar
   3. Handle
   4. Device Logo
   5. Body
   6. Lever
   7. Marker Lumen
   8. QuickCut™ Mechanism
   9. Proximal Guide
   10. Depth Reference Markers
   11. Suture with Pre-tied Knot
   12. a. Anterior Needle
       b. Posterior Needle
   13. Marker Port
   14. Foot (with Cuffs)
   15. Link
   16. Suture Bearing
   17. Distal Guide
   18. Guide Wire Exit Port
   19. Sheath

B. Perclose™ ProStyle™ Suture Trimmer
   1. Thumb Knob
   2. Trimming Lever (Red)
   3. Sheath
   4. Depth Reference Markers
   5. Suture Gate

C. Perclose™ Snared Knot Pusher
   1. Snare Tab
   2. Sheath
   3. Snare

3.0 HOW SUPPLIED

The Perclose™ ProStyle™ SMCR System is provided sterile and non-pyrogenic in unopened, undamaged packages. Products are sterilized with ethylene oxide and intended for single use only. Do not resterilize. Store in a cool, dry place.

Perclose ProStyle SMCR System includes:
One (1) Perclose™ ProStyle™ Device
One (1) Perclose™ ProStyle™ Suture Trimmer
One (1) Perclose™ Snared Knot Pusher

4.0 INDICATIONS

The Perclose™ ProStyle™ Suture-Mediated Closure and Repair System is indicated for the percutaneous delivery of suture for closing the common femoral artery and vein access sites of patients who have undergone diagnostic or interventional catheterization procedures.

The Perclose ProStyle SMCR System is indicated for closing the common femoral vein in single or multiple access sites per limb.

The Perclose ProStyle SMCR System is used without or, if required, with adjunctive manual compression.

For access sites in the common femoral artery using 5F to 21F sheaths. For arterial sheath sizes greater than 8F, at least two devices and the pre-close technique are required.

For access sites in the common femoral vein using 5F to 24F sheaths. For venous sheath sizes greater than 14F, at least two devices and the pre-close technique are required.

5.0 CONTRAINDICATIONS

There are no known contraindications to the use of this device.

6.0 WARNINGS

Do not use the Perclose™ ProStyle™ SMCR System if the packaging or sterile barrier has been previously opened or damaged or if the components appear to be damaged or defective.

DO NOT RESTERILIZE OR REUSE. The Perclose ProStyle SMCR System is intended for single use only.

Do not use the Perclose ProStyle SMCR System if the sterile field has been broken where bacterial contamination of the sheath or surrounding tissues may have occurred, since such a broken sterile field may result in infection.

Do not use the Perclose ProStyle SMCR System if the puncture site is located above the most inferior border of the inferior epigastric artery (IEA) and / or above the inguinal ligament based upon bony landmarks, since such a puncture site may result in a retroperitoneal hematoma. Perform a femoral angiogram to verify the location of the puncture site. **Note:** This may require

both a right anterior oblique (RAO) and left anterior oblique (LAO) angiogram to adequately visualize where the sheath enters the femoral vessel.

Do not use the Perclose ProStyle SMCR System in arterial or venous access if the puncture is through the posterior wall or if there are multiple punctures in the same access site, since such punctures may result in a hematoma or retroperitoneal bleed.

Do not use the Perclose ProStyle SMCR System if the puncture site is located in the superficial femoral artery or the profunda femoris artery, or the bifurcation of these vessels, since such puncture sites may result in a pseudoaneurysm, intimal dissection, or an acute vessel closure (thrombosis of small artery lumen). Perform a femoral angiogram to verify the location of the puncture site. **Note:** This may require both a right anterior oblique (RAO) and left anterior oblique (LAO) angiogram to adequately visualize where the sheath enters the vessel.

7.0 PRECAUTIONS

1. Prior to use, inspect the Perclose™ ProStyle™ SMCR System to ensure that the sterile packaging has not been damaged during shipment. Examine all components prior to use to verify proper function. Exercise care during device handling to reduce the possibility of accidental device breakage.
2. As with all catheter-based procedures, infection is a possibility. Observe sterile technique at all times when using the Perclose ProStyle SMCR System. Employ appropriate groin management, as per hospital protocol, post-procedure, and post-hospital discharge to prevent infection.
3. Use a single wall puncture technique. Do not puncture the posterior wall of the vessel in arterial and venous access.
4. Do not deploy the Perclose™ ProStyle™ Device at an elevated angle against resistance as this may cause a cuff miss or device breakage.
5. There are no reaccess restrictions if previous arteriotomy / venotomy repairs were achieved with Abbott Medical SMC or SMCR systems.
6. If significant blood flow is present around the Perclose ProStyle Device, do not deploy needles. Remove the device over a 0.038" (0.97 mm) (or smaller) guide wire and insert an appropriately sized sheath.
7. Prior to depressing the plunger to advance the needles, stabilize the device by the body to ensure the foot is apposed to the vessel wall and the device does not twist during deployment. Twisting (torquing) the device could lead to needle deflection resulting in a cuff miss. Do not use excessive force or repeatedly depress the plunger. Excessive force on the plunger during deployment could potentially cause breakage of the device, which may necessitate intervention and / or surgical removal of the device and vessel repair.
8. Do not apply excessive force to the lever when opening the foot and returning the foot to its original position down to the body of the device. Do not attempt to remove the device without closing the lever. Excessive force on the lever or attempting to remove the device without closing the lever could cause breakage of the device and / or lead to vessel trauma, which may necessitate intervention and / or surgical removal of the device and vessel repair.

9. **Do not advance or withdraw the Perclose ProStyle Device against resistance until the cause of that resistance has been determined. Excessive force used to advance or torque the Perclose ProStyle Device should be avoided, as this may lead to significant vessel damage and / or breakage of the device, which may necessitate intervention and / or surgical removal of the device and vessel repair.**
10. If excessive resistance in advancing the Perclose ProStyle Device is encountered, withdraw the device over a 0.038" (0.97 mm) (or smaller) guide wire and reinsert the introducer sheath or use manual compression.
11. Remove the Perclose ProStyle sheath before tightening the suture. Failure to remove the sheath prior to tightening the suture may result in detachment of the tip of the sheath.
12. Care should be taken to avoid damage to the suture from handling. Avoid crushing damage due to application of surgical instruments such as clamps, forceps or needle holders.
13. For catheterization procedures using a 5 – 8F procedural sheath, use manual compression in the event that bleeding from the femoral access site persists after the use of the Perclose ProStyle SMCR System to obtain hemostasis.
14. For catheterization procedures using a procedural sheath > 8F, use manual compression, compression assisted devices, surgical repair, and / or other appropriate treatment methods in the event that bleeding from the femoral access site persists after the use of the Perclose ProStyle SMCR System to obtain hemostasis.
15. For catheterization procedures using a procedural sheath > 8F, where the operating physician is not a vascular surgeon, it is recommended that a vascular surgeon or a surgeon with vascular training be available during the procedure to perform any necessary vascular surgical intervention.
16. If the Perclose ProStyle Device is used to close and repair multiple access sites in the same vessel, space the access sites apart adequately to minimize sheath-device interference.

8.0 SPECIAL PATIENT POPULATION

As with any catheter-based procedures, vessel damage and / or device breakage is a possibility. Observe Warnings and Precautions at all times when using this device, and be prepared for necessary intervention and / or surgical removal of the device and vessel repair as per facility protocol.

The safety and effectiveness of the Perclose™ ProStyle™ SMCR System have not been established in the following special patient populations:

- Patients in whom introducer sheaths < 5F or > 21F were used in the femoral artery during the catheterization procedure.
- Patients in whom introducer sheaths < 5F or > 24F were used in the femoral vein during the catheterization procedure.
- Patients with small femoral vessels (< 5 mm in diameter).
- Patients with access sites above the most inferior border of the inferior epigastric artery (IEA) and / or above the inguinal ligament based upon bony landmarks.
- Patients having access in vessels other than the common femoral artery or vein.

- Patients having a hematoma, pseudoaneurysm or arteriovenous fistula present prior to sheath removal.
- Patients with femoral artery calcium which is fluoroscopically visible at access site.
- Patients with severe claudication, iliac or femoral vessel diameter stenosis greater than 50% or previous bypass surgery or stent placement in the vicinity of access site.
- Patients with access sites in vascular grafts.
- Patients with prior intra-aortic balloon pump at access site at any time prior to the procedure.
- Patients with ipsilateral arterial access sites punctured and externally compressed within 48 hours of closure. **Note:** The previous / initial access site may have the potential to re-bleed due to an unstable clot and / or anticoagulants, even if the new access site is successfully closed and repaired with Perclose ProStyle SMCR System.
- Patients with whom there is difficulty inserting the sheath or greater than one ipsilateral vascular puncture at the start of the catheterization procedure that are not actively managed.
- Patients with antegrade punctures.
- Patients with intra-procedural bleeding around access site.
- Patients receiving glycoprotein IIb/IIIa inhibitors before, during, or after the catheterization procedure.
- Patients who are pregnant or lactating.
- Patients with bleeding diathesis or coagulopathy.
- Patients younger than 18 years of age.
- Patients who are morbidly obese (Body Mass Index ≥ 40 kg/m²).
- Patients with active systemic or cutaneous infection or inflammation.

Before considering early discharge, assess the patient for the following clinical conditions:

- Anticoagulation, thrombolytic, or antiplatelet therapy
- Any comorbid condition requiring observation
- Bleeding at the closure site
- Conscious sedation
- Hematoma at the closure site
- Hypotension
- Pain while walking
- Unstable cardiac status

The presence of any of the above factors has generally led to the deferral of early discharge recommendations.

9.0 POTENTIAL ADVERSE EVENTS

Potential adverse events associated with use of vessel closure devices may include, but are not limited to, the following:

- Allergic reaction or hypersensitivity to device components
- Vascular access complications which may require transfusion or vessel repair, including:
    - Anemia
    - Aneurysm
    - Arteriovenous fistula
    - Bleeding / hemorrhage / re-bleeding

  - Bruising / hematoma
  - Embolism
  - Inflammation
  - Intimal tear / dissection
  - Perforation
  - Pseudoaneurysm
  - Retroperitoneal hematoma / bleeding
  - Scar formation
  - Wound dehiscence
- Cardiac arrhythmias (including conduction disorders, atrial and ventricular arrhythmias)
  - Atrial arrhythmias
  - Ventricular arrhythmias
- Femoral artery / venous complications which may require additional intervention, including:
  - Arterial / venous stenosis
  - Arterial / venous occlusion
  - Arteriovenous fistula
  - Intimal tear / dissection
  - Ischemia distal to closure site
  - Nerve injury
  - Numbness
  - Thrombus formation
  - Vascular injury
- Venous thromboembolism (including deep vein thrombosis, pulmonary embolism, post-procedure pulmonary embolism):
- Infection – local or systemic
- Pain
- Hemodynamic instability:
  - Hypotension / hypertension
  - Vasovagal episode
- Death
- Device complications
- Device failure
- Device malfunction

10.0 CLINICAL STUDIES

10.1 The PEVAR Clinical Trial

The PEVAR trial was a prospective, multicenter, randomized concurrently controlled clinical trial. Patients with AAA who were suitable candidates for endovascular repair using the Endologix's Powerlink Stent Graft with the 21F IntuiTrak Delivery System and for percutaneous femoral artery closure who met the prospectively defined inclusion / exclusion criteria were randomized to treatment with the IntuiTrak System via a totally percutaneous access approach (PEVAR = Test) or via a standard vascular exposure cutdown approach (SEVAR = Control). Randomization was carried out in a 2:1 PEVAR:SEVAR manner. PEVAR patients had their femoral artery access sites closed using either the Perclose ProGlide™ Suture-Mediated

Closure System[1] or another closure system. Prior to the randomization of the first patient at each investigational site, a minimum of two patients were treated in a roll-in phase at the investigational site. Roll-in patients underwent the same treatment and follow-up as the randomized patients.

The PEVAR trial included the Independent Access Site Closure Study which was a set of analyses designed to evaluate the safety and effectiveness of the ProGlide using the pre-close technique to percutaneously close ipsilateral femoral artery access sites up to 21F sheath size. The primary analysis was based on a non-inferiority hypothesis test to demonstrate the ProGlide arm is non-inferior to the SEVAR arm. Data from the ProGlide (N = 50) and SEVAR (N = 50) arms are briefly presented below.

10.1.1 Methods

All patients underwent pre-procedure assessments prior to enrollment in the trial. The protocol required clinical assessments prior to discharge, at 1 month and 6 months. An independent clinical events committee adjudicated potential endpoint events of both major and minor ipsilateral access site vascular complications. The enrollment has been completed and all 6-month visits have been completed. The following assessments were required at pre-discharge, 1 month, and 6 months:

- Medication review (1 and 6 months only)
- Physical exam, including overall health and physical assessment, lower extremity sensorimotor exam and access site assessment
- Serum creatinine, blood urea nitrogen, hematocrit and hemoglobin
- ABI (Ankle-Brachial Index)
- Contrast-enhanced CT scan of the abdomen and pelvis (1 month only)
- Bilateral femoral duplex ultrasound (pre-discharge and 6 months only)
- SF-36 QOL (Quality of Life) (1 and 6 months only)
- Pain scale
- Adverse events

10.1.2 Results of the Independent Access Site Closure Study for the Randomized ProGlide vs. SEVAR Arms

Patient Demographics

In general, baseline demographics were comparable between the ProGlide and the SEVAR patients. There was a difference in age between the ProGlide and SEVAR arms (69.9 ± 6.6 vs. 73.2 ± 8.8) which did not appear to affect the overall study outcome, based on additional adjusted analysis.

Primary Endpoint

The primary endpoint for the Independent Access Site Closure Study of the PEVAR trial was the major ipsilateral access site vascular complication rate at 30 days for patients treated

[1] Perclose ProStyle SMCR System is a design evolution of the Perclose ProGlide SMC System. The results of the PEVAR Clinical Trial are applicable to the Perclose ProStyle SMCR System because of system similarities.

percutaneously (PEVAR ProGlide arm [Test]) compared to that of patients treated using standard surgical vascular access (SEVAR group [Control]).

Major ipsilateral access site vascular complications are a composite of the following events:

- Access site vascular injury requiring surgical repair, angioplasty, or ultrasound-guided compression, or thrombin injection
- New onset lower extremity ischemia that is attributed to arterial access or closure causing a threat to the viability of the limb and requiring surgical or additional percutaneous intervention
- Access site-related bleeding requiring transfusion
- Access site-related infection requiring intravenous antibiotics or a prolonged hospitalization
- Access site-related nerve injury that is permanent or requires surgery

The study results show that at 30 days, ProGlide patients had a 6.0% (3/50) major ipsilateral access site vascular complication rate vs. the SEVAR patients who had a 10% (5/50) major ipsilateral access site vascular complication rate. The non-inferiority test for the primary endpoint revealed a *p*-value = 0.0048 and resulted in the rejection of the null hypothesis, demonstrating that ProGlide is non-inferior to SEVAR in the closure of femoral artery access sites up to 21F sheath size (**Table 10.1.2-1**).

Table 10.1.2-1: Non-inferiority Test for Primary Endpoint – Per Subject Analysis (Modified Intent-to-Treat Population[1] - ProGlide vs. SEVAR)

	ProGlide N = 50	**SEVAR N = 50**	***p*-value[3]**
Major Ipsilateral Access Site Vascular Complication at 30 Days [95% Confidence Interval][2]	6.0% (3/50) [1.3%, 16.5%]	10.0% (5/50) [3.3%, 21.8%]	0.0048

[1] Defined as all patients who were randomized and treated
[2] By Clopper-Pearson exact confidence interval
[3] One-sided p-value and 95% confidence interval for non-inferiority test by using asymptotic test statistics with non-inferiority margin of 10%

Select Secondary Endpoints

In the Independent Access Site Closure Study of the PEVAR trial, the following select secondary endpoints were also evaluated.

- Procedure time was defined as elapsed time from the first skin break to final closure (skin to skin time)
- Minor ipsilateral access site complications included minor ipsilateral access site vascular complications and narcotic analgesic use for ipsilateral access site pain at 30 days. Minor ipsilateral access site vascular complications included:
    - Access site pseudoaneurysm or AV fistula documented by ultrasound
    - Access site hematoma ≥ 6 cm
    - Post-discharge access site-related bleeding requiring > 30 minutes to re-achieve hemostasis

  - Lower extremity arterial emboli or stenosis that is attributed to arterial access or closure
  - Deep vein thrombosis
  - Access site-related vessel laceration
  - Transient access site-related nerve injury
  - Access site wound dehiscence
  - Access site-related lymphocele
  - Localized access site infection treated with intramuscular or oral antibiotics
- Time to actual hospital discharge was defined as elapsed time from sheath removal to actual physical discharge from the hospital.
- Time to ambulation was defined as elapsed time between sheath removal and time when the patient stands and walks at least 20 feet without re-bleeding.
- Ipsilateral pain score at pre-discharge
- Time to hemostasis for the ipsilateral access site was defined as elapsed time from sheath removal to first observed cessation of CFA bleeding (excluding cutaneous or subcutaneous oozing).
- Closure device success was defined as successful achievement of index procedure ipsilateral access site hemostasis with percutaneous closure without surgical intervention.
- Ipsilateral access site closure success was defined as successful achievement of hemostasis with percutaneous closure devices and without surgical intervention and freedom from major ipsilateral access site vascular complications within 48 hours of the index procedure or hospital discharge, whichever occurs first.

As shown in **Table 10.1.2-2**, the ProGlide arm had a 25% shorter procedure time than the SEVAR arm (106.5 ± 44.9 vs. 141.1 ± 73.4, $p = 0.0076$). There were no differences in the minor ipsilateral access site complications, time to actual hospital discharge, time to ambulation and ipsilateral pain score at pre-discharge between the ProGlide and SEVAR arms. In the ProGlide arm, the time to hemostasis for the ipsilateral access site was 57% shorter than in the SEVAR arm (9.8 ± 17 vs. 22.7 ± 22.9 minutes, 95% CI of the difference [-21.1, -4.7]). In addition, the ProGlide arm achieved a closure device success rate and access site closure success rate at 96% and 94%, respectively.

Table 10.1.2-2: Select Secondary Endpoints

Secondary Endpoints	ProGlide N = 50	SEVAR N = 50	Difference (95% CI)[1]	Superiority Test *p*-value
Procedure Time (minutes) [95% Confidence Interval][1]	106.5 ± 44.9 (50) [93.7, 119.2]	141.1 ± 73.4 (50) [120.3, 162.0]	-34.7 [-58.9, -10.4]	0.0076[3]
Minor Ipsilateral Access Site Complications at 30 Days[5] [95% Confidence Interval][2]	22.0% (11/50) [11.5%, 36.0%]	30.0% (15/50) [17.9%, 44.6%]	-8.0% [-25.1%, 9.1%]	0.4954[4]
Minor Ipsilateral Access Site Vascular Complications at 30 Days [95% Confidence Interval][2]	4.0% (2/50) [0.5%, 13.7%]	8.0% (4/50) [2.2%, 19.2%]	-4.0% [Assumptions not met] [6]	--
Narcotic Analgesic Use for Ipsilateral Access Site Pain at 30 Days [95% Confidence Interval][2]	18.0% (9/50) [8.6%, 31.4%]	28.0% (14/50) [16.2%, 42.5%]	-10.0% [-26.4%, 6.4%]	--
Time to Actual Hospital Discharge (hours) [95% Confidence Interval][1]	31.4 ± 16.9 (50) [26.6, 36.2]	45.7 ± 59.9 (48) [28.3, 63.1]	-14.3 [-32.3, 3.7]	--
Time to Ambulation (hours) [95% Confidence Interval][1]	17.8 ± 7.2 (50) [15.7, 19.9]	20.5 ± 16.9 (48) [15.6, 25.5]	-2.7 [-8.0, 2.5]	--
Ipsilateral Pain Scale Score at Pre-Discharge [95% Confidence Interval][1]	2.1 ± 2.2 (50) [1.5, 2.7]	2.6 ± 2.4 (49) [1.9, 3.3]	-0.5 [-1.4, 0.4]	--
Time to Hemostasis for Ipsilateral Access Site (minutes)[3] [95% Confidence Interval][2]	9.8 ± 17.0 (50) [5.0, 14.7]	22.7 ± 22.9 (47) [16.0, 29.4]	-12.9 [-21.1, -4.7]	--
Closure Device Success [95% Confidence Interval][2]	96.0% (48/50) [86.3%, 99.5%]	N/A	N/A	--
Access Site Closure Success [95% Confidence Interval][2]	94.0% (47/50) [83.5%, 98.7%]	N/A	N/A	--

[1] By normal approximation
[2] By Clopper-Pearson exact confidence interval
[3] By two-sample t-test, pre-specified hypothesis test based hierarchical test procedure.
[4] By Fisher's Exact Test, pre-specified hypothesis test based hierarchical test procedure.
[5] A composite endpoint including minor Ipsilateral Access site vascular complications and narcotic analgesic use for Ipsilateral access site pain at 30 days
[6] Insufficient sample size or small frequency in the numerator for the validity of normal approximation assumption

Adverse Events

Adverse events related to major and minor ipsilateral access site vascular complications that occurred within the first 30 days are listed in **Table 10.1.2-3**.

Table 10.1.2-3: Major and Minor Ipsilateral Access Site Vascular Complications Through 30 Days[1]

	ProGlide N = 50	SEVAR N = 50
Major Ipsilateral Access Site Vascular Complications at 30 Days	6.0% (3/50)	10.0% (5/50)
Access site vascular injury requiring surgical repair, angioplasty, or ultrasound-guided compression, or thrombin injection	2.0% (1/50)	2.0% (1/50)
New onset lower extremity ischemia that is attributed to arterial access or closure causing a threat to the viability of the limb and requiring surgical or additional percutaneous intervention	4.0% (2/50)	4.0% (2/50)
Access site-related bleeding requiring transfusion	2.0% (1/50)	4.0% (2/50)
Access site-related infection requiring intravenous antibiotics or a prolonged hospitalization	0.0% (0/50)	0.0% (0/50)
Access site-related nerve injury that is permanent or requires surgery	0.0% (0/50)	2.0% (1/50)
Minor Ipsilateral Access Site Vascular Complications at 30 Days	4.0% (2/50)	8.0% (4/50)
Access site pseudoaneurysm or AV fistula documented by ultrasound	0.0% (0/50)	0.0% (0/50)
Access site hematoma ≥ 6 cm	0.0% (0/50)	2.0% (1/50)
Post-discharge access site-related bleeding requiring > 30 minutes to re-achieve hemostasis	0.0% (0/50)	0.0% (0/50)
Lower extremity arterial emboli or stenosis that is attributed to arterial access or closure	4.0% (2/50)	4.0% (2/50)
Deep vein thrombosis	0.0% (0/50)	0.0% (0/50)
Access site-related vessel laceration	0.0% (0/50)	0.0% (0/50)
Transient access site-related nerve injury	0.0% (0/50)	2.0% (1/50)
Access site wound dehiscence	0.0% (0/50)	0.0% (0/50)
Access site-related lymphocele	0.0% (0/50)	0.0% (0/50)
Localized access site infection treated with intramuscular or oral antibiotics	0.0% (0/50)	0.0% (0/50)

[1] Include only each subject's first occurrence of each event

10.1.3 Clinical Data from the Roll-in Phase

There were 22 patients treated in the ProGlide roll-in phase of the PEVAR trial. The mean age of this treatment group was 71.1 ± 6.9 years. The major ipsilateral access site vascular complication rate was 4.5 % (1/22). The mean procedure time was 118.2 ± 43.4 minutes and the average time to ipsilateral hemostasis was 7.7 ± 6.8 minutes for the roll-in phase. Additionally, the closure device success rate and the access site closure success rate were both

95.5%, respectively. These results were comparable to the ProGlide arm in the randomized phase and substantiated the safety and effectiveness of the ProGlide device.

Conclusion

The Perclose ProGlide SMC device, using a pre-close technique, is non-inferior to the standard vascular surgical cutdown in the closure of femoral artery access sites up to 21F sheath size. The Perclose ProGlide SMC device can be safely and effectively used to close femoral artery access sites up to 21F sheath size. Additionally, use of the ProGlide pre-close technique can result in shorter procedure time and shorter time to achieve hemostasis.

10.2 The CLOSER IDE Clinical Trial

The previous generation suture mediated closure device was known as the Closer and Closer S SMC Systems. The CLOSER IDE trial provided safety and effectiveness data which supported an indication for closing femoral arteries up to 8F and the addition of interventional catheterization procedures.

The CLOSER IDE trial[2] was designed as an equivalency trial for the 30-day primary combined safety endpoint of freedom from major complications and a primary efficacy endpoint of time to discharge when compared to the control group (STAND II Trial). The study prospectively examined the safety and effectiveness of femoral artery closure using the Closer 6F SMC device following interventional catheterization procedures using 5F to 8F sheaths. Two hundred twenty-five (225) patients were enrolled in post-close arm and one hundred sixty (160) patients were enrolled in the pre-close arm of the CLOSER IDE trial. In the post-close arm, the deployment of the Closer device occurred at the end of the catheterization procedure. In the pre-close arm, the Closer device was deployed in two steps with suture delivery at the beginning of the catheterization procedure with knot tying and knot delivery occurring at the end of the procedure.

Procedural success was achieved in 223 patients (99.1%) in the post-close arm and 158 patients (98.8%) in the pre-close arm. Time to discharge was 28.9 $\pm$ 22.7 hours and 30.1 $\pm$ 33.9 hours for the post-close and pre-close patients, respectively. The secondary endpoint of time to hemostasis was 10.9 $\pm$ 42.0 minutes and 8.2 $\pm$ 51.0 minutes for the post-close and pre-close patients, respectively, versus 7.9 $\pm$ 6.4 hours for the control group patients, $p < 0.0001$, and the secondary endpoint of time to ambulation was 4.7 $\pm$ 7.1 hours and 6.5 $\pm$ 11.4 hours for the post-close and pre-close patients, respectively.

Device success was 92.0% (207/225 patients) in the post-close arm and 89.4% (143/160 patients) in the pre-close arm. Failure to deploy the Closer occurred in 17 (7.6%) patients in the post-close arm and 15 (9.4%) patients in the pre-close arm.

A major complication was defined as surgical repair of vascular injury, ultrasound-guided compression, groin-related transfusion, or groin-related infection requiring IV antibiotics and extended hospitalization. The primary safety endpoint was the combined rate of major complications at 30 days. For the post-close arm, one patient received a blood transfusion

[2] Perclose ProStyle SMCR System and Perclose ProGlide SMC System are design evolutions of the Closer 6F SMC system. The results of the CLOSER IDE trial are applicable to the Perclose ProStyle SMCR and Perclose ProGlide SMC Systems because of system similarities.

subsequent to a retroperitoneal bleed. Another patient underwent surgical repair of a vascular injury and received a blood transfusion subsequent to the intervention. Both patients were free of symptoms at time of follow-up. For the pre-close arm, one patient developed a hematoma > 6 cm as a result of insufficient hemostasis. Subsequently, the patient required vascular surgery to repair the femoral artery and received blood transfusions intraoperatively. The second patient received IV antibiotic therapy for a local infection that presented post discharge. Both patients reported no further sequelae at time of follow-up.

The incidence of vascular complication other than major was a secondary safety endpoint of the study and in the post-close arm consisted of one (0.4%) false aneurysm, one (0.4%) infection requiring IM and PO antibiotics, two (0.9%) ≥ 6 cm hematomas, and two (0.9%) retroperitoneal bleeds not requiring intervention. For the pre-close arm, the incidence of vascular complication other than major consisted of one (0.6%) ≥ 6 cm hematoma and one (0.6%) groin infection requiring PO antibiotics. All patients were free of symptoms at time of follow up. The results of the effectiveness measures are summarized in **Table 10.2-1**.

Table 10.2-1: Principal Effectiveness Results

(All patients enrolled in the CLOSER IDE trial;
N = 225 for the post-close arm; N = 160 for the pre-close arm)

Effectiveness Measures*	**The CLOSER IDE Trial Post-Close Patients**	**The CLOSER IDE Trial Pre-Close Patients**
Treated patients (per event)	**N = 225**	**N = 160**
Procedural success	223 (99.1%)	158 (98.8%)
Device success	207 (92.0%)	143 (89.4%)
Device failure	17 (7.6%)	15 (9.4%)
Device malfunction	16 (7.1%)	14 (8.8%)
Device complication	1 (0.4%)	1 (0.6%)
Time to Hemostasis (mins)	N = 224	N = 160
mean±SD	10.9±42.0	8.2±51.0
(min. max.)	(1.0, 324.0)	(0.1, 639.0)
Median	3.0	1.5
[quartiles]	[2.0, 5.0]	[0.0, 5.0]
Time to Ambulation (hrs)	N = 225	N = 160
mean±SD	4.7±7.1	6.5±11.4
(min. max.)	(0.1, 71.4)	(0.05, 100.9)
Median	2.4	2.2
[quartiles]	[1.6, 4.5]	[1.2, 5.0]
Time to Discharge (hrs)	N = 225	N = 160
mean±SD	28.9±22.7	30.1±33.9
(min. max.)	(2.2, 240.2)	(2.7, 292.6)
Median	24.4	22.5
[quartiles]	[22.0, 27.2]	[20.2, 26.1]

*The number of patients listed under effectiveness measures is less than the total patients studied due to missing data for some patients. Device success = acute success using the device only or the device + adjunctive (non-arterial) compression.

Thus, the Perclose ProGlide SMC System reduced the time to hemostasis, ambulation (10 feet) and discharge in patients who had undergone diagnostic or interventional catheterization

procedures without complicating clinical conditions (refer to sections **7.0 PRECAUTIONS** and **8.0 SPECIAL PATIENT POPULATION)**.

Adverse Events in the CLOSER IDE Trial

The CLOSER IDE trial was designed as a multi-center, multi-operator, prospective registry enrolling 225 patients in the post-close arm and 160 patients in the pre-close arm. The post-close arm studied the use of the Closer 6F system following interventional procedures using 5F to 6F sheaths. The pre-close arm studied the use of the Closer 6F system following interventional procedures using 7F to 8F sheaths utilizing the pre-close technique. The pre-specified analysis of the primary safety endpoint of the IDE trial was the incidence of the combined rate of major complications at 30 days of patients undergoing interventional catheterization procedures. Post-treatment, ultrasound evaluations were performed 0 to 15 days post-discharge to verify detection of clinical complications. Two major complications were reported in each of the post-close and pre-close arms of the CLOSER IDE trial. Neither of the two major complications reported in the post-close or pre-close arms were considered unanticipated events. No delayed major hemorrhagic events were reported despite early ambulation and early discharge of the patients with the Closer SMC device. The adverse events that were observed during the trial are reported in **Table 10.2-2**.

Table 10.2-2: Percentage of Patients Who Experienced Adverse Events

(All patients enrolled in the CLOSER IDE trial;
N = 225 for post-close arm; N = 160 for pre-close arm)

Safety Measures, n (percent)	The CLOSER IDE Trial Post-Close Patients	The CLOSER IDE Trial Pre-Close Patients
Treated patients (per event)	**N = 225**	**N = 160**
Device Failure	17 (7.6%)	15 (9.4%)
Surgical repair*	1 (0.4%)	1 (0.6%)
U/S guided compression*	0 (0.0%)	0 (0.0%)
Transfusion*	2 (0.9%)	1 (0.6%)
Infection requiring IV Abx*	0 (0.0%)	1 (0.6%)
Hematoma $\geq$ 6 cm	2 (0.9%)	1 (0.6%)
AV-fistula	0 (0.0%)	0 (0.0%)
Pseudoaneurysm	1 (0.4%)	0 (0.0%)
Vascular narrowing	0 (0.0%)	0 (0.0%)
Infection requiring IM\PO Abx	1 (0.4%)	1 (0.6%)
Retroperitoneal bleed	2 (0.9%)	0 (0.0%)
Incidence of Complications (per patient)		
Any complication¶	6 (2.7%)	3 (1.9%)
Major complication¶	2 (0.9%)	2 (1.2%)
No major complication	223 (99.1%)	158 (98.8%)

* Major complication

¶ Per patient; some patients may have experienced more than one complication.

No groin or device related deaths were reported in the Closer IDE trial among the post-close or

pre-close study patients. Other adverse events potentially associated with the use of the Closer SMC System were reported as an underlying event or did not occur during the clinical study. These include: deep vein thrombosis, infection extending hospitalization, late bleeding, wound dehiscence, vessel laceration, local pulse deficits or ischemia, embolization, transitory local irritation, nerve injury and vascular spasm. In addition, polyester surgical sutures elicit a minimal acute inflammatory reaction in tissues, followed by gradual encapsulation of the suture by fibrous connective tissue. Polyester surgical sutures are not absorbed, nor are any significant change in tensile strength known to occur *in vivo*.

10.3 The REALISM Clinical Trial – ProGlide Cohort

A retrospective analysis was performed to evaluate the safety and effectiveness of the Perclose ProGlide SMC System[3] in closing large-sized venous access sites through a retrospective data collection from the EVEREST II/REALISM Continued Access Registry Study (REALISM). The retrospective analysis included subjects in whom ProGlide was used as the primary method for large bore venous access-site closure during the MitraClip index procedure with a 24F vascular sheath.

10.3.1 Methods

The analysis population was derived from a subset of REALISM subjects who were enrolled in the REALISM High Risk (HR) cohort, REALISM Non-High Risk (NHR) cohort, and REALISM Compassionate Use (CU) cohort. REALISM was a continued access study within the EVEREST II trial, which included subjects receiving the MitraClip index procedure with MitraClip sheath of 24F. REALISM enrolled 958 subjects, of whom 899 subjects were enrolled per the protocol and 59 as compassionate use. The **ProGlide cohort** was selected from subjects enrolled in the seven (7) REALISM sites with high frequency use of vessel closure devices (VCD ≥ 15 cases), and who received at least one ProGlide as their primary closure device during the MitraClip index procedure. Of the seven (7) sites, one (1) site did not use ProGlide and another site only used ProGlide for arterial access, and therefore the ProGlide cohort comprised of five (5) sites with a total of 159 subjects. Similarly, a **Manual Compression cohort (MC cohort)** of 230 subjects was identified from seven (7) sites that reported high frequency MC usage of ≥ 25 cases each without the use of any VCD. Subjects in both cohorts had MitraClip implanted into the mitral valve with access through the common femoral vein.

In the ProGlide Cohort, three (3) sub-group analyses were predefined: ProGlide Alone vs. ProGlide Plus, Male vs. Female, and One ProGlide vs. Two ProGlides. The ProGlide Alone group included subjects in whom at least one ProGlide was used without any secondary method(s) other than brief adjunctive MC ≤ 10 minutes. The ProGlide Plus group included subjects in whom at least one ProGlide with prolonged MC > 10 minutes or other secondary closure methods were used. None of the sub-group analyses are powered for statistical significance.

This retrospective analysis reports baseline subject characteristics and comorbidities, ProGlide usage information, effectiveness of achieving hemostasis (including time to hemostasis) during

[3] Perclose ProStyle SMCR System is a design evolution of the Perclose ProGlide SMC System. The results of the REALISM Clinical Trial are applicable to the Perclose ProStyle SMCR System because of system similarities

the index procedure, and adverse events up to 30 days. The primary endpoint was the rate of freedom from major femoral vein access-site related complications at 30-days post MitraClip index procedure. The pre-specified acceptance criterion for the rate of freedom from major femoral vein access-site related complications at 30-days post-procedure was ≥ 90%.
Major complication is defined as any event leading to death, life-threatening or major bleeding, surgical intervention, hospitalization, visceral ischemia, or neurological impairment. This list includes development of the following:

- Femoral vein stenosis (> 50%) development at the puncture site related to closure technique
- Development of deep vein thrombosis in the target limb
- Significant venous bleeding, retroperitoneal bleeding / hematoma, or hematoma at the access site requiring transfusion or surgical intervention
- Hematoma that does not require transfusion or surgical intervention
- Access site-related wound dehiscence or venous access site infection requiring intravenous, intramuscular or oral antibiotics, and / or leading to a prolonged hospitalization
- Venous access site injury, including vessel laceration, requiring surgical repair, angioplasty, ultrasound-guided compression or thrombin injection
- Re-bleeding at access site that requires treatment or re-hospitalization
- AV fistula
- Pseudoaneurysm
- Access site-related nerve injury

Minor complications are defined as those complications that did not require transfusion, surgery, or re-hospitalization. Adverse events from baseline to 30 days were reviewed to identify any potential femoral vein access-site related complications, which upon identification, were subsequently adjudicated by an independent Clinical Event Committee (CEC).

10.3.2 Results – ProGlide Cohort

Subject Selection: Of the 159 subjects in the ProGlide cohort, 98 subjects (61.6%) were from the REALISM High Risk cohort, 37 subjects (23.3%) from the REALISM Non-High Risk cohort, and 24 subjects (15.1%) from the REALISM Compassionate Use cohort. All subjects completed their discharge evaluations. Four (4) subjects died before their 30-day visits and two (2) missed their 30-day visits, and therefore 153 subjects reported 30-day assessments.

Subject Demographics: The ProGlide cohort reflected subjects with varying degrees of heart failure. The cohort included elderly subjects with a mean age of 76 years. Male subjects accounted for 52.8%. Subjects presented with multiple comorbidities including high rates of congestive heart failure (CHF) (89.2%), atrial fibrillation (AF) (64.7%), coronary artery disease (CAD) (67.7%), hypertension (84.8%), diabetes (26.4%) moderate to severe renal disease (24.5%), chronic obstructive pulmonary disease (COPD) (23.3%), and NYHA class III (59.7%) and IV (24.5%). History of prior percutaneous interventions (37.7%) and cardiovascular surgery (42.1%) were common in this cohort.

Primary Endpoint: The freedom from major femoral vein access-site related complications was 98.1% at 30 days, which met the pre-specified safety acceptance criteria of 90% for the ProGlide cohort (**Table 10.3.2-1**). ProGlide group is defined as subjects who had received at least one ProGlide as the primary intended method to close femoral vein access site during the index procedure with or without adjunctive closure methods (manual compression or subcutaneous stitch). A total of 16 adjudicated complications, in 13 subjects, were reported through 30 days, of which only five (5) events in three (3) subjects were major complications. The remaining 11 adjudicated complications, in 10 subjects, were considered minor.

Table 10.3.2-1: Freedom from Major Femoral Vein Access-Site Related Complication Through 30 Days (ProGlide Cohort[4]) (Per Subject Analysis)

Events[1]	ProGlide (N = 159[3])	Clinical Acceptance Criteria
Freedom from Major Femoral Vein Access-Related Complication[2]	98.1% (156/159)	90%

[1] Includes only each subject's first occurrence of each event.

[2] The major femoral vein access-related complication is defined as access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment.

[3] The denominator excludes subjects who withdrew or lost to follow up before the 30-day visit early window (27 days post-procedure) without any femoral vein access-related complication.

[4] ProGlide group is defined as subjects who had received at least one ProGlide as the primary intended method to close femoral vein access site during the index procedure with or without adjunctive closure methods (manual compression or subcutaneous stitch).

Summary of Safety: The adjudicated major femoral vein access-site related complications through 30 days were reported as non-hierarchical subject counts (**Table 10.3.2-2**). The major complication rate was low at 1.9%. Five (5) major complications in three (3) subjects were reported within 30 days: one (1) hematoma requiring intervention and one (1) pseudo-aneurysm, one (1) hematoma and one (1) re-bleeding within 48 hours, and one (1) deep vein thrombosis in the target limb 6-days post-procedure. All cases achieved hemostasis within 2 minutes without MC or secondary closure devices.

Table 10.3.2-2: Summary of Adjudicated Major Femoral Vein Access-Site Related Complications Through 30 Days (ProGlide Cohort[3]): Non-Hierarchical by Subject

Non-Hierarchical Major Events[1]	0 – 48 hours (Subject count)	> 48 hours – 30 days (Subject count)	0 – 30 days (Subject count)	Total number of events from 0 to 30 days
Major Femoral Vein Access-Related Complications[2]	1.3% (2/159)	0.6% (1/159)	1.9% (3/159)	5
Femoral vein stenosis (>50% development at the puncture site related to closure technique)	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0

Non-Hierarchical Major Events[1]	0 – 48 hours (Subject count)	> 48 hours – 30 days (Subject count)	0 – 30 days (Subject count)	Total number of events from 0 to 30 days
Development of deep vein thrombosis in the target limb	0.0% (0/159)	0.6% (1/159)	0.6% (1/159)	1
Significant venous bleeding, retroperitoneal bleeding / hematoma, or hematoma at the access site requiring transfusion or surgical intervention	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
Hematoma that does not require transfusion or surgical intervention	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
Access site-related wound dehiscence or venous access site infection requiring intravenous, intramuscular or oral antibiotics, and / or leading to a prolonged hospitalization	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0
Venous access site injury, including vessel laceration, requiring surgical repair, angioplasty, ultrasound-guided compression or thrombin injection	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0
Re-bleeding at access site that requires treatment or re-hospitalization	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
AV Fistula	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0
Pseudoaneurysm	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
Access site-related nerve injury	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0

[1] Includes only each subject's first occurrence of each event.
[2] The major femoral vein access-related complication is defined as access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment.
[3] ProGlide group is defined as subjects who had received at least one ProGlide as the primary intended method to close femoral vein access site during the index procedure with or without adjunctive closure methods (manual compression or subcutaneous stitch).

The adjudicated minor femoral vein access-site related complications through 30 days were also reported as non-hierarchical subject counts. There were 10 subjects with minor complications (6.3%). The total number of minor complications through 30 days was 11, including four (4) hematoma events not requiring treatment (2.5%; 4/159) and seven (7) re-bleeds requiring treatment (4.4%; 7/159). All minor complications occurred within 48-hours post-procedure and were resolved by 30 days.

Summary of Effectiveness: ProGlide was an effective device for primary intended hemostasis of venous closure sites. Majority of subjects (69.2%) achieved hemostasis with ProGlide alone without additional secondary closure methods. Adjunctive closure methods included MC (17.6%, 28/159) and subcutaneous stitch (12.6%, 20/159), and one (1) subject received an AngioSeal along with ProGlide and MC (0.6%, 1/159). Within the ProGlide cohort, two (2) ProGlide devices were used predominantly to achieve hemostasis (90.6%, 144/159), a practice attributed to the arterial closure IFU which requires at least two (2) ProGlides if the transcatheter device sheath is greater than 8F as is the case with the 24F MitraClip. The remaining 9.4% (15/159) cases used single ProGlide for access-site closure.

On average, hemostasis was achieved in 5.92 ± 6.19 minutes in the ProGlide cohort. The mean time to achieve hemostasis with ProGlide alone was 5.15 minutes. This time increased to 9.3 minutes when adjunctive MC was used. When a secondary vessel closure method (namely subcutaneous stitch) was used, the mean time to achieve hemostasis was 5.8 minutes (**Table 10.3.2-3**). Overall, secondary closures were mostly initiated when there was a failure to achieve hemostasis using ProGlide and MC, which occurred in 12.6% of patients.

Table 10.3.2-3: Summary of ProGlide Effectiveness on Hemostasis (ProGlide Cohort[5])

Characteristics	ProGlide (N = 159)
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	5.92 ± 6.19 (134)
Median (Q1, Q3)	4.50 (1.00, 8.00)
Range (min, max)	(0.00, 30.00)
ProGlide Without Any Adjunctive Closure Method	69.2% (110/159)
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	5.15 ± 6.05 (95)
Median (Q1, Q3)	3.00 (1.00, 7.00)
Range (min, max)	(0.00, 29.00)
ProGlide and Adjunctive Manual Compression (MC) Only	17.6% (28/159)
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	9.3 ± 7.3 (23)
Median (Q1, Q3)	6.0 (5.0, 14.0)
Range (min, max)	(1, 30)
ProGlide and Adjunctive Manual Compression <=5 Minutes[1]	6.3% (10/159)
Time to Achieve Hemostasis (min)	4.0 ± 1.7 (10)
Mean ± SD (n)	5.0 (3.0, 5.0)
Median (Q1, Q3)	(1, 5)
Range (min, max)	
ProGlide and Adjunctive Manual Compression <=10 Minutes[1]	10.1% (16/159)
Time to Achieve Hemostasis (min)	5.1 ± 2.1 (16)
Mean ± SD (n)	5.0 (5.0, 6.0)
Median (Q1, Q3)	(1, 9)
Range (min, max)	
ProGlide and Adjunctive Manual Compression >10 Minutes or Unknown [1, 2]	7.5% (12/159)
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	

Characteristics	ProGlide (N = 159)
Median (Q1, Q3) Range (min, max)	18.7 ± 5.9 (7) 18.0 (14.0, 22.0) (13, 30)
ProGlide and Secondary Vessel Closure Method Only **Time to Achieve Hemostasis (min)** Mean ± SD (n) Median (Q1, Q3) Range (min, max)	12.6% (20/159) 5.8 ± 3.3 (16) 6.0 (3.0, 7.0) (1, 12)
Type of Secondary Closure Method Subcutaneous Stitch Other Closure Device Surgical Repair Data Not Available	 100.0% (20/20) 0.0% (0/20) 0.0% (0/20) 0.0% (0/20)
Reason to use Secondary Vessel Closure Method ProGlide Device Deficiency Access Complication (s) Failure to Achieve Hemostasis Data Not Available[4]	 0.0% (0/20) 0.0% (0/20) 95.0% (19/20) 5.0% (1/20)
Hemostasis Achieved by Using ProGlide, Manual Compression and Secondary Vessel Closure Method [3]	0.6% (1/159)

[1] For subjects with missing manual compression time, the non-missing time to achieve hemostasis is used to determine the sub-category.
[2] Subjects with both manual compression time and time to achieve hemostasis missing are also included in this category.
[3] One (1) subject used Angio-seal as the secondary vessel closure method in addition to ProGlide and Manual Compression due to unknown reason. The subject had both manual compression time and time to achieve hemostasis unknown.
[4] Subject who used Secondary closure method with unknown reason was categorized in the Data not available category.
[5] ProGlide group is defined as subjects who had received at least one ProGlide as the primary intended method to close femoral vein access site during the index procedure with or without adjunctive closure methods (manual compression or subcutaneous stitch).

10.3.3 Sub-Group Analyses

Three (3) sub-group analyses were pre-specified: ProGlide Alone vs. ProGlide Plus, Male vs. Female, and One ProGlide vs. Two ProGlides. These sub-group analyses were not powered.

10.3.3.1 ProGlide Alone vs. ProGlide Plus

The ProGlide Alone group involved 126 subjects in whom at least one ProGlide was used along with adjunctive MC ≤ 10 minutes. These subjects generally had numerically higher baseline comorbidities, such as atrial fibrillation, coronary artery disease, diabetes, hypercholesterolemia, angina, MI, prior percutaneous interventions and cardiovascular surgery, liver disease, and NYHA II compared to the ProGlide Plus group. The ProGlide Plus group included fewer subjects (n = 33) all of whom required at least one ProGlide with either prolonged MC > 10 minutes or a secondary closure device to achieve hemostasis.

Safety: The major complications were low and occurred in the ProGlide Alone group (2.4% [3/126]) with 1.6% (2/126) complications occurring within the first 48 hours. There were no major complications in the ProGlide Plus group, through 30 days. Minor complications were similar in both groups with approximately 94% freedom from events (ProGlide Alone 6.3% [8/126] and

ProGlide Plus 6.1% [2/33]). Within the limits of sample sizes, these results support the safe and effective use of ProGlide with or without adjunctive MC.

Effectiveness: The ProGlide Plus group had a numerically greater time to achieve hemostasis compared to the ProGlide Alone group (9.70 ± 7.34 [23] vs. 5.14 ± 5.65 [111]). In the ProGlide Alone group, 87.3% of subjects achieved hemostasis by using ProGlide without any adjunctive closure method, and 12.7% achieved hemostasis by using ProGlide and adjunctive manual compression. Additionally, the ProGlide Plus group compared to the ProGlide Alone group had a numerically higher percentage of subjects achieving hemostasis using ProGlide and adjunctive manual compression (36.4% [12/33] vs. 12.7% [16/126]).

10.3.3.2 Male vs. Female

A total of 84 male subjects and 75 female subjects were included in this sub-group analysis. Both groups had a similar mean age (males: 77 years; females: 74 years). Males reported numerically higher baseline incidences of key comorbidities including congestive heart failure, hypercholesterolemia, coronary and peripheral vascular disease (PVD), diabetes, COPD, and NYHA III/IV.

Safety: All 30-day major complications were reported in males 3.6% (3/84). There were no major complications in female through 30 days. However, because the event rates are low, larger dataset would be needed to confirm a gender difference. Among minor events, men 8.3% (7/84) had a numerically higher rate compared with women 4.0% (3/75).

Effectiveness: On average, both groups took comparable time to achieve hemostasis (men: 5.69 ± 6.37 [70] vs. women: 6.18 ± 6.02 [64]). Males achieved numerically faster hemostasis than females when adjunctive MC (6.9 ± 4.7 [11] vs. 11.4 ± 8.7 [12]) or other secondary closure devices (4.2 ± 2.9 [9] vs. 7.7 ± 2.7 [7]) were used.

10.3.3.3 One ProGlide vs. Two ProGlides

Most of the subjects in this study received two (2) ProGlides (n = 144) and only fifteen (15) subjects received one (1) ProGlide. The most common reason for using more than one ProGlide was per IFU recommendation (93.8% [135/144] of the cases). Within the Two ProGlides group, 70.8% (102/144) did not require any adjunctive closure methods compared with 53.3% (8/15) in the One ProGlide group.

Both groups were similar in age (one ProGlide 75 years vs. two ProGlides 76 years). Both groups had approximately same rates of key risk factors of CHF, atrial fibrillation, angina, and COPD. The One ProGlide subjects had numerically higher rates of CAD, PVD, renal disease, and NYHA III, while the Two ProGlide subjects had numerically higher rates of cardiomyopathy, diabetes, history of CABG, and NYHA IV.

Safety: Major complication rates at 30 days were numerically higher in the One ProGlide group at 6.7% (1/15) compared with 1.4% (2/144) in Two ProGlides group. The very small sample size of the One ProGlide group must be considered when assessing the 30-day rate. Each group

reported only one (1) major access-site complications within 48 hours post-procedure. The 30-day minor complication rate remained unchanged from the 30-day major complication rate for the one ProGlide group (6.7%) and was 6.3% (9/144) for the two ProGlide group. Given the disproportionate sample sizes of the two groups, the outcomes must be interpreted with caution.

Effectiveness: The subjects in the One ProGlide group took numerically longer to achieve hemostasis than those who received two (2) ProGlides (7.93 ± 6.58 [14] vs. 5.69 ± 6.13 [120]). Additionally, the One ProGlide group reported a smaller percentage of subjects achieving hemostasis without any adjunctive methods compared to Two ProGlide (53.3% [8/15] vs. 70.8% [102/144]), a numerically higher percentage of use of adjunctive MC (33.3% [5/15] vs. 16.0% [23/144]) and a numerically higher percentage of MC of ≥ 10 mins compared with the Two ProGlides group (20.0% [3/15] vs. 6.3% [9/144]).

10.3.4 RESULTS: Manual Compression Cohort

The MC Cohort consisted of 230 subjects: 156 (67.8%) from the REALISM High Risk cohort, 58 (25.2%) from the REALISM Non-High Risk cohort, and 16 (7.0%) from the REALISM Compassionate Use cohort. Their mean age was 77 years (230) and subjects in the MC cohort had high rates of CHF (94.8% [218/230]), AF (62.9% [134/213]), CAD (76.4% [175/229]), diabetes (33.0% [76/230]), moderate to severe renal (27.8% [64/230]), and COPD (28.4% [65/229]), and prior percutaneous intervention (35.4% [81/229]). In the MC cohort, 50% of the subjects achieved hemostasis with MC only; 49.6% and 0.4% of the subjects received MC plus a subcutaneous stitch or MC plus other closure device as a secondary method to facilitate hemostasis, respectively.

Safety: Thirty-two adjudicated access site complications were reported through 30 days: 10 major (4.4% [10/227]) and 22 (9.7% [22/227]) minor. The 30-day major complications were mostly venous bleeding (3.1% [7/227]) with the remaining being development of deep vein thrombosis (0.4% [1/227]), hematoma (0.4% [1/227]), re-bleeding (0.9% [2/227]), venous access site injury (0.9% [2/227]) and pseudo-aneurysm 0.9% (2/227). Minor complications mostly developed within 48-hours post-index procedure and were largely due to hematoma, and re-bleeding at the access site that requires treatment.

Effectiveness: In the MC cohort, 50% (115/230) of the subjects received MC alone as the intended hemostasis method; 49.6% (114/230) and 0.4% (1/230) of the subjects received MC plus a subcutaneous stitch or MC plus other closure device as a secondary method to facilitate hemostasis, respectively.

Conclusion

In summary, the primary objective of the study was to evaluate the safety and performance of ProGlide in closure of venous access site in subjects with a large-caliber femoral vein sheath (24F). The study results have demonstrated that the safety assessment of the ProGlide met the predefined acceptance safety criterion. Taken together, the study results show that ProGlide is safe and effective in the closure of the venous access site with up to 24F sheath.

Study Limitations

THE STUDY HAD LIMITATIONS SINCE IT WAS A RETROSPECTIVE ANALYSIS OF A SELECTED DATASET WITHIN A TRIAL IN WHICH THE MAIN OBJECTIVE WAS THE EVALUATION OF THE MITRACLIP DEVICE. THE DESIGN OF THE TRIAL WAS NOT SPECIFIC TO THE EVALUATION OF PROGLIDE FOR LARGE BORE VENOUS CLOSURE.

10.4 The Perclose SMC Investigator Sponsored Studies (ISS)

The primary objective of the Perclose SMC Multi-Access ISS analysis was to evaluate the safety and effectiveness of Perclose SMC in subjects with multiple access sites in a single vein, with focus on use of Perclose SMC for more than one access site per femoral vein; and use of 2 or more Perclose SMCs for a femoral vein access site that is >8F.

10.4.1 Methods

The Perclose Multi-Access ISS analysis consisted of a prospective/retrospective data analysis of the three real-world studies: Santa Barbara Cottage Hospital Study (SBCH), conducted at Santa Barbara Cottage Hospital, Santa Barbara, CA; Emory School of Medicine Study (ESM), conducted at the Emory School of Medicine, Atlanta, GA; and VAscular Closure for Cardiac Ablation Registry (VACCAR), conducted at Saint Luke's Hospital, Kansas City, MO.

The ESM study was a prospective trial while both the VACCAR and the SBCH studies were retrospective. The analysis of the three studies was performed by Abbott using datasets provided by the investigators.

10.4.1.1 SBCH Study

The SBCH trial, a retrospective, single-arm, subject-level study, enrolled 519 subjects between November 2016 and March 2020, over a period of 40.3 months, to evaluate the safety and effectiveness of the Perclose SMC in closure of multiple access sites of the ipsilateral femoral vein following Atrial Fibrillation (AF) ablation. The right femoral vein for vessel access/closure was used per the site standard, with at least one access site using Perclose SMC device. Majority of access sites were treated with one Perclose SMC based on site's standard of care, if Perclose SMC was used for that access site.

The subject population was comprised of men and women ages 25 to 92 that underwent AF ablation with post-ablation closure of the femoral vein using the Perclose SMC System, and who were discharged the same day of the procedure with 30-day follow-up.

10.4.1.2 ESM Study

The ESM study, a prospective, randomized controlled trial, was conducted at three participating sites – Emory University Hospital, Emory University Hospital Midtown, and Emory St Joseph's Hospital; enrolled subjects between January 2020 and December 2020, over a period of 10.8 months, and evaluated the safety and efficacy of Perclose SMC in comparison with manual hemostasis. The trial enrolled 55 subjects in the Perclose SMC arm and 54 subjects in the MC arm. All access sites were treated with only one Perclose SMC regardless of sheath size as

standard of care. Subjects underwent routine ablation for AF as standard of care and were followed through 30 days before exiting the trial.

Additional comparisons of this study were time to hemostasis and time to ambulation. Several other secondary endpoints including frequency of access site related complications, pain and need for post-procedure narcotics, subject satisfaction, as well as cost and overall resource utilization.

10.4.1.3 VACCAR Study

The VACCAR study, a retrospective chart review, subject-level study, enrolled subjects between October 2017 and November 2020 over a period of 37.1 months, comparing 3 groups aimed to find if there was a difference in subject satisfaction and rate of vascular and bleeding complications with use of the Perclose SMC System for venous closure post AF and atrial flutter procedures in comparison to manual compression (MC). Other parameters measured included the time to achieve hemostasis, time to ambulate and length of hospital stay. The trial enrolled 75 subjects in the Perclose SMC arm, 156 subjects in the MC arm, and 203 subjects in the Figure of 8 stitch (Fo8) arm. Unilateral or bilateral femoral veins were used during the index procedure, and the right femoral vein was used for the first 3 access sites. If there were more than 3 access sites, then the remainders used the left femoral vein. For a cryoablation procedure that used 3 or more access sites, one access site used two Perclose devices and all other access sites used one Perclose SMC. If a radio-frequency ablation procedure was done using Perclose SMC in closure of multiple access sites, then every access site only used one Perclose device.

Clinical Study Endpoints

The primary safety endpoint was freedom from femoral vein access-related major vascular complications at 30-days post procedure, including but not limited to:

- Femoral vein stenosis (> 50%) development at the puncture site related to closure technique;
- Development of deep vein thrombosis in the target limb;
- Significant venous bleeding, retroperitoneal bleeding / hematoma, or hematoma at the access site requiring transfusion or surgical intervention;
- Hematoma that did not require transfusion or surgical intervention;
- Access site-related wound dehiscence or venous access site infection requiring intravenous, intramuscular or oral antibiotics, and / or leading to a prolonged hospitalization;
- Venous access site injury, including vessel laceration, requiring surgical repair, angioplasty, ultrasound-guided compression or thrombin injection;
- Re-bleeding at access site that required treatment or re-hospitalization;
- AV fistula;
- Pseudoaneurysm;
- Access site-related nerve injury;
- Pulmonary embolism

Results were compared to a clinical acceptance criterion of ≥95%. A 95% clinical acceptance criterion was applied to both the SBCH Study and ESM Study but was not applied to the VACCAR Registry results as it did not have 30-day follow-up.

Primary performance endpoints included the following procedure details:

1. Type of ablation procedure
2. Number of access sites per subject
3. Number of access sites per single vein
4. Number of Perclose SMCs used per vein and per access site and per closure procedure
5. Number of Perclose SMCs used access site > 8F access sites
6. Distribution of sheath size
7. Procedure duration
8. Success rate
9. Anticoagulant and antiplatelet medications
10. Use of protamine for heparin reversal

10.4.2 Results

10.4.2.1 Subject Selection

A total of 1062 subjects underwent ablation procedure at 3 investigational sites in the United States between November 2016 and December 2020. Of these 1062 subjects, 649 were treated with the Perclose SMC System, 210 were treated by MC, and 203 were treated using Fo8 stitch.

The SBCH Study treated 519 subjects with Perclose SMC. All subjects were assessed for performance endpoints and for safety endpoints to 30 days.

The ESM Study treated 55 subjects with Perclose SMC arm, and 54 subjects with MC. Of the 55 subjects in the Perclose SMC arm, 2 subjects were randomized without procedure, therefore, only 53 subjects were assessed for safety endpoints to 30 days.

The VACCAR Study treated 75 subjects with Perclose SMC arm, 156 subjects with MC, and 203 subjects with Fo8. All subjects were assessed for performance endpoints and for safety endpoints in-hospital.

10.4.2.2 Subject Demographics

Demographics and primary diagnosis of subjects in the 3 studies is given in **Table 0-1** below. Use of oral anticoagulants and oral antiplatelets pre and post procedure for 30 days is given in **Table 0-2** and **Table 10.4.2-3**.

Table 0-1 Demographics and Primary Diagnosis

	SBCH Study Perclose Device (N=519)	**ESM Study Perclose Device (N=55)**	**VACCAR Study Perclose Device (N=75)**
Age (year)			
Mean ± SD (n)	69.1 ± 10.1 (519)	61.1 ± 10.0 (55)	67.2 ± 8.6 (74)
Median (Q1, Q3)	70.0 (63.0, 76.0)	64.0 (55.0, 68.0)	68.5 (63.0, 73.0)

Range (min, max)	(25, 92)	(31, 80)	(43, 81)
Sex			
Male	65.9% (342/519)	70.9% (39/55)	57.3% (43/75)
Female	34.1% (177/519)	29.1% (16/55)	42.7% (32/75)
Primary Diagnosis			
Paroxysmal AF	44.5% (231/519)	67.9% (36/53)	73.3% (55/75)
Persistent AF	47.6% (247/519)	32.1% (17/53)	16.0% (12/75)
Atrial Flutter	1.7% (9/519)	Not reported	10.7% (8/75)
Other	6.2% (32/519)	Not reported	Not reported
Diabetes	Not reported	10.9% (6/55)	26.7% (20/75)
Coronary Artery Disease	Not reported	10.9% (6/55)	21.3% (16/75)

Note: N is the total number of subjects.

Table 0-2 Oral Anticoagulant Use Pre- and Post-Procedure

	SBCH Study Perclose Device (N=519)	ESM Study Perclose Device (N=55)	VACCAR Study Perclose Device (N=75)
Pre-Procedure			
Any Oral Anticoagulant	29.2% (151/517)	89.1% (49/55)	100.0% (75/75)
Warfarin	4.3% (22/517)	7.3% (4/55)	10.7% (8/75)
Apixaban	25.0% (129/517)	65.5% (36/55)	68.0% (51/75)
Rivaroxaban	0.0% (0/517)	14.5% (8/55)	17.3% (13/75)
Dabigatran	0.0% (0/517)	1.8% (1/55)	4.0% (3/75)
Post-Procedure for 30 Days			
Any Oral Anticoagulant	30.8% (159/517)	100.0% (53/53)	Not reported
Warfarin	4.3% (22/517)	3.8% (2/53)	Not reported
Apixaban	26.7% (138/517)	79.2% (42/53)	Not reported
Rivaroxaban	0.0% (0/517)	17.0% (9/53)	Not reported
Dabigatran	0.0% (0/517)	1.9% (1/53)	Not reported

Oral anti-coagulant use post-procedure not available for the VACCAR study.

Table 0-3 Oral Antiplatelet Use Pre- and Post-Procedure

	SBCH Study Perclose Device (N=519)	ESM Study Perclose Device (N=55)
Pre-Procedure		
Any Oral Antiplatelet	22.4% (116/517)	20.0% (11/55)
Aspirin	20.9% (108/517)	18.2% (10/55)
Clopidogrel	3.3% (17/517)	1.8% (1/55)
Ticagrelor	0.4% (2/517)	0.0% (0/55)
Prasugrel	0.0% (0/517)	0.0% (0/55)
Post-Procedure during 30 Days		
Any Oral Antiplatelet	19.5% (101/517)	79.2% (42/53)
Aspirin	18.2% (94/517)	77.4% (41/53)
Clopidogrel	3.1% (16/517)	0.0% (0/53)
Ticagrelor	0.4% (2/517)	1.9% (1/53)
Prasugrel	0.0% (0/517)	0.0% (0/53)

Oral antiplatelet use pre-and post-procedure not available for the VACCAR study.

10.4.2.3 Key Results

Freedom from major access-site related complications was 99.2% for the SBCH study and 96.2% for the ESM study (**Table 0-4**) up to 30 days post index procedure, compared to the 95% clinical acceptance criterion. Both studies met the clinical acceptance criterion.
The major access-site related complications included hematomas, major bleeding, pseudoaneurysm, and vascular surgery.

Although the VACCAR study did not have 30-day follow-up, it also demonstrated a complete freedom of access site-related major complications (0.0%, 0/75) in the Perclose SMC arm at discharge. Minor complication rate included hematoma (1.3%), pseudoaneurysm (1.3%) and other complications (1.3%). MC and Fo8 minor complication rates were 2.6% and 1.5%, all of which were hematomas (**Table 10.4.2-5**).

Table 0-4 Primary Safety Endpoint - Freedom from Major Access-Site Related Complications at 30-Days Compared to Clinical Acceptance Criteria for SBCH and ESM Study

	SBCH Study Perclose Device (N=519)	ESM Study Perclose Device (N=53*)	Clinical Acceptance Criteria
Freedom from Major Access-site Related Complications	99.2% (515/519)	96.2% (51/53)	95%
Hematoma	99.8% (518/519)	96.2% (51/53)	-
Major Bleeding	100.0% (519/519)	96.2% (51/53)	-
Pseudoaneurysm	99.8% (518/519)	Not reported	-
Vascular Surgery	99.6% (517/519)	Not reported	-

Note: N is the total number of subjects.
* Two subjects were randomized without procedure. They are included in the baseline tables but not others.

Table 0-5 Safety Endpoints (In-hospital) - VACCAR Study

	Perclose Device (N=75)	Manual Compression (N=156)	Figure of 8 Stitch (N=203)
Major Complications	0.0% (0/75)	0.6% (1/156)	0.0% (0/203)
Hematoma	0.0% (0/75)	0.6% (1/156)	0.0% (0/203)
Minor Complications	4.0% (3/75)	2.6% (4/156)	1.5% (3/203)
Hematoma	1.3% (1/75)	2.6% (4/156)	1.5% (3/203)
Pseudoaneurysm	1.3% (1/75)	0.0% (0/156)	0.0% (0/203)
Other Complications	1.3% (1/75)	0.0% (0/156)	0.0% (0/203)
Additional Manual Compression	13.5% (10/74)	4.5% (7/156)	4.9% (10/203)

Note: N is the total number of subjects.

10.4.2.5 Effectiveness Endpoints and Other Key Measures

The acceptance criterion for freedom from femoral vein access-related major vascular complications at 30-days post procedure was ≥95%. The 95% clinical acceptance criterion was applied to ESM Study but not to the VACCAR Registry results as it does not have 30-day results. A brief summary of the procedural variables for the 3 studies is summarized in **Table 0-6** Procedural Information
. Hospitalization information for the 3 studies is summarized in **Table 0-7**.

Time to Hemostasis, Time to Ambulation, Total Index Hospitalization Duration

In the SBCH study. time to hemostasis and time to ambulation were not collected. All 519 subjects were discharged at the same day, so the total hospitalization duration is 0 day for all subjects. Protamine heparin reverse was administered in 90.1% of all subjects.

In the ESM study, the mean times to hemostasis were 7.46 minutes for Perclose SMC vs. 11.66 minutes for MC. The mean times to ambulation were 167.9 minutes for Perclose SMC vs. 280.1 minutes for MC. The mean total index hospitalization duration days was the same for both groups (0.3 days for both Perclose SMC and MC). Protamine heparin reverse was administered in 66.0% of subjects in the Perclose SMC arm, whereas 70.4% in the MC arm were administered protamine.

In the VACCAR study, the mean times to hemostasis were 8.63 minutes for Perclose SMC vs. 165.83 minutes for MC vs. 10.19 minutes for Figure of 8 Stitch. The mean times to ambulation were 157.29 minutes for Perclose SMC vs. 390.20 minutes for MC vs. 157.42 minutes for Figure of 8 Stitch. The total index hospitalization duration days was not collected. Only 2.7% of subjects in the Perclose SMC arm were administered Protamine heparin reverse, whereas 11.8% in the MC arm and 90.1% in the Fo8 arm were administered protamine.

It is important to note that no analysis was done by Abbott specifically to assess safety in the population that did not use Protamine heparin reverse.

Table 0-6 Procedural Information

SBCH Study (n=519)	ESM Study (n=53)	VACCAR Study (n=75)
Type of Ablation Procedure		
Not Available (NA)*	Cryoablation: 66% Radiofrequency: 34%	Cryoablation: 64% Radiofrequency: 36%
# of Access Sites Per Subject		
Mean: 3.6 Range: 2-5	Mean: 3.0 Range: 2-4	Mean: 3.4 Range: 2-6
# of Access Sites Per Single Vein		
Mean: 3.6 Range: 2-5	Mean: 2.3 Range: 1-3	Mean: not available Range: 1-3
# of Perclose SMCs Used Per Vein and Per Access Site and Per Closure Procedure		
Per Vein Mean: 3.5 Range: 1-6 Per Access Site Mean: NA Range: NA Per Closure Procedure Mean:3.5 Range: 1-6	Per Vein Mean: 2.3 Range: 1-4 Per Access Site Mean: NA Range: 1-2 Per Closure Procedure Mean: 3.0 Range: 2-5	Per Vein Mean: NA Range: NA Per Access Site Mean: NA Range: 1-2 Per Closure Procedure Mean: 4.0 Range: 2-7
% of access site > 8F		
30%	68.2%	NA
# of Perclose SMCs Used Access Site for subjects with > 8F Access Sites		
NA	>8F: 1 Perclose SMC: 96.2%	>8F: NA

SBCH Study (n=519)	ESM Study (n=53)	VACCAR Study (n=75)
	2 Perclose SMC: 3.8%	
Distribution of Sheath Size		
Mean: 8.8F Range: 4F-12F	Mean: 10.24F Range: 7F-16F	Mean: NA Range: NA
Procedure Duration		
Mean: 181.8 minutes	Mean: 158.1 minutes	NA
Success Rate – Per Access Site**		
NA	98.7%	NA
Anticoagulant and Antiplatelet Medications		
Anticoagulant Pre Procedure: 29.2% 30 Days Post: 30.8% Antiplatelet Medications Pre Procedure: 22.4% 30 Days Post: 19.5%	Anticoagulant Pre Procedure: 89.1% 30 Days Post: 100% Antiplatelet Medications Pre Procedure: 20% 30 Days Post: 79.2%	Anticoagulant Pre Procedure: 100% 30 Days Post: NA Antiplatelet Medications Pre Procedure: NA 30 Days Post: NA

* Not available (NA) means data were not available.
** Success rate is defined as either complete success (immediate complete hemostasis) or partial success (more hemostatic than without any intervention but some manual pressure required) achieved. Failure is defined as no effect by Perclose SMC System for access site closure as if the Perclose SMC weren't there.

Table 0-7 Hospitalization Information

	SBCH Study Perclose Device (N=519)	ESM Study Perclose Device (N=55)	VACCAR Study Perclose Device (N=75)
Total Index Hospitalization Duration (day) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	0.0 ± 0.0 (519) 0.0 (0.0, 0.0) (0, 0)	0.3 ± 0.5 (53) 0.0 (0.0, 1.0) (0, 1)	Not reported
Time to Hemostasis (min) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	Not reported	7.46 ± 7.53 (53) 4.45 (1.05, 11.30) (0.07, 26.98)	8.63 ± 9.32 (75) 7.00 (4.00, 10.25) (0.10, 71.13)
Time to Ambulation (min) # Mean ± SD (n) Median (Q1, Q3) Range (min, max)	Not reported	167.9 ± 136.4 (49) 135.0 (87.0, 201.0) (60, 944)	157.29 ± 94.41 (75) 135.00 (84.90, 207.00) (28.95, 509.00)

#Time to ambulation is time to move outside the bed.
Note: N is the total number of subjects.

To summarize, all subjects of the 3 ISSs had at least 2 access sites. Except for the VACCAR study that did not collect access site level information, majority of the SBCH and the ESM studies had at least one access site that was > 8F (517/519 for SBCH and 52/53 for ESM). For the access sites > 8F, most of them used one Perclose SMC only (site operation rule for SBCH, 149/154 access sites for ESM).

Both the SBCH and the ESM studies met the 95% clinical acceptance criterion as the primary safety endpoint (99.2% for SBCH and 96.2% for ESM). The VACCAR also demonstrated a complete freedom of access site related major complications (0.0%, 0/75) in the Perclose SMC arm at discharge.

10.4.3 Subgroup Analyses

As pre-specified in the Perclose Multi-Access Project Plan, subgroup analyses for procedural details and safety evaluation were performed for procedures using sheath size ≤8F (at least one access site using sheath >8F vs. ≤8F), number of access sites (2 or 3 vs. ≥4), access sites per vein (at least 1 vein with 3 access sites vs. all veins with 1 or 2 access sites), gender (male vs. female), age (age ≥65 vs. <65 years), race (white vs. non-white), and diabetes (diabetes vs. non-diabetes). All subgroup analyses were descriptive without pre-specified power hypothesis.

10.4.3.1 Sheath Size > 8F vs ≤ 8F

Safety: Almost all subjects (517/519) in the SBCH study and 52/53 in the ESM study received at least one sheath with size >8F. A per subject analysis at 30-days showed low major access-site related complication of 0.8% (4/517) in the SBCH study and 3.8% (2/52) in the ESM study. Major complications for subjects with sheath size >8F in the SBCH study included hematoma (0.2%), pseudoaneurysm (0.2%) and vascular surgery (0.4%) and in the ESM study included hematoma (3.8%) and major bleeding (3.8%) (**Table 0-8**). ESM study mostly used only one Perclose SMC for closure of access sites > 8F (96.2%). Standard practice of the SBCH study was to use only one Perclose for access sites > 8F. Largest sheath size used of these studies was 12F in the SBCH study and 16F in the ESM study. The results confirmed safety of single Perclose for closure of access sites > 8F.

Table 0-8 Major Access-site Related Complications in Subjects with > 8F Sheaths

	SBCH Study Perclose Device (N=517)	ESM Study Perclose Device (N=52*)
Major Access-site Related Complications	0.8% (4/517)	3.8% (2/52)
Hematoma	0.2% (1/517)	3.8% (2/52)
Major Bleeding	0.0% (0/517)	3.8% (2/52)
Pseudoaneurysm	0.2% (1/517)	Not reported
Vascular Surgery	0.4% (2/517)	Not reported

Note: N is the total number of subjects.
* Two subjects were randomized without procedure. They are included into the baseline tables but not others.

Effectiveness: In the SBCH study, subjects receiving at least one sheath size > 8F had numerically shorter procedure time (181.8 mins) compared to subjects with all sheaths ≤ 8F (200 mins).

In the ESM study, subjects receiving at least one sheath size > 8F had numerically longer procedure time (158.4 mins) compared to subjects with all sheaths ≤ 8F (142 mins).

10.4.3.2 2 or 3 Access Sites versus ≥ 4 Access Sites

Safety: In the SBCH study, only right femoral veins were used for the access sites. Subjects that used 2 or 3 access sites per right femoral vein were 212, compared to procedures with ≥4 access sites were 307. Major complication rates were 0.5% (1/212) and 1.0% (3/307) respectively (**Table 0-9**).

The ESM study used both right and left femoral arteries for the ablation procedures. Thirty-nine (39) subjects had 2 or 3 access sites and 14 had ≥4 access sites. The subgroups used a mean of 2.5 and 2 access sites per vein respectively. Major complication rates were 5.1% and 0% respectively (**Table 0-10**).
Major complication rates in subjects with ≥4 access sites were low and below the pre-specified acceptance criteria of 5%.

The VACCAR study did not report any major in-hospital complications (**Table 0-11**).

Table 0-9 Major Access-site Related Complications, 2 or 3 Access Sites vs ≥ 4 Access Sites, SBCH Study

	2 or 3 Access Sites (N=212)	≥ 4 Access Sites (N=307)
Major Access-site Related Complications	0.5% (1/212)	1.0% (3/307)
Hematoma	0.0% (0/212)	0.3% (1/307)
Major Bleeding	0.0% (0/212)	0.0% (0/307)
Pseudoaneurysm	0.0% (0/212)	0.3% (1/307)
Vascular Surgery	0.5% (1/212)	0.3% (1/307)

Note: N is the total number of subjects.

Table 0-10 Major Access-site Related Complications, 2 or 3 Access Sites vs ≥ 4 Access Sites, ESM Study

	2 or 3 Access Sites (N=39)	≥ 4 Access Sites (N=14)
Major Access-site Related Complications	5.1% (2/39)	0.0% (0/14)
Hematoma	5.1% (2/39)	0.0% (0/14)
Major Bleeding	5.1% (2/39)	0.0% (0/14)

Note: N is the total number of subjects.

Table 0-11 Safety Endpoints (In-Hospital), 2 or 3 Access Sites vs ≥ 4 Access Sites, VACCAR Study

	2 or 3 Access Sites (N=48)	≥ 4 Access Sites (N=27)
Major Complications	0.0% (0/48)	0.0% (0/27)
Hematoma	0.0% (0/48)	0.0% (0/27)

Note: N is the total number of subjects.

Access Sites Per Vein

Safety: In the ESM study, procedures that used at least 1 vein with 3 access sites had a success rate of 100% and those in which all veins had 1 or 2 access sites had a success rate of 97.1%, similar major complications (3.7%, 1/27 vs. 3.8%, 1/26) with no other complications (0%) to 30 days but higher rates of minor complications (11.1%, 3/27 vs. 3.8%, 1/26). Data were not reported for the SBCH and VACCAR study for this subgroup.

Effectiveness: In the ESM study, procedures that used at least 1 vein with 3 access sites compared to those in which all veins had 1 or 2 access sites had longer procedure times (170.7 vs. 144.9 min), needed more time to ambulation (177.3 vs. 156.3 min) but required lesser time to achieve hemostasis (6.96 vs. 7.98 min).

Study Limitations: THE STUDIES HAD LIMITATIONS SINCE TWO OF THE STUDIES (SBCH STUDY AND VACCAR STUDY) WERE RETROSPECTIVE AND HAD ONLY SUBJECT LEVEL DATA. Further, all subgroup analyses were descriptive without pre-specified power hypothesis.

10.5 The Perclose Multi-Access DUS IDE Trial

The objective of the trial was to evaluate the safety of multiple access site closure in a single vein with the Perclose SMC by scheduled duplex ultrasound (DUS) at discharge and at 30 days (if vascular complications observed at discharge) in subjects with asymptomatic or non-visible complications, with focus on use of Perclose SMC for more than one access site per femoral vein; and use of 2 or more Perclose SMCs for a femoral vein access site that is >8F.

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 some hematomas) and/or symptomatic. Therefore, a scheduled femoral DUS was performed in subjects with asymptomatic or non-visible complications to evaluate the overall safety of Perclose SMC in multiple access site closures in a single vein.

10.5.1 Methods

The trial was a prospective, single arm, multicenter, descriptive study and enrolled 36 subjects to evaluate the safety of multiple access site closure in a single vein with the Perclose SMC.The first subject was enrolled on September 1, 2021, and the last subject was enrolled on May 4, 2022. The last subject's 30-day follow-up occurred on May 27, 2022. All subjects were required

to have femoral DUS at discharge and at a 30-day follow-up visit (in case of any access site-related vascular complications {either symptomatic/visible or asymptomatic/non-visible}, nerve injury, or infection at discharge, as assessed by either the investigator or the core laboratory). All subjects underwent routine ablation for cardiac arrythmias as standard of care and similar information was captured including device usage and adverse events (AEs).

Clinical Study Endpoints

The primary endpoint of this study was vascular complications detected by scheduled DUS at discharge or 30 days in subjects with asymptomatic/non-visible complications. The primary endpoint was further categorized as major or minor. Major complications were defined as those which required surgical, interventional, or pre-specified repair and/or hospitalization. All other complications were considered to be minor complications.

Vascular access-site related complications included but were 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
- Non-flow limiting suture material
- Access site-related nerve injury
- Pulmonary embolism
- Other (specify)

Any vascular complications and access site complications were also analyzed as the descriptive endpoints.

Procedural information analyzed included the following:

- Procedure duration
- Type of Procedure (Cryoablation, 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 MC 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

10.5.2 Results

10.5.2.1 Subject Selection

A total of 36 subjects were enrolled in the study and all subjects completed their 30-day follow-ups without any major complications. Thirty-four (34) subjects had DUS assessments at discharge**.**

10.5.2.2 Subject Demographics

The mean age of the study population was 62.9 years, and most subjects were male (66.7%), had a mean body mass index (BMI) of 31.25 kg/mm^2, range of 17.9 kg/mm^2 to 43.4 kg/mm^2, and were diagnosed with either Paroxysmal AF (47.2%), Persistent AF (30.6%) or Atrial Flutter (16.7%). Major co-morbidities included hypertension (61.1%), dyslipidemia (52.8%), diabetes (33.3%), and coronary artery disease (30.6%). A majority of the subjects (91.7%) were on anticoagulants, primarily Apixaban (86.1%). Medication status at discharge and 30-day follow-up is given in **Table 10.5.2-1**.

Table 0-1 Medication Status at Discharge and at 30-day Follow-up

	Perclose SMC (N=36)
At Discharge	
Any Oral Anticoagulant	91.7% (33/36)
Apixaban	86.1% (31/36)
Rivaroxaban	5.6% (2/36)
Any Oral Antiplatelet	25.0% (9/36)
Aspirin	22.2% (8/36)
Clopidogrel	2.8% (1/36)
Ticagrelor	2.8% (1/36)
At 30-Day Visit	
Any Oral Anticoagulant	91.7% (33/36)
Apixaban	86.1% (31/36)
Rivaroxaban	5.6% (2/36)
Any Oral Antiplatelet	19.4% (7/36)
Aspirin	13.9% (5/36)
Clopidogrel	2.8% (1/36)

Ticagrelor	2.8% (1/36)

Note: Medication taken at the time of discharge or at the 30-day follow-up visit is included.
Note: N is the total number of subjects

10.5.2.3 Key Results

10.5.2.3.1 Primary Endpoint

Starting with an intent-to-treat population of 36 subjects (N=36; ITT), there were no major complications detected symptomatically or by DUS for all 36 subjects. However, there were 2 subjects who had minor symptomatic/visible complications and were excluded from the primary endpoint analysis. Of the remaining 34 subjects with no symptomatic/visible complications, 2 subjects did not have DUS at discharge and were excluded from the primary endpoint analysis as well. **The remaining 32 subjects constituted the primary endpoint analysis population (N=32; primary endpoint population).** These 32 subjects in the primary endpoint analysis group were asymptomatic at discharge. Further, DUS at discharge detected no major vascular complications. The overall rate of minor complications in these 32 subjects at discharge was low, as assessed by DUS, with only 4 of 32 (12.5%) having minor complications. The minor complications in the 4 subjects included deep vein thrombosis in the target limb (3 subjects; 1 out of the 3 subjects also had mobile Perclose common femoral vein (CFV) as a complication), and hematoma (1 subject).

As required by the protocol, the 4 subjects in the primary endpoint analysis group who had minor complications at discharge had a scheduled DUS at 30 days and had no additional complications (major or minor). All minor complications were resolved at 30 days. Similarly, at 30 days, there were no additional symptomatic major or minor complications for any of the other subjects in the primary endpoint analysis population.

Table 0-22-2 presents the vascular complications detected by scheduled DUS at discharge in both the intent-to-treat and primary endpoint populations. As detailed above, at discharge, there were no major complications (100% major complication-free) detected symptomatically or by DUS for all 36 subjects.

Table 0-2 Vascular Complications at Discharge

	Intent-to-Treat Population (N=36)	Primary Endpoint Population (N=32)
Major Complications by DUS Detection or CEC Adjudication	**0.0% (0/34)**	**0.0% (0/32)**
Minor Complications by DUS Detection or CEC Adjudication	**17.6% (6/34)**	**12.5% (4/32)**
Deep Vein Thrombosis in the Target Limb	11.8% (4/34)	9.4% (3/32)
Venous Bleeding, Retroperitoneal Bleeding	5.6% (2/36)	N/A
Venous Access Site Injury Including Vessel Laceration	5.6% (2/36)	N/A

	Intent-to-Treat Population (N=36)	Primary Endpoint Population (N=32)
Hematoma	5.9% (2/34)	3.1% (1/32)
Other Vascular Complication	2.9% (1/34)	3.1% (1/32)
Arterial Stenosis	0.0% (0/34)	0.0% (0/32)
Mobile Perclose Common Femoral Vein*	2.9% (1/34)	3.1% (1/32)

* Linear echodensity or filamentous structure visible in two different planes on DUS was the linear thrombus labeled by the core lab as “mobile Perclose CFV”.
Note: Major complications are defined as those which requiring surgical or percutaneous repair if not specified. All other complications are considered to be minor complications.
Note: N is the total number of subjects.

10.5.2.3.2 Summary of Safety

Adverse Event Reporting

A total of 5 adverse events in 3 subjects were reported for the duration of the study. Of those 5, 4 non-serious events - one venous bleeding, one thrombus, one re-bleeding at the access site, and one deep vein thrombosis in the target limb were adjudicated by CEC as device and procedure related event. No device/procedure related serious adverse events were reported and no serious adverse events qualified for the CEC adjudication during the study.

10.5.2.3.3 Summary of Effectiveness

Table 0-3 displays a summary of the procedure and post procedure information
Per subject, the study used a mean of 3.5 (median 4.0) access sites (sheaths) and a mean of 3.8 (median 4.0) Perclose devices in 36 subjects. A majority of subjects received Heparin Reversal (Protamine) after the procedure, as the site standard of care. Mean procedure duration was 138.6 minutes and TTH was 3.1 minutes per access site and 9.5 minutes per subject. Mean time to ambulation[4] was 233.7 minutes and mean time to discharge was 10.92 hours.

Success rate for Perclose SMC per access site was 99.2%.

A mean of 2.3 sheaths and 2.4 Perclose devices were used per vein (n=56).

The study used sheath sizes from ≤ 8F to ≥ 15F. The most commonly used sheath sizes per access site were ≤ 8F (62/126 access sites; 49.2%) and 8.5 – 14F (62/126 access sites; 49.2%). A majority of the access sites (84.9%) used 1 Perclose device to achieve vascular closure. Even in access sites using sheath size >8F also largely (47 of 64 access sites; 73.4%) used 1 Perclose device for vascular closure. Thus, irrespective of whether 1 or 2 Perclose devices were used in >8F access sites, with a majority of the cases using one device, with sheath sizes between 8F and 14F.

[4] Time to ambulation is time to move outside the bed.

Table 0-3 Procedural Results

	Perclose Device (N=36) (V=56) (AS=126)
PER SUBJECT ANALYSIS	
Type of Ablation Procedure	
Cryoablation only	38.9% (14/36)
Radiofrequency Ablation only	58.3% (21/36)
Both	2.8% (1/36)
Number of Access Site (Based on the number of sheath used)	
Mean ± SD (n)	3.5 ± 0.8 (36)
Median (Q1, Q3)	4.0 (3.0, 4.0)
Range (min, max)	(2, 5)
Number of Perclose Used	
Mean ± SD (n)	3.8 ± 1.3 (36)
Median (Q1, Q3)	4.0 (3.0, 5.0)
Range (min, max)	(0, 5)
Procedure Length (minute)	
Mean ± SD (n)	138.6 ± 47.4 (36)
Median (Q1, Q3)	140.0 (120.5, 159.0)
Range (min, max)	(42, 279)
Time to Hemostasis (minute)	
Mean ± SD (n)	9.5 ± 12.4 (36)
Median (Q1, Q3)	6.5 (4.0, 9.5)
Range (min, max)	(1, 74)
Heparin Reverse (Protamine)	79.4% (27/34)
PER VEIN ANALYSIS	
Number of Access Site (Based on the number of sheath used)	
Mean ± SD (n)	2.3 ± 0.8 (56)
Median (Q1, Q3)	2.0 (2.0, 3.0)
Range (min, max)	(1, 3)
1	23.2% (13/56)
2	28.6% (16/56)
3	48.2% (27/56)
Number of Perclose Used	
Mean ± SD (n)	2.4 ± 0.7 (56)
Median (Q1, Q3)	2.0 (2.0, 3.0)
Range (min, max)	(0, 4)
1 unit	1.8% (1/56)
2 units	46.4% (26/56)
3 units	46.4% (26/56)
4 units	1.8% (1/56)

	Perclose Device (N=36) (V=56) (AS=126)
PER ACCESS SITE ANALYSIS	
Sheath Size Used	
≥ 15F	1.6% (2/126)
12 - 14F	11.9% (15/126)
8.5 - 11F	37.3% (47/126)
≤ 8F	49.2% (62/126)
Number of Perclose Used*	
1 unit	84.9% (107/126)
2 units	11.1% (14/126)
Number of Perclose Used* per Access Site > 8F	
1 unit	73.4% (47/64)
2 units	21.9% (14/64)
Time to Hemostasis (minute) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	 3.1 ± 7.3 (126) 1.0 (1.0, 3.0) (0, 74)
Success Rate	99.2% (120/121)
POST PROCEDURE INFORMATION	
Time to Ambulation (minute) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	 233.7 ± 188.7 (36) 193.5 (129.5, 275.5) (58, 1199)
Delay >30 minutes	100.0% (36/36)
Time to Discharge (hour) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	 10.92 ± 9.69 (36) 5.95 (4.00, 19.35) (2.4, 43.8)

Note: N is the total number of subjects, V is the total number of Veins, and AS is total numbers of Access Site.
* Subject US0047-45 had two femoral veins, 5 access sites (3 were >8F). None of the 5 access sites was treated by Perclose SMC due to device deficiencies.

10.5.3 Subgroup Analysis

A summary of post procedure information and mean time to hemostasis per subject for the 4 main subgroups below is given in Error! Reference source not found..

Table 10.5.3-1 Summary of Time to Hemostasis and Post-Procedure Information for 4 Main Subgroups

	Subgroup 1	Subgroup 2	Subgroup 3		Subgroup 4	
	Subjects Treated with 2 Perclose SMC for Access Sites > 8F Perclose SMC (N=14)	Subjects having 3 or 4 Access Sites per Vein Perclose SMC (N=27)	At least One Sheath > 8F (N=32)	All ≤ 8F (N=4)	2 or 3 Access Sites (N=16)	≥ 4 Access Sites (N=20)
Time to Hemostasis (minute) – Per Subject Mean ± SD (n) Median (Q1, Q3) Range (min, max)	9.2 ± 6.6 (14) 7.5 (3.0, 16.0) (2, 21)	8.0 ± 6.3 (27) 7.0 (3.0, 10.0) (1, 24)	10.2 ± 13.0 (32) 7.0 (4.0, 10.0) (1, 74)	3.8 ± 3.6 (4) 2.5 (1.5, 6.0) (1, 9)	11.2 ± 17.6 (16) 6.0 (4.0, 9.5) (1, 74)	8.1 ± 6.0 (20) 7.5 (3.5, 12.0) (1, 21)
Time to Ambulation (minute) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	203.7 ± 106.5 (14) 185.5 (127.0, 266.0) (58, 464)	213.0 ± 91.6 (27) 211.0 (131.0, 266.0) (58, 464)	234.3 ± 198.3 (32) 193.5 (127.5, 258.0) (58, 1199)	228.8 ± 93.5 (4) 224.5 (150.0, 307.5) (136, 330)	246.1 ± 263.9 (16) 154.0 (129.5, 235.0) (106, 1199)	223.9 ± 101.8 (20) 210.5 (137.0, 312.5) (58, 464)
Delay >30 minutes	100.0% (14/14)	100.0% (27/27)	100.0% (32/32)	100.0% (4/4)	100.0% (16/16)	100.0% (20/20)
Time to Discharge (hour) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	13.28 ± 11.41 (14) 7.45 (4.80, 20.10) (2.7, 43.8)	11.00 ± 9.99 (27) 6.10 (4.10, 19.60) (2.4, 43.8)	11.74 ± 9.98 (32) 6.20 (4.20, 19.85) (2.4, 43.8)	4.33 ± 1.46 (4) 4.25 (3.20, 5.45) (2.7, 6.1)	6.39 ± 6.88 (16) 3.80 (3.10, 5.25) (2.4, 23.9)	14.54 ± 10.22 (20) 13.05 (5.95, 20.15) (4.1, 43.8)

10.5.3.1 2 Perclose SMC for Access Sites > 8F

Safety: No major complications (0%) were detected by DUS in the 14 asymptomatic subjects treated with 2 Perclose SMC for access sites using >8F sheaths. The overall minor complication rate (7.1%) was low based on DUS examination with 1 (7.1%, n=1/14) subject experiencing a minor hematoma.

Effectiveness: Mean time to hemostasis was 9.2 mins and time to ambulation was 203.7 mins. Per subject, a mean of 4.8 Perclose SMC (range 3-5 units) were used with 85.7% using 5 Perclose SMC. Heparin (92.9%) and Heparin Reversal (92.3%) were administered to the majority of subjects.

Per vein, a mean of 2.0 sheaths and 2.6 Perclose SMC units were used.

The overall success rate per access site was 100%. Per access site, a sheath size ≤8F (49.1%) was most commonly used followed by 8.5-11F (28.3%) and 12-14F (22.6%). Overall, most procedures used 1 Perclose SMC (73.6%) per access site.

Of the 53 access sites, 27 access sites used a sheath size >8F (27/53; 50.9%) among 14 subjects (from 36 ITT subjects) treated with 2 Perclose SMC for at least one access site >8F. Of these 27 access sites, a little more than half (14/27; 51.9%) of the access sites required 2 Perclose SMC devices, and less than half (13/27; 48.1%) of the access sites required 1 Perclose SMC device to achieve vascular closure. Of these 14, 12 had 4 access sites (3 in one leg and 1 in another leg), 1 had 3 access sites (all in one leg) and 1 had 2 access sites (all in one leg).

10.5.3.2 3 or 4 Access Sites Per Vein

Safety: No major complications (0%) were detected in the 25 asymptomatic subjects having 3 or 4 access sites per vein. The overall minor complication rate (12.0%) was low when analyzed by DUS and included deep vein thrombosis in the target limb (8.0%) and hematoma (4.0%).

Effectiveness: The mean TTH overall was 8.0 min, with 4 access sites (9.2 min) requiring the most TTH; subjects with 5 access sites tended to have the lowest TTH (5.7 min), but the sample size is too small to make meaningful comparisons. Mean time to ambulation was 213 mins. Per subject, a mean of 3.7 (range 3-5 units) sheaths and a mean of 4.0 Perclose SMC were used. Heparin (92.6%) and Heparin Reversal (88.0%) were administered to the majority of subjects.

Per vein, a mean of 2.3 sheaths and a mean of 2.5 Perclose SMC.

Per access site, the overall success rate was 100%. Approximately half the subjects used at least 1 sheath >8F (≤8F, 49.0%; 8.5-11F, 36.0%) with 15% using sheaths larger than 12F (12-14F and ≥15F). While the majority used 1 Perclose SMC (82.0%) per access site, 13.0% used 2 Perclose SMC.

10.5.3.3 Sheath Size > 8F versus ≤ 8F

The majority of subjects in subgroup used at least one >8F (n=32/36) compared to ≤8F only (n=4/36). Due to small number of subjects treated with ≤8F only, comparing of these subgroups was not meaningful.

Safety: No major complications (0%) were detected by DUS in this subgroup. Minor complication rates by DUS at discharge in subjects with at least 1 access site using sheaths >8F compared with all ≤8F were 14.3% (4/28) and 0% (0/4) respectively.

Effectiveness: Time to ambulation for subjects that used at least 1 access site >8F compared to procedures with all ≤8F was 234.3 mins and 228.8 min and time to discharge was 11.74 hours and 4.33 hours respectively. TTH was 10.2 min and 3.8 min respectively.

Per subject, procedure time for subjects that used at least 1 access site >8F compared to procedures with all ≤8F was 139.8 min and. 128.8 min respectively. Mean sheath number used were 3.6 and 3.0 respectively and mean Perclose used were 3.8 and 3.0 units respectively.
Per vein, subjects with 1 access site using >8F compared with all ≤8F used a similar number of sheaths (2.2 vs. 2.4 units) and Perclose SMC (2.4 vs. 2.4 units).
The overall success rate per access site was 99.1% for 1 access site using sheaths >8F and 100% for all ≤8F. TTH per access site, was 3.2 min and 2.3 min respectively.

10.5.3.4 2 or 3 Access Sites versus ≥ 4 Access Sites

Safety No major complications (0%) at discharge were detected by DUS in this subgroup. Minor complication rates at discharge detected by DUS were numerically lower with 2 or 3 access sites versus ≥4 access sites (7.1%, 1/14 vs. 16.7%, 3/18); minor complications in the group using 2 or 3 access sites included deep vein thrombosis in the target limb (7.1%), and in the group using ≥4 access sites included deep vein thrombosis in the target limb (11.1%) and hematoma (5.6%).

Effectiveness: Procedures that used 2 or 3 access sites compared to procedures requiring ≥4 access sites required less time to discharge (6.39 vs. 14.54 hours) but more time to ambulation (246.1 vs. 223.9 min). Subjects with 2 or 3 access sites compared with ≥4 access sites required more overall TTH (11.2 vs 8.1 min). The difference in TTH can be attributed to the high range of TTH (1-74 minutes) in the 2 or 3 access sites subgroup.

Per subject, subjects with 2 or 3 access sites compared with ≥4 access sites used fewer sheaths (mean 2.7 vs. 4.2) and Perclose SMC (2.8 vs. 4.5 units) and had shorter procedure time (128.3 vs. 146.8 min).

Per vein, subjects with 2 or 3 access sites compared with all ≥ 4 access sites used a more sheaths (2.7 vs. 2.1 units) and Perclose SMC (2.8 vs. 2.3 units).

The overall success rate per access site was 97.7% for 2 or 3 access sites and 100% for ≥4 access. Per access site, sheath sizes used were similar across both groups. More 1 Perclose SMC (95.3% vs. 79.5%) were used per access site >8F. Subjects with 2 or 3 access sites compared with ≥4 access sites required more overall TTH (6.9 vs. 1.1 min) and TTH per access site >8F (9.3 vs 1.3 min) which is counterintuitive and could be interpreted as a coincidental study finding due to the high range of TTH in the 2 or 3 access site group.

Conclusion:

All subjects had at least 2 access sites for vessel closure, majority of them had 3 or 4 access sites (28/36) and at least one >8F (n=32/36) sheath used for an access site. In addition, 13/36 subjects used two Perclose SMC units in one access site.

No major complications were found symptomatically or detected by DUS at discharge, or at 30 days for all 36 subjects. Only minor vascular complications were detected at discharge either symptomatically or by DUS in subjects with asymptomatic/non-visible complications. Importantly, all these complications resolved, and no minor complications were found at 30 days for all 36 subjects. None of the asymptomatic or non-visible complications detected by DUS were index-procedure or Perclose SMC related.

Further, subgroup analyses detected no major complications, irrespective of whether 1 or 2 Perclose devices were used in >8F access sites, with a majority of the cases using one device, with sheath sizes between 8F and 14F. However, since there were no major complications detected in the asymptomatic subjects in any of the subgroups, this precluded any meaningful analyses of major complications in different subgroup populations. Additionally, the numbers of subjects in different subgroups were low and this study was not designed and powered to evaluate the differences between various subgroups.

The use of a scheduled DUS at discharge and at 30 days has successfully demonstrated the overall safety of using Perclose SMC in achieving vascular closure for multiple venous access sites in a single vein. Additionally, Perclose SMC was found safe for vascular closure of access sites that use sheath sizes ranging from ≤8F to ≥15F, and also for those that use 2 or more Perclose SMCs per femoral vein access site.

In conclusion, the results of the Perclose Multi-Access DUS trial demonstrate that Perclose SMC is safe to use for multiple access site closure in a single vein and when 2 or more Perclose SMC units are used per femoral vein access site.

11.0 THE PERCLOSE™ PROSTYLE™ SMCR SYSTEM CLINICAL PROCEDURE

The following instructions provide technical direction but do not obviate the necessity of formal training in the use of the Perclose ProStyle SMCR System. The techniques and procedures described below are not intended as a substitute for the operator's experience and judgment in treating any specific patients.

11.1 Examination and Selection of Products

1. Select the Perclose ProStyle SMCR Systems(s) for closure and repair of 5F to 21F sheath access sites in the common femoral artery and 5F to 24F sheath access sites in the common femoral vein.
2. After carefully inspecting the packaging of the Perclose ProStyle SMCR System for damage to the sterile barrier, remove the device from the package.
3. Exercise care when using additional instruments, such as clamps, forceps or needle holders during device handling, to reduce the possibility of accidental device breakage or damage to the suture.

11.2 Access Site and Puncture Considerations

1. An extremely deep tissue tract can prevent the Perclose ProStyle needles from engaging the cuffs. In extremely deep tissue tracts, the Perclose™ ProStyle™ Suture Trimmer and / or the Perclose™ Snared Knot Pusher may not be able to advance the knot completely to the external vessel wall before locking the knot. In extremely deep tissue tracts, inserting the Perclose™ ProStyle™ Device can require lifting of the panniculus and / or compression of the subcutaneous tissue (with the body of the device) to be able to obtain flow of blood ("mark") through the marker lumen.

2. Before inserting the access needle, use of ultrasound guidance to visualize the access site or fluoroscopy to visualize the femoral head is recommended. When using the femoral head as a reference point, target the medial third of the femoral head as the puncture site. Performing a femoral angiogram through the introducer sheath (or procedural sheath) to verify that the access site is in the common femoral artery or vein is recommended before anticoagulants are given.
3. If the Perclose ProStyle Device is used to close and repair multiple access sites in the same vessel, space the access sites apart adequately to minimize sheath-device interference. Use of ultrasound guidance to visualize the spacing between each needle entry point in the vessel while maintaining approximately the same angle of entry for all punctures is recommended. Consider puncturing the access sites from the most caudal to the most cranial location.
4. Puncture the anterior wall of the common femoral artery or vein at an angle of approximately 45 degrees. Avoid side wall or posterior wall punctures.
5. Prior to deployment of the Perclose ProStyle Device, perform a femoral angiogram to evaluate the access site for vessel size, calcium deposits, tortuosity, and for disease or dissections of the wall to avoid device cuff misses (device needles not engaging with the cuffs), posterior wall suture placement, and / or possible ligation of the anterior and posterior walls of the vessel. Angiographically verify that the puncture is on the anterior wall of the common femoral artery or vein. In arteries the puncture should be proximal to the bifurcation of the superficial femoral artery and the profunda femoris branch and distal to the inferior margin of the inferior epigastric artery.
6. There are **no** re-access restrictions after using Abbott Medical vessel closure devices.

   Note: For arterial sheath sizes less than or equal to 8F, one device may be used. For arterial sheath sizes greater than 8F, at least two devices and the pre-close technique are required. For venous sheath sizes less than or equal to 14F, one device may be used. For venous sheath sizes greater than 14F, at least two devices and the pre-close technique are required.

11.3 Device Preparation

1. Verify marker lumen patency by flushing the marker lumen with saline until saline exits the marker port. **Do not use the device if the marker lumen is not patent.**
2. Place a 0.038” (0.97 mm) (or smaller) hydrophilic or general purpose guide wire (minimum 50 cm in length) through the procedural (or introducer) sheath. Remove the procedural sheath while applying pressure on the groin to maintain hemostasis.
3. Advance the device over the guide wire until the guide wire exit port is just above the skin line.
4. Remove the guide wire before the guide wire exit port crosses the skin line.

11.4 Suture Deployment

1. STEP 1: Advance Device and Lift Lever to Open Foot

a. Position and maintain the device at approximately a 45-degree angle, continue gently to advance the device in the vessel until flow of blood (“mark”) is observed from the marker lumen. Anticipate tactile sensation when distal guide enters the vessel. **In the**

artery, brisk pulsatile flow of blood can be expected. In the vein, the flow of blood may not be pulsatile or blood may only fill the marker lumen.

Note: Stop device advancement once “mark” is observed from the marker lumen to ensure the foot is open near or at the access site to minimize intraluminal travel during pull back. To confirm foot location, retract device until “mark” ceases and re-advance, stop device advancement once “mark” is observed again. **Do not open the foot if “mark” is not observed from the marker lumen**.

b. Using the left hand, maintain the device at approximately a 45-degree angle with the device logo facing the ceiling (approximately 12 o'clock). Lift the lever (**marked 1**) with the right thumb pad or forefinger to open the foot. **Do not lift the lever against resistance.**

Note: To deploy multiple sutures (**Section 11.4.2**), position the device at approximately a 45-degree angle and rotate the device logo approximately 30 degrees towards the patient’s medial or lateral side before lifting the lever to open the foot.

c. Maintain the device logo position while keeping the device at approximately a 45-degree angle, gently retract the device to ensure that the foot is apposed to the vessel wall. It is recommended to place the right forefinger and middle finger on the device handles in an open palm position while pulling back the device. If proper position of the foot has been achieved against the vessel wall, slight tactile sensation will be felt to confirm foot location**. Do not raise the device angle against resistance. In the artery, blood marking will cease or be significantly reduced to a slight drip. In the vein, there may be no change in blood marking.**

Note: If blood marking does not stop or significantly change, evaluate the angiogram for device position in the vessel, vessel size, calcium deposits, tortuosity, disease and for location of the puncture (ensure the footplate is not in bifurcation or side branch). Reposition the device to stop blood marking. Alternatively, reinsert a guide wire, remove the device to hold manual compression, insert a new device or insert a new sheath.

2. **STEP 2: Depress Plunger to Deploy Needles**

a. While maintaining device logo position and keeping the device at approximately a 45-degree angle with gentle retraction against the vessel wall, stabilize the device to ensure the foot is apposed to the vessel wall and depress the plunger with the right thumb (**in the arrow direction marked 2**) until the black collar on the plunger meets the blue body to deploy the needles. In addition to the visual confirmation, an audible “click” should be heard to confirm needle and cuff engagement.

Note: Do not use excessive force or repeatedly push the plunger or depress the plunger repeatedly as this may prevent the needles from engaging the cuffs. After the visual and audible confirmation, **STEP 2** is complete.

3. **Use of Depth Reference Markers (Optional)**

a. After completing **STEP 1** and before performing **STEP 3**, maintain device at approximately a 45-degree angle with the foot apposed to the vessel wall, and observe the depth reference mark closest to the skin line.

Note: The depth reference marks on the device provide depth estimation of the tissue tract and may be used in combination with the corresponding depth reference mark on the Perclose ProStyle Suture Trimmer as a visual reference for approximating the

advancement of the Perclose ProStyle Suture Trimmer into the tissue tract during suture management (**Section 11.5.1**).

4. **STEP 3: Pull Back Plunger to Deploy Suture**
   a. Using the right thumb or forefinger as a fulcrum on the handle, pull out the plunger assembly from the body (**in the arrow direction marked 3**) and completely remove the plunger and needles from the body. Continue to pull back on the plunger until the suture is taut, which confirms that the suture has been fully retracted from the body of the device. The anterior needle will be attached to the link with the suture limb. The posterior needle will be free of suture.

      Note: Do not attempt to reinsert the needles if the suture limb is not attached to the anterior needle. Reinsert a guide wire through the guide wire exit port and remove the device with the detached suture over the wire while maintaining guide wire access. Insert a new Perclose ProStyle Device over the guide wire to complete the procedure.

   b. While holding the plunger, place the needles under the QuickCut™ Mechanism. Use the needles as the guide, slide the suture against the QuickCut Mechanism to trim the suture from the anterior needle distal of the link. Alternately, use a sterile scalpel or scissors to cut the suture.

5. **STEP 4: Lower Lever to Close Foot**
   a. Release the gentle retraction against the vessel wall. Advance device slightly to restore marker flow, if necessary. Push the lever (**marked 4**) down to the body of the device to return the foot to its original closed position.

      Note: Do not attempt to remove the device without closing the lever fully to its original closed position, “1” is visible on top of the lever.

   b. Retract the device out of the tissue tract deliberately. Slight resistance should be felt when the suture exits the suture bearing on the distal guide. Continue to gently withdraw the device until the guide wire exit port is visible above the skin line.

   c. Rotate the body of the device slightly, if needed, to locate the two suture limbs in the bend of the distal guide. Grasp both suture limbs together and gently pull the suture end through the distal end of the proximal guide.

   d. Reinsert a guide wire through the guide wire exit port to maintain guide wire access. There should be adequate length of guide wire inside of the vessel and outside the guide wire exit port for device or sheath exchange.

      Note: Care should be taken to avoid suture limbs and guide wire entanglement. If preferred to secure and maintain guide wire access first, perform **Step 5b** before **Step 5c** above.

   e. Identify the rail and non-rail suture limbs. The longer, rail suture limb is blue and is used to advance the pre-tied suture knot. The distal end of the shorter, non-rail suture limb is white and is used to lock the pre-tied suture knot.

      Note: Do not pull on the individual suture limbs to prevent knot advancement or locking of the knot.

6. Do not remove the device. Continue with suture management steps in **Section 11.5** for single suture using the pre-close technique, by following the steps in **Section 11.4.1**. For multiple sutures using the pre-close technique, follow the steps in **Section 11.4.2**.

11.4.1 Single Suture using Pre-Close Technique

When using the pre-close technique, the suture can be placed around the access site at the beginning of the procedure and suture management can be placed on hold until the procedure is complete.

1. After completing suture deployment steps in **Section 11.4,** immediately secure the two suture limbs together with a shodded hemostat or clamp at the distal end of the non-rail suture limb.

   Note: Do not pull on the individual suture limbs to prevent knot advancement or locking of the knot.
2. Gently pull on the clamp until the suture is taut to **remove any suture slack from the tissue tract**. Place the clamped suture under a sterile towel during the procedure.

   Note: The monofilament suture can be damaged by opening and closing the clamp. In order to attach the suture to the drape, it is recommended to use a second clamp with the tip placed through the handle of the first clamp and attach the second clamp to the drape.
3. Exchange the Perclose ProStyle Device for an appropriately sized procedural sheath over the guide wire and proceed with the catheterization procedure.
4. At the end of the catheterization procedure, reinsert the guide wire into the procedural sheath. It is recommended to reinsert the dilator into the sheath for a smooth transition of suture at the end of the sheath. Maintain adequate length of guide wire in the vessel and outside the sheath to maintain guide access.
5. Heavily irrigate the secured suture with heparinized saline to remove any dry blood. Remove the clamp from the suture limbs. Continue with the suture management steps in **Section 11.5**.

11.4.2 Multiple Sutures using Pre-close Technique

1. To deploy the first suture, follow the suture deployment steps in **Section 11.4**. At **Step 1b**, rotate the device logo approximately 30 degrees towards the patient's **medial side**. Proceed to the pre-close technique in **Section 11.4.1** (up to **Step 2**). Place the clamped suture for the first device on the **medial side** of the patient under a sterile towel. It is important to identify which suture is deployed first, as this is the suture knot that needs to be advanced first at the end of the procedure.
2. Maintain adequate length of guide wire in the vessel and outside the guide wire exit port. Remove the first Perclose ProStyle Device while holding compression above the puncture site. Advance a second Perclose ProStyle Device over the guide wire.
3. To deploy the second suture, follow the suture deployment steps in **Section 11.4**. At **Step 1b**, rotate the device logo approximately 30 degrees towards the patient's **lateral side**. Proceed to pre-close technique in **Section 11.4.1** (up to **Step 2**). Place the clamped suture for the second device on the **lateral side** of the patient under a sterile towel.
   Note: It is important to identify which suture was deployed first and which suture was deployed second. At the completion of the procedure, the pre-tied suture knots will be advanced in the order they were placed. The pre-tied suture knot from the first device would be advanced first followed by the pre-tied suture knot from the second device.
4. Exchange the Perclose ProStyle Device for an appropriately sized procedural sheath over the guide wire and proceed with the catheterization procedure.
5. At the end of the catheterization procedure, reinsert a guide wire into the procedural sheath. It is recommended to reinsert the dilator into the sheath for a smooth transition of suture at

the end of the sheath. Maintain adequate length of guide wire in the vessel and outside the sheath to maintain guide wire access.

6. Heavily irrigate the secured sutures with heparinized saline to remove any dry blood. Remove the clamp from the first suture. Follow the suture management steps using the Perclose ProStyle Suture Trimmer (**Section 11.5.1, Steps 1-5**) or Perclose Snared Knot Pusher (**Section 11.5.2, Steps 1-4**). Place the suture limbs on the **medial side** of the patient for easy identification as the first suture deployed. **DO NOT lock or excessively tighten the suture knot while the guide wire is still in the vessel.**
7. Remove the clamp from the second suture. Follow the same steps as the first suture. Place the suture limbs on the **lateral side** of the patient for easy identification as the second suture deployed. **Again, DO NOT lock or excessively tighten the suture knot while the guide wire is still in the vessel.**
8. Assess for hemostasis. If brisk bleeding is observed, advance the first (**patient's medial side**) suture knot again and then advance the second (**patient's lateral side**) suture knot again. Multiple knot advancements are common when closing larger sheath sizes. **Until the guide wire is removed, some bleeding will be visible, but it should not be pulsatile blood flow.**
9. If adequate hemostasis is not observed, additional Perclose ProStyle Devices may be deployed at this point. Repeat the above steps to deploy a third suture. The third device should not be rotated. The third device will be deployed with the device logo facing the ceiling (approximately 12 o'clock). **Again, DO NOT lock the knot or excessively tighten the suture knot while the guide wire remains in the vessel.**
10. Assess the access site for adequate hemostasis. **Remove the guide wire if bleeding is controlled.**
11. Complete advancing and locking the first suture knot using the Perclose ProStyle Suture Trimmer (**Section 11.5.1, Steps 6-9**) or Perclose Snared Knot Pusher (**Section 11.5.2, Steps 5-9**). Follow the same steps to advance and lock the second suture knot. If applicable, advance and lock any additional suture knots in the order that they were placed (first, second, third).
12. If hemostasis is deemed adequate, cut the suture limbs below the surface of the skin using the Perclose ProStyle Suture Trimmer (**Section 11.5.1, Step 10**).

11.5 Suture Management

1. Use the Perclose ProStyle Suture Trimmer (**Section 11.5.1**) or the Perclose Snared Knot Pusher (**Section 11.5.2**) to advance and tighten the pre-tied suture knot.
2. For 5F - 8F sheaths, confirm hemostasis and the security of the suture knot by having the patient cough and / or bend his / her leg. **Active testing for hemostasis is only for 5F – 8F sheaths. For sheath closures greater than 8F, active confirmation should not be performed; only visual confirmation of hemostasis should be employed**.

   Note: Patients may be able to move freely in bed without head of bed or leg restrictions if the close is successful.

11.5.1 Suture Management Using the Perclose ProStyle Suture Trimmer

1. Securely wrap the rail suture limb around the left forefinger close to the skin. While maintaining guide wire access, simultaneously pull the rail suture limb coaxial to the tissue tract with slow, consistent increasing tension to advance the pre-tied suture knot to the access site and remove the Perclose ProStyle Device (or the entire procedural sheath system if using pre-close technique) completely from the vessel with the right hand.

   Note: Do not tighten the suture around the device or the procedural sheath. Avoid quick or jerky type movements with the suture limbs. Manual pressure should be applied proximal to the puncture site for hemostasis, while the sheath is removed and during initial suture advancement.
2. While maintaining tension and keeping the rail suture limb securely wrapped around the left forefinger and coaxial to the tissue tract, place the rail suture limb into the suture gate following the steps below:
   a. Hold the Perclose ProStyle Suture Trimmer with the right hand. Retract the thumb knob on the Perclose ProStyle Suture Trimmer with the right thumb to open the suture gate.
   b. Place the Perclose ProStyle Suture Trimmer shaft **under** the rail suture limb making an “x” or a “cross”. Slide the shaft back to load the rail suture limb into the suture gate.
   c. Keeping the thumb knob retracted, turn the shaft coaxial to the rail suture limb and then release the thumb knob to capture the suture in the suture gate. Once the rail suture limb is loaded in the suture gate correctly, the Perclose ProStyle Suture Trimmer should slide easily coaxial on the rail suture limb.

      Note: Releasing the thumb knob before the rail suture limb is coaxial to the Perclose ProStyle Suture Trimmer can cause the suture to be caught within the sliding mechanism in the suture gate and damage the suture.
3. While maintaining tension on the rail suture limb, keeping the Perclose ProStyle Suture Trimmer and the rail suture limbs coaxial to the tissue tract and the thumb knob at approximately 12 o’clock (facing the ceiling), advance the Perclose ProStyle Suture Trimmer on the rail suture limb coaxial to the tissue tract until the pre-tied suture knot is at the vessel surface.

   Note: The Perclose ProStyle Suture Trimmer should not be rotated during advancement to avoid having the rail suture limb wrapped around the sheath.
4. While maintaining tension on the rail suture limb and keeping the rail suture limb securely wrapped around the left forefinger, place the left thumb on the top of the Perclose ProStyle Suture Trimmer to assume a single-handed position. Complete knot advancement by applying slow, consistent increasing tension using the left forefinger until the rail suture limb is taut (guitar string tightness in artery and gentle tension in vein).
5. **Use of Depth Reference Markers (Optional)**

   Note: If the depth reference mark on the device is used to provide an estimation of the tissue tract depth during suture deployment in **Section 11.4**, the corresponding depth reference mark on the Perclose ProStyle Suture Trimmer may be used as a visual reference to appropriate the depth for advancing the Perclose ProStyle Suture Trimmer.
   a. While maintaining the Perclose ProStyle Suture Trimmer at a 45-degree angle, observe the depth reference mark closest to the skin level.

   Note: The depth reference markers are only to be used as a reference tool and are not intended to replace tactile feel during the advancement of the Perclose ProStyle Suture

Trimmer into the tissue tract. Do not solely depend on these depth reference markers for approximating the tissue tract depth when advancing the Perclose ProStyle Suture Trimmer.

6. Assess the access site for adequate hemostasis. If bleeding is controlled, the guide wire can be removed. Resume the single-handed position to advance the pre-tied suture knot after guide wire removal.

   Note: DO NOT lock or excessively tighten the suture knot while the guide wire is still in the vessel.

7. While maintaining the single-handed position with the Perclose ProStyle Suture Trimmer, keeping the rail suture limb taught and the tip of the Perclose ProStyle Suture Trimmer on top of the knot, pull gently on the non-rail suture limb coaxial to the tissue tract with the right hand to remove suture slack, tighten and lock the suture knot at the vessel surface.
8. Hemostasis of the access site is achieved when the suture knot is fully advanced to the vessel surface, and the tissue is in complete apposition. Remove the Perclose ProStyle Suture Trimmer from the tissue tract, relax tension on the suture limbs.
9. For 5F–8F sheaths, confirm hemostasis and the security of the suture knot by having the patient cough or bend his/her leg. **Active testing for hemostasis is only for 5F–8F sheaths. For sheath closures greater than 8F, active confirmation should not be performed; only visual confirmation of hemostasis should be employed.** If hemostasis has not been achieved, resume the single-handed position for 20 seconds or until hemostasis is achieved. Secure the knot again by gently pulling coaxial on the non-rail suture limb. **DO NOT** apply excessive pressure to the suture.
10. After confirming hemostasis, use the Perclose ProStyle Suture Trimmer to trim the suture limbs below the skin. While holding both suture limbs together and pulling them taut, load both suture limbs into the suture gate and advance the Perclose ProStyle Suture Trimmer to the vessel surface. Trim the suture limbs by pulling back on the red trimming lever. If only one suture limb has been loaded and trimmed, repeat the same steps to trim the other suture limb. Alternatively, use a sterile scalpel or scissor.

    Note: Patients may be able to move freely in bed without head of bed or leg restrictions if the close is successful.

11.5.2 Suture Management Using the Perclose Snared Knot Pusher

1. Place approximately 2 cm of the rail suture limb into the snare at the distal end of the Perclose Snared Knot Pusher. Detach the snare tab completely from the shaft and pull the tab coaxial to the shaft to load the rail suture limb through the Perclose Snared Knot Pusher. Keep snare tab for re-snaring the rail suture limb as needed.
2. Grab the distal end of the rail suture limb with the left hand and advance the Perclose Snared Knot Pusher coaxial over the rail suture limb to skin level. If the rail suture limb is loaded on the Perclose Snared Knot Pusher correctly, the Perclose Snared Knot Pusher should slide easily coaxially on the rail suture limb.
3. Securely wrap the rail suture limb around the left forefinger close to skin level. While maintaining guide wire access, simultaneously pull the rail suture limb coaxial to the tissue tract with slow, consistent increasing tension to advance the pre-tied suture knot to the access site and remove the Perclose ProStyle Device (or the entire procedural sheath system if using the pre-close technique) completely from the vessel with the right hand.

   Note: Do not tighten the suture around the device or procedural sheath. Avoid quick or jerky type movements with the suture limbs. Manual pressure should be applied proximal to the

puncture site for hemostasis, while the sheath is removed and during initial suture advancement.

4. While maintaining tension on the rail suture limb and keeping the Perclose Snared Knot Pusher and the rail suture limbs coaxial to the tissue tract, advance the Perclose Snared Knot Pusher on the rail suture limb coaxial into the tissue tract with the right hand until the pre-tied suture knot is at the vessel surface.

   Note: The Perclose Snared Knot Pusher should not be rotated during advancement to avoid having the rail suture limb wrapped around the shaft.

5. While maintaining tension on the rail suture limb, keeping the rail suture limb securely wrapped around the left forefinger, place the left thumb on the top of the Perclose Snared Knot Pusher to assume a single-handed position. Complete knot advancement by applying slow, consistent increasing tension on the left forefinger until the rail suture limb is taut (guitar string tightness in artery and gentle tension in vein).
6. Assess the access site for adequate hemostasis. If bleeding is controlled, the guide wire can be removed. Resume the single-handed position to advance the suture knot after guide wire removal.

   Note: DO NOT lock or excessively tighten the suture knot while the guide wire is still in the vessel.

7. While maintaining the single-handed position with the Perclose Snared Knot Pusher and keeping the rail suture limb taut and the tip of the Perclose Snared Knot Pusher on top of the suture knot, pull gently on the non-rail suture limb coaxial to the tissue tract with the right hand to remove suture slack, tighten and lock the suture knot at the vessel surface.
8. Hemostasis of the access site is achieved when the suture knot is fully advanced to the vessel surface, and the tissue is in complete apposition. Remove the Perclose Snared Knot Pusher from the tissue tract, relax tension on the suture limbs.
9. For 5F–8F sheaths, confirm hemostasis and security of the suture knot by having the patient cough or bend his / her leg. **Active testing for hemostasis is only for 5F–8F sheaths. For sheath closures greater than 8F, active confirmation should not be performed; only visual confirmation of hemostasis should be employed**. If hemostasis has not been achieved, assume the single-handed position for 20 seconds or until hemostasis is achieved. Secure the suture knot again by gently pulling coaxial on the non-rail suture limb. **DO NOT** apply excessive pressure to the suture.
10. After confirming hemostasis, use the Perclose ProStyle Suture Trimmer (**Section 11.5.1, Step 10**) to trim the suture limbs below the skin.

    Note: Patients may be able to move freely in bed without head of bed or leg restrictions if the close is successful.

11.6 Suture Breakage

1. To prevent suture breakage, always pull on the suture limbs with slow, consistent increasing tension. Avoid quick or jerky type movements with the suture limbs.
2. To prevent damage to the suture and subsequent suture breakage, the Perclose ProStyle Suture Trimmer, the Perclose Snared Knot Pusher and suture limbs should always remain coaxial to the tissue tract.

3. The Perclose ProStyle Suture Trimmer should not be rotated and the thumb knob should be maintained at approximately 12 o'clock (facing the ceiling). When loading suture into the Perclose ProStyle Suture Trimmer, keep the thumb knob retracted until the suture and Perclose ProStyle Suture Trimmer are coaxial, then release the thumb knob to capture the suture in the suture gate.
4. If suture breakage occurs during knot advancement **before the knot** is tightened, and a guide wire is still in place, use another Perclose ProStyle SMCR Device to complete the procedure.
5. If suture breakage occurs **after a knot** has been advanced and / or tightened, and a wire is still in place, use an introducer sheath to open the knot before inserting another Perclose ProStyle Device can be used to complete the procedure.

   Note: Care should be taken to avoid excessive force if another Perclose ProStyle Device or an introducer sheath is required. Use an introducer sheath small enough to avoid undue force.
6. To remove the broken suture limbs, cut the suture limbs close to the suture knot using the Perclose ProStyle Suture Trimmer or a sterile scalpel or scissor.

11.7 Post Procedure Patient Management

1. Apply an appropriate dressing to the access site.
2. Assess the access site as per hospital standard of care.

11.8 Recommendation for Patient Ambulation and Discharge

Patients may be able to move freely in bed without head of bed or leg restrictions if the close is successful.

Patients who have undergone a diagnostic or interventional procedure using 5–8F sheaths may be ambulated two hours after the Perclose ProStyle SMCR procedures.

Patients who have undergone an interventional catheterization procedure using sheaths greater than 8F, may be ambulated at a time-point 2 hours or more after the Perclose ProStyle SMCR procedure, with the time-point based on the judgement of the physician.

Patients who have undergone cardiac arrhythmia treatments with multiple access sites in a single femoral vein of one or both limbs may be ambulated one hour or more and may be eligible for same-day discharge two hours or more after the Perclose ProStyle SMCR procedures based on the judgement of the physician.

In determining whether to ambulate or discharge an individual patient, it is important to consider all clinical factors including, but not limited to, anticoagulation regimen, antiplatelet and thrombolytic agents administered, oozing or bleeding from the arterial or venous access site, the general cardiovascular condition of the patient, anesthetic levels, and the overall clinical condition of the patient.

12.0 PRODUCT INFORMATION DISCLOSURE

Abbott has exercised reasonable care in the manufacture of this device. Abbott excludes all warranties, whether expressed or implied, by operation of law or otherwise, including but not limited to, any implied warranties of merchantability or fitness, since handling and storage of this device, as well as factors relating to the patient, diagnosis, treatment, surgical procedures, and other matters beyond the control of Abbott directly affect this device and the results obtained from its use. Abbott shall not be liable for any incidental or consequential loss, damage, or expense, directly or indirectly arising from the use of this device. Abbott neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this device.

Reference Abbott website for patent markings: www.abbott.com/patents

Abbott Medical
3200 Lakeside Drive
Santa Clara, CA 95054 USA

CUSTOMER SERVICE
TEL: (800) 227-9902
FAX: (800) 601-8874
Outside USA TEL: (951) 914-4669
Outside USA FAX: (951) 914-2531

Graphical Symbols for Medical Device Labeling

LOT	Batch code		Do not resterilize
	Date of manufacture		Do not re-use
	Use-by date		Non-pyrogenic
REF	Catalogue number	STERILE EO	Sterilized using ethylene oxide
CONTENTS	Contents (component included with device)		Do not use if package is damaged and consult instructions for use
	Packaging unit		Keep away from sunlight
Rx ONLY	CAUTION: Federal law restricts this device to sale by or on the order of a physician		Keep dry
	Consult instructions for use or consult electronic instructions for use		Manufacturer
		UDI	Unique device identifier

Perclose™ ProStyle™

Rx ONLY

Suture-Mediated Closure and Repair System

Instructions for Use

Table of Contents

TO ENSURE PROPER DEPLOYMENT AND USE OF THIS DEVICE AND TO PREVENT INJURY TO PATIENTS, READ ALL INFORMATION CONTAINED IN THESE INSTRUCTIONS FOR USE.

Note: This IFU may be revised from time to time. Please refer to the Abbott website (www.abbottvascular.com/ifu) for the most current version at the time of the procedure.

If you have difficulties accessing this document or would like to request a paper copy at no extra cost, please contact: Abbott Customer Service at 1-800-227-9902.

1.0 CAUTION

Federal law restricts this medical device to sale by or on the order of a physician (or allied healthcare professionals, authorized by, or under the direction of, such physicians) who is trained in diagnostic and / or interventional catheterization procedures and who has been trained by an authorized representative of Abbott.

Prior to use, the operator must review the Instructions for Use and be familiar with the deployment techniques associated with the use of this device.

During closure of access sites using a procedural sheath greater than 8F, it is recommended that a vascular surgeon or a surgeon with vascular training be available in case surgical conversion to control bleeding and to repair the vessel is needed.

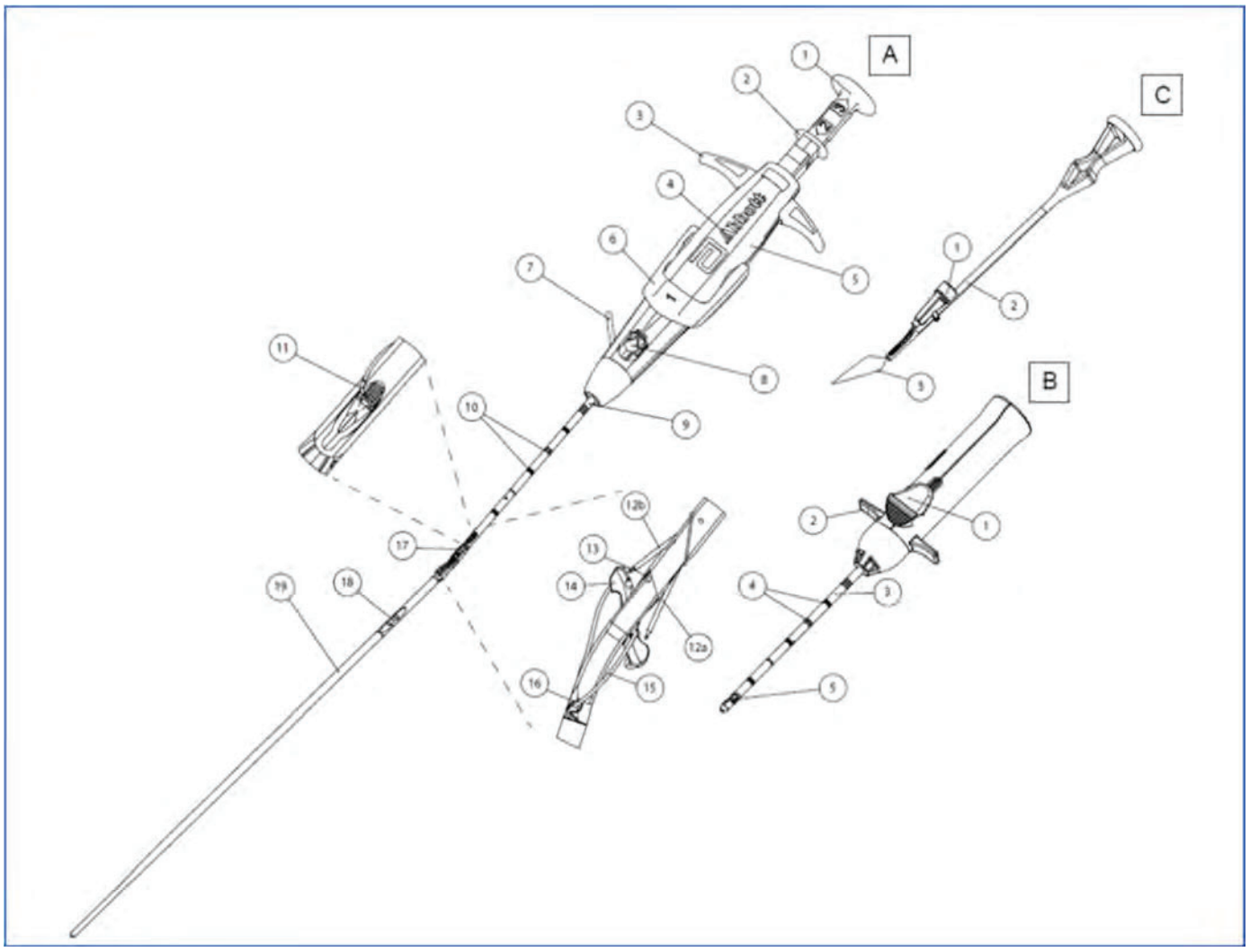
2.0 DEVICE DESCRIPTION

The Perclose™ ProStyle™ Suture-Mediated Closure and Repair (SMCR) System (Figure 2.0-1) is designed to deliver a single monofilament polypropylene suture for use in closing and repairing femoral vessel access sites following diagnostic or interventional catheterization procedures.

This Perclose ProStyle Device is composed of a plunger, handle, guide, and sheath. The Perclose ProStyle Device tracks over a standard 0.038" (0.97 mm) (or smaller) guide wire. A hemostasis valve restricts the blood flow through the sheath with or without a guide wire in place. The guide houses the anterior and posterior needles, and the foot with cuffs, and precisely controls the placement of the needles around the access site. The handle is used to stabilize the device during use. The plunger advances the needles and is used to retrieve the suture. A marker lumen is contained within the guide, with the intraluminal marker port positioned at the distal end of the guide. Proximally, the marker lumen exits from the body of the device. The marker lumen allows a pathway for back-bleeding (obtaining mark) from the femoral vessel to ensure proper device positioning.

The Perclose™ ProStyle™ Suture Trimmer and Perclose™ Snared Knot Pusher are designed to position the pre-tied suture knot to the top of the access site. The Perclose ProStyle Suture Trimmer is also designed to trim the trailing limbs of suture below the skin.

Figure 2.0-1



A. **Perclose™ ProStyle™ Device**
   1. Plunger
   2. Collar
   3. Handle
   4. Device Logo
   5. Body
   6. Lever
   7. Marker Lumen
   8. QuickCut™ Mechanism
   9. Proximal Guide
   10. Depth Reference Markers
   11. Suture with Pre-tied Knot
   12. a. Anterior Needle
       b. Posterior Needle
   13. Marker Port
   14. Foot (with Cuffs)
   15. Link
   16. Suture Bearing
   17. Distal Guide
   18. Guide Wire Exit Port
   19. Sheath

B. Perclose™ ProStyle™ Suture Trimmer
   1. Thumb Knob
   2. Trimming Lever (Red)
   3. Sheath
   4. Depth Reference Markers
   5. Suture Gate

C. Perclose™ Snared Knot Pusher
   1. Snare Tab
   2. Sheath
   3. Snare

3.0 HOW SUPPLIED

The Perclose™ ProStyle™ SMCR System is provided sterile and non-pyrogenic in unopened, undamaged packages. Products are sterilized with ethylene oxide and intended for single use only. Do not resterilize. Store in a cool, dry place.

Perclose ProStyle SMCR System includes:
One (1) Perclose™ ProStyle™ Device
One (1) Perclose™ ProStyle™ Suture Trimmer
One (1) Perclose™ Snared Knot Pusher

4.0 INDICATIONS

The Perclose™ ProStyle™ Suture-Mediated Closure and Repair System is indicated for the percutaneous delivery of suture for closing the common femoral artery and vein access sites of patients who have undergone diagnostic or interventional catheterization procedures.

The Perclose ProStyle SMCR System is indicated for closing the common femoral vein in single or multiple access sites per limb.

The Perclose ProStyle SMCR System is used without or, if required, with adjunctive manual compression.

For access sites in the common femoral artery using 5F to 21F sheaths. For arterial sheath sizes greater than 8F, at least two devices and the pre-close technique are required.

For access sites in the common femoral vein using 5F to 24F sheaths. For venous sheath sizes greater than 14F, at least two devices and the pre-close technique are required.

5.0 CONTRAINDICATIONS

There are no known contraindications to the use of this device.

6.0 WARNINGS

Do not use the Perclose™ ProStyle™ SMCR System if the packaging or sterile barrier has been previously opened or damaged or if the components appear to be damaged or defective.

DO NOT RESTERILIZE OR REUSE. The Perclose ProStyle SMCR System is intended for single use only.

Do not use the Perclose ProStyle SMCR System if the sterile field has been broken where bacterial contamination of the sheath or surrounding tissues may have occurred, since such a broken sterile field may result in infection.

Do not use the Perclose ProStyle SMCR System if the puncture site is located above the most inferior border of the inferior epigastric artery (IEA) and / or above the inguinal ligament based upon bony landmarks, since such a puncture site may result in a retroperitoneal hematoma. Perform a femoral angiogram to verify the location of the puncture site. **Note:** This may require

both a right anterior oblique (RAO) and left anterior oblique (LAO) angiogram to adequately visualize where the sheath enters the femoral vessel.

Do not use the Perclose ProStyle SMCR System in arterial or venous access if the puncture is through the posterior wall or if there are multiple punctures in the same access site, since such punctures may result in a hematoma or retroperitoneal bleed.

Do not use the Perclose ProStyle SMCR System if the puncture site is located in the superficial femoral artery or the profunda femoris artery, or the bifurcation of these vessels, since such puncture sites may result in a pseudoaneurysm, intimal dissection, or an acute vessel closure (thrombosis of small artery lumen). Perform a femoral angiogram to verify the location of the puncture site. **Note:** This may require both a right anterior oblique (RAO) and left anterior oblique (LAO) angiogram to adequately visualize where the sheath enters the vessel.

7.0 PRECAUTIONS

1. Prior to use, inspect the Perclose™ ProStyle™ SMCR System to ensure that the sterile packaging has not been damaged during shipment. Examine all components prior to use to verify proper function. Exercise care during device handling to reduce the possibility of accidental device breakage.
2. As with all catheter-based procedures, infection is a possibility. Observe sterile technique at all times when using the Perclose ProStyle SMCR System. Employ appropriate groin management, as per hospital protocol, post-procedure, and post-hospital discharge to prevent infection.
3. Use a single wall puncture technique. Do not puncture the posterior wall of the vessel in arterial and venous access.
4. Do not deploy the Perclose™ ProStyle™ Device at an elevated angle against resistance as this may cause a cuff miss or device breakage.
5. There are no reaccess restrictions if previous arteriotomy / venotomy repairs were achieved with Abbott Medical SMC or SMCR systems.
6. If significant blood flow is present around the Perclose ProStyle Device, do not deploy needles. Remove the device over a 0.038" (0.97 mm) (or smaller) guide wire and insert an appropriately sized sheath.
7. Prior to depressing the plunger to advance the needles, stabilize the device by the body to ensure the foot is apposed to the vessel wall and the device does not twist during deployment. Twisting (torquing) the device could lead to needle deflection resulting in a cuff miss. Do not use excessive force or repeatedly depress the plunger. Excessive force on the plunger during deployment could potentially cause breakage of the device, which may necessitate intervention and / or surgical removal of the device and vessel repair.
8. Do not apply excessive force to the lever when opening the foot and returning the foot to its original position down to the body of the device. Do not attempt to remove the device without closing the lever. Excessive force on the lever or attempting to remove the device without closing the lever could cause breakage of the device and / or lead to vessel trauma, which may necessitate intervention and / or surgical removal of the device and vessel repair.

9. **Do not advance or withdraw the Perclose ProStyle Device against resistance until the cause of that resistance has been determined. Excessive force used to advance or torque the Perclose ProStyle Device should be avoided, as this may lead to significant vessel damage and / or breakage of the device, which may necessitate intervention and / or surgical removal of the device and vessel repair.**
10. If excessive resistance in advancing the Perclose ProStyle Device is encountered, withdraw the device over a 0.038" (0.97 mm) (or smaller) guide wire and reinsert the introducer sheath or use manual compression.
11. Remove the Perclose ProStyle sheath before tightening the suture. Failure to remove the sheath prior to tightening the suture may result in detachment of the tip of the sheath.
12. Care should be taken to avoid damage to the suture from handling. Avoid crushing damage due to application of surgical instruments such as clamps, forceps or needle holders.
13. For catheterization procedures using a 5 – 8F procedural sheath, use manual compression in the event that bleeding from the femoral access site persists after the use of the Perclose ProStyle SMCR System to obtain hemostasis.
14. For catheterization procedures using a procedural sheath > 8F, use manual compression, compression assisted devices, surgical repair, and / or other appropriate treatment methods in the event that bleeding from the femoral access site persists after the use of the Perclose ProStyle SMCR System to obtain hemostasis.
15. For catheterization procedures using a procedural sheath > 8F, where the operating physician is not a vascular surgeon, it is recommended that a vascular surgeon or a surgeon with vascular training be available during the procedure to perform any necessary vascular surgical intervention.
16. If the Perclose ProStyle Device is used to close and repair multiple access sites in the same vessel, space the access sites apart adequately to minimize sheath-device interference.

8.0 SPECIAL PATIENT POPULATION

As with any catheter-based procedures, vessel damage and / or device breakage is a possibility. Observe Warnings and Precautions at all times when using this device, and be prepared for necessary intervention and / or surgical removal of the device and vessel repair as per facility protocol.

The safety and effectiveness of the Perclose™ ProStyle™ SMCR System have not been established in the following special patient populations:

- Patients in whom introducer sheaths < 5F or > 21F were used in the femoral artery during the catheterization procedure.
- Patients in whom introducer sheaths < 5F or > 24F were used in the femoral vein during the catheterization procedure.
- Patients with small femoral vessels (< 5 mm in diameter).
- Patients with access sites above the most inferior border of the inferior epigastric artery (IEA) and / or above the inguinal ligament based upon bony landmarks.
- Patients having access in vessels other than the common femoral artery or vein.

- Patients having a hematoma, pseudoaneurysm or arteriovenous fistula present prior to sheath removal.
- Patients with femoral artery calcium which is fluoroscopically visible at access site.
- Patients with severe claudication, iliac or femoral vessel diameter stenosis greater than 50% or previous bypass surgery or stent placement in the vicinity of access site.
- Patients with access sites in vascular grafts.
- Patients with prior intra-aortic balloon pump at access site at any time prior to the procedure.
- Patients with ipsilateral arterial access sites punctured and externally compressed within 48 hours of closure. **Note:** The previous / initial access site may have the potential to re-bleed due to an unstable clot and / or anticoagulants, even if the new access site is successfully closed and repaired with Perclose ProStyle SMCR System.
- Patients with whom there is difficulty inserting the sheath or greater than one ipsilateral vascular puncture at the start of the catheterization procedure that are not actively managed.
- Patients with antegrade punctures.
- Patients with intra-procedural bleeding around access site.
- Patients receiving glycoprotein IIb/IIIa inhibitors before, during, or after the catheterization procedure.
- Patients who are pregnant or lactating.
- Patients with bleeding diathesis or coagulopathy.
- Patients younger than 18 years of age.
- Patients who are morbidly obese (Body Mass Index ≥ 40 kg/m²).
- Patients with active systemic or cutaneous infection or inflammation.

Before considering early discharge, assess the patient for the following clinical conditions:

- Anticoagulation, thrombolytic, or antiplatelet therapy
- Any comorbid condition requiring observation
- Bleeding at the closure site
- Conscious sedation
- Hematoma at the closure site
- Hypotension
- Pain while walking
- Unstable cardiac status

The presence of any of the above factors has generally led to the deferral of early discharge recommendations.

9.0 POTENTIAL ADVERSE EVENTS

Potential adverse events associated with use of vessel closure devices may include, but are not limited to, the following:

- Allergic reaction or hypersensitivity to device components
- Vascular access complications which may require transfusion or vessel repair, including:
    - Anemia
    - Aneurysm
    - Arteriovenous fistula
    - Bleeding / hemorrhage / re-bleeding

  - Bruising / hematoma
  - Embolism
  - Inflammation
  - Intimal tear / dissection
  - Perforation
  - Pseudoaneurysm
  - Retroperitoneal hematoma / bleeding
  - Scar formation
  - Wound dehiscence
- Cardiac arrhythmias (including conduction disorders, atrial and ventricular arrhythmias)
  - Atrial arrhythmias
  - Ventricular arrhythmias
- Femoral artery / venous complications which may require additional intervention, including:
  - Arterial / venous stenosis
  - Arterial / venous occlusion
  - Arteriovenous fistula
  - Intimal tear / dissection
  - Ischemia distal to closure site
  - Nerve injury
  - Numbness
  - Thrombus formation
  - Vascular injury
- Venous thromboembolism (including deep vein thrombosis, pulmonary embolism, post-procedure pulmonary embolism):
- Infection – local or systemic
- Pain
- Hemodynamic instability:
  - Hypotension / hypertension
  - Vasovagal episode
- Death
- Device complications
- Device failure
- Device malfunction

10.0 CLINICAL STUDIES

10.1 The PEVAR Clinical Trial

The PEVAR trial was a prospective, multicenter, randomized concurrently controlled clinical trial. Patients with AAA who were suitable candidates for endovascular repair using the Endologix's Powerlink Stent Graft with the 21F IntuiTrak Delivery System and for percutaneous femoral artery closure who met the prospectively defined inclusion / exclusion criteria were randomized to treatment with the IntuiTrak System via a totally percutaneous access approach (PEVAR = Test) or via a standard vascular exposure cutdown approach (SEVAR = Control). Randomization was carried out in a 2:1 PEVAR:SEVAR manner. PEVAR patients had their femoral artery access sites closed using either the Perclose ProGlide™ Suture-Mediated

Closure System[1] or another closure system. Prior to the randomization of the first patient at each investigational site, a minimum of two patients were treated in a roll-in phase at the investigational site. Roll-in patients underwent the same treatment and follow-up as the randomized patients.

The PEVAR trial included the Independent Access Site Closure Study which was a set of analyses designed to evaluate the safety and effectiveness of the ProGlide using the pre-close technique to percutaneously close ipsilateral femoral artery access sites up to 21F sheath size. The primary analysis was based on a non-inferiority hypothesis test to demonstrate the ProGlide arm is non-inferior to the SEVAR arm. Data from the ProGlide (N = 50) and SEVAR (N = 50) arms are briefly presented below.

10.1.1 Methods

All patients underwent pre-procedure assessments prior to enrollment in the trial. The protocol required clinical assessments prior to discharge, at 1 month and 6 months. An independent clinical events committee adjudicated potential endpoint events of both major and minor ipsilateral access site vascular complications. The enrollment has been completed and all 6-month visits have been completed. The following assessments were required at pre-discharge, 1 month, and 6 months:

- Medication review (1 and 6 months only)
- Physical exam, including overall health and physical assessment, lower extremity sensorimotor exam and access site assessment
- Serum creatinine, blood urea nitrogen, hematocrit and hemoglobin
- ABI (Ankle-Brachial Index)
- Contrast-enhanced CT scan of the abdomen and pelvis (1 month only)
- Bilateral femoral duplex ultrasound (pre-discharge and 6 months only)
- SF-36 QOL (Quality of Life) (1 and 6 months only)
- Pain scale
- Adverse events

10.1.2 Results of the Independent Access Site Closure Study for the Randomized ProGlide vs. SEVAR Arms

Patient Demographics

In general, baseline demographics were comparable between the ProGlide and the SEVAR patients. There was a difference in age between the ProGlide and SEVAR arms (69.9 ± 6.6 vs. 73.2 ± 8.8) which did not appear to affect the overall study outcome, based on additional adjusted analysis.

Primary Endpoint

The primary endpoint for the Independent Access Site Closure Study of the PEVAR trial was the major ipsilateral access site vascular complication rate at 30 days for patients treated

[1] Perclose ProStyle SMCR System is a design evolution of the Perclose ProGlide SMC System. The results of the PEVAR Clinical Trial are applicable to the Perclose ProStyle SMCR System because of system similarities.

percutaneously (PEVAR ProGlide arm [Test]) compared to that of patients treated using standard surgical vascular access (SEVAR group [Control]).

Major ipsilateral access site vascular complications are a composite of the following events:

- Access site vascular injury requiring surgical repair, angioplasty, or ultrasound-guided compression, or thrombin injection
- New onset lower extremity ischemia that is attributed to arterial access or closure causing a threat to the viability of the limb and requiring surgical or additional percutaneous intervention
- Access site-related bleeding requiring transfusion
- Access site-related infection requiring intravenous antibiotics or a prolonged hospitalization
- Access site-related nerve injury that is permanent or requires surgery

The study results show that at 30 days, ProGlide patients had a 6.0% (3/50) major ipsilateral access site vascular complication rate vs. the SEVAR patients who had a 10% (5/50) major ipsilateral access site vascular complication rate. The non-inferiority test for the primary endpoint revealed a *p*-value = 0.0048 and resulted in the rejection of the null hypothesis, demonstrating that ProGlide is non-inferior to SEVAR in the closure of femoral artery access sites up to 21F sheath size (**Table 10.1.2-1**).

Table 10.1.2-1: Non-inferiority Test for Primary Endpoint – Per Subject Analysis (Modified Intent-to-Treat Population[1] - ProGlide vs. SEVAR)

	ProGlide N = 50	**SEVAR N = 50**	***p*-value[3]**
Major Ipsilateral Access Site Vascular Complication at 30 Days [95% Confidence Interval][2]	6.0% (3/50) [1.3%, 16.5%]	10.0% (5/50) [3.3%, 21.8%]	0.0048

[1] Defined as all patients who were randomized and treated
[2] By Clopper-Pearson exact confidence interval
[3] One-sided p-value and 95% confidence interval for non-inferiority test by using asymptotic test statistics with non-inferiority margin of 10%

Select Secondary Endpoints

In the Independent Access Site Closure Study of the PEVAR trial, the following select secondary endpoints were also evaluated.

- Procedure time was defined as elapsed time from the first skin break to final closure (skin to skin time)
- Minor ipsilateral access site complications included minor ipsilateral access site vascular complications and narcotic analgesic use for ipsilateral access site pain at 30 days. Minor ipsilateral access site vascular complications included:
    - Access site pseudoaneurysm or AV fistula documented by ultrasound
    - Access site hematoma ≥ 6 cm
    - Post-discharge access site-related bleeding requiring > 30 minutes to re-achieve hemostasis

  - Lower extremity arterial emboli or stenosis that is attributed to arterial access or closure
  - Deep vein thrombosis
  - Access site-related vessel laceration
  - Transient access site-related nerve injury
  - Access site wound dehiscence
  - Access site-related lymphocele
  - Localized access site infection treated with intramuscular or oral antibiotics
- Time to actual hospital discharge was defined as elapsed time from sheath removal to actual physical discharge from the hospital.
- Time to ambulation was defined as elapsed time between sheath removal and time when the patient stands and walks at least 20 feet without re-bleeding.
- Ipsilateral pain score at pre-discharge
- Time to hemostasis for the ipsilateral access site was defined as elapsed time from sheath removal to first observed cessation of CFA bleeding (excluding cutaneous or subcutaneous oozing).
- Closure device success was defined as successful achievement of index procedure ipsilateral access site hemostasis with percutaneous closure without surgical intervention.
- Ipsilateral access site closure success was defined as successful achievement of hemostasis with percutaneous closure devices and without surgical intervention and freedom from major ipsilateral access site vascular complications within 48 hours of the index procedure or hospital discharge, whichever occurs first.

As shown in **Table 10.1.2-2**, the ProGlide arm had a 25% shorter procedure time than the SEVAR arm (106.5 ± 44.9 vs. 141.1 ± 73.4, $p = 0.0076$). There were no differences in the minor ipsilateral access site complications, time to actual hospital discharge, time to ambulation and ipsilateral pain score at pre-discharge between the ProGlide and SEVAR arms. In the ProGlide arm, the time to hemostasis for the ipsilateral access site was 57% shorter than in the SEVAR arm (9.8 ± 17 vs. 22.7 ± 22.9 minutes, 95% CI of the difference [-21.1, -4.7]). In addition, the ProGlide arm achieved a closure device success rate and access site closure success rate at 96% and 94%, respectively.

Table 10.1.2-2: Select Secondary Endpoints

Secondary Endpoints	ProGlide N = 50	SEVAR N = 50	Difference (95% CI)[1]	Superiority Test *p*-value
Procedure Time (minutes) [95% Confidence Interval][1]	106.5 ± 44.9 (50) [93.7, 119.2]	141.1 ± 73.4 (50) [120.3, 162.0]	-34.7 [-58.9, -10.4]	0.0076[3]
Minor Ipsilateral Access Site Complications at 30 Days[5] [95% Confidence Interval][2]	22.0% (11/50) [11.5%, 36.0%]	30.0% (15/50) [17.9%, 44.6%]	-8.0% [-25.1%, 9.1%]	0.4954[4]
Minor Ipsilateral Access Site Vascular Complications at 30 Days [95% Confidence Interval][2]	4.0% (2/50) [0.5%, 13.7%]	8.0% (4/50) [2.2%, 19.2%]	-4.0% [Assumptions not met] [6]	--
Narcotic Analgesic Use for Ipsilateral Access Site Pain at 30 Days [95% Confidence Interval][2]	18.0% (9/50) [8.6%, 31.4%]	28.0% (14/50) [16.2%, 42.5%]	-10.0% [-26.4%, 6.4%]	--
Time to Actual Hospital Discharge (hours) [95% Confidence Interval][1]	31.4 ± 16.9 (50) [26.6, 36.2]	45.7 ± 59.9 (48) [28.3, 63.1]	-14.3 [-32.3, 3.7]	--
Time to Ambulation (hours) [95% Confidence Interval][1]	17.8 ± 7.2 (50) [15.7, 19.9]	20.5 ± 16.9 (48) [15.6, 25.5]	-2.7 [-8.0, 2.5]	--
Ipsilateral Pain Scale Score at Pre-Discharge [95% Confidence Interval][1]	2.1 ± 2.2 (50) [1.5, 2.7]	2.6 ± 2.4 (49) [1.9, 3.3]	-0.5 [-1.4, 0.4]	--
Time to Hemostasis for Ipsilateral Access Site (minutes)[3] [95% Confidence Interval][2]	9.8 ± 17.0 (50) [5.0, 14.7]	22.7 ± 22.9 (47) [16.0, 29.4]	-12.9 [-21.1, -4.7]	--
Closure Device Success [95% Confidence Interval][2]	96.0% (48/50) [86.3%, 99.5%]	N/A	N/A	--
Access Site Closure Success [95% Confidence Interval][2]	94.0% (47/50) [83.5%, 98.7%]	N/A	N/A	--

[1] By normal approximation
[2] By Clopper-Pearson exact confidence interval
[3] By two-sample t-test, pre-specified hypothesis test based hierarchical test procedure.
[4] By Fisher's Exact Test, pre-specified hypothesis test based hierarchical test procedure.
[5] A composite endpoint including minor Ipsilateral Access site vascular complications and narcotic analgesic use for Ipsilateral access site pain at 30 days
[6] Insufficient sample size or small frequency in the numerator for the validity of normal approximation assumption

Adverse Events

Adverse events related to major and minor ipsilateral access site vascular complications that occurred within the first 30 days are listed in **Table 10.1.2-3**.

Table 10.1.2-3: Major and Minor Ipsilateral Access Site Vascular Complications Through 30 Days[1]

	ProGlide N = 50	SEVAR N = 50
Major Ipsilateral Access Site Vascular Complications at 30 Days	6.0% (3/50)	10.0% (5/50)
Access site vascular injury requiring surgical repair, angioplasty, or ultrasound-guided compression, or thrombin injection	2.0% (1/50)	2.0% (1/50)
New onset lower extremity ischemia that is attributed to arterial access or closure causing a threat to the viability of the limb and requiring surgical or additional percutaneous intervention	4.0% (2/50)	4.0% (2/50)
Access site-related bleeding requiring transfusion	2.0% (1/50)	4.0% (2/50)
Access site-related infection requiring intravenous antibiotics or a prolonged hospitalization	0.0% (0/50)	0.0% (0/50)
Access site-related nerve injury that is permanent or requires surgery	0.0% (0/50)	2.0% (1/50)
Minor Ipsilateral Access Site Vascular Complications at 30 Days	4.0% (2/50)	8.0% (4/50)
Access site pseudoaneurysm or AV fistula documented by ultrasound	0.0% (0/50)	0.0% (0/50)
Access site hematoma ≥ 6 cm	0.0% (0/50)	2.0% (1/50)
Post-discharge access site-related bleeding requiring > 30 minutes to re-achieve hemostasis	0.0% (0/50)	0.0% (0/50)
Lower extremity arterial emboli or stenosis that is attributed to arterial access or closure	4.0% (2/50)	4.0% (2/50)
Deep vein thrombosis	0.0% (0/50)	0.0% (0/50)
Access site-related vessel laceration	0.0% (0/50)	0.0% (0/50)
Transient access site-related nerve injury	0.0% (0/50)	2.0% (1/50)
Access site wound dehiscence	0.0% (0/50)	0.0% (0/50)
Access site-related lymphocele	0.0% (0/50)	0.0% (0/50)
Localized access site infection treated with intramuscular or oral antibiotics	0.0% (0/50)	0.0% (0/50)

[1] Include only each subject's first occurrence of each event

10.1.3 Clinical Data from the Roll-in Phase

There were 22 patients treated in the ProGlide roll-in phase of the PEVAR trial. The mean age of this treatment group was 71.1 ± 6.9 years. The major ipsilateral access site vascular complication rate was 4.5 % (1/22). The mean procedure time was 118.2 ± 43.4 minutes and the average time to ipsilateral hemostasis was 7.7 ± 6.8 minutes for the roll-in phase. Additionally, the closure device success rate and the access site closure success rate were both

95.5%, respectively. These results were comparable to the ProGlide arm in the randomized phase and substantiated the safety and effectiveness of the ProGlide device.

Conclusion

The Perclose ProGlide SMC device, using a pre-close technique, is non-inferior to the standard vascular surgical cutdown in the closure of femoral artery access sites up to 21F sheath size. The Perclose ProGlide SMC device can be safely and effectively used to close femoral artery access sites up to 21F sheath size. Additionally, use of the ProGlide pre-close technique can result in shorter procedure time and shorter time to achieve hemostasis.

10.2 The CLOSER IDE Clinical Trial

The previous generation suture mediated closure device was known as the Closer and Closer S SMC Systems. The CLOSER IDE trial provided safety and effectiveness data which supported an indication for closing femoral arteries up to 8F and the addition of interventional catheterization procedures.

The CLOSER IDE trial[2] was designed as an equivalency trial for the 30-day primary combined safety endpoint of freedom from major complications and a primary efficacy endpoint of time to discharge when compared to the control group (STAND II Trial). The study prospectively examined the safety and effectiveness of femoral artery closure using the Closer 6F SMC device following interventional catheterization procedures using 5F to 8F sheaths. Two hundred twenty-five (225) patients were enrolled in post-close arm and one hundred sixty (160) patients were enrolled in the pre-close arm of the CLOSER IDE trial. In the post-close arm, the deployment of the Closer device occurred at the end of the catheterization procedure. In the pre-close arm, the Closer device was deployed in two steps with suture delivery at the beginning of the catheterization procedure with knot tying and knot delivery occurring at the end of the procedure.

Procedural success was achieved in 223 patients (99.1%) in the post-close arm and 158 patients (98.8%) in the pre-close arm. Time to discharge was 28.9 $\pm$ 22.7 hours and 30.1 $\pm$ 33.9 hours for the post-close and pre-close patients, respectively. The secondary endpoint of time to hemostasis was 10.9 $\pm$ 42.0 minutes and 8.2 $\pm$ 51.0 minutes for the post-close and pre-close patients, respectively, versus 7.9 $\pm$ 6.4 hours for the control group patients, $p < 0.0001$, and the secondary endpoint of time to ambulation was 4.7 $\pm$ 7.1 hours and 6.5 $\pm$ 11.4 hours for the post-close and pre-close patients, respectively.

Device success was 92.0% (207/225 patients) in the post-close arm and 89.4% (143/160 patients) in the pre-close arm. Failure to deploy the Closer occurred in 17 (7.6%) patients in the post-close arm and 15 (9.4%) patients in the pre-close arm.

A major complication was defined as surgical repair of vascular injury, ultrasound-guided compression, groin-related transfusion, or groin-related infection requiring IV antibiotics and extended hospitalization. The primary safety endpoint was the combined rate of major complications at 30 days. For the post-close arm, one patient received a blood transfusion

[2] Perclose ProStyle SMCR System and Perclose ProGlide SMC System are design evolutions of the Closer 6F SMC system. The results of the CLOSER IDE trial are applicable to the Perclose ProStyle SMCR and Perclose ProGlide SMC Systems because of system similarities.

subsequent to a retroperitoneal bleed. Another patient underwent surgical repair of a vascular injury and received a blood transfusion subsequent to the intervention. Both patients were free of symptoms at time of follow-up. For the pre-close arm, one patient developed a hematoma > 6 cm as a result of insufficient hemostasis. Subsequently, the patient required vascular surgery to repair the femoral artery and received blood transfusions intraoperatively. The second patient received IV antibiotic therapy for a local infection that presented post discharge. Both patients reported no further sequelae at time of follow-up.

The incidence of vascular complication other than major was a secondary safety endpoint of the study and in the post-close arm consisted of one (0.4%) false aneurysm, one (0.4%) infection requiring IM and PO antibiotics, two (0.9%) ≥ 6 cm hematomas, and two (0.9%) retroperitoneal bleeds not requiring intervention. For the pre-close arm, the incidence of vascular complication other than major consisted of one (0.6%) ≥ 6 cm hematoma and one (0.6%) groin infection requiring PO antibiotics. All patients were free of symptoms at time of follow up. The results of the effectiveness measures are summarized in **Table 10.2-1**.

Table 10.2-1: Principal Effectiveness Results

(All patients enrolled in the CLOSER IDE trial;
N = 225 for the post-close arm; N = 160 for the pre-close arm)

Effectiveness Measures*	**The CLOSER IDE Trial Post-Close Patients**	**The CLOSER IDE Trial Pre-Close Patients**
Treated patients (per event)	**N = 225**	**N = 160**
Procedural success	223 (99.1%)	158 (98.8%)
Device success	207 (92.0%)	143 (89.4%)
Device failure	17 (7.6%)	15 (9.4%)
Device malfunction	16 (7.1%)	14 (8.8%)
Device complication	1 (0.4%)	1 (0.6%)
Time to Hemostasis (mins)	N = 224	N = 160
mean±SD	10.9±42.0	8.2±51.0
(min. max.)	(1.0, 324.0)	(0.1, 639.0)
Median	3.0	1.5
[quartiles]	[2.0, 5.0]	[0.0, 5.0]
Time to Ambulation (hrs)	N = 225	N = 160
mean±SD	4.7±7.1	6.5±11.4
(min. max.)	(0.1, 71.4)	(0.05, 100.9)
Median	2.4	2.2
[quartiles]	[1.6, 4.5]	[1.2, 5.0]
Time to Discharge (hrs)	N = 225	N = 160
mean±SD	28.9±22.7	30.1±33.9
(min. max.)	(2.2, 240.2)	(2.7, 292.6)
Median	24.4	22.5
[quartiles]	[22.0, 27.2]	[20.2, 26.1]

*The number of patients listed under effectiveness measures is less than the total patients studied due to missing data for some patients. Device success = acute success using the device only or the device + adjunctive (non-arterial) compression.

Thus, the Perclose ProGlide SMC System reduced the time to hemostasis, ambulation (10 feet) and discharge in patients who had undergone diagnostic or interventional catheterization

procedures without complicating clinical conditions (refer to sections **7.0 PRECAUTIONS** and **8.0 SPECIAL PATIENT POPULATION)**.

Adverse Events in the CLOSER IDE Trial

The CLOSER IDE trial was designed as a multi-center, multi-operator, prospective registry enrolling 225 patients in the post-close arm and 160 patients in the pre-close arm. The post-close arm studied the use of the Closer 6F system following interventional procedures using 5F to 6F sheaths. The pre-close arm studied the use of the Closer 6F system following interventional procedures using 7F to 8F sheaths utilizing the pre-close technique. The pre-specified analysis of the primary safety endpoint of the IDE trial was the incidence of the combined rate of major complications at 30 days of patients undergoing interventional catheterization procedures. Post-treatment, ultrasound evaluations were performed 0 to 15 days post-discharge to verify detection of clinical complications. Two major complications were reported in each of the post-close and pre-close arms of the CLOSER IDE trial. Neither of the two major complications reported in the post-close or pre-close arms were considered unanticipated events. No delayed major hemorrhagic events were reported despite early ambulation and early discharge of the patients with the Closer SMC device. The adverse events that were observed during the trial are reported in **Table 10.2-2**.

Table 10.2-2: Percentage of Patients Who Experienced Adverse Events

(All patients enrolled in the CLOSER IDE trial;
N = 225 for post-close arm; N = 160 for pre-close arm)

Safety Measures, n (percent)	The CLOSER IDE Trial Post-Close Patients	The CLOSER IDE Trial Pre-Close Patients
Treated patients (per event)	**N = 225**	**N = 160**
Device Failure	17 (7.6%)	15 (9.4%)
Surgical repair*	1 (0.4%)	1 (0.6%)
U/S guided compression*	0 (0.0%)	0 (0.0%)
Transfusion*	2 (0.9%)	1 (0.6%)
Infection requiring IV Abx*	0 (0.0%)	1 (0.6%)
Hematoma $\geq$ 6 cm	2 (0.9%)	1 (0.6%)
AV-fistula	0 (0.0%)	0 (0.0%)
Pseudoaneurysm	1 (0.4%)	0 (0.0%)
Vascular narrowing	0 (0.0%)	0 (0.0%)
Infection requiring IM\PO Abx	1 (0.4%)	1 (0.6%)
Retroperitoneal bleed	2 (0.9%)	0 (0.0%)
Incidence of Complications (per patient)		
Any complication¶	6 (2.7%)	3 (1.9%)
Major complication¶	2 (0.9%)	2 (1.2%)
No major complication	223 (99.1%)	158 (98.8%)

* Major complication

¶ Per patient; some patients may have experienced more than one complication.

No groin or device related deaths were reported in the Closer IDE trial among the post-close or

pre-close study patients. Other adverse events potentially associated with the use of the Closer SMC System were reported as an underlying event or did not occur during the clinical study. These include: deep vein thrombosis, infection extending hospitalization, late bleeding, wound dehiscence, vessel laceration, local pulse deficits or ischemia, embolization, transitory local irritation, nerve injury and vascular spasm. In addition, polyester surgical sutures elicit a minimal acute inflammatory reaction in tissues, followed by gradual encapsulation of the suture by fibrous connective tissue. Polyester surgical sutures are not absorbed, nor are any significant change in tensile strength known to occur *in vivo*.

10.3 The REALISM Clinical Trial – ProGlide Cohort

A retrospective analysis was performed to evaluate the safety and effectiveness of the Perclose ProGlide SMC System[3] in closing large-sized venous access sites through a retrospective data collection from the EVEREST II/REALISM Continued Access Registry Study (REALISM). The retrospective analysis included subjects in whom ProGlide was used as the primary method for large bore venous access-site closure during the MitraClip index procedure with a 24F vascular sheath.

10.3.1 Methods

The analysis population was derived from a subset of REALISM subjects who were enrolled in the REALISM High Risk (HR) cohort, REALISM Non-High Risk (NHR) cohort, and REALISM Compassionate Use (CU) cohort. REALISM was a continued access study within the EVEREST II trial, which included subjects receiving the MitraClip index procedure with MitraClip sheath of 24F. REALISM enrolled 958 subjects, of whom 899 subjects were enrolled per the protocol and 59 as compassionate use. The **ProGlide cohort** was selected from subjects enrolled in the seven (7) REALISM sites with high frequency use of vessel closure devices (VCD ≥ 15 cases), and who received at least one ProGlide as their primary closure device during the MitraClip index procedure. Of the seven (7) sites, one (1) site did not use ProGlide and another site only used ProGlide for arterial access, and therefore the ProGlide cohort comprised of five (5) sites with a total of 159 subjects. Similarly, a **Manual Compression cohort (MC cohort)** of 230 subjects was identified from seven (7) sites that reported high frequency MC usage of ≥ 25 cases each without the use of any VCD. Subjects in both cohorts had MitraClip implanted into the mitral valve with access through the common femoral vein.

In the ProGlide Cohort, three (3) sub-group analyses were predefined: ProGlide Alone vs. ProGlide Plus, Male vs. Female, and One ProGlide vs. Two ProGlides. The ProGlide Alone group included subjects in whom at least one ProGlide was used without any secondary method(s) other than brief adjunctive MC ≤ 10 minutes. The ProGlide Plus group included subjects in whom at least one ProGlide with prolonged MC > 10 minutes or other secondary closure methods were used. None of the sub-group analyses are powered for statistical significance.

This retrospective analysis reports baseline subject characteristics and comorbidities, ProGlide usage information, effectiveness of achieving hemostasis (including time to hemostasis) during

[3] Perclose ProStyle SMCR System is a design evolution of the Perclose ProGlide SMC System. The results of the REALISM Clinical Trial are applicable to the Perclose ProStyle SMCR System because of system similarities

the index procedure, and adverse events up to 30 days. The primary endpoint was the rate of freedom from major femoral vein access-site related complications at 30-days post MitraClip index procedure. The pre-specified acceptance criterion for the rate of freedom from major femoral vein access-site related complications at 30-days post-procedure was ≥ 90%.
Major complication is defined as any event leading to death, life-threatening or major bleeding, surgical intervention, hospitalization, visceral ischemia, or neurological impairment. This list includes development of the following:

- Femoral vein stenosis (> 50%) development at the puncture site related to closure technique
- Development of deep vein thrombosis in the target limb
- Significant venous bleeding, retroperitoneal bleeding / hematoma, or hematoma at the access site requiring transfusion or surgical intervention
- Hematoma that does not require transfusion or surgical intervention
- Access site-related wound dehiscence or venous access site infection requiring intravenous, intramuscular or oral antibiotics, and / or leading to a prolonged hospitalization
- Venous access site injury, including vessel laceration, requiring surgical repair, angioplasty, ultrasound-guided compression or thrombin injection
- Re-bleeding at access site that requires treatment or re-hospitalization
- AV fistula
- Pseudoaneurysm
- Access site-related nerve injury

Minor complications are defined as those complications that did not require transfusion, surgery, or re-hospitalization. Adverse events from baseline to 30 days were reviewed to identify any potential femoral vein access-site related complications, which upon identification, were subsequently adjudicated by an independent Clinical Event Committee (CEC).

10.3.2 Results – ProGlide Cohort

Subject Selection: Of the 159 subjects in the ProGlide cohort, 98 subjects (61.6%) were from the REALISM High Risk cohort, 37 subjects (23.3%) from the REALISM Non-High Risk cohort, and 24 subjects (15.1%) from the REALISM Compassionate Use cohort. All subjects completed their discharge evaluations. Four (4) subjects died before their 30-day visits and two (2) missed their 30-day visits, and therefore 153 subjects reported 30-day assessments.

Subject Demographics: The ProGlide cohort reflected subjects with varying degrees of heart failure. The cohort included elderly subjects with a mean age of 76 years. Male subjects accounted for 52.8%. Subjects presented with multiple comorbidities including high rates of congestive heart failure (CHF) (89.2%), atrial fibrillation (AF) (64.7%), coronary artery disease (CAD) (67.7%), hypertension (84.8%), diabetes (26.4%) moderate to severe renal disease (24.5%), chronic obstructive pulmonary disease (COPD) (23.3%), and NYHA class III (59.7%) and IV (24.5%). History of prior percutaneous interventions (37.7%) and cardiovascular surgery (42.1%) were common in this cohort.

Primary Endpoint: The freedom from major femoral vein access-site related complications was 98.1% at 30 days, which met the pre-specified safety acceptance criteria of 90% for the ProGlide cohort (**Table 10.3.2-1**). ProGlide group is defined as subjects who had received at least one ProGlide as the primary intended method to close femoral vein access site during the index procedure with or without adjunctive closure methods (manual compression or subcutaneous stitch). A total of 16 adjudicated complications, in 13 subjects, were reported through 30 days, of which only five (5) events in three (3) subjects were major complications. The remaining 11 adjudicated complications, in 10 subjects, were considered minor.

Table 10.3.2-1: Freedom from Major Femoral Vein Access-Site Related Complication Through 30 Days (ProGlide Cohort[4]) (Per Subject Analysis)

Events[1]	ProGlide (N = 159[3])	Clinical Acceptance Criteria
Freedom from Major Femoral Vein Access-Related Complication[2]	98.1% (156/159)	90%

[1] Includes only each subject's first occurrence of each event.

[2] The major femoral vein access-related complication is defined as access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment.

[3] The denominator excludes subjects who withdrew or lost to follow up before the 30-day visit early window (27 days post-procedure) without any femoral vein access-related complication.

[4] ProGlide group is defined as subjects who had received at least one ProGlide as the primary intended method to close femoral vein access site during the index procedure with or without adjunctive closure methods (manual compression or subcutaneous stitch).

Summary of Safety: The adjudicated major femoral vein access-site related complications through 30 days were reported as non-hierarchical subject counts (**Table 10.3.2-2**). The major complication rate was low at 1.9%. Five (5) major complications in three (3) subjects were reported within 30 days: one (1) hematoma requiring intervention and one (1) pseudo-aneurysm, one (1) hematoma and one (1) re-bleeding within 48 hours, and one (1) deep vein thrombosis in the target limb 6-days post-procedure. All cases achieved hemostasis within 2 minutes without MC or secondary closure devices.

Table 10.3.2-2: Summary of Adjudicated Major Femoral Vein Access-Site Related Complications Through 30 Days (ProGlide Cohort[3]): Non-Hierarchical by Subject

Non-Hierarchical Major Events[1]	0 – 48 hours (Subject count)	> 48 hours – 30 days (Subject count)	0 – 30 days (Subject count)	Total number of events from 0 to 30 days
Major Femoral Vein Access-Related Complications[2]	1.3% (2/159)	0.6% (1/159)	1.9% (3/159)	5
Femoral vein stenosis (>50% development at the puncture site related to closure technique)	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0

Non-Hierarchical Major Events[1]	0 – 48 hours (Subject count)	> 48 hours – 30 days (Subject count)	0 – 30 days (Subject count)	Total number of events from 0 to 30 days
Development of deep vein thrombosis in the target limb	0.0% (0/159)	0.6% (1/159)	0.6% (1/159)	1
Significant venous bleeding, retroperitoneal bleeding / hematoma, or hematoma at the access site requiring transfusion or surgical intervention	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
Hematoma that does not require transfusion or surgical intervention	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
Access site-related wound dehiscence or venous access site infection requiring intravenous, intramuscular or oral antibiotics, and / or leading to a prolonged hospitalization	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0
Venous access site injury, including vessel laceration, requiring surgical repair, angioplasty, ultrasound-guided compression or thrombin injection	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0
Re-bleeding at access site that requires treatment or re-hospitalization	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
AV Fistula	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0
Pseudoaneurysm	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
Access site-related nerve injury	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0

[1] Includes only each subject's first occurrence of each event.
[2] The major femoral vein access-related complication is defined as access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment.
[3] ProGlide group is defined as subjects who had received at least one ProGlide as the primary intended method to close femoral vein access site during the index procedure with or without adjunctive closure methods (manual compression or subcutaneous stitch).

The adjudicated minor femoral vein access-site related complications through 30 days were also reported as non-hierarchical subject counts. There were 10 subjects with minor complications (6.3%). The total number of minor complications through 30 days was 11, including four (4) hematoma events not requiring treatment (2.5%; 4/159) and seven (7) re-bleeds requiring treatment (4.4%; 7/159). All minor complications occurred within 48-hours post-procedure and were resolved by 30 days.

Summary of Effectiveness: ProGlide was an effective device for primary intended hemostasis of venous closure sites. Majority of subjects (69.2%) achieved hemostasis with ProGlide alone without additional secondary closure methods. Adjunctive closure methods included MC (17.6%, 28/159) and subcutaneous stitch (12.6%, 20/159), and one (1) subject received an AngioSeal along with ProGlide and MC (0.6%, 1/159). Within the ProGlide cohort, two (2) ProGlide devices were used predominantly to achieve hemostasis (90.6%, 144/159), a practice attributed to the arterial closure IFU which requires at least two (2) ProGlides if the transcatheter device sheath is greater than 8F as is the case with the 24F MitraClip. The remaining 9.4% (15/159) cases used single ProGlide for access-site closure.

On average, hemostasis was achieved in 5.92 ± 6.19 minutes in the ProGlide cohort. The mean time to achieve hemostasis with ProGlide alone was 5.15 minutes. This time increased to 9.3 minutes when adjunctive MC was used. When a secondary vessel closure method (namely subcutaneous stitch) was used, the mean time to achieve hemostasis was 5.8 minutes (**Table 10.3.2-3**). Overall, secondary closures were mostly initiated when there was a failure to achieve hemostasis using ProGlide and MC, which occurred in 12.6% of patients.

Table 10.3.2-3: Summary of ProGlide Effectiveness on Hemostasis (ProGlide Cohort[5])

Characteristics	ProGlide (N = 159)
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	5.92 ± 6.19 (134)
Median (Q1, Q3)	4.50 (1.00, 8.00)
Range (min, max)	(0.00, 30.00)
ProGlide Without Any Adjunctive Closure Method	69.2% (110/159)
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	5.15 ± 6.05 (95)
Median (Q1, Q3)	3.00 (1.00, 7.00)
Range (min, max)	(0.00, 29.00)
ProGlide and Adjunctive Manual Compression (MC) Only	17.6% (28/159)
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	9.3 ± 7.3 (23)
Median (Q1, Q3)	6.0 (5.0, 14.0)
Range (min, max)	(1, 30)
ProGlide and Adjunctive Manual Compression <=5 Minutes[1]	6.3% (10/159)
Time to Achieve Hemostasis (min)	4.0 ± 1.7 (10)
Mean ± SD (n)	5.0 (3.0, 5.0)
Median (Q1, Q3)	(1, 5)
Range (min, max)	
ProGlide and Adjunctive Manual Compression <=10 Minutes[1]	10.1% (16/159)
Time to Achieve Hemostasis (min)	5.1 ± 2.1 (16)
Mean ± SD (n)	5.0 (5.0, 6.0)
Median (Q1, Q3)	(1, 9)
Range (min, max)	
ProGlide and Adjunctive Manual Compression >10 Minutes or Unknown [1, 2]	7.5% (12/159)
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	

Characteristics	ProGlide (N = 159)
Median (Q1, Q3) Range (min, max)	18.7 ± 5.9 (7) 18.0 (14.0, 22.0) (13, 30)
ProGlide and Secondary Vessel Closure Method Only **Time to Achieve Hemostasis (min)** Mean ± SD (n) Median (Q1, Q3) Range (min, max)	12.6% (20/159) 5.8 ± 3.3 (16) 6.0 (3.0, 7.0) (1, 12)
Type of Secondary Closure Method Subcutaneous Stitch Other Closure Device Surgical Repair Data Not Available	 100.0% (20/20) 0.0% (0/20) 0.0% (0/20) 0.0% (0/20)
Reason to use Secondary Vessel Closure Method ProGlide Device Deficiency Access Complication (s) Failure to Achieve Hemostasis Data Not Available[4]	 0.0% (0/20) 0.0% (0/20) 95.0% (19/20) 5.0% (1/20)
Hemostasis Achieved by Using ProGlide, Manual Compression and Secondary Vessel Closure Method [3]	0.6% (1/159)

[1] For subjects with missing manual compression time, the non-missing time to achieve hemostasis is used to determine the sub-category.
[2] Subjects with both manual compression time and time to achieve hemostasis missing are also included in this category.
[3] One (1) subject used Angio-seal as the secondary vessel closure method in addition to ProGlide and Manual Compression due to unknown reason. The subject had both manual compression time and time to achieve hemostasis unknown.
[4] Subject who used Secondary closure method with unknown reason was categorized in the Data not available category.
[5] ProGlide group is defined as subjects who had received at least one ProGlide as the primary intended method to close femoral vein access site during the index procedure with or without adjunctive closure methods (manual compression or subcutaneous stitch).

10.3.3 Sub-Group Analyses

Three (3) sub-group analyses were pre-specified: ProGlide Alone vs. ProGlide Plus, Male vs. Female, and One ProGlide vs. Two ProGlides. These sub-group analyses were not powered.

10.3.3.1 ProGlide Alone vs. ProGlide Plus

The ProGlide Alone group involved 126 subjects in whom at least one ProGlide was used along with adjunctive MC ≤ 10 minutes. These subjects generally had numerically higher baseline comorbidities, such as atrial fibrillation, coronary artery disease, diabetes, hypercholesterolemia, angina, MI, prior percutaneous interventions and cardiovascular surgery, liver disease, and NYHA II compared to the ProGlide Plus group. The ProGlide Plus group included fewer subjects (n = 33) all of whom required at least one ProGlide with either prolonged MC > 10 minutes or a secondary closure device to achieve hemostasis.

Safety: The major complications were low and occurred in the ProGlide Alone group (2.4% [3/126]) with 1.6% (2/126) complications occurring within the first 48 hours. There were no major complications in the ProGlide Plus group, through 30 days. Minor complications were similar in both groups with approximately 94% freedom from events (ProGlide Alone 6.3% [8/126] and

ProGlide Plus 6.1% [2/33]). Within the limits of sample sizes, these results support the safe and effective use of ProGlide with or without adjunctive MC.

Effectiveness: The ProGlide Plus group had a numerically greater time to achieve hemostasis compared to the ProGlide Alone group (9.70 ± 7.34 [23] vs. 5.14 ± 5.65 [111]). In the ProGlide Alone group, 87.3% of subjects achieved hemostasis by using ProGlide without any adjunctive closure method, and 12.7% achieved hemostasis by using ProGlide and adjunctive manual compression. Additionally, the ProGlide Plus group compared to the ProGlide Alone group had a numerically higher percentage of subjects achieving hemostasis using ProGlide and adjunctive manual compression (36.4% [12/33] vs. 12.7% [16/126]).

10.3.3.2 Male vs. Female

A total of 84 male subjects and 75 female subjects were included in this sub-group analysis. Both groups had a similar mean age (males: 77 years; females: 74 years). Males reported numerically higher baseline incidences of key comorbidities including congestive heart failure, hypercholesterolemia, coronary and peripheral vascular disease (PVD), diabetes, COPD, and NYHA III/IV.

Safety: All 30-day major complications were reported in males 3.6% (3/84). There were no major complications in female through 30 days. However, because the event rates are low, larger dataset would be needed to confirm a gender difference. Among minor events, men 8.3% (7/84) had a numerically higher rate compared with women 4.0% (3/75).

Effectiveness: On average, both groups took comparable time to achieve hemostasis (men: 5.69 ± 6.37 [70] vs. women: 6.18 ± 6.02 [64]). Males achieved numerically faster hemostasis than females when adjunctive MC (6.9 ± 4.7 [11] vs. 11.4 ± 8.7 [12]) or other secondary closure devices (4.2 ± 2.9 [9] vs. 7.7 ± 2.7 [7]) were used.

10.3.3.3 One ProGlide vs. Two ProGlides

Most of the subjects in this study received two (2) ProGlides (n = 144) and only fifteen (15) subjects received one (1) ProGlide. The most common reason for using more than one ProGlide was per IFU recommendation (93.8% [135/144] of the cases). Within the Two ProGlides group, 70.8% (102/144) did not require any adjunctive closure methods compared with 53.3% (8/15) in the One ProGlide group.

Both groups were similar in age (one ProGlide 75 years vs. two ProGlides 76 years). Both groups had approximately same rates of key risk factors of CHF, atrial fibrillation, angina, and COPD. The One ProGlide subjects had numerically higher rates of CAD, PVD, renal disease, and NYHA III, while the Two ProGlide subjects had numerically higher rates of cardiomyopathy, diabetes, history of CABG, and NYHA IV.

Safety: Major complication rates at 30 days were numerically higher in the One ProGlide group at 6.7% (1/15) compared with 1.4% (2/144) in Two ProGlides group. The very small sample size of the One ProGlide group must be considered when assessing the 30-day rate. Each group

reported only one (1) major access-site complications within 48 hours post-procedure. The 30-day minor complication rate remained unchanged from the 30-day major complication rate for the one ProGlide group (6.7%) and was 6.3% (9/144) for the two ProGlide group. Given the disproportionate sample sizes of the two groups, the outcomes must be interpreted with caution.

Effectiveness: The subjects in the One ProGlide group took numerically longer to achieve hemostasis than those who received two (2) ProGlides (7.93 ± 6.58 [14] vs. 5.69 ± 6.13 [120]). Additionally, the One ProGlide group reported a smaller percentage of subjects achieving hemostasis without any adjunctive methods compared to Two ProGlide (53.3% [8/15] vs. 70.8% [102/144]), a numerically higher percentage of use of adjunctive MC (33.3% [5/15] vs. 16.0% [23/144]) and a numerically higher percentage of MC of ≥ 10 mins compared with the Two ProGlides group (20.0% [3/15] vs. 6.3% [9/144]).

10.3.4 RESULTS: Manual Compression Cohort

The MC Cohort consisted of 230 subjects: 156 (67.8%) from the REALISM High Risk cohort, 58 (25.2%) from the REALISM Non-High Risk cohort, and 16 (7.0%) from the REALISM Compassionate Use cohort. Their mean age was 77 years (230) and subjects in the MC cohort had high rates of CHF (94.8% [218/230]), AF (62.9% [134/213]), CAD (76.4% [175/229]), diabetes (33.0% [76/230]), moderate to severe renal (27.8% [64/230]), and COPD (28.4% [65/229]), and prior percutaneous intervention (35.4% [81/229]). In the MC cohort, 50% of the subjects achieved hemostasis with MC only; 49.6% and 0.4% of the subjects received MC plus a subcutaneous stitch or MC plus other closure device as a secondary method to facilitate hemostasis, respectively.

Safety: Thirty-two adjudicated access site complications were reported through 30 days: 10 major (4.4% [10/227]) and 22 (9.7% [22/227]) minor. The 30-day major complications were mostly venous bleeding (3.1% [7/227]) with the remaining being development of deep vein thrombosis (0.4% [1/227]), hematoma (0.4% [1/227]), re-bleeding (0.9% [2/227]), venous access site injury (0.9% [2/227]) and pseudo-aneurysm 0.9% (2/227). Minor complications mostly developed within 48-hours post-index procedure and were largely due to hematoma, and re-bleeding at the access site that requires treatment.

Effectiveness: In the MC cohort, 50% (115/230) of the subjects received MC alone as the intended hemostasis method; 49.6% (114/230) and 0.4% (1/230) of the subjects received MC plus a subcutaneous stitch or MC plus other closure device as a secondary method to facilitate hemostasis, respectively.

Conclusion

In summary, the primary objective of the study was to evaluate the safety and performance of ProGlide in closure of venous access site in subjects with a large-caliber femoral vein sheath (24F). The study results have demonstrated that the safety assessment of the ProGlide met the predefined acceptance safety criterion. Taken together, the study results show that ProGlide is safe and effective in the closure of the venous access site with up to 24F sheath.

Study Limitations

THE STUDY HAD LIMITATIONS SINCE IT WAS A RETROSPECTIVE ANALYSIS OF A SELECTED DATASET WITHIN A TRIAL IN WHICH THE MAIN OBJECTIVE WAS THE EVALUATION OF THE MITRACLIP DEVICE. THE DESIGN OF THE TRIAL WAS NOT SPECIFIC TO THE EVALUATION OF PROGLIDE FOR LARGE BORE VENOUS CLOSURE.

10.4 The Perclose SMC Investigator Sponsored Studies (ISS)

The primary objective of the Perclose SMC Multi-Access ISS analysis was to evaluate the safety and effectiveness of Perclose SMC in subjects with multiple access sites in a single vein, with focus on use of Perclose SMC for more than one access site per femoral vein; and use of 2 or more Perclose SMCs for a femoral vein access site that is >8F.

10.4.1 Methods

The Perclose Multi-Access ISS analysis consisted of a prospective/retrospective data analysis of the three real-world studies: Santa Barbara Cottage Hospital Study (SBCH), conducted at Santa Barbara Cottage Hospital, Santa Barbara, CA; Emory School of Medicine Study (ESM), conducted at the Emory School of Medicine, Atlanta, GA; and VAscular Closure for Cardiac Ablation Registry (VACCAR), conducted at Saint Luke's Hospital, Kansas City, MO.

The ESM study was a prospective trial while both the VACCAR and the SBCH studies were retrospective. The analysis of the three studies was performed by Abbott using datasets provided by the investigators.

10.4.1.1 SBCH Study

The SBCH trial, a retrospective, single-arm, subject-level study, enrolled 519 subjects between November 2016 and March 2020, over a period of 40.3 months, to evaluate the safety and effectiveness of the Perclose SMC in closure of multiple access sites of the ipsilateral femoral vein following Atrial Fibrillation (AF) ablation. The right femoral vein for vessel access/closure was used per the site standard, with at least one access site using Perclose SMC device. Majority of access sites were treated with one Perclose SMC based on site's standard of care, if Perclose SMC was used for that access site.

The subject population was comprised of men and women ages 25 to 92 that underwent AF ablation with post-ablation closure of the femoral vein using the Perclose SMC System, and who were discharged the same day of the procedure with 30-day follow-up.

10.4.1.2 ESM Study

The ESM study, a prospective, randomized controlled trial, was conducted at three participating sites – Emory University Hospital, Emory University Hospital Midtown, and Emory St Joseph's Hospital; enrolled subjects between January 2020 and December 2020, over a period of 10.8 months, and evaluated the safety and efficacy of Perclose SMC in comparison with manual hemostasis. The trial enrolled 55 subjects in the Perclose SMC arm and 54 subjects in the MC arm. All access sites were treated with only one Perclose SMC regardless of sheath size as

standard of care. Subjects underwent routine ablation for AF as standard of care and were followed through 30 days before exiting the trial.

Additional comparisons of this study were time to hemostasis and time to ambulation. Several other secondary endpoints including frequency of access site related complications, pain and need for post-procedure narcotics, subject satisfaction, as well as cost and overall resource utilization.

10.4.1.3 VACCAR Study

The VACCAR study, a retrospective chart review, subject-level study, enrolled subjects between October 2017 and November 2020 over a period of 37.1 months, comparing 3 groups aimed to find if there was a difference in subject satisfaction and rate of vascular and bleeding complications with use of the Perclose SMC System for venous closure post AF and atrial flutter procedures in comparison to manual compression (MC). Other parameters measured included the time to achieve hemostasis, time to ambulate and length of hospital stay. The trial enrolled 75 subjects in the Perclose SMC arm, 156 subjects in the MC arm, and 203 subjects in the Figure of 8 stitch (Fo8) arm. Unilateral or bilateral femoral veins were used during the index procedure, and the right femoral vein was used for the first 3 access sites. If there were more than 3 access sites, then the remainders used the left femoral vein. For a cryoablation procedure that used 3 or more access sites, one access site used two Perclose devices and all other access sites used one Perclose SMC. If a radio-frequency ablation procedure was done using Perclose SMC in closure of multiple access sites, then every access site only used one Perclose device.

Clinical Study Endpoints

The primary safety endpoint was freedom from femoral vein access-related major vascular complications at 30-days post procedure, including but not limited to:

- Femoral vein stenosis (> 50%) development at the puncture site related to closure technique;
- Development of deep vein thrombosis in the target limb;
- Significant venous bleeding, retroperitoneal bleeding / hematoma, or hematoma at the access site requiring transfusion or surgical intervention;
- Hematoma that did not require transfusion or surgical intervention;
- Access site-related wound dehiscence or venous access site infection requiring intravenous, intramuscular or oral antibiotics, and / or leading to a prolonged hospitalization;
- Venous access site injury, including vessel laceration, requiring surgical repair, angioplasty, ultrasound-guided compression or thrombin injection;
- Re-bleeding at access site that required treatment or re-hospitalization;
- AV fistula;
- Pseudoaneurysm;
- Access site-related nerve injury;
- Pulmonary embolism

Results were compared to a clinical acceptance criterion of ≥95%. A 95% clinical acceptance criterion was applied to both the SBCH Study and ESM Study but was not applied to the VACCAR Registry results as it did not have 30-day follow-up.

Primary performance endpoints included the following procedure details:

1. Type of ablation procedure
2. Number of access sites per subject
3. Number of access sites per single vein
4. Number of Perclose SMCs used per vein and per access site and per closure procedure
5. Number of Perclose SMCs used access site > 8F access sites
6. Distribution of sheath size
7. Procedure duration
8. Success rate
9. Anticoagulant and antiplatelet medications
10. Use of protamine for heparin reversal

10.4.2 Results

10.4.2.1 Subject Selection

A total of 1062 subjects underwent ablation procedure at 3 investigational sites in the United States between November 2016 and December 2020. Of these 1062 subjects, 649 were treated with the Perclose SMC System, 210 were treated by MC, and 203 were treated using Fo8 stitch.

The SBCH Study treated 519 subjects with Perclose SMC. All subjects were assessed for performance endpoints and for safety endpoints to 30 days.

The ESM Study treated 55 subjects with Perclose SMC arm, and 54 subjects with MC. Of the 55 subjects in the Perclose SMC arm, 2 subjects were randomized without procedure, therefore, only 53 subjects were assessed for safety endpoints to 30 days.

The VACCAR Study treated 75 subjects with Perclose SMC arm, 156 subjects with MC, and 203 subjects with Fo8. All subjects were assessed for performance endpoints and for safety endpoints in-hospital.

10.4.2.2 Subject Demographics

Demographics and primary diagnosis of subjects in the 3 studies is given in **Table 0-1** below. Use of oral anticoagulants and oral antiplatelets pre and post procedure for 30 days is given in **Table 0-2** and **Table 10.4.2-3**.

Table 0-1 Demographics and Primary Diagnosis

	SBCH Study Perclose Device (N=519)	**ESM Study Perclose Device (N=55)**	**VACCAR Study Perclose Device (N=75)**
Age (year)			
Mean ± SD (n)	69.1 ± 10.1 (519)	61.1 ± 10.0 (55)	67.2 ± 8.6 (74)
Median (Q1, Q3)	70.0 (63.0, 76.0)	64.0 (55.0, 68.0)	68.5 (63.0, 73.0)

Range (min, max)	(25, 92)	(31, 80)	(43, 81)
Sex			
Male	65.9% (342/519)	70.9% (39/55)	57.3% (43/75)
Female	34.1% (177/519)	29.1% (16/55)	42.7% (32/75)
Primary Diagnosis			
Paroxysmal AF	44.5% (231/519)	67.9% (36/53)	73.3% (55/75)
Persistent AF	47.6% (247/519)	32.1% (17/53)	16.0% (12/75)
Atrial Flutter	1.7% (9/519)	Not reported	10.7% (8/75)
Other	6.2% (32/519)	Not reported	Not reported
Diabetes	Not reported	10.9% (6/55)	26.7% (20/75)
Coronary Artery Disease	Not reported	10.9% (6/55)	21.3% (16/75)

Note: N is the total number of subjects.

Table 0-2 Oral Anticoagulant Use Pre- and Post-Procedure

	SBCH Study Perclose Device (N=519)	ESM Study Perclose Device (N=55)	VACCAR Study Perclose Device (N=75)
Pre-Procedure			
Any Oral Anticoagulant	29.2% (151/517)	89.1% (49/55)	100.0% (75/75)
Warfarin	4.3% (22/517)	7.3% (4/55)	10.7% (8/75)
Apixaban	25.0% (129/517)	65.5% (36/55)	68.0% (51/75)
Rivaroxaban	0.0% (0/517)	14.5% (8/55)	17.3% (13/75)
Dabigatran	0.0% (0/517)	1.8% (1/55)	4.0% (3/75)
Post-Procedure for 30 Days			
Any Oral Anticoagulant	30.8% (159/517)	100.0% (53/53)	Not reported
Warfarin	4.3% (22/517)	3.8% (2/53)	Not reported
Apixaban	26.7% (138/517)	79.2% (42/53)	Not reported
Rivaroxaban	0.0% (0/517)	17.0% (9/53)	Not reported
Dabigatran	0.0% (0/517)	1.9% (1/53)	Not reported

Oral anti-coagulant use post-procedure not available for the VACCAR study.

Table 0-3 Oral Antiplatelet Use Pre- and Post-Procedure

	SBCH Study Perclose Device (N=519)	ESM Study Perclose Device (N=55)
Pre-Procedure		
Any Oral Antiplatelet	22.4% (116/517)	20.0% (11/55)
Aspirin	20.9% (108/517)	18.2% (10/55)
Clopidogrel	3.3% (17/517)	1.8% (1/55)
Ticagrelor	0.4% (2/517)	0.0% (0/55)
Prasugrel	0.0% (0/517)	0.0% (0/55)
Post-Procedure during 30 Days		
Any Oral Antiplatelet	19.5% (101/517)	79.2% (42/53)
Aspirin	18.2% (94/517)	77.4% (41/53)
Clopidogrel	3.1% (16/517)	0.0% (0/53)
Ticagrelor	0.4% (2/517)	1.9% (1/53)
Prasugrel	0.0% (0/517)	0.0% (0/53)

Oral antiplatelet use pre-and post-procedure not available for the VACCAR study.

10.4.2.3 Key Results

Freedom from major access-site related complications was 99.2% for the SBCH study and 96.2% for the ESM study (**Table 0-4**) up to 30 days post index procedure, compared to the 95% clinical acceptance criterion. Both studies met the clinical acceptance criterion.
The major access-site related complications included hematomas, major bleeding, pseudoaneurysm, and vascular surgery.

Although the VACCAR study did not have 30-day follow-up, it also demonstrated a complete freedom of access site-related major complications (0.0%, 0/75) in the Perclose SMC arm at discharge. Minor complication rate included hematoma (1.3%), pseudoaneurysm (1.3%) and other complications (1.3%). MC and Fo8 minor complication rates were 2.6% and 1.5%, all of which were hematomas (**Table 10.4.2-5**).

Table 0-4 Primary Safety Endpoint - Freedom from Major Access-Site Related Complications at 30-Days Compared to Clinical Acceptance Criteria for SBCH and ESM Study

	SBCH Study Perclose Device (N=519)	ESM Study Perclose Device (N=53*)	Clinical Acceptance Criteria
Freedom from Major Access-site Related Complications	99.2% (515/519)	96.2% (51/53)	95%
Hematoma	99.8% (518/519)	96.2% (51/53)	-
Major Bleeding	100.0% (519/519)	96.2% (51/53)	-
Pseudoaneurysm	99.8% (518/519)	Not reported	-
Vascular Surgery	99.6% (517/519)	Not reported	-

Note: N is the total number of subjects.
* Two subjects were randomized without procedure. They are included in the baseline tables but not others.

Table 0-5 Safety Endpoints (In-hospital) - VACCAR Study

	Perclose Device (N=75)	Manual Compression (N=156)	Figure of 8 Stitch (N=203)
Major Complications	0.0% (0/75)	0.6% (1/156)	0.0% (0/203)
Hematoma	0.0% (0/75)	0.6% (1/156)	0.0% (0/203)
Minor Complications	4.0% (3/75)	2.6% (4/156)	1.5% (3/203)
Hematoma	1.3% (1/75)	2.6% (4/156)	1.5% (3/203)
Pseudoaneurysm	1.3% (1/75)	0.0% (0/156)	0.0% (0/203)
Other Complications	1.3% (1/75)	0.0% (0/156)	0.0% (0/203)
Additional Manual Compression	13.5% (10/74)	4.5% (7/156)	4.9% (10/203)

Note: N is the total number of subjects.

10.4.2.5 Effectiveness Endpoints and Other Key Measures

The acceptance criterion for freedom from femoral vein access-related major vascular complications at 30-days post procedure was ≥95%. The 95% clinical acceptance criterion was applied to ESM Study but not to the VACCAR Registry results as it does not have 30-day results. A brief summary of the procedural variables for the 3 studies is summarized in **Table 0-6** Procedural Information
. Hospitalization information for the 3 studies is summarized in **Table 0-7**.

Time to Hemostasis, Time to Ambulation, Total Index Hospitalization Duration

In the SBCH study. time to hemostasis and time to ambulation were not collected. All 519 subjects were discharged at the same day, so the total hospitalization duration is 0 day for all subjects. Protamine heparin reverse was administered in 90.1% of all subjects.

In the ESM study, the mean times to hemostasis were 7.46 minutes for Perclose SMC vs. 11.66 minutes for MC. The mean times to ambulation were 167.9 minutes for Perclose SMC vs. 280.1 minutes for MC. The mean total index hospitalization duration days was the same for both groups (0.3 days for both Perclose SMC and MC). Protamine heparin reverse was administered in 66.0% of subjects in the Perclose SMC arm, whereas 70.4% in the MC arm were administered protamine.

In the VACCAR study, the mean times to hemostasis were 8.63 minutes for Perclose SMC vs. 165.83 minutes for MC vs. 10.19 minutes for Figure of 8 Stitch. The mean times to ambulation were 157.29 minutes for Perclose SMC vs. 390.20 minutes for MC vs. 157.42 minutes for Figure of 8 Stitch. The total index hospitalization duration days was not collected. Only 2.7% of subjects in the Perclose SMC arm were administered Protamine heparin reverse, whereas 11.8% in the MC arm and 90.1% in the Fo8 arm were administered protamine.

It is important to note that no analysis was done by Abbott specifically to assess safety in the population that did not use Protamine heparin reverse.

Table 0-6 Procedural Information

SBCH Study (n=519)	ESM Study (n=53)	VACCAR Study (n=75)
Type of Ablation Procedure		
Not Available (NA)*	Cryoablation: 66% Radiofrequency: 34%	Cryoablation: 64% Radiofrequency: 36%
# of Access Sites Per Subject		
Mean: 3.6 Range: 2-5	Mean: 3.0 Range: 2-4	Mean: 3.4 Range: 2-6
# of Access Sites Per Single Vein		
Mean: 3.6 Range: 2-5	Mean: 2.3 Range: 1-3	Mean: not available Range: 1-3
# of Perclose SMCs Used Per Vein and Per Access Site and Per Closure Procedure		
Per Vein Mean: 3.5 Range: 1-6 Per Access Site Mean: NA Range: NA Per Closure Procedure Mean:3.5 Range: 1-6	Per Vein Mean: 2.3 Range: 1-4 Per Access Site Mean: NA Range: 1-2 Per Closure Procedure Mean: 3.0 Range: 2-5	Per Vein Mean: NA Range: NA Per Access Site Mean: NA Range: 1-2 Per Closure Procedure Mean: 4.0 Range: 2-7
% of access site > 8F		
30%	68.2%	NA
# of Perclose SMCs Used Access Site for subjects with > 8F Access Sites		
NA	>8F: 1 Perclose SMC: 96.2%	>8F: NA

SBCH Study (n=519)	ESM Study (n=53)	VACCAR Study (n=75)
	2 Perclose SMC: 3.8%	
Distribution of Sheath Size		
Mean: 8.8F Range: 4F-12F	Mean: 10.24F Range: 7F-16F	Mean: NA Range: NA
Procedure Duration		
Mean: 181.8 minutes	Mean: 158.1 minutes	NA
Success Rate – Per Access Site**		
NA	98.7%	NA
Anticoagulant and Antiplatelet Medications		
Anticoagulant Pre Procedure: 29.2% 30 Days Post: 30.8% Antiplatelet Medications Pre Procedure: 22.4% 30 Days Post: 19.5%	Anticoagulant Pre Procedure: 89.1% 30 Days Post: 100% Antiplatelet Medications Pre Procedure: 20% 30 Days Post: 79.2%	Anticoagulant Pre Procedure: 100% 30 Days Post: NA Antiplatelet Medications Pre Procedure: NA 30 Days Post: NA

* Not available (NA) means data were not available.
** Success rate is defined as either complete success (immediate complete hemostasis) or partial success (more hemostatic than without any intervention but some manual pressure required) achieved. Failure is defined as no effect by Perclose SMC System for access site closure as if the Perclose SMC weren't there.

Table 0-7 Hospitalization Information

	SBCH Study Perclose Device (N=519)	ESM Study Perclose Device (N=55)	VACCAR Study Perclose Device (N=75)
Total Index Hospitalization Duration (day) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	0.0 ± 0.0 (519) 0.0 (0.0, 0.0) (0, 0)	0.3 ± 0.5 (53) 0.0 (0.0, 1.0) (0, 1)	Not reported
Time to Hemostasis (min) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	Not reported	7.46 ± 7.53 (53) 4.45 (1.05, 11.30) (0.07, 26.98)	8.63 ± 9.32 (75) 7.00 (4.00, 10.25) (0.10, 71.13)
Time to Ambulation (min) # Mean ± SD (n) Median (Q1, Q3) Range (min, max)	Not reported	167.9 ± 136.4 (49) 135.0 (87.0, 201.0) (60, 944)	157.29 ± 94.41 (75) 135.00 (84.90, 207.00) (28.95, 509.00)

#Time to ambulation is time to move outside the bed.
Note: N is the total number of subjects.

To summarize, all subjects of the 3 ISSs had at least 2 access sites. Except for the VACCAR study that did not collect access site level information, majority of the SBCH and the ESM studies had at least one access site that was > 8F (517/519 for SBCH and 52/53 for ESM). For the access sites > 8F, most of them used one Perclose SMC only (site operation rule for SBCH, 149/154 access sites for ESM).

Both the SBCH and the ESM studies met the 95% clinical acceptance criterion as the primary safety endpoint (99.2% for SBCH and 96.2% for ESM). The VACCAR also demonstrated a complete freedom of access site related major complications (0.0%, 0/75) in the Perclose SMC arm at discharge.

10.4.3 Subgroup Analyses

As pre-specified in the Perclose Multi-Access Project Plan, subgroup analyses for procedural details and safety evaluation were performed for procedures using sheath size ≤8F (at least one access site using sheath >8F vs. ≤8F), number of access sites (2 or 3 vs. ≥4), access sites per vein (at least 1 vein with 3 access sites vs. all veins with 1 or 2 access sites), gender (male vs. female), age (age ≥65 vs. <65 years), race (white vs. non-white), and diabetes (diabetes vs. non-diabetes). All subgroup analyses were descriptive without pre-specified power hypothesis.

10.4.3.1 Sheath Size > 8F vs ≤ 8F

Safety: Almost all subjects (517/519) in the SBCH study and 52/53 in the ESM study received at least one sheath with size >8F. A per subject analysis at 30-days showed low major access-site related complication of 0.8% (4/517) in the SBCH study and 3.8% (2/52) in the ESM study. Major complications for subjects with sheath size >8F in the SBCH study included hematoma (0.2%), pseudoaneurysm (0.2%) and vascular surgery (0.4%) and in the ESM study included hematoma (3.8%) and major bleeding (3.8%) (**Table 0-8**). ESM study mostly used only one Perclose SMC for closure of access sites > 8F (96.2%). Standard practice of the SBCH study was to use only one Perclose for access sites > 8F. Largest sheath size used of these studies was 12F in the SBCH study and 16F in the ESM study. The results confirmed safety of single Perclose for closure of access sites > 8F.

Table 0-8 Major Access-site Related Complications in Subjects with > 8F Sheaths

	SBCH Study Perclose Device (N=517)	ESM Study Perclose Device (N=52*)
Major Access-site Related Complications	0.8% (4/517)	3.8% (2/52)
Hematoma	0.2% (1/517)	3.8% (2/52)
Major Bleeding	0.0% (0/517)	3.8% (2/52)
Pseudoaneurysm	0.2% (1/517)	Not reported
Vascular Surgery	0.4% (2/517)	Not reported

Note: N is the total number of subjects.
* Two subjects were randomized without procedure. They are included into the baseline tables but not others.

Effectiveness: In the SBCH study, subjects receiving at least one sheath size > 8F had numerically shorter procedure time (181.8 mins) compared to subjects with all sheaths ≤ 8F (200 mins).

In the ESM study, subjects receiving at least one sheath size > 8F had numerically longer procedure time (158.4 mins) compared to subjects with all sheaths ≤ 8F (142 mins).

10.4.3.2 2 or 3 Access Sites versus ≥ 4 Access Sites

Safety: In the SBCH study, only right femoral veins were used for the access sites. Subjects that used 2 or 3 access sites per right femoral vein were 212, compared to procedures with ≥4 access sites were 307. Major complication rates were 0.5% (1/212) and 1.0% (3/307) respectively (**Table 0-9**).

The ESM study used both right and left femoral arteries for the ablation procedures. Thirty-nine (39) subjects had 2 or 3 access sites and 14 had ≥4 access sites. The subgroups used a mean of 2.5 and 2 access sites per vein respectively. Major complication rates were 5.1% and 0% respectively (**Table 0-10**).
Major complication rates in subjects with ≥4 access sites were low and below the pre-specified acceptance criteria of 5%.

The VACCAR study did not report any major in-hospital complications (**Table 0-11**).

Table 0-9 Major Access-site Related Complications, 2 or 3 Access Sites vs ≥ 4 Access Sites, SBCH Study

	2 or 3 Access Sites (N=212)	≥ 4 Access Sites (N=307)
Major Access-site Related Complications	0.5% (1/212)	1.0% (3/307)
Hematoma	0.0% (0/212)	0.3% (1/307)
Major Bleeding	0.0% (0/212)	0.0% (0/307)
Pseudoaneurysm	0.0% (0/212)	0.3% (1/307)
Vascular Surgery	0.5% (1/212)	0.3% (1/307)

Note: N is the total number of subjects.

Table 0-10 Major Access-site Related Complications, 2 or 3 Access Sites vs ≥ 4 Access Sites, ESM Study

	2 or 3 Access Sites (N=39)	≥ 4 Access Sites (N=14)
Major Access-site Related Complications	5.1% (2/39)	0.0% (0/14)
Hematoma	5.1% (2/39)	0.0% (0/14)
Major Bleeding	5.1% (2/39)	0.0% (0/14)

Note: N is the total number of subjects.

Table 0-11 Safety Endpoints (In-Hospital), 2 or 3 Access Sites vs ≥ 4 Access Sites, VACCAR Study

	2 or 3 Access Sites (N=48)	≥ 4 Access Sites (N=27)
Major Complications	0.0% (0/48)	0.0% (0/27)
Hematoma	0.0% (0/48)	0.0% (0/27)

Note: N is the total number of subjects.

Access Sites Per Vein

Safety: In the ESM study, procedures that used at least 1 vein with 3 access sites had a success rate of 100% and those in which all veins had 1 or 2 access sites had a success rate of 97.1%, similar major complications (3.7%, 1/27 vs. 3.8%, 1/26) with no other complications (0%) to 30 days but higher rates of minor complications (11.1%, 3/27 vs. 3.8%, 1/26). Data were not reported for the SBCH and VACCAR study for this subgroup.

Effectiveness: In the ESM study, procedures that used at least 1 vein with 3 access sites compared to those in which all veins had 1 or 2 access sites had longer procedure times (170.7 vs. 144.9 min), needed more time to ambulation (177.3 vs. 156.3 min) but required lesser time to achieve hemostasis (6.96 vs. 7.98 min).

Study Limitations: THE STUDIES HAD LIMITATIONS SINCE TWO OF THE STUDIES (SBCH STUDY AND VACCAR STUDY) WERE RETROSPECTIVE AND HAD ONLY SUBJECT LEVEL DATA. Further, all subgroup analyses were descriptive without pre-specified power hypothesis.

10.5 The Perclose Multi-Access DUS IDE Trial

The objective of the trial was to evaluate the safety of multiple access site closure in a single vein with the Perclose SMC by scheduled duplex ultrasound (DUS) at discharge and at 30 days (if vascular complications observed at discharge) in subjects with asymptomatic or non-visible complications, with focus on use of Perclose SMC for more than one access site per femoral vein; and use of 2 or more Perclose SMCs for a femoral vein access site that is >8F.

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 some hematomas) and/or symptomatic. Therefore, a scheduled femoral DUS was performed in subjects with asymptomatic or non-visible complications to evaluate the overall safety of Perclose SMC in multiple access site closures in a single vein.

10.5.1 Methods

The trial was a prospective, single arm, multicenter, descriptive study and enrolled 36 subjects to evaluate the safety of multiple access site closure in a single vein with the Perclose SMC.The first subject was enrolled on September 1, 2021, and the last subject was enrolled on May 4, 2022. The last subject's 30-day follow-up occurred on May 27, 2022. All subjects were required

to have femoral DUS at discharge and at a 30-day follow-up visit (in case of any access site-related vascular complications {either symptomatic/visible or asymptomatic/non-visible}, nerve injury, or infection at discharge, as assessed by either the investigator or the core laboratory). All subjects underwent routine ablation for cardiac arrythmias as standard of care and similar information was captured including device usage and adverse events (AEs).

Clinical Study Endpoints

The primary endpoint of this study was vascular complications detected by scheduled DUS at discharge or 30 days in subjects with asymptomatic/non-visible complications. The primary endpoint was further categorized as major or minor. Major complications were defined as those which required surgical, interventional, or pre-specified repair and/or hospitalization. All other complications were considered to be minor complications.

Vascular access-site related complications included but were 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
- Non-flow limiting suture material
- Access site-related nerve injury
- Pulmonary embolism
- Other (specify)

Any vascular complications and access site complications were also analyzed as the descriptive endpoints.

Procedural information analyzed included the following:

- Procedure duration
- Type of Procedure (Cryoablation, 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 MC 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

10.5.2 Results

10.5.2.1 Subject Selection

A total of 36 subjects were enrolled in the study and all subjects completed their 30-day follow-ups without any major complications. Thirty-four (34) subjects had DUS assessments at discharge**.**

10.5.2.2 Subject Demographics

The mean age of the study population was 62.9 years, and most subjects were male (66.7%), had a mean body mass index (BMI) of 31.25 kg/mm^2, range of 17.9 kg/mm^2 to 43.4 kg/mm^2, and were diagnosed with either Paroxysmal AF (47.2%), Persistent AF (30.6%) or Atrial Flutter (16.7%). Major co-morbidities included hypertension (61.1%), dyslipidemia (52.8%), diabetes (33.3%), and coronary artery disease (30.6%). A majority of the subjects (91.7%) were on anticoagulants, primarily Apixaban (86.1%). Medication status at discharge and 30-day follow-up is given in **Table 10.5.2-1**.

Table 0-1 Medication Status at Discharge and at 30-day Follow-up

	Perclose SMC (N=36)
At Discharge	
Any Oral Anticoagulant	91.7% (33/36)
Apixaban	86.1% (31/36)
Rivaroxaban	5.6% (2/36)
Any Oral Antiplatelet	25.0% (9/36)
Aspirin	22.2% (8/36)
Clopidogrel	2.8% (1/36)
Ticagrelor	2.8% (1/36)
At 30-Day Visit	
Any Oral Anticoagulant	91.7% (33/36)
Apixaban	86.1% (31/36)
Rivaroxaban	5.6% (2/36)
Any Oral Antiplatelet	19.4% (7/36)
Aspirin	13.9% (5/36)
Clopidogrel	2.8% (1/36)

Ticagrelor	2.8% (1/36)

Note: Medication taken at the time of discharge or at the 30-day follow-up visit is included.
Note: N is the total number of subjects

10.5.2.3 Key Results

10.5.2.3.1 Primary Endpoint

Starting with an intent-to-treat population of 36 subjects (N=36; ITT), there were no major complications detected symptomatically or by DUS for all 36 subjects. However, there were 2 subjects who had minor symptomatic/visible complications and were excluded from the primary endpoint analysis. Of the remaining 34 subjects with no symptomatic/visible complications, 2 subjects did not have DUS at discharge and were excluded from the primary endpoint analysis as well. **The remaining 32 subjects constituted the primary endpoint analysis population (N=32; primary endpoint population).** These 32 subjects in the primary endpoint analysis group were asymptomatic at discharge. Further, DUS at discharge detected no major vascular complications. The overall rate of minor complications in these 32 subjects at discharge was low, as assessed by DUS, with only 4 of 32 (12.5%) having minor complications. The minor complications in the 4 subjects included deep vein thrombosis in the target limb (3 subjects; 1 out of the 3 subjects also had mobile Perclose common femoral vein (CFV) as a complication), and hematoma (1 subject).

As required by the protocol, the 4 subjects in the primary endpoint analysis group who had minor complications at discharge had a scheduled DUS at 30 days and had no additional complications (major or minor). All minor complications were resolved at 30 days. Similarly, at 30 days, there were no additional symptomatic major or minor complications for any of the other subjects in the primary endpoint analysis population.

Table 0-22-2 presents the vascular complications detected by scheduled DUS at discharge in both the intent-to-treat and primary endpoint populations. As detailed above, at discharge, there were no major complications (100% major complication-free) detected symptomatically or by DUS for all 36 subjects.

Table 0-2 Vascular Complications at Discharge

	Intent-to-Treat Population (N=36)	Primary Endpoint Population (N=32)
Major Complications by DUS Detection or CEC Adjudication	**0.0% (0/34)**	**0.0% (0/32)**
Minor Complications by DUS Detection or CEC Adjudication	**17.6% (6/34)**	**12.5% (4/32)**
Deep Vein Thrombosis in the Target Limb	11.8% (4/34)	9.4% (3/32)
Venous Bleeding, Retroperitoneal Bleeding	5.6% (2/36)	N/A
Venous Access Site Injury Including Vessel Laceration	5.6% (2/36)	N/A

	Intent-to-Treat Population (N=36)	Primary Endpoint Population (N=32)
Hematoma	5.9% (2/34)	3.1% (1/32)
Other Vascular Complication	2.9% (1/34)	3.1% (1/32)
Arterial Stenosis	0.0% (0/34)	0.0% (0/32)
Mobile Perclose Common Femoral Vein*	2.9% (1/34)	3.1% (1/32)

* Linear echodensity or filamentous structure visible in two different planes on DUS was the linear thrombus labeled by the core lab as “mobile Perclose CFV”.
Note: Major complications are defined as those which requiring surgical or percutaneous repair if not specified. All other complications are considered to be minor complications.
Note: N is the total number of subjects.

10.5.2.3.2 Summary of Safety

Adverse Event Reporting

A total of 5 adverse events in 3 subjects were reported for the duration of the study. Of those 5, 4 non-serious events - one venous bleeding, one thrombus, one re-bleeding at the access site, and one deep vein thrombosis in the target limb were adjudicated by CEC as device and procedure related event. No device/procedure related serious adverse events were reported and no serious adverse events qualified for the CEC adjudication during the study.

10.5.2.3.3 Summary of Effectiveness

Table 0-3 displays a summary of the procedure and post procedure information
Per subject, the study used a mean of 3.5 (median 4.0) access sites (sheaths) and a mean of 3.8 (median 4.0) Perclose devices in 36 subjects. A majority of subjects received Heparin Reversal (Protamine) after the procedure, as the site standard of care. Mean procedure duration was 138.6 minutes and TTH was 3.1 minutes per access site and 9.5 minutes per subject. Mean time to ambulation[4] was 233.7 minutes and mean time to discharge was 10.92 hours.

Success rate for Perclose SMC per access site was 99.2%.

A mean of 2.3 sheaths and 2.4 Perclose devices were used per vein (n=56).

The study used sheath sizes from ≤ 8F to ≥ 15F. The most commonly used sheath sizes per access site were ≤ 8F (62/126 access sites; 49.2%) and 8.5 – 14F (62/126 access sites; 49.2%). A majority of the access sites (84.9%) used 1 Perclose device to achieve vascular closure. Even in access sites using sheath size >8F also largely (47 of 64 access sites; 73.4%) used 1 Perclose device for vascular closure. Thus, irrespective of whether 1 or 2 Perclose devices were used in >8F access sites, with a majority of the cases using one device, with sheath sizes between 8F and 14F.

[4] Time to ambulation is time to move outside the bed.

Table 0-3 Procedural Results

	Perclose Device (N=36) (V=56) (AS=126)
PER SUBJECT ANALYSIS	
Type of Ablation Procedure	
Cryoablation only	38.9% (14/36)
Radiofrequency Ablation only	58.3% (21/36)
Both	2.8% (1/36)
Number of Access Site (Based on the number of sheath used)	
Mean ± SD (n)	3.5 ± 0.8 (36)
Median (Q1, Q3)	4.0 (3.0, 4.0)
Range (min, max)	(2, 5)
Number of Perclose Used	
Mean ± SD (n)	3.8 ± 1.3 (36)
Median (Q1, Q3)	4.0 (3.0, 5.0)
Range (min, max)	(0, 5)
Procedure Length (minute)	
Mean ± SD (n)	138.6 ± 47.4 (36)
Median (Q1, Q3)	140.0 (120.5, 159.0)
Range (min, max)	(42, 279)
Time to Hemostasis (minute)	
Mean ± SD (n)	9.5 ± 12.4 (36)
Median (Q1, Q3)	6.5 (4.0, 9.5)
Range (min, max)	(1, 74)
Heparin Reverse (Protamine)	79.4% (27/34)
PER VEIN ANALYSIS	
Number of Access Site (Based on the number of sheath used)	
Mean ± SD (n)	2.3 ± 0.8 (56)
Median (Q1, Q3)	2.0 (2.0, 3.0)
Range (min, max)	(1, 3)
1	23.2% (13/56)
2	28.6% (16/56)
3	48.2% (27/56)
Number of Perclose Used	
Mean ± SD (n)	2.4 ± 0.7 (56)
Median (Q1, Q3)	2.0 (2.0, 3.0)
Range (min, max)	(0, 4)
1 unit	1.8% (1/56)
2 units	46.4% (26/56)
3 units	46.4% (26/56)
4 units	1.8% (1/56)

	Perclose Device (N=36) (V=56) (AS=126)
PER ACCESS SITE ANALYSIS	
Sheath Size Used	
≥ 15F	1.6% (2/126)
12 - 14F	11.9% (15/126)
8.5 - 11F	37.3% (47/126)
≤ 8F	49.2% (62/126)
Number of Perclose Used*	
1 unit	84.9% (107/126)
2 units	11.1% (14/126)
Number of Perclose Used* per Access Site > 8F	
1 unit	73.4% (47/64)
2 units	21.9% (14/64)
Time to Hemostasis (minute) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	 3.1 ± 7.3 (126) 1.0 (1.0, 3.0) (0, 74)
Success Rate	99.2% (120/121)
POST PROCEDURE INFORMATION	
Time to Ambulation (minute) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	 233.7 ± 188.7 (36) 193.5 (129.5, 275.5) (58, 1199)
Delay >30 minutes	100.0% (36/36)
Time to Discharge (hour) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	 10.92 ± 9.69 (36) 5.95 (4.00, 19.35) (2.4, 43.8)

Note: N is the total number of subjects, V is the total number of Veins, and AS is total numbers of Access Site.
* Subject US0047-45 had two femoral veins, 5 access sites (3 were >8F). None of the 5 access sites was treated by Perclose SMC due to device deficiencies.

10.5.3 Subgroup Analysis

A summary of post procedure information and mean time to hemostasis per subject for the 4 main subgroups below is given in Error! Reference source not found..

Table 10.5.3-1 Summary of Time to Hemostasis and Post-Procedure Information for 4 Main Subgroups

	Subgroup 1	Subgroup 2	Subgroup 3		Subgroup 4	
	Subjects Treated with 2 Perclose SMC for Access Sites > 8F Perclose SMC (N=14)	Subjects having 3 or 4 Access Sites per Vein Perclose SMC (N=27)	At least One Sheath > 8F (N=32)	All ≤ 8F (N=4)	2 or 3 Access Sites (N=16)	≥ 4 Access Sites (N=20)
Time to Hemostasis (minute) – Per Subject Mean ± SD (n) Median (Q1, Q3) Range (min, max)	9.2 ± 6.6 (14) 7.5 (3.0, 16.0) (2, 21)	8.0 ± 6.3 (27) 7.0 (3.0, 10.0) (1, 24)	10.2 ± 13.0 (32) 7.0 (4.0, 10.0) (1, 74)	3.8 ± 3.6 (4) 2.5 (1.5, 6.0) (1, 9)	11.2 ± 17.6 (16) 6.0 (4.0, 9.5) (1, 74)	8.1 ± 6.0 (20) 7.5 (3.5, 12.0) (1, 21)
Time to Ambulation (minute) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	203.7 ± 106.5 (14) 185.5 (127.0, 266.0) (58, 464)	213.0 ± 91.6 (27) 211.0 (131.0, 266.0) (58, 464)	234.3 ± 198.3 (32) 193.5 (127.5, 258.0) (58, 1199)	228.8 ± 93.5 (4) 224.5 (150.0, 307.5) (136, 330)	246.1 ± 263.9 (16) 154.0 (129.5, 235.0) (106, 1199)	223.9 ± 101.8 (20) 210.5 (137.0, 312.5) (58, 464)
Delay >30 minutes	100.0% (14/14)	100.0% (27/27)	100.0% (32/32)	100.0% (4/4)	100.0% (16/16)	100.0% (20/20)
Time to Discharge (hour) Mean ± SD (n) Median (Q1, Q3) Range (min, max)	13.28 ± 11.41 (14) 7.45 (4.80, 20.10) (2.7, 43.8)	11.00 ± 9.99 (27) 6.10 (4.10, 19.60) (2.4, 43.8)	11.74 ± 9.98 (32) 6.20 (4.20, 19.85) (2.4, 43.8)	4.33 ± 1.46 (4) 4.25 (3.20, 5.45) (2.7, 6.1)	6.39 ± 6.88 (16) 3.80 (3.10, 5.25) (2.4, 23.9)	14.54 ± 10.22 (20) 13.05 (5.95, 20.15) (4.1, 43.8)

10.5.3.1 2 Perclose SMC for Access Sites > 8F

Safety: No major complications (0%) were detected by DUS in the 14 asymptomatic subjects treated with 2 Perclose SMC for access sites using >8F sheaths. The overall minor complication rate (7.1%) was low based on DUS examination with 1 (7.1%, n=1/14) subject experiencing a minor hematoma.

Effectiveness: Mean time to hemostasis was 9.2 mins and time to ambulation was 203.7 mins. Per subject, a mean of 4.8 Perclose SMC (range 3-5 units) were used with 85.7% using 5 Perclose SMC. Heparin (92.9%) and Heparin Reversal (92.3%) were administered to the majority of subjects.

Per vein, a mean of 2.0 sheaths and 2.6 Perclose SMC units were used.

The overall success rate per access site was 100%. Per access site, a sheath size ≤8F (49.1%) was most commonly used followed by 8.5-11F (28.3%) and 12-14F (22.6%). Overall, most procedures used 1 Perclose SMC (73.6%) per access site.

Of the 53 access sites, 27 access sites used a sheath size >8F (27/53; 50.9%) among 14 subjects (from 36 ITT subjects) treated with 2 Perclose SMC for at least one access site >8F. Of these 27 access sites, a little more than half (14/27; 51.9%) of the access sites required 2 Perclose SMC devices, and less than half (13/27; 48.1%) of the access sites required 1 Perclose SMC device to achieve vascular closure. Of these 14, 12 had 4 access sites (3 in one leg and 1 in another leg), 1 had 3 access sites (all in one leg) and 1 had 2 access sites (all in one leg).

10.5.3.2 3 or 4 Access Sites Per Vein

Safety: No major complications (0%) were detected in the 25 asymptomatic subjects having 3 or 4 access sites per vein. The overall minor complication rate (12.0%) was low when analyzed by DUS and included deep vein thrombosis in the target limb (8.0%) and hematoma (4.0%).

Effectiveness: The mean TTH overall was 8.0 min, with 4 access sites (9.2 min) requiring the most TTH; subjects with 5 access sites tended to have the lowest TTH (5.7 min), but the sample size is too small to make meaningful comparisons. Mean time to ambulation was 213 mins. Per subject, a mean of 3.7 (range 3-5 units) sheaths and a mean of 4.0 Perclose SMC were used. Heparin (92.6%) and Heparin Reversal (88.0%) were administered to the majority of subjects.

Per vein, a mean of 2.3 sheaths and a mean of 2.5 Perclose SMC.

Per access site, the overall success rate was 100%. Approximately half the subjects used at least 1 sheath >8F (≤8F, 49.0%; 8.5-11F, 36.0%) with 15% using sheaths larger than 12F (12-14F and ≥15F). While the majority used 1 Perclose SMC (82.0%) per access site, 13.0% used 2 Perclose SMC.

10.5.3.3 Sheath Size > 8F versus ≤ 8F

The majority of subjects in subgroup used at least one >8F (n=32/36) compared to ≤8F only (n=4/36). Due to small number of subjects treated with ≤8F only, comparing of these subgroups was not meaningful.

Safety: No major complications (0%) were detected by DUS in this subgroup. Minor complication rates by DUS at discharge in subjects with at least 1 access site using sheaths >8F compared with all ≤8F were 14.3% (4/28) and 0% (0/4) respectively.

Effectiveness: Time to ambulation for subjects that used at least 1 access site >8F compared to procedures with all ≤8F was 234.3 mins and 228.8 min and time to discharge was 11.74 hours and 4.33 hours respectively. TTH was 10.2 min and 3.8 min respectively.

Per subject, procedure time for subjects that used at least 1 access site >8F compared to procedures with all ≤8F was 139.8 min and. 128.8 min respectively. Mean sheath number used were 3.6 and 3.0 respectively and mean Perclose used were 3.8 and 3.0 units respectively.
Per vein, subjects with 1 access site using >8F compared with all ≤8F used a similar number of sheaths (2.2 vs. 2.4 units) and Perclose SMC (2.4 vs. 2.4 units).
The overall success rate per access site was 99.1% for 1 access site using sheaths >8F and 100% for all ≤8F. TTH per access site, was 3.2 min and 2.3 min respectively.

10.5.3.4 2 or 3 Access Sites versus ≥ 4 Access Sites

Safety No major complications (0%) at discharge were detected by DUS in this subgroup. Minor complication rates at discharge detected by DUS were numerically lower with 2 or 3 access sites versus ≥4 access sites (7.1%, 1/14 vs. 16.7%, 3/18); minor complications in the group using 2 or 3 access sites included deep vein thrombosis in the target limb (7.1%), and in the group using ≥4 access sites included deep vein thrombosis in the target limb (11.1%) and hematoma (5.6%).

Effectiveness: Procedures that used 2 or 3 access sites compared to procedures requiring ≥4 access sites required less time to discharge (6.39 vs. 14.54 hours) but more time to ambulation (246.1 vs. 223.9 min). Subjects with 2 or 3 access sites compared with ≥4 access sites required more overall TTH (11.2 vs 8.1 min). The difference in TTH can be attributed to the high range of TTH (1-74 minutes) in the 2 or 3 access sites subgroup.

Per subject, subjects with 2 or 3 access sites compared with ≥4 access sites used fewer sheaths (mean 2.7 vs. 4.2) and Perclose SMC (2.8 vs. 4.5 units) and had shorter procedure time (128.3 vs. 146.8 min).

Per vein, subjects with 2 or 3 access sites compared with all ≥ 4 access sites used a more sheaths (2.7 vs. 2.1 units) and Perclose SMC (2.8 vs. 2.3 units).

The overall success rate per access site was 97.7% for 2 or 3 access sites and 100% for ≥4 access. Per access site, sheath sizes used were similar across both groups. More 1 Perclose SMC (95.3% vs. 79.5%) were used per access site >8F. Subjects with 2 or 3 access sites compared with ≥4 access sites required more overall TTH (6.9 vs. 1.1 min) and TTH per access site >8F (9.3 vs 1.3 min) which is counterintuitive and could be interpreted as a coincidental study finding due to the high range of TTH in the 2 or 3 access site group.

Conclusion:

All subjects had at least 2 access sites for vessel closure, majority of them had 3 or 4 access sites (28/36) and at least one >8F (n=32/36) sheath used for an access site. In addition, 13/36 subjects used two Perclose SMC units in one access site.

No major complications were found symptomatically or detected by DUS at discharge, or at 30 days for all 36 subjects. Only minor vascular complications were detected at discharge either symptomatically or by DUS in subjects with asymptomatic/non-visible complications. Importantly, all these complications resolved, and no minor complications were found at 30 days for all 36 subjects. None of the asymptomatic or non-visible complications detected by DUS were index-procedure or Perclose SMC related.

Further, subgroup analyses detected no major complications, irrespective of whether 1 or 2 Perclose devices were used in >8F access sites, with a majority of the cases using one device, with sheath sizes between 8F and 14F. However, since there were no major complications detected in the asymptomatic subjects in any of the subgroups, this precluded any meaningful analyses of major complications in different subgroup populations. Additionally, the numbers of subjects in different subgroups were low and this study was not designed and powered to evaluate the differences between various subgroups.

The use of a scheduled DUS at discharge and at 30 days has successfully demonstrated the overall safety of using Perclose SMC in achieving vascular closure for multiple venous access sites in a single vein. Additionally, Perclose SMC was found safe for vascular closure of access sites that use sheath sizes ranging from ≤8F to ≥15F, and also for those that use 2 or more Perclose SMCs per femoral vein access site.

In conclusion, the results of the Perclose Multi-Access DUS trial demonstrate that Perclose SMC is safe to use for multiple access site closure in a single vein and when 2 or more Perclose SMC units are used per femoral vein access site.

11.0 THE PERCLOSE™ PROSTYLE™ SMCR SYSTEM CLINICAL PROCEDURE

The following instructions provide technical direction but do not obviate the necessity of formal training in the use of the Perclose ProStyle SMCR System. The techniques and procedures described below are not intended as a substitute for the operator's experience and judgment in treating any specific patients.

11.1 Examination and Selection of Products

1. Select the Perclose ProStyle SMCR Systems(s) for closure and repair of 5F to 21F sheath access sites in the common femoral artery and 5F to 24F sheath access sites in the common femoral vein.
2. After carefully inspecting the packaging of the Perclose ProStyle SMCR System for damage to the sterile barrier, remove the device from the package.
3. Exercise care when using additional instruments, such as clamps, forceps or needle holders during device handling, to reduce the possibility of accidental device breakage or damage to the suture.

11.2 Access Site and Puncture Considerations

1. An extremely deep tissue tract can prevent the Perclose ProStyle needles from engaging the cuffs. In extremely deep tissue tracts, the Perclose™ ProStyle™ Suture Trimmer and / or the Perclose™ Snared Knot Pusher may not be able to advance the knot completely to the external vessel wall before locking the knot. In extremely deep tissue tracts, inserting the Perclose™ ProStyle™ Device can require lifting of the panniculus and / or compression of the subcutaneous tissue (with the body of the device) to be able to obtain flow of blood ("mark") through the marker lumen.

2. Before inserting the access needle, use of ultrasound guidance to visualize the access site or fluoroscopy to visualize the femoral head is recommended. When using the femoral head as a reference point, target the medial third of the femoral head as the puncture site. Performing a femoral angiogram through the introducer sheath (or procedural sheath) to verify that the access site is in the common femoral artery or vein is recommended before anticoagulants are given.
3. If the Perclose ProStyle Device is used to close and repair multiple access sites in the same vessel, space the access sites apart adequately to minimize sheath-device interference. Use of ultrasound guidance to visualize the spacing between each needle entry point in the vessel while maintaining approximately the same angle of entry for all punctures is recommended. Consider puncturing the access sites from the most caudal to the most cranial location.
4. Puncture the anterior wall of the common femoral artery or vein at an angle of approximately 45 degrees. Avoid side wall or posterior wall punctures.
5. Prior to deployment of the Perclose ProStyle Device, perform a femoral angiogram to evaluate the access site for vessel size, calcium deposits, tortuosity, and for disease or dissections of the wall to avoid device cuff misses (device needles not engaging with the cuffs), posterior wall suture placement, and / or possible ligation of the anterior and posterior walls of the vessel. Angiographically verify that the puncture is on the anterior wall of the common femoral artery or vein. In arteries the puncture should be proximal to the bifurcation of the superficial femoral artery and the profunda femoris branch and distal to the inferior margin of the inferior epigastric artery.
6. There are **no** re-access restrictions after using Abbott Medical vessel closure devices.

   Note: For arterial sheath sizes less than or equal to 8F, one device may be used. For arterial sheath sizes greater than 8F, at least two devices and the pre-close technique are required. For venous sheath sizes less than or equal to 14F, one device may be used. For venous sheath sizes greater than 14F, at least two devices and the pre-close technique are required.

11.3 Device Preparation

1. Verify marker lumen patency by flushing the marker lumen with saline until saline exits the marker port. **Do not use the device if the marker lumen is not patent.**
2. Place a 0.038” (0.97 mm) (or smaller) hydrophilic or general purpose guide wire (minimum 50 cm in length) through the procedural (or introducer) sheath. Remove the procedural sheath while applying pressure on the groin to maintain hemostasis.
3. Advance the device over the guide wire until the guide wire exit port is just above the skin line.
4. Remove the guide wire before the guide wire exit port crosses the skin line.

11.4 Suture Deployment

1. STEP 1: Advance Device and Lift Lever to Open Foot

a. Position and maintain the device at approximately a 45-degree angle, continue gently to advance the device in the vessel until flow of blood (“mark”) is observed from the marker lumen. Anticipate tactile sensation when distal guide enters the vessel. **In the**

artery, brisk pulsatile flow of blood can be expected. In the vein, the flow of blood may not be pulsatile or blood may only fill the marker lumen.

Note: Stop device advancement once “mark” is observed from the marker lumen to ensure the foot is open near or at the access site to minimize intraluminal travel during pull back. To confirm foot location, retract device until “mark” ceases and re-advance, stop device advancement once “mark” is observed again. **Do not open the foot if “mark” is not observed from the marker lumen**.

b. Using the left hand, maintain the device at approximately a 45-degree angle with the device logo facing the ceiling (approximately 12 o'clock). Lift the lever (**marked 1**) with the right thumb pad or forefinger to open the foot. **Do not lift the lever against resistance.**

Note: To deploy multiple sutures (**Section 11.4.2**), position the device at approximately a 45-degree angle and rotate the device logo approximately 30 degrees towards the patient’s medial or lateral side before lifting the lever to open the foot.

c. Maintain the device logo position while keeping the device at approximately a 45-degree angle, gently retract the device to ensure that the foot is apposed to the vessel wall. It is recommended to place the right forefinger and middle finger on the device handles in an open palm position while pulling back the device. If proper position of the foot has been achieved against the vessel wall, slight tactile sensation will be felt to confirm foot location**. Do not raise the device angle against resistance. In the artery, blood marking will cease or be significantly reduced to a slight drip. In the vein, there may be no change in blood marking.**

Note: If blood marking does not stop or significantly change, evaluate the angiogram for device position in the vessel, vessel size, calcium deposits, tortuosity, disease and for location of the puncture (ensure the footplate is not in bifurcation or side branch). Reposition the device to stop blood marking. Alternatively, reinsert a guide wire, remove the device to hold manual compression, insert a new device or insert a new sheath.

2. **STEP 2: Depress Plunger to Deploy Needles**

a. While maintaining device logo position and keeping the device at approximately a 45-degree angle with gentle retraction against the vessel wall, stabilize the device to ensure the foot is apposed to the vessel wall and depress the plunger with the right thumb (**in the arrow direction marked 2**) until the black collar on the plunger meets the blue body to deploy the needles. In addition to the visual confirmation, an audible “click” should be heard to confirm needle and cuff engagement.

Note: Do not use excessive force or repeatedly push the plunger or depress the plunger repeatedly as this may prevent the needles from engaging the cuffs. After the visual and audible confirmation, **STEP 2** is complete.

3. **Use of Depth Reference Markers (Optional)**

a. After completing **STEP 1** and before performing **STEP 3**, maintain device at approximately a 45-degree angle with the foot apposed to the vessel wall, and observe the depth reference mark closest to the skin line.

Note: The depth reference marks on the device provide depth estimation of the tissue tract and may be used in combination with the corresponding depth reference mark on the Perclose ProStyle Suture Trimmer as a visual reference for approximating the

advancement of the Perclose ProStyle Suture Trimmer into the tissue tract during suture management (**Section 11.5.1**).

4. **STEP 3: Pull Back Plunger to Deploy Suture**
   a. Using the right thumb or forefinger as a fulcrum on the handle, pull out the plunger assembly from the body (**in the arrow direction marked 3**) and completely remove the plunger and needles from the body. Continue to pull back on the plunger until the suture is taut, which confirms that the suture has been fully retracted from the body of the device. The anterior needle will be attached to the link with the suture limb. The posterior needle will be free of suture.

      Note: Do not attempt to reinsert the needles if the suture limb is not attached to the anterior needle. Reinsert a guide wire through the guide wire exit port and remove the device with the detached suture over the wire while maintaining guide wire access. Insert a new Perclose ProStyle Device over the guide wire to complete the procedure.

   b. While holding the plunger, place the needles under the QuickCut™ Mechanism. Use the needles as the guide, slide the suture against the QuickCut Mechanism to trim the suture from the anterior needle distal of the link. Alternately, use a sterile scalpel or scissors to cut the suture.

5. **STEP 4: Lower Lever to Close Foot**
   a. Release the gentle retraction against the vessel wall. Advance device slightly to restore marker flow, if necessary. Push the lever (**marked 4**) down to the body of the device to return the foot to its original closed position.

      Note: Do not attempt to remove the device without closing the lever fully to its original closed position, “1” is visible on top of the lever.

   b. Retract the device out of the tissue tract deliberately. Slight resistance should be felt when the suture exits the suture bearing on the distal guide. Continue to gently withdraw the device until the guide wire exit port is visible above the skin line.

   c. Rotate the body of the device slightly, if needed, to locate the two suture limbs in the bend of the distal guide. Grasp both suture limbs together and gently pull the suture end through the distal end of the proximal guide.

   d. Reinsert a guide wire through the guide wire exit port to maintain guide wire access. There should be adequate length of guide wire inside of the vessel and outside the guide wire exit port for device or sheath exchange.

      Note: Care should be taken to avoid suture limbs and guide wire entanglement. If preferred to secure and maintain guide wire access first, perform **Step 5b** before **Step 5c** above.

   e. Identify the rail and non-rail suture limbs. The longer, rail suture limb is blue and is used to advance the pre-tied suture knot. The distal end of the shorter, non-rail suture limb is white and is used to lock the pre-tied suture knot.

      Note: Do not pull on the individual suture limbs to prevent knot advancement or locking of the knot.

6. Do not remove the device. Continue with suture management steps in **Section 11.5** for single suture using the pre-close technique, by following the steps in **Section 11.4.1**. For multiple sutures using the pre-close technique, follow the steps in **Section 11.4.2**.

11.4.1 Single Suture using Pre-Close Technique

When using the pre-close technique, the suture can be placed around the access site at the beginning of the procedure and suture management can be placed on hold until the procedure is complete.

1. After completing suture deployment steps in **Section 11.4,** immediately secure the two suture limbs together with a shodded hemostat or clamp at the distal end of the non-rail suture limb.

   Note: Do not pull on the individual suture limbs to prevent knot advancement or locking of the knot.
2. Gently pull on the clamp until the suture is taut to **remove any suture slack from the tissue tract**. Place the clamped suture under a sterile towel during the procedure.

   Note: The monofilament suture can be damaged by opening and closing the clamp. In order to attach the suture to the drape, it is recommended to use a second clamp with the tip placed through the handle of the first clamp and attach the second clamp to the drape.
3. Exchange the Perclose ProStyle Device for an appropriately sized procedural sheath over the guide wire and proceed with the catheterization procedure.
4. At the end of the catheterization procedure, reinsert the guide wire into the procedural sheath. It is recommended to reinsert the dilator into the sheath for a smooth transition of suture at the end of the sheath. Maintain adequate length of guide wire in the vessel and outside the sheath to maintain guide access.
5. Heavily irrigate the secured suture with heparinized saline to remove any dry blood. Remove the clamp from the suture limbs. Continue with the suture management steps in **Section 11.5**.

11.4.2 Multiple Sutures using Pre-close Technique

1. To deploy the first suture, follow the suture deployment steps in **Section 11.4**. At **Step 1b**, rotate the device logo approximately 30 degrees towards the patient's **medial side**. Proceed to the pre-close technique in **Section 11.4.1** (up to **Step 2**). Place the clamped suture for the first device on the **medial side** of the patient under a sterile towel. It is important to identify which suture is deployed first, as this is the suture knot that needs to be advanced first at the end of the procedure.
2. Maintain adequate length of guide wire in the vessel and outside the guide wire exit port. Remove the first Perclose ProStyle Device while holding compression above the puncture site. Advance a second Perclose ProStyle Device over the guide wire.
3. To deploy the second suture, follow the suture deployment steps in **Section 11.4**. At **Step 1b**, rotate the device logo approximately 30 degrees towards the patient's **lateral side**. Proceed to pre-close technique in **Section 11.4.1** (up to **Step 2**). Place the clamped suture for the second device on the **lateral side** of the patient under a sterile towel.
   Note: It is important to identify which suture was deployed first and which suture was deployed second. At the completion of the procedure, the pre-tied suture knots will be advanced in the order they were placed. The pre-tied suture knot from the first device would be advanced first followed by the pre-tied suture knot from the second device.
4. Exchange the Perclose ProStyle Device for an appropriately sized procedural sheath over the guide wire and proceed with the catheterization procedure.
5. At the end of the catheterization procedure, reinsert a guide wire into the procedural sheath. It is recommended to reinsert the dilator into the sheath for a smooth transition of suture at

the end of the sheath. Maintain adequate length of guide wire in the vessel and outside the sheath to maintain guide wire access.

6. Heavily irrigate the secured sutures with heparinized saline to remove any dry blood. Remove the clamp from the first suture. Follow the suture management steps using the Perclose ProStyle Suture Trimmer (**Section 11.5.1, Steps 1-5**) or Perclose Snared Knot Pusher (**Section 11.5.2, Steps 1-4**). Place the suture limbs on the **medial side** of the patient for easy identification as the first suture deployed. **DO NOT lock or excessively tighten the suture knot while the guide wire is still in the vessel.**
7. Remove the clamp from the second suture. Follow the same steps as the first suture. Place the suture limbs on the **lateral side** of the patient for easy identification as the second suture deployed. **Again, DO NOT lock or excessively tighten the suture knot while the guide wire is still in the vessel.**
8. Assess for hemostasis. If brisk bleeding is observed, advance the first (**patient's medial side**) suture knot again and then advance the second (**patient's lateral side**) suture knot again. Multiple knot advancements are common when closing larger sheath sizes. **Until the guide wire is removed, some bleeding will be visible, but it should not be pulsatile blood flow.**
9. If adequate hemostasis is not observed, additional Perclose ProStyle Devices may be deployed at this point. Repeat the above steps to deploy a third suture. The third device should not be rotated. The third device will be deployed with the device logo facing the ceiling (approximately 12 o'clock). **Again, DO NOT lock the knot or excessively tighten the suture knot while the guide wire remains in the vessel.**
10. Assess the access site for adequate hemostasis. **Remove the guide wire if bleeding is controlled.**
11. Complete advancing and locking the first suture knot using the Perclose ProStyle Suture Trimmer (**Section 11.5.1, Steps 6-9**) or Perclose Snared Knot Pusher (**Section 11.5.2, Steps 5-9**). Follow the same steps to advance and lock the second suture knot. If applicable, advance and lock any additional suture knots in the order that they were placed (first, second, third).
12. If hemostasis is deemed adequate, cut the suture limbs below the surface of the skin using the Perclose ProStyle Suture Trimmer (**Section 11.5.1, Step 10**).

11.5 Suture Management

1. Use the Perclose ProStyle Suture Trimmer (**Section 11.5.1**) or the Perclose Snared Knot Pusher (**Section 11.5.2**) to advance and tighten the pre-tied suture knot.
2. For 5F - 8F sheaths, confirm hemostasis and the security of the suture knot by having the patient cough and / or bend his / her leg. **Active testing for hemostasis is only for 5F – 8F sheaths. For sheath closures greater than 8F, active confirmation should not be performed; only visual confirmation of hemostasis should be employed**.

   Note: Patients may be able to move freely in bed without head of bed or leg restrictions if the close is successful.

11.5.1 Suture Management Using the Perclose ProStyle Suture Trimmer

1. Securely wrap the rail suture limb around the left forefinger close to the skin. While maintaining guide wire access, simultaneously pull the rail suture limb coaxial to the tissue tract with slow, consistent increasing tension to advance the pre-tied suture knot to the access site and remove the Perclose ProStyle Device (or the entire procedural sheath system if using pre-close technique) completely from the vessel with the right hand.

   Note: Do not tighten the suture around the device or the procedural sheath. Avoid quick or jerky type movements with the suture limbs. Manual pressure should be applied proximal to the puncture site for hemostasis, while the sheath is removed and during initial suture advancement.
2. While maintaining tension and keeping the rail suture limb securely wrapped around the left forefinger and coaxial to the tissue tract, place the rail suture limb into the suture gate following the steps below:
   a. Hold the Perclose ProStyle Suture Trimmer with the right hand. Retract the thumb knob on the Perclose ProStyle Suture Trimmer with the right thumb to open the suture gate.
   b. Place the Perclose ProStyle Suture Trimmer shaft **under** the rail suture limb making an “x” or a “cross”. Slide the shaft back to load the rail suture limb into the suture gate.
   c. Keeping the thumb knob retracted, turn the shaft coaxial to the rail suture limb and then release the thumb knob to capture the suture in the suture gate. Once the rail suture limb is loaded in the suture gate correctly, the Perclose ProStyle Suture Trimmer should slide easily coaxial on the rail suture limb.

      Note: Releasing the thumb knob before the rail suture limb is coaxial to the Perclose ProStyle Suture Trimmer can cause the suture to be caught within the sliding mechanism in the suture gate and damage the suture.
3. While maintaining tension on the rail suture limb, keeping the Perclose ProStyle Suture Trimmer and the rail suture limbs coaxial to the tissue tract and the thumb knob at approximately 12 o’clock (facing the ceiling), advance the Perclose ProStyle Suture Trimmer on the rail suture limb coaxial to the tissue tract until the pre-tied suture knot is at the vessel surface.

   Note: The Perclose ProStyle Suture Trimmer should not be rotated during advancement to avoid having the rail suture limb wrapped around the sheath.
4. While maintaining tension on the rail suture limb and keeping the rail suture limb securely wrapped around the left forefinger, place the left thumb on the top of the Perclose ProStyle Suture Trimmer to assume a single-handed position. Complete knot advancement by applying slow, consistent increasing tension using the left forefinger until the rail suture limb is taut (guitar string tightness in artery and gentle tension in vein).
5. **Use of Depth Reference Markers (Optional)**

   Note: If the depth reference mark on the device is used to provide an estimation of the tissue tract depth during suture deployment in **Section 11.4**, the corresponding depth reference mark on the Perclose ProStyle Suture Trimmer may be used as a visual reference to appropriate the depth for advancing the Perclose ProStyle Suture Trimmer.
   a. While maintaining the Perclose ProStyle Suture Trimmer at a 45-degree angle, observe the depth reference mark closest to the skin level.

   Note: The depth reference markers are only to be used as a reference tool and are not intended to replace tactile feel during the advancement of the Perclose ProStyle Suture

Trimmer into the tissue tract. Do not solely depend on these depth reference markers for approximating the tissue tract depth when advancing the Perclose ProStyle Suture Trimmer.

6. Assess the access site for adequate hemostasis. If bleeding is controlled, the guide wire can be removed. Resume the single-handed position to advance the pre-tied suture knot after guide wire removal.

   Note: DO NOT lock or excessively tighten the suture knot while the guide wire is still in the vessel.

7. While maintaining the single-handed position with the Perclose ProStyle Suture Trimmer, keeping the rail suture limb taught and the tip of the Perclose ProStyle Suture Trimmer on top of the knot, pull gently on the non-rail suture limb coaxial to the tissue tract with the right hand to remove suture slack, tighten and lock the suture knot at the vessel surface.
8. Hemostasis of the access site is achieved when the suture knot is fully advanced to the vessel surface, and the tissue is in complete apposition. Remove the Perclose ProStyle Suture Trimmer from the tissue tract, relax tension on the suture limbs.
9. For 5F–8F sheaths, confirm hemostasis and the security of the suture knot by having the patient cough or bend his/her leg. **Active testing for hemostasis is only for 5F–8F sheaths. For sheath closures greater than 8F, active confirmation should not be performed; only visual confirmation of hemostasis should be employed.** If hemostasis has not been achieved, resume the single-handed position for 20 seconds or until hemostasis is achieved. Secure the knot again by gently pulling coaxial on the non-rail suture limb. **DO NOT** apply excessive pressure to the suture.
10. After confirming hemostasis, use the Perclose ProStyle Suture Trimmer to trim the suture limbs below the skin. While holding both suture limbs together and pulling them taut, load both suture limbs into the suture gate and advance the Perclose ProStyle Suture Trimmer to the vessel surface. Trim the suture limbs by pulling back on the red trimming lever. If only one suture limb has been loaded and trimmed, repeat the same steps to trim the other suture limb. Alternatively, use a sterile scalpel or scissor.

    Note: Patients may be able to move freely in bed without head of bed or leg restrictions if the close is successful.

11.5.2 Suture Management Using the Perclose Snared Knot Pusher

1. Place approximately 2 cm of the rail suture limb into the snare at the distal end of the Perclose Snared Knot Pusher. Detach the snare tab completely from the shaft and pull the tab coaxial to the shaft to load the rail suture limb through the Perclose Snared Knot Pusher. Keep snare tab for re-snaring the rail suture limb as needed.
2. Grab the distal end of the rail suture limb with the left hand and advance the Perclose Snared Knot Pusher coaxial over the rail suture limb to skin level. If the rail suture limb is loaded on the Perclose Snared Knot Pusher correctly, the Perclose Snared Knot Pusher should slide easily coaxially on the rail suture limb.
3. Securely wrap the rail suture limb around the left forefinger close to skin level. While maintaining guide wire access, simultaneously pull the rail suture limb coaxial to the tissue tract with slow, consistent increasing tension to advance the pre-tied suture knot to the access site and remove the Perclose ProStyle Device (or the entire procedural sheath system if using the pre-close technique) completely from the vessel with the right hand.

   Note: Do not tighten the suture around the device or procedural sheath. Avoid quick or jerky type movements with the suture limbs. Manual pressure should be applied proximal to the

puncture site for hemostasis, while the sheath is removed and during initial suture advancement.

4. While maintaining tension on the rail suture limb and keeping the Perclose Snared Knot Pusher and the rail suture limbs coaxial to the tissue tract, advance the Perclose Snared Knot Pusher on the rail suture limb coaxial into the tissue tract with the right hand until the pre-tied suture knot is at the vessel surface.

   Note: The Perclose Snared Knot Pusher should not be rotated during advancement to avoid having the rail suture limb wrapped around the shaft.

5. While maintaining tension on the rail suture limb, keeping the rail suture limb securely wrapped around the left forefinger, place the left thumb on the top of the Perclose Snared Knot Pusher to assume a single-handed position. Complete knot advancement by applying slow, consistent increasing tension on the left forefinger until the rail suture limb is taut (guitar string tightness in artery and gentle tension in vein).
6. Assess the access site for adequate hemostasis. If bleeding is controlled, the guide wire can be removed. Resume the single-handed position to advance the suture knot after guide wire removal.

   Note: DO NOT lock or excessively tighten the suture knot while the guide wire is still in the vessel.

7. While maintaining the single-handed position with the Perclose Snared Knot Pusher and keeping the rail suture limb taut and the tip of the Perclose Snared Knot Pusher on top of the suture knot, pull gently on the non-rail suture limb coaxial to the tissue tract with the right hand to remove suture slack, tighten and lock the suture knot at the vessel surface.
8. Hemostasis of the access site is achieved when the suture knot is fully advanced to the vessel surface, and the tissue is in complete apposition. Remove the Perclose Snared Knot Pusher from the tissue tract, relax tension on the suture limbs.
9. For 5F–8F sheaths, confirm hemostasis and security of the suture knot by having the patient cough or bend his / her leg. **Active testing for hemostasis is only for 5F–8F sheaths. For sheath closures greater than 8F, active confirmation should not be performed; only visual confirmation of hemostasis should be employed**. If hemostasis has not been achieved, assume the single-handed position for 20 seconds or until hemostasis is achieved. Secure the suture knot again by gently pulling coaxial on the non-rail suture limb. **DO NOT** apply excessive pressure to the suture.
10. After confirming hemostasis, use the Perclose ProStyle Suture Trimmer (**Section 11.5.1, Step 10**) to trim the suture limbs below the skin.

    Note: Patients may be able to move freely in bed without head of bed or leg restrictions if the close is successful.

11.6 Suture Breakage

1. To prevent suture breakage, always pull on the suture limbs with slow, consistent increasing tension. Avoid quick or jerky type movements with the suture limbs.
2. To prevent damage to the suture and subsequent suture breakage, the Perclose ProStyle Suture Trimmer, the Perclose Snared Knot Pusher and suture limbs should always remain coaxial to the tissue tract.

3. The Perclose ProStyle Suture Trimmer should not be rotated and the thumb knob should be maintained at approximately 12 o'clock (facing the ceiling). When loading suture into the Perclose ProStyle Suture Trimmer, keep the thumb knob retracted until the suture and Perclose ProStyle Suture Trimmer are coaxial, then release the thumb knob to capture the suture in the suture gate.
4. If suture breakage occurs during knot advancement **before the knot** is tightened, and a guide wire is still in place, use another Perclose ProStyle SMCR Device to complete the procedure.
5. If suture breakage occurs **after a knot** has been advanced and / or tightened, and a wire is still in place, use an introducer sheath to open the knot before inserting another Perclose ProStyle Device can be used to complete the procedure.

   Note: Care should be taken to avoid excessive force if another Perclose ProStyle Device or an introducer sheath is required. Use an introducer sheath small enough to avoid undue force.
6. To remove the broken suture limbs, cut the suture limbs close to the suture knot using the Perclose ProStyle Suture Trimmer or a sterile scalpel or scissor.

11.7 Post Procedure Patient Management

1. Apply an appropriate dressing to the access site.
2. Assess the access site as per hospital standard of care.

11.8 Recommendation for Patient Ambulation and Discharge

Patients may be able to move freely in bed without head of bed or leg restrictions if the close is successful.

Patients who have undergone a diagnostic or interventional procedure using 5–8F sheaths may be ambulated two hours after the Perclose ProStyle SMCR procedures.

Patients who have undergone an interventional catheterization procedure using sheaths greater than 8F, may be ambulated at a time-point 2 hours or more after the Perclose ProStyle SMCR procedure, with the time-point based on the judgement of the physician.

Patients who have undergone cardiac arrhythmia treatments with multiple access sites in a single femoral vein of one or both limbs may be ambulated one hour or more and may be eligible for same-day discharge two hours or more after the Perclose ProStyle SMCR procedures based on the judgement of the physician.

In determining whether to ambulate or discharge an individual patient, it is important to consider all clinical factors including, but not limited to, anticoagulation regimen, antiplatelet and thrombolytic agents administered, oozing or bleeding from the arterial or venous access site, the general cardiovascular condition of the patient, anesthetic levels, and the overall clinical condition of the patient.

12.0 PRODUCT INFORMATION DISCLOSURE

Abbott has exercised reasonable care in the manufacture of this device. Abbott excludes all warranties, whether expressed or implied, by operation of law or otherwise, including but not limited to, any implied warranties of merchantability or fitness, since handling and storage of this device, as well as factors relating to the patient, diagnosis, treatment, surgical procedures, and other matters beyond the control of Abbott directly affect this device and the results obtained from its use. Abbott shall not be liable for any incidental or consequential loss, damage, or expense, directly or indirectly arising from the use of this device. Abbott neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this device.

Reference Abbott website for patent markings: www.abbott.com/patents

Abbott Medical
3200 Lakeside Drive
Santa Clara, CA 95054 USA

CUSTOMER SERVICE
TEL: (800) 227-9902
FAX: (800) 601-8874
Outside USA TEL: (951) 914-4669
Outside USA FAX: (951) 914-2531

Graphical Symbols for Medical Device Labeling

LOT	Batch code		Do not resterilize
	Date of manufacture		Do not re-use
	Use-by date		Non-pyrogenic
REF	Catalogue number	STERILE EO	Sterilized using ethylene oxide
CONTENTS	Contents (component included with device)		Do not use if package is damaged and consult instructions for use
	Packaging unit		Keep away from sunlight
Rx ONLY	CAUTION: Federal law restricts this device to sale by or on the order of a physician		Keep dry
	Consult instructions for use or consult electronic instructions for use		Manufacturer
		UDI	Unique device identifier