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Instructions for Use
Silk Road Medical ENROUTE™ Transcarotid Stent System

READ ALL INSTRUCTIONS CAREFULLY. Failure to properly follow the instructions, warnings and precautions may lead to serious consequences or injury to the patient.

ONLY PHYSICIANS WHO HAVE RECEIVED APPROPRIATE TRAINING FOR TRANSCAROTID STENTING AND WHO ARE FAMILIAR WITH THE PRINCIPLES, CLINICAL APPLICATIONS, COMPLICATIONS, SIDE EFFECTS AND HAZARDS COMMONLY ASSOCIATED WITH CAROTID INTERVENTIONAL PROCEDURES SHOULD USE THIS DEVICE.
Use only with ENROUTE Transcarotid Neuroprotection System (NPS).

EO STERILE. ENROUTE Transcarotid Stent System is sterilized with ethylene oxide (EO) gas.
Non-pyrogenic.
DO NOT USE THIS PRODUCT WITH POWER INJECTION SYSTEMS.
FOR ONE USE ONLY.
DO NOT RESTERILIZE.
DO NOT USE THIS PRODUCT PAST ITS EXPIRATION DATE.
THIS PRODUCT IS RADIOPAQUE.
STORE IN A COOL, DARK, DRY PLACE.

Explanation of symbols on labels and packaging

Manufacturer

Sterilized with ethylene oxide gas

Do not resterilize

For one use only

REF

Catalog No.

Lot No.

Use By

MR Conditional

Caution, Attention See Instructions for Use.

Nonpyrogenic

Do not use if the package is open or damaged.

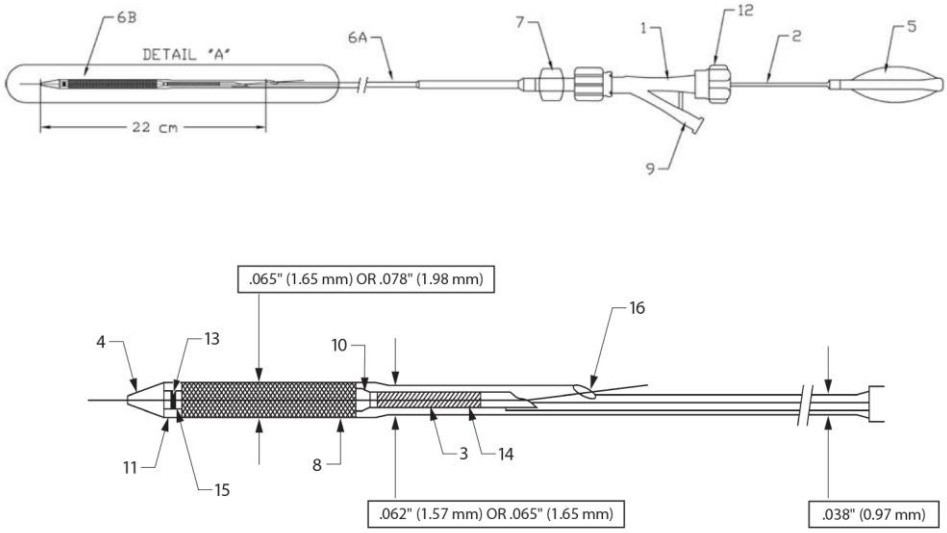
Store in a cool, dark, dry place.

Instructions for Use, ENROUTE Transcarotid Stent System, Table of Contents

1.0 Device Name
The device brand name is the ENROUTE™ Transcarotid Stent System.

2.0 Description
The ENROUTE Transcarotid Stent System consists of a nitinol self-expanding stent preloaded on a 5F (.065" / 1.65 mm) or 6F (.078" / 1.98 mm) sheathed delivery system. The rapid exchange delivery system consists mainly of an inner shaft and an outer sheath with radiopaque markers, and a Tuohy Borst valve. The inner shaft consists of a support member and wire lumen. The proximal portion of the support member is comprised of a hub connected to a stainless steel wire and hypotube and distally of a stainless steel coil. The wire lumen originates distally in a catheter tip and terminates proximally at a guidewire exit port designed to accept a .014" (0.36 mm) guidewire. The outer sheath has a proximal shaft and distal outer sheath with a nominal working length of 57 cm. The self-expanding ENROUTE Transcarotid Stent System is constrained within the space between the inner shaft and the distal outer sheath, located between distal and proximal stent markers on the inner shaft. The stent expands to its unconstrained diameter when released from the deployment catheter into the carotid artery. Upon deployment, the stent forms a lattice to cover the diseased arterial segment and to push outward on the luminal surface, helping to maintain the patency of the artery. Due to the self-expanding behavior of nitinol, the stents are indicated for placement into vessels that are 1-2 mm smaller in diameter than the unconstrained diameter of the stent. Device depictions and components are provided in **Figure 1**.

Figure 1. ENROUTE TRANSCAROTID STENT SYSTEM



1. Tuohy Borst valve
2. Hypotube
3. Coil
4. Catheter Inner Shaft Tip
5. Inner Shaft Hub
6A. Proximal Shaft
6B. Distal Outer Sheath
7. Outer Sheath Luer Hub
8. Pod Housing Crimped Stent
9. Tuohy Borst Y-Connection
10. Proximal Inner Shaft Marker (Stop) Marks
11. Outer Sheath Radiopaque Marker
12. Proximal Valve End
13. Distal Inner Shaft Stent Marker
14. Coil Sleeve
15. Wire Lumen
16. Guidewire Exit Port

The ENROUTE Transcarotid Stent System is provided as noted in **Table 1** below.

Table 1
ENROUTE Transcarotid Stent System
57 cm Working Length
Guidewire Lumen: Accepts .014" (0.36 mm) Guidewire
For use with ENROUTE Transcarotid Arterial Sheath (8F ID, 2.7 mm)

.065" (1.65 mm) ENROUTE CODES	UNCONSTRAINED STENT DIMENSIONS Diameter x Length (mm)	CROSSING PROFILE
SR-0520-CS	5 x 20	5F (.078", 1.98 mm)
SR-0530-CS	5 x 30	5F (.078", 1.98 mm)
SR-0540-CS	5 x 40	5F (.078", 1.98 mm)
SR-0620-CS	6 x 20	5F (.078", 1.98 mm)
SR-0630-CS	6 x 30	5F (.078", 1.98 mm)
SR-0640-CS	6 x 40	5F (.078", 1.98 mm)
SR-0720-CS	7 x 20	5F (.078", 1.98 mm)
SR-0730-CS	7 x 30	5F (.078", 1.98 mm)
SR-0740-CS	7 x 40	5F (.078", 1.98 mm)
SR-0820-CS	8 x 20	5F (.078", 1.98 mm)
SR-0830-CS	8 x 30	5F (.078", 1.98 mm)
SR-0840-CS	8 x 40	5F (.078", 1.98 mm)
SR-0920-CS	9 x 20	6F (.087", 2.21 mm)
SR-0930-CS	9 x 30	6F (.087", 2.21 mm)
SR-0940-CS	9 x 40	6F (.087", 2.21 mm)
SR-1020-CS	10 x 20	6F (.087", 2.21 mm)
SR-1030-CS	10 x 30	6F (.087", 2.21 mm)
SR-1040-CS	10 x 40	6F (.087", 2.21 mm)

3.0 Indications for Use

The ENROUTE Transcarotid Stent System used in conjunction with the ENROUTE Transcarotid Neuroprotection System (NPS) is indicated for the treatment of patients at high risk for adverse events from carotid endarterectomy, who require carotid revascularization and meet the criteria outlined below.

1. Patients with neurological symptoms and $\geq$ 50% stenosis of the common or internal carotid artery by ultrasound or angiogram **OR** patients without neurological symptoms and $\geq$ 80% stenosis of the common or internal carotid artery by ultrasound or angiogram, **AND**
2. Patients must have a vessel diameter of 4-9 mm at the target lesion, **AND**
3. Carotid bifurcation is located at minimum 5 cm above the clavicle to allow for placement of the ENROUTE Transcarotid NPS.

4.0 Contraindications

Use of the ENROUTE Transcarotid Stent System is contraindicated in the following patients:

1. Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated.
2. Patients in whom the ENROUTE Transcarotid NPS is unable to be placed.
3. Patients with uncorrected bleeding disorders.
4. Patients with known allergies to nitinol.
5. Lesions in the ostium of the common carotid artery.

5.0 Warnings

5.1 General Warnings

1. Only physicians who have received appropriate training for transcarotid stenting and who are familiar with the principles, clinical applications, complications, side effects and hazards commonly associated with carotid interventional procedures should use this device.
2. The safety and efficacy of the ENROUTE Transcarotid Stent System have not been demonstrated with embolic protection systems other than the ENROUTE Transcarotid NPS. Use the ENROUTE Transcarotid Stent System only with the ENROUTE Transcarotid NPS.
3. The long term performance (> 3 years) of carotid stents has not yet been established.
4. As with any type of vascular implant, infection secondary to contamination of the stent may lead to thrombosis, pseudoaneurysm or rupture.
5. The stent may cause a thrombus, distal embolization or may migrate from the site of implant through the arterial lumen. Appropriate sizing of the stent to the vessel is required to reduce the possibility of stent migration (see Section 9.3 of these instructions). In the event of thrombosis of the expanded stent, thrombolysis and PTA should be attempted.
6. Overstretching of the artery may result in rupture and life-threatening bleeding.
7. In patients requiring the use of antacids and/or H2-antagonists before or immediately after stent placement, oral absorption of antiplatelet agents (e.g. aspirin) may be adversely affected.
8. The appropriate antiplatelet and anticoagulation therapy should be administered pre- and post-procedure as suggested in Section 9.1 of these instructions.
9. In the event of complications such as infection, pseudoaneurysm or fistulization, surgical removal of the stent may be required.

5.2 Patient Selection Warnings

1. Safety and effectiveness of the ENROUTE Transcarotid Stent System has **NOT** yet been established in patients with the characteristics noted below.

Lesion Characteristics:

- Patients with evidence of intraluminal thrombus thought to increase the risk of plaque fragmentation and distal embolization.
- Patients whose lesion(s) may require more than two stents.
- Patients with total occlusion of the target vessel.

• Patients with lesions of the ostium of the common carotid.
• Patients with highly calcified lesions resistant to PTA.
• Concurrent treatment of bilateral lesions.

Patient Characteristics:
• Patients at low-to-moderate risk for adverse events from carotid endarterectomy.
• Patients experiencing acute ischemic neurologic stroke or who experienced a stroke within 48 hours.
• Patient has had a recent (<7 days) stroke of sufficient size (on CT or MRI) to place him or her at risk of hemorrhagic conversion during the procedure.
• Patients with ipsilateral intracranial or extracranial arterial stenosis greater in severity than the lesion to be treated, cerebral aneurysm > 5 mm, AVM (arteriovenous malformation) of the cerebral vasculature, or intracranial tumor.
• Patients with arterio-venous malformations in the territory of the target carotid artery.
• Patients with diathesis or coagulopathies.
• Patients with poor renal function, who, in the physician's opinion, may be at high risk for a reaction to contrast medium.
• Patients with perforated vessels evidenced by extravasation of contrast media.
• Patients with aneurismal dilation immediately proximal or distal to the lesion.
• Pregnant patients or patients under the age of 18.

Access Characteristics:
• Patients with known internal carotid artery tortuosity that would preclude the use of catheter-based techniques.
• Patients with known common carotid or internal carotid artery tortuosity that would preclude the use of catheter-based techniques.
• Patients in whom common carotid access is not possible.

2. Risk of distal embolization may be higher if the ENROUTE Transcarotid Stent System cannot be used in conjunction with the ENROUTE Transcarotid NPS during the carotid stenting procedure.

5.3 Device Use Warnings
1. USE OF A SMALLER THAN INDICATED ACCESSORY DEVICE OTHER THAN THE ENROUTE TRANSCAROTID ARTERIAL SHEATH MAY LEAD TO INTRODUCTION OF AIR INTO THAT DEVICE AS THE STENT DELIVERY SYSTEM IS ADVANCED, WHICH MAY NOT BE REMOVED DURING AIR ASPIRATION.
2. Ensure that the catheter system is flushed according to the steps outlined in "Introduction of Stent Delivery System" (**Section 9.4**). Failure to do so could result in air entering the ENROUTE's Transcarotid Arterial Sheath.
3. Ensure that there is a tight seal between the ENROUTE catheter and the valve for the ENROUTE Transcarotid Arterial Sheath during aspiration. Failure to do so could result in air entering the ENROUTE Transcarotid Arterial Sheath.
4. The black dotted pattern on the gray temperature exposure indicator found on the pouch must be clearly visible.
DO NOT USE THE PRODUCT IF THE ENTIRE TEMPERATURE EXPOSURE INDICATOR IS COMPLETELY BLACK as the pre-programmed stent diameter may have been compromised.
5. Do not use the device if there are abnormalities in the sterile barrier (e.g. broken seal, torn or breached barrier) or the product.
6. This device is intended for one-time use only. Do not re-sterilize and/or reuse. Structural integrity and/or function may be impaired through reuse or cleaning.
7. Do not use the ENROUTE Transcarotid Stent System after the "Use By" date specified on the package.
8. Do not use with Ethiodol or Lipiodol* contrast media, which may adversely affect the stent delivery system.
*Ethiodol and Lipiodol are Trademarks of Gerbert S.A.
9. Do not expose the delivery system to organic solvents (e.g., alcohol) as structural integrity and/or function of the device may be impaired.

10. The stent is not designed for dragging or repositioning.
11. Once the stent is partially deployed, it cannot be recaptured using the stent delivery system.
12. As with any type of vascular implant, infection secondary to contamination of the stent may lead to thrombosis, pseudoaneurysm or rupture.
13. When multiple stents are used, they should be of similar composition.
14. Long-term outcomes following repeat dilatation of endothelialized stents are unknown.

6.0 Precautions

6.1 Stent Handling Precautions

1. The ENROUTE Transcarotid Stent System is supplied **STERILE** and is intended for single use only. DO NOT resterilize and/or reuse the device.
2. The ENROUTE Transcarotid Stent System is shipped with the Tuohy Borst valve in the **OPEN** position. Care should be taken not to pre-deploy the stent. The device should be prepped in the tray. (See **Section 9.3** of these instructions).
3. Do not use the ENROUTE Transcarotid Stent System after the "Use By" date specified on the package.
4. Do not use if the pouch is opened or damaged.
5. Store in a cool, dark, dry place.

6.2 Stent Placement Precautions

1. Venous access should be available during carotid stenting in order to manage bradycardia and/or hypotension either by pharmaceutical intervention or placement of a temporary pacemaker, if needed.
2. When catheters are in the body, they should be manipulated only under fluoroscopy. Radiographic equipment that provides high quality images is needed.
3. The delivery system is not designed for the use of power injection. Use of power injection may adversely affect device performance.
4. If resistance is met during delivery system introduction, the system should be withdrawn and another system used.
5. Prior to stent deployment, remove all slack from the catheter delivery system (see **Section 9.4, 4** of these instructions).
6. Adequate distance must be maintained from the distal tip of the transcarotid access sheath and the proximal edge of the stent to avoid stent delivery within the lumen of the sheath.
7. When treating multiple lesions, the distal lesion should be initially stented, followed by stenting of the proximal lesion. Stenting in this order obviates the need to cross the proximal stent in placement of the distal stent and reduces the chance for dislodging stents that have already been placed.
8. Overlap of sequential stents is necessary, but the amount of overlap should be kept to a minimum (approximately 5 mm). In no instance should more than 2 stents overlap.
9. Fractures of this stent may occur. Fractures may also occur with the use of multiple overlapping stents. Fractures have been reported most often in clinical uses for which the safety and effectiveness have not been established. The causes and clinical implications of stent fractures are not well characterized. Care should also be taken when deploying the stent as excessive force could, in rare instances, lead to stent deformation and/or fracture.

6.3 Post Stent Placement Precautions

1. Recrossing a deployed stent with adjunct devices must be performed with caution.
2. In the event of thrombosis of the expanded stent, thrombolysis and PTA should be attempted.

6.4 MRI Safety Information

Non-clinical testing has demonstrated that the ENROUTE Transcarotid Stent is *MR Conditional.* A patient with this device can be scanned safely in an MR system meeting the following conditions:
- Static magnetic field of 1.5-Tesla or 3-Tesla, only
- Maximum spatial gradient magnetic field of 4,000 Gauss/cm (40 Tesla/m) or less
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2-W/kg (Normal Operating Mode).

Under the scan conditions defined above, the ENROUTE Transcarotid Stent is expected to produce a maximum temperature rise of 2.4°C after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends approximately 5 mm from the ENROUTE Transcarotid Stent when imaged with a gradient echo pulse sequence and a 3-Tesla MRI system. The artifact does obscure the device lumen.

7.0 Adverse Events

The ENROUTE Transcarotid Stent System is a stenting platform based upon the FDA-approved Cordis PRECISE Nitinol Stent System (PRECISE). The ENROUTE Transcarotid Stent System is identical to the PRECISE Stent System with the exception of the working length of the delivery system. The ENROUTE Transcarotid Stent System has a working length of 57 cm whereas the PRECISE Stent System has a working length of 135 cm. The adverse event information presented herein encompasses clinical trial data on the use of the PRECISE Stent System in combination with the ENROUTE Transcarotid NPS (see Section 7.1, Observed Adverse Events). Additional adverse event information is derived from clinical trial data on the use of the PRECISE Stent System and the ANGIOGUARD® XP Emboli Capture Guidewire.

7.1 Observed Adverse Events – Clinical Studies

Carotid stenting with reverse flow proximal embolic protection using the PRECISE Stent System and the ENROUTE Transcarotid Neuroprotection System was conducted in 65 patients in the ROADSTER study (n=52) and the PROOF study (n=13). In the ROADSTER study, a sub-study of 52 patients who were at high risk for complications from carotid endarterectomy (CEA) were enrolled to evaluate the safety and effectiveness of the PRECISE Stent System when used with the ENROUTE Transcarotid Neuroprotection System. In the PROOF Study, 13 patients who were at standard and high risk for complications from CEA were enrolled to evaluate the feasibility of the carotid angioplasty and stenting with ENROUTE Transcarotid NPS. These data serve as the basis for the safety and effectiveness of the ENROUTE Transcarotid Stent System which differs from the PRECISE Stent System only in the working length of the delivery system. Safety and effectiveness data for the PRECISE Stent System when used with the ANGIOGUARD XP Emboli Capture Guidewire can be found on FDA's website at the following URL: http://www.accessdata.fda.gov/cdrh_docs/pdf3/P030047b.pdf. 510(k) clearance of the ENROUTE Transcarotid NPS was supported by data from the full cohort of patients enrolled in the ROADSTER study (n=141) when used with any FDA-approved carotid stent system.

The Major Adverse Event rate in the ROADSTER sub-study population (subjects treated with a combination of the PRECISE Stent and the ENROUTE Transcarotid NPS) was 1.9%. One subject experienced a minor ipsilateral stroke within the 30-day follow-up period.

7.2 ROADSTER Study – Sub-Study of Patients Treated with a Combination of the PRECISE Stent System and the ENROUTE Transcarotid Neuroprotection System

This prospective, single arm, multi-center study included 52 patients at high risk for complications from CEA. The PRECISE Stent System was used as a surrogate for the ENROUTE Transcarotid Stent System as the two systems differ only in the working length. The major adverse event (MAE) rate was defined as death, stroke, or MI to 30 days. The 30-day MAE rate for these patients was 1.9%. Serious adverse events to 30 days from the ROADSTER sub-study are presented in the following table:

Table 2
Serious Adverse Events to 30 Days

System Organ Class **Preferred Term**	**All PRECISE Stent Subjects in ROADSTER (N=52)**
Number (%) of Subjects with one or more Serious Adverse Events	7 (13.5%)
Blood And Lymphatic System Disorders	1 (1.9%)
Anaemia	1 (1.9%)
Cardiac Disorders	1 (1.9%)
Cardiac Failure Congestive	1 (1.9%)
Injury, Poisoning And Procedural Complications	1 (1.9%)
Post Procedural Haemorrhage	1 (1.9%)
Nervous System Disorders	1 (1.9%)
Cerebrovascular Accident	1 (1.9%)
Respiratory, Thoracic And Mediastinal Disorders	1 (1.9%)
Atelectasis	1 (1.9%)
Vascular Disorders	2 (3.8%)
Artery Dissection	1 (1.9%)
Hypotension	1 (1.9%)

Results from the ROADSTER sub-study of subjects receiving the PRECISE stent (N=52) were comparable to results seen in the ROADSTER pivotal study cohort (N=141).

7.3 PROOF Pivotal Study – Sub-Study of Patients Treated with a Combination of the PRECISE Stent System and the ENROUTE Transcarotid Neuroprotection System

This prospective, single arm, multi-center study included 13 patients at standard and high risk for complications from CEA. The PRECISE Stent System was used as a surrogate for the ENROUTE Transcarotid Stent System as the two systems differ only in the working length. The major adverse event (MAE) rate was defined as death, major stroke, or MI to 30 days. It should be noted that, although the primary endpoint for stroke included only major stroke, there were no minor strokes in this sub-study population. The 30-day MAE rate for these patients was 0.0%. Serious adverse events to 30 days from the PROOF sub-study are presented in the following table:

Table 3
ENROUTE Transcarotid Stent System
Serious Adverse Events

System Organ Class	All PRECISE Stent Subjects in PROOF (N=13)
Number (%) of Subjects with one or more Serious Adverse Events	13 (100%)
Cardiac Disorders	2 (15.4%)
Gastrointestinal Disorders	2 (15.4%)
General Disorders and Administration Site Conditions	1 (7.7%)
Infections and Infestations	1 (7.7%)
Investigations	2 (15.4%)
Nervous System Disorders	7 (53.8%)
Respiratory, Thoracic, and Mediastinal Disorders	1 (7.7%)
Skin and Subcutaneous Tissue Disorders	2 (15.4%)
Surgical and Medical Procedures	1 (7.7%)
Vascular Disorders	7 (53.8%)

7.4 Potential Adverse Events

Adverse Events (in alphabetical order) that may be associated with the use of the ENROUTE Transcarotid Stent System when used in conjunction with the ENROUTE Transcarotid NPS include, but may not be limited to (based upon clinical trial data for the PRECISE Stent System and the ANGIOGUARD XP Emboli Capture Guidewire and clinical trial data from the ROADSTER and PROOF studies):

- Air embolism
- Allergic/anaphylactoid reaction
- Aneurysm
- Angina/coronary ischemia
- Arrhythmia (including bradycardia, possibly requiring need for a temporary or permanent pacemaker)
- Arterial occlusion/restenosis of the treated vessel
- Arterial occlusion/thrombus, at puncture site
- Arterial occlusion/thrombus, remote from puncture site
- Arteriovenous fistula
- Bacteremia or septicemia
- Cerebral edema
- Death
- Embolization, arterial
- Embolization, stent
- Emergent repeat hospital intervention
- Fever
- GI bleeding from anticoagulation/antiplatelet medication
- Hematoma bleed, access site
- Hematoma bleed, remote site
- Hemorrhage
- Hyperperfusion syndrome
- Hypotension/hypertension
- Infection
- Intimal injury/dissection
- Ischemia/infarction of tissue/organ
- Local infection and pain at insertion site

• Malposition (failure to deliver the stent to the intended site)
• Myocardial infarction
• Pain
• Pseudoaneurysm
• Renal failure
• Restenosis of the vessel (> 50% obstruction)
• Seizure
• Severe unilateral headache
• Stent migration
• Stent thrombosis
• Stroke
• Transient ischemic attack
• Transient intolerance to reverse flow
• Vasospasm
• Venous occlusion/thrombosis, at puncture site
• Venous occlusion/thrombosis, remote from puncture site
• Vessel rupture, dissection, perforation

7.5 Device Related Adverse Event Reporting

Any adverse event (clinical incident) involving the ENROUTE Transcarotid Stent System should be reported to Silk Road Medical, Inc. immediately. To report an incident, call Silk Road Medical, Inc. at 408-720-9002.

8.0 Clinical Study Information

The ROADSTER clinical study was conducted to evaluate the safety and effectiveness of the PRECISE Stent System when used with the ENROUTE Transcarotid NPS. The PRECISE Stent System was used as a surrogate for the ENROUTE Transcarotid Stent System as the two systems differ only in the working length. The ROADSTER pivotal study data are presented below.

8.1 The ROADSTER Study

The ROADSTER study was a prospective, single-arm, multi-center clinical trial of the ENROUTE Transcarotid NPS in conjunction with all FDA-approved carotid artery stents including the PRECISE Stent System used for revascularization in patients with carotid disease who were at high risk for complications from carotid endarterectomy (CEA). There was a lead-in phase of up to five (5) patients per investigator to allow investigators to gain experience with the study device prior to pivotal study enrollment. Sixty-seven (67) lead-in and 141 pivotal (ITT) subjects at high risk for complications from CEA were enrolled between November 2012 and July 2014. A sub-study of 18 lead-in and 34 pivotal subjects at high risk for complications from CEA and treated with the PRECISE Stent System was also conducted. The study included patients with atherosclerotic extracranial internal carotid stenosis (ICA) with or without involvement of the contiguous common artery (CCA) determined by duplex ultrasound, CT/CTA, MR/MRA or angiography. The study population consisted of male and female subjects at least 18 years of age meeting one of the following criteria regarding neurological symptom status and degree of stenosis:

Symptomatic: Stenosis must be >50% as determined by angiogram and the patient has a history of stroke (minor or non-disabling), TIA and/or amaurosis fugax within 180 days of the procedure, OR

Asymptomatic: Stenosis must be >70% as determined by angiogram without any neurological symptoms within the prior 180 days.

Eligible subjects were scheduled to undergo carotid revascularization any FDA-approved carotid artery stent system with the ENROUTE Transcarotid NPS. Subjects were followed for 30 days post-procedure. Patients met at least one of the surgical high-risk criteria listed below.

Anatomic High Risk Inclusion Criteria:

A. Contralateral carotid artery occlusion
B. Tandem stenoses >70%

C. High cervical carotid artery stenosis
D. Restenosis after carotid endarterectomy
E. Bilateral carotid artery stenosis requiring treatment (Treatment of the contralateral vessel must be scheduled at least 30 days post index procedure).
F. Hostile Necks which the Investigator deems safe for transcarotid access including:
   I. Prior neck irradiation
   II. Radical neck dissection
   III. Cervical spine immobility

Clinical High Risk Inclusion Criteria:

G. Patient is ≥ 75 years of age
H. Patient has ≥ 2-vessel coronary artery disease and history of angina
I. Patient has a history of angina
   - Canadian Cardiovascular Society (CCS) angina class 3 or 4
   or
   - unstable angina
J. Patient has congestive heart failure (CHF) - New York Heart Association (NYHA)
   - Functional Class III or IV
K. Patient has known severe left ventricular dysfunction
   - LVEF <30%.
L. Patient has had a myocardial infarction > 72 hours and < 6 weeks prior to procedure.
M. Patient has severe pulmonary disease (COPD) with either:
   - FEV1 <50% predicted or
   - chronic oxygen therapy or
   - resting PO2 of ≤60mmHg (room air)
N. Patient has permanent contralateral cranial nerve injury
O. Patient has chronic renal insufficiency (serum creatinine > 2.5 mg/dL).

The following effectiveness endpoints were assessed 0 to 30 days in the lead-in and ITT pivotal populations comprised of subjects deemed to be at high risk for complications from CEA and treated with the PRECISE Stent System:

- Acute Device Success
- Technical Success
- Procedural Success

The following safety endpoints were assessed 0 to 30 days in the lead-in and ITT populations comprised of subjects deemed to be at high risk for complications from CEA and treated with the PRECISE System:

- Major Adverse Events (stroke, death and myocardial infarction)
- Adverse Events
- Access Site Complications

Compulsory clinical follow-up included neurological examinations (NIH Stroke Scale, Barthel ADL Index, Modified Rankin Scale, and Cranial Nerve Palsy assessment), duplex ultrasound, and laboratory assessments of cardiac enzymes and 12-lead EKG. Subjects who were suspected of having a stroke were asked to return at 3 months post-procedure for a follow-up neurological exam. Subjects suspected of having a procedure related cranial nerve injury were asked to return at 6 months post-procedure for a follow up neurological examination.

Patient follow-up and accountability are presented in the following table for the sub-study population:

Table 4
Patient Follow-Up and Accountability

30-Day Follow-Up		90-Day Follow-Up[1]		6-Month Follow-Up[2]	
N	**%**	**N**	**%**	**N**	**%**
52/52	100%	1/1	100%	N/A	N/A

Patient demographics in the sub-study population are presented in the following table:

Table 5
Patient Demographics in the Sub-Study Population

Observation	All PRECISE Stent Patients in ROADSTER (N=52)
Age (Years)	73.0 ± 9.07
Symptomatic	23.1%
Male	57.7%
Diabetes	34.6%
Hypertension	94.2%
History of Peripheral Artery Disease	34.6%
History of Coronary Artery Disease	48.1%
History of Angina	19.2%
Congestive Heart Failure	11.5%
Recent MI	1.9%
Severe Pulmonary Disease	9.6%
Dyslipidemia	88.5%
History of Stroke	15.4%
History of TIA	21.2%
History of Amaurosis Fugax	13.5%
Current Nicotine Use	25.0%
Age >75 Years	51.9%
Age >80 Years	23.1%
Contralateral Carotid Occlusion	9.6%
High Cervical Carotid Stenosis	15.4%
Restenosis after CEA	28.8%
Bilateral Stenosis Requiring Treatment	32.7%
Hostile Neck	15.4%
>2 Vessel Coronary Disease	7.7%
Chronic Renal Insufficiency	1.9%

The primary effectiveness outcomes include acute device success, technical success, and procedural success. In the sub-study population, acute device success was defined as the ability to insert the device, establish flow reversal, and remove the device was 100%. Technical success defined as acute device success plus the ability to deliver interventional tools was 100% in the sub-study population. Procedural success defined as technical success in the absence of a Major Adverse Event (S/D/MI) was 98.1% in the sub-study population.

[1] For only those subjects suspected of having a stroke.
[2] For only those patients suspected of having a Cranial Nerve Injury (CNI)

Table 6: ROADSTER Sub-study - Summary of Baseline Vessel and Lesion Characteristics

Observation	All PRECISE Stent Subjects (n=52)
Target Lesion Location	
Left	27 (51.9%)
Right	25 (48.1%)
Vessel to be Treated	
ICA	37 (71.2%)
ICA + CCA	15 (28.8%)
Distance between clavicle and bifurcation (cm)	
N	52
Mean	6.6
Standard Deviation	1.21
Median	6.5
Minimum, Maximum	5, 10
95% Confidence Interval	(6.3, 6.9)
Target Vessel Calcification	
Normal	26 (50.0%)
Mild	17 (32.7%)
Moderate	6 (11.5%)
Severe	1 (1.9%)
Unknown / NA	2 (3.8%)
Target Vessel Tortuosity	
Normal	10 (19.2%)
Mild	26 (50.0%)
Moderate	10 (19.2%)
Severe	2 (3.8%)
Unknown / NA	4 (7.7%)
Pre-Procedure Vessel Diameter (mm)	
N	52
Mean	6.7
Standard Deviation	1.78
Median	6.8
Minimum, Maximum	4, 11
95% Confidence Interval	(6.2, 7.2)
Target Lesion Length (mm)	
N	52
Mean	18.7
Standard Deviation	8.05
Median	17.6
Minimum, Maximum	5, 39
95% Confidence Interval	(16.4, 20.9)
Pre-Procedure Percent Stenosis (%)	
N	52
Mean	86.1
Standard Deviation	9.01
Median	90.0
Minimum, Maximum	60, 99
95% Confidence Interval	**(83.6, 88.6)**

Table 7
Acute Device, Technical and Procedural Success in Subjects Treated with the PRECISE Stent

Observations	All PRECISE Stent Subjects (N=52)
Acute Device Success	52 (100%)
Technical Success	52 (100%)
Procedural Success	51 (98.1%)

The Major Adverse Event rate in the sub-study population (subjects treated with a combination of the PRECISE Stent System and the ENROUTE Transcarotid NPS, N=52) was 1.9%. One sub-study subject experienced a minor ipsilateral stroke within the 30-day follow-up period. The following table presents the Major Adverse Event rate in the sub-study population along with other endpoints from the ROADSTER study:

Table 8
Major Adverse Event Rate

Observations (at 30 days)	All PRECISE Stent Patients in ROADSTER (N=52)
PRIMARY ENDPOINTS	
Safety:	
30 Day MAE (Stroke, Death, or MI)	1 (1.9%)
Effectiveness:	
Acute Device Success	52 (100%)
Technical Success	52 (100%)
Procedural Success	51 (98.1%)
SECONDARY ENDPOINTS	
All Death (non-hierarchical)	0 (0.0%)
All Stroke (non-hierarchical)	1 (1.9%)
All Myocardial Infarction (non-hierarchical)	0 (0.0%)
All Cardiac Death (non-hierarchical)	0 (0.0%)
Ipsilateral Stroke (non-hierarchical)	1 (1.9%)
Access Site Complications	
Oozing	0 (0.0%)
Limited Surgical Wound Hematoma	0 (0.0%)
Surgical Wound Hematoma	0 (0.0%)
Arterial Access Site Hematoma	0 (0.0%)
Femoral Vein Access Site Hematoma	0 (0.0%)
Re-bleeding	1 (1.9%)
Contrast Usage (cc)	
N	47
Mean	66.1
Standard Deviation	42.14
Median	55.0
Minimum, Maximum	12, 220

Table 9: Summary of All Adverse Events (Sub-study Subjects)

System Organ Class Preferred Term	All PRECISE Stent Subjects (N=52)
Number (%) of Subjects with one or more Adverse Events	21 (40.4%)
Blood And Lymphatic System Disorders	2 (3.8%)
Anaemia	2 (3.8%)
Cardiac Disorders	1 (1.9%)
Atrial Fibrillation	1 (1.9%)
Cardiac Failure Congestive	1 (1.9%)
Gastrointestinal Disorders	6 (11.5%)
Nausea	5 (9.6%)
Vomiting	3 (5.8%)
General Disorders And Administration Site Conditions	5 (9.6%)
Pain	5 (9.6%)
Infections And Infestations	3 (5.8%)
Adenoviral Upper Respiratory Infection	1 (1.9%)
Infection	1 (1.9%)
Urinary Tract Infection	1 (1.9%)
Injury, Poisoning And Procedural Complications	1 (1.9%)
Post Procedural Haemorrhage	1 (1.9%)
Investigations	3 (5.8%)
Blood Creatine Phosphokinase Increased	1 (1.9%)
Oxygen Saturation Decreased	1 (1.9%)
Troponin Increased	1 (1.9%)
Metabolism And Nutrition Disorders	1 (1.9%)
Hypomagnesaemia	1 (1.9%)
Hypophosphataemia	1 (1.9%)
Nervous System Disorders	4 (7.7%)
Cerebrovascular Accident	1 (1.9%)
Headache	3 (5.8%)
Psychiatric Disorders	1 (1.9%)
Hallucination, Visual	1 (1.9%)
Respiratory, Thoracic And Mediastinal Disorders	3 (5.8%)
Atelectasis	1 (1.9%)
Rales	1 (1.9%)
Rhinorrhoea	1 (1.9%)
Wheezing	1 (1.9%)
Vascular Disorders	8 (15.4%)
Artery Dissection	1 (1.9%)
Hypotension	6 (11.5%)
Orthostatic Hypotension	1 (1.9%)

The patient demographics and results from the ROADSTER sub-study including subjects receiving the PRECISE stent (N=52) were comparable those of the ROADSTER pivotal study cohort (N=141).

9.0 Directions for Use

Only physicians who have received appropriate training for transcarotid stenting and who are familiar with the principles, clinical applications, complications, side effects and hazards commonly associated with carotid interventional procedures should use this device.

9.1 Peri-Procedural Care

Table 10
Pre-Procedure Medications

Medication	Dose	Time prior to procedure	Notes
Aspirin	75-325 mg*	At least 72 hrs	A 650 mg loading dose of aspirin, provided that it is not enteric coated or extended release, at least 4 hours prior to procedure is acceptable if 325 mg dosing was not administered prior to procedure or per the Institution's standard of care.
Clopidogrel	75 mg	At least 72 hrs	A 450 mg clopidogrel loading dose at least 4 hours prior to procedure is acceptable if 75 mg dosing was not administered prior to procedure. The physician may substitute prasugrel, ticlopidine, or a generic version of clopidogrel per the manufacturer's published guidelines. If ticlopidine is prescribed, it must be administered with the appropriate safety monitoring at two weeks and at one month.

*As stated in the "2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease: executive summary." and "ESVS Guidelines. Invasive Treatment for Carotid Stenosis: Indications, Techniques."

Table 11
Post-Procedure Medications

Medication	Dose	Duration post-procedure	Notes
Aspirin	75-325 mg*	Daily, continued indefinitely	Aspirin dosage may be adjusted at the discretion of the Investigator and/or if warranted by the patient's medical condition, i.e., documented intolerance, GI bleed, etc. All change in medications are to be documented on the Concomitant Medication CRF.
Clopidogrel	75 mg	Daily, for minimum of 4 weeks	Clopidogrel dosing may extend at physician's discretion. The physician may substitute prasugrel, ticlopidine, or a generic version of clopidogrel per the manufacturer's published guidelines.

*As stated in the "2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease: executive summary." and "ESVS Guidelines. Invasive Treatment for Carotid Stenosis: Indications, Techniques."

In addition to the usual care and the suggested peri-procedure pharmacological regimen, special attention to diagnosis and management of the following conditions are critical for optimal patient care:

- Bradycardia or tachycardia
- Hypertension or hypotension
- Acute and subacute stent thrombosis
- Hyperfusion syndrome

9.2 Pre-Procedure

Refer to **Section 9.1** of these instructions for the suggested pre-procedure pharmacological treatment regimen. The placement of the stent in a stenotic or obstructed carotid artery should be done in a procedure room equipped with angiography. Angiography should be performed to map out the extent of the lesion(s) and the collateral flow. If thrombus is present, do not proceed with stent deployment. Patient preparation and sterile precautions should be the same as for any angioplasty procedure.
CAUTION: Venous access should be available during carotid stenting in order to manage bradycardia and/or hypotension either by pharmaceutical intervention or placement of a temporary pacemaker if needed.
CAUTION: When catheters are in the body, they should be manipulated only under fluoroscopy. Radiographic equipment that provides high quality images is needed.
a. **Inject contrast media** – Perform an angiogram using the technique described in the ENROUTE Transcarotid NPS's Instructions for Use.
b. **Identify and mark the lesion** – Fluoroscopically identify and mark the lesion, observing the most distal level of the stenosis.

9.3 Device Selection and Preparation
1. Select Stent Size
Measure the length of the target lesion to determine the length of stent(s) required. When more than one stent is required to cover the lesion, the more distal stent should be placed first. Overlap of sequential stents is necessary, but the amount of overlap should be kept to a minimum (approximately 5 mm).

Measure the diameter of the reference vessel (proximal and distal to the lesion). It is necessary to select a stent, which has an unconstrained diameter that is 1 to 2 mm larger than the largest reference vessel diameter to achieve secure placement according to the following Stent Size Selection Table (**Table 12**).

Table 12
ENROUTE Transcarotid Stent System - Stent Size Selection Table

Vessel Lumen Diameter (mm)	Unconstrained Stent Diameter (mm)	% Length Foreshortening* (%)
3.0 – 4.0	5.0	1.2
4.0 – 5.0	6.0	2.4
5.0 – 6.0	7.0	4.1
6.0 – 7.0	8.0	6.2
7.0 – 8.0	9.0	5.8
8.0 – 9.0	10.0	8.0

*Calculated

2. Preparation of Stent Delivery System
CAUTION: The ENROUTE Transcarotid Stent System is supplied **STERILE** and is intended for single use only. **DO NOT** resterilize and/or reuse the device. Assure that the device had been properly stored in a cool, dark, dry place prior to use.
CAUTION: Use the ENROUTE Transcarotid Stent System prior to the "Use By" date specified on the package. Do not use if the pouch is opened or damaged.
CAUTION: The ENROUTE Transcarotid Stent System is shipped with the Tuohy Borst valve **OPEN.** Be careful not to prematurely deploy the stent during preparation. The system should be prepped in the sterile tray per the below instructions. Close the Tuohy Borst valve prior to removing the device from the tray.
a. Open the outer box to reveal the pouch containing the stent and delivery system.

b. Check the temperature exposure indicator on the pouch to confirm that the black dotted pattern with a gray background is clearly visible. Do not use if entire temperature exposure indicator is completely black as the unconstrained stent diameter may have been compromised.
c. After careful inspection of the pouch looking for damage to the sterile barrier, carefully peel the pouch open and remove the tray. Without removing the device from the tray, examine the device for any damage. If it is suspected that the sterility or performance of the device has been compromised, the device should not be used.
d. With the device in the tray, attach a stopcock to the Y connection on the Tuohy Borst valve.
e. (Refer to Fig. 2) With the device still in the tray, attach a 5-cc syringe filled with heparinized saline solution to the opened stopcock attached to the Y connection (9) on the Tuohy Borst valve (1). Ensure that the Tuohy Borst proximal end valve (12) is in the open position. Apply positive pressure to the syringe until saline weeps from the proximal end of the Tuohy Borst valve (12). Lock the Tuohy Borst valve.
f. Close the stopcock attached to the Tuohy Borst Y connection.
g. Extract the stent delivery system from the tray. Examine the device for any damage. Evaluate the distal end of the catheter to ensure that the stent is contained within the outer sheath. Do not use if the stent is partially deployed. If a gap between the catheter tip and outer sheath tip exists, open the Tuohy Borst valve and gently pull the inner shaft in a proximal direction until the gap is closed. Lock the Tuohy Borst valve after the adjustment by rotating the proximal valve end in a clockwise direction.

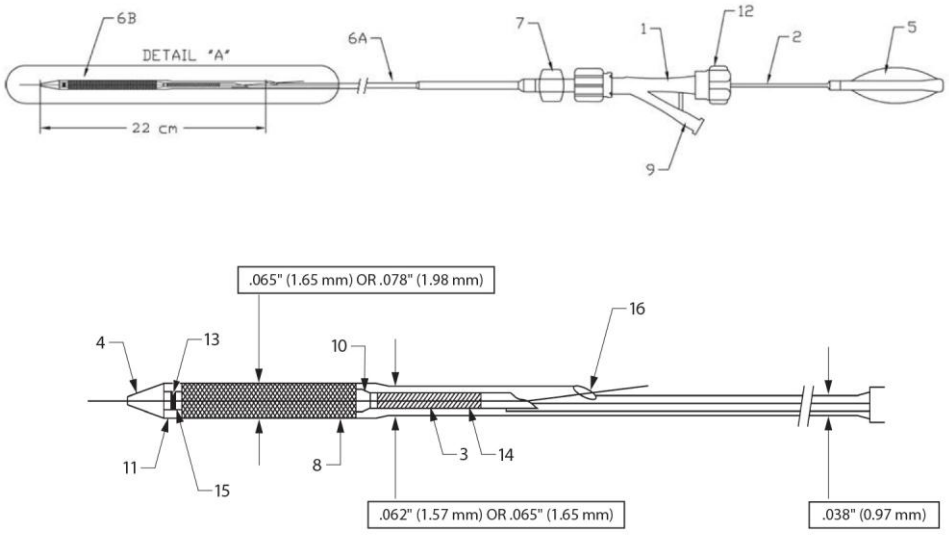
9.4 Stent Deployment Procedure
WARNING: Ensure that the catheter system is flushed according to the steps outlined in "Introduction of Stent Delivery System". Failure to do so could result in air entering the ENROUTE Transcarotid Arterial Sheath.
WARNING: Ensure that there is a tight seal between the ENROUTE Transcarotid Stent System and the valve for the ENROUTE Transcarotid Arterial Sheath during aspiration. Failure to do so could result in air entering the ENROUTE Transcarotid Arterial Sheath.
WARNING: Do not use with Ethiodol or Lipiodol* contrast media, which may adversely affect the stent delivery system.
*Ethiodol and Lipiodol are Trademarks of Gerbert S.A.
WARNING: Do not expose the delivery system to organic solvents (e.g., alcohol), as structural integrity and/or function of the device may be impaired.
CAUTION: The delivery system is not designed for the use of power injection. Use of power injection may adversely affect device performance.

1. Insertion of ENROUTE Transcarotid Neuroprotection System
a. Access the treatment site utilizing the ENROUTE Transcarotid NPS in accordance with the Instructions for Use.
b. The ENROUTE Transcarotid Stent System is compatible with a .014" (0.36 mm) or smaller guidewire.

2. Dilation of Lesion
a. If appropriate, pre-dilate the lesion using standard PTA techniques.
b. Remove the PTA balloon catheter from the patient maintaining lesion access with the guidewire.

3. Introduction of Stent Delivery System

Fig. 2 ENROUTE Transcarotid Stent System Description
(Refer to Fig. 1 for component list)



a. Flush the guidewire lumen of the stent delivery system with heparinized saline by connecting a 5-cc syringe filled with heparinized saline solution to the stopcock attached to the Y connection (9) on the Tuohy Borst valve (1) to expel air. Ensure that the Tuohy Borst proximal end valve (12) is in the locked position to prevent premature stent deployment. Apply positive pressure to the syringe until saline weeps from the guidewire exit port (16). While covering the guidewire exit port (16) with thumb and forefinger, apply positive pressure to the syringe until saline weeps from the catheter tip (4) and the space between the outer sheath radiopaque marker (11) and the catheter tip (4). Continue to flush to ensure all air is removed from the system, then close the stopcock attached to the Y connection (9) on the Tuohy Borst valve.
b. Ensure the Tuohy Borst valve (1) connecting the inner shaft and outer sheath is locked by rotating the proximal valve end (12) in a clockwise direction to prevent premature stent deployment.
c. Advance the ENROUTE Transcarotid Stent System over the .014" (0.36 mm) guidewire until the guidewire exit port (16) is just outside the ENROUTE Transcarotid Arterial Sheath valve. Look for and confirm back flow through the guidewire exit port (16) opening.
d. After confirming back flow, advance the ENROUTE Transcarotid Stent System to the lesion site.
e. Perform contrast injections in accordance to ENROUTE Transcarotid NPS Instructions for Use.
CAUTION: If resistance is met during delivery system introduction, the system should be withdrawn and another system should be used, while the ENROUTE Transcarotid NPS remains in place.

4. Slack Removal
a. Advance the stent delivery system past the lesion site.
b. Pull back the stent delivery system until the radiopaque inner shaft markers (leading and trailing ends) move in position so that they are proximal and distal to the target lesion.
c. Ensure the stent delivery system outside the patient remains flat and straight.
CAUTION: Prior to stent deployment, remove all slack from the catheter delivery system. Slack in the catheter shaft either outside or inside the patient may result in deployment of the stent beyond the lesion site.

5. Stent Deployment
WARNING: The stent is not designed for dragging or repositioning. Once the stent is partially deployed, it cannot be recaptured using the stent delivery system. The mechanism for stent deployment is outer sheath retraction.

Deployment is completed by maintaining inner shaft position while retracting the outer sheath and allowing the stent to expand.
NOTE: It is recommended that heparin (intravenous) be given during the procedure before the ENROUTE Transcarotid NPS is placed. The initial bolus doses of heparin should be approximately 3,000 to 5,000 units (with necessary weight adjustments). Additional bolus doses of heparin should be given to maintain an ACT near 250 seconds during the entire procedure. No heparin should be given after the procedure until hemostasis at the puncture site is achieved.
a. Verify that the delivery system's radiopaque inner shaft markers (leading and trailing ends) are proximal and distal to the target lesion.
b. Verify that the delivery system's radiopaque inner shaft marker (trailing end) is distal to the radiopaque marker at the tip of the ENROUTE Transcarotid Arterial Sheath.
c. Unlock the Tuohy Borst proximal valve end connecting the inner shaft and outer sheath of the delivery system.
d. Ensure that the ENROUTE Transcarotid Arterial Sheath does not move during deployment.
e. Initiate stent deployment by retracting the outer sheath while holding the inner shaft in a fixed position. Deployment is complete when the outer sheath marker passes the proximal inner shaft stent marker.

CAUTION: When more than one stent is required to cover the lesion, or if there are multiple lesions, the more distal stent should be placed first. Stenting in this order obviates the need to cross the proximal stent in placement of the distal stent and reduces the chance for dislodging stents that have already been placed.
CAUTION: Overlap of sequential stents is necessary but the amount of overlap should be kept to a minimum (approximately 5 mm). In no instance, should more than two (2) stents ever overlap.

6. Post-Deployment Stent Dilatation
WARNING: Long-term outcomes following repeat dilatation of endothelialized stents are unknown.
CAUTION: The delivery system is not designed for the use of power injection. Use of power injection may adversely affect device performance.
CAUTION: Re-crossing a deployed stent with adjunct devices must be performed with caution.
a. While using fluoroscopy, withdraw the entire delivery system as one unit, over the guidewire and out of the body. Remove the delivery device from the guidewire.
NOTE: If any resistance is met during delivery system withdrawal, advance the outer sheath until the outer sheath marker contacts the catheter tip and withdraw the system as one unit. (Do not remove guidewire.)
b. Using fluoroscopy, visualize the stent to verify full deployment.
c. If incomplete expansion exists within the stent at any point along the lesion, post-deployment balloon dilatation (standard PTA technique) can be performed.
d. Select an appropriate size PTA balloon dilatation catheter and dilate the lesion with conventional technique. The inflation diameter of the PTA balloon dilatation catheter used for post-dilatation should not exceed the diameter of the reference vessel.
e. Remove the PTA balloon from the patient.

7. Post Stent Placement
a. A post-stent angiogram can be obtained per institutional protocol.
b. Remove the ENROUTE Transcarotid NPS in accordance with that device's Instructions for Use.
c. Follow the suggested post-procedure pharmacological treatment regimen described in **Section 9.1** of these instructions.
WARNING: In the event of thrombosis of the expanded stent, thrombolysis and PTA should be attempted.
WARNING: In the event of complications such as infection, pseudoaneurysm or fistulization, surgical removal of the stent may be required.

8. Patient Information

In addition to these Instructions for Use, the ENROUTE Transcarotid Stent System is packaged with a Stent Implant Card for the patient that contains specific information about the ENROUTE Transcarotid Stent System. All patients should be instructed to keep this card in their possession at all times for procedure/stent identification.

9. How Supplied

ENROUTE Transcarotid Stent System is supplied sterile by ethylene oxide gas and is intended for SINGLE USE ONLY. It has not been validated for resterilization or reuse. Silk Road Medical shall not be responsible for any damages, including without limitation direct, incidental or consequential damages, resulting from reuse or resterilization of this product.

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ENROUTE™ Transcarotid Stent and Neuroprotection Systems

This guidebook...

This guidebook is provided as a courtesy from Silk Road Medical intended to help you learn more about carotid artery disease.

For your convenience, a glossary of medical terms is included at the end of this booklet. You will find many words that are in bold throughout the text are defined in the glossary.

This booklet is only a guideline. It provides basic information about carotid artery disease and its treatment with the **ENROUTE™ Transcarotid Stent System** and the **ENROUTE™ Transcarotid Neuroprotection System**. It is not intended to diagnose a medical condition. The treatment of carotid artery disease may vary according to each individual's unique needs and doctor assessments. As with any medical procedure, the best source for information and advice is your doctor.

Table of Contents

Introduction

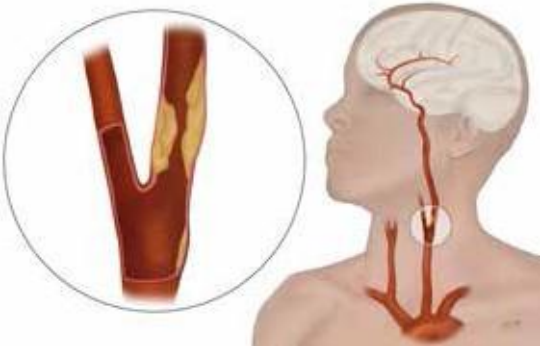
This guidebook is designed to help you and your family understand vascular disease of the **carotid arteries** of your neck and transcarotid treatment with a vascular **stent**. If you have any questions as you read, please write them down and discuss them with your doctor or nurse.

Vascular disease in the carotid arteries of the neck

Vascular disease is caused by the build-up of fatty substances that collect and stick to the linings of your arteries, in a process known as **atherosclerosis**. You may also hear the terms **"plaque"**, "blockage", **"lesion"**, or **"stenosis"**. As the **plaque** build-up continues, the internal lining of your artery thickens which causes the artery to narrow and limit blood flow to vital tissues and organs. Some of the more commonly affected arteries are those located in the heart, legs, arms, neck, and kidneys. The symptoms from these blockages depend on what artery is affected and the severity of the blockage causing limited blood flow. This guidebook describes peripheral vascular disease of the arteries in your neck, which are called **carotid arteries**.

The carotid arteries

Function - Arteries are vessels that carry blood away from the heart. The carotid arteries extend from the main artery (aortic arch) coming directly from your heart and supply oxygen-rich blood to the brain.



Carotid Artery Narrowing (stenosis) - When **plaque** builds up in the **carotid arteries**, they begin to narrow and slow down blood flow to the brain. This is called carotid artery **stenosis**. Severe carotid artery **stenosis** can be a major cause of stroke.

The carotid arteries

Diagnosis - You should be screened for carotid artery stenosis if you have:

- Weakness, numbness, tingling or paralysis of the arm, leg, or face on one side of your body
- Trouble swallowing
- Loss of eyesight or blurry eyesight in one eye
- Dizziness, confusion, fainting, or coma
- Unexplained slurred or garbled speech

Sometimes, patients are screened for carotid artery **stenosis** if the doctor knows the patient has vascular disease elsewhere in the body. Blockages can also be found when your physician hears a sound through a stethoscope placed on the neck. The sound is caused by blood flowing past the blockage.

The carotid arteries (continued)

The following tests may be performed if carotid artery disease is suspected.

Carotid artery ultrasound: This test uses sound waves that produce an image of the **carotid arteries** on a TV screen, and can be helpful in identifying narrowing in the **carotid arteries**. This test is painless and does not require the use of needles, dye, or x-rays.

Angiography: An **angiogram** uses x-rays to take a picture of your carotid artery. In order for the x-ray to "see" your arteries, a dye is injected through a small tube **(catheter)** inserted into an artery in the groin or arm. This procedure will determine exactly where the narrowing is located and will help to guide further treatments. You will be awake for the test, although you will be given a light sedative to relax you. The injection of dye may cause a warm sensation. After the test is complete, you will need to lie flat for 5-6 hours to allow the puncture site in your groin or arm to heal.

If carotid disease is diagnosed during one of these tests, your doctor will discuss your treatment options with you.

Treatment options

There are four basic treatment options for patients with carotid artery stenosis. It is important to inform your doctor about your entire medical history. Be sure to ask your doctor to explain the risks and benefits of your treatment options and answer any questions you or your family may have.

Diet modification and exercise: Decreasing the amount of fat and **cholesterol** in your diet in combination with exercise (especially 30 minutes of walking) in your daily activities may be recommended. Your doctor will make specific dietary and exercise recommendations for you. Other lifestyle changes may also need to be made, including stopping smoking.

Medical Management: Your doctor may prescribe medicine to help thin your blood **(anticoagulants)**, which will improve blood flow and help prevent your blood from clotting. Additionally, medications that help to lower your **cholesterol** and fats may be prescribed. If you have diabetes, your physician may change your medications to help reduce your blood sugar levels.

Both of the above options do not require any physical intervention, but each of them may not be enough to manage your disease completely. If neither of the above options is sufficient to manage your disease, one of the following interventional options may be recommended.

Treatment Options

Carotid Endarterectomy (open surgery): This surgical procedure removes **plaque** from inside of your carotid artery in order to restore normal blood flow to your brain. You are often put to sleep for this procedure using general anesthesia. The surgeon exposes your carotid artery through an incision (cut) in the side of the neck. The artery is clamped on both sides of the blockage and the artery is then opened. If the brain is not getting enough blood flow, a tube called a "shunt" may be placed around the blockage to keep blood flow during the procedure. The **plaque** inside of the artery is then removed and the artery is sewn back together. Sometimes, it is necessary to use a patch or graft when sewing the artery walls together to make the artery wider.

Doctors have been successfully conducting the procedure for over 50 years. Be sure to ask your doctor about the risks associated with this surgical procedure.

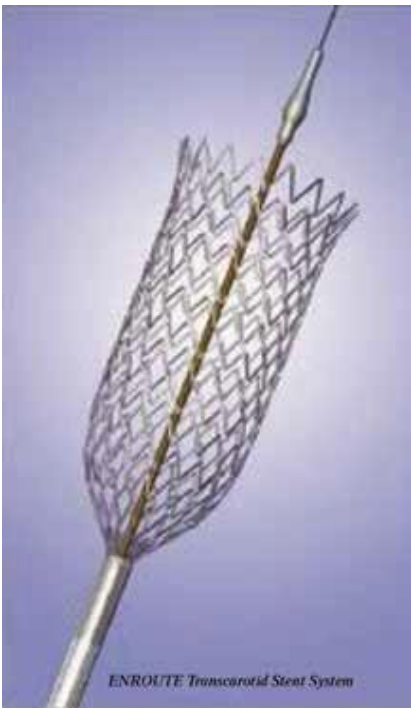
Treatment Options

Transfemoral Carotid Artery Stenting is a procedure in which your physician inserts a slender, metal-mesh tube, called a stent, (introduced through your femoral artery) which expands inside your carotid artery to increase blood flow in areas blocked by plaque. This procedure has been performed safely for over 10 years.

Carotid Artery Stenting with the ENROUTE Transcarotid Stent and Neuroprotection Systems: This procedure is presently available to you only if you have other conditions that place you at a high risk for carotid endarterectomy (open surgery). The procedure involves placement of a **stent** into your carotid artery. The Silk Road Procedure is performed through a small incision at your neckline just above your clavicle. The incision is smaller than a typical Carotid Artery Endarterectomy (CEA) incision. Your surgeon will temporarily place a tube directly into your carotid artery and connect it to a system that will temporarily direct blood flow away from your brain, to protect against particles that may come loose during the procedure. Your blood will flow through the system and very small particles may be captured in a filter. Your filtered blood will then be returned through a tube in your upper leg. While flow is reversed, a stent is placed at the area of your blockage. The stent holds the artery open to allow normal blood flow to the brain. The stent is approximately ¾ to 1½ inches in length and ¼ inch in diameter when expanded. You may remain awake during the stenting procedure. Please refer to “Stent implantation procedure” in this booklet for a more detailed description of the procedure. After the stent is placed successfully, flow reversal is turned off and blood flow resumes in its normal direction.

Device Description

ENROUTE Transcarotid Stent System: The ENROUTE Transcarotid Stent is made of a metal called nitinol. The **stent** is inside a tube (delivery system) for passage into the body to the **carotid arteries**, where it is released to hold open the blockage.



Device Description

ENROUTE Transcarotid Neuroprotection System: The ENROUTE Transcarotid Neuroprotection System draws upon proven surgical techniques to reduce the risk of stroke during carotid artery stenting. It allows physicians to deliver a stent directly from the neck, which is intended to avoid complications associated with starting from the femoral artery in the groin, which is typically used in carotid artery stenting procedures. To provide protection for the patient's brain during the entire procedure, the ENROUTE Transcarotid Neuroprotection System temporarily reverses blood flow in order to move any potential particles away from the brain.

Clinical Studies

The ENROUTE Transcarotid Stent System was approved via two clinical studies.

The ROADSTER study was a multi-center clinical study of the ENROUTE Transcarotid Neuroprotection System used together with any FDA- approved carotid artery stent used for treatment of carotid artery disease in patients who are at high risk for complications from carotid endarterectomy surgery. A sub-study of ROADSTER patients received the Cordis PRECISE stent, which is the same as the ENROUTE Transcarotid stent.

Clinical Studies

The ROADSTER sub-study demonstrated that the safety and effectiveness of the approved PRECISE stent system was not impacted when delivered through a transcarotid approach using the ENROUTE Transcarotid Neuroprotection System (i.e., via an incision in your neck instead of the typical femoral artery approach for carotid stenting, which involves an incision in your leg). One out of 52 patients in the sub-study experienced a minor stroke within 30 days following the procedure.

The Silk Road Medical Embolic Protection System: First In Man Study (PROOF) was a clinical study that collected short-term data from 75 patients in Germany using an early design of the ENROUTE Transcarotid Neuroprotection System. A subset of patients in the PROOF study (13 patients) was treated with a combination of the PRECISE Stent and the ENROUTE Transcarotid Neuroprotection System. None of the 13 patients experienced a major stroke, myocardial infarction, or death during the 30-day post-procedural period.

Potential Risks

Treatment with the ENROUTE Transcarotid and Neuroprotection Systems may involve the following risks. Your doctor can help you understand these risks.

- Air embolism (air bubbles in arteries or veins)
- Allergic reaction to device materials
- Anemia (lack of healthy red blood cells)
- Aneurysm (weakened area of the artery)
- Angina/coronary ischemia (chest pain/reduced blood flow to heart tissue)
- Arrhythmia (irregular heart beat that may require medical correction)
- Arterial dissection (separation of the walls of the artery)
- Arterial occlusion/restenosis of the treated vessel (blockage of the artery or recurrence of blockage)
- Arterial occlusion/thrombus at puncture site (blockage at the puncture site or blood clot)
- Arterial occlusion/thrombus remotely (blockage or blood clot somewhere else in the body)
- Arteriovenous fistula (abnormal blood flow from an artery to a vein)
- Atelectasis (collapsed lung)
- Atrial Fibrillation (irregular heart rate)
- Bacteremia or septicemia (harmful bacteria in the blood)
- Cerebral edema (excess fluid in the brain)
- Congestive heart failure (poor functioning of the heart)
- Death
- Embolization, arterial (debris in the artery)
- Embolization, stent (debris in the stent)
- Emergent repeat hospital intervention
- Fever
- Gastrointestinal disorders (digestive system problems)
- GI bleeding from anticoagulation/antiplatelet medication (bleeding in the digestive system from medications)
- Hallucination (false sensations cause by the brain)
- Hematoma bleed, access site (abnormal collection of blood at the access site)
- Hematoma bleed, remote site (abnormal collection of blood away from the access site)
- Hemorrhage (bleeding from an artery or vein)
- Hyperperfusion syndrome (leaking of fluid from blood vessels that cause brain swelling or headache)
- Hypotension/hypertension (abnormally low or high blood pressure)

Potential Risks

- Hypomagnesaemia (abnormal magnesium levels in the blood)
- Hypophosphatemia (abnormal levels of phosphate in the blood)
- Infection
- Intimal injury/dissection (injury to the walls of an artery)
- Ischemia/infarction of tissue/organ (lack of blood flow to tissue or organ/permanent damage to tissue or organ)
- Local infection and pain at insertion site
- Malposition (failure to deliver the stent to the intended site)
- Myocardial infarction or cardiac enzyme increase (heart attack or abnormal increase in heart muscle proteins that could signify heart muscle damage)
- Nausea
- Oxygen saturation decrease (decreased concentration of oxygen in the blood)
- Pain
- Pseudoaneurysm (injured blood vessel causing blood to leak)
- Rales (clicking or bubbling sounds in the lungs)
- Renal failure (liver failure)
- Respiratory Infection (lung infection)
- Restenosis of the vessel (> 50% obstruction) (re-blockage of the vessel)
- Rhinorrhea (runny nose)
- Seizure
- Severe unilateral headache
- Stent migration
- Stent thrombosis (blood clots in the stent)
- Stroke
- Transient ischemic attack (mini-stroke lasting a short time)
- Transient intolerance to reverse flow (temporary loss of consciousness or reduced consciousness)
- Urinary tract infection
- Vasospasm (abnormal constriction of a blood vessel)
- Venous occlusion/thrombosis, at puncture site (blockage or blood clots in a vein used for access)
- Venous occlusion/thrombosis, remote from puncture site (blockage or blood clots in a vein not used for access)
- Vessel rupture, dissection, perforation (burst or damaged artery or vein)
- Vomiting (throwing up)
- Wheezing (difficulty breathing)

Potential Risks

Contraindications:

If you cannot take antiplatelet medication and/or anticoagulation therapy medications, if you have a bleeding problem, or if you have a known allergy to nickel or Nitinol, then this procedure is not suitable for you.

Preparing for your procedure

When **plaque** builds up in your **carotid arteries**, they begin to narrow and slow down blood flow to your brain. This is called carotid artery stenosis. Severe carotid artery stenosis is a major cause of stroke. The benefit of having **carotid artery** stenting is to reduce carotid artery stenosis.

As with any intervention, the stenting procedure involves some risks. These risks include, but are not limited to:

- Stroke, heart attack, allergic reaction to the dye, slow heartbeat which requires treatment, or death
- Rupture or damage to your carotid artery, excessive bleeding, infection/fever
- Bleeding, bruising or swelling at the access site in your neck
- Failure to deliver the stent to the site of your blockage (treatment failure)

Be sure that your doctor has discussed the procedure and the possible benefit and risks with you and that any questions you have are answered.

Preparing for your procedure (continued)

Upon admission to the hospital, you will have had tests such as carotid artery ultrasound, angiography and routine blood tests. Be sure to tell your doctor what medications you are currently taking and any allergies you might have. You will probably be asked not to eat or drink anything after midnight on the night before your procedure. You will be asked to take aspirin for one to two days before the procedure and your doctor may ask you to change other medications.

The procedure will be performed in a **catheterization** laboratory or an operating room. You will lie on a table, and an x-ray camera will pass over your neck during the procedure. Your heart and blood pressure will be monitored during the course of the procedure.

The procedure will involve little to moderate pain and you will experience mild to moderate discomfort during the first few hours following the procedure. Dye injected through **catheters** will allow the doctor to see the area of blockage in your vessels. Although rare, dye may produce an allergic reaction causing low blood pressure and breathing difficulties.

Flow reversal and stent implantation procedure

Your procedure will be performed in a room equipped with special instruments and x-ray equipment. Once you enter this room, you will be moved onto an x-ray table. You will be covered with sterile sheets and the areas where the incision will be made and the **catheters** will be inserted (groin & neck) will be shaved and washed with an antiseptic solution to prevent infection.

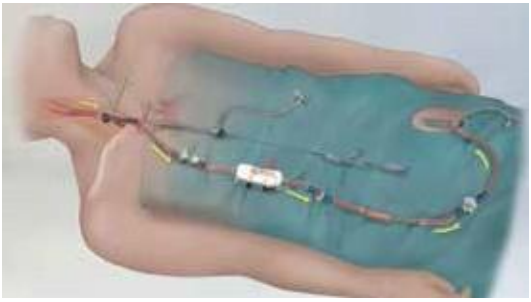
You may be awake during your procedure. Your doctor or a hospital member may give you instructions. It is important to listen for these instructions and do what is asked.

A numbing medication **(local anesthetic)** will be used at the sites where the **catheter** is inserted and where the incision will be made. You may feel a stinging sensation when this medication is given. After the medication takes effect, you should only feel dull pressure where the doctor is working with the **catheters**. Where the neck is cut, a small tube called a sheath will be inserted into your carotid artery. The sheath provides a passageway through which the doctor can insert the ENROUTE Transcarotid Neuroprotection System, the ENROUTE Transcarotid Stent System, and other potential catheters.

Flow reversal and stent implantation procedure (continued)

Dye injected through the **catheters** will allow the doctor to see the area of blockage in your arteries. An x-ray machine with a TV screen allows the doctor to see your arteries and any **catheters** that are moved in your arteries. Once your doctor has taken pictures of the blockage, the ENROUTE Transcarotid Neuroprotection System is activated and flow reversal begins. Your filtered blood will then be returned through a tube in your upper leg.

The ENROUTE Transcarotid **Stent** is then put into the **carotid artery** on a delivery system and moved to stabilize the blocked area of the artery. The **stent** will open to fit the artery when it is released. One or more **stents** may be implanted. After the **stent** is placed, the delivery system is taken out. The **stent** stays in place permanently, holding the artery open. After **stent** placement is completed, the ENROUTE Transcarotid Neuroprotection System is turned off and taken out of the body. The small incision in your neck is then sutured closed. Your procedure will take approximately 60-90 minutes.



After your procedure

The sheath that was put in your leg at the beginning of the procedure is removed at the end of the procedure and handheld pressure will be administered to stop the bleeding. After the procedure, you will be moved to a special care unit where you will be closely monitored by the hospital staff. Your blood pressure and heart rhythm will be monitored continuously.

While you are in the hospital, notify your doctor if you feel lightheaded or dizzy, have trouble swallowing, have trouble seeing, or have blurry eyesight in one eye. Also notify them if you have weakness, numbness, or tingling or can't move your arm, leg, or face on one side of your body, or have unexplained slurred or garbled speech, or if you notice any bleeding, swelling, or discomfort from where your neck was cut or where the sheath was placed in your leg.

Your recovery

Before you leave the hospital, your doctor will give you advice for activity, diet and medications. You will be asked to avoid hard activities like lifting for at least a week. You will be told when you can resume normal activity and return to work. Your doctor will prescribe medications for you to take to prevent blood clots from forming in your newly opened artery. Please notify your doctor if these medications cause unpleasant reactions. Do not stop taking them unless your doctor tells you to do so. Different medications may be prescribed that suit you better.

Patients who undergo carotid **stent** implantation are usually discharged from the hospital the next day. You should arrange to have someone take you home rather than driving yourself. After you leave the hospital, it is important to keep all of your scheduled appointments so that your progress can continue to be monitored.

If you have any pain, discomfort or bleeding from where your neck was cut or where the sheath was placed in your leg, call your doctor immediately. Also call your doctor immediately if you are lightheaded or dizzy, have trouble swallowing, have trouble seeing, or have blurry eyesight in one eye. Also notify your doctor if you have weakness, numbness, tingling or can't move your arm, leg, or face on one side of your body, or have unexplained slurred or garbled speech. If your doctor can not be reached immediately, call 911 to be taken to the nearest hospital emergency room.

After **stent** placement, you will be followed closely to monitor your recovery. An **ultrasound** will be performed at a later date to determine if any narrowing has occurred in the treated artery.

Lifestyle changes

You and your doctor have formed a team in an effort to reduce the risk of **restenosis** (re-occurring blockage) in the area of your **stent**.

To help stay healthy in the future, you are encouraged to make important diet, exercise, and lifestyle changes. Some patients may need few modifications while others may need to make many changes. It is extremely important to avoid smoking. If you need help quitting, please notify your healthcare provider.

Stent implant card

Be sure your doctor gives you a completed "Stent implant card" that you can keep as a record of your procedure. Carry the card with you at all times and show it to any doctors or healthcare workers who may be treating you. The card will have the date of the **stent** procedure, location of the **stent** in your body, the name of the doctor who performed the procedure, and other important information.

If you require magnetic resonance imaging (MRI) after carotid artery stenting

If you require **MRI** after carotid artery stenting, tell your healthcare providers that you have a stent and show them your stent implant card, which will advise them to refer to the ENROUTE Transcarotid Stent System Instructions for Use or to call 408-720-9002 for more information about **MRI** compatibility of the ENROUTE Transcarotid Stent System.

Conclusion

You have a very important role to play in order to ensure that your stent implantation is successful. It is essential that you cooperate with your doctor and follow through with your responsibilities as part of the patient/doctor medical team. Keep your appointments, live a healthy lifestyle, and continue to follow your doctor's advice with respect to any other medical conditions that you are being treated for. If you have any questions or concerns, please contact your doctor to discuss them. It is important that you get the most benefit from your treatment and join the thousands of people with vascular disease who are leading healthy, productive lives.

Glossary

Angiogram: A procedure in which contrast dye is injected into the arteries to diagnose a narrowing or blockage of an artery.

Anticoagulant: A medicine that slows or prevents the clotting of blood.

Atherosclerosis: The process of fatty deposits and/or calcium buildup (plaque) on the inside of the arteries.

Carotid Arteries: Arteries are vessels that carry blood away from the heart. The carotid arteries extend from the main artery (aortic arch) coming directly from the heart and supply oxygen rich blood to the brain.

Catheter: A long hollow tube used to introduce a device, drug, or dye into a blood vessel,

Catheterization: A procedure that involves passing a tube (catheter) through blood vessels and injecting dye to detect blockages.

Cholesterol: A substance that circulates in the blood and when deposited in the artery, plays a role in the formation of blockages. Cholesterol originates in foods that are rich in animal fat.

Lesion: A blockage in a blood vessel. Also known as plaque or stenosis.

Local Anesthetic: A substance used to numb the area to which it is applied.

MRI (Magnetic Resonance Imaging): A diagnostic test that uses magnetic waves to obtain images of the inside of your body.

Plaque: An accumulation or build-up of fatty deposits, calcium, and/or cell debris in an artery that leads to narrowing of the artery.

Restenosis: The recurrence of a narrowing of blockage in an artery after treatment.

Stent: An expandable, metallic tubular shaped device that provides structural support for a vessel.

Stenosis: A narrowing in your arteries caused by plaque build-up, which restricts blood flow.

Ultrasound: A non-invasive test using sound waves to determine the presence of arterial narrowing.

Please visit www.silkroadmed.com

Contact Information:
Your doctor or nurse will review this material with you. We encourage you to ask them any questions regarding your treatment and recovery.

Additionally, your doctor may recommend that you join a support group to speak with others who have undergone similar procedures. Ask your doctor for contact information about these groups and possible web site addresses.

Caution: Federal law restricts this device to sale by or on the order of a physician.

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