ENROUTE®
Transcarotid Neuroprotection System

SILKROAD MEDICAL®

Indications for Use

The ENROUTE Transcarotid Neuroprotection System (ENROUTE Transcarotid NPS) is intended to provide transcarotid vascular access, introduction of diagnostic agents and therapeutic devices, and embolic protection during carotid artery angioplasty and stenting procedures for patients diagnosed with carotid artery stenosis and who have appropriate anatomy described below:

- Adequate femoral venous access
- Common carotid artery reference diameter of at least 6 mm
- Carotid bifurcation is a minimum of 5 cm above the clavicle as measured by duplex Doppler ultrasound (DUS) or computerized axial tomography (CT) angiography or magnetic resonance (MR) angiography.

Contraindications

The ENROUTE Transcarotid NPS is contraindicated for use in patients exhibiting the following conditions:

- Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated
- Patients with unresolved bleeding disorders
- Patients with severe disease of the ipsilateral common carotid artery
- Uncontrollable intolerance to flow reversal (i.e. pre-conditioning does not result in in tolerance to vessel occlusion/flow reversal)

Device Description

The ENROUTE Transcarotid NPS consists of four primary components:

Component
Transcarotid Arterial Sheath with Arterial Dilator
Venous Return Sheath with Venous Dilator
Flow Controller with Filter
0.035" (0.9 mm) Extra Support, J-Tip Guidewire

When assembled, the ENROUTE Transcarotid NPS creates an arteriovenous shunt that has the ability to reverse the flow of blood at the treatment site of the carotid arteries from antegrade to retrograde, shunting embolic particles away from the cerebral circulation (see Figure 1 below).

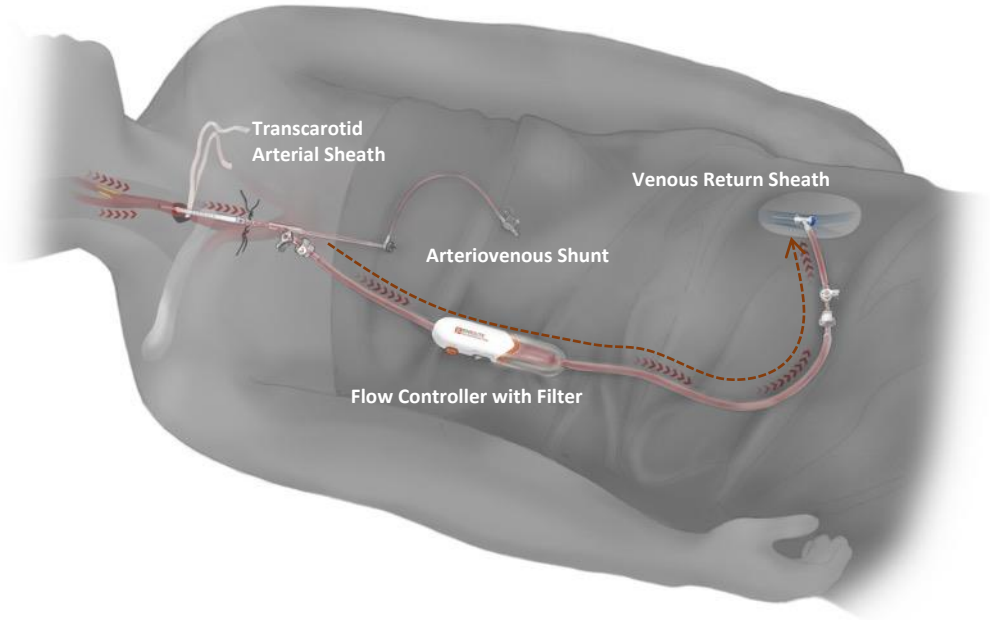

Figure 1 - ENROUTE Transcarotid Neuroprotection System

The symbols glossary is provided in this IFU on page 19.

Table 1: Key Dimensions of the ENROUTE Transcarotid NPS

Attribute	Transcarotid Arterial Sheath	Venous Return Sheath	Arteriovenous Shunt**
Working Length	11 cm	11 cm	
Total Length	33.2 cm	13.6 cm	102cm
Inner Diameter	8 Fr (2.6 mm)	8 Fr (2.6 mm)	
Outer Diameter	10.5 Fr (3.5 mm)	10.5 Fr (3.5 mm)	

** The Arteriovenous Shunt total length includes the large diameter tubing from the Arterial Sheath to the Venous Return Sheath as shown by the dotted line in Table 1.

Each component of the ENROUTE Transcarotid NPS is described in the following sections.

Transcarotid Arterial Sheath

The Transcarotid Arterial Sheath with Uber-Flex™ Angled Tip consists of an 8 Fr. Arterial Sheath and an Arterial Dilator (see Figure 2). The Transcarotid Arterial Sheath permits access to the common carotid artery (CCA), and includes the following features:

- A radiopaque tip which allows visualization of the sheath tip under fluoroscopy.
- Printed centimeter markers to measure sheath insertion depth.
- A removable Sheath Stopper, which prevents the Arterial Sheath from entering more than 2.5 cm into the artery. The body of the Sheath Stopper has suture grooves for which sutures may be placed across for sheath stability.
- A Hemostasis Valve on the proximal end of the Sheath to provide hemostasis after Dilator removal and to allow introduction of interventional devices into the Sheath.
- An Extension Tube which extends the Hemostasis Valve of the Arterial Sheath away from the radiation field.
- Suture Eyelets for securement of the Arterial Sheath.
- An Arterial Side Arm with Stopcock to permit saline prep, contrast injection, and aspiration.
- An Arterial Stopcock which connects the Arterial Sheath to the Flow Controller via a "quick connect" type fitting. The handle on the Arterial Stopcock is used to shunt flow once the Arterial Sheath is connected to the Flow Controller.

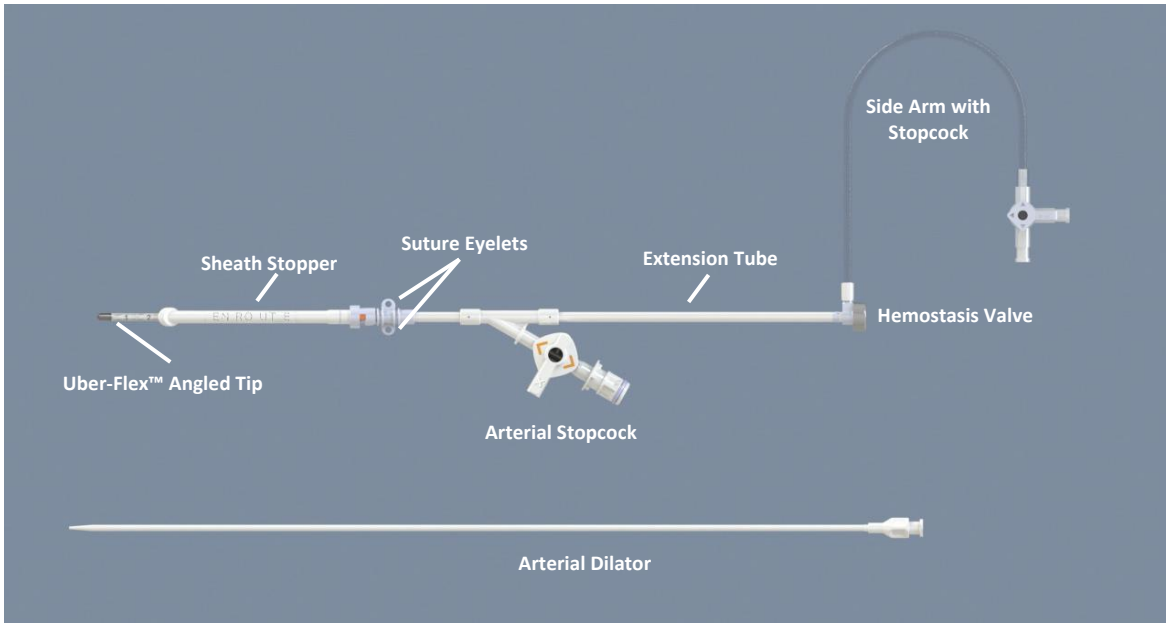

Figure 2 - ENROUTE Transcarotid Arterial Sheath

Venous Return Sheath

The Venous Return Sheath consists of an 8 Fr. Venous Sheath and a Venous Dilator (see Figure 3). The Venous Return Sheath is used to gain femoral vein access, and includes the following features:

- A radiopaque tip which allows visualization of the sheath tip under fluoroscopy.
- A Hemostasis Valve on the proximal end of the Sheath to provide hemostasis after removal of the Dilator.
- Suture Eyelets for securement of the Venous Return Sheath.
- A Venous Flow Line and Stopcock which connects the Venous Return Sheath to the Flow Controller via a "quick connect" type fitting. The Venous Stopcock also permits saline prep, saline and contrast injections, and aspiration.

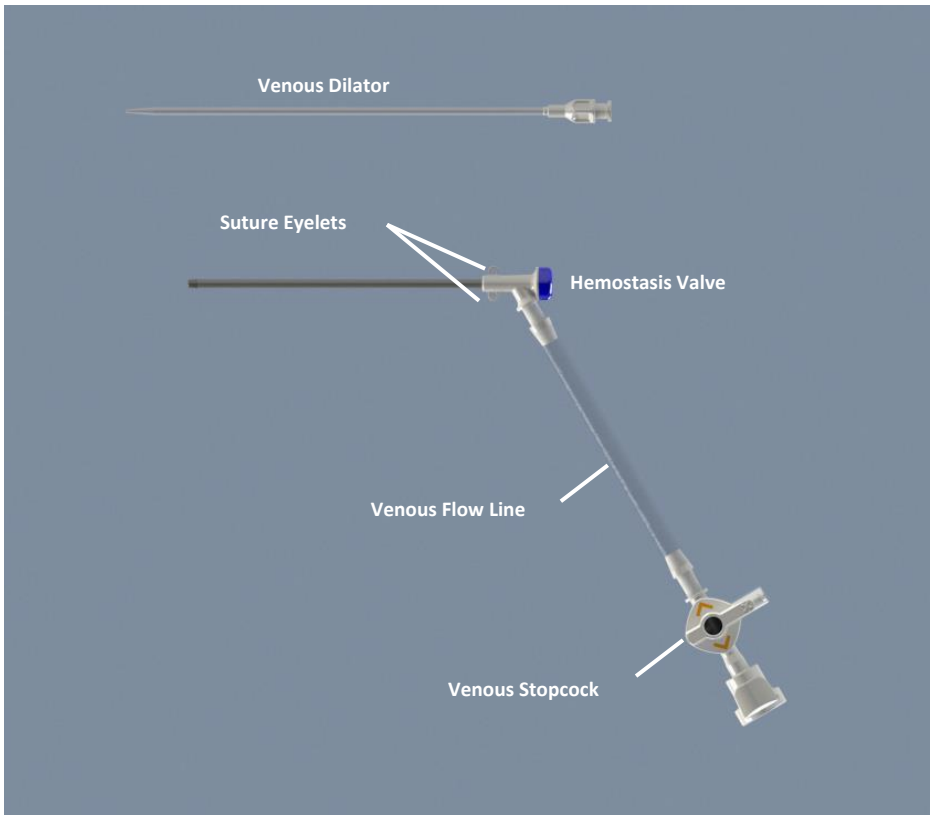

Figure 3 – ENROUTE Venous Return Sheath

Flow Controller

The Flow Controller (see Figure 4) connects the Transcarotid Arterial Sheath to the Venous Return Sheath. The Flow Controller includes the following features:

- A Flow Controller which regulates the rate of reverse flow via the High/Low Switch and which allows temporary shut off of the Controller/Filter Line during contrast injections via the Flow "Stop" Button. (Detail in Figure 5). Pressing the switch towards "Low" sets the flow setting to low flow and pressing the switch towards "High" sets the flow setting to high flow.
- An in-line Filter which captures embolic debris from the blood flow through the shunt.
- An in-line Check Valve which prevents inadvertent flow or injection of blood or fluid through the shunt in the arterial direction.
- "Quick-Connect" type connections to the Transcarotid Arterial Sheath and Venous Return Sheath.
- A "Pull to Prep" Toggle Loop that is removed and discarded prior to system prep and usage.

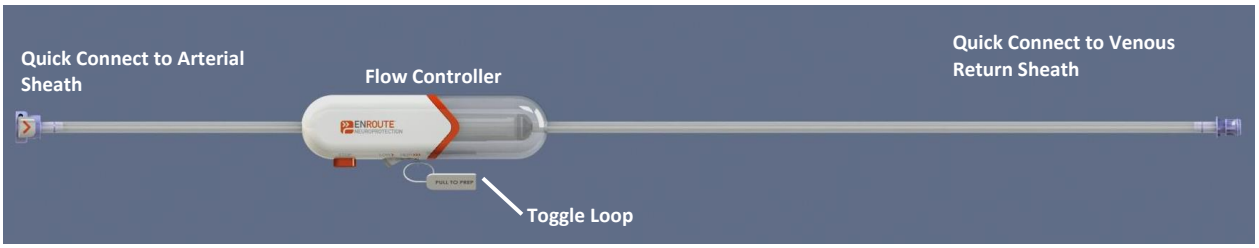

Figure 4 – ENROUTE Flow Controller

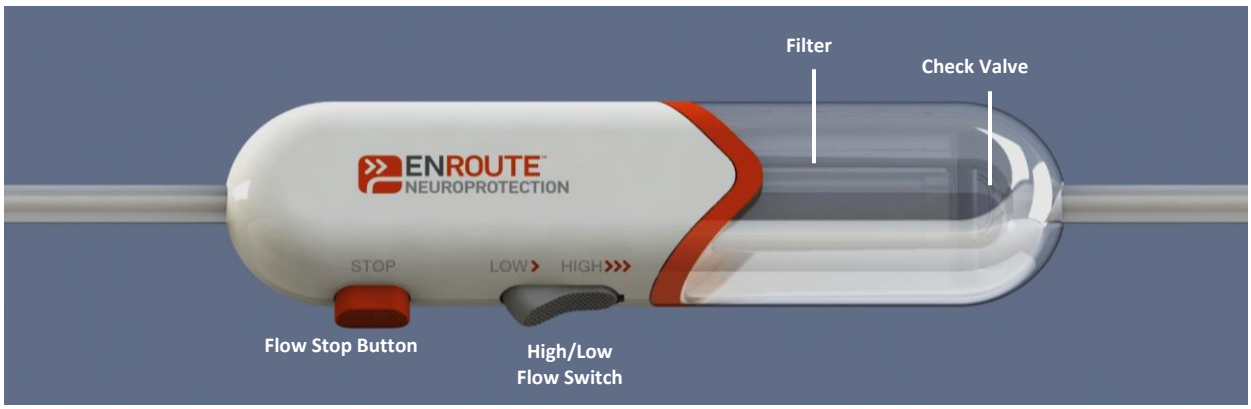

Figure 5 – Flow Controller Detail

Guidewire

The Guidewire (see Figure 6) is a 90 cm (35.4”) long 0.035” (0.9 mm) Extra Support J-Tip Guidewire. The Guidewire consists of a polytetrafluoroethylene (PTFE) coated Nickel-Titanium Alloy (Nitinol) core with a stainless-steel coil covering the distal tip. The flexible, 7.5 mm (0.30”) outer diameter, J-Tip is an atraumatic interface with the carotid artery and central vein. The 0.035” (0.9 mm) Nitinol core provides additional support to facilitate the insertion of the ENROUTE Transcarotid Arterial Sheath and the ENROUTE Venous Return Sheath into the vasculature.

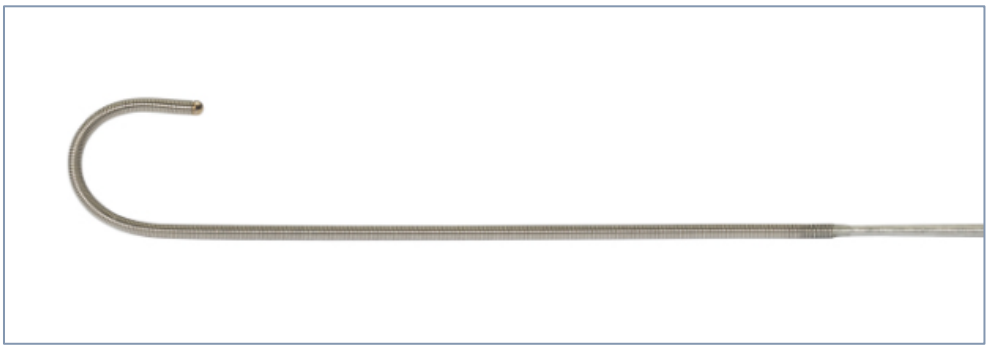

Figure 6 – ENROUTE 0.035" (0.9mm) Guidewire

How Supplied/Storage and Handling:

- The ENROUTE Transcarotid Neuroprotection System (ENROUTE Transcarotid NPS) is provided as a system in a single package. The product is sterile and non-pyrogenic in unopened and undamaged packaging.
- The System is sterilized with ethylene oxide and is intended for single use only. Do not reuse or resterilize. Structural integrity and/or function may be impaired through reuse or cleaning. Do not use after the “Use By” date specified on the package.
- Keep away from sunlight, keep dry.
- After the procedure, all components used, and packaging materials may be a potential biohazard. Handle and discard the ENROUTE Transcarotid Neuroprotection System in accordance with accepted medical practice, institutional guidelines, and with applicable laws and regulations.

Recommended Accessories (not provided):

- 20 cc Luer Lock Syringe (for device preparation and flush)
- 10 cc Luer Lock Syringe (for contrast injections and flush of Sheaths)
- 4 or 5 Fr. Micropuncture Introducer Set

Warnings

- *Only physicians who have received appropriate training and are familiar with the principles, clinical applications, complications, side effects and hazards commonly associated with carotid interventional procedures should use this device.*
- *Do not advance any part of the ENROUTE Transcarotid NPS if resistance is felt. Stop and assess the cause of resistance. Failure to do so may cause vessel or product component damage.*
- *If excess resistance is encountered during flushing, preparation, or injection of fluids into any of the ENROUTE Transcarotid NPS system components, stop and assess cause of resistance. Failure to do so may result in damage to the product or harm to the patient.*
- *The safety and efficacy of the ENROUTE Transcarotid Neuroprotection System has not been demonstrated with carotid stent systems other than Precise® ProRx Carotid Stent, Acculink® Carotid Stent, Xact® Carotid Stent, PROTÉGÉ® Carotid Stent, Carotid WALLSTENT™ Endoprosthesis and ENROUTE® Transcarotid Stent.*
- *Consider severe disease of the contralateral arteries and ipsilateral posterior arteries which may affect adequate cerebral blood flow during flow reversal.*
- *Systemic antiplatelet and anticoagulation therapy should be used before, during and after the procedure based on hospital and physician preferred protocol.*

Precautions

- *Carefully read all instructions prior to use. Observe all warnings and precautions noted throughout these instructions. Failure to do so may result in complications.*
- *Refer to Instructions for Use supplied with other interventional devices to be used in conjunction with the ENROUTE Transcarotid NPS for their intended uses, contraindications and potential complications.*
- *The ENROUTE Transcarotid NPS is not recommended in patients who cannot tolerate contrast agents necessary for intra-operative imaging.*
- *Common carotid artery and femoral vein size and morphology should be compatible at the respective access site with the 8 Fr. Transcarotid Arterial and Venous Return Sheaths using standard vascular access techniques.*
- *Proper placement of the ENROUTE Transcarotid NPS Sheaths should be monitored and confirmed fluoroscopically.*
- *Monitoring of patients' neurological status during carotid artery stenting procedure is recommended.*
- *The J-tipped wire provided is not intended to be rotated or torqued during use.*
- *Do not withdraw or manipulate the coated wire in a metal cannula or sharp-edged object.*
- *Avoid wiping the wire with dry gauze as this may damage the wire coating.*
- *Avoid using alcohol, antiseptic solutions or other solvents to pre-treat the guidewire as this may cause unpredictable changes in the coating which can affect the wire safety and performance.*
- *Always inspect the guidewire carefully for bends, kinks or other damage prior to insertion or re-insertion. Do not use damaged guidewires.*

Adverse Events

Summary of Clinical Results (G120143)
The intent of the ROADSTER study was to assess the safety and effectiveness of the ENROUTE Transcarotid Neuroprotection System in providing cerebral embolic protection during angioplasty and stenting procedures in carotid arteries in subjects at high risk for complications from CEA. A comprehensive list of the MAEs is provided in Table 2. In summary, outcomes in subcategories of the Major Adverse Event endpoint included death (1.4% for the pivotal population and 0.0% for the extended enrollment population), stroke (1.4% for the pivotal population and 1.3% for the extended enrollment population) and myocardial infarction (0.7% for the pivotal population and 2.6% for the extended enrollment population).

Table 2: Hierarchical Major Adverse Event Rate (30 days)
- Pivotal Patient Population and Extended Enrollment Population

Observations	Pivotal Population (N=141)	Extended Enrollment Population (N=78)
Stroke/Death/Myocardial Infarction	5 (3.5%)	3 (3.8%)
Death	2 (1.4%)	0 (0.0%)
Cardiac	1 (0.7%)	0 (0.0%)
Neurological	0 (0.0%)	0 (0.0%)
Non-Cardiac/Non-Neurological	1 (0.7%)	0 (0.0%)
Stroke	2 (1.4%)	1 (1.3%)
Major Ipsilateral	0 (0.0%)	0 (0.0%)
Major Contralateral	0 (0.0%)	0 (0.0%)
Minor Ipsilateral	2 (1.4%)	1 (1.3%)
Minor Contralateral	0 (0.0%)	0 (0.0%)
Myocardial Infarction	1 (0.7%)	2 (2.6%)
Stroke/Death	4 (2.8%)	1 (1.3%)

The serious adverse events that were reported during the ROADSTER Clinical Trial are summarized in Table 3. Adverse events were defined as any undesirable medical occurrence in a patient. This definition does not depend on the causal relationship with the device or protocol requirements.

Table 3: Summary of ROADSTER Serious Adverse Events

System Organ Class Preferred Term	Pivotal Population (N=141)	Extended Enrollment Population (N=78)
Number (%) of Subjects with one or more Serious Adverse Events	20 (14.2%)	9 (11.5%)
Anemia	5 (3.5%)	0 (0.0%)
Angina Pectoris	1 (0.7%)	0 (0.0%)
Bradycardia	1 (0.7%)	0 (0.0%)
Cardiac Arrest	0 (0.0%)	1 (1.3%)
Cardiac Failure Acute	1 (0.7%)	0 (0.0%)
Myocardial Infarction	2 (1.4%)	1 (1.3%)
Gastrointestinal Hemorrhage	1 (0.7%)	0 (0.0%)
Pyrexia	1 (0.7%)	0 (0.0%)
Pneumonia	2 (1.4%)	0 (0.0%)
Post Procedural Cellulitis	1 (0.7%)	0 (0.0%)
Incision Site Hematoma	0 (0.0%)	2 (2.6%)
Wound Hematoma	1 (0.7%)	2 (2.6%)
Troponin Increased	1 (0.7%)	0 (0.0%)
Diabetic Ketoacidosis	1 (0.7%)	0 (0.0%)
Cerebrovascular Accident	1 (0.7%)	0 (0.0%)
Ischemic Stroke	0 (0.0%)	1 (1.3%)
Metabolic Encephalopathy	1 (0.7%)	0 (0.0%)
Psychomotor Seizures	1 (0.7%)	0 (0.0%)
Renal Failure	2 (1.4%)	0 (0.0%)
Urinary Retention	1 (0.7%)	1 (1.3%)
Acute Respiratory Failure	2 (1.4%)	0 (0.0%)
Dyspnea	1 (0.7%)	0 (0.0%)
Epistaxis	1 (0.7%)	0 (0.0%)
Pneumothorax	0 (0.0%)	1 (1.3%)
Pulmonary Embolism	1 (0.7%)	0 (0.0%)
Respiratory Failure	0 (0.0%)	1 (1.3%)
Aortic Aneurysm	1 (0.7%)	0 (0.0%)
Artery Dissection	3 (2.1%)	1 (1.3%)
Hypotension	4 (2.8%)	0 (0.0%)
Hypertension	1 (0.7%)	0 (0.0%)

POTENTIAL PROCEDURE AND / OR DEVICE RELATED ADVERSE EVENTS
Complications and adverse events can occur when using any embolic protection device in carotid artery stenting procedures. These complications include, but are not limited to:
abrupt vessel closure; allergic reactions; aneurysm; angina / coronary ischemia; arteriovenous fistula; bacteremia or septicemia; bleeding from anticoagulant or antiplatelet medications; bradycardia / arrhythmia and other conduction disturbances; cerebral edema; cerebral hemorrhage; component damage; congestive heart failure; cranial nerve injury (CNI); death; deployment and retrieval failure; distal embolization; drug reactions; embolism (which includes thrombus, plaque, air, device and / or component); emergent / urgent endarterectomy; fever; fluid overload; groin hematoma; headache; hemorrhage / hematoma; hemorrhagic stroke; hyperperfusion syndrome; hypertension / hypotension; infection / sepsis; ischemia / infarction of tissue / organ; ischemic stroke; intolerance to vessel occlusion and / or flow reversal; myocardial infarction; pain and tenderness; pseudoaneurysm; reduced blood flow; renal failure / insufficiency; restenosis of the stented artery; seizure; stent deformation; stroke or other neurological complications (e.g., paralysis, paraplegia or aphasia); surgery required due to device failure; temporary or total occlusion of the artery; thromboembolic episodes; thrombophlebitis; transient ischemic attacks (TIAs); vascular access complications (e.g., bleeding, vessel damage, pseudoaneurysm and infection); ventricular fibrillation; vessel spasm, dissection, rupture, or perforation; vessel thrombosis (partial blockage); unstable angina pectoris.

SUMMARY OF CLINICAL RESULTS
The results of this clinical study support the safety and effectiveness of the ENROUTE Transcarotid Neuroprotection System.

Objective: The objective of the ROADSTER study was to establish the safety and effectiveness of the ENROUTE Transcarotid Neuroprotection System in providing cerebral embolic protection during angioplasty and stenting procedures in carotid arteries in subjects at high risk for complications from CEA. The ENROUTE Transcarotid Neuroprotection System also facilitates access to the carotid and neuro anatomy for the introduction of therapeutic or diagnostic endovascular devices and/or agents.

Study Design: The ROADSTER study was a prospective, single-arm, multi-center clinical trial of the ENROUTE Transcarotid Neuroprotection System used in conjunction with all FDA-approved carotid artery stents used for revascularization in patients with carotid disease who are 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.

Study Enrollment: Sixty-seven (67) lead-in, one hundred forty-one (141) pivotal and seventy-eight (78) extended enrollment subjects at high risk for complications from CEA were enrolled between November 2012 and July 2016 in 17 sites in the United States and one (1) site in the European Union. The lead-in subjects were excluded from the primary analysis.

Primary Endpoint: The primary endpoint was a hierarchical composite of any stroke, myocardial infarction and death during a 30-day post-procedural period in the pivotal population and extended enrollment population comprised of subjects deemed to be at high risk for complications from CEA. Results from the analysis of the primary endpoint are based on a 2-sided binomial test, compared to an a priori threshold of 11.0%. The 2-sided 95% exact binomial confidence intervals is also presented.

Secondary Endpoints: The following secondary endpoints were assessed 0 to 30 days in the pivotal population and extended enrollment population comprised of subjects deemed to be at high risk for complications from CEA:

- Technical success
- Acute Device success
- Procedural success
- Access Site Complications
- All death
- All stroke
- All MI
- Cardiac death
- Ipsilateral stroke
- Contrast Usage

Patients Studied: The study included patients at high risk for complications from CEA with atherosclerotic extracranial internal carotid stenosis (ICA) with or without involvement of the contiguous common carotid artery (CCA) determined by duplex ultrasound, CT/CTA, MR/MRA or angiography. Eligible patients met one of the following criteria regarding neurological symptom status and degree of stenosis:

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

Subjects included in the study were considered high-risk for complications from carotid endarterectomy and had to meet at least one surgical high-risk criterion outlined in the Inclusion Criteria section of this report. These criteria were divided into two groups: anatomic and clinical. The frequency of occurrence of each high-risk criterion is tabulated and presented in Table 4. A subject could have multiple high-risk criteria at the time of inclusion in the study.

Table 4: ROADSTER High Surgical Risk Inclusion Criteria

	Pivotal Population	Extended Enrollment Population
Number of Subjects Enrolled	141	78
Anatomic Risk		
Contralateral carotid artery occlusion	11 (7.8%)	10 (12.8%)
Tandem stenoses >70%	1 (0.7%)	2 (2.6%)
High cervical carotid artery stenosis	42 (29.8%)	13 (16.7%)
Restenosis after carotid endarterectomy	29 (20.6%)	31 (39.7%)
Bilateral carotid artery stenosis requiring treatment	6 (4.3%)	1 (1.3%)
Hostile Necks safe for Transcarotid access	22 (15.6%)	8 (10.3%)
Clinical Risk		
> 75 years of age	66 (46.8%)	25 (32.1%)
> 2-vessel CAD and history of angina	15 (10.6%)	14 (17.9%)
History of angina	2 (1.4%)	3 (3.8%)
Congestive heart failure – NYHA Functional Class III or IV	1 (0.7%)	0 (0.0%)
Known severe left ventricular dysfunction: LVEF <30%	2 (1.4%)	1 (1.3%)
MI >72 hours and < 6 weeks prior to procedure	1 (0.7%)	1 (1.3%)
Severe pulmonary disease (COPD)	6 (4.3%)	6 (7.7%)
Permanent contralateral cranial nerve injury	0 (0.0%)	0 (0.0%)
Patient has chronic renal insufficiency	1 (0.7%)	0 (0.0%)

The pre-procedure demographics for the pivotal subjects and extended enrollment subjects are summarized in Table 5.

Table 5: Subject Demographics

	Pivotal Population	Extended Enrollment Population
Number of Subjects	**N=141**	**N=78**
Subject Age		
Mean (Min, Max)	72.9 (40, 90)	71.14 (43, 88)
Gender		
Male	92 (65.2%)	44 (56.4%)
Female	49 (34.8%)	34 (43.6%)
Medical History		
Hypertension	122 (86.5%)	71 (91.0%)
Hyperlipidemia	109 (77.3%)	75 (96.2%)
Diabetes	52 (36.9%)	29 (37.2%)
Respiratory	15 (10.6%)	6 (7.7%)
Current Smoker	32 (22.7%)	21 (26.9%)
History of Stroke/TIA		
Prior Stroke	42 (29.8%)	13 (16.7%)
Prior TIA	24 (17.0%)	11 (14.1%)
Non-Carotid Vascular Disease		
Coronary	59 (41.8%)	42 (53.8%)
Peripheral	41 (29.1%)	27 (34.6%)
Symptom Status		
Symptomatic	36 (25.5%)	8 (10.3%)
Asymptomatic	105 (74.5%)	70 (89.7%)
Lesion and Vessel Characteristics		
Mean Lesion Length (min, max)	16.5 (5, 39)	17.1 (1, 41)
Mean % Diameter Stenosis	85.9 (55, 99)	85.0 (50, 99)

Study Results:
A summary of the distribution of stents used in the study is provided in Table 6.

Table 6: Distribution of FDA-Approved Stents in ROADSTER

Stent Brand	Pivotal Population	% of Pivotal enrollment	Extended Enrollment population	% of Extended Enrollment Population
Abbott Acculink®	17	12%	16	21%
Abbott Xact®	45	32%	22	28%
Boston Scientific Wallstent®	36	26%	0	0%
Cordis Precise ProRx®	34	24%	25	32%
Ev3 Protégé™	7	5%	15	19%

Procedural outcomes for the study are summarized in Table 7. The non-hierarchical stroke and death rate was 2.8% (n=4) for the pivotal population and 1.3% (n=1) for the extended enrollment population. There was one cardiac death (0.7%) and one death due to sequelae from respiratory failure (0.7%) in the pivotal population. There were no deaths in the extended enrollment population. There were two (2) strokes (1.4%) in the pivotal population and one (1) stroke (1.3%) in the extended enrollment population all of which were minor. There were zero (0) major strokes (0.0%) in both the pivotal and extended enrollment populations. There were two (2) non-hierarchical myocardial infarctions (1.4%) in the pivotal population, both of which were characterized by enzyme rises with non-specific changes on ECG and no reports of chest pain. There were two (2) non-hierarchical myocardial infarctions (2.6%) in the extended enrollment population, one of which was characterized as a non-ST elevation myocardial infarction (NSTEMI) with shortness of breath, the other characterized by ECG findings consistent with left ventricular hypertrophy/strain pattern but unconvincing for acute ischemic changes with sub-sternal chest pain. There was one report of transient cranial nerve injury (0.7%) that was fully resolved at six (6) months follow up in the pivotal population and no reports of cranial nerve injury in the extended enrollment population. Access Site Complications were included as a secondary endpoint. In total, of the Access Site Complications reported and stratified by the wound management definitions in the study protocol, for the pivotal population, fourteen (14) were deemed non-serious or minor; four (4) resolved with nominal therapy contemplated in the wound management definitions and ten (10) resolved without treatment. One (1) wound complication was deemed serious (0.7%) but was resolved with standard wound exploration and evacuation. Intolerance to high flow reversal (non-serious adverse event) was reported in one (1) subject (0.7%), however the procedure was completed on low flow. No permanent neurological deficits were associated with flow reversal intolerance when antegrade flow was re-established. In the extended enrollment population, six (6) were deemed non-serious or minor; four (4) resolved with nominal therapy contemplated in the wound management definitions and two (2) resolved without treatment. Four (4) wound complications were deemed serious (5.1%). Intolerance to high flow reversal (non-serious adverse event) was reported in one (1) subject, however the procedure was completed on low flow. No permanent neurological deficits were associated with flow reversal intolerance when antegrade flow was re-established.

Table 7: Procedural Outcomes for ROADSTER

	Pivotal Population	Extended Enrollment
Number of Subjects Enrolled	141	78
Procedure Time (minutes)	N = 140	N = 77
Mean (Std Dev)	73.6 (27.76)	72.4 (31.26)
Median	68.0	60.0
Range	29, 257	32, 179
Total Reverse Flow Time (minutes)	N = 140	N = 78
Mean (Std Dev)	12.9 (8.57)	13.1 (10.12)
Median	10.0	10.0
Range	4, 63	5, 78
Contrast Usage (cc)	N=135	N = 75
Mean (Std Dev)	72.0 (41.57)	79.3 (77.82)
Median	65.0	65.0
Range	17, 250	15, 585

Table 8: ROADSTER Primary Endpoints

Observations	Pivotal Population (N=141)	Extended Enrollment Population (N=78)
Number of Patients Who Experienced an MAE		
N (%)	5 (3.5%)	3 (3.8%)
95% Exact Binomial Confidence Intervals	(1.16, 8.08)	(0.80, 10.83)
p-value	0.0047	N/A
Number of Patients Who Died Within 30 Days of the Index Procedure		
N (%)	2 (1.4%)	0 (0.0%)
Number of Patients Who had a Stroke Within 30 Days of the Index Procedure		
N (%)	2 (1.4%)	1 (1.3%)
Number of Patients Who had an MI Within 30 Days of the Index Procedure		
N (%)	1 (0.7%)	2 (2.6%)

The ROADSTER study met the primary endpoint for efficacy (hierarchical rate of stroke, death and myocardial infarction) in the pivotal population (comprised of subjects deemed to be at high risk for complications from CEA) based upon the upper 95% confidence interval as compared to the a priori performance goal of 11.0%.

Table 9: ROADSTER Secondary Endpoints

Secondary Endpoints	Pivotal Population %(n/N)	Extended Enrollment Population %(n/N)
Acute Device Success	140 (99.3%)	78 (100.0%)
Technical Success	140 (99.3%)	78 (100.0%)
Procedural Success	135 (95.7%)	75 (96.2%)

Acute Device Success is defined as successful delivery of the subject device, establishment of reverse flow, and successful retrieval/removal from the vasculature. Technical Success is Acute Device Success plus the successful introduction of interventional tools. Procedural Success is Technical Success plus the absence of a Major Adverse Event 30-days post-procedure.

Pre-procedure Assessment

Perform a duplex Doppler ultrasound exam, Magnetic Resonance Angiogram, or Computerized Axial Tomography Angiogram to assess the location of the carotid artery bifurcation relative to the location of the clavicle and the suitability of the common carotid artery for direct access (e.g. size, prevalence of disease and vessel calcification)

Caution: *The Transcarotid Arterial Sheath and Dilator together protrude beyond the Sheath Stopper when assembled. Ensure there is sufficient distance between the clavicle and the carotid artery bifurcation to safely introduce the Transcarotid Arterial Sheath into the CCA while avoiding advancement into the bifurcation. Take care to ensure the system is not inadvertently advanced further into the CCA while manipulating the Sheath, Dilator, and/or Guidewire. (Refer to Figure 7).*

Directions for Use

Inspection Prior to Use

- Inspect the product and packaging prior to use.
- Do not use if the sterile barrier is opened or damaged or the product is damaged.

Sheath Preparation

- Flush the Transcarotid Arterial Sheath, Venous Return Sheath and respective dilators with heparinized saline using a 20 cc syringe to ensure patency of all lumens and to lubricate the system.
- Turn the handle on the Arterial Sheath Stopcock with the “X” position towards the CCA.
- Insert each Dilator into each Sheath until it snaps into the hemostasis valve cap.

Venous and Arterial Sheath Placement Procedural Steps

- Venous Return Sheath Placement
    - Access the femoral vein with a 4 or 5 Fr. Micropuncture set using the modified Seldinger technique or ultrasound guidance. Insert 0.035" (0.9 mm) Extra Support J-Tip Guidewire and confirm venous placement using fluoroscopy.
    - Advance the Venous Return Sheath and Dilator into the vein over the 0.035" (0.9 mm) Guidewire. Secure the Venous Return Sheath to the patient's skin using the suture eyelet(s) on the Y-arm of the sheath. Unsnap the Dilator hub from the Sheath hub, then carefully withdraw the Dilator and Guidewire, aspirate blood from the Venous Flow Line, flush the Venous Flow Line with heparinized saline, then close the Venous stopcock.
- Arterial Sheath Placement
    - Gain access to the Common Carotid Artery (CCA) cephalad to the clavicle using surgical techniques.
    - Place umbilical tape, clamp, or a vessel loop around the CCA for control and/or occlusion.
    - Administer patient appropriate therapy to provide systemic anticoagulation.
    - At the operator's discretion, sutures may be pre-placed at the planned puncture site to provide rapid hemostasis upon Transcarotid Arterial Sheath removal.
    - Access the CCA with a Micropuncture Introducer Set. Advance the 0.035" (0.9 mm) Extra Support J-Tip Guidewire into the CCA under fluoroscopy, taking care not to advance the 0.035" (0.9 mm) Guidewire into the lesion.
    - To limit sheath entry to 2.5 cm, verify that the Arterial Sheath Stopper is attached to the Transcarotid Arterial Sheath (see Figure 7). Do not trim the sheath stopper.

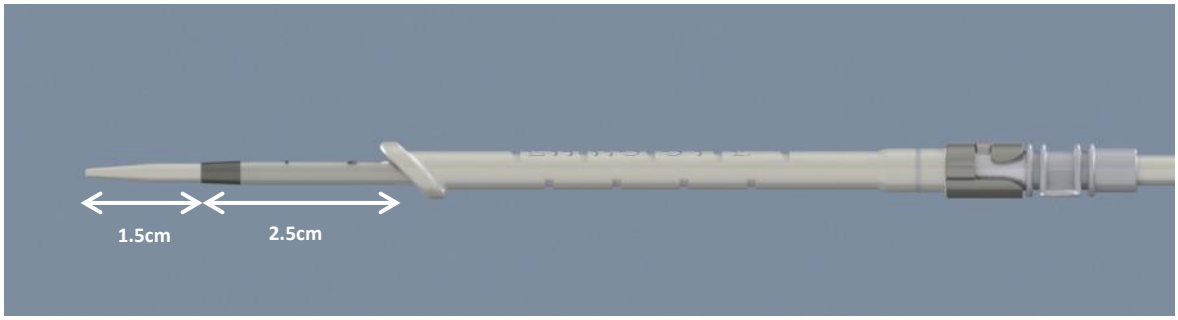

Figure 7 – Transcarotid Arterial Sheath with Included Arterial Dilator and Sheath Stopper

- Verify proper Arterial Sheath Stopper orientation by confirming text on the Arterial Sheath Stopper being in-line with the depth markers on the Arterial Sheath body and the orange marker on the Arterial Mid-Body Connector (see Figure 8).

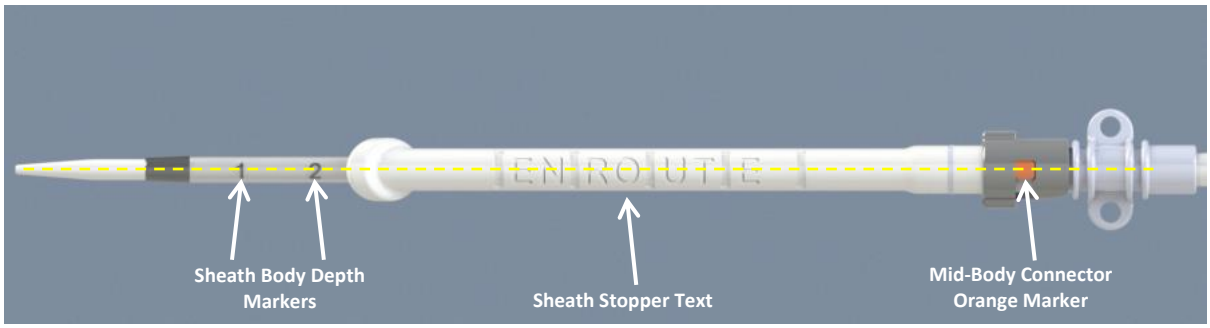

Figure 8 – Arterial Sheath Stopper Orientation

- NOTE: When the Arterial Sheath Stopper is properly oriented relative to the Arterial Sheath, the angle of the Arterial Sheath tip should be in the same plane as the tip angle of the Arterial Sheath Stopper (see Figure 9).

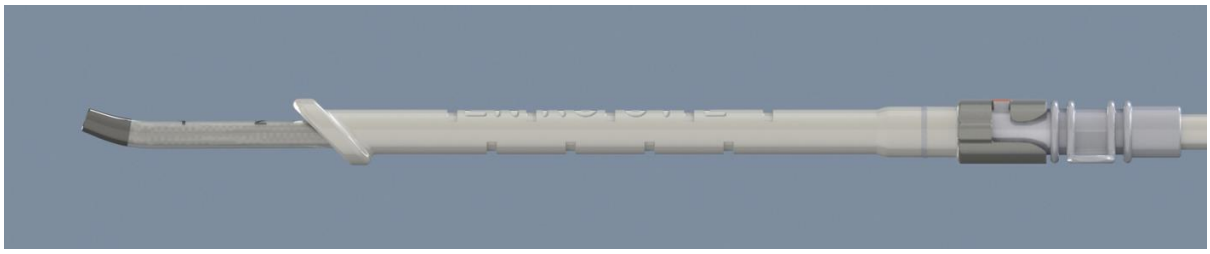

Figure 9 – Uber-Flex™ Angled Tip Arterial Sheath Orientation with respect to the Arterial Sheath Stopper

- NOTE: To remove the Arterial Sheath Stopper from the Arterial Sheath, first insert the Arterial Dilator into the Arterial Sheath for support. Disengage the grey Sheath Stopper Hub from the Mid-Body Connector and carefully withdraw the Sheath Stopper.

Caution: *Ensure the Arterial Dilator is fully inserted into the Transcarotid Arterial Sheath prior to removing or reattaching the Arterial Sheath Stopper. Failure to do so may result in damage to the tip of the Arterial Sheath.*

- Advance the Transcarotid Arterial Sheath and Dilator over the 0.035” (0.9 mm) Extra Support J-Tip Guidewire. Using gentle counter traction to elevate the vessel, advance the Transcarotid Arterial Sheath over the 0.035” (0.9 mm) Guidewire into the CCA until the distal foot of the Sheath Stopper contacts the arterial wall. Relax the umbilical tape or vessel loop and unsnap the Dilator hub from the Sheath hub, then carefully withdraw the Dilator and 0.035” (0.9 mm) Guidewire. Aspirate blood from the Side Arm, flush the Side Arm with heparinized saline, then close the sidearm stopcock.
- Under fluoroscopy and with contrast injections, in the anterior/posterior and lateral views, confirm the Transcarotid Arterial Sheath is placed centrally in the common carotid lumen. Reposition Sheath as needed for central common carotid lumen placement. Once the Sheath is in the desired position, with slight forward tension, secure the Sheath to the patient’s skin using the suture eyelet(s) on the mid-body connector of the Sheath. Sutures may also be placed across the grooves of the Sheath Stopper to provide additional sheath stability closer to the arteriotomy.

Caution: *Ensure the Transcarotid Arterial Sheath is centrally located in the common carotid arterial vessel lumen. Failure to do so may result in inadvertent damage to the vessel.*

Caution: *Ensure the Transcarotid Arterial Sheath is well-secured to the patient. Failure to do so may result in inadvertent sheath removal during the procedure.*

Flow Controller in situ Preparation

- With the Venous Return Sheath and Transcarotid Arterial Sheath in place, prepare the ENROUTE Flow Controller in situ using the following steps:
  - Confirm Arterial Stopcock is "X" to the artery (see Figure 10).
  - Confirm Venous Stopcock is "X" to the Venous Flow Line.
  - On the Flow Controller, pull and remove the Toggle Loop that reads "Pull to Prep". Confirm that the High/Low Switch on the Flow Controller has been set to Low (see Figure 10).

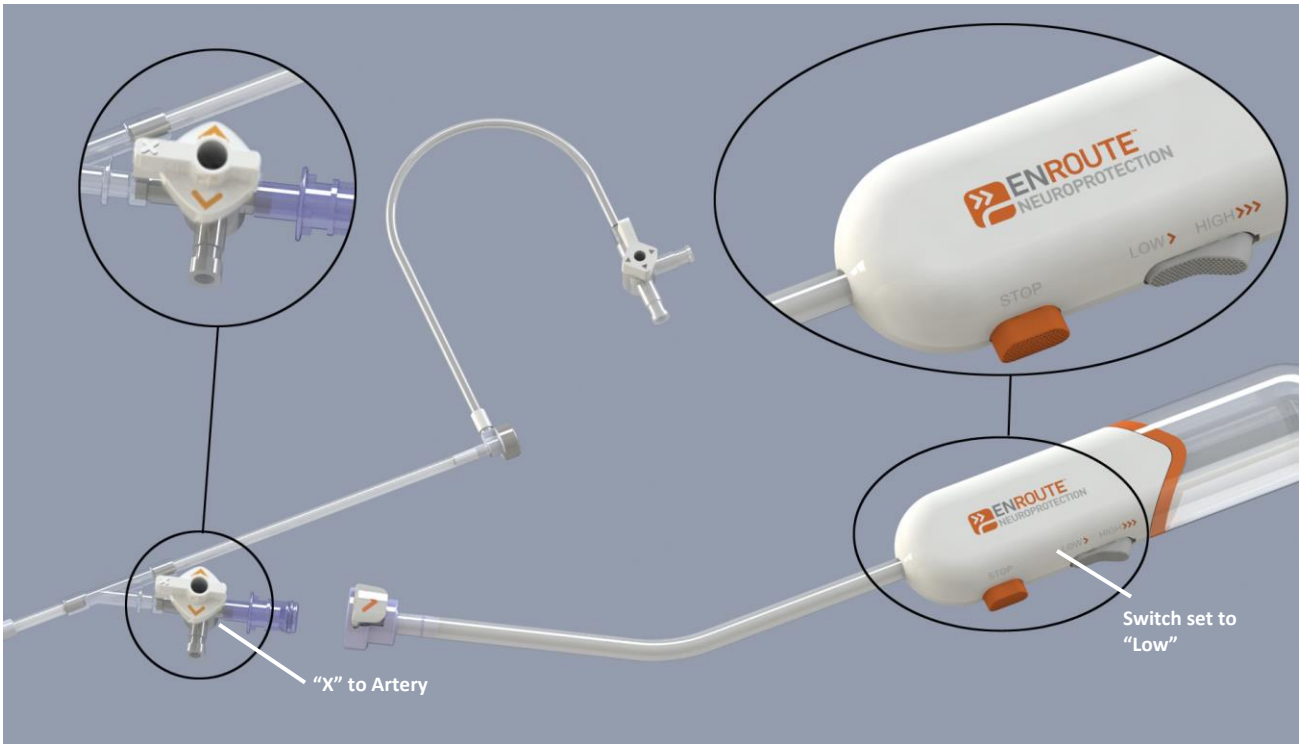

Figure 10 Flow Controller Featuring High/Low Switch

- Connect the female quick connect of the Flow Controller to the male quick connect of the Arterial Stopcock (see Figure 11).

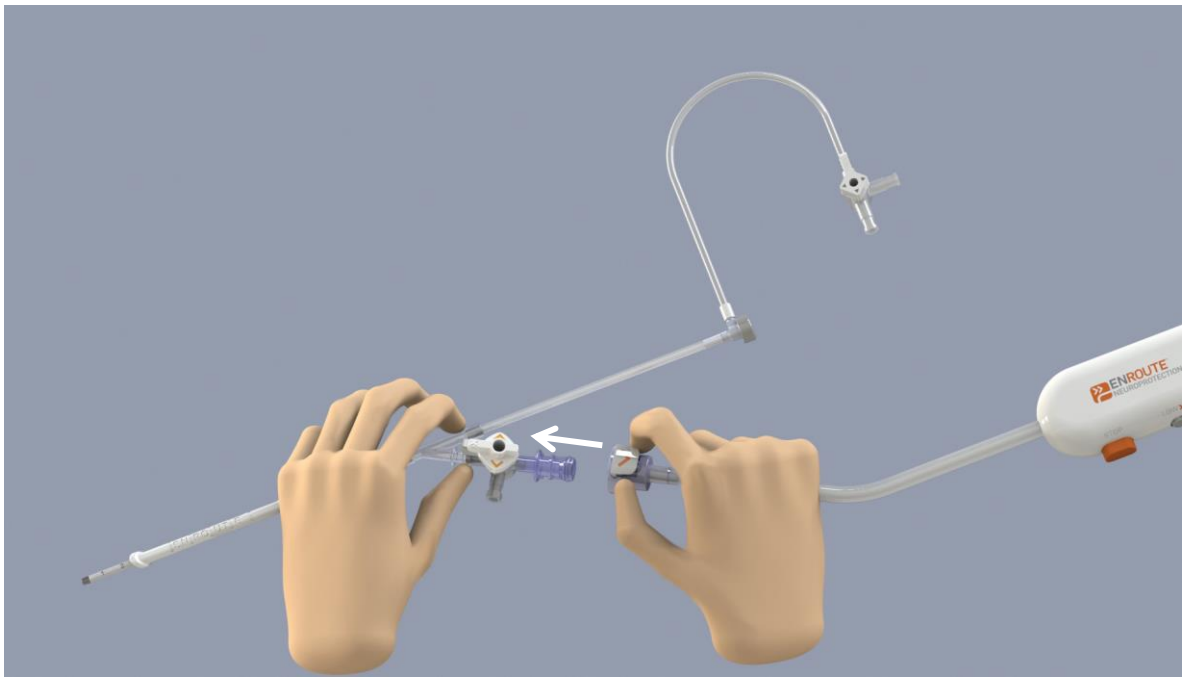

Figure 11 Male Quick Connect to Flow Controller

- To start the flow of blood into the Flow Controller, open the Arterial Stopcock to the Flow Controller to allow the Flow Controller to fill (see Figure 12).

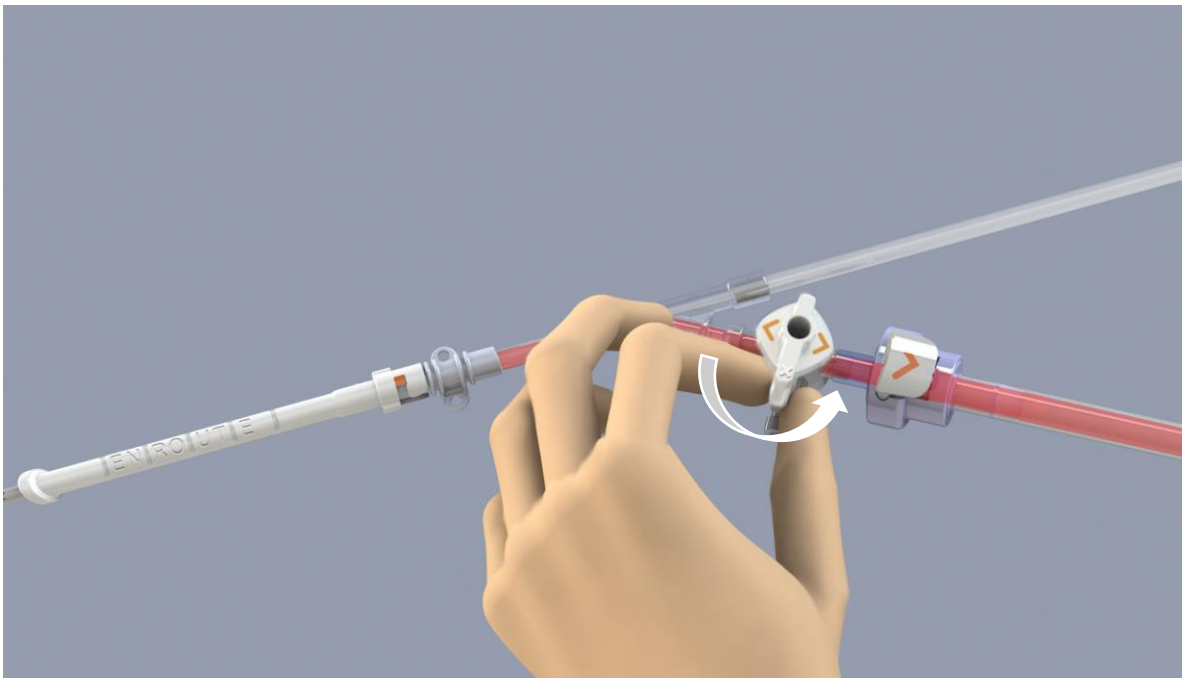

Figure 12 Arterial Stopcock in “Open” Position

- Immediately raise the venous end of the Flow Controller so the end is vertical.
- Allow blood to fill the filter chamber, check valve, and the remainder of the Flow Controller line (see Figure 13).

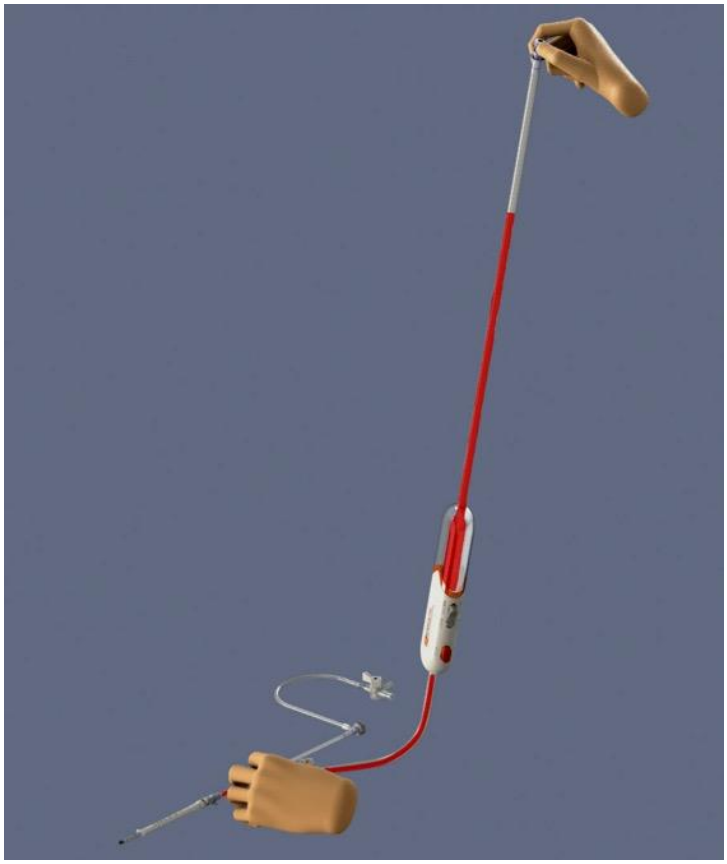

Figure 13 Filter Chamber, Check Valve and Flow Controller Line

- Once blood has filled the filter, check valve, and the remainder of the Flow Controller line, connect the venous end of the Flow Controller to the quick connect fitting of the Venous Stopcock (which should be closed to the Venous Return Sheath flow line) (see Figure 14).

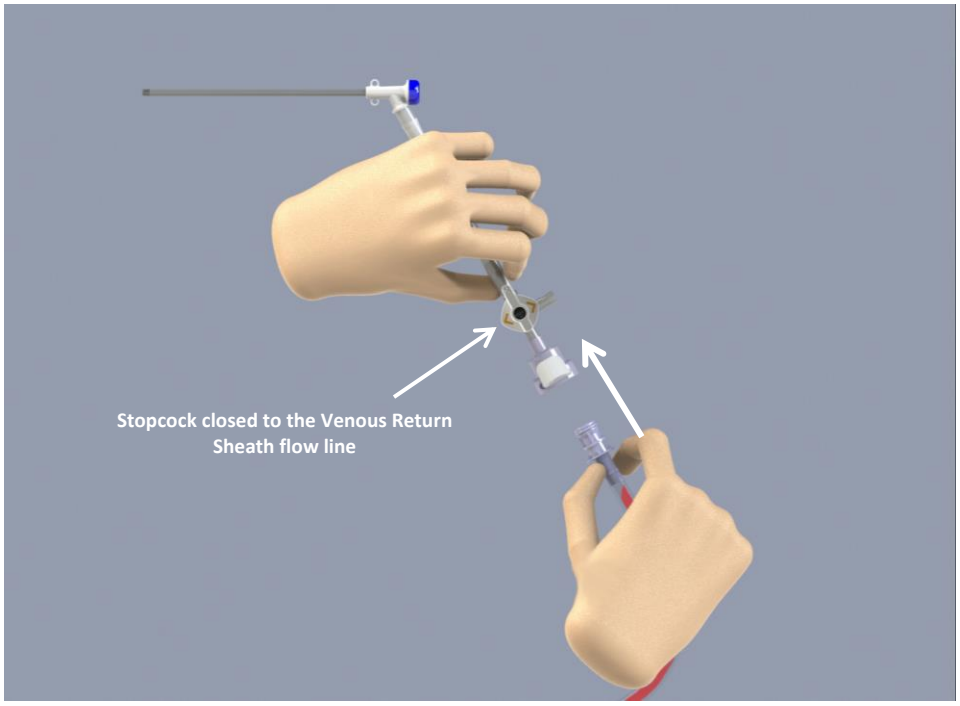

Figure 14 Venous Return Sheath and Flow Controller Connection

- Allow any air to exit the Venous Stopcock side port (see Figure 15).

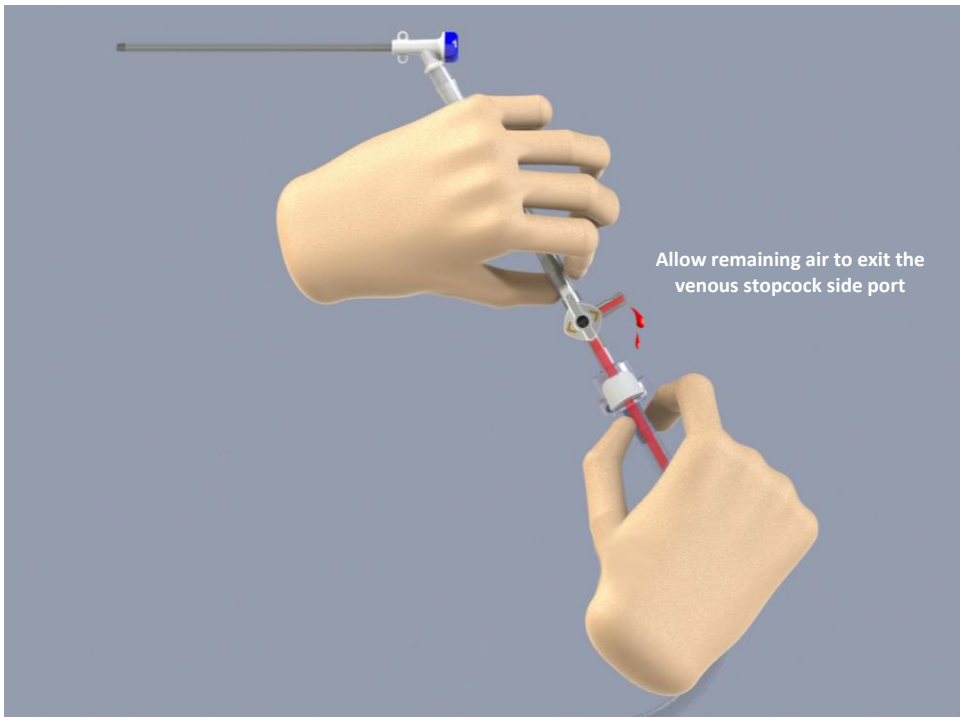

Figure 15 Venous Stopcock Side Port

- After all air has been removed from the Flow Controller and Flow Controller Line, close the stopcock to the side port to establish the arteriovenous shunt flow (see Figure 16).

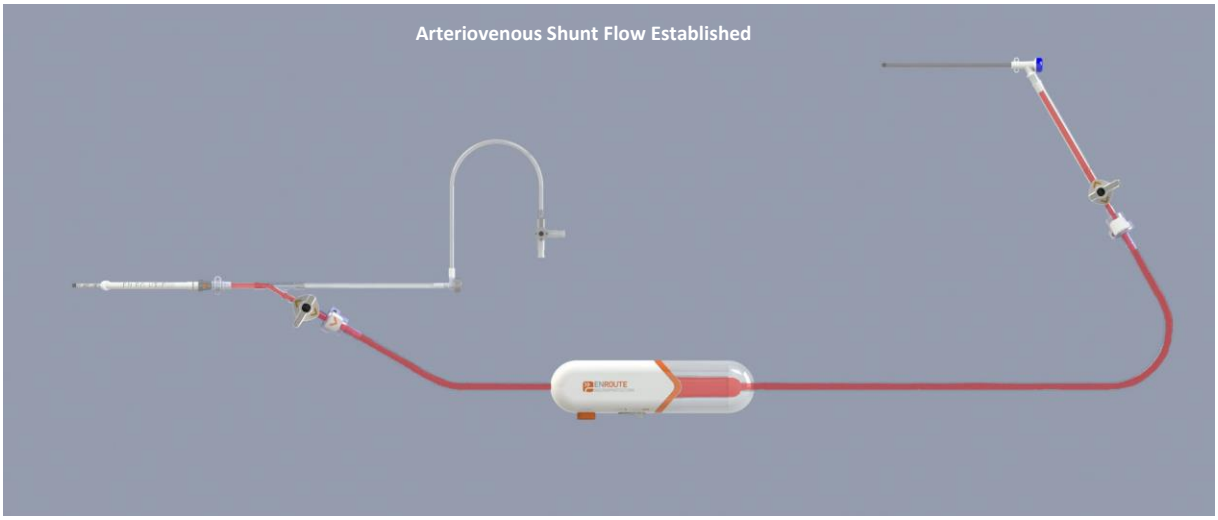

Figure 16 Arteriovenous Shunt Flow Established

- Flow rate through the Flow Controller Line is regulated by use of the High/Low Switch on the Flow Controller. To change to high flow, depress the Switch to High. To revert to low flow, depress the Switch to Low.

Caution: *Ensure the Arterial Stopcock and the Venous Stopcock are fully open to the Flow Controller line for optimal arteriovenous flow rates.*

- Occlude the CCA using standard surgical technique (e.g., vascular clamp, Rummel loop, silastic vessel loop). Active, robust flow reversal is now established.

Caution: *If at any time during the procedure the patient exhibits signs of intolerance to flow reversal, modulate or discontinue the reverse flow using the Flow Controller High/Low Switch, Flow Stop Button, and/or the Arterial Stopcock. Re-establish antegrade CCA flow as necessary for patient tolerance. Avoid manipulating devices at the lesion site while reverse flow is inactive.*

- Verify reversal of flow through the arteriovenous shunt:
  - With the Flow Controller High/Low Switch on Low, ensure the Venous Stopcock and Arterial Stopcock are open to the Flow Controller.
  - Attach a 20 cc Luer tipped syringe with heparinized saline to the side port of the Venous Stopcock and close the Venous Stopcock to the Flow Controller.
  - Flush 10-15 cc of heparinized saline into the Venous Return Sheath Flow Line, such that the blood is cleared.
  - Re-open the Venous Stopcock to the Flow Controller and observe the passage of blood pushing the clear heparinized saline bolus toward the Venous Return Sheath.
  - Repeat the above steps with the High/Low Switch set to High.
- To perform carotid angiography under flow reversal:
  - Connect a 10 cc syringe to the Side Arm of the Transcarotid Arterial Sheath. Aspirate 5 cc of fluid and discard.
  - Attach a 10 cc contrast syringe or manifold with contrast syringe to the Side Arm of the Transcarotid Arterial Sheath.
  - Set High/Low Switch to High.
  - Depress the Flow Stop Button with one hand while injecting contrast.
  - After the contrast is injected, release the Flow Stop Button to reestablish reverse flow and to clear the contrast into the arteriovenous shunt.
- Perform the carotid interventional steps under High reverse flow using the Transcarotid Arterial Sheath to insert the interventional devices into the carotid artery.
  - During non-critical periods of the intervention, flow may be modulated to the Low setting as needed for patient tolerance.
- Use conventional interventional catheter techniques to periodically aspirate and flush the device lumens with heparinized saline if blood flow is stopped for any prolonged period.

- After completion of the interventional procedure, loosen or remove the CCA occlusion device. Turn the Venous Stopcock and Arterial Stopcock to the off position to the Flow Controller "X", thereby closing the arteriovenous shunt and restoring antegrade flow into the carotid artery.
- Remove the Transcarotid Arterial Sheath and Venous Return Sheath and close the puncture sites and incisions using standard surgical techniques.

Definitions of Symbols

Symbol	Title/Description	Standard and reference number
	Caution	ISO 15223-1 5.4.4
www.silkroadmed.com/ifu	Consult Instructions for Use	ISO 15223-1 5.4.3
STERILE EO	Sterilized using Ethylene Oxide	ISO 15223-1 5.2.3
R_X Only	Caution: Federal (US) law restricts this device to sale by or on the order of a physician	N/A
LOT	Batch code /Lot Number	ISO 15223-1 5.1.5
Date format: YYYY-MM-DD	Manufacturer (may include date of manufacture)	ISO 15223-1 5.1.1
	Do Not Use if Package is Damaged and consult instructions for use	ISO 15223-1 5.2.8
LATEX	Not Made with Natural Rubber Latex	ISO 15223-1 5.4.5
	Use by Date	ISO 15223-1 5.1.4
REF	Catalog Number	ISO 15223-1 5.1.6
	Do Not Reuse	ISO 15223-1 5.4.2
STERILIZE	Do Not Resterilize	ISO 15223-1 5.2.6
	Non-pyrogenic	ISO 15223-1 5.6.3
	Keep dry	ISO 15223-1 5.3.4
	Keep away from sunlight	ISO 15223-1 5.3.2
MD	Medical device or Device name	ISO 15223-1 5.7.7
UDI	Unique Device Identifier	ISO 15223-1 5.7.10
	Single sterile barrier system with protective packaging inside	ISO 15223-1 5.2.13

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