INSTRUCTIONS FOR USE FOR:

GORE

CARDIOFORM

SEPTAL
OCCLUDER

en
English

INSTRUCTIONS FOR USE FOR:
GORE® CARDIOFORM SEPTAL OCCLUDER

Carefully read all instructions prior to use. Observe all warnings and precautions noted throughout these instructions.
Failure to do so may result in complications.

DESCRIPTION
The GORE® CARDIOFORM Septal Occluder consists of an implantable Occluder and a Delivery System. The Occluder is comprised of a platinum-filled nickel-titanium (Nitinol) wire frame covered with expanded polytetrafluoroethylene (ePTFE). The ePTFE includes a hydrophilic surface treatment to facilitate echocardiographic imaging of the Occluder and surrounding tissue during implantation. When fully deployed, the Occluder assumes a double-disc configuration to prevent shunting of blood between the right and left atria. The Delivery System consists of a 75 cm working length 10 Fr outer diameter Delivery Catheter that is coupled to a Handle. The Handle facilitates loading, deployment, and locking of the Occluder. The Handle also allows repositioning and retrieval of the Occluder via the Retrieval Cord, if necessary.
The Occluder is available in diameters of 20, 25, and 30 mm. The Occluder is delivered using conventional catheter delivery techniques and may be delivered with the aid of a 0.035" guidewire (or smaller), if desired.

FIGURE 1: GORE® CARDIOFORM Septal Occluder

FIGURE 1a: Left Atrial View

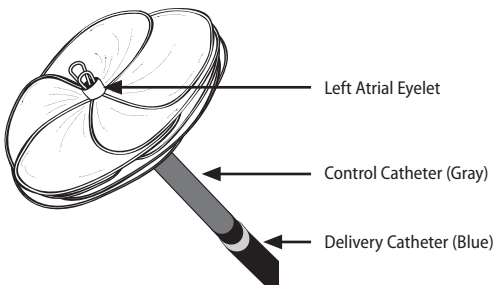


FIGURE 1b: Right Atrial View

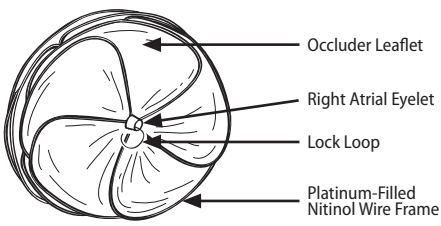
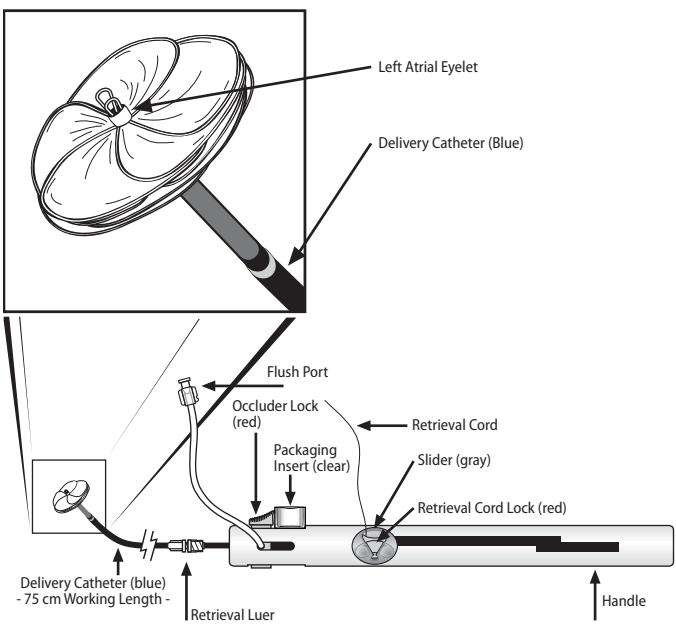


FIGURE 2: GORE® CARDIOFORM Septal Occluder Delivery System



INDICATIONS / INTENDED USE
The GORE® CARDIOFORM Septal Occluder is a permanently implanted device indicated for the percutaneous, transcatheter closure of the following defects of the atrial septum:

- ostium secundum atrial septal defects (ASDs).
- patent foramen ovale (PFO) to reduce the risk of recurrent ischemic stroke in patients, predominantly between the ages of 18 and 60 years, who have had a *cryptogenic* stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke.

CONTRAINDICATIONS

The GORE® CARDIOFORM Septal Occluder is contraindicated for use in patients:

- Unable to take antiplatelet or anticoagulant medications such as aspirin, heparin, or warfarin.
- With anatomy where the GORE® CARDIOFORM Septal Occluder size or position would interfere with other intracardiac or intravascular structures, such as cardiac valves or pulmonary veins.
- With active endocarditis, or other infections producing bacteremia, or patients with known sepsis within one month of planned implantation, or any other infection that cannot be treated successfully prior to device placement.
- With known intracardiac thrombi.

WARNINGS

- The GORE® CARDIOFORM Septal Occluder is not recommended for, and has not been studied in, patients with other anatomical types of ASDs that are eccentrically located on the septum (e.g., sinus venosus ASD and ostium primum ASD), or fenestrated Fontan.
- The GORE® CARDIOFORM Septal Occluder has not been studied in patients with multiple defects requiring placement of more than one device.
- The GORE® CARDIOFORM Septal Occluder is not recommended for defects larger than 17 mm.
- Regarding device sizing:
  - The defect and atrial chamber size should be evaluated by Transesophageal (TEE) or Intracardiac Echo (ICE) with color flow Doppler measurement to confirm that there is adequate space to accommodate the selected occluder size without impinging on adjacent cardiac structures (e.g., A-V valves, ostia of the pulmonary veins, coronary sinus, or other critical features).
  - There must be adequate room in the atrial chambers to allow the right and left atrial discs to lie flat against the septum with disc spacing equal to the septal thickness, and without interference with critical cardiac structures or the free wall of the atria.
  - An occluder that pulls through the defect after disc conformation may be too small and should be removed and replaced with a larger size.
- Embolized devices must be removed. An embolized device should not be withdrawn through intracardiac structures unless the occluder has been adequately collapsed within a sheath.
- The GORE® CARDIOFORM Septal Occluder should be used only by physicians trained in its use, and in transcatheter defect closure techniques.
- Patients allergic to nickel may suffer an allergic reaction to this device. Certain allergic reactions can be serious; patients should be instructed to notify their physicians immediately if they suspect they are experiencing an allergic reaction such as difficulty breathing or inflammation of the face or throat. Some patients may also develop an allergy to nickel if this device is implanted.

PRECAUTIONS

Handling

- The GORE® CARDIOFORM Septal Occluder is intended for single use only. An unlocked and removed occluder cannot be reused. Gore does not have data regarding reuse of this device. Reuse may cause device failure or procedural complications including device damage, compromised device biocompatibility, and device contamination. Reuse may result in infection, serious injury, or patient death.
- Inspect the package before opening. If seal is broken, contents may not be sterile.
- Inspect the product prior to use in the patient. Do not use if the product has been damaged.
- Do not use after the labeled "use by" (expiration) date.
- Do not resterilize.

Procedure

- The GORE® CARDIOFORM Septal Occluder should only be used in patients whose vasculature is adequate to accommodate a 10 Fr delivery sheath (or 12 Fr delivery sheath when a guidewire is used).
- Retrieval equipment such as large diameter sheaths, loop snares, and retrieval forceps should be available for emergency or elective removal of the occluder.
- An Activated Clotting Time (ACT) greater than 200 seconds should be maintained throughout the procedure.
- The GORE® CARDIOFORM Septal Occluder should be used only in conjunction with appropriate imaging techniques to assess the septal anatomy and to visualize the wire frame.
- If successful deployment cannot be achieved after three attempts, an alternative device or treatment for septal defect closure is recommended. Consideration should be given to the patient's total exposure to radiation and anesthesia if prolonged or multiple attempts are required for the placement of the GORE® CARDIOFORM Septal Occluder.
- Expansion of an occluder disc may occur in the periprocedural time period. If there is uncertainty that an expanded device remains locked, fluoroscopic examination is recommended in order to identify if the Lock Loop captures all three eyelets.
- Removal of the Occluder should be considered if:
  - The Lock Loop does not capture all three eyelets
  - The Occluder will not come to rest in a planar position apposing the septal tissue
  - The selected Occluder allows excessive shunting
  - There is impingement on adjacent cardiac structures

Post Procedure

- Patients should take appropriate prophylactic antibiotic therapy consistent with the physician's routine procedures following device implantation.
- Patients treated for ostium secundum atrial septal defect closure should be treated with antiplatelet therapy for six months post-implant. The decision to continue antiplatelet therapy beyond six months is at the discretion of the physician. Patients treated for patent foramen ovale septal defect closure should be treated with antiplatelet therapy post-implant indefinitely. In the pivotal REDUCE clinical trial, all patients implanted with the GORE® CARDIOFORM Septal Occluder were prescribed clopidogrel alone (75 mg) for three days and were required to continue taking anti-platelet medications for the remainder of the study follow-up (5 years). Most subjects implanted with the GORE® CARDIOFORM Septal Occluder in the REDUCE trial took aspirin alone (81-325 mg daily); alternatively, combination aspirin (50-100 mg daily) and dipyridamole (225-400 mg daily), or clopidogrel (75 mg daily) could be used. The decision to discontinue antiplatelet therapy is at the discretion of the physician.
- Patients should be advised to avoid strenuous physical activity for a period of at least two weeks after occluder placement.
- Patients should have Transthoracic Echocardiographic (TTE) exams prior to discharge, and at 1, 6, and 12 months after occluder placement to assess defect closure. Attention should be given to the stability of the device on the atrial septum during these assessments, as a lack of device stability may be indicative of wire frame fractures. In instances where device stability is questionable, fluoroscopic examination without contrast is recommended in order to identify and assess wire frame fractures.

PATIENT SELECTION FOR PFO CLOSURE

In considering the use of the GORE® CARDIOFORM Septal Occluder, the rationale for seeking PFO closure and the safety and effectiveness of the device compared to antithrombotic therapy alone should be taken into account. A shared decision-making process with the patient and their medical team is recommended when considering the use of the GORE® CARDIOFORM Septal Occluder. See "Patient Counseling Information" and "Summary of Clinical Studies" sections for additional information.

Ischemic Stroke. Most ischemic strokes are due to a known mechanism unrelated to a PFO including thromboembolism from an intracardiac source, large vessel atherosclerosis, artery-to-artery thromboembolism, or small vessel disease. The following are potential etiologies of ischemic stroke:

- Thromboembolic stroke in the setting of atrial fibrillation
- Thromboembolic stroke due to left ventricular mural thrombus
- Thromboembolic stroke due to infectious or non-infectious endocarditis
- Thromboembolic stroke associated with prosthetic heart valves
- Atheroembolic stroke due to thoracic aortic or carotid artery atherosclerotic disease
- Intracranial atherosclerotic disease
- Arterial dissection
- Vasculitis
- Migraine/vasospasm
- Hypercoagulable states
- Thromboembolic stroke via a right-to-left shunt

Ischemic strokes are considered to be *cryptogenic* when there is no identified cause following a comprehensive evaluation to exclude an underlying known stroke etiology.

PFO and Ischemic Stroke. A PFO persists into adulthood in 25-30% of individuals, and in the vast majority of cases, a PFO is an incidental finding that is not associated with any disease condition. Specifically, the presence of a PFO is not associated with an increased stroke risk among asymptomatic individuals. However, in some patients with cryptogenic ischemic stroke, the presence of a PFO raises the possibility that a thromboembolism from the venous circulation passed through the PFO into the arterial circulation (paradoxical thromboembolism) leading to an ischemic stroke.

In carefully selected cryptogenic stroke patients with a PFO and evidence of a right-to-left shunt, PFO closure with the GORE® CARDIOFORM Septal Occluder has demonstrated a reduction in the risk of recurrent stroke beyond what can be achieved with antiplatelet therapy alone, while taking into account the risks and benefits of the device. Although a paradoxical embolism through a PFO is one potential mechanism for causing an ischemic stroke, it is an uncommon cause. The GORE® CARDIOFORM Septal Occluder prevents a recurrent ischemic stroke due to a paradoxical embolism through the PFO, but it would not reduce the risk of a stroke from mechanisms or diseases that are unrelated to a paradoxical embolism through the PFO.

Before considering implantation of the GORE® CARDIOFORM Septal Occluder, other potential mechanisms for an ischemic stroke should be investigated including atrial fibrillation, left atrial appendage thrombus, left ventricular thrombus, significant cardiac valve pathology, aortic arch atheroma, intracranial and extra cranial cerebrovascular disease, small vessel disease, and a hypercoagulable state. Patients selected should undergo an evaluation by a neurologist to confirm the diagnosis of a cryptogenic ischemic stroke. This evaluation should exclude the presence of other known ischemic stroke mechanisms that are unrelated to a paradoxical embolism through the PFO. It is recommended that the evaluation follow the latest professional society guidelines for diagnosing a cryptogenic ischemic stroke, and should include at a minimum the following assessments:

- MRI or CT scanning of the head to rule out small vessel disease or lacunar infarct
- Echocardiography (e.g., transesophageal echocardiography with or without intra-cardiac echocardiography) to rule out non-PFO intra-cardioembolic sources or conditions or aortic arch atheroma
- ECG and prolonged cardiac rhythm monitoring (~30 days) to rule out atrial fibrillation and other heart rhythm disturbances that may be associated with stroke

- Intra and extracranial artery imaging: MRA, CT angiography, or contrast angiography to rule out an ischemic stroke associated with atherosclerotic plaque, arterial dissection, or other vascular diseases.
- Hematological evaluation to rule out an underlying hypercoagulable state

Patients with a PFO that are first deemed by a neurologist and a cardiologist to have had a cryptogenic stroke following an evaluation to exclude known causes of ischemic stroke should next be evaluated by a GORE® CARDIOFORM Septal Occluder implanting physician to ensure that the device can be implanted safely. Specific factors that need to be considered for the GORE® CARDIOFORM Septal Occluder and implantation procedure include the following:

- Overall medical status, including conditions which might preclude the safety of a percutaneous, transcatheter procedure.
- Suitability for percutaneous procedures, including considerations of:
  - Cardiac anatomy relating to the size of the PFO
  - Vascular access anatomy (e.g., femoral vein size, thrombus, or tortuosity)
  - Ability of the patient to tolerate general or local anesthesia
  - Ability of the patient to undergo required imaging (i.e., fluoroscopy, intra-cardiac echocardiography, and/or transesophageal echocardiography)
  - Ability to comply with the recommended post-implant antiplatelet pharmacologic regimen. In the pivotal REDUCE clinical trial, all patients implanted with the GORE® CARDIOFORM Septal Occluder were prescribed clopidogrel alone (75 mg) for three days and were required to continue taking anti-platelet medications for the remainder of the study follow-up (5 years). Most subjects implanted with the GORE® CARDIOFORM Septal Occluder the REDUCE trial took aspirin alone (81-325 mg daily); alternatively, combination aspirin (50-100 mg daily) and dipyridamole (225-400 mg daily), or clopidogrel (75 mg daily) could be used.

PATIENT COUNSELING INFORMATION FOR PFO TREATMENT

Physicians should review the following information when counseling patients about the GORE® CARDIOFORM Septal Occluder and the implant procedure:

- The safety and effectiveness of PFO closure with the GORE® CARDIOFORM Septal Occluder in combination with the required post-implant antiplatelet therapy.
- PFO closure with the GORE® CARDIOFORM Septal Occluder has demonstrated reduction in the risk of recurrent ischemic stroke.
  - However, PFO closure can only reduce the risk of those strokes due to a paradoxical embolism through a PFO.
  - With aging there is an increased likelihood that non-PFO related risks for stroke may develop and cause a recurrent ischemic stroke independent of PFO closure.
- The procedural risks associated with the GORE® CARDIOFORM Septal Occluder. **Table 11** and **Table 12** detail the major clinical events related to the device or procedure as observed in the REDUCE clinical study.
- The need for adherence to a defined adjunctive antiplatelet therapy following implantation of the GORE® CARDIOFORM Septal Occluder.

It is recommended that the medical team (neurologist and cardiologist) and the patient engage in a shared decision-making process where the risks and benefits of PFO closure in comparison to using antiplatelet therapy alone are discussed while taking into account the patient's values and preferences. Additional counseling information can be found in the Patient Information Brochure and in the Clinical Studies section of the Instructions for Use.

POTENTIAL DEVICE- OR PROCEDURE-RELATED ADVERSE EVENTS

Adverse Events associated with the use of the Occluder may include, but are not limited to:

- Access site pain or complications requiring surgery, interventional procedure, transfusion, or prescription medication
- Air embolism
- Anxiety
- Arrhythmia, such as atrial fibrillation or flutter, requiring treatment
- Bleeding requiring surgery, interventional procedure, transfusion, or prescription medication
- Cardiac arrest
- Chest pain or discomfort
- Death
- Device disc expansion resulting in clinical sequelae or intervention
- Device embolization
- Device failure or ineffectiveness requiring repeat atrial septal defect interventions or procedures
- Device fracture resulting in clinical sequelae or surgical intervention
- Device thrombosis or thromboembolic event resulting in clinical sequelae
- Endocarditis
- Fatigue
- Headache or migraine
- Hypotension
- Myocardial infarction
- Palpitations
- Perforation or damage of a cardiovascular structure by the device
- Pericardial tamponade
- Renal failure
- Respiratory arrest
- Sepsis
- Significant pleural or pericardial effusion requiring drainage
- Stroke or TIA
- Thrombosis or thromboembolic event resulting in clinical sequelae

SUMMARY OF CLINICAL STUDIES

Investigational Device Exemption (IDE) clinical studies were conducted to evaluate the safety and effectiveness of the GORE® CARDIOFORM Septal Occluder in the closure of ostium secundum septal defects (ASDs, the GORE® Septal Occluder Clinical Study) and patent foramen ovale (PFO, the Gore REDUCE Clinical Study). A summary of these studies is provided below that includes study information and clinical data, which supports the safety and effectiveness of the GORE® CARDIOFORM Septal Occluder and its approved indications for use.

GORE® Septal Occluder Clinical Study (Ostium Secundum ASD Closure)

Design

The GORE® CARDIOFORM Septal Occluder was evaluated in a multi-center, non-randomized, Pivotal Study that included 50 subjects enrolled for closure of ostium secundum ASDs. An Independent Data Reviewer provided external oversight and review of subject safety data, including evaluation of all reported adverse events for accuracy of event coding, seriousness, and relationship to the device. An event was considered a Serious Adverse Event if it led to death or serious deterioration in health that resulted in a life threatening illness or injury or in permanent impairment. Device Events, a type of Serious Adverse Event, were defined as any post-procedure embolization, post-procedural device removal, or any other reintervention to the septal defect.

The primary endpoint for the study was Composite Clinical Success, evaluated at 6 months post-procedure. Composite Clinical Success was defined as: 1) Successful deployment and retention of a GORE® CARDIOFORM Septal Occluder, 2) No Serious Adverse Events during 30-day follow-up, 3) No Device Events through 6-month follow-up, and 4) Clinical closure success, where the defect was classified as either completely occluded or having a clinically insignificant shunt at the 6-month follow-up as determined by echocardiography core lab evaluation.

Secondary endpoints evaluated specific safety and efficacy results. Safety endpoints were defined as the proportion of subjects who experienced a Serious Adverse Event in the first 30 days or a Device Event through the 6-month follow-up. Technical Success was defined as successful deployment and retention of a GORE® CARDIOFORM Septal Occluder. Closure success endpoints were evaluated for those subjects with Technical Success. Procedure Success was defined as a residual shunt of ≤ 2 mm at the end of the implant procedure as measured by the investigational site. Closure Success was defined as a residual shunt ≤ 2 mm at 6-month follow-up as measured by the echocardiography core lab.

Procedure and Follow-up

Dimensional verification and characterization of the ASD, interatrial septum, and surrounding cardiac structures were performed during the implant procedure. The measurement of ASD size was determined utilizing the stop-flow technique (a balloon was placed across the defect and slowly expanded until it filled the defect space and blood flow through the defect was prevented). The measurement of the balloon's waist (i.e., the narrowest portion) was recorded as the defect diameter and used to determine the appropriate size GORE® CARDIOFORM Septal Occluder. Fluoroscopic and echocardiographic guidance were used throughout the procedure for placement and assessment of the GORE® CARDIOFORM Septal Occluder. All subjects were placed on the investigator's choice of antiplatelet therapy for six months following device implantation, and on prophylactic, post-procedure antibiotic therapy consistent with the investigator's routine procedure.

Follow-up evaluations, which included a physical exam, ECG, and an assessment of residual shunt status by echocardiography, were performed at hospital discharge, and at 1 and 6 months post-procedure. At the 6-month follow-up visit, fluoroscopic examination was performed to assess device integrity.

Patients Studied

Inclusion Criteria

Subjects enrolled in the Pivotal Study were required to have an ostium secundum atrial septal defect with evidence of right heart volume overload. Subjects were eligible for enrollment if their defect measured ≤ 17 mm in diameter by stop-flow balloon sizing and had adequate septal rims to successfully retain the occluder.

Exclusion Criteria

- Significant known pre-existing electrophysiologic, structural cardiovascular defect, or other comorbidities that could elevate morbidity / mortality beyond what is common in ASD patients or would be expected to require surgical treatment within three years of device placement.
- Systemic or inherited conditions that would significantly increase subject risk of major morbidity and mortality during the term of the study.
- Anatomy where the size or position of the occluder would interfere with other intracardiac or intravascular structures, such as cardiac valves or pulmonary veins.
- Active endocarditis, other infections producing bacteremia, or known sepsis within one month of planned implantation, or any other infection that could not be treated successfully prior to device placement.
- One or more known intracardiac thrombi.
- Uncontrolled arrhythmia.
- History of stroke resulting in a significant morbidity or disability.
- Pregnant or lactating at time of enrollment.
- Contraindication to antiplatelet therapy.
- Pulmonary artery systolic pressure greater than half the systemic systolic arterial pressure unless the indexed pulmonary arteriolar resistance was <5 Woods units.
- Multiple defects based on screening imaging and stop-flow balloon sizing that would require placement of more than one device.

Subjects provided informed consent prior to enrollment. No training cases were required by study investigators prior to enrollment in the Pivotal Study.

Demographics and Defect Characteristics

Subject demographics at enrollment and defect characteristics assessed at the implant procedure by the investigational site are listed in **Table 1**. Subject medical history is shown in **Table 2**.

Table 1. Subject Demographics and Defect Characteristics – Pivotal Study

Number of Subjects (N=50)	n (%)
Patient Demographics	
Gender	
Male	23 (46.0%)
Female	27 (54.0%)
Race	
Black or African American	8 (16.0%)
White or Caucasian	39 (78.0%)
Other Race	4 (8.0%)
Age (years)	N = 50
Mean (Std Dev)	19.7 (21.0)
Median	7.4
(Min, Max)	(3.4, 68.3)
Height (cm)	N = 50
Mean (Std Dev)	133.0 (33.6)
Median	121.5
(Min, Max)	(40.5, 188.0)
Weight (kg)	N = 50
Mean (Std Dev)	45.1 (32.3)
Median	27.6
(Min, Max)	(11.9, 133.6)
Defect Characteristics	
Stop Flow Balloon Defect Size (mm)	N=49
Mean (Std Dev)	11.9 (3.4)
Median	12.0
(Min, Max)	(5.7, 17)
Atrial Septal Aneurysm[1]	14.0% (7/50)
Deficient Retroaortic Rim[2]	26.0% (13/50)
Multiple Fenestrations	20.0% (10/50)

[1] Protrusion of the septum ≥10 mm from baseline in either direction or ≥15 mm total septal excursion
[2] Measured as <5 mm

Table 2. Subject Medical History – Pivotal Study

Number of Subjects (N=50)	n (%)
Cardiac Arrhythmia	8 (16.0%)
Hypertension	5 (10.0%)
Migraines	8 (16.0%)
Diabetes Mellitus	4 (8.0%)
Previous Cardiac Surgeries	2 (4.0%)
Non-ASD Cardiac Disorders	27 (54.0%)
Vascular Disorders	3 (6.0%)
History of Stroke and/or TIA	4 (8.0%)
Birth/Genetic Defects	9 (18.0%)
Neurological Disorders	7 (14.0%)
Pulmonary/Respiratory Disorders	14 (28.0%)

Effectiveness and Safety Results

Primary safety, and efficacy endpoint results through 6 months are shown in **Table 3**. All subjects with an atrial septal aneurysm, multiple fenestrations or deficient retroaortic rim who received a GORE® CARDIOFORM Septal Occluder had complete clinical closure and no Serious Adverse Events at 6 months.

Table 3. Primary, Safety, and Efficacy Endpoints – Pivotal Study

Primary Endpoint	
Composite Clinical Success[1]	40/43 (93.0%)
Safety Endpoints	
30-Day Serious Adverse Events	0.0% (0/50)
6-Month Serious Adverse Events	0.0% (0/50)
6-Month Device Events[2]	0.0% (0/50)
Efficacy Endpoints	
Technical Success[3]	47/50 (94.0%)
Procedure Success[4]	46/47 (97.9%)
6-Month Closure Success[5]	43/45 (95.6%)
6-Month Clinical Closure Success[6]	40/40 (100%)

[1] Technical Success and 6-Month Clinical Closure Success without Serious Adverse Events through 30 days or Device Events through 6 months
[2] Post-procedural device embolization, post-procedural device removal, or any reintervention to the septal defect
[3] Successful delivery and retention of the device in subjects with a delivery attempted
[4] Technical Success with completely occluded defect or residual shunt ≤ 2 mm at the completion of the implant procedure
[5] Technical Success with completely occluded defect or residual shunt ≤ 2 mm at 6 months
[6] Technical Success with completely occluded defect or clinically insignificant residual shunt at 6 months

Deaths
No deaths have been reported in study subjects.
Serious Adverse Events
No Serious Adverse Events, including Device Events, were observed in any study subjects through the 6-month follow-up.
Non-Serious Adverse Events
Non-Serious Adverse Events reported through the 6-month follow-up for Pivotal Study subjects and determined to be potentially or definitely related to the implant procedure or the device are presented in **Table 4**.

Table 4. Subjects with Non-Serious Adverse Events Through 6 Months Related to the Device or Implant Procedure – Pivotal Study

Subjects Evaluable for Safety (N=50)	n (%)
Subjects With One or More Non-Serious Adverse Events	12 (24.0%)
Anesthesia or Procedural	8 (16.0%)
Incision site complication	4 (8.0%)
Anesthesia complication	3 (6.0%)
Procedural pain	2 (4.0%)
Nervous System	2 (4.0%)
Burning sensation	1 (2.0%)
Migraine	1 (2.0%)
Other	3 (6.0%)
Respiratory, thoracic and mediastinal	2 (4.0%)
Gastrointestinal	1 (2.0%)

A wire frame fracture was observed in 9.3% (4/43) of subjects with fluoroscopic evaluation completed at 6 months. No fractures were associated with device instability or clinical sequelae.

Gore REDUCE Clinical Study (PFO Closure)
Design
The GORE® CARDIOFORM Septal Occluder was evaluated in a prospective, randomized, multinational, multicenter evaluation (the Gore REDUCE Clinical Study). This study compared antiplatelet medical management (MM Group) to PFO closure with the GORE® CARDIOFORM Septal Occluder or GORE® HELEX® Septal Occluder (Device Group) plus antiplatelet medical management (Device Group) for the reduction of recurrent stroke in subjects with a PFO and history of cryptogenic stroke.
A total of 664 eligible subjects were randomized using a 2:1 randomization scheme to either the Device Group (n = 441) or the MM Group (n = 223). There were 63 study sites in the US, Canada, Denmark, Finland, Norway, Sweden, and the UK with 50% of subjects enrolled in the US.
The co-primary endpoints were:
- Co-Primary Endpoint 1: Freedom from recurrent ischemic stroke through at least 24 months post-randomization,
- Co-primary Endpoint 2: Proportion of subjects with new brain infarction defined as clinical ischemic stroke or at least one new T2 hyperintense MRI lesion with diameter ≥3 mm from screening through 24 months or last follow-up visit, whichever occurred first.

The secondary endpoints were:
- Adverse events (AEs) directly related to the device, procedure, and/or antiplatelet medical therapy
- PFO closure in Device Group subjects assessed by echocardiography
- Device Success – the proportion of Device Group subjects with successful implant and retention of the occluder after the procedure.
- Clinical Success
  - Device Group - defined as the composite of Device Success, effective PFO closure, and absence of a recurrent stroke at 24 months post-procedure
  - MM Group - defined as the freedom from a recurrent stroke at 24 months post-randomization
- Overall Survival – time from randomization to death from any cause or last known contact
- Freedom from any stroke/TIA

Procedure and Follow-up
Investigators prescribed antiplatelet medical therapy regimens for all device and medical management subjects, based on their best medical judgment for the duration of the study. Subjects at each site were to be treated with the same antiplatelet therapy regardless of study arm. Investigators chose one of the following options: aspirin alone (75-325 mg once daily), combination aspirin (50-100 mg) and dipyridamole (225-400 mg), or clopidogrel (75 mg once daily). Other combinations or the use of anticoagulants was not permitted.
Subjects randomized to the device arm had PFO closure attempted with a study device (the GORE® HELEX® Septal Occluder from 2008 through late 2012 or the GORE® CARDIOFORM Septal Occluder from late 2012 through 2015) in addition to continued antiplatelet therapy. Patients in the Device Group were treated with pre-procedural antiplatelet therapy per the institutional standard of care or physician discretion (usually 300 mg of clopidogrel), followed by 75 mg of clopidogrel daily for 3 days post-procedure, and then resumed the antiplatelet option chosen as above.
Dimensional verification and characterization of the PFO, interatrial septum, and surrounding cardiac structures were performed during the implant procedure. The measurement of PFO size was taken utilizing the stop-flow technique (a balloon was placed across the defect and slowly expanded until it filled the defect space, and blood flow through the defect was prevented). The measurement of the balloon's waist (i.e., the narrowest portion) was recorded as the defect diameter and used to determine the appropriate septal occluder

size. Fluoroscopic and echocardiographic (TEE or intra-cardiac echocardiography) guidance were used throughout the procedure for placement and assessment of the septal occluder.
All subjects were followed for a minimum of 2 years and a maximum of 5 years. All subjects received follow-up evaluations with neurology investigators at 1, 6, 12, 18, 24, 36, 48, and 60 months. Each neurology follow-up evaluation included a standardized and validated questionnaire to detect potential stroke or transient ischemic attack. Subjects in the Device Group also had follow-up echocardiography with agitated saline bubble study at 1, 12, and 24 months and underwent a fluoroscopic examination without contrast at 12 months. If a primary endpoint event was suspected, an evaluation was performed by a neurologist and brain imaging was required by protocol.
All subjects in both treatment groups were planned for follow-up MRI imaging at 24 months, if not already performed for a primary endpoint event.
The intention-to-treat (ITT) population was the pre-specified primary analysis population. Analyses were also performed on the Per Protocol population, which consisted of subjects who received their randomly assigned treatment and complied with protocol-mandated medical treatment and excluded subjects who did not receive their randomized therapy, did not comply with the protocol-mandated medical treatment, or had a major inclusion/exclusion criterion violation.

Patients Studied

Major Inclusion Criteria

- Patient with a cryptogenic, ischemic stroke of presumed embolic etiology, verified by a neurologist within 180 days prior to randomization with either:
  - Ischemic stroke clinical symptoms persisting ≥ 24 hours.
  - Clinical symptoms persisting < 24 hours and has MRI evidence of infarction.
- Presence of PFO, as determined by positive bubble study utilizing TEE, demonstrating spontaneous right-to-left shunting or right-to-left shunting during Valsalva maneuver.
- Absence of an identifiable source of thromboembolism in the systemic circulation.
- Patient has no evidence of hypercoagulable state, which requires anticoagulation therapy.
- Age range: 18 - 59 years

Major Exclusion Criteria

- Other co-morbidities including, but not limited to, intracardiac thrombus, dilated cardiomyopathy, atrial fibrillation/flutter, prosthetic heart valves, mitral valve stenosis, aortic dissection, significant atherosclerosis, vasculitis, pre-existing neurologic disorders, multiple sclerosis, arteriovenous malformations, prior intracranial hemorrhage, severe CNS disease, severe disability related to prior stroke, and autoimmune disorders that would increase the risk of mortality or morbidity above what is typical for the treatment
- Previous myocardial infarction
- Uncontrolled diabetes mellitus at the time of randomization, in the opinion of the investigator
- Pulmonary hypertension (mean pulmonary artery pressure >25 mm Hg)
- Uncontrolled systemic hypertension at the time of screening, in the opinion of the investigator
- Presentation with a lacunar stroke syndrome
- Neurological deficits not due to stroke that may affect neurologic assessments
- Intracranial pathology that made the patient inappropriate for study participation based on discretion of the Investigator (e.g., brain tumor other than meningioma, AVM, cerebral hemorrhage, cerebral venous sinus thrombosis on CT or MRI, or cerebral aneurysm >7 mm)
- Active infection that cannot be treated successfully prior to randomization
- Sensitivity or contraindication to all proposed medical treatments, including antiplatelet therapy
- Requirement for chronic anticoagulation therapy that cannot be discontinued prior to randomization
- Patient is pregnant, lactating, or intent on becoming pregnant through 24-months after randomization
- In the opinion of the Investigator, anatomic criteria identified during the screening evaluation and/or the screening TEE that are unfavorable for successful placement of the GORE® HELEX® Septal Occluder/GORE® CARDIOFORM Septal Occluder or the patient has contraindications for device placement, which may include:
  - Inability to accommodate a 10 Fr delivery catheter
  - The need for trans-septal puncture
  - Requires placement of more than one device
  - PFO estimated to be too large for successful device placement
  - Device would impinge on cardiac structure(s)
  - Anatomy would likely prevent discs from apposing the septal tissue

Screening to establish the diagnosis of cryptogenic stroke

- Work-up of qualifying stroke evaluated by a neurologist
- Brain MRI (CT acceptable for MRI-incompatible patients)
- TEE to exclude left atrial appendage thrombus or other mural thrombus
- ECG
- MRA, CTA, duplex color Doppler carotid ultrasound, or conventional angiography of the head, neck, and aortic arch to rule out arterial atherosclerotic sources of embolism (aortic arch may also be evaluated by TEE)
- Evaluation to exclude a hypercoagulable state

Demographics and Defect Characteristics

The REDUCE trial subject demographics and baseline characteristics and baseline stroke risk factors for the intention-to-treat (ITT) population are shown in **Table 5** and **Table 6**. There were no significant differences between the groups in any of the characteristics listed.

Table 5. Subject Demographics and Baseline Characteristics – ITT Population

Variable	Device Group (N=441)	MM Group (N=223)	p-value[1]
Age-yr	45.4 ± 9.3	44.8 ± 9.6	0.410
Days from qualifying event to randomization	100 ± 52	101 ± 53	0.901
Male sex	261 (59.2%)	138 (61.9%)	0.557
Medical history			0.218
Stroke or TIA prior to qualifying event	62 (14.1%)	23 (10.3%)	
Previous stroke	42 (9.5%)	13 (5.8%)	
Previous TIA	26 (5.9%)	11 (4.9%)	
Qualifying event			0.483
Stroke with symptoms ≥ 24 hrs	402 (91.2%)	199 (89.2%)	
Stroke with symptoms < 24 hrs but with imaging confirmation of infarct	39 (8.8%)	24 (10.8%)	
Patent foramen ovale shunt grade[2]	(n=425)	(n=216)	0.317
Grade I Trivial/Small (1-5 bubbles)	77 (18.1%)	43 (19.9%)	
Grade II Moderate (6-25 bubbles)	166 (39.1%)	94 (43.5%)	
Grade III Large (>25 bubbles)	182 (42.8%)	79 (36.6%)	
Atrial septal aneurysm	86/422 (20.4%)	n/a	

Continuous variables reported as means ± SD and categorical variables as n (%).
MM = Medical Management
[1]p-value based upon Fisher's Exact Test for categorical variables and Wilcoxon Test for continuous variables
[2]Shunt size was graded based on the estimated number of microbubbles detected in the left atrium within 3 cardiac cycles after appearance in the right atrium, as observed on transesophageal echocardiography, either at rest or with Valsalva maneuver.

Table 6. Baseline Stroke Risk Factors – ITT Population

Variable	Device Group (N = 441)	MM Group (N=223)	p-value[1]
Diabetes	18 (4.1%)	10 (4.5%)	0.839
Hypertension	112 (25.4%)	58 (26.0%)	0.925
Hyperlipidemia	213 (48.3%)	103 (46.2%)	0.622
Tobacco Use:			0.299
Current	63 (14.3%)	25 (11.2%)	
Previous: stopped > 12 months ago	87 (19.7%)	45 (20.2%)	
Previous: stopped < 12 months ago	42 (9.5%)	31 (13.9%)	
Never used	249 (56.5%)	122 (54.7%)	

MM = Medical Management
[1]p-value based upon Fisher's Exact Test

Effectiveness and Safety Results

Subject Follow-up

There were 1529 patient-years of follow-up (mean 3.5 years) in the Device Group and 703 patient-years of follow-up (mean 3.2 years) in the MM Group. Discontinuation rates were higher in the MM Group (14.8% in the MM Group vs. 8.8% in the Device Group). The ITT Device Group included 250 subjects implanted with the GORE® CARDIOFORM Septal Occluder and 158 subjects implanted with the GORE® HELEX® Septal Occluder.

Medical Therapy Use

Patients were required to take antiplatelet therapy for the duration of the clinical study. Single antiplatelet therapy was used in approximately 85% of patients in both the Device Group and MM Group. Aspirin alone was the most commonly prescribed medication and used by 61.2% of patients in the Device Group and 54.7% of patients the MM Group.

Primary Endpoint Analysis Results – ITT Population

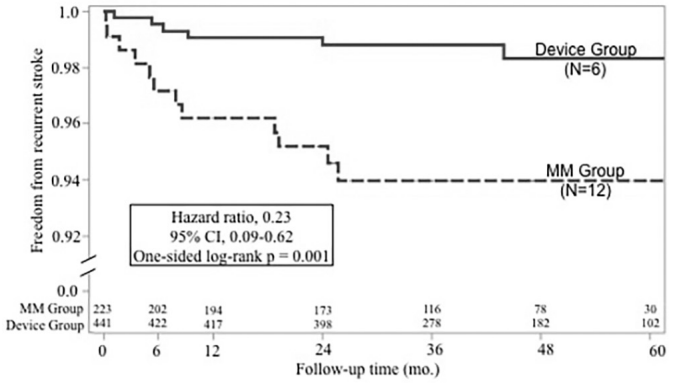
Co-Primary Endpoint 1: Recurrent ischemic stroke. Recurrent clinical ischemic stroke occurred in 6 subjects (0.39 per 100-patient-years) in the Device Group and 12 subjects (1.71 per 100-patient-years) in the MM Group (hazard ratio [HR] 0.23; 95% confidence interval [CI], 0.09-0.62; nominal one-sided p=0.001). This 77% hazard reduction in recurrent ischemic stroke achieved statistical significance at the pre-specified alpha=0.025 with a multiplicity adjusted one-sided p=0.001 (**Table 7** and **Figure 3**). The number needed-to-treat to prevent one recurrent stroke in 2 years was approximately 28 patients (the reciprocal of the absolute difference in Kaplan-Meier recurrent stroke rate between Device and MM Groups).

Table 7. Summary of Co-Primary Endpoint 1 Analysis – ITT Population

Primary Endpoint	# Subjects (Rate per 100 Pt-Yrs)[1]		Hazard Ratio (95% CI)	Hazard Reduction	p-value[2]
	Device Group (N=441)	MM Group (N=223)			
Recurrent Clinical Stroke	6 (0.39)	12 (1.71)	0.23 (0.09-0.62)	77%	0.001

MM = Medical Management
[1]100 x (Total number of events / total patient years follow-up)
[2]One-sided log-rank test

Figure 3: Intention-to-treat Kaplan-Meier plot of freedom from recurrent stroke (Co-Primary Endpoint 1)



Co-Primary Endpoint 2: New brain infarction. New brain infarction (the composite of clinical ischemic stroke or at least one new T2 hyperintense MRI lesion with diameter ≥3 mm from screening through 24 months) occurred in 22 subjects (5.7%) in the Device Group and 20 subjects (11.3%) in the MM Group (absolute difference 5.6%; 95% CI 0.3-10.8%, relative risk [RR] 0.51; 95% CI 0.29-0.91, nominal one-sided p=0.018). This 49% relative risk reduction for incidence of new brain infarct achieved statistical significance at the pre-specified alpha=0.025 with a multiplicity adjusted one-sided p=0.024 (**Table 8**). Of Device Group subjects with new brain infarcts, 5 (1.3%) had recurrent clinical strokes, and 17 (4.4%) had silent brain infarcts only. Of MM Group subjects with new brain infarcts, 12 (6.8%) had recurrent clinical strokes, and 8 (4.5%) had silent brain infarcts only.

Table 8. Summary of Co-Primary Endpoint 2 Analysis – ITT Population

Primary Endpoint	# Subjects[1]		Relative Risk (95% CI)	Relative Risk Reduction	p-value[2]
	Device Group (N=383)	MM Group (N=177)			
New Brain Infarction	22 (5.7%)	20 (11.3%)	0.51 (0.29-0.91)	49%	0.018
Recurrent Clinical Stroke	5 (1.3%)	12 (6.8%)	-	-	-
Silent Brain Infarction Only	17 (4.4%)	8 (4.5%)	-	-	-

MM = Medical Management
[1]The sample sizes (N=383 in the Device Group and N=177 in the MM Group) represent the number of evaluable patients; 58 Device Group subjects (13.2%) and 46 MM Group subjects (20.6%) were not evaluable for the New Brain Infarction co-primary endpoint due to early discontinuation or missing MRI assessments.
[2]One-sided binomial proportions test

Primary Endpoint Analysis Results – Per Protocol Population

Co-Primary Endpoint 1: Recurrent ischemic stroke. Recurrent clinical ischemic stroke occurred in 6 subjects in the Device Group and 12 subjects in the MM Group (HR 0.25; 95% CI, 0.09-0.65; nominal one-sided p=0.001) (**Table 9A**).

Co-Primary Endpoint 2: New brain infarction. New brain infarction occurred in 22 subjects (6.4%) in the Device Group and 19 subjects (11.5%) in the MM Group (absolute difference 5.0%; 95% CI -0.5-10.5%, relative risk [RR] 0.56; 95% CI 0.31-1.01, nominal one-sided p=0.037). Of Device Group subjects with new brain infarcts, 5 (1.5%) had recurrent clinical strokes, and 17 (5.0%) had silent brain infarcts only. Of MM Group subjects with new brain infarcts, 12 (7.2%) had recurrent clinical strokes, and 7 (4.2%) had silent brain infarcts only (**Table 9B**).

Table 9A. Summary of Co-Primary Endpoint 1 Analysis – Per Protocol Population

Co-Primary Endpoint 1	# Subjects (Rate per 100 Pt-Yrs)[1]		Hazard Ratio (95% CI)	Hazard Reduction	p-value[2]
	Device Group (N=380)	MM Group (N=203)			
Recurrent Clinical Stroke	6 (0.45)	12 (1.87)	HR 0.25 (0.09-0.65)	75%	0.001

MM = Medical Management
[1]100x (Total number of events / total patient years follow-up)
[2]One-sided log-rank test

Table 9B. Summary of Co-Primary Endpoint 2 Analysis – Per Protocol Population

Co-Primary Endpoint 2	Device Group (N=342)	MM Group (N=166)	Relative Risk (95% CI)	Relative Risk Reduction	p-value[1]
New Brain Infarction	22 (6.4%)	19 (11.5%)	0.56 (0.31-1.01)	44%	0.037
Recurrent Clinical Stroke	5 (1.5%)	12 (7.2%)	-	-	-
Silent Brain Infarction Only	17 (5.0%)	7 (4.2%)	-	-	-

MM = Medical Management
[1] One-sided binomial proportions test

Secondary Endpoint Analyses Results

Table 10 provides a summary of the results of Technical Success, Device Success, Clinical Success, and PFO Closure for the Device Group along with a summary of the results of Clinical Success for the MM Group.

Table 10. Secondary Endpoint Summary

Performance Outcome	Device Group n/N (%)	MM Group n/N (%)
Technical Success[1]	408/413 (98.8%)	-
Device Success[2]	408/423 (96.5%)	-
Clinical Success[3]	308/334 (92.2%)	186/198 (93.9%)
Effective PFO Closure[4]		
12 months	290/307 (94.5%)	-
24 months	309/315 (98.1%)	-
Complete PFO Closure[5]		
12 months	232/307 (75.6%)	-
24 months	257/315 (81.6%)	-

MM = Medical Management
[1] proportion of Device Group subjects with successful implant and retention of a study device after study device implant attempt.
[2] proportion of Device Group subjects with successful implant and retention of the study device after procedure.
[3] Device Group is defined as the composite of Device Success, PFO closure, and absence of recurrent stroke at 24 months post-procedure. MM Group is defined as the freedom from a recurrent stroke at 24 months post-randomization.
[4] freedom from large shunt (> 25 bubbles), adjudicated by echo core lab. Note that PFO closure results are provided for Device Group subjects who received a study device
[5] shunt status of occluded in subject with retained study device, adjudicated by echo core lab.

Overall survival, defined as time from randomization to death from any cause or last known contact, was not different between groups (p=0.335) with 24-month survival of 99.8% and 100% in the Device and MM groups, respectively. Freedom from any stroke / TIA at 24-months was 95.1% for the Device Group and 91.8% for the MM Group (p=0.096).

Safety Evaluation

Serious adverse events (SAEs) occurred in 102 (23.1%) subjects in the Device Group and 62 (27.8%) subjects in the MM Group (p=0.22) (**Table 11**). There were 2 patient deaths in the Device Group and no deaths in the MM Group; neither was device- or procedure-related. No unanticipated adverse device effects were reported. In the Device Group, procedure- and device-related SAEs occurred in 2.5% and 1.4% of subjects, respectively.

Table 11. Overall Subject-Based Rate of SAEs

	Device Group (N=441)	MM Group (N=223)
Device- or procedure-related death	**0 (0.0%)**	**N/A**
Any SAE[1]	**102 (23.1%)**	**62 (27.8%)**
Related to device	6 (1.4%)	N/A
Related to procedure	11 (2.5%)	N/A

MM = Medical Management
[1] Subjects could have more than one event

Six (6) device-related SAEs occurred in 6 subjects (1.4%) and 18 procedure-related SAEs occurred in 11 subjects (2.5%), and are summarized in **Table 12**. One subject (0. 2%) with a device- or procedure-related SAE (a device-related thrombosis) had a recurrent stroke.

Table 12. Device-related and procedure-related SAEs in the Device Group (N = 441)

Device-related SAE	**n (%)**
Atrial fibrillation	2 (0.5%)
Device-related thrombosis	2 (0.5%)
Device embolization	1 (0.2%)
Tachycardia	1 (0.2%)
Procedure-related SAE	**n (%)**
Device embolization	2 (0.5%)
Hypotension	2 (0.5%)
Anxiety	1 (0.2%)
Aortic dissection	1 (0.2%)
Arteriovenous fistula	1 (0.2%)
Cardiac tamponade	1 (0.2%)
Chest discomfort	1 (0.2%)
Complication of device removal	1 (0.2%)
Fatigue	1 (0.2%)
Hemiparesis	1 (0.2%)
Incision site hematoma	1 (0.2%)
Incision site hemorrhage	1 (0.2%)
Non-cardiac chest pain	1 (0.2%)
Post procedural hemorrhage	1 (0.2%)
Puncture site hemorrhage	1 (0.2%)
Respiratory arrest	1 (0.2%)

Atrial Fibrillation or Flutter Events

There was a higher incidence of atrial fibrillation or flutter in the Device Group than in the MM Group (6.6% vs. 0.4%, p<0.001) (**Table 13**).

Table 13. Atrial fibrillation and atrial flutter events

	Device Group (N=441)			MM Group (N=223)		
	# Patients	# Events	Rate Per 100 Pt-Yrs	# Patients	# Events	Rate Per 100 Pt-Yrs
Atrial fibrillation	29	31	2.0	1	1	0.1
Implant Procedure-Related	7	7	0.5	N/A	N/A	N/A
Non-Procedure-Related	22	24	1.6	N/A	N/A	N/A
Atrial flutter	2	2	0.1	0	0	0

MM = Medical Management

Of the 33 atrial fibrillation or flutter events in the Device Group, 33% were categorized as serious, and 67% were categorized as non-serious. One Device Group subject (0.2%) with atrial fibrillation had a recurrent stroke.

Wire Frame Fracture

Wire frame fracture was noted on 12-month fluoroscopy in 4.6% of Device Group subjects. No fractures were associated with device instability or clinical sequelae.

Additional Analyses

GORE® HELEX® Septal Occluder and GORE® CARDIOFORM Septal Occluder Poolability

Study device poolability was analyzed for baseline characteristics, device performance, and treatment effect for primary efficacy endpoints. There was no significant difference in the baseline characteristics (age, gender, PFO diameter and length, atrial septal aneurysm, qualifying event) of subjects treated with either study device. In addition, the following effectiveness and safety measures were not significantly different between study devices:

- Freedom from recurrent stroke (Co-Primary Endpoint 1)
- New brain infarction (Co-Primary Endpoint 2)
- Technical success
- 24 month PFO effective closure
- Device- and procedure-related SAEs
- Unrelated SAEs through two year follow-up
- Atrial fibrillation or flutter
- Wire frame fracture
- Antiplatelet-related SAEs

There was a significant difference in all unrelated (not procedure- or device-related) SAEs between study devices (24.1% for the GORE® HELEX® Septal Occluder subjects vs. 14.4% for the GORE® CARDIOFORM Septal Occluder subjects, p=0.017), which was due to the longer follow-up duration available on the earliest implanted subjects (i.e., those subjects who received a GORE® HELEX® Septal Occluder).

There was also a significant difference in effective closure at 12 months (98.0% for the GORE® CARDIOFORM Septal Occluder vs. 88.1% for the GORE® HELEX® Septal Occluder, p=0.001).

HOW SUPPLIED

The GORE® CARDIOFORM Septal Occluder is supplied sterile in a protective tray and pouch. Provided that the integrity of the pouch is not compromised in any way, it will serve as an effective barrier until the "use by" (expiration) date printed on the box.

REQUIRED ACCESSORIES

- 10 Fr Introducer Sheath
- Heparinized saline
- Flushing syringe
- Stopcock
- Sizing balloon
- Sterile bowl for flushing catheter

OPTIONAL ACCESSORIES

0.035" / 0.89 mm guidewire, or smaller (if necessary for defect access) 12 Fr Introducer Sheath when a guidewire is utilized.

RECOMMENDED PROCEDURES (applicable for both ASD and PFO closure)

A. Sizing the Defect and Selecting the Proper Occluder Size

1. Use echocardiography to measure the septal length.
2. Measure the septal defect using fluoroscopy or echocardiography; the stop flow balloon technique is recommended, as described below:
   a. Place a contrast filled, compliant balloon across the defect and gently inflate until shunting through the defect has stopped.
   b. Measure the diameter of the defect using either echocardiography or calibrated fluoroscopy.
3. Select the appropriate occluder size for the defect, taking the following recommendations into consideration:
   - A minimum occluder to defect size ratio of 1.75:1 is recommended (reference **Table 14**). The defect size should be no greater than 17 mm. An occluder that pulls through the defect after disc conformation may be too small and should be removed and replaced with a larger size.
   - There must be adequate space to accommodate the discs within the atrial chambers. To assure that there is adequate space to accommodate the discs within the atrial chambers, the selected occluder diameter should be less than 90% of the measured septal length.
   - The septal tissue margins surrounding the defect must be of sufficient size and integrity to prevent disc prolapse through the defect and Occluder embolization.

Table 14. GORE® CARDIOFORM Septal Occluder Device Sizing

Labeled Occluder Diameter (mm)	Maximum Recommended Defect Size Measured with Stop Flow Balloon Sizing (mm)
20	11
25	14
30	17

B. Access Site Preparation

1. Prepare the venous access site according to standard practice.
2. Place appropriately sized Introducer Sheath.

C. Occluder Preparation and Loading

1. Check the "use by" (expiration date) and the condition of the package.
2. Using aseptic technique, remove the sterile tray from the pouch, and remove the packaging tray lid.
3. Remove the device from the package and visually inspect the device for shipping damage. Ensure that the Retrieval Luer is tight.
4. Remove the Packaging Insert from the handle (**Figure 4**).
5. Loading and Flushing the Occluder:
   a. Submerge the Occluder and catheter tip in a heparinized saline bath during loading to reduce the chance of air entrapment in the delivery system.
   b. Fill a syringe with heparinized saline.
   c. Attach the syringe to a stopcock and the Flush Port.
   d. Flush the device until air no longer exits the tip of the Delivery Catheter.
   e. When the initial flushing is completed, begin loading the Occluder by pushing the Slider up and then to the right until the Slider stops (**Figure 5a**).
   f. Complete Occluder loading by pushing the Slider down and then to the right until it stops (**Figure5b**).
   g. Flush the device again until air no longer exits the tip of the Delivery Catheter.
   h. If additional air removal is desired, it is recommended to deploy the Occluder (refer to Section E "Occluder Deployment") and repeat steps d - g above.

The Occluder Lock should not be moved before or during Occluder loading or deployment. Partial or complete Occluder locking may prevent Occluder loading and deployment.

FIGURE 4: Packaging Insert Removal

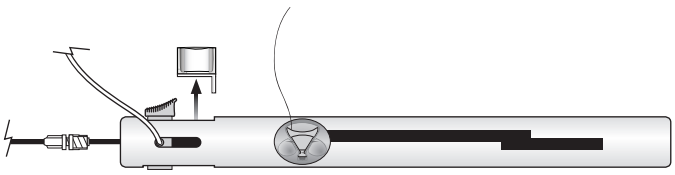


FIGURE 5: Occluder Loading

FIGURE 5a: Initial Occluder Loading

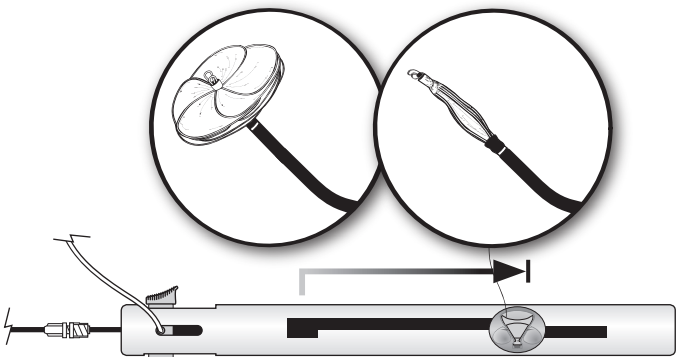
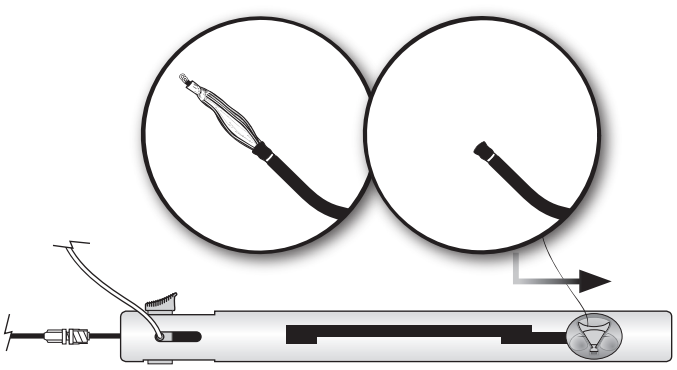


FIGURE 5b: Completion of Occluder Loading

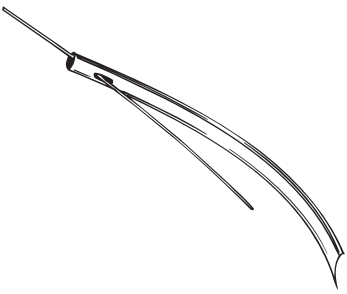


D. Occluder Delivery

1. If applicable, load the Delivery Catheter onto the guidewire by threading the guidewire into the lumen of the Delivery Catheter from the tip and out the Guidewire Slot (**Figure 6**).

2. While flushing the device, load the Delivery Catheter into the appropriately sized introducer sheath. Close the stopcock and remove the flushing syringe from the stopcock.

FIGURE 6



E. Occluder Deployment

1. Advance the Delivery Catheter across the atrial septum until the tip is positioned within the left atrium.
2. If a guidewire was utilized, remove the guidewire before attempting to deploy the Occluder.
3. Begin deploying the Occluder left disc by pushing the Slider to the left until it stops (**Figure 7a**).
4. Complete Occluder left disc deployment by pushing the Slider up and then to the left until a flat left disc has formed (**Figure 7b**). This step may be performed while simultaneously retracting the Delivery System to minimize advancement of the Occluder within the left atrial chamber.
5. Gently pull on the Handle to bring the left atrial disc onto the surface of the left atrial septum..
6. Deploy the right atrial disc by pushing the Slider to the left until it stops and then down. Confirm that the Slider has moved completely to the left and down position (**Figure 7c**). Failure to move the Slider completely to the left and down position may prevent Occluder locking.
7. Confirm that both left and right discs appear planar and apposed to the septum with septal tissue between the discs.

If the position is not correct, refer to Section G, "Reloading the Occluder". Note that the Occluder can only be Reloaded prior to Occluder Locking.

FIGURE 7: Occluder Deployment

FIGURE 7a: Initial Occluder Deployment

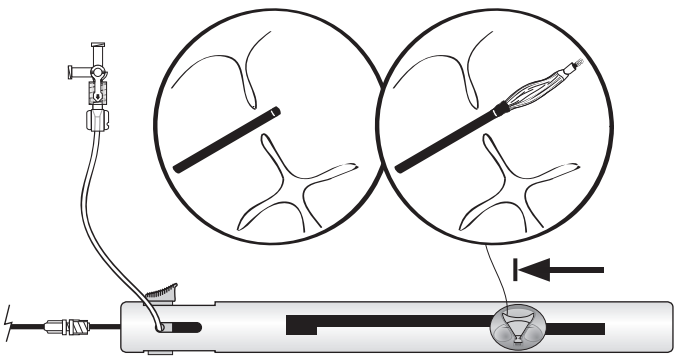


FIGURE 7b: Left Atrial Disc Deployment

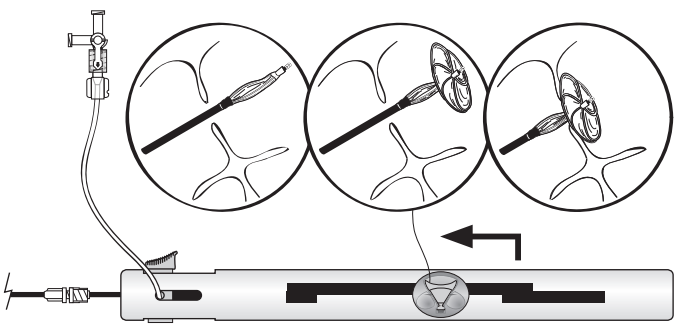
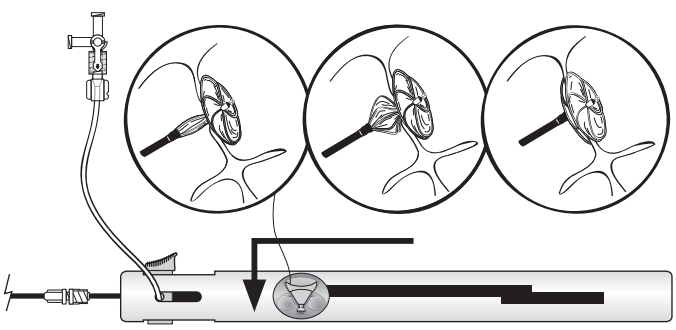


FIGURE 7c: Right Atrial Disc Deployment



F. Occluder Locking and Delivery System Removal

1. Prior to Occluder locking, assess that the Occluder position and defect closure are acceptable and that the Delivery System is not exerting tension on the septum and Occluder.
2. Lock the Occluder by holding the Handle in a fixed position to prevent applying tension on the Occluder. Note that excessive compression of the handle may prevent Occluder locking. Next, squeeze and then slide the Occluder Lock decisively and with a consistent amount of force to the right (**Figure 8**). At the completion of Occluder locking, the Occluder is still attached to the Delivery System by the Retrieval Cord.
   During the Occluder locking step, the Delivery Catheter moves proximally and may exert minimal tension on the introducer sheath. It is recommended to confirm adequate introducer sheath insertion prior to Occluder locking.
3. If the Occluder position is not acceptable, refer to Section H, "Removing the Occluder with the Retrieval Cord After Occluder Locking".
4. If the Occluder position is acceptable, hold the Handle in a fixed position, pull up on the red Retrieval Cord Lock (**Figure 9a**), disengage it from the Slider, and gently pull the Retrieval Cord Lock until the Retrieval Cord has been completely removed from the Handle (**Figure 9b**).
5. The Occluder is now released from the Delivery System and the Delivery System can be removed.
6. Once the Retrieval Cord is removed, the Occluder cannot be removed using the Delivery System, refer to Section I, "Recapture".

FIGURE 8: Occluder Locking

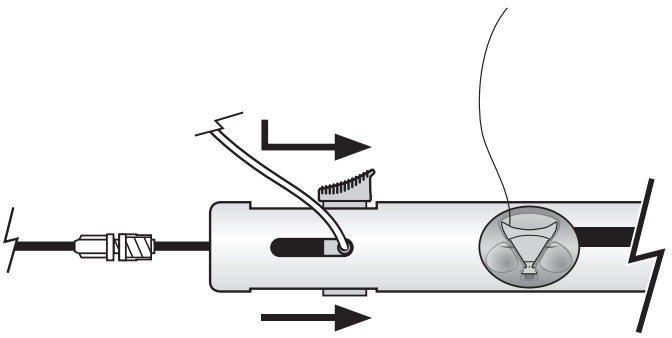


FIGURE 9: Occluder Release

FIGURE 9a: Retrieval Cord Lock Release

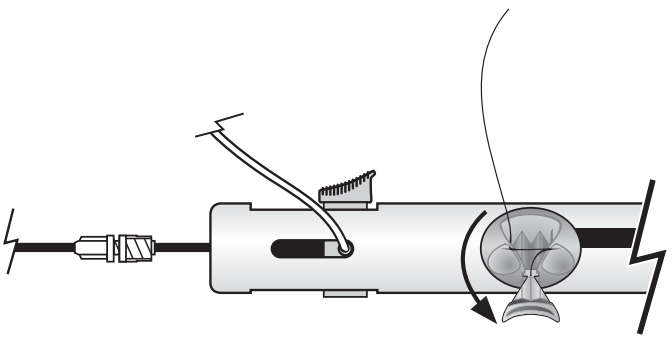
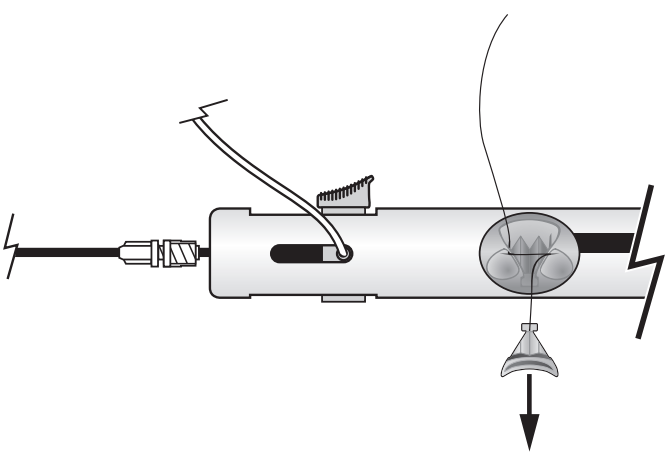


FIGURE 9b: Retrieval Cord Removal



G. Reloading the Occluder Before Occluder Locking

1. Reload the Occluder by pushing the Slider up and then to the right until the desired portion of the Occluder discs is reloaded or until the Slider stops, if complete disc reloading is desired (**Figure 5a**).
2. If desired, complete Occluder reloading by pushing the Slider down and then to the right until it stops (**Figure 5b**). Ensure that the Delivery Catheter tip remains across the defect to maintain defect access.

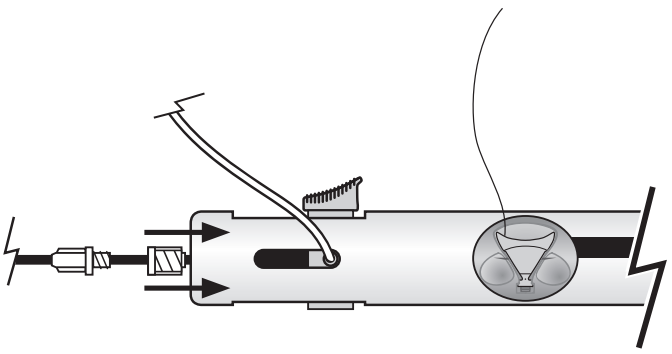
3. Refer to Section E, "Occluder Deployment" to re-deploy the Occluder.
   - If desired device placement cannot be achieved after multiple deployment attempts, consideration should be given to minimize the patient's exposure to radiation and prolonged anesthesia time. If the patient's septal anatomy is determined to be unsuitable for the GORE® CARDIOFORM Septal Occluder, alternative treatment options such as other devices or surgical closure of the defect should be considered.

H. Removing the Occluder with the Retrieval Cord After Occluder Locking

1. Unscrew the Retrieval Luer, hold the Delivery Catheter in place and withdraw the Handle until the Occluder has unlocked (**Figure 9**). This step requires that the Delivery Catheter is sufficiently spaced away from the Occluder to permit full extension of the Lock Loop.
2. Continue to withdraw the Handle to pull the entire Occluder into the Delivery Catheter. Do not use excessive force in an attempt to withdraw all of the Occluder into the Delivery Catheter. Doing so could cause the Retrieval Cord to break or result in Occluder damage.
   - The operator must ensure that the Occluder does not catch on the Delivery Catheter tip or introducer sheath. If the Lock Loop or eyelet catch and the Delivery System is forcibly retracted, the Retrieval Cord or Occluder frame is at risk of damage.
3. If necessary, remove the introducer sheath and Occluder together.
   - If the Occluder is removed, it should be disposed of and a new Occluder should be used.

   Note that without a hemostatic valve at the Delivery Catheter proximal end, care should be taken to avoid air entry or blood loss if the Occluder is completely removed from the Delivery Catheter.

FIGURE 10: Occluder Retrieval



I. Recapture

1. In the event that the Occluder is malpositioned, embolized, or otherwise requires removal, it may be recaptured with the aid of a loop snare or other suitable means. A long sheath (11 Fr or greater) positioned close to the device is recommended for recapture.
2. Attempt to recapture the device by first snaring the left or right atrial eyelet to facilitate Occluder retraction into the sheath. If necessary, the loop snare may be placed around any portion of the Occluder frame.
3. Pull the Occluder into the long sheath using the snare. If a portion of the Occluder frame cannot be retracted into the long sheath, it may be necessary to remove the Occluder, loop snare, and long sheath as one unit. Do not use excessive force in an attempt to withdraw all of the Occluder into the long sheath. Doing so could result in Occluder damage.
4. Bring the recaptured Occluder into the sheath to avoid pulling the unlocked device across valve tissue.

MR CONDITIONAL **MR Conditional**

J. MRI Information

Non-clinical testing demonstrated that the GORE® CARDIOFORM Septal Occluder is MR Conditional. A patient with this device can be scanned safely in a MR system under the following conditions:

- Static magnetic field of 1.5 T or 3.0 T only
- Maximum spatial gradient magnetic field of 4,000 gauss/cm (40 T/m)
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 4 W/kg for 15 minutes of scanning (i.e., per pulse sequence) in the First Level Controlled Operating Mode

Under the scan conditions defined, the GORE® CARDIOFORM Septal Occluder is expected to produce a maximum temperature rise of less than 3.3 °C after 15 minutes of continuous scanning (i.e., per pulse sequence).

In non-clinical testing, the image artifact caused by the GORE® CARDIOFORM Septal Occluder extends approximately 10 mm from this implant when imaged using a gradient echo pulse sequence and a 3.0 T MR system.

The effect of overlapping Occluders has not been studied and is not understood.

DEFINITIONS

EC REP Authorised Representative in the European Community

REF Catalogue Number

Caution

℞ Only CAUTION: USA Federal Law restricts the sale, distribution, or use of this device to, by, or on the order of a physician.

Consult Instructions for Use

Date of Manufacture

Do Not Resterilize

Do Not Reuse

Do Not Use if Package is Damaged

Keep Dry

Manufacturer

MR Conditional

SN Serial Number

STERILE Sterile

STERILE EO Sterilized using Ethylene Oxide

Store in a Cool Place

Use By

Catheter Working Length

Delivery Profile

Diameter

Guidewire Compatibility

20054136

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For international contact and additional product information, visit **www.goremedical.com**

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