PROTEGE™ RX

Carotid Stent System

INSTRUCTIONS FOR USE

CAUTION: Federal (U.S.A.) law restricts this device to sale by or on the order of a physician.

1. DEVICE DESCRIPTION

The PROTÉGÉ™ RX Carotid Stent System (**Table 1**) is a self-expanding Nitinol stent system intended for permanent implantation. The self-expanding stent is made of a nickel titanium alloy (Nitinol) and comes pre-mounted on a 6 Fr, 0.014" rapid exchange delivery system. The stent is cut from a Nitinol tube in an open lattice design, and is designed with tantalum radiopaque markers at the proximal and distal ends of the stent. Upon deployment, the stent achieves its predetermined diameter and exerts a constant, gentle outward force to establish patency.

The Delivery System, as shown in **Figure 1**, is comprised of an inner shaft and outer sheath, which are locked together with a Tuohy-Borst valve (1). The inner shaft terminates distally in a flexible catheter tip (2) and originates at the proximal end of the catheter. Two tantalum radiopaque markers, one marker distal (3) and one marker/retainer proximal (4) to the constrained stent (9), are on the inner shaft. Delivery systems with tapered stents have an additional radiopaque marker that reveals where the stent diameter transition begins. Tapered stents are mounted onto the delivery catheter with the smallest diameter toward the distal end of the catheter. The outer sheath connects proximally to the Y-connector (5). The self-expanding stent is constrained within the space between the inner shaft and outer sheath. This space is flushed prior to the procedure through the side port of the Y-connector (6).

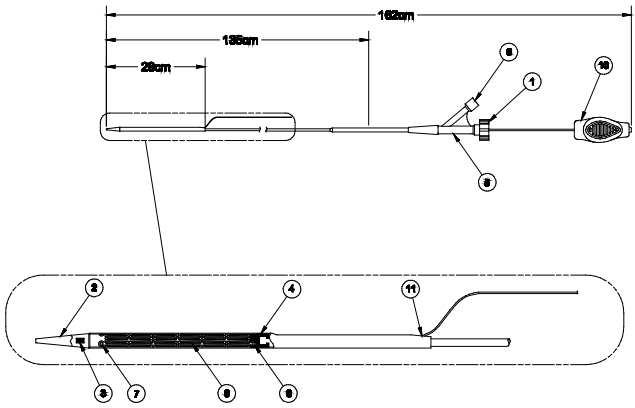
Stent positioning at the targeted lesion is achieved prior to deployment utilizing the tantalum radiopaque markers (7, 8) on the constrained stent. For stent deployment, the Tuohy-Borst valve is turned counter-clockwise to unlock the outer sheath.

The outer sheath retraction is achieved by pulling the Y-connector (5) toward the proximal grip (10) resulting in stent deployment.

TABLE 1: Device Range

Unconstrained Stent Diameter (mm)	Stent Length (mm)	Configuration	Lumen Diameter (mm)
6	20, 30, 40, 60	Straight	4.5 - 5.5
7	20, 30, 40, 60	Straight	5.5 - 6.5
8	20, 30, 40, 60	Straight	6.5 - 7.5
9	20, 30, 40, 60	Straight	7.5 - 8.5
10	20, 30, 40, 60	Straight	8.5 - 9.5
8 - 6	30, 40	Tapered	(6.5 - 7.5) - (4.5 - 5.5)
10 - 7	30, 40	Tapered	(8.5 - 9.5) - (5.5 - 6.5)

FIGURE 1: PROTÉGÉ™ RX Delivery Catheter



1. Tuohy-Borst Valve
2. Catheter Distal Tip
3. Distal Marker Band
4. Proximal Retainer/Marker Band
5. Y-Connector
6. Y-Connector Port
7. Distal Stent Tantalum Markers
8. Proximal Stent Tantalum Markers
9. Constrained Stent
10. Proximal Grip
11. Guidewire Exit Port

2. INDICATIONS

The PROTÉGÉ RX Carotid Stent System, when used in conjunction with the ev3, Inc. embolic protection systems, is indicated for the treatment of patients at high-risk for adverse events from carotid endarterectomy who require percutaneous carotid revascularization and meet the criteria outlined below:

1. Patients with carotid artery stenosis (> 50% for symptomatic patients by ultrasound or angiography or ≥ 80% for asymptomatic patients by ultrasound or angiography) of the common or internal carotid artery, AND
2. Patients must have a reference vessel diameter within the range of 4.5 mm and 9.5 mm at the target lesion.

3. CONTRAINDICATIONS

Use of the PROTÉGÉ RX Carotid Stent System is contraindicated under these circumstances:

- Patients in whom anticoagulant, antiplatelet therapy or thrombolytic drugs is contraindicated.
- Patients with vascular tortuosity or anatomy, which precludes the safe introduction of the sheath, guide catheter, embolic protection device, or stent system.
- Patients with known hypersensitivity to nickel-titanium.
- Patients with uncorrected bleeding disorders.
- Lesions in the ostium of the common carotid artery.

4. 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.

4.1 General

Refer to the Instructions for Use supplied with all interventional devices to be used in conjunction with the PROTÉGÉ RX Carotid Stent System for their intended uses, contraindications and potential complications.

The clinical data contained within this document reflects data generated using the PROTÉGÉ GPS™ Carotid Stent System and the PROTÉGÉ RX Carotid Stent Systems.

The safety and efficacy of the PROTÉGÉ RX Carotid Stent System in the carotid indication has not been demonstrated with embolic protection devices other than with the ev3 embolic protection devices. The long-term performance (> 3 years) of the PROTÉGÉ RX Carotid Stent System has not been established.

As with any type of vascular implant, infection secondary to contamination of the stent may lead to thrombosis, pseudoaneurysm, or rupture.

Stenting across a major bifurcation may hinder or prevent future diagnostic or therapeutic procedures.

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.

The appropriate antiplatelet and anticoagulation therapy should be administered pre- and post-procedure as suggested in these instructions. Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease.

When multiple stents are required, stent materials should be of similar composition. The safety and effectiveness of the PROTÉGÉ RX Carotid Stent System have NOT yet been established in patients with the characteristics noted below.

General Characteristics

- Low to moderate risk for adverse events from carotid endarterectomy.
- Pregnant patients or patients under the age of 18.
- Patients in whom femoral access is not possible.
- Chronic or paroxysmal atrial fibrillation that is not treated by Coumadin®.
- Prior stenting of the target carotid artery.
- Documented intolerance to both heparin and Angiomax.
- Allergy or contraindication to aspirin, or to clopidogrel AND ticlopidine, or to nickel or titanium.
- Active bleeding diathesis requiring blood transfusion within 1 month prior to procedure.
- Myocardial infarction (total CK > 3 times lab normal and MB above the normal limit) within 72 hours prior to procedure.
- Coronary artery bypass graft or vascular surgery within 30 days prior to procedure.
- Major residual neurological deficit (stroke scales: Barthel < 60, NIH > 15 or Rankin > 3) at pre-procedure neurological exam.
- Transient ischemic attack or amaurosis fugax within 48 hours prior to procedure.
- Cerebral vascular accident or retinal artery occlusion within 1 month prior to procedure.
- Allergy to radiographic contrast that cannot be pre-treated.
- Abnormal blood counts with platelets < 50,000 or > 700,000 mm^3 or white blood cell count < 3000 mm^3.
- Current radiation treatment for cerebral carcinoma or sarcoma presenting with occluded or sclerosed vessels.
- Patients who exhibit persistent acute intraluminal thrombus of the proposed lesion site, post thrombolytic therapy.
- Perforation at the angioplasty site evidenced by extravasation of contrast medium.
- Patients contraindicated for PTA.

Angiographic Characteristics

- Peripheral vascular disease that precludes safe sheath insertion.
- Total occlusion of target carotid artery.
- Ostial common carotid artery stenosis requiring treatment.
- Multiple carotid stenoses in the same vessel that cannot be covered by one stent.
- Ipsilateral intracranial stenosis that requires treatment.
- Presence of any intracranial tumor(s), arteriovenous malformations (AVMs), or an aneurysm requiring treatment.

The safety and effectiveness of concurrent treatment of lesions in patients with bilateral carotid artery disease have not been established.

4.2 Specific

The device is provided sterile for single use only. DO NOT reprocess or resterilize. Reprocessing and resterilizing increase the risk of patient infection and risk of compromised device performance.

Do not use the product after the “Use By Date” printed on the package.

Maintain the patient’s Activated Clotting Time (ACT) at > 250 seconds throughout PROTÉGÉ RX Carotid Stent System usage to prevent thrombus formation on the device.

Maintain continuous flush while removing and reinserting devices on the guidewire. Perform all exchanges slowly to prevent air embolism or trauma to the artery.

Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stent and may cause acute closure of the vessel, requiring additional intervention (carotid endarterectomy, further dilatation, or placement of additional stents).

The stent may cause thrombus, distal embolization or may migrate from the site of implant down the arterial lumen. Appropriate sizing of the stent to the vessel is required to reduce the possibility of stent migration. In the event of thrombosis of the expanded stent, thrombolysis and PTA should be attempted.

In the event of complications such as infection, pseudoaneurysm or fistulization, surgical removal of the stent may be required.

Overstretching of the artery may result in rupture and life-threatening bleeding.

Never withdraw or move an intravascular device against any resistance until the cause is determined. Advancing with such resistance may lead to embolization of debris, and vessel and/or device damage.

Frequently observe the PROTÉGÉ RX Carotid Stent System under fluoroscopy during stent deployment.

Exercise caution when advancing or withdrawing the PROTÉGÉ RX Carotid Stent System through any previously placed devices.

Allow for and maintain adequate distance between the embolic protection device and the stent delivery system or deployed stent to avoid potential entanglement.

Ensure optimal positioning of the stent prior to deployment. Once deployment is initiated, the stent cannot be repositioned or recaptured. Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the carotid vasculature and/or the vascular access site. Complications may include death, stroke, bleeding, hematoma or pseudoaneurysm.

5. PRECAUTIONS

Carefully inspect the sterile package and device prior to use to verify that neither has been damaged during shipment. Do not use damaged equipment.

Do not remove the stent from its delivery system as removal may damage the stent. The stent and delivery system are intended to perform as a system. If removed, the stent cannot be put back on the delivery system.

The delivery system should not be used in conjunction with other stents.

Ensure the stent system is fully flushed with heparinized saline prior to use.

Venous access should be available during carotid stenting to manage bradycardia and/or hypotension by either pharmaceutical intervention or placement of a temporary pacemaker, if needed.

Advancement and deployment of the PROTÉGÉ RX Carotid Stent System should only be performed under fluoroscopic observation.

If resistance occurs during movement through the sheath, carefully withdraw the stent system.

If resistance is felt when initially retracting the outer deployment sheath, do not force deployment. Carefully withdraw the stent system without deploying the stent.

Only one stent should be used to cover the target lesion. If more than one stent is required to cover the lesion after initial stent placement, or if there are multiple lesions, the distal lesion should be stented first, followed by stenting of the proximal lesion.

If use of sequential stents is necessary, the sequential stents must be overlapped; however, the amount of overlap should be kept to a minimum.

Use caution when crossing a deployed stent with any adjunct device.

5.1 MRI Compatibility

Through non-clinical testing, the PROTÉGÉ RX Carotid Stent has been shown to be MR Conditional[1] at field strengths of 3 Tesla or less and a maximum whole body average specific absorption rate (SAR) of 3 W/kg for 20 min of MR. The stent should not migrate in this MR environment. Non-clinical testing has not been performed to rule out the possibility of stent migration at field strengths higher than 3 Tesla.

In this testing, the stent produced a temperature rise of less than 0.54° C at a maximum whole body averaged specific absorption rate (SAR) of 3 W/kg for 20 minutes of MR. The effect of heating in the MRI environment for overlapping stents or stents with

fractured struts is not known.

MR image quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the stent.

[1]MR Conditional as defined in ASTM F2503-05

6. ADVERSE EVENTS

6.1 Observed Adverse Events

The PROTÉGÉ GPS Carotid Stent System was evaluated for the treatment of internal and/or common carotid artery stenoses in high-risk patients via the Carotid Revascularization with ev3 Arterial Technology Evolution (CREATE) Trial. A total of 419 patients were enrolled in the CREATE Pivotal Trial. The primary objective of the study was to demonstrate the safety and effectiveness of the PROTÉGÉ GPS Carotid Stent System and SPIDER™ Embolic Protection Device in the treatment of common and/or internal carotid artery stenoses for subjects that are at high-risk for carotid endarterectomy.

Table 2 presents the serious adverse events that were reported within the first 30 and 365 days for registry patients enrolled in the CREATE Pivotal Trial.

Table 3 presents the cause of all patient deaths.

The numbers and types of adverse events observed were anticipated given the high co-morbid state of these patients.

TABLE 2: Serious Adverse Event Summary (≤ 30 Days, ≤ 365 Days)

Description of Event	≤30 Days (N=417)		≤365 Days (N=395)*	
	n	%	n	%
All Death, Stroke and MI	26 / 417	6.2%	37 / 395	9.4%
Death (study-defined[1]) Stroke-Related Not Stroke-Related	8 / 417 5 / 417 3 / 417	1.9% 1.2% 0.7%	21 / 395 9 / 395 12 / 395	5.3% 2.3% 3.0%
All-cause Death	8 / 417	1.9%	35 / 395	8.7%
Ipsilateral Stroke Major Minor Non-ipsilateral Stroke	16 / 417 14 / 417 3 / 417 4 / 417	3.8% 3.4% 0.7% 1.0%	19 / 395 16 / 395 4 / 395 4 / 395	4.8% 4.1% 1.0% 1.0%
Non-stroke Neurological[2]	8 / 417	1.9%	8 / 395	2.0%
Restenosis (≥70% stenosis as measured by ultrasound)[3]	0 / 417	0.0%	1 / 395	0.3%
Restenosis (≥50% stenosis as measured by ultrasound)[4]	14 / 417	3.4%	27 / 395	6.8%
Target Lesion Revascularization (TLR)[5]	0 / 417	0.0%	1 / 395	0.3%
Cardiac MI Arrhythmia Angina Congestive Heart Failure (CHF) Coronary Artery Disease (CAD)	14 / 417 4 / 417 2 / 417 0 / 417 7 / 417 1 / 417	3.4% 1.0% 0.5% 0.0% 1.7% 0.2%	16 / 395 4 / 395 3 / 395 0 / 395 8 / 395 1 / 395	4.1% 1.0% 0.8% 0.0% 2.0% 0.3%
Procedural Complication Hypotension Arrhythmia Vasospasm Dissection In-stent Thrombosis Emergent CEA Emergent Intervention	81 / 417 71 / 417 12 / 417 0 / 417 5 / 417 0 / 417 0 / 417 3 / 417	19.4% 17.0% 2.9% 0.0% 1.2% 0.0% 0.0% 0.7%	81 / 395 71 / 395 12 / 395 0 / 395 5 / 395 0 / 395 0 / 395 3 / 395	20.5% 18.0% 3.0% 0.0% 1.3% 0.0% 0.0% 0.8%
Access Site Complication[6] Requiring Repair/Transfusion	11 / 417 8 / 417	2.6% 1.9%	11 / 395 8 / 395	2.8% 2.0%
Vascular[7]	3 / 417	0.7%	4 / 395	1.0%
Hemodynamic[8]	4 / 417	1.0%	4 / 395	1.0%
Bleeding[9] Requiring transfusion GI bleeding	22 / 417 20 / 417 7 / 417	5.3% 4.8% 1.7%	25 / 395 22 / 395 12 / 395	6.3% 5.6% 3.0%
Blood Dyscrasia[10]	0 / 417	0.0%	0 / 395	0.0%
Respiratory[11]	5 / 417	1.2%	5 / 395	1.3%
Gastrointestinal[12]	0 / 417	0.0%	5 / 395	1.3%
Genitourinary[13]	3 / 417	0.7%	5 / 395	1.3%
Infection[14]	3 / 417	0.7%	3 / 395	0.8%
Metabolic[15]	7 / 417	1.7%	7 / 395	1.8%
Musculoskeletal[16]	0 / 417	0.0%	0 / 395	0.0%
Other[17]	4 / 417	1.0%	6 / 395	1.5%

Patients may have had multiple events and therefore can be counted in more than one category / subcategory of event. Counts represent the number of patients who have experienced one or more events.

* Patients were excluded if they missed the one-year visit, withdrew or were lost-to-follow-up and did not have any reported adverse events.

Events are categorized by body system and are defined as follows:

[1] **Death (study-defined):** The Clinical Events Committee (CEC) adjudicated all deaths to determine if the death was considered a study adverse event (i.e., device-related, procedure related, and/or a study endpoint). Study-defined deaths do not include 14 deaths adjudicated as non-study related by the CEC including accident, cancer, respiratory failure, renal failure, cardiac death, and unknown death.

[2] **Non-stroke neurological:** includes visual/speech disturbances, confusion, seizure, weakness and TIA.

[3] **Restenosis:** re-narrowing of lesion as defined in the protocol by a ≥ 70% stenosis as determined via duplex ultrasound scan

[4] **Restenosis rates:** representing ≥ 50% stenosis in the target lesion as determined by duplex ultrasound are also reported, as this definition is commonly employed for surgical revascularization outcomes.

[5] **Target Lesion Revascularization (TLR):** any repeat invasive procedure, including angioplasty, stenting, endarterectomy, or thrombolysis, performed to open or increase the luminal diameter inside or within 10 mm of the previously treated lesion.

[6] **Access site complications:** bruising, hematoma and bleeding.

[7] **Vascular:** peripheral arterial disease, artery perforation and deep vein thrombosis.

[8] **Hemodynamic:** includes hypotension and hypertension (that are not procedural complications), syncope and dizziness.

[9] **Bleeding:** includes non-access site bleeding, anemia up to 30 days, GI bleed up to 30 days and subarachnoid hemorrhage.

[10] **Blood dyscrasia:** includes anemia later than 30 days and thrombocytopenia.

[11] **Respiratory:** includes pneumonia, embolism, chronic obstructive pulmonary disease (COPD) and respiratory failure.

[12] **Gastrointestinal:** includes nausea, ulcer, bowel obstruction and GI bleed later than 30 days.

[13] **Genitourinary:** includes urinary tract infection, hematuria, urosepsis and prostatic hyperplasia.

[14] **Infection:** includes laryngitis, puncture site infection, sepsis, endocarditis and bacteremia from IV site.

[15] **Metabolic:** includes diabetes, electrolyte imbalance, metabolic acidosis, renal insufficiency and renal failure.

[16] **Musculoskeletal:** includes pain, fractures and joint replacements.

[17] **Other:** Subconjunctival hemorrhage and clot in left eye secondary to fall (n=1), stent misplacement (n=1), filter perforation through delivery catheter (n=1), psychiatric admission for major depression (n=1), drug side effect (n=2).

TABLE 3: Cause of All Death (≤ 30 Days, ≤ 365 Days)

Cause of Death	≤30 Days		≤365 Days	
	Pivotal N=8	%	Pivotal N=35	%
Stroke	5/417	1.2%	9/395	2.3%
Cardiac	3/417	0.7%	14/395	3.5%
Cancer	NA	NA	4/395	1.0%
Infection	NA	NA	2/395	0.5%
Accidental	NA	NA	2/395	0.5%
Other	NA	NA	2/395	0.5%
Unknown	NA	NA	2/395	0.5%

6.2 Potential Adverse Events

Based on the literature, and on clinical and commercial experience with carotid stents and embolic protection devices, the following alphabetical list includes possible adverse events associated with the use of these devices:

- Abrupt closure
- Allergic reactions to procedural medications, contrast dye or device materials
- Amaurosis fugax
- Aneurysm
- Angina/coronary ischemia
- Arrhythmia
- Arterial occlusion or thrombosis at puncture site or remote site
- Arteriovenous fistula
- Bacteremia or septicemia
- Bleeding from anticoagulant or antiplatelet medications
- Bleeding, with or without transfusion
- Cerebral edema
- Cerebral hemorrhage
- Cerebral ischemia or transient ischemic attack (TIA)
- Congestive heart failure (CHF)
- Death
- Detachment of a component of the device system
- Embolism (air, tissue, thrombus)
- Emergent or urgent endarterectomy surgery (CEA)
- Fever
- Filter thrombosis or occlusion
- Fluid overload
- Groin hematoma, with or without surgical repair
- Hemorrhage, with or without transfusion
- Hyperperfusion syndrome
- Hypotension or hypertension
- Infection and/or pain at the puncture site
- Ischemia or infarction of tissue/organ
- Myocardial infarction (MI)
- Pain (head, neck)
- Pseudoaneurysm, femoral
- Renal failure/insufficiency (new or worsening)
- Restenosis of stented segment
- Seizure
- Severe unilateral headache
- Slow/no flow during procedure
- Stent/filter collapse or fracture
- Stent/filter entanglement or damage
- Stent/filter failure to deploy
- Stent embolization, migration or misplacement
- Stent or vessel thrombosis/occlusion
- Stroke/cerebrovascular accident (CVA)
- Total occlusion of carotid artery
- Vessel dissection, flap, perforation, or rupture
- Vessel spasm or recoil

Any device-related adverse event occurring involving the PROTÉGÉ RX Carotid Stent System should be reported immediately to ev3 Inc. Customer Service: 1-800-716-6700.

7. CLINICAL STUDIES

7.1 Create Pivotal

The Carotid Revascularization with ev3 Inc. Arterial Technology Evolution (CREATE) Pivotal Trial was a prospective, non-randomized, multi-center, single-arm clinical trial. The trial was performed to demonstrate the safety and efficacy of the PROTÉGÉ GPS Carotid Stent System and the SPIDER Embolic Protection Device when used to treat high-risk symptomatic and asymptomatic patients with internal and/or common carotid artery stenoses. A total of 419 patients were enrolled at 31 clinical sites in the United States. Of these 419, twenty-five underwent staged stenting of both carotid arteries. For these subjects, both lesions were enrolled into the CREATE Pivotal Trial, bringing the total lesion count to 444.

An overview of the CREATE Pivotal Trial is presented in **Table 4**.

TABLE 4: Overview of CREATE Pivotal Trial

Products Evaluated	Over-the-wire PROTÉGÉ GPS Carotid Stent System and over-the-wire SPIDER Embolic Protection Device
Study Design	Non-randomized, multi-center, single-arm, prospective clinical trial
Patients Enrolled	419
Number of Sites	31
Primary Endpoint	30-day composite of myocardial infarction (MI), ipsilateral stroke, procedure-related contralateral stroke or death AND ipsilateral stroke from 31 to 365 days post-implantation
Secondary Endpoints	- Ipsilateral stroke, procedure-related contralateral stroke, or death within 30 days of implantation; and ipsilateral stroke from 31 to 365 days post-implantation. - Target lesion revascularization through 1 year - Target vessel revascularization through 1 year - Primary patency at 1 year (defined as < 70% stenosis as measured by duplex scan) - Technical Success (defined as successful delivery and retrieval of the filter and stent deployment with final residual stenosis < 50%)
Study Hypothesis	The primary endpoint rate for the treatment is significantly less than the upper limit of an objective performance criterion (uOPC) of 16%.
Patient Follow-up	25-45 days post procedure: neurological evaluation by neurologist or NIH-approved surrogate, adverse event assessment, ultrasound 150-240 days post procedure: Telephone follow-up including evaluation of Barthel Index and Rankin Score, adverse event reporting, current anticoagulation/antiplatelet regimen 335-425 days post procedure: neurological evaluation by neurologist or NIH-approved surrogate, adverse event assessment, ultrasound

Core laboratories provided independent assessments of angiographic and ultrasound data. Monitors reviewed all data to ensure appropriate reporting of adverse events and adherence to the study protocol. A Clinical Events Committee (CEC) consisting of non-investigators adjudicated adverse events reports for study subjects. A Data Safety Monitoring Board (DSMB) monitored study progress and adverse events to ensure patient safety.

Statistical Methods

The statistical analysis of the CREATE Pivotal Trial demonstrated that the primary endpoint is significantly less than an objective performance criterion (uOPC). The upper bound of the confidence interval around the primary endpoint observed was expected to be less than the uOPC of 16%. The estimated rate for the carotid artery stent system would be similar to the rate observed in the SAPPHIRE study at one year of 9.8%. Conservatively, an 11% rate was estimated for the primary endpoint. The sample size estimation was determined by assuming an exact confidence interval for this primary endpoint. The following assumptions were made to determine sample size:

- Although the estimated endpoint rate for the ev3 carotid stent is 9.8%, a conservative estimate for sample size assumed a rate of 11%.
- The Type I error rate $\alpha = 0.05$
- This Type I error is one-sided
- The Type II error rate $\beta = 0.20$, which is equivalent to 80% power
- uOPC of 16%

Hypothesis

H_0: $p \geq 16\%$

H_A: $p < 16\%$

where p is the observed primary endpoint rate for the PROTÉGÉ GPS Carotid Stent System. A one-sided upper 95% confidence bound that is less than 16% is equivalent to rejecting H_0 at the 0.05 level of significance and concluding the primary endpoint rate is significantly less than the uOPC of 16% (p-value <0.0001). Exact methods were used to form the confidence bound.

Eligibility Criteria Summary

Male and female patients who presented for percutaneous treatment of an internal and/or common carotid artery intervention were considered for enrollment. To be included, the patients were required to be at least 18 years old and considered to be at high-risk for carotid endarterectomy.

Patients were considered symptomatic if their target stenosis was associated with ipsilateral transient or visual TIA evidenced by amaurosis fugax, ipsilateral hemispheric TIAs or ipsilateral ischemic stroke within 6 months prior to enrollment. Patients who were characterized as symptomatic were also required to have a target lesion stenosis (as defined in the NASCET trial) >50%. Asymptomatic patients were required to have a target lesion stenosis ≥ 70%.

High-risk criteria are included in **Table 5**.

TABLE 5: High Surgical Risk Criteria

Clinical Criteria[1]	Anatomic Criteria[1]
1. Age >75 2. CCS angina class 3-4 or unstable angina 3. CHF class III-IV 4. LVEF <35% 5. Myocardial infarction <6 weeks pre- procedure 6. Coronary artery disease with >two-vessel disease in major vessel and history of angina 7. Severe pulmonary disease: home oxygen,resting pO^2 <60 or FEV^1 <50% 8. Permanent contralateral cranial nerve injury	1. Contralateral carotid artery occlusion 2. High cervical lesion (above the angle of the jaw) 3. Infraclavicular lesion 4. Tandem lesions >70% 5. Previous cervical radiation treatment, tracheostomy/stoma, or radical neck dissection 6. Restenosis from previous carotid endarterectomy 7. Cervical immobility due to fusion or arthritis 8. Bilateral carotid stenoses, both requiring treatment

[1] The subjects were required to meet at least ONE or more high-risk criterion in EITHER the clinical or anatomical section.

Description of Patients Evaluated

Table 6 summarizes patient follow-up compliance in the CREATE Pivotal Trial.

TABLE 6: CREATE Pivotal Trial Patient Follow-up

Time	Compliance
Procedure	419 / 419 (100%)
Discharge	417 / 419 (99.5%)
30 Days	405 / 419 (96.7%)

Time	Compliance
6 Months	386 / 419 (92.1%)
12 Months	353 / 419 (84.2%)
Primary Endpoint	370 / 419 (88.3%)

Baseline demographics and lesion characteristics for subjects enrolled in the CREATE Pivotal trial are presented in **Table 7**.

TABLE 7: Baseline Demographics and Lesion Characteristics (All Patients Treated)

Patient Characteristics	Pivotal (N=419)
Age (yrs.) Mean SD (N) Range (min, max)	 73.6 9.1 (419) 48 (46, 94)
Male	(255 / 419) 60.9%
Diabetes Mellitus	(131 / 419) 31.3%
Hypertension	(377 / 419) 90.0%
Hyperlipidemia	(367 / 419) 87.6%
Renal Insufficiency	(80 / 419) 19.1%
Smoking Never Current Former >1 Year	 (96 / 419) 22.9% (69 / 419) 16.5% (254 / 419) 60.6%
History of Arrhythmia	(84 / 419) 20.0%
History of Myocardial Infarction	(126 / 419) 30.1%
History of previous PTCA/CABG	(219 / 419) 52.3%
History of CEA	(123 / 419) 29.4%
History of Other Treatment to Target Artery	(3 / 419) 0.7%
History of TIA	(97 / 419) 23.2%
History of Stroke	(85 / 419) 20.3%
Current Carotid Bruit	(318 / 411) 77.4%
Lesion Location Common Internal Both	 (25 / 444) 5.6% (334 / 444) 75.2% (85 / 444) 19.1%
Lesion Length (mm)	17.5
Eccentric Lesion	(337 / 442) 76.2%
Calcified Lesion	(222 / 442) 50.2%
Ulcerated Lesion	(173 / 442) 39.1%
Symptomatic	(73 / 419) 17.4%
Pre-procedure % Stenosis	82.2
Pre-reference Vessel Diameter	5.5
Pre-vessel Diameter (minimum lumen diameter) Mean SD (N) Range (min, max)	 1.9 0.8 (377) 7.3 (0.4, 7.7)
Post-vessel Diameter Mean SD (N) Range (min, max)	 4.4 0.83 (365) 4.8 (2.4, 7.2)
High Risk Factors Anatomical Clinical Both	 (100 / 419) 23.9% (196 / 419) 46.8% (123 / 419) 29.4%
Clinical Risk Factors Age >75 CCS Angina 3-4 CHF NYHA III-IV CAD LVEF <35% MI <6 weeks Perm. Contralateral Injury Severe Pulmonary Disease	 (209 / 419) 49.9% (17 / 419) 4.1% (28 / 419) 6.7% (146 / 419) 34.8% (41 / 419) 9.8% (3 / 419) 0.7% (0 / 419) 0.0% (16 / 419) 3.8%
Anatomical Risk Factors Bilateral Carotid Stenosis CEA Restenosis Cervical Immobility High Cervical Lesion Contralateral Occlusion Hostile Neck Infraclavicular Lesion Tandem Lesions >70%	 (43 / 419) 10.3% (100 / 419) 23.9% (11 / 419) 2.6% (26 / 419) 6.2% (40 / 419) 9.5% (29 / 419) 6.9% (1 / 419) 0.20% (3 / 419) 0.70%

Clinical Results Summary

The primary endpoint of the CREATE Pivotal Trial was a composite of MI, ipsilateral stroke, procedure-related contralateral stroke or death within 30 days of implantation and ipsilateral stroke within one year of implantation (also referred to as MACCE). Reported primary endpoint events in the CREATE Pivotal Trial included four myocardial infarctions; 16 ipsilateral strokes, 14 of which were classified as major; three procedure-related contralateral strokes, eight deaths and three ipsilateral strokes between 31 and 365 days. Of these events, 14 of the 34 were classified as device-related by the Clinical Events Committee. **Figures 2 and 3** contain primary endpoint Kaplan-Meier Survival Estimates overall and by symptom group. In **Table 8**, each component of the overall MACCE definition is listed with its corresponding occurrence. When the overall 30-day MACCE number was calculated, it was done in a hierarchical fashion and only the worst event that occurred in any subject was counted. The individual components of MACCE were actually counted per occurrence.

Kaplan-Meier Analysis of Time to Primary Endpoint (All Patients)

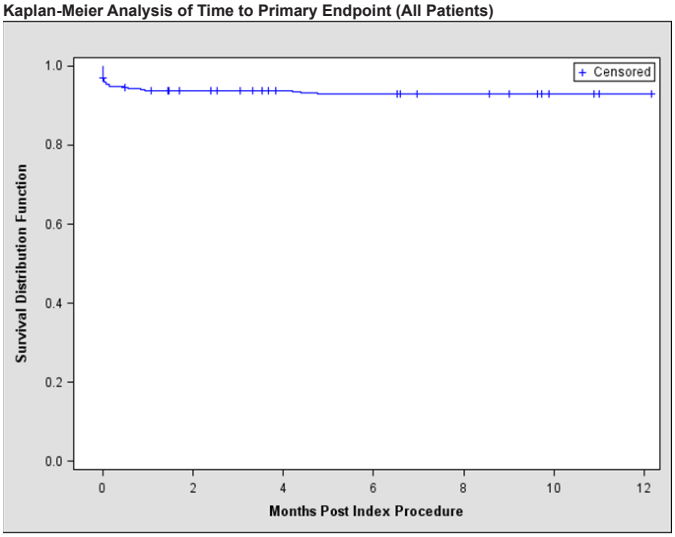


FIGURE 2: Primary Endpoint Overall Pivotal Cohort

All Patients					
Months After Index Procedure	0	1	3	6	12
Number At Risk	419	391	384	376	366
Number Censored	0	2	9	14	24
Number of Events	0	26	26	29	29
Percent Event Free	100%	93.8%	93.8%	93.0%	93.0%

Kaplan-Meier Analysis of Time to Primary Endpoint (Symptomatic vs. Asymptomatic Subjects)

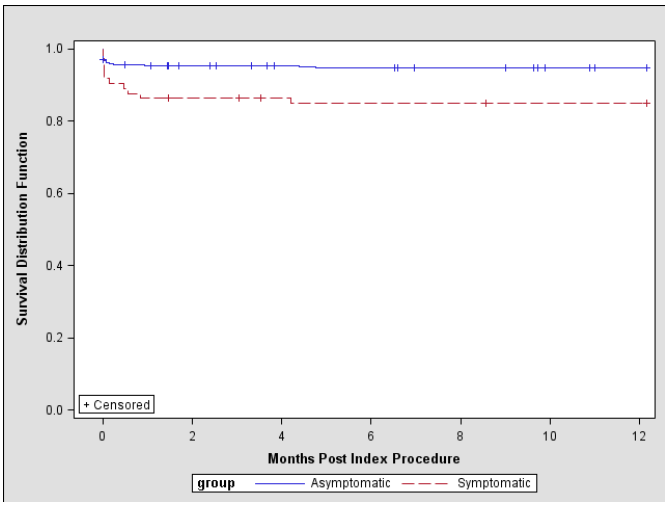


FIGURE 3: Primary Endpoint by Symptom Group

Asymptomatic Patients					
Months After Index Procedure	0	1	3	6	12
Number At Risk	346	328	322	317	308
Number Censored	0	2	8	11	20
Number of Events	0	16	16	18	18
Percent Event Free	100%	95.4%	95.4%	94.8%	94.8%

Symptomatic Patients					
Months After Index Procedure	0	1	3	6	12
# At Risk	73	63	62	59	58
# Censored	0	0	1	3	4
# Events	0	10	10	11	11
% Event Free	100%	86.3%	86.3%	84.9%	84.9%

TABLE 8: Safety and Efficacy Measures (All Patients Treated)

Safety and Efficacy Measures	Pivotal (N=419)
Primary Endpoint	29 / 370 (7.8%)
30-Day MACCE*	26 / 414 (6.3%)
Myocardial Infarction	4 / 414 (1.0%)
Ipsilateral CVA	16 / 414 (3.9%)
- Major	14 / 414 (3.4%)
- Minor	3 / 414 (0.7%)
Procedure-Related Contralateral CVA	3 / 414 (0.7%)
Death	8 / 414 (1.9%)
1 year Ipsilateral CVA	3 / 370 (0.8%)
Secondary Endpoints	
MANE**	26 / 370 (7.0%)
TLR	1 / 370 (0.2%)
TVR	1 / 370 (0.2%)
Primary Patency at 1 year	286 / 304 (94.1%)
Technical Success	408 / 419 (97.4%)
Acute Procedure Success (QCA)	397 / 397 (100.0%)
Acute Procedure Success (Site)	437 / 441 (98.4%)

* 30-day MACCE is done via a hierarchical calculation. Only the worst event that occurred in any subject is counted. The individual components of MACCE are counted per occurrence.

** Major Adverse Neurological Events (MANE) includes 11 elements of the primary endpoint **except** myocardial infarction.

In the CREATE Pivotal Trial, 29 of the 370 subjects followed to one year were observed to have at least one primary endpoint. This leads to an overall primary endpoint rate of 7.8% (29/370 = 7.8%). This estimate of the primary endpoint rate was performed only on subjects with recorded endpoints, excluding subjects with missing endpoint information. Using exact confidence methods, the upper 95% confidence limit for the primary endpoint rate was 11.3%. The corresponding p-value for the above null hypothesis is less than 0.0001. Thus, the null hypothesis that the primary efficacy of the carotid stent system is equal to or greater than 16% is rejected and the primary endpoint event rate is significantly less than 16% (p-value < 0.0001).

7.2 CREATE Post Approval Study

The Carotid Revascularization with ev3 Arterial Technology Protégé Stent with the SpiderFX Evolution Post Approval Study (CREATE PAS) was a prospective multicenter study initiated after FDA's approval of the PROTÉGÉ RX Carotid Stent System. The objectives of the study were:

- To confirm the safety and effectiveness of the PROTÉGÉ GPS and PROTÉGÉ RX Carotid Stent Systems and ev3 embolic protection devices when used in the treatment of common and/or internal carotid artery stenoses for subjects with a high-risk for complications during endarterectomy.
- To evaluate rare and unanticipated adverse events among subjects treated with carotid stenting using the PROTÉGÉ stent with the ev3 embolic protection devices when used in the treatment of common and/or internal carotid artery stenoses for subjects with a high-risk for complications during carotid endarterectomy.

Eligibility Criteria Summary

This section summarizes data on 1500 subjects enrolled in CREATE PAS at 57 investigational sites within the United States. The first 500 subjects were enrolled in the one-year follow-up cohort. The required visit schedule consisted of a baseline visit, procedure, pre-discharge visit, 30-day clinic visit, 6-month telephone contact and one-year clinic visit. The subsequent 1,000 subjects were enrolled in the 30-day follow-up cohort. The required visit schedule consisted of a baseline visit, procedure, pre-discharge visit and a 30-day clinic visit. The subjects were enrolled in CREATE PAS between May 2007 and October 2011.

Description of Pateints Evaluated

Table 9 summarizes patient follow-up compliance in CREATE PAS.

TABLE 9: CREATE PAS: Follow-up Compliance Rate

Follow-up visit	Cohort		Overall (N=1500)
	30-day (N=1000)	1-Year (N=500)	
30-day	951/1000 (95.1%)	473/500 (94.6%)	1424/1500 (94.9%)
6-month	-	452/500 (90.4%)	452/500 (90.4%)
1-year	-	397/500 (79.4%)	397/500 (79.4%)

Baseline Patient Demographics

Baseline demographic and clinical characteristic for all subjects enrolled in CREATE PAS are presented in **Table 10**.

TABLE 10: Baseline Demographics & Clinical Characteristics

Subject Characteristics	All Subjects (N = 1500)
Age (yrs.)	
Mean ± SD (N)	72.5 ± 9.5 (1500)
Range (min, max)	(37.2, 96.6)
Male	61.5% (923/1500)
Medical History	
Diabetes	35.8% (537/1500)
Hypertension	89.0% (1335/1500)
Hyperlipidemia	85.3% (1279/1500)
Renal insufficiency	15.4% (231/1500)
Tobacco Use	
Current Smoker	22.4% (335/1496*)
Former Smoker	52.1% (779/1496*)
Non Smoker	25.5% (382/1496*)

Subject Characteristics	All Subjects (N = 1500)
Arrhythmia	18.9% (284/1500)
Myocardial infarction	24.6% (368/1498*)
Previous PTCA/CABG	50.4% (756/1500)
Baseline Lesion and Vessel Characteristics	
Lesion Location	
Both	10.1% (151/1499*)
Common	2.7% (41/1499*)
Internal	87.0% (1304/1499*)
Eccentric lesion	63.3% (949/1500)
Calcified lesion	46.5% (698/1500)
Ulcerated lesion	31.8% (477/1500)
Lesion length (mm)	
Mean ± SD (N)	17.2 ± 8.4 (1497*)
Range (min, max)	(1.0, 65.0)
Pre-Procedure diameter stenosis (%)	
Mean ± SD (N)	85.7 ± 7.6 (1499*)
Range (min, max)	(50.0, 100.0)
Reference Vessel diameter (mm)	
Mean ± SD (N)	5.3 ± 1.0 (1492*)
Range (min, max)	(0.3, 20.0)
Symptomatic Carotid Stenosis	19.9% (298/1500)
High Risk Factors	
Clinical	51.5% (771/1496*)
Anatomical	28.2% (422/1496*)
Both	20.3% (303/1496*)

*Note: Data were not available for some subjects.

Results

The primary analysis of the one-year cohort was an assessment of Major Adverse Cardiac and Cerebrovascular Events (MACCE), defined as the combined incidence of death, myocardial infarction (MI), ipsilateral cerebrovascular accident (CVA) and procedure-related contralateral CVA through 30 days post-implantation. It also included an assessment of ipsilateral CVA from 31 days to one year post-implantation.

The primary analysis of the 30-day cohort was an assessment of MACCE, defined as the combined incidence of death, myocardial infarction (MI), ipsilateral CVA and procedure-related contralateral CVA through 30 days post-implantation.

The combined 30-day MACCE rate for both cohorts was 6.6%. The data are presented in **Table 11**.

TABLE 11: MACCE in Both Cohorts

	Percent of Subjects with Event (N=1500)
Death	1.3% (20/1500)
MI	0.7% (11/1500)
Ipsilateral CVA	5.1% (76/1500)
Procedure Related Contralateral CVA	0.1% (2/1500)
Total	6.6% (99/1500)

All physicians enrolling subjects in the CREATE PAS were stratified into three categories with respect to their carotid stenting experience at the time of each subject's procedure:

- **Level One (1):** Physicians who had performed at least 25 CAS procedures as the primary operator.
- **Level Two (2):** Physicians who had performed at least 25 CAS procedures as the primary or secondary operator.
- **Level Three (3):** Physicians who had performed less than 25 CAS procedures.

Primary endpoint data for both cohorts are presented in **Table 12** for the three levels of physician experience.

TABLE 12: MACCE in Both Cohorts by Physician Level of Experience

		CREATE PAS (N=1500)				
Physician Experience Level	**% of Subjects in Each Level**	**Death**	**MI**	**Ipsilateral CVA**	**Procedure-Related Contralateral CVA**	**Total MACCE**
Level 1	92.5% (1388/1500)	1.1% (15/1388)	0.8% (11/1388)	4.8% (67/1388)	0.1% (2/1388)	6.2% (86/1388)
Level 2	3.6% (54/1500)	5.6% (3/54)	0.0% (0/54)	9.3% (5/54)	0.0% (0/54)	13.0% (7/54)
Level 3	3.9% (58/1500)	3.4% (2/58)	0.0% (0/58)	6.9% (4/58)	0.0% (0/58)	10.3% (6/58)
Total	100.0% (1500/1500)	1.3% (20/1500)	0.7% (11/1500)	5.1% (76/1500)	0.1% (2/1500)	6.6% (99/1500)

There were no unanticipated adverse device effects (UADE) identified during the study. A UADE was defined as any serious adverse experience leading to injury, illness, or death of a subject not previously identified in nature, severity or degree of incidence in the protocol that may be directly related to the use of the device.

Conclusion: The results of the CREATE PAS study are comparable to those observed in the CREATE Pivotal study (in which a

6.3% rate of MACCE was observed). These data confirm that the PROTÉGÉ RX Carotid Stent System in conjunction with an ev3 embolic protection device is safe to use in a broader community setting for treating common and/or internal carotid artery stenoses in subjects at high-risk for complications during carotid endarterectomy.

Strenths and Weaknesses

- Over 90% follow-up for the entire study but the study was not powered to detect long-term rare adverse events since follow-up beyond 30 days was limited to the 1-Year cohort.
- CREATE PAS enrolled patients from high, moderate and low volume centers and were treated by physicians that represent Level 1, 2, and 3 experience. However, the overwhelming majority of subjects were treated by physicians with level 1 experience (92.5%). The low number of level 2 and level 3 operators makes it difficult to make any conclusions on the training program.

8. CLINICIAN USE INFORMATION

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.

WARNING: The device is provided sterile for single use only. DO NOT reprocess or resterilize. Reprocessing and resterilizing increase the risk of patient infection and risk of compromised device performance.

WARNING: Do not use the product after the "Use By Date" printed on the package.

8.1 Materials Required

Confirm the compatibility of the PROTÉGÉ RX Carotid Stent System with all interventional devices before actual use.

- 6 F hemostatic introducer sheath or 8 F guiding catheter compatible with the vascular anatomy.
- Balloon dilation catheter (optional)
- 0.014" exchange guidewire
- ev3 Embolic Protection Device
- 5 or 10 cc syringe filled with heparinized saline

CAUTION: The PROTÉGÉ RX Carotid Stent System is not compatible with any guidewire larger than 0.014" (0.36 mm).

8.2 Periprocedural Care

Pre-procedure anticoagulation and antiplatelet requirements were specified in the CREATE Pivotal trial. A baseline dose of acetylsalicylic acid (ASA) of 325 mg was required the day prior and the day of the procedure. For patients on regular Coumadin® therapy, the dose could be reduced to 81 mg.

Several options were given with respect to the loading dose of antiplatelet medication:

- Clopidogrel 75 mg for three days prior to the procedure and the day of the procedure **or**
- Clopidogrel 450 mg the day before the procedure and 75 mg the day of the procedure **or**
- Ticlopidine 1000 mg the day before the procedure and two 250 mg doses the day of the procedure.

Patients were required to take 325 mg ASA **and** either 75 mg of clopidogrel each day or 250 mg of ticlopidine twice a day for three months following the procedure. For patients on regular Coumadin® therapy, the post-procedure ASA dose could be reduced to 81 mg.

WARNING: The appropriate antiplatelet and anticoagulation therapy should be administered pre- and post-procedure as suggested in these instructions. Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease.

8.3 Pre-procedure

Refer to Section 8.2 of these instructions for the suggested pre-procedure pharmacological treatment regimen. The placement of the stent in astenotic or obstructed carotid artery should be done in an angiography procedure room. 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. Access vessels must be sufficiently patent or sufficiently recanalized to proceed with further intervention. Patient preparation and sterile precautions should be the same as for any angioplasty procedure.

8.4 Stent Size Determination

Measure the diameter of the reference vessel (proximal and distal to lesion). Measure the length of the target lesion to determine the length of stent required. Refer to **Table 13** for stent diameter sizing. Choose a stent length at least as long as the targeted stricture. There is no foreshortening of the stent length during deployment.

NOTE: Ensure tapered stent diameters are properly sized to lumen diameters.

TABLE 13: Stent Diameter Sizing

Stent Diameter (mm)	Lumen Diameter (mm)
6	4.5 - 5.5
7	5.5 - 6.5
8	6.5 - 7.5
9	7.5 - 8.5
10	8.5 - 9.5
8-6*	(6.5 - 7.5) - (4.5 - 5.5)
10-7*	(8.5 - 9.5) - (5.5 - 6.5)

*Tapered

WARNING: The PROTÉGÉ RX Carotid Stent System is contraindicated for use with lesions in the ostium of the common carotid artery.

8.5 Preparation of Stent Delivery System

- Open the shelf box to reveal the pouch containing the stent and delivery catheter.

CAUTION: Carefully inspect the sterile package and device prior to use to verify that no damage occurred during shipment.

- After careful inspection of the pouch, looking for damage to the sterile barrier, carefully peel open the outer pouch and extract the tray with contents.
- Set the tray on a flat surface. Carefully pull the lid off the tray and remove the stent/delivery system. Examine the device for damage. If it is suspected that the sterility has been compromised or the device is damaged, do not use the device.
- Examine the distal end of the catheter to ensure the stent is contained within the outer sheath. Do not use if the stent is partially deployed.
- If a gap exists between the catheter tip and outer sheath, 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.
- Flush delivery system with heparinized saline immediately before backloading guidewire. Do not power inject. Apply constant, steady pressure to syringe to ensure delivery system is fully flushed.
  - System is fully flushed when saline exits the distal end of the outer sheath and the RX port while applying constant steady pressure.
  - Attach a 5-10 cc syringe filled with heparinized saline to the Y-connector side port.
  - Loosen Tuohy-Borst valve (counter clockwise) and inject saline until it seeps from the proximal end of the Tuohy-Borst valve.
  - Close Tuohy-Borst valve by turning clockwise.
  - Continue to flush system by injecting saline until it comes out between the distal end of the outer sheath and tip.
  - Cover distal end of outer sheath with fingers and continue to inject until the saline exits the RX Port.

– Just prior to loading onto the guidewire, submerge the catheter distal section into saline.

8.6 Introduction of the Stent Delivery System

- Gain access at the femoral artery using an introducer sheath or guide catheter with a hemostatic valve.
- Insert a 0.014" guidewire of appropriate length across the target stricture via the introducer sheath.
- Refer to the manufacturer's instructions for placement of the ev3 Embolic Protection Device.
- Per physician discretion, pre-dilate the lesion using standard PTA techniques. Remove the PTA balloon from the patient while maintaining lesion access with the guidewire/filter embolic protection device.

CAUTION: During dilation, never expand the balloon such that bleeding or dissection complications could occur.

Advance the device over the embolic protection device through the hemostatic valve and sheath introducer until it exits through the RX Port. Use one hand to hold the proximal end of the guidewire and the other hand to advance the delivery system through the hemostatic valve and guide catheter or introducer sheath to the site of the stricture.

NOTE: If resistance is met during delivery system introduction or advancement, the system should be withdrawn and another system used.

CAUTION: Always use an introducer sheath for the implant procedure to protect both the vessel and puncture site.

8.7 Stent Deployment

- Advance the delivery system until the radiopaque inner shaft markers (distal and proximal ends of the stent) are proximal and distal to the target lesion. For tapered stents, ensure the middle radiopaque inner shaft marker is positioned at the location in which the artery begins to widen.
- Loosen the Tuohy-Borst valve to unlock the system.
- Initiate stent deployment by retracting the outer sheath (Y-connector) while holding the inner shaft (proximal grip) in a fixed position. During release of the stent, the whole length of the flexible deployment system should be kept as straight as possible. A slight back tension on the delivery catheter using the back handgrip is recommended to ensure that the deployment system is stationary and straight. Deployment is complete when the outer sheath passes the proximal inner shaft stent marker and the stent is released from the retainer.

NOTE: When more than one stent is required to open the lesion, place the more distal stent first. Overlap of sequential stents is necessary but the amount of overlap should be kept to a minimum.

8.8 Post Stent Deployment

- While using fluoroscopy, withdraw the entire delivery system as one unit, over the guidewire/embolic protection device, into the catheter introducer sheath and out of the body. Remove the delivery device from the guidewire/embolic protection device.

NOTE: If resistance is met during delivery system withdrawal, advance the outer sheath until the outer sheath contacts the catheter tip and withdraw the system as one unit.

- Using fluoroscopy, visualize the stent to verify full deployment.
- If incomplete expansion exists within the stent at any point along the lesion, post deployment balloon dilation (standard rapid exchange PTA technique) can be performed.

NOTE: The stent cannot be expanded past its predetermined diameter.

- To dilate the stent, select an appropriate size rapid exchange PTA balloon catheter and dilate with conventional technique. The inflation diameter of the PTA balloon should approximate the diameter of the reference vessel.
- Remove the PTA balloon from the patient.
- Recover the embolic protection device.
- Remove the guidewire/embolic protection device and sheath from the body.
- Close entry wound as appropriate.
- Discard the delivery system, guidewire/embolic protection device and sheath.

NOTE: Physician experience and discretion will determine the appropriate drug regimen for each patient.

9. PATIENT INFORMATION

A Patient Brochure, which includes information on carotid artery disease and the carotid stent implant procedure, is available from ev3 upon request. Please contact Customer Service at 1-800-716-6700 to obtain copies.

Patients will also be provided a Stent Implant Card that is filled in during the procedure, which will contain specific information about the PROTÉGÉ RX Carotid Stent System. Patients should keep this card in their possession at all times for procedure/stent identification.

10. HOW SUPPLIED

Sterile: This device is sterilized with Ethylene Oxide. Non-pyrogenic.

Contents: One (1) PROTÉGÉ RX Carotid Stent System

Storage: Store in a dry, dark, cool place.

WARRANTY DISCLAIMER

Although this product has been manufactured under carefully controlled conditions, ev3 has no control over the conditions under which this product is used. ev3 therefore disclaims all warranties, both express and implied, with respect to the product including, but not limited to, any implied warranty of merchantability or fitness for a particular purpose. ev3 Inc. shall not be liable to any person or entity for any medical expenses or any direct, incidental or consequential damages caused by any use, defect, failure or malfunction of the product, whether a claim for such damages is based upon warranty, contract, tort or otherwise. No person has any authority to bind ev3 Inc. to any representation or warranty with respect to the product. The exclusions and limitations set out above are not intended to, and should not be construed so as to contravene mandatory provisions of applicable law. If any part or term of this Disclaimer of Warranty is held to be illegal, unenforceable or in conflict with applicable law by a court of competent jurisdiction, the validity of the remaining portions of this Disclaimer of Warranty shall not be affected, and all rights and obligations shall be construed and enforced as if this Disclaimer of Warranty did not contain the particular part or term held to be invalid.

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