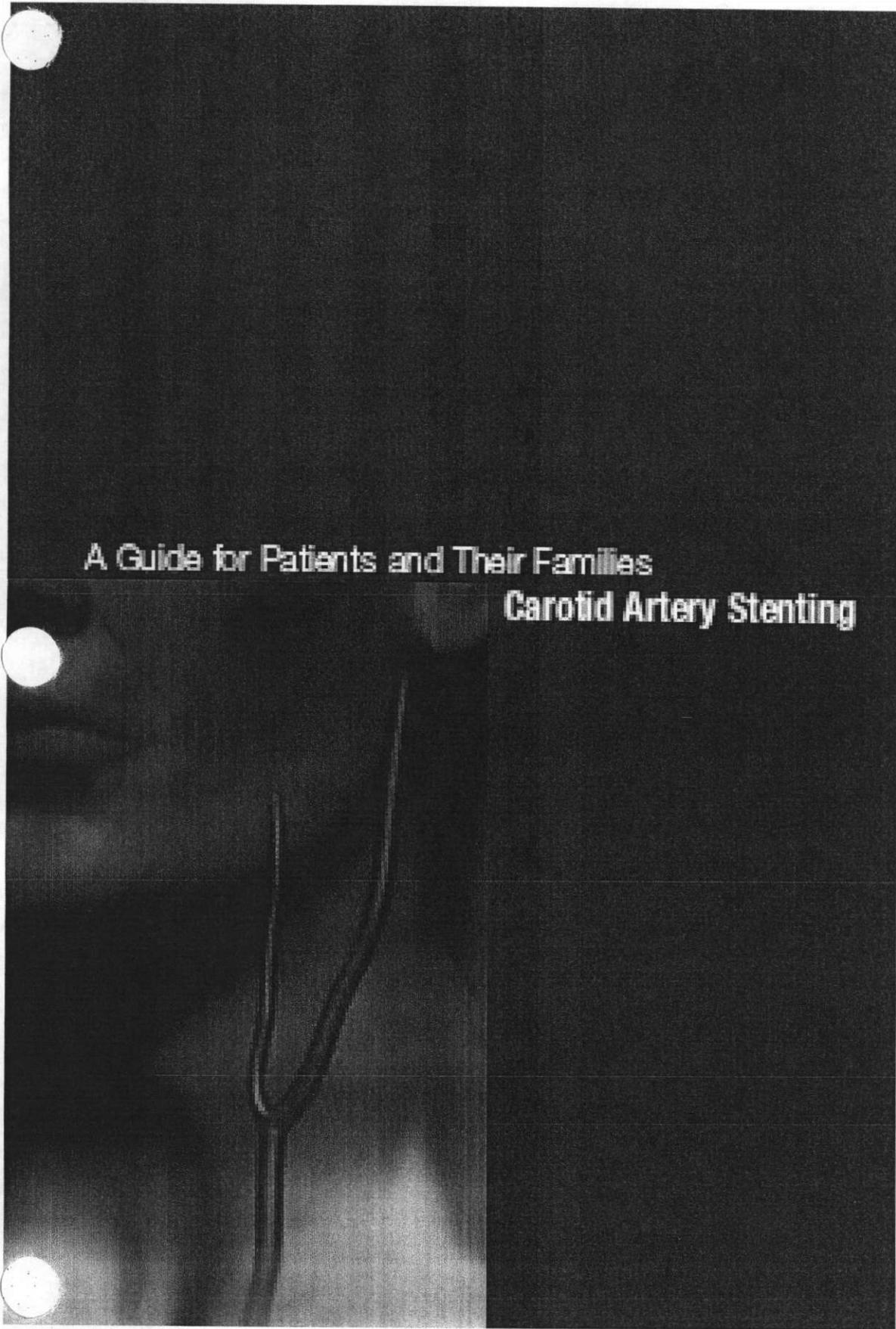


Abbott Vascular Carotid Artery Stenting

A Guide for Patients and Their Families





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Carotid Artery Stenting

Abbott Vascular Carotid Artery Stenting

A Guide for Patients and Their Families

This guide provides you with information about carotid artery disease (narrowing of the neck arteries) and the treatment options. Endovascular treatment (procedures that are done through the blood vessels) using Abbott Vascular's RX Acculink[®] Carotid Stent System or the Xact[™] Carotid Stent System, and the RX Accunet[®] Embolic Protection System or the Emboshield NAV^{6®} Embolic Protection System is one treatment option to reopen your narrowed neck arteries.

Abbott Vascular's Carotid Stent Systems are authorized by Federal (U.S.) law for use in the treatment of carotid artery disease for patients who are ineligible for carotid surgery (endarterectomy) or at risk for surgical or anesthesia-related complications.

This guide provides you with information about the RX Acculink[®] and Xact[™] Carotid Stents and the procedure used to insert a stent into your carotid arteries. As you read, you might think of questions you would like to discuss with your doctor or nurse. You will find a place in the back of this guide for your questions and notes.

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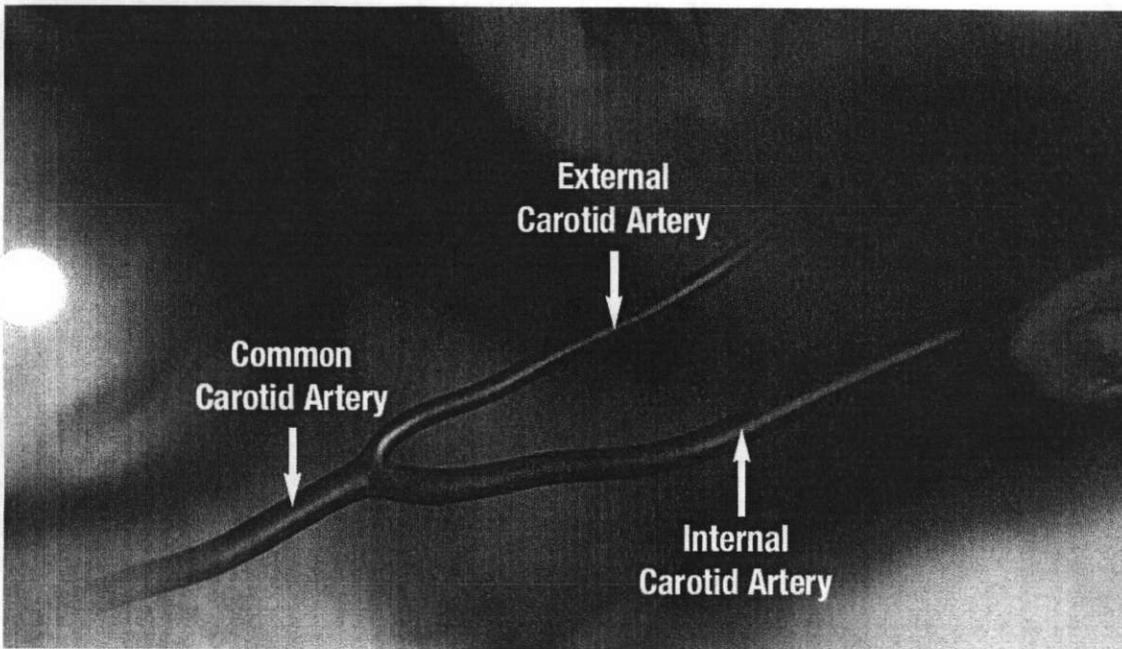
Frequently Asked Questions

Carotid Artery Disease

Your Brain

Your brain is a very active organ. It is the control center of your body. To work well, your brain needs a constant supply of oxygen and other nutrients found in your blood. Most of the blood flow to your brain comes from the carotid arteries which are large blood vessels on either side of your neck. The common carotid arteries (CCA), located on both sides of your neck, divide into two vessels. These vessels are called the external carotid arteries (ECA) and the internal carotid arteries (ICA) see Figure 1. The carotid arteries also bring blood to your face.

Figure 1 – Carotid Arteries



What is Carotid Artery Disease?

Carotid artery disease is a condition that occurs when the arteries that supply oxygen-rich blood to the brain become narrowed or blocked. Usually this narrowing is caused by a build-up of "plaque." Plaque is made up of fatty deposits (cholesterol), white blood cells, calcium, and other substances that collect over time in the wall of a carotid artery. This process is called "atherosclerosis."

Atherosclerosis in the carotid artery may lead to stroke in one of two ways:

1. Plaque buildup narrows the blood vessel so that the flow of blood to the brain is blocked.
2. The plaque or blood clots formed on the plaque break off and travel to a smaller artery in the brain, resulting in a blockage of that artery.

In other case, an artery becomes blocked and the brain doesn't receive enough blood. This lack of blood can cause a medical condition called a stroke also known as an ischemic ("lack of blood") stroke. Lack of blood to your brain can also create temporary symptoms that seem like a stroke, known as a transient ischemic attack or TIA. (For more information on stroke, please go to page 6).

This is why it is important for you and your doctor to know about any risk factors you might have for stroke.

What are the Risk Factors for Carotid Artery Disease?

Certain factors, such as your lifestyle or family history, can increase your risk of carotid artery disease. While some of these risk factors cannot be modified or changed, others can be reduced, treated, or controlled.

Risk factors that cannot be changed:

- Increasing age
- Gender
- Family history of stroke
- A relative with atherosclerosis
- Prior history of stroke and/or heart attack
- Race

Risk factors that can be reduced, treated or controlled:

- High blood pressure
- Smoking
- Diabetes
- Heart disease (e.g., heart attack, heart failure)
- Artery disease outside the heart and the major vessels
- Obesity
- High blood cholesterol level
- Lack of exercise

What are the Symptoms of Carotid Artery Disease?

Many people do not have any symptoms from carotid artery disease. Some people may experience TIA or stroke. A stroke or "brain attack" is an injury to the brain caused by lack of oxygen.

Transient ischemic attacks (TIAs), also called "temporary strokes" or "mini strokes", are warning signs that you are at high risk for experiencing a stroke. Because there are no specific symptoms of carotid artery disease, it is important to know these warning signs. If you have any of the warning signs of a stroke or TIA, it may be a sign of blockage in the carotid arteries.

What are the Symptoms of Stroke or TIA?

During a stroke or TIA the blood flow to the brain is interrupted. Symptoms of stroke and TIA are very similar and depend on the area of the brain affected, how long your symptoms last, and the amount of the injury.

Common signs and symptoms of a stroke or TIA may include:

- Sudden numbness or weakness of the face, arm or leg, especially on one side
- Sudden confusion or dizziness
- Sudden trouble speaking or understanding
- Sudden trouble seeing in one or both eyes
- Sudden trouble walking, loss of balance or coordination

Sudden, severe headache with no known cause

Sudden trouble swallowing

Call your doctor immediately if you have any of these symptoms.

If the symptoms go away within 24 hours or so, this may be due to a TIA. But be aware that TIA's are extremely important stroke warning signs so it is important to let your doctor know that you've had these symptoms.

How Can My Doctor Tell if I Have Carotid Artery Disease?

Your doctor may use one or more of the following tests to help diagnose carotid artery disease:

- **Medical History:** Your doctor will ask you about your risk factors for carotid artery disease, and may ask you if you have had any signs or symptoms of a TIA or stroke. It is important to tell the doctor all of your symptoms, even if some were only temporary.
- **Physical Exam:** Often there are no symptoms of carotid artery disease, which is why it is important to have regular physical examinations. During an exam, your doctor may listen to your carotid arteries with a stethoscope. If he or she hears an abnormal sound, that may indicate a reduction or change in blood flow due to atherosclerosis. Your doctor may then recommend additional tests.
- **Carotid Ultrasound:** Ultrasound uses sound waves to create images of the inside of your carotid artery. It is a painless test that is done from outside the body.
- **Angiogram:** This is a procedure carried out by a doctor in the catheterization laboratory (cath lab). Angiography is a procedure in which the carotid arteries are visualized using X-rays. A catheter (long, thin, hollow tube) is inserted into an artery in the groin or arm. The tip of this tube is positioned at the beginning of the arteries supplying blood to the brain, and a special fluid called contrast dye is injected through the tube to visualize the blood vessels on X-rays so that pictures, called angiograms, can be taken. These angiograms allow the doctor to see any blockage and/or narrowings in your carotid arteries and determine their severity.
- **Computerized Axial Tomography Scan (CT or CAT Scan):** A CT scan, also called a CAT scan, uses X-rays to create three-dimensional images of a part of the body. Your doctor may use contrast dye to highlight the carotid arteries on the image.
- **Magnetic Resonance Imaging (MRI):** An MRI uses a very strong magnet to make three-dimensional images of a part of the body. An MRI can show atherosclerosis of the carotid arteries, or areas of the brain damaged by a previous stroke, in addition to other abnormalities. It can be done with contrast dye if the doctor wants to see the vessels more clearly (Magnetic Resonance Angiogram, also called an MRA).

Using the information gathered from one or more of these tests, your doctor will be better able to recommend the most appropriate treatment. The doctor will explain the risks and benefits of your treatment options and answer any questions you or your family may have.

ur Treatment Options

Once you have been diagnosed with carotid artery disease, your doctor will recommend the most appropriate form of treatment depending on the condition and severity of your carotid artery disease. Carotid artery disease can be managed by a combination of changes in lifestyle (eating a healthy, low-saturated fat diet, regular exercise, quitting smoking, and properly controlling other physical ailments). Your treatment may include medications to lower the risk of blood clots, or lower your blood pressure or cholesterol.

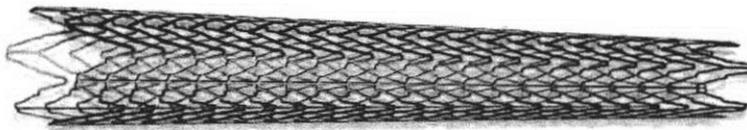
Surgery

Carotid Endarterectomy (CEA) is a surgical procedure that removes the blockage in the carotid artery. An incision is made in your neck and into the carotid artery, the plaque is removed from the artery, and then the artery is closed with stitches. The procedure is usually done under general anesthesia, although some doctors use local anesthesia. CEA is one of the most common surgical procedures in the United States and has been performed for over 50 years.

Carotid Stenting

Carotid stenting is an endovascular treatment (done through or inside the blood vessels) for carotid artery disease. You and your physician might decide that carotid stenting is a better option for you.

Figure 2 – Carotid Stent



A stent is a metal mesh tube that is designed to open up the narrowed carotid artery and help maintain the opening. Figure 2, above, shows a carotid stent. This stent will be permanently implanted.

An embolic protection device is a wire with a small filter on the end that looks like a basket. It was developed to capture material that could break off from the narrowed area of the artery while the stent is being implanted. This material could block blood flow to the arteries beyond the narrowing and be harmful to the brain. During the stenting procedure, the filter system is first positioned beyond the narrowed part of the artery and is opened like an umbrella to capture any material that breaks off. Next, the stent will be placed in the required area of the artery. Once the stent is implanted, the filter system will be completely removed.

Carotid Stent Procedure

Preparing For Your Procedure

In the days prior to your treatment, make sure you:

- Take all of your prescription medications. Tell your doctor if you are taking any medication.
- Tell your doctor about any allergies you have, especially to contrast dye or iodine, or to materials such as metals (nickel-titanium or stainless steel) or plastics (polyurethane).
- Tell your doctor if you cannot take aspirin, since aspirin and other medications are usually started prior to a procedure and continued for several months thereafter.
- Do not eat or drink anything after midnight on the night before your procedure.
- Follow all instructions given to you by your doctor or your nurse.

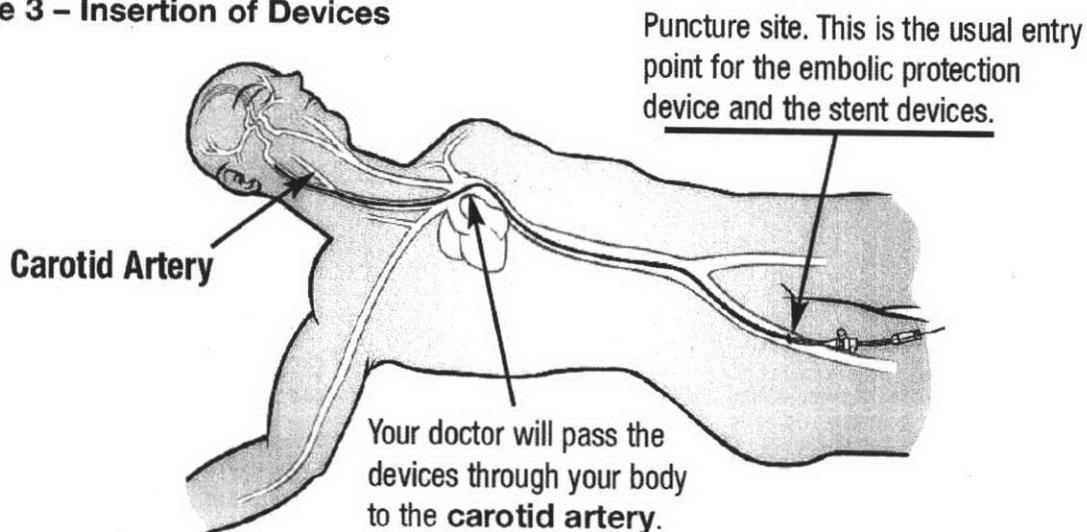
Before Your Procedure

- Your doctor will explain the possible risks and benefits of the stenting procedure and answer any questions you or your family may have.
- You may be given a sedative, a medication to relax you, before the procedure. The sedative may also make you sleepy.

During Your Procedure

- Once you are in the cath lab, you will be moved onto an xray table. The procedure will be done through an artery in your leg, so your groin area (at the top of the leg) will be washed with an antibiotic solution and then covered with a sterile sheet.
- Your doctor will inject a local anesthetic (numbing medicine) into the area where the catheters will be inserted. You may feel a sting when the needle is put into your groin and a brief warm sensation when the medicine is injected.
- Next, your doctor will put a needle into the artery in your groin to feed the guiding catheter into your artery (Figure 3). When the needle is first placed in the artery in your groin, you may feel some pressure.

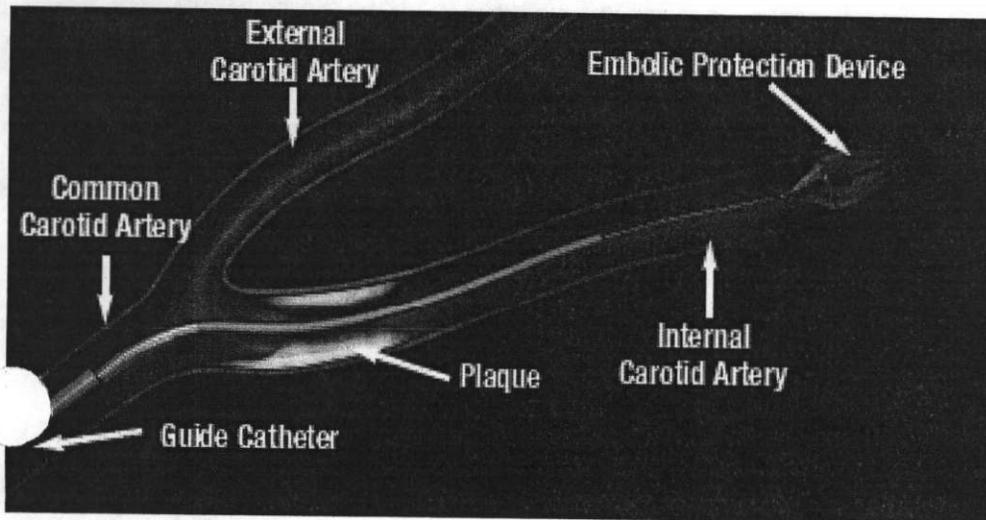
Figure 3 – Insertion of Devices



Your doctor will inject contrast dye into the guiding catheter to allow him or her to see the arteries in your neck and brain. Your face and neck may feel warm or flushed when this happens, but this usually goes away after a short time.

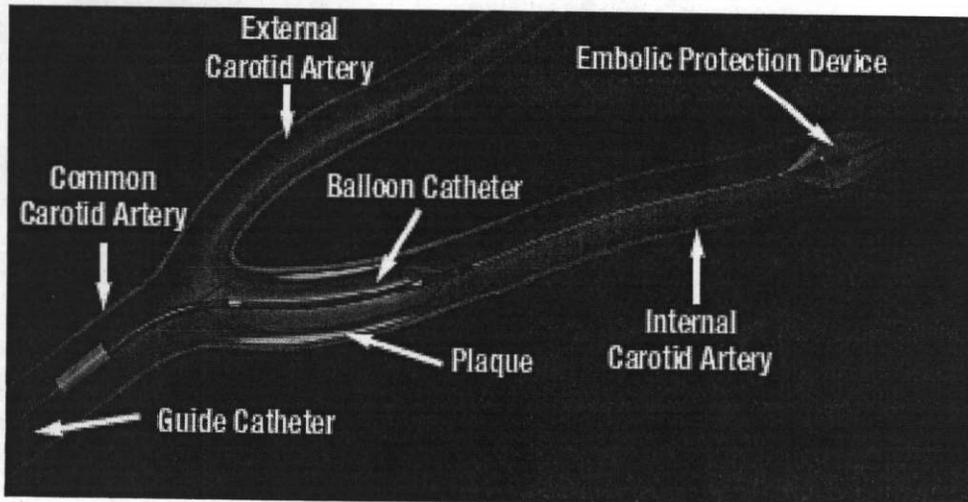
- Your doctor will pass the embolic protection device into the carotid artery. The embolic protection device is a wire with a small filter on the end that looks like a basket. You should not feel any discomfort during this part of the procedure.
- Once your doctor crosses the diseased area of the artery with the embolic protection device, the doctor will open the small filter. The embolic protection device will stay in place during the procedure to help capture any plaque or particles that could travel into the smaller vessels in the brain (Figure 4).

Figure 4 - Placement of Embolic Protection Device



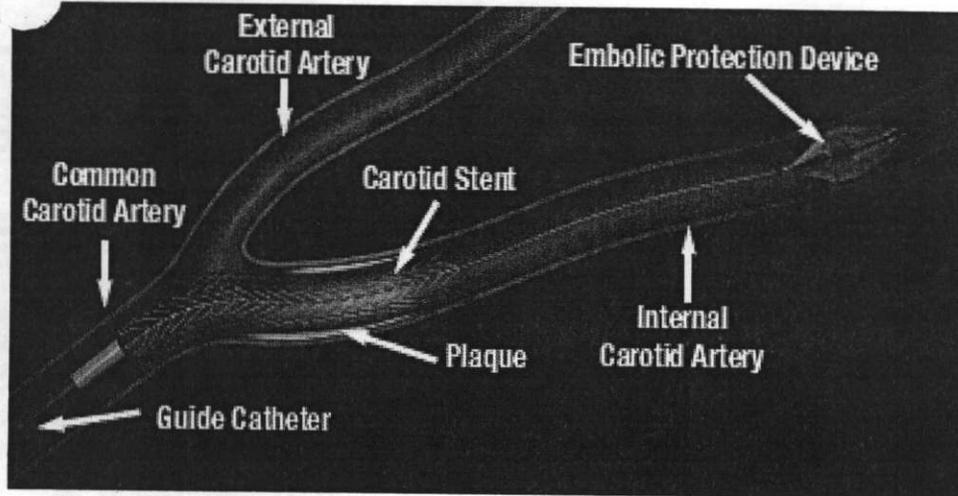
- The doctor may insert a balloon catheter into the narrowed area and then temporarily inflate the balloon in order to open up the artery. Your doctor will then remove the balloon catheter from your body (Figure 5).

Figure 5 - Embolic Protection Device and Balloon Inflation



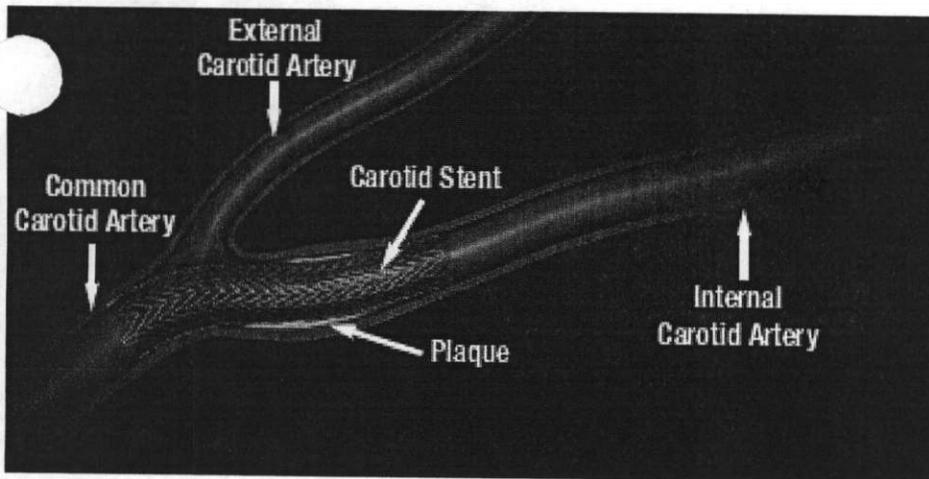
Your doctor will feed the carotid stent system through the vessels to the area of the plaque. After careful positioning, the doctor will open the carotid stent to cover the plaque (Figure 6).

Figure 6 - Placement of Carotid Stent



- Your doctor may, if necessary, insert a balloon catheter into the carotid stent to open it wider. The stent will remain in place permanently, but the balloon will be removed.
- The doctor will then remove the embolic protection device and all other devices from your body (Figure 7).

Figure 7 - Embolic Protection Device Removed



- Pressure will be applied to your puncture site until bleeding stops. Your doctor may use a special vascular closure device to close the small incision in your groin.

Following Your Procedure

- Immediately after your procedure you may feel sleepy from the sedation. This will clear as the medication wears off.
- You will be taken to a special area where nurses and doctors will monitor you closely.
- Your vital signs (heart rate and blood pressure) and the area in which the catheter was inserted will be checked frequently.
- A nurse will ask you questions, instruct you to move your fingers and toes, and check your pupils with a flashlight.
- Your blood pressure and puncture site will also be closely watched.
- You should drink plenty of fluids to flush the dye out of your system.

While you are in the hospital, you should let your doctor know if you have any dizziness, severe headache, sudden numbness in your legs, arms, or just on one side of your body, sudden weakness, blurred vision, blindness in one or both eyes, difficult swallowing or speaking, or pain at the puncture site in your groin.

- You will have to stay in bed for several hours, keeping your leg straight to allow your puncture site to heal.
- Your doctor will allow you to gradually become more active. You should avoid lifting and straining for as long as your doctor tells you.

Your Recovery

You may need to stay in the hospital for one or two days. Before you leave the hospital, your doctor will give you guidelines for activities, diet, and medications. Your doctor will also give you your Stent Implant Card, which has important information regarding your carotid stent.

After you are discharged, be sure to call your doctor or hospital immediately if you have any new symptoms or worsening of the symptoms you had before the stent placement, such as:

- severe headache
- dizziness
- slurred speech
- problems at your puncture site such as increasing swelling, pain or bleeding
- fever
- weakness or numbness affecting one side of your body (for instance, your right arm, leg, or face becomes weaker than your left)
- blurry vision or sudden loss of vision in one or both eyes

These symptoms may mean that your brain is not receiving enough blood flow and may be signs of a () or stroke.

Because medications will be an important part of your treatment, your doctor will prescribe drugs to take at home. It is important to take all your medicines according to your doctor's instructions. These medications will help prevent blood clots from forming in the newly opened carotid artery. These medications can also slow or prevent clotting if you have bleeding resulting from your stenting procedure, from an injury, or from any other medical treatment. Notify your doctor if your medications cause unpleasant reactions, but do not stop taking your medications unless instructed to do so. Your doctor may be able to prescribe new medications that better suit you.

It is important to keep all scheduled follow-up appointments. Your doctor will want to follow your progress closely and may want you to have tests to make sure that your carotid arteries are open and that blood flow through the treated area is sufficient. Most of the patients who go home after a successful procedure have no further problems. In some patients, narrowing within, or around the carotid stent may occur (restenosis) and your doctor may suggest additional treatment. If you have any questions, ask your doctor.

Make sure to notify your doctor if your address or telephone number changes so that your doctor can contact you if any information about your stent becomes available in the future.

Follow your doctor's advice about lifestyle changes. You should stop smoking if you currently smoke, eat a healthy diet, get enough exercise, and make sure to take all of the medicines regularly that your doctor has prescribed for you.

Safety Information

Benefits

Carotid stenting is another treatment for carotid artery disease. The safety and effectiveness of carotid stenting was compared to carotid surgery in several clinical studies. These clinical studies demonstrated that carotid stenting is as safe and effective as carotid surgery. Your doctor can help explain the risks and benefits that are specific to you. For additional information regarding the above-mentioned clinical studies, refer to page 18.

Contraindications

Your doctor can help explain the possible complications and treatments related to endovascular procedures.

Your doctor should not use the stent if:

- The narrowed area in your carotid artery is located beyond sharply curved vessels, making it difficult to place the stent and embolic protection device
- You can't take anticoagulants (medicines that make your blood take longer to form a clot)
- You can't take antiplatelets (medicines that make it harder for cells in your blood to form a blood clot)
- You are allergic to nickel-titanium, the metal used to make the RX Acculink and Xact Carotid Stents
- You have an uncorrected bleeding disorder
- You have lesions at the opening of the common carotid artery
- You are allergic to contrast (dye)

If anything you have read in this booklet raises further questions about the stenting procedure, now is the time to discuss them with your doctor.

Precautions

You may need to have a procedure to look at your arteries some time after your stent implant (MRI or MRA). You can have an MRI or MRA at any time after your stent is implanted. **IMPORTANT: you must tell the people running the MRI test that you have a stent.** Give them your Stent Implant Card so they use the right kind of MRI machine.

Potential Complications

Complications can occur during any endovascular procedure. The following lists the possible complications of the carotid stent or the carotid stenting procedure.

Common Complications

- Decrease in blood pressure
- Headaches and/or fever
- Problems with the rhythm of your heart such as slow heartbeat, irregular heartbeat or uneven heartbeats
- Infection or bruising of your groin area at the catheter insertion site

- Use of icepacks or pressure bandages to treat bruising or bleeding at the catheter insertion site

Uncommon Complications

The following serious complications occurred in fewer than ten out of a hundred patients who received a carotid stent.

- Use of antibiotics or other medications to treat an infection or allergic reaction
- Allergic reactions
- Bleeding
- Chest pain
- Excessive trauma to your blood vessels
- Blood clots or restenosis blocking blood flow through the stent
- Use of a second stent or surgery to treat a damaged or blocked artery
- Renal failure: failure of the kidneys to filter toxins and waste from your blood
- Stent deformation, collapse, fracture, movement of stent (possibly requiring emergency surgery); failures of the stent structure or stability that may require repeat endovascular treatment or surgery
- Emboli (air, blood clots, or even the stent) moving upstream from where the doctor is working
- Swelling or bleeding in the brain
- Stroke or TIAs
- Heart attack
- Death

If any of these complications happen to you, your doctor will treat you as needed. Treatments will vary widely depending upon the type of complication and your medical history.

Preventing Carotid Artery Disease

Carotid artery disease can be treated, but it has no cure. You can help to prevent your carotid artery disease from progressing by carefully following your doctor's advice. Your carotid stent is designed to keep your carotid artery open. However, to stay healthy, you need to keep all appointments with your doctor, take all of the medications regularly that have been prescribed for you, and call your doctor if you are not feeling well. Your doctor may also recommend some of the following lifestyle changes.

Lifestyle Changes:

Stop smoking. If you smoke, quitting is the single most important thing you can do to lower your risk of carotid artery disease. Chemicals in cigarette smoke may make it easier for plaque to build up on your artery walls. And smoking increases your heart rate and blood pressure, raising your risk of heart attack and stroke. If you are ready to quit, ask your doctor for advice — he or she can recommend tools to help you quit.

Increase your activity. Regular exercise can help you lower your blood pressure and blood cholesterol and reach a healthy weight. It can also help you manage the daily stresses of modern life more easily. Your doctor can recommend an activity program tailored for your situation.

a healthy diet. Choose a healthy diet. A diet low in saturated fats and cholesterol, and rich in lean protein, fresh fruits, vegetables, and whole grains, can help you achieve a healthy weight, as well as help you control your blood pressure, and cholesterol levels.

Manage your stress. You can help lessen the negative health effects of stress by practicing the "relaxation response." Research has shown that reducing stress can decrease your heart rate, blood pressure, and stress hormone levels.

Abbott Vascular Family of Carotid Clinical Studies

More than 25,000 patients have received an Abbott Vascular carotid stent during one of 8 clinical studies conducted in the United States and Canada. Of these, more than 7,500 patients were implanted with the Xact Carotid Stent and more than 17,500 patients were implanted with the Acculink Carotid Stent.

The health of the patients that received a carotid stent and those that had surgery was determined through the months or years following their procedures. The results of these studies showed that receiving an Abbott Vascular carotid stent is a safe and effective alternative to carotid surgery. The healing process after carotid stenting is usually faster and may be less painful compared to surgery.

Your Stent Implant Card

Tell any dentist or doctor who treats you for any reason that you have a stent implant in your neck, and keep your Stent Implant Card with you at all times. Your Stent Implant Card identifies the doctor who implanted your stent and how to reach him/her, the hospital where you received your carotid stent, the date it was implanted, and where it was placed in your carotid artery. It also identifies important information about your stent, such as the size of the stent and the date the stent was manufactured. The card gives your doctor valuable information that is necessary if you need an MRI or MRA. There are also phone numbers on the card that your doctor can call if he/she has any questions.

Below is a sample of a stent card you may receive:

Please carry this card at all times.
Show it to any medical personnel who may be treating you.



Through non-clinical testing, the Acculink Carotid Stent has been shown to be MR Conditional at field strengths of 3.0 Tesla or less, a maximum spatial gradient of 3.3 Tesla / meter and a maximum whole body averaged specific absorption rate (SAR) of 2.0 W / kg for 15 min of MRI. The Acculink Carotid Stent should not migrate in this MRI environment. Non-clinical testing has not been performed to rule out the possibility of stent migration at field strengths higher than 3.0 Tesla or a maximum spatial gradient higher than 3.3 Tesla / meter.

In this testing, the stent produced a temperature rise of less than or equal to 0.5°C at a maximum whole body averaged specific absorption rate (SAR) of 2.0 W / kg for 15 min of MRI. The effect of heating in the MRI environment for overlapping stents or stents with fractured struts is not known.

MRI quality may be compromised if the area of interest is in the exact same area as or adjacent to those to the position of the stent.

Acculink
Carotid Stent

Abbott Vascular
 Santa Clara, CA 95054-2807 USA

TEL: (800) 227-9902
 FAX: (800) 601-8874
 Outside U.S. TEL: (951) 914-4669
 Outside U.S. FAX: (951) 914-2531



PPL2079611 (2/9/11)

Stent Patient Implant Card

Patient Name _____ Date of Birth _____

Implanting Physician's Name _____ Phone Number _____

Hospital Name _____

City/State _____ Date of Implant _____

Stent Identification Information			
Affix Product Label Here or complete:			
Product Part # (REF)			
Product Lot #	Product Lot #	Product Lot #	Product Lot #
Location of First Stent	Location of Second Stent	Location of Third Stent	Location of Fourth Stent

Frequently Asked Questions

How long will the stent stay in my body?

Stents are designed to stay in your body permanently.

What are the restrictions or cautions after I've received a stent?

If you require magnetic resonance imaging (MRI), tell your doctor or MRI technician that you have an implanted stent.

When can I resume my regular activities?

Your doctor will advise you. Many patients can return to work and follow their normal routine about a week after their stent procedure.

Will my stent set off the metal detector at airport security checkpoints?

No, your stent implant will not trigger alarms at security checkpoints.

Will I be able to feel the stent inside me?

No, you will not be able to feel the stent once it has been implanted in your artery.

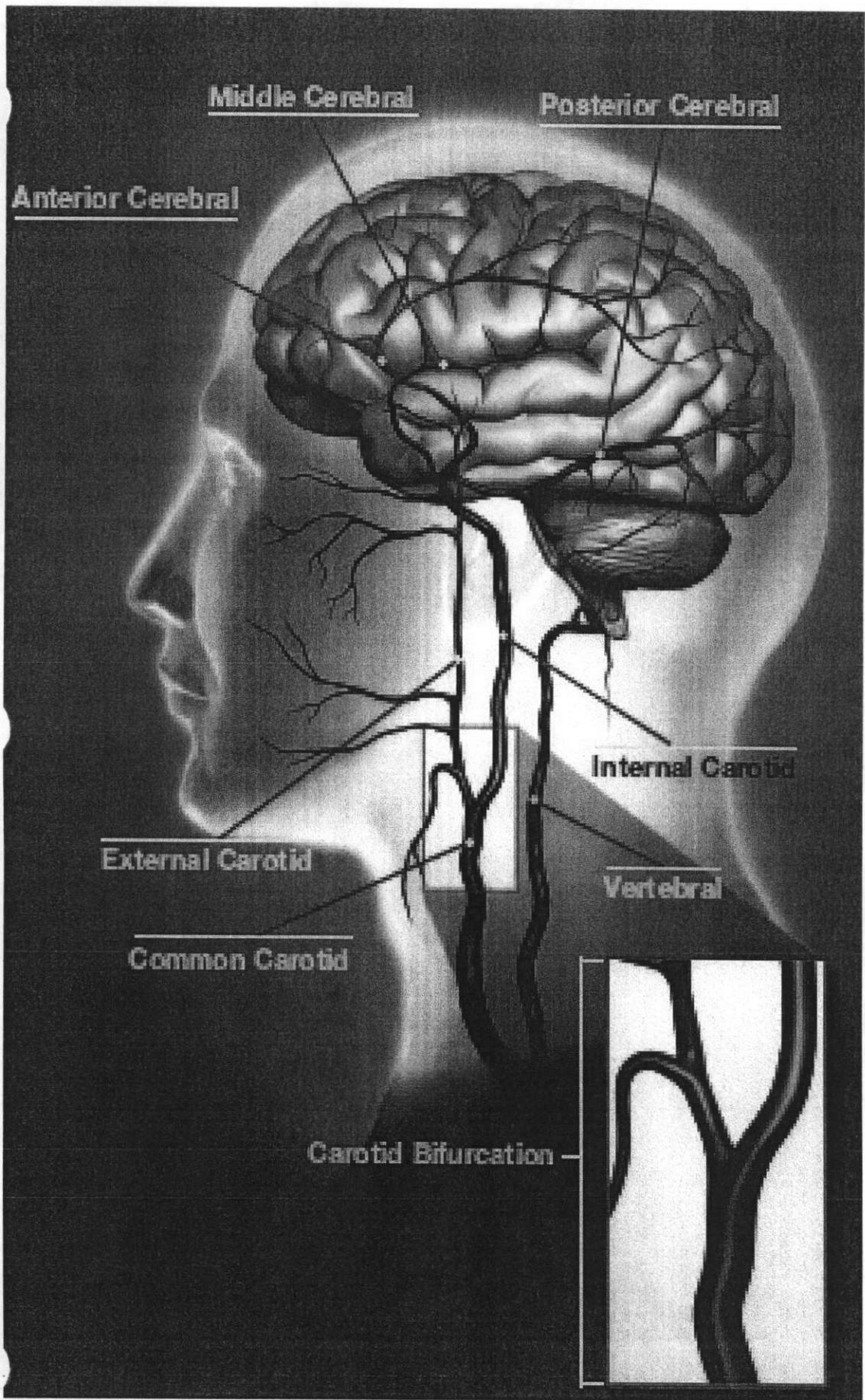
Could I have recurring symptoms?

Yes, it is possible that you will experience symptoms again, either due to a new blockage in the region treated with the stent or due to a blockage at another place in your carotid arteries. Your doctor will monitor your progress.

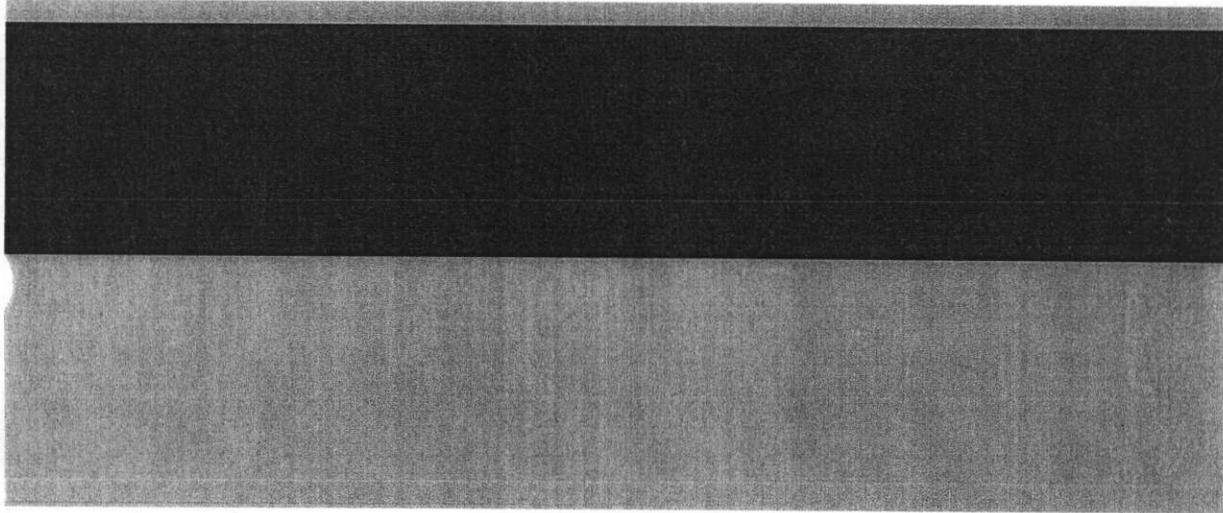
How can I help prevent a recurrence of symptoms?

While there is no sure way to prevent a recurrence of symptoms, you can reduce the risk through exercise, not smoking, and eating a healthy diet. Your doctor can advise you about lifestyle changes.

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Abbott Vascular
8200 Lakeside Drive Santa Clara, CA 95054 Customer Service 1.800.227.9902

All illustrations included are artificial conditions.
All tests performed by and data on file at Abbott Vascular.

CAUTION: This product is intended for use by or under the direction of a physician. Prior to use, it is important to read the package insert thoroughly for instructions for use, warnings and potential complications associated with the use of this device.

FX Acculink®, Xact™, FX Accuset® and Emboshield NAs™ are trademarks of the Abbott Group of Companies.

For more information, visit our web site at www.AbbottVascular.com
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**SECTION 6.0
PROPOSED INSERT****INSTRUCTIONS FOR USE****RX Acculink® Carotid Stent System**
Information for Prescribers

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

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CAUTION:

CAREFULLY READ ALL INSTRUCTIONS PRIOR TO USE. FAILURE TO OBSERVE ALL WARNINGS AND PRECAUTIONS MAY RESULT IN COMPLICATIONS.

1.0 DEVICE DESCRIPTION

The RX Acculink Carotid Stent System (RX Acculink) includes a self-expanding nickel-titanium stent pre-mounted on a rapid exchange stent delivery catheter. Radiopaque markers on the shaft mark the stent location, as illustrated in Figure 1.

The delivery system is comprised of a retractable sheath covering the stent during delivery, a radiopaque tip, an internal guide wire lumen, a handle assembly with a safety lock (Figure 2), and a pullback handle. The entire system is shown in Figure 3. With the handle in the unlocked position, retracting the pullback handle removes the sheath and deploys the stent. Upon deployment, the stent forms an open lattice, providing the scaffolding necessary to hold the artery open and ensure blood flow through the artery.

Figure 1. Tip Detail Showing Stent Location Markers

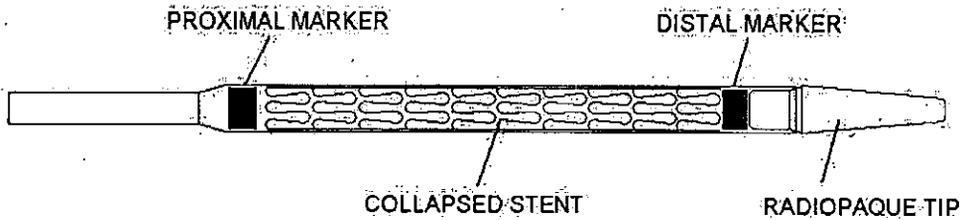
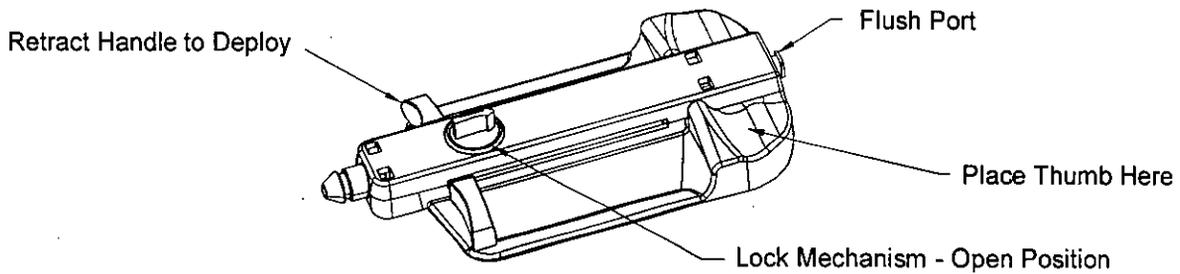
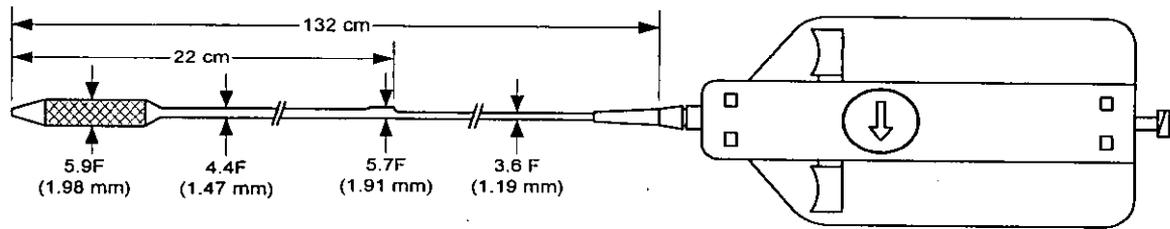


Figure 2. Handle Detail



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Figure 3. Delivery System Schematic



The RX Acculink Carotid Stent System is available in a range of stent lengths and diameters, and in straight and tapered configurations. Stent ends should be sized between the 1.1:1 and 1.4:1 stent-to-artery ratio. Tapered stents are designed to provide appropriate stent apposition when there is a distinct difference between vessel diameters at each stent end. The proximal stent end is sized to the common carotid artery (CCA) and the distal end is sized to the internal carotid artery (ICA). See Tables 1 and 2 for stent sizes and diameters and recommended reference vessel diameters.

The RX Acculink Carotid Stent System is compatible with either an 8 F guiding catheter (min. ID 0.085" / 2.2 mm) or a 6 F introducer sheath (min. ID 0.085" / 2.2 mm). It is also compatible with Abbott Vascular's AccUNET or Emboshield family of Embolic Protection Systems (EPS).

Table 1. RX Acculink Carotid Stent System - Stent Diameters

Unconstrained Stent Diameter (mm)	Stent Length (mm)	Reference Vessel Diameter (mm)
5.0	20, 30, 40	3.6 – 4.5
6.0	20, 30, 40	4.3 – 5.4
7.0	20, 30, 40	5.0 – 6.4
8.0	20, 30, 40	5.7 – 7.3
9.0	20, 30, 40	6.4 – 8.2
10.0	20, 30, 40	7.1 – 9.1

Table 2. RX Acculink Carotid Stent System – Tapered Stent Diameters

Unconstrained Stent Diameter (mm)	Stent Length (mm)	ICA Reference Vessel Diameter (mm)	CCA Reference Vessel Diameter (mm)
6 – 8 Taper	30, 40	4.3 - 5.4	5.7 – 7.3
7 – 10 Taper	30, 40	5.0 - 6.4	7.1 – 9.1

2.0 INDICATIONS

The RX Acculink Carotid Stent System, used in conjunction with the Abbott Vascular embolic protection system specified below, is indicated for the treatment of patients at high and standard risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below:

	High Risk	Standard Risk
Embolic Protection System	Abbott Vascular's Accunet or Emboshield Family	Abbott Vascular's Accunet only
With neurological symptoms	≥ 50% stenosis of the common or internal carotid artery by ultrasound or angiogram	≥ 70% stenosis of the common or internal carotid artery by ultrasound or ≥ 50% stenosis of the common or internal carotid artery by angiogram
Without neurological symptoms	≥ 80% stenosis of the common or internal carotid artery by ultrasound or angiogram	≥ 70% stenosis of the common or internal carotid artery by ultrasound or ≥ 60% stenosis of the common or internal carotid artery by angiogram
Reference vessel diameter	Must be within 4.0 mm – 9.0 mm at the target lesion	

3.0 CONTRAINDICATIONS

The RX Acculink Carotid Stent System is contraindicated for use in:

- Patients in whom anti-coagulant and / or anti-platelet therapy is contraindicated.
- Patients with severe vascular tortuosity or anatomy that would preclude the safe introduction of a guide catheter, sheath, embolic protection system, or stent system.
- Patients with known hypersensitivity to nickel-titanium.
- Patients with uncorrected bleeding disorders.
- Lesions in the ostium of the common carotid artery.

4.0 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 stent placement should use this device.

General

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

The safety and efficacy of the RX Acculink Carotid Stent System have not been demonstrated with embolic protection systems other than Abbott Vascular's Accunet or Emboshield family of Embolic Protection Systems (EPS). Refer to the Instructions for Use document for the Embolic Protection System that will be used for specific device instructions.

Clinical study results suggest lower event rates when the RX Acculink Carotid Stent System is used in conjunction with an embolic protection device.

The long-term performance (> 3 years) of the Acculink Carotid Stent 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.

Patient Selection

The safety and effectiveness of the RX Acculink Carotid Stent System have NOT yet been established in patients with the characteristics noted below.

Patient Characteristics:

- Patients experiencing acute ischemic neurologic stroke or who experience a stroke within 7 days prior to the procedure.
- Patients with an intracranial mass lesion (i.e., abscess, tumor, or infection) or aneurysm > 5 mm.
- Patients with arteriovenous malformations of the territory of the target carotid artery.
- Patients with coagulopathies.
- Patients with poor renal function who, in the physician's opinion, may be at high risk for a reaction to contrast medium.
- Patients with perforated vessels evidenced by extravasation of contrast media.
- Patients with aneurysmal dilation immediately proximal or distal to the lesion.
- Pregnant patients or patients under the age of 18.

Lesion Characteristics:

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

Access Characteristics:

- Patients with known peripheral vascular, supra-aortic or internal carotid artery tortuosity that would preclude the use of catheter-based techniques.
- Patients in whom femoral access is not possible.
- Risk of distal embolization may be higher if the RX Acculink System cannot be used in conjunction with an embolic protection system during the carotid stenting procedure.

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

Device Use

This device is intended for single-use only. Do not reuse. Do not resterilize, as this can compromise device performance and increase the risk of cross contamination due to inappropriate reprocessing.

Do not use the product after the "Use By" date specified on the package.

Do not use the product if the temperature indicator on inner pouch is black.

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

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

Caution should be used if pre-dilating the lesion without embolic protection as this may increase the risk of an adverse outcome.

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 a 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.

If a filter-based embolic protection system (EPS) is used, allow for and maintain adequate distance between the RX Acculink and the EPS to avoid potential filter engagement with the RX Acculink tip and / or filter entanglement with the deployed stent. If filter engagement and / or entanglement or filter detachment occurs, surgical conversion or additional catheter based intervention may be required.

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.

5.0 PRECAUTIONS

5.1 Stent Handling - Precautions

Carefully inspect the RX Acculink Carotid Stent System to verify that the device has not been damaged in shipment. Do not use damaged equipment.

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The delivery system has an internal hypotube. Take care to avoid unnecessary handling, which may kink or damage the delivery system. Do not use if device is kinked.

Do not expose the delivery system to organic solvents (e.g. alcohol) as structural integrity and / or function of the device may be impaired.

Do not remove the stent from its delivery system as removal may damage the stent. The stent on the delivery system is 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.

Special care must be taken not to handle or in any way disrupt the stent on the delivery system. This is most important during catheter removal from packaging, mandrel removal, placement over the guide wire, and advancement through a Rotating Hemostatic Valve (RHV) adapter and guiding catheter hub.

Do not hold the sheath or stent during mandrel removal.

5.2 Stent Placement - Precautions

Use with bleedback control hemostatic valves is not recommended.

The RX Acculink System is not compatible with any guide wire larger than 0.014" (0.36 mm).

Leave the safety lock closed until the stent is ready to deploy.

The RX Acculink Carotid Stent System must be used with a guiding catheter or introducer sheath to maintain adequate support of the 0.014" guide wire throughout the procedure.

For best device performance, the guide wire exit notch should remain within the guiding catheter or sheath.

Ensure the stent system is fully flushed with heparinized saline prior to use. Do not use the delivery system if flush is not observed exiting at the distal end of the sheath.

Do not attempt to pull a partially expanded stent back through the guiding catheter or sheath; dislodgment of the stent from the delivery system may occur.

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.

When catheters are in the body, they should be manipulated only under fluoroscopy. Radiographic equipment that provides high quality images is needed.

The delivery system is not designed for use with power injection. Use of power injection may adversely affect device performance.

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

Prior to stent deployment, remove all slack from the delivery system.

When more than one stent is required to cover the lesion, or if there are multiple lesions, the distal lesion should be stented first, followed by stenting of the proximal lesion. Stenting in this order obviates the need to cross the proximal stent for placement of the distal stent and reduces the chance of dislodging stents that have already been placed.

If overlap of sequential stents is necessary, the amount of overlap should be kept to a minimum (approximately 5 mm). In no instance should more than 2 stents overlap.

5.3 Post-Implant - Precautions

Care must be exercised when crossing a newly deployed stent with other interventional devices to avoid disrupting the stent geometry and placement of the stent.

In the event of thrombosis of the expanded stent, thrombolysis and PTA should be attempted.

5.3.1 MRI Compatibility

Through non-clinical testing, the Acculink Carotid Stent has been shown to be MR conditional. Patients may undergo MRI at field strengths of 3.0 Tesla or less, a maximum spatial gradient of 3.3 Tesla / meter and a maximum whole body averaged specific absorption rate (SAR) of 2.0 W / kg for 15 min of MRI. The Acculink Carotid Stent should not migrate in this MRI environment. Non-clinical testing has not been performed to rule out the possibility of stent migration at field strengths higher than 3.0 Tesla or a maximum spatial gradient higher than 3.3 Tesla / meter.

In this testing, the stent produced a temperature rise of less than or equal to 0.5°C at a maximum whole body averaged specific absorption rate (SAR) of 2.0 W / kg for 15 min of MRI. The effect of heating in the MRI environment for overlapping stents or stents with fractured struts is not known.

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

6.0 ADVERSE EVENTS

6.1 Observed Adverse Events

The Acculink Carotid Stent System and Accunet Embolic Protection System were evaluated for the treatment of high surgical risk patients and non-surgical patients with lesions in the internal carotid artery, in three separate ARChER clinical trials. In addition, an evaluation for the treatment of standard surgical risk patients was conducted in the CREST clinical trial. A total of 3083 patients were enrolled in the trials as follows:

- ARChER 1 evaluated the over-the-wire (OTW) Acculink Carotid Stent System only and included 158 registry patients. The primary objective of the study was to determine if the occurrence rate of the composite primary endpoint of stroke, death, and myocardial infarction (MI) at 30 days and ipsilateral stroke at one year for carotid stenting is not inferior to the occurrence rate for carotid endarterectomy (CEA) in the population under evaluation.
- ARChER 2 evaluated the OTW Acculink Carotid Stent System and OTW Accunet Embolic Protection System and included 278 registry patients. The primary objective of the study was the same as ARChER 1. A second primary endpoint for this study was Accunet device success.

- ARCHEr 3 evaluated the rapid exchange (RX) Acculink Carotid Stent System and RX Accunet Embolic Protection System and included 145 registry patients. The primary objective of the study was to establish equivalence (non-inferiority) to the ARCHEr 2 results with respect to 30-day death, stroke and MI as a means of establishing equivalency between the OTW and RX devices.
- CREST evaluated the OTW and RX Acculink Carotid Stent System and the OTW and RX Accunet Embolic Protection and included 2502 patients. The primary objective of the study was to demonstrate that the 1-year composite endpoint (death, stroke and myocardial infarction (DSMI) at 30 days plus ipsilateral stroke between 31 and 365 days) to treat standard surgical risk symptomatic and asymptomatic subjects with disease in the internal carotid artery is not inferior to that of CEA.

Tables 3 and 4 present the adverse events reported for registry patients enrolled in each ARCHEr trial. P values are given for the comparison of rates observed in the ARCHEr 2 and ARCHEr 3 trials. Because the ARCHEr 1 trial did not use embolic protection, it is not compared statistically to the other trials. Table 5 details the cause of any patient deaths in the ARCHEr studies. Tables 6 through 9 present the adverse events reported for CREST. Events are categorized by body system.

Table 3. ARChER - Serious Adverse Events Summary, ≤ 30 days

Event Categories ^{1,2}	ARChER 2 (N=278)		ARChER 3 ³ (N=145)		P value ³	ARChER 1 (N=158)	
	n	%	n	%		n	%
All Death, Stroke, and MI ⁴	23	8.27	11	7.59	0.824	12	7.59
Death	6	2.16	2	1.38	0.625	4	2.53
Stroke-Related	2	0.72	0	0.00	0.406	1	0.63
Not Stroke-Related	4	1.44	2	1.38	0.965	3	1.90
Ipsilateral Stroke	14	5.04	7	4.83	0.933	6	3.80
Major	3	1.08	2	1.38	0.802	2	1.27
Minor ⁴	11	3.96	5	3.45	0.816	4	2.53
Non-ipsilateral Stroke	1	0.36	1	0.69	0.653	1	0.63
Non-stroke Neurological	6	2.16	1	0.69	0.341	3	1.90
Target Lesion Revascularization (TLR), Clinically Indicated	0	0.00	0	0.00	1.000	0	0.00
Cardiac	23	8.27	13	8.97	0.826	22	13.92
MI	8	2.88	2	1.38	0.406	4	2.53
Arrhythmia	3	1.08	3	2.07	0.433	4	2.53
Angina	3	1.08	3	2.07	0.433	1	0.63
Congestive Heart Failure (CHF)	5	1.80	4	2.76	0.542	4	2.53
Coronary Artery Disease (CAD)	0	0.00	1	0.69	0.087	3	1.90
Procedural Complication	27	9.71	8	5.52	0.194	11	6.96
Hypotension	15	5.40	2	1.38	0.092	6	3.80
Arrhythmia	11	3.96	0	0.00	0.048	5	3.16
Vasospasm	4	1.44	0	0.00	0.238	0	0.00
Dissection ⁵	2	0.72	3	2.07	0.223	0	0.00
In-stent Thrombosis	1	0.36	1	0.69	0.653	0	0.00
Emergent CEA ⁶	2	0.72	0	0.00	0.406	0	0.00
Emergent Intervention ⁷	1	0.36	1	0.69	0.653	0	0.00
Access Site Complication	13	4.68	4	2.76	0.405	9	5.70
Requiring Repair / Transfusion	8	2.88	2	1.38	0.406	6	3.80
Vascular	3	1.08	0	0.00	0.308	2	1.27
Hemodynamic	6	2.16	4	2.76	0.722	3	1.90
Bleeding	7	2.52	6	4.14	0.387	11	6.96
Requiring transfusion	5	1.80	5	3.45	0.310	9	5.70
GI bleeding	0	0.00	2	1.38	0.015	2	1.27
Blood Dyscrasia	5	1.80	2	1.38	0.776	0	0.00
Respiratory	5	1.80	0	0.00	0.186	2	1.27
Gastrointestinal	2	0.72	0	0.00	0.406	0	0.00
Genitourinary	1	0.36	1	0.69	0.653	1	0.63
Infection	4	1.44	0	0.00	0.238	1	0.63
Metabolic	5	1.80	0	0.00	0.186	1	0.63
Musculoskeletal	0	0.00	0	0.00	1.000	1	0.63
Miscellaneous ⁸	0	0.00	0	0.00	1.000	3	1.90

¹Patients 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.

²Three of the reported adverse events were related to device failures / malfunctions. The three are described below in footnotes 5 – 7.

³Because of the multiple tests of significance performed, the individual test level for significance was set conservatively at $p < .01$ after a Bonferroni adjustment. Therefore, none of the AE rates were deemed significantly different statistically between ARChE2 and ARChE3.

⁴Two patients suffered strokes that were determined to be non-serious adverse events. Patient 249-3715 (ARChE2) suffered blurred vision that was subsequently diagnosed by an ophthalmologist as “central retinal artery occlusion with multiple refractile emboli and macular edema.” Patient 074-4804 had mild facial weakness that was subsequently diagnosed by MRI as an acute lacunar infarct. Both events resolved without treatment. The Clinical Events Adjudication Committee adjudicated both of these events as strokes. However, because the events did not meet the criteria for a serious adverse event (no intervention to prevent permanent impairment, no persistent or significant disability), they are not included in this table. The events are included as strokes in the composite endpoints.

⁵One dissection in the ARChE2 study was attributed by the physician to the OTW Accunet System. The physician was not able to cross the lesion with the device.

⁶One CEA in the ARChE2 study resulted when the OTW Accunet System became entangled with the deployed stent and could not be retrieved by the physician.

⁷The emergent intervention in the ARChE3 study resulted when the RX Accunet Filter Basket became entangled with the deployed stent and detached from the guidewire during the retrieval attempt. The physician opted to stent the basket in place in the artery. No additional adverse events related to this device malfunction were reported as of the last patient follow-up (9 months post-procedure).

⁸The 3 miscellaneous adverse events reported in the ARChE1 study were bladder tumor, headache, and rash.

Table 4. ARCHeR - Serious Adverse Events Summary, Up to 365 Days¹

Event Categories ^{2,3}	31 – 365 Days				0 – 365 Days			
	ARCHeR 1 N = 154		ARCHeR 2 N = 272		ARCHeR 1 N = 158		ARCHeR 2 N = 278	
	n	%	n	%	n	%	n	%
Death	10	6.49	18	6.62	14	8.86	24	8.63
Stroke-Related	0	0.00	1	0.37	1	0.63	3	1.08
Not Stroke-Related	8	5.19	16	5.88	11	6.96	20	7.19
Unknown	2	1.30	1	0.37	2	1.27	1	0.36
Ipsilateral Stroke	1	0.65	3	1.10	7	4.43	17	6.12
Major	0	0.00	0	0.00	2	1.27	3	1.08
Minor	1	0.65	3	1.10	5	3.16	14	5.04
Non-ipsilateral Stroke	1	0.65	3	1.10	2	1.27	4	1.44
Non-stroke Neurological	1	0.65	3	1.10	4	2.53	9	3.24
Target Lesion Revascularization (TLR), Clinically Indicated	7	4.55	6	2.21	7	4.43	6	2.16
Cardiac	26	16.88	50	18.38	46	29.11	69	24.82
MI	1	0.65	8	2.94	4	2.53	16	5.76
Arrhythmia	6	3.90	4	1.47	10	6.33	7	2.52
Angina	6	3.90	13	4.78	7	4.43	16	5.76
Congestive Heart Failure (CHF)	5	3.25	7	2.57	8	5.06	11	3.96
Coronary Artery Disease (CAD)	6	3.90	6	2.21	9	5.70	6	2.16
Procedural Complication	0	0.00	0	0.00	11	6.96	27	9.71
Hypotension	0	0.00	0	0.00	6	3.80	15	5.40
Arrhythmia	0	0.00	0	0.00	5	3.16	11	3.96
Vasospasm	0	0.00	0	0.00	0	0.00	4	1.44
Dissection	0	0.00	0	0.00	0	0.00	2	0.72
In-stent Thrombosis	0	0.00	0	0.00	0	0.00	1	0.36
Emergent CEA	0	0.00	0	0.00	0	0.00	2	0.72
Emergent Intervention	0	0.00	0	0.00	0	0.00	1	0.36
Access Site Complication	0	0.00	1	0.37	9	5.70	14	5.04
Requiring Repair / Transfus.	0	0.00	0	0.00	6	3.80	8	2.88
Vascular	14	9.09	25	9.19	15	9.49	27	9.71
Hemodynamic	4	2.60	4	1.47	7	4.43	10	3.60
Bleeding	0	0.00	3	1.10	11	6.96	10	3.60
Requiring transfusion	0	0.00	2	0.74	9	5.70	7	2.52
GI bleeding	0	0.00	0	0.00	2	1.27	0	0.00
Blood Dyscrasia	2	1.30	1	0.37	2	1.27	6	2.16
Respiratory	5	3.25	5	1.84	7	4.43	10	3.60
Gastrointestinal	10	6.49	5	1.84	10	6.33	6	2.16
Genitourinary	0	0.00	1	0.37	1	0.63	2	0.72
Infection	2	1.30	4	1.47	4	2.53	8	2.88
Metabolic	2	1.30	3	1.10	3	1.90	8	2.88
Musculoskeletal	1	0.65	5	1.84	2	1.27	5	1.80
Miscellaneous ⁴	5	3.25	9	3.31	8	5.06	9	3.24

¹Data > 30 days for ARCHeR 3 is not available because not all subjects have completed 1-year follow-up.

²Patients 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.

³None of the adverse events reported in the period 31 – 365 days were related to device failures / malfunctions.

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⁴The 5 miscellaneous adverse events reported in the ARCHeR 1 during the 31 – 365 day period study include hospitalization for planned surgery (1), bladder cancer (1), biopsy (1), non-responsive episode adjudicated as chronic subdural hematoma (1), and a fall (1). The additional 3 events in the 0 – 365 day period were bladder tumor (1), headache (1), and rash (1).

The 9 miscellaneous adverse events reported in the ARCHeR 2 study during the 31 – 365 day period included cancer (4), weakness accompanying a GI bleed (1), glaucoma (1), cataract surgery (1), post-thoracotomy syndrome (1), and hospitalization for elective surgery (1)

Table 5. ARCHeR - Cause of Death¹

Events	ARCHeR 1		ARCHeR 2		ARCHeR 3	
	n	%	n	%	n	%
0 – 30 days²	N=158		N=278		N=145	
Stroke	1	0.63	2	0.72	0	0.00
Cardiac	3	1.90	4	1.44	1	0.69
Bleeding (GI)	0	0.00	0	0.00	1	0.69
31 – 365 days³	N=154		N=272		N/A⁴	
Stroke	0	0.00	1	0.36		
Cardiac	3	1.94	9	3.31		
Cancer	1	0.65	2	0.74		
Bleeding (GI)	0	0.00	0	0.00		
Respiratory	2	1.30	2	0.74		
Gastrointestinal	0	0.00	1	0.36		
Genitourinary	1	0.65	0	0.00		
Infection	1	0.65	2	0.74		
Unknown	2	1.30	1	0.36		
Total Deaths (0 – 365 days)	14	8.90	24	8.63		

¹None of the reported deaths were due to a device malfunction or failure.

²Of the deaths 0 – 30 days, 5 were considered device or procedure related: 3 strokes, 2 cardiac.

³Of the deaths 31 – 365 days, 1 was considered device or procedure related: 1 stroke.

⁴Data > 30 days for ARCHeR 3 is not available because not all subjects have completed 1-year follow-up.

Table 6. CREST – Endpoint Adverse Events Summary, ≤ 30 days for the Per-Protocol Population

Event Category	CAS (N = 1131)		CEA (N = 1176)	
	n	%	n	%
Death	6	0.5%	3	0.3%
All Stroke	46	4.1%	22	1.9%
Major Stroke	10	0.9%	5	0.4%
Ipsilateral to Treated Hemisphere	10	0.9%	4	0.3%
Non-ipsilateral to Treated Hemisphere	0	0.0%	1	0.1%
Minor Stroke	36	3.2%	18	1.5%
Ipsilateral to Treated Hemisphere	33	2.9%	15	1.3%
Non-ipsilateral to Treated Hemisphere	3	0.3%	3	0.3%
MI	22	2.0%	40	3.4%

Note: The analysis only includes each 30-day DSMI evaluable subject's first occurrence of the event.

Table 7. CREST – Major Adverse Events Summary, Up to 30 Days Post Procedure (PP Population)

Up to 30 days	CAS N= 1131		CEA N= 1176	
	n	%	n	%
Access Site Complication Requiring Treatment	13	1.1	42	3.6
Procedure-related Cranial Nerve Injury	0	0.0	59	5.0
Unresolved at One Month	0	0.0	40	3.4
Unresolved at Six Months	0	0.0	24	2.0
Bleeding	10	0.9	6	0.5
Neurologic Other than stroke	48	4.2	51	4.3
Procedure-related				
Arrhythmia	45	4.0	12	1.0
Bleeding	15	1.3	20	1.7
Hypertension	65	5.7	161	13.7
Hypotension	243	21.5	117	9.9
Vascular				
Aneurysm	0	0.0	2	0.2
Fistula/Pseudoaneurysm/Dissection	0	0.0	0	0.0
Clinically indicated - Target Lesion Revascularization	1	0.1	2	0.2

Table 8. CREST – Major Adverse Events Summary, 31 to 365 Days Post Procedure (PP Population)

31 to 365 days	CAS N= 1120		CEA N= 1166	
	n	%	n	%
All Stroke	26	2.3	24	2.1
Major Stroke	5	0.4	3	0.3
Ipsilateral to Treated Hemisphere	5	0.4	2	0.2
Non-ipsilateral to Treated Hemisphere	0	0.0	1	0.1
Minor Stroke	21	1.9	21	1.8
Ipsilateral to Treated Hemisphere	14	1.3	16	1.4
Non-ipsilateral to Treated Hemisphere	7	0.6	5	0.4
Death	26	2.3	16	1.4
Access Site Complication Requiring Treatment	0	0.0	1	0.1
Procedure-related Cranial Nerve Injury	0	0.0	3	0.3
Unresolved at One Month	0	0.0	2	0.2
Unresolved at Six Months	0	0.0	1	0.1
Bleeding	24	2.1	23	2.0
Neurologic Other than stroke	70	6.3	73	6.3
Vascular				
Aneurysm	1	0.1	2	0.2
Fistula/Pseudoaneurysm/Dissection	1	0.1	1	0.1
Clinically indicated - Target Lesion Revascularization	9	0.8	10	0.9

Table 9. CREST - Major Adverse Events from 1 year Up to 4 year for Per-Protocol Population

	1 to 2 years		2 to 3 years		3 to 4 years	
	CAS N= 1069	CEA N= 1122	CAS N= 870	CEA N= 883	CAS N= 563	CEA N= 566
All Stroke	16	15	12	10	4	4
Death	30	19	25	31	15	19
Bleeding	15	19	8	13	3	3
Neurologic other than stroke	53	45	28	35	18	13
Target Lesion Revascularization	9	3	3	6	2	0

Note: Not all patients have reached 4 year follow-up.

6.2 Potential Adverse Events

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

- Allergic reactions to anti-platelet agents / contrast medium
- Aneurysm
- Angina / coronary ischemia
- Arrhythmia
- Arterial occlusion / thrombosis at puncture site or remote site
- Arteriovenous fistula
- Bacteremia or septicemia
- Bleeding from anticoagulant or antiplatelet medications
- Cerebral edema
- Cerebral hemorrhage
- Cerebral ischemia / transient ischemic attack (TIA)
- Congestive heart failure (CHF)
- Death
- Detachment and / or implantation of a component of the system
- Emboli, distal (air, tissue or thrombotic emboli)
- Emergent or urgent endarterectomy surgery (CEA)
- Fever
- Filter thrombosis / occlusion
- Groin hematoma, with or without surgical repair
- Hemorrhage, with or without transfusion
- Hyperperfusion syndrome
- Hypotension / hypertension
- Infection and pain at insertion site
- Ischemia / infarction of tissue / organ
- Myocardial infarction (MI)

- Pain (head, neck)
- Pseudoaneurysm, femoral
- Renal failure / insufficiency
- Restenosis of stented segment
- Seizure
- Severe unilateral headache
- Stent / filter entanglement / damage
- Stent embolization
- Stent malposition
- Stent migration
- Stent thrombosis / occlusion
- Stroke / cerebrovascular accident (CVA)
- Total occlusion of carotid artery
- Vessel dissection, perforation, or rupture
- Vessel spasm or recoil

Any device related adverse event occurring involving the RX Acculink Carotid Stent System should be reported immediately to Abbott Vascular, Customer Service, at (800) 227-9902. If outside the USA, call (951) 914-4669.

7.0 CLINICAL STUDIES

7.1 ARChER Pivotal Clinical Study

The Acculink for Revascularization of Carotids in High Risk Patients (ARChER) Clinical Trials were a series of prospective, non-randomized, multi-center, single-arm clinical trials. These trials were performed to demonstrate the safety and efficacy of the Acculink and RX Acculink Carotid Stent Systems and Accunet and RX Accunet Embolic Protection Systems when used to treat high-risk, surgical and non-surgical, symptomatic ($\geq 50\%$ stenosis) and asymptomatic ($\geq 80\%$ stenosis) subjects with disease in the internal carotid artery. A total of 581 registry patients were enrolled at 45 clinical sites in the United States and five sites outside of the United States.^a These trials are summarized in Table 10.

^a The ARChER 1 and 2 trials each had a lead-in phase for initial clinical experience. An additional 76 patients were enrolled in this phase of the clinical study, 51 in ARChER 1 and 25 in ARChER 2. The natures and frequencies of endpoints and adverse events reported in lead-in patients were consistent with those reported in the pivotal trials, and thus are not reported here.

Table 10. An Overview of the ARCHeR Trials

	ARCHeR 1	ARCHeR 2	ARCHeR 3
Products Evaluated	Over-the-wire Acculink Carotid Stent System	Over-the-wire Acculink and Over-the-wire Accunet Systems	Rapid Exchange Acculink and Rapid Exchange Accunet Systems
Study Design	Non-randomized, multi-center, single-arm, prospective clinical trials		
Sample Size	158 (plus 51 lead-in patients)	278 (plus 25 lead-in patients)	145 patients
Number of Sites	25 Sites in the U.S.	37 Sites in the U.S. and 1 Site in South America	19 Sites in the U.S., 4 Sites in Europe, and 1 Site in South America
Primary Endpoint	30-day death, stroke, MI and ipsilateral stroke at 31-365 days	30-day death, stroke, and MI and ipsilateral stroke at 31-365 days; Accunet device success ²	30-day death, stroke, and MI
Secondary Endpoints-All Trials	-Device Success ^{1,2} -Clinical Success ³ -Target Lesion Revascularization -Access Site complications requiring treatment		
Specific Secondary Endpoints	-Six and 12 month ultrasound (annually thereafter)	-Six and 12 month ultrasound (annually thereafter) -Medical Resource Utilization	-Six and 12 month ultrasound -Ipsilateral stroke between 31 and 365 days ⁴
Study Hypothesis	Non-inferiority to historical control	Non-inferiority to historical control	Non-inferiority to ARCHeR 2 results at 30 days
Patient Follow-up	-Neurologic evaluation by an <u>independent neurologist</u> and patient assessment at 24 hours, 30 days, 6 months, 12 months (every 6 months thereafter for ARCHeR 1 and 2 only) -TIA / Stroke Questionnaire and adverse event assessment at 30 days and 3, 6, 9 and 12 months. -ECG at 30 days -Ultrasound at 30 days, 6 and 12 months (annually thereafter for ARCHeR 1 and 2 only)		

¹Attainment of final result, < 50% residual stenosis covering an area no longer than the original lesion, using the Acculink System as described in the protocol.

²Device delivered, placed, and retrieved as described in the protocol.

³Acculink device / procedure success without death, emergency endarterectomy, repeat PTA / thrombolysis of the target vessel, stroke, or MI within seven days of the procedure.

⁴Data collection for the ARCHeR 3 study is not complete beyond 30 days. Secondary endpoints have not been evaluated.

The study hypothesis of the ARCHeR 1 and ARCHeR 2 trials was to show equivalence (non-inferiority) between carotid stenting and a historical control, based on the standard of care. The historical control was established based on a review of the current literature on carotid endarterectomy and medical therapy. From this review, the rate of 30-day death, stroke, MI and ipsilateral stroke at 31 – 365 days was estimated at 15% for patients with medical co-morbidities, and estimated at 11% for patients with anatomy unfavorable for

CEA. A weighted historical control (WHC) was calculated based on the proportion of each of these patient groups enrolled in the study.

$$WHC = pc \cdot 15\% + pa \cdot 11\%$$

Where: pc = the proportion of patients with medical co-morbidities, and
pa = the proportion of patients with unfavorable anatomy.

Using this equation, the WHC rate at one year was calculated for both ARCHeR 1 and ARCHeR 2 to be 14.5%. The ARCHeR 3 trial was designed to demonstrate equivalence (non-inferiority) of the safety and performance of the rapid exchange RX Acculink and RX Accunet Systems to results observed in the ARCHeR 2 trial for the OTW Acculink and Accunet Systems based on 30-day results.

As shown in Table 10, the protocol required regular patient follow-up by the treating physician and follow-up neurological assessments by an independent neurologist. Core laboratories provided independent assessments for angiographic, ultrasound, ECG, and pathologic evaluation of captured debris (Accunet only). Medical monitors reviewed all safety data to ensure appropriate reporting of adverse events. A Clinical Events Adjudication Committee adjudicated suspected primary endpoint events. A Data Safety Monitoring Board monitored adverse events to ensure patient safety.

Eligibility Criteria Summary

The study population consisted of male and female patients, at least 18 years of age, with discrete lesions in the internal carotid artery. Patients had to be high-risk candidates for surgery or non-surgical candidates; both symptomatic ($\geq 50\%$ stenosis) and asymptomatic ($\geq 80\%$ stenosis) patients were eligible.

The inclusion criteria for ARCHeR 1, 2, and 3 were essentially identical. Key inclusion criteria included the following:

- Symptomatic patient: Transient ischemic attack (TIA), amaurosis fugax, or minor / non-disabling stroke (in the hemisphere supplied by the target vessel) within 180 days of enrollment; carotid stenosis had to be $\geq 50\%$ by angiography, using NASCET^b methodology to determine degree of stenosis.
- Asymptomatic patient: meets angiographic and clinical inclusion criteria; carotid stenosis had to be $\geq 80\%$ by angiography, using NASCET methodology to determine degree of stenosis.
- Patient had to meet two or more of the criteria listed in a-e **OR** one or more of the criteria listed in f-q to qualify as a high-risk or non-surgical candidate:
 - a) Knowledge of two or more proximal or major diseased coronary arteries with $\geq 70\%$ stenosis that have not, or cannot be revascularized;
 - b) Unstable angina defined as rest angina with electrocardiogram (ECG) changes;
 - c) MI within the previous 30 days and current need for carotid artery revascularization;
 - d) Concurrent requirement for aortocoronary bypass or cardiac valve surgery within 30 days;
 - e) Contralateral occlusion of the ICA.

^b NASCET, North American Symptomatic Carotid Endarterectomy Trial. Methods, patient characteristics, and progress. Stroke, 1991. 22(6): p. 711-20.

- f) Currently on a list for major organ transplantation (i.e. heart, lung, liver, kidney) or is being evaluated for such;
 - g) Ejection fraction < 30% or New York Heart Association (NYHA) Functional Class III or higher;
 - h) FEV₁ < 30% (Predicted);
 - i) Dialysis-dependent renal failure;
 - j) Uncontrolled diabetes defined as fasting glucose > 400 mg / dl and ketones > 2+;
 - k) Restenosis after previous CEA;

 - l) Patient is status / post radiation treatment to the neck;
 - m) Patient is status / post radical neck surgery;
 - n) Surgically inaccessible lesions (e.g. lesions above the level of C2 or below the clavicle, lesions obstructed by tumors in the neck);
 - o) Spinal immobility – inability to flex neck beyond neutral or kyphotic deformity;
 - p) Presence of tracheostomy stoma;
 - q) Contralateral laryngeal nerve paralysis.
- Patient had a discrete lesion located in the ICA (with or without involvement of the contiguous CCA).
 - Target ICA vessel reference diameter had to be ≥ 4.0 mm and ≤ 9.0 mm by angiography.

Specific Inclusion Criteria for the OTW and RX Accunet System (ARChER 2 and 3 only)

- The vessel distal to the lesion had to have an absence of excessive tortuosity and an available straight or mildly angulated segment ≥ 4 cm, by angiography, in the distal ICA (prior to the petrous portion of the vessel) in which to place the embolic protection device.
- The diameter of the straight or mildly angulated segment, in the distal ICA prior to the petrous portion of the vessel, had to be ≥ 3.25 mm and ≤ 7.5 mm (ARChER 2) or ≥ 3.25 mm and ≤ 7.0 mm (ARChER 3) by angiography.

Description of Patients Evaluated

Table 11 summarizes patient follow-up at the endpoint evaluation time points of 30 days and 365 days. Patients were considered to have been evaluated if they had physician contact including one or more of the following at the given time point: office visit, neurologic evaluation, TIA / Stoke questionnaire, hospital admission, or lab tests including ultrasound, angiogram, or ECG.

Table 11. ARChER - Patient Follow-up

	ARChER 1	ARChER 2	ARChER 3
30 Days			
Patients Enrolled	158	278	145
Cumulative Death	4	4	2
Cumulative Withdrawn or LTF	2	1	1
Patients evaluable	152	273	142
Patients evaluated ¹	152	272	141
Neurological Evaluation	128	256	130
Ultrasound Evaluation	133	256	136
Other Clinical Evaluation only ²	14	10	5
365 Days			
Cumulative Death	12	21	
Cumulative Withdrawn / LTF	14	11	
Patients evaluable	132	246	

Patients evaluated ¹	131	239	
Neurological Evaluation	116	207	
Ultrasound Evaluation	121	213	
Other Clinical Evaluation only ²	9	19	

¹Patients evaluated may have one or more of the evaluations listed: neurological, ultrasound, or clinical.

²Other Clinical Evaluation includes: Office visit, telephone conversation with site, TIA / Stroke Questionnaire, Hospitalization.

Baseline demographics and lesion characteristics for the three studies are presented in Table 12. All reported angiographic data on the treated lesions are based on measurements obtained by a centralized angiographic core laboratory.

Table 12. ARChER - Baseline Patient Demographics

Demographics and Medical History	ARChER 2 N=278	ARChER 3 N=145	P value	ARChER 1 N=158
Age				
Mean ± SD	70.48± 9.38	71.13± 9.40	0.499	69.21± 9.65
Range (min, max)	(278) (45.29, 92.67)	(145) (38.94, 88.78)		(158) (40.28, 90.14)
Age ≥ 80 year	15.5% (43/278)	17.9% (26/145)	0.579	13.3% (21 / 158)
Gender				
Male	68.3% (190/278)	68.3% (99/145)	1.000	63.9% (101 / 158)
Medical History				
Diabetes	39.9% (111/278)	34.5% (50/145)	0.293	37.3% (59 / 158)
Hypertension	84.2% (234/278)	83.3% (120/144)	0.889	83.5% (132/158)
Hypercholesterolemia	71.9% (200/278)	82.4% (117/142)	0.022	64.7% (101/156)
Current Smoker	17.7% (49/277)	17.7% (25/141)	1.000	23.7% (37 / 156)
Number of Symptomatic Patients (TIA, Stroke or Amaurosis Fugax Within 180 Days)	24.1% (67/278)	21.4%(31/145)	0.547	25.3% (40 / 158)
Baseline Lesion & Vessel Characteristics				
No Calcification	50.4% (139/276)	42.3% (60/142)	0.122	64.9% (98/151)
Unilateral Calcification	27.2% (75/276)	23.2% (33/142)	0.411	27.2% (41/151)
Bilateral Calcification	22.5% (62/276)	34.5% (49/142)	0.010	7.9% (12/151)
Lesion Length (mm)				
Mean ± SD (N)	14.55± 7.14	14.84± 7.82	0.707	16.17± 7.45
Range (min, max)	(276) (0.00, 56.51)	(142) (3.57, 43.81)		(157) (4.72, 50.37)
Minimum Lumen Diameter (MLD, mm)				

Mean ± SD (N) Range (min, max)	1.35± 0.56 (276) (0.10, 3.57)	1.21± 0.53 (142) (0.00, 3.03)	0.013	1.37± 0.64 (156) (0.10, 3.15)
Percent Diameter Stenosis (%DS)				
Mean ± SD (N) Range (min, max)	69.93±10.86 (276) (31.03, 95.95)	73.04±10.13 (142) (47.40, 100.0)	0.005	72.62±10.99 (156) (42.96, 98.14)
High-Risk Inclusion Criteria	% (n/N)	% (n/N)		% (n/N)
Medical/Surgical Co-morbidities				
Two or More Diseased Coronary Arteries	27.7% (77/ 278)	25.5%(37/ 145)	0.647	28.5% (45/ 158)
Unstable Angina	7.9% (22/ 278)	6.9%(10/ 145)	0.847	7.6% (12/ 158)
MI Prior 30d & Need Carotid Artery Revasc.	3.6% (10/ 278)	2.1% (3/ 145)	0.556	4.4% (7/ 158)
Need CABG or Valve Surgery	14.0% (39/ 278)	15.2% (22/ 145)	0.772	19.0% (30/ 158)
Contralateral Occlusion of ICA	16.2% (45/ 278)	12.4% (18/ 145)	0.318	20.9% (33/ 158)
On List For Major Organ Transplant	0.0% (0/ 278)	0.7% (1/ 145)	0.343	0.0% (0/ 158)
Ejection fraction < 30% or NYHA ≥ III	38.8% (108/ 278)	27.6% (40/ 145)	0.024	29.7% (47/ 158)
FEV ₁ < 30% (Predicted)	3.2% (9/ 278)	4.8% (7/ 145)	0.429	5.1% (8/ 158)
Dialysis-dependent Renal Failure	2.2% (6/ 278)	2.1% (3/ 145)	1.000	5.1% (8/ 158)
Uncontrolled Diabetes	0.0% (0/ 278)	0.7% (1/ 145)	0.343	0.0% (0/ 158)
Restenosis after previous CEA	34.2% (95/ 278)	35.9% (52/ 145)	0.748	36.1% (57/ 158)
Unfavorable Anatomic Conditions				
Radiation Treatment to Neck	6.5% (18/ 278)	6.9% (10/ 145)	0.840	7.0% (11/ 158)
Radical Neck Surgery	2.2% (6/ 278)	4.8% (7/ 145)	0.146	3.2% (5/ 158)
Surgically Inaccessible Lesions	6.5% (18/ 278)	9.0% (13/ 145)	0.432	8.9% (14/ 158)
Spinal Immobility	2.9% (8/ 278)	6.2% (9/ 145)	0.119	0.0% (0/ 158)
Presence of Tracheostomy Stoma	1.4% (4/ 278)	2.1% (3/ 145)	0.695	1.9% (3/ 158)
Contralateral Laryngeal Nerve Paralysis	0.4% (1/ 278)	0.7% (1/ 145)	1.000	0.6% (1/ 158)

¹Statistical test of difference between ARCHeR 2 and ARCHeR 3, using Fisher's exact test for categorical values and t-Test for continuous variables.

Results

The primary and secondary endpoints presented in Table 10 for the three studies were evaluated and categorized as either safety or efficacy endpoints.

Table 13 presents the periprocedural (30 day) safety endpoints related to short-term patient outcome. The 30-day primary endpoint rate (death, stroke, or MI within 30 days) was 7.59%, 8.63%, and 8.28% for ARCHeR 1, 2, and 3 respectively. Rates for each of the contributors to the composite rate are presented, as well as rates of other adverse events related to evaluation of procedure safety.

Table 14 presents efficacy endpoint and procedural success data. The one-year primary endpoint event rates (30-day primary endpoint + ipsilateral stroke between 31 and 365 days) were 8.28% and 10.22% for ARCHeR *98*

1 and 2 respectively. These rates are estimated via Kaplan-Meier analysis presented in Figures 4 and 5. Device, procedural and clinical success rates for all devices in all trials exceeded 91%.

To investigate the long-term stroke prevention capabilities of the Acculink Carotid Stent, the primary endpoint Kaplan-Meier curves shown in Figures 4 and 5 were extended out with all available follow-up data for the ARCHEr 1 and ARCHEr 2 studies. Median time for follow-up of the ARCHEr 1 study is 726 days; the accompanying table presents the Kaplan-Meier analysis at 1, 6, 12, 24, and 30 months. Median time for follow-up in the ARCHEr 2 study is 378 days; the accompanying table presents the Kaplan-Meier analysis at 1, 3, 6, 12, and 24 months.

A meta-analysis of all ARCHEr registry patients was conducted to evaluate the clinical efficacy of carotid stenting in symptomatic (n = 138) and asymptomatic (n = 443) subsets. Because MI has not historically been included in the primary endpoint of the landmark symptomatic (NASCET^c) and asymptomatic (ACAS^d) trials, a composite of all death and stroke within 30 days plus ipsilateral stroke beyond 30 days is presented in Figures 6A and 6B as Kaplan-Meier freedom-from functions. The rate of this composite at 1 and 2.5 years is 12.6% and 14.5% in the symptomatic subset and 6.8% and 11.0% in the asymptomatic subset. Another relevant outcome is the composite of all death and major stroke within 30 days and major ipsilateral stroke beyond 30 days (Figures 6C and 6D). The rate of this composite at 1 and 2.5 years is 5.1% and 6.9% in the symptomatic subset and 2.6% and 4.3% in the asymptomatic subset.

The relationship of patient and lesion characteristics to periprocedural outcomes (specifically stroke within 30 days and the composite of stroke, death and MI within 30 days) was examined in a multi-variate analysis. The statistically significant predictors of the composite endpoint events of stroke, death or MI were: requirement for coronary artery bypass graft (CABG) or valve surgery, hypertension, and symptomatic carotid stenosis (all p < 0.05). The statistically significant predictors of stroke at 30 days were: symptomatic carotid stenosis, hypercholesterolemia, male gender, advanced age, and anatomic risk factors (all p < 0.05).

The primary objectives of the ARCHEr 1 and ARCHEr 2 trials were met. The upper confidence limits for primary endpoint rates fell below the 14.5% WHC for both studies, demonstrating that carotid stenting is non-inferior to carotid endarterectomy in the studied high-risk population.

The primary objective of the ARCHEr 3 study, that the 30-day primary endpoint for the ARCHEr 3 study was non-inferior to that of the ARCHEr 2 study, was met. The upper bound of the 95% confidence interval of the difference between ARCHEr 3 and ARCHEr 2 is 4.75%, which is less than the delta of 8% (p = 0.005). Thus, results from ARCHEr 3 are determined to be non-inferior to those of ARCHEr 2 and the RX and OTW devices are determined to yield similar clinical results.

Table 13. ARCHEr Pivotal Trials - Safety Assessment Event Rates (≤ 30 days)

Event Categories ¹	ARCHEr 2 (N=278)		ARCHEr 3 (N=145)		P value ²	ARCHEr 1 (N=158)	
	n	%	n	%		n	%
30-Day Primary Endpoint (Death, Stroke, MI)	24	8.63	12	8.28	1.000	12	7.59
All Stroke, Death Endpoint	19	6.83	11	7.59	0.842	10	6.33

^c Barnett, H.J., D.W. Taylor, M. Eliasziw, A.J. Fox, G.G. Ferguson, R.B. Haynes, R.N. Rankin, G.P. Clagett, V.C. Hachinski, D.L. Sackett, K.E. Thorpe, and H.E. Meldrum. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med*, 1998. 339(20): p. 1415-25.

^d ACAS, Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA*, 1995. 273(18): p. 1421-8.

Death	6	2.16	2	1.38	0.625	4	2.53
Stroke-Related	2	0.72	0	0.00	0.406	1	0.63
Not Stroke-Related	4	1.44	2	1.38	0.965	3	1.90
Ipsilateral Stroke	14	5.04	7	4.83	0.933	6	3.80
Major	3	1.08	2	1.38	0.802	2	1.27
Minor ²	11	3.96	5	3.45	0.816	4	2.53
Non-ipsilateral Stroke	1	0.36	1	0.69	0.653	1	0.63
Non-stroke Neurological ³	6	2.16	1	0.69	0.341	3	1.90
MI	8	2.88	2	1.38	0.406	4	2.53
Procedural Complication	27	9.71	8	5.52	0.194	11	6.96
Hypotension	15	5.40	2	1.38	0.092	6	3.80
Arrhythmia	11	3.96	0	0.00	0.048	5	3.16
Vasospasm	4	1.44	0	0.00	0.238	0	0.00
Dissection	2	0.72	3	2.07	0.223	0	0.00
In-stent Thrombosis	1	0.36	1	0.69	0.653	0	0.00
Emergent CEA	2	0.72	0	0.00	0.406	0	0.00
Emergent Intervention	1	0.36	1	0.69	0.653	0	0.00
Access Site Complication ⁴	13	4.68	4	2.76	0.405	9	5.70
Requiring Repair / Transfusion	8	2.88	2	1.38	0.406	6	3.80
Bleeding ⁵	7	2.52	6	4.14	0.387	11	6.96
Requiring transfusion	5	1.80	5	3.45	0.310	9	5.70
GI bleeding	0	0.00	2	1.38	0.015	2	1.27
Adverse events related to device failure or malfunction ⁶	2	0.72	1	0.69	1.000	0	0.00

¹Patients 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.

²Two patients suffered strokes that were determined to be non-serious adverse events. Patient 249-3715 (ARCHEr 2) suffered blurred vision that was subsequently diagnosed by an ophthalmologist as "central retinal artery occlusion with multiple refractile emboli and macular edema." Patient 074-4804 had mild facial weakness that was subsequently diagnosed by MRI as an acute lacunar infarct. Both events resolved without treatment. The Clinical Events Adjudication Committee adjudicated both of these events as strokes. However, because the events did not meet the criteria for a serious adverse event (no intervention to prevent permanent impairment, no persistent or significant disability), they are not included in the accounting of serious adverse events. The events are included as strokes in the composite endpoints.

³Includes events such as visual / speech disturbances, confusion, seizure, and TIA.

⁴Includes events such as bruising, hematoma, and bleeding.

⁵Includes events such as non-access site bleeding, anemia up to 30 days, and GI bleed up to 30 days.

⁶Three adverse events counted above were categorized as related to device failure / malfunction:

One dissection in the ARCHEr 2 study was attributed by the physician to the OTW Accunet System. The physician was not able to cross the lesion with the device.

One CEA in the ARCHEr 2 study resulted when the OTW Accunet System became entangled with the deployed stent and could not be retrieved by the physician.

One emergent intervention in the ARCHEr 3 study resulted when the RX Accunet Filter Basket became entangled with the deployed stent and detached from the guidewire during the retrieval attempt. The physician opted to stent the basket in place in the artery. No additional adverse events related to this device malfunction were reported as of the last patient follow-up (9 months post-procedure).

Table 14. ARCHeR Pivotal Trial Results – Efficacy Assessment Event Rates

Events	ARCHeR 2		ARCHeR 3		P value	ARCHeR 1		
	n/N	%	n/N	%		n/N	%	
One-Year Primary Endpoint (30-Day Primary Endpoint + Ipsilateral Stroke Between 31 and 365 Days) ¹ [95% Conf. Interval] ²		10.22% [–, 13.48%]		N/A		N/A	8.28% [–, 12.25%]	
AccUNET Device Success ³	264/277	95.3	139/145	95.9	1.000		N/A	
Acculink Device/Procedural Success ⁴	268/271	98.9	141/142	99.3	1.000	153/156	98.1	
Clinical Success ⁵	249/272	91.5	133/142	93.7	0.562	143/156	91.7	
Post-procedure In-lesion Minimal Lumen Diameter Mean ± SD (N) Range (min, max)	3.64± 0.78 (272) (1.93, 6.89)		3.79± 0.75 (143) (1.93, 6.29)		0.064		3.95± 0.86 (156) (1.52, 6.67)	
Post-procedure In-lesion Percent Diameter Stenosis Mean ± SD (N) Range (min, max)	18.66±11.88 (272) (0.00, 51.07)		15.85±12.47 (143) (–12.1, 55.66)		0.025		20.40±12.38 (156) (–12.1, 56.06)	
Target Lesion Revascularization (Clinically Indicated) ^{1, 6}								
at 6 months	1	0.4%		N/A		N/A	1	0.7%
at 12 months	7	2.8%					3	2.2%
at 24 months	8	3.8%					4	3.0%
Ultrasound (Same or decreased stenosis from Baseline exam)								
at 6 months	143/196	73.0		N/A		N/A	84/102	82.4
at 12 months	124/173	71.7					78/97	80.4

¹ Estimated via Kaplan-Meier analysis.

² 95% 1-sided confidence interval by normal approximation, using Peto's formula for the Kaplan Meier standard error.

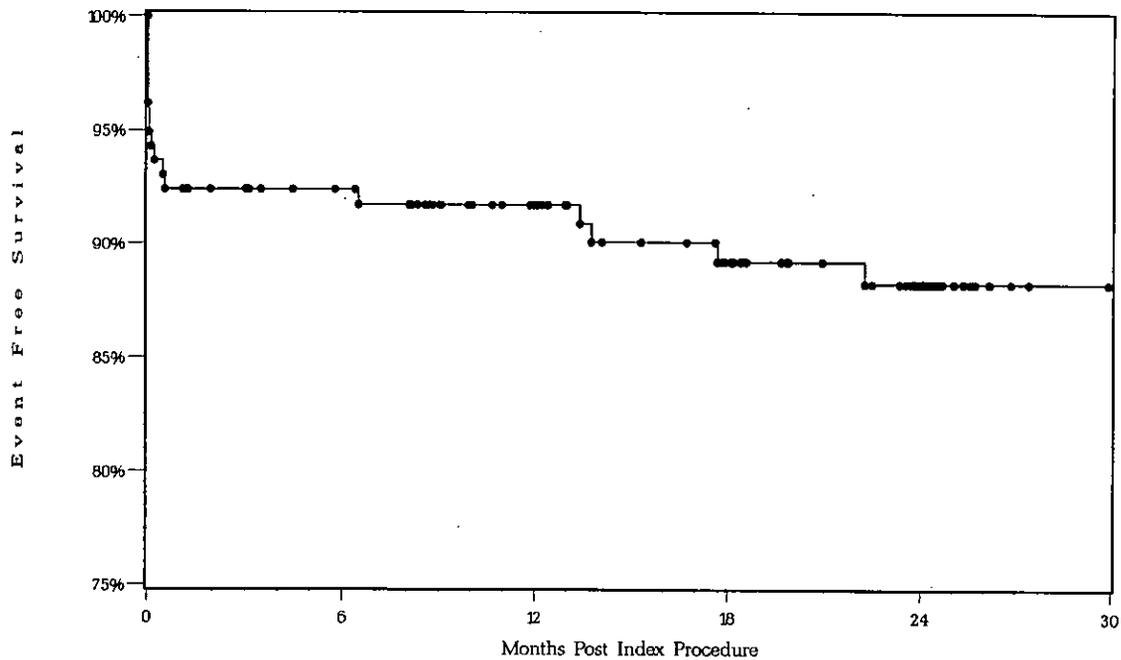
³ Device delivered, placed, and retrieved as described in protocol.

⁴ Stent successfully deployed and residual stenosis < 50% following stent placement, per core lab reading.

⁵ Acculink device / procedural success in the absence of death, emergency endarterectomy, repeat PTA / thrombolysis of the target vessel, stroke, or MI, within seven days of procedure.

⁶ TLR is defined as 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. To be considered clinically indicated, the patient must be symptomatic with ≥ 50% stenosis or asymptomatic with ≥ 80% stenosis.

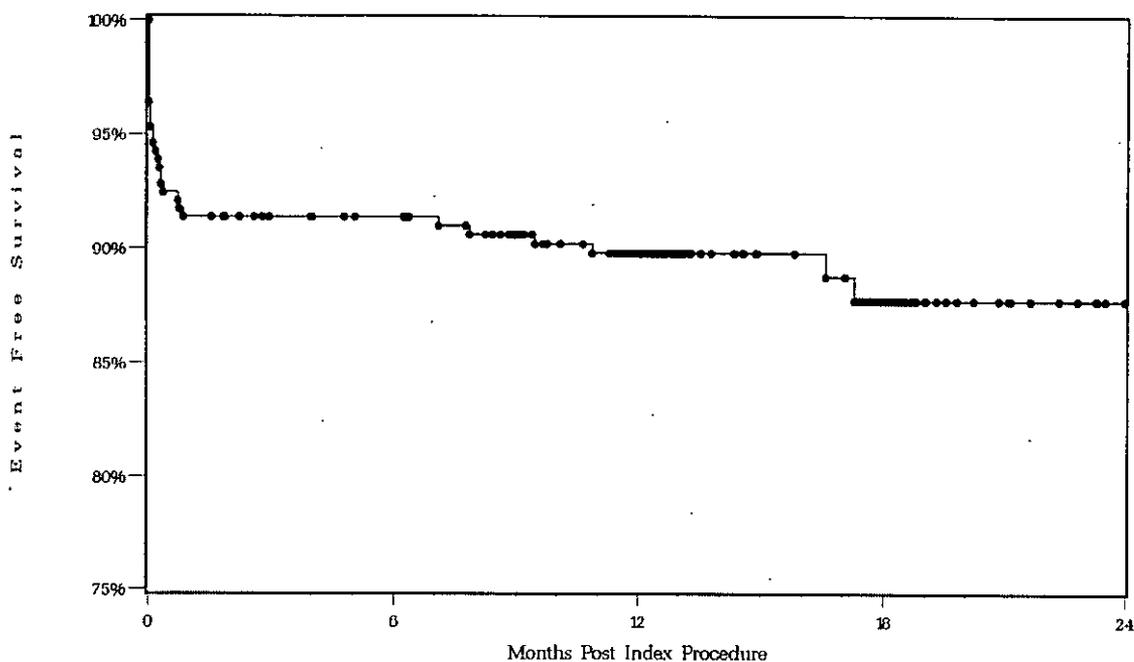
Figure 4. ARChER 1 Study, Freedom from composite endpoint of Stroke, Death, and MI within 30 days and Ipsilateral Stroke between days 31 and 910



Months After Index Procedure	0	1	6	12	24	30
# At Risk	158	152	146	135	102	70
# Events	6	12	12	13	17	17
% Event Free	96.2%	92.4%	92.4%	91.7%	88.2%	88.2%

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Figure 5. ARCHeR 2 Study, Freedom from composite endpoint of Stroke, Death, and MI within 30 days and Ipsilateral Stroke between days 31 and 730

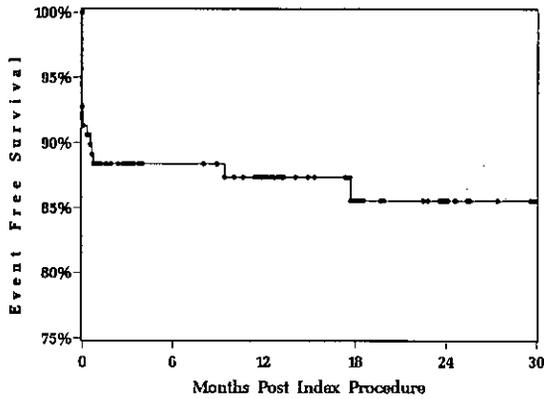


Months After Index Procedure	0	1	3	6	12	24
# At Risk	278	268	254	246	231	164
# Events	10	24	24	24	28	30
% Event Free	96.4%	91.4%	91.4%	91.4%	89.8%	87.7%

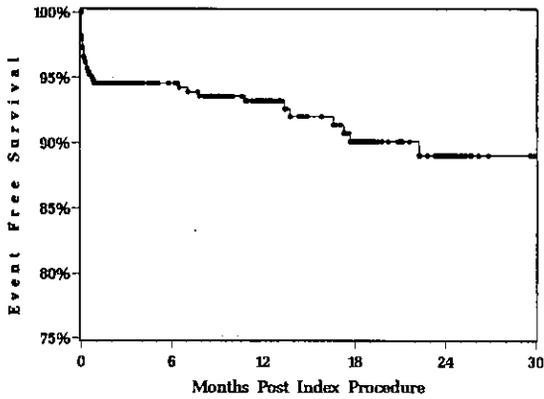
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Figure 6. Symptomatic and asymptomatic registry patients in ARCHeR 1, 2 and 3

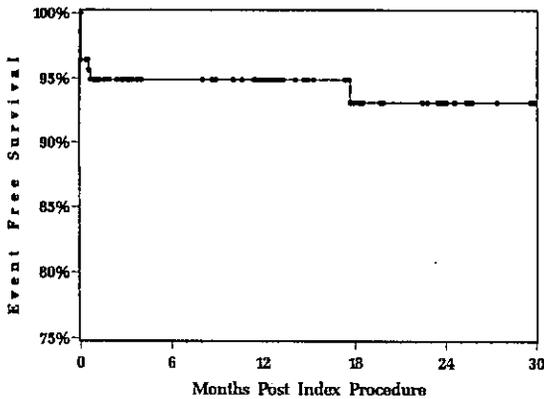
A. Symptomatic patients, freedom from composite of all Death or Stroke < 30 days, and Ipsilateral Stroke days 31-910



B. Asymptomatic patients, freedom from composite of all Death or Stroke < 30 days, and Ipsilateral Stroke days 31-910

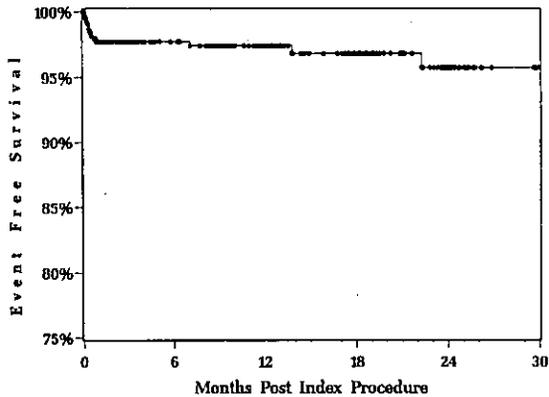


C. Symptomatic patients, freedom from composite of all Death or Major Stroke < 30 days, and Major Ipsilateral Stroke days 31-910



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D. Asymptomatic patients, freedom from composite of all Death or Major Stroke < 30 days, and Major Ipsilateral Stroke days 31-910



7.2 CREST Pivotal Clinical Study

Purpose: The objective of CREST was to demonstrate that the 1-year composite endpoint (stroke, MI and death at 30 days plus ipsilateral stroke between 31 days and 1 year) resulting from use of the Acculink Carotid Stent Systems to treat standard surgical risk symptomatic ($\geq 50\%$ stenosis) and asymptomatic ($\geq 70\%$ stenosis) subjects with carotid artery stenosis was non-inferior to CEA.

Conclusions: CAS when using the Acculink Carotid Stent System was shown to be non-inferior to CEA. The outcomes of CREST confirm the safety and effectiveness of the Acculink Carotid Stent System when used with the Accunet Embolic Protection System for treatment of standard surgical risk subjects with disease of the internal carotid artery.

Design: A multi-center, prospective, randomized, controlled, clinical trial with blinded endpoint evaluation, conducted at 107 sites in the U.S. and 9 sites in Canada. A total of 2502 patients were randomized 1:1 to CAS or CEA between December 21, 2000 and July 18, 2008. Patients had to be at least 18 years of age or older and had either symptomatic ($\geq 50\%$) or asymptomatic ($\geq 70\%$) carotid artery stenosis. The primary endpoint and selected secondary endpoints were analyzed for a Per-Protocol population.

Patients who satisfied the eligibility criteria were enrolled if they had a discrete lesion located in the ICA with or without the involvement of the contiguous common carotid artery (CCA) confirmed by angiography or ultrasound prior to randomization. Target ICA vessel reference diameter had to be ≥ 4.0 mm and ≤ 9.0 mm by angiography.

The primary analysis of CREST was performed on the Per-Protocol (PP) analysis population. Four additional analyses of the primary endpoint were performed on the Intent-to-Treat (ITT), As-Treated (AT), Modified As-Treated (MAT) [defined as the AT population minus the subjects who crossed over after an attempted procedure], and propensity score-adjusted PP population. In all five analyses, the CREST trial results met the criteria for statistical non-inferiority of CAS using the Acculink stent as compared to CEA with $p < 0.05$.

The safety and effectiveness of the Acculink Carotid Stent System when used with the Accunet Embolic Protection System was analyzed to demonstrate non-inferiority of CAS versus CEA for the standard surgical risk population.

Demographics: Key baseline demographics and risk factors are comparable and well balanced between CAS and CEA arms. The mean age was 69.1 years and 9.7% (243/2502) of the study population were octogenarians. Male subjects comprised 65.1% (1630/2502) of the study population which is consistent with recently published data from an observational study in which 60.9% of subjects with atherosclerotic lesions who underwent CAS were male. This is also consistent with the 66%-78% proportion of males enrolled in several randomized CAS and CEA clinical trials that studied similar patient populations.

Baseline characteristics that occurred most frequently in greater than 10% of the CREST population were prior cardiovascular disease 43.7% (1046/2394), previous CABG 20.7% (514/2480), diabetes using oral anti-diabetic agents only 22.8% (567/2488), hypertension 85.9% (2141/2492), dyslipidemia 84.4% (2093/2481) and history of / or current smoker 65.7% (1619/2465).

Methods: The CEC was used to adjudicate potential endpoint events of MI and death up to 30 days and any potential stroke. An NIH appointed DSMB monitored the safety and efficacy of treatments. Angiographic, ECG and ultrasound core labs were used to determine respective outcomes. The enrollment has been completed and long-term follow-up continues.

Results: CREST met the primary endpoint of the trial with $p < 0.05$. In the primary analysis of the one-year composite primary endpoint, the event rate of death, stroke and MI during the 30-day peri-procedural period plus ipsilateral stroke between 31 and 365 days was 7.1% in the CAS arm and 6.6% in the CEA arm in the PP population. The difference between the primary endpoint event rates for CAS and CEA arms was 0.5% with 95% upper confidence limit of 2.26% meeting the non-inferiority margin of 2.6% with $p = 0.0245$. CAS was shown to be non-inferior to CEA in the PP, ITT, AT, MAT, and propensity score adjusted per-protocol populations. Table 15 presents the one year primary endpoint event rates.

Table 15. Summary of Non-Inferiority Testing for the Primary Endpoint for the CREST Study

Analyses	One Year Primary Endpoint Event Rate (%) ± SE (%) (N)			Non-inferiority Test	
	CAS	CEA	Difference [95% CI] ^a	Non- inferiority Test Margins	p-Value ^b
Per-protocol ¹	7.1% ± 0.77% (N = 1131)	6.6% ± 0.73% (N = 1176)	0.5% [-∞, 2.26%]	2.6%	0.0245
Per-protocol (Adjusted) ²	7.2% ± 0.77% (N = 1131)	6.5% ± 0.72% (N = 1176)	0.7% [-∞, 2.41%]	2.6%	0.0342
Intent-to-treat ¹	7.0% ± 0.73% (N = 1259)	6.9% ± 0.73% (N = 1237)	0.1% [-∞, 1.80%]	2.6%	0.0077
As-treated ¹	7.2% ± 0.76% (N = 1151)	6.7% ± 0.71% (N = 1246)	0.4% [-∞, 2.16%]	2.6%	0.0193
Modified As- treated ¹	7.2% ± 0.76% (N = 1149)	6.7% ± 0.71% (N = 1239)	0.5% [-∞, 2.22%]	2.6%	0.0221

¹ Event rate is estimated by the Kaplan-Meier method and standard error is estimated by the Greenwood method.

² Event rate and standard error are estimated by the propensity score adjusted Kaplan-Meier estimators.

³ One-sided p-value and 95% confidence interval for non-inferiority test by using asymptotic test statistics with non-inferiority test margins as indicated in the table.

Note: -∞ means Not Applicable for this one-sided test

An analysis of the composite endpoint in randomized subjects in the PP analysis population was performed to assess the interaction between revascularization treatment and gender. There were 64.6% (731/1131) male subjects in the CAS arm and 66.7% (784/1176) male subjects in the CEA arm of the PP analysis population.

Table 16 presents the results of the Cox regression analysis of the interaction between treatment and the gender for the one-year composite endpoint. There is no evidence of an interaction and the *p*-value for the interaction term was 0.9168. The result of the analysis indicates that there is no differential treatment effect modification between CAS and CEA in relation to the subject's gender.

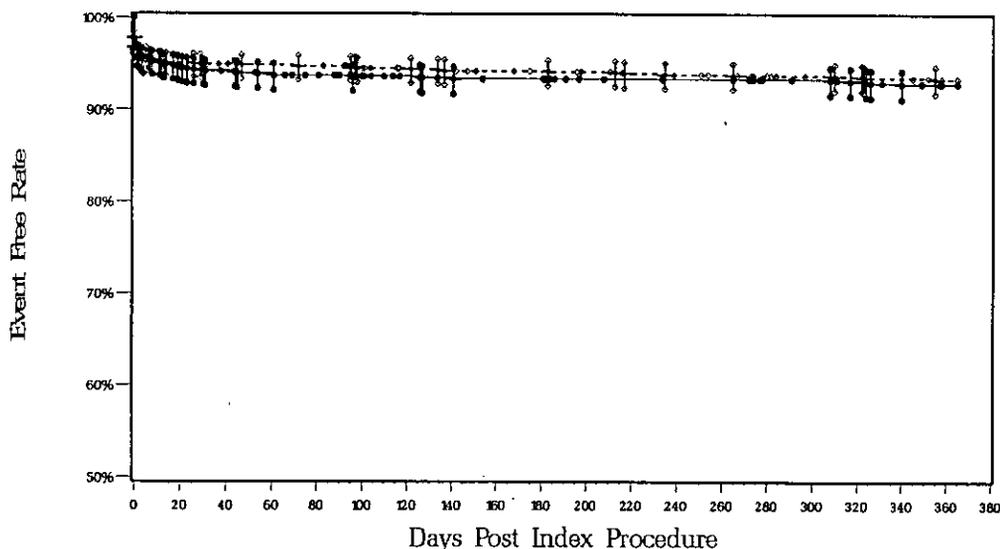
Table 16. Interaction Analysis between Treatment and Gender on One-Year Composite Endpoint by Cox Regression (PP Population)

Variable	Coefficient (SE)	Hazard Ratio [95% CI]	<i>p</i> -Value ¹
Treatment (CAS vs. CEA)	0.06 (0.26)	1.06 [0.64, 1.76]	0.8233
Gender (male vs. female)	-0.19 (0.24)	0.83 [0.52, 1.31]	0.4182
Treatment * Gender	0.03 (0.33)	1.03 [0.54, 1.97]	0.9168

¹ Wald Chi-Square *p*-value.

In the Kaplan-Meier survival analyses, a subject was counted as having an event when a subject experienced death, stroke, or myocardial infarction (DSMI) within 30 days, or ipsilateral stroke between 31 and 365 days following the index procedure. The Kaplan-Meier estimated CAS freedom from event rate was 92.9%. The Kaplan-Meier estimated CEA freedom from event rate was 93.4%.

Figure 7. CREST - Freedom from Primary Endpoint Events (PP Population)



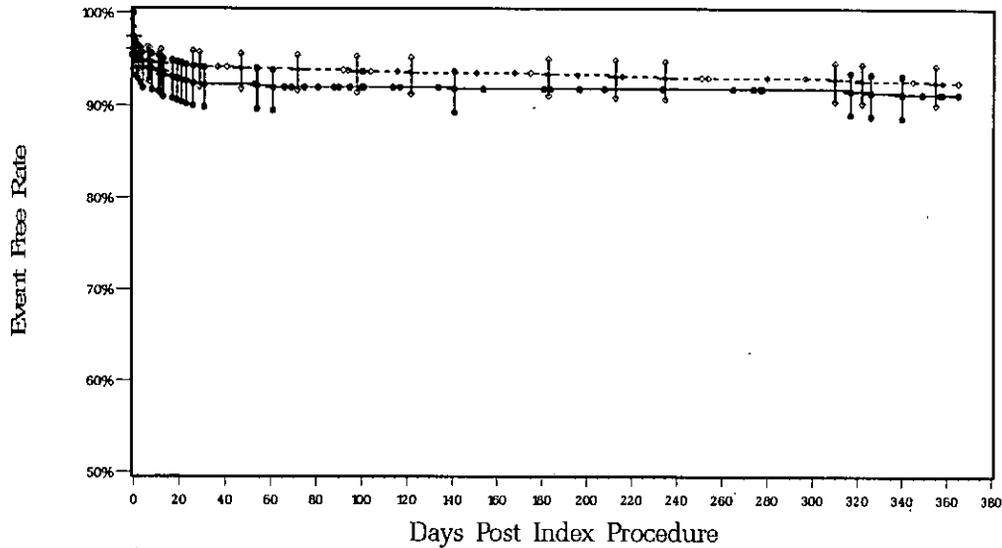
Solid line: CAS Subjects (n= 1131)
 Dashed line: CEA Subjects (n= 1176)
 Vertical bar: 95% Confidence Limit

Days Post Index Procedure	0	(0, 2]	(2, 30]	(30, 180]	(180, 365]
CAS					
Subjects at Risk	1131	1094	1082	1062	1031
Subjects Censored	0	1	3	21	1026
Number of Events	37	11	17	10	5
% Event Free	96.7%	95.8%	94.2%	93.4%	92.9%
% Standard Error	0.5%	0.6%	0.7%	0.7%	0.8%
CEA					
Subjects at Risk	1176	1150	1127	1110	1083
Subjects Censored	0	1	5	19	1074
Number of Events	26	22	12	8	9
% Event Free	97.8%	95.9%	94.9%	94.2%	93.4%
% Standard Error	0.4%	0.6%	0.6%	0.7%	0.7%
Tests Between Groups					
	Test	Chi-Square	DF	p-value	
	Log-Rank	0.268	1	0.6047	
	Wilcoxon	0.304	1	0.5815	

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The freedom from the estimated one-year composite primary endpoint event rates are 91.3% in the CAS arm and 92.5% in the CEA arm for symptomatic subjects. The Kaplan-Meier survival curves of CAS and CEA are comparable.

Figure 8. CREST - Symptomatic CAS and CEA Subjects -- Freedom from One-Year Composite Endpoint (PP Population)



Solid line: CAS Subjects (n=599)
 Dashed line: CEA Subjects (n=620)
 Vertical bar: 95% Confidence Limit

Days Post Index Procedure	0	(0, 2]	(2, 30]	(30, 180]	(180, 365]
CAS					
Subjects at Risk	599	576	568	552	531
Subjects Censored	0	1	1	17	528
Number of Events	23	7	15	4	3
% Event Free	96.2%	95.0%	92.5%	91.8%	91.3%
% Standard Error	0.8%	0.9%	1.1%	1.1%	1.2%
CEA					
Subjects at Risk	620	604	589	579	563
Subjects Censored	0	0	5	12	557
Number of Events	16	15	5	4	6
% Event Free	97.4%	95.0%	94.2%	93.5%	92.5%
% Standard Error	0.6%	0.9%	0.9%	1.0%	1.1%
Tests Between Groups					
	Test	Chi-Square	DF	p-value	
	Log-Rank	0.685	1	0.4078	

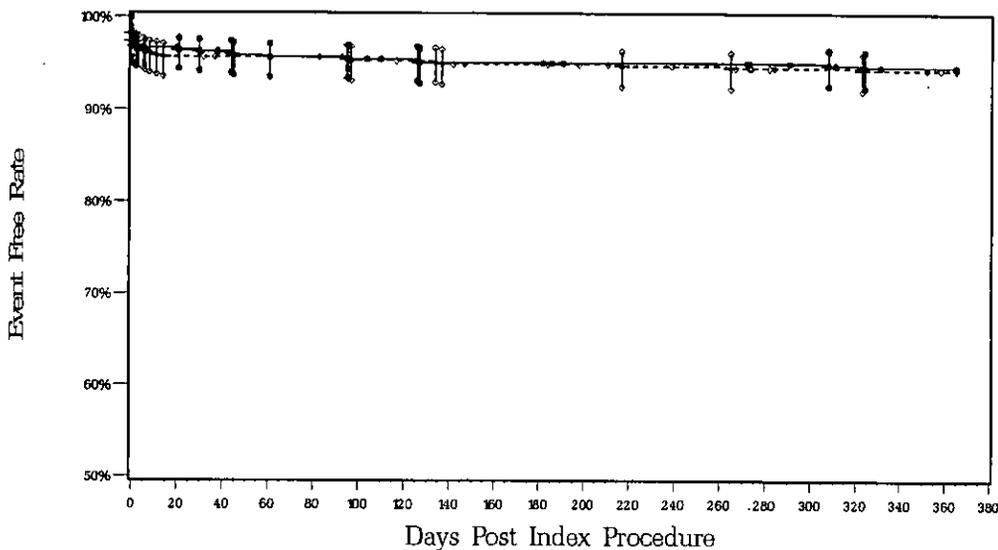
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	Wilcoxon	0.731	1	0.3926
<i>Note: Subjects at risk gives the number of subjects at risk of an event at the start of the interval, while subjects censored and number of events are the incremental counts of subjects censored or with events during the interval. The intervals are denoted as half-open bracket expression, where the start of interval '(' is exclusive and the end of the interval ']' is inclusive.</i>				

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The freedom from the estimated one-year composite primary endpoint event rates are 94.7% in the CAS arm and 94.4% in the CEA arm for asymptomatic subjects. The Kaplan-Meier survival curves of CAS and CEA are comparable.

Figure 9. CREST - Asymptomatic CAS and CEA Subjects -- Freedom from One-Year Composite Endpoint (PP Population)



Solid line: CAS Subjects (n=532)
Dashed line: CEA Subjects (n=550)
Vertical bar: 95% Confidence Limit

Days Post Index Procedure	0	(0, 2]	(2, 30]	(30, 180]	(180, 365]
CAS					
Subjects at Risk	532	518	514	510	500
Subjects Censored	0	0	2	4	498
Number of Events	14	4	2	6	2
% Event Free	97.4%	96.6%	96.2%	95.1%	94.7%
% Standard Error	0.7%	0.8%	0.8%	0.9%	1.0%
CEA					
Subjects at Risk	556	546	538	531	520
Subjects Censored	0	1	0	7	517
Number of Events	10	7	7	4	3
% Event Free	98.2%	96.9%	95.7%	95.0%	94.4%
% Standard Error	0.6%	0.7%	0.9%	0.9%	1.0%
Tests Between Groups	Test	Chi-Square	DF	p-value	
	Log-Rank	0.049	1	0.8240	

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	Wilcoxon	0.041	1	0.8390	
Note: Subjects at risk gives the number of subjects at risk of an event at the start of the interval, while subjects censored and number of events are the incremental counts of subjects censored or with events during the interval. The intervals are denoted as half-open bracket expression, where the start of interval '(' is exclusive and the end of the interval ']' is inclusive.					

For both the symptomatic and the asymptomatic subgroups, the difference in DSMI rates was not statistically significant between the CAS and the CEA arms. The peri-procedural death and stroke rate for both CAS 5.9% (35/597) and CEA 2.4% (15/620) were within the AHA guideline of 6% death and stroke for treating symptomatic subjects. The peri-procedural death and stroke rates for CAS 2.5% (13/530) and for CEA 1.3% (7/555) for asymptomatic subjects were both within the AHA guideline of 3% death and stroke for treating asymptomatic subjects. These findings suggest that CAS and CEA are comparable with respect to peri-procedural safety when treating symptomatic and asymptomatic subjects.

Table 17. CREST - Death, Stroke and MI within 30 Days -- Hierarchical Events by Symptomatic Status (PP Population)

Hierarchical Events	Symptomatic			Asymptomatic		
	CAS N = 599	CEA N = 620	Difference [95% CI] ¹	CAS N = 532	CEA N = 556	Difference [95% CI] ¹
All Death, Stroke, and MI [95% Conf. Interval] ²	7.5% (45/597) [5.6%, 10.0%]	5.8% (36/620) [4.1%, 7.9%]	1.7% [-1.1%, 4.5%]	3.8% (20/530) [2.3%, 5.8%]	4.3% (24/555) [2.8%, 6.4%]	-0.6% [-2.9%, 1.8%]
Death	5	1	--	1	2	--
All Stroke	30	14	--	12	5	--
Major Stroke	4	2	--	2	0	--
Ipsilateral to Treated Hemisphere	4	2	--	2	0	--
Non-ipsilateral to Treated Hemisphere	0	0	--	0	0	--
Minor Stroke	26	12	--	10	5	--
Ipsilateral to Treated Hemisphere	25	10	--	8	4	--
Non-ipsilateral to Treated Hemisphere	1	2	--	2	1	--
MI	10	21	--	7	17	--
All Stroke and Death [95% Conf. Interval] ²	5.9% (35/597) [4.1%, 8.1%]	2.4% (15/620) [1.4%, 4.0%]	3.4% [1.2%, 5.7%]	2.5% (13/530) [1.3%, 4.2%]	1.3% (7/555) [0.5%, 2.6%]	1.2% [-0.4%, 2.8%]
Major Stroke and Death [95% Conf. Interval] ²	1.5% (9/597) [0.7%, 2.8%]	0.5% (3/620) [0.1%, 1.4%]	1.0% Assumptions not met	0.6% (3/530) [0.1%, 1.6%]	0.4% (2/555) [0.0%, 1.3%]	0.2% Assumptions not met

Note: Only includes the first occurrence of the most serious event for each subject.

¹ By normal approximation.

² Clopper-Pearson exact confidence interval.

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The results show that the stroke rate was higher in CAS and the MI rate was higher in CEA. The stroke rate in CAS was 4.1% (46/1127), compared to 1.9% (22/1175) in the CEA arm. The MI rate in CAS was 2.0% (22/1127), compared to 3.4% (40/1175) in the CEA arm. Both of these differences in rates are statistically significant.

Table 18. CREST - Death, Stroke and MI within 30 Days – Non-Hierarchical Events (PP Population)

Events Category	CAS N= 1131	CEA N= 1176
Death [95% Conf. Interval] ¹	0.5% (6/1127) [0.2%, 1.2%]	0.3% (3/1175) [0.1%, 0.7%]
All Stroke [95% Conf. Interval] ¹	4.1% (46/1127) [3.0%, 5.4%]	1.9% (22/1175) [1.2%, 2.8%]
Major Stroke [95% Conf. Interval] ¹	0.9% (10/1127) [0.4%, 1.6%]	0.4% (5/1175) [0.1%, 1.0%]
Ipsilateral to Treated Hemisphere [95% Conf. Interval] ¹	0.9% (10/1127) [0.4%, 1.6%]	0.3% (4/1175) [0.1%, 0.9%]
Non-ipsilateral to Treated Hemisphere [95% Conf. Interval] ¹	0.0% (0/1127) [0.0%, 0.3%]	0.1% (1/1175) [0.0%, 0.5%]
Minor Stroke [95% Conf. Interval] ¹	3.2% (36/1127) [2.2%, 4.4%]	1.5% (18/1175) [0.9%, 2.4%]
Ipsilateral to Treated Hemisphere [95% Conf. Interval] ¹	2.9% (33/1127) [2.0%, 4.1%]	1.3% (15/1175) [0.7%, 2.1%]
Non-ipsilateral to Treated Hemisphere [95% Conf. Interval] ¹	0.3% (3/1127) [0.1%, 0.8%]	0.3% (3/1175) [0.1%, 0.7%]
MI [95% Conf. Interval] ¹	2.0% (22/1127) [1.2%, 2.9%]	3.4% (40/1175) [2.4%, 4.6%]

Note: The analysis only includes each 30-day DSMI evaluable subject's first occurrence of the event. An evaluable subject for 30-day DSMI Analysis is a subject who has either 30-day DSMI event or 30-day follow up.

¹ Clopper-Pearson exact confidence interval.

Table 19. CREST - Death, Stroke and MI within 30 Days -- Non-hierarchical Events by Symptomatic Status (PP Population)

Non-hierarchical Events	Symptomatic			Asymptomatic		
	CAS N = 599	CEA N = 620	Difference [95% CI] ¹	CAS N = 532	CEA N = 556	Difference [95% CI] ¹
Death [95% Conf. Interval] ²	0.8% (5/597) [0.3%, 1.9%]	0.2% (1/620) [0.0%, 0.9%]	0.7% Assumptions not met	0.2% (1/530) [0.0%, 1.0%]	0.4% (2/555) [0.0%, 1.3%]	-0.2% Assumptions not met
All Stroke [95% Conf. Interval] ²	5.5% (33/597) [3.8%, 7.7%]	2.4% (15/620) [1.4%, 4.0%]	3.1% [0.9%, 5.3%]	2.5% (13/530) [1.3%, 4.2%]	1.3% (7/555) [0.5%, 2.6%]	1.2% [-0.4%, 2.8%]
Major Stroke [95% Conf. Interval] ²	1.2% (7/597) [0.5%, 2.4%]	0.5% (3/620) [0.1%, 1.4%]	0.7% Assumptions not met	0.6% (3/530) [0.1%, 1.6%]	0.4% (2/555) [0.0%, 1.3%]	0.2% Assumptions not met
Ipsilateral to Treated Hemisphere [95% Conf. Interval] ²	1.2% (7/597) [0.5%, 2.4%]	0.5% (3/620) [0.1%, 1.4%]	0.7% Assumptions not met	0.6% (3/530) [0.1%, 1.6%]	0.2% (1/555) [0.0%, 1.0%]	0.4% Assumptions not met
Non-ipsilateral to Treated Hemisphere [95% Conf. Interval] ²	0.0% (0/597) [0.0%, 0.6%]	0.0% (0/620) [0.0%, 0.6%]	0.0% Assumptions not met	0.0% (0/530) [0.0%, 0.7%]	0.2% (1/555) [0.0%, 1.0%]	-0.2% Assumptions not met
Minor Stroke [95% Conf. Interval] ²	4.4% (26/597) [2.9%, 6.3%]	2.1% (13/620) [1.1%, 3.6%]	2.3% [0.3%, 4.2%]	1.9% (10/530) [0.9%, 3.4%]	0.9% (5/555) [0.3%, 2.1%]	1.0% [-0.4%, 2.4%]
Ipsilateral to Treated Hemisphere [95% Conf. Interval] ²	4.2% (25/597) [2.7%, 6.1%]	1.8% (11/620) [0.9%, 3.2%]	2.4% [0.5%, 4.3%]	1.5% (8/530) [0.7%, 3.0%]	0.7% (4/555) [0.2%, 1.8%]	0.8% Assumptions not met
Non-ipsilateral to Treated Hemisphere [95% Conf. Interval] ²	0.2% (1/597) [0.0%, 0.9%]	0.3% (2/620) [0.0%, 1.2%]	-0.2% Assumptions not met	0.4% (2/530) [0.0%, 1.4%]	0.2% (1/555) [0.0%, 1.0%]	0.2% Assumptions not met
MI [95% Conf. Interval] ²	2.2% (13/597) [1.2%, 3.7%]	3.7% (23/620) [2.4%, 5.5%]	-1.5% [-3.4%, 0.4%]	1.7% (9/530) [0.8%, 3.2%]	3.1% (17/555) [1.8%, 4.9%]	-1.4% [-3.2%, 0.4%]

Note: Only includes each subject's first occurrence of the event.

¹ By normal approximation.

² Clopper-Pearson exact confidence interval.

Table 20. CREST - Death, Stroke, and MI within 30 Days - Hierarchical Events (PP Population)

Hierarchical Events	CAS N = 1131	CEA N = 1176	Total N = 2307	Difference [95% CI] ¹
All Death, Stroke, and MI [95% Conf. Interval] ²	5.8% (65/1127) [4.5%, 7.3%]	5.1% (60/1175) [3.9%, 6.5%]	5.4% (125/2302) [4.5%, 6.4%]	0.7% [-1.2%, 2.5%]
Death	6	3	9	--
All Stroke	42	19	61	--
Major Stroke	6	2	8	--
Ipsilateral to Treated Hemisphere	6	2	8	--
Non-ipsilateral to Treated Hemisphere	0	0	0	--
Minor Stroke	36	17	53	--
Ipsilateral to Treated Hemisphere	33	14	47	--
Non-ipsilateral to Treated Hemisphere	3	3	6	--
MI	17	38	55	--
All Stroke and Death [95% Conf. Interval] ²	4.3% (48/1127) [3.2%, 5.6%]	1.9% (22/1175) [1.2%, 2.8%]	3.0% (70/2302) [2.4%, 3.8%]	2.4% [1.0%, 3.8%]
Major Stroke and Death [95% Conf. Interval] ²	1.1% (12/1127) [0.6%, 1.9%]	0.4% (5/1175) [0.1%, 1.0%]	0.7% (17/2302) [0.4%, 1.2%]	0.6% [-0.1%, 1.3%]

Note: Only includes the first occurrence of the most serious event for each subject.

¹ By normal approximation.

² Clopper-Pearson exact confidence interval.

The 30-day DSMI rate was 5.5% in the CAS arm and 4.8% in the CEA arm in non-octogenarians and 8.5% in the CAS arm and 8.7% in the CEA arm in octogenarians. No significant difference was shown between the CAS and the CEA treatment arms for both the octogenarian and non-octogenarian subgroups.

Table 21. CREST - Death, Stroke and MI within 30 Days -- Hierarchical Events by Octogenarian Status (PP Population)

Hierarchical Events	Octogenarian			Non-octogenarian		
	CAS N = 106	CEA N = 103	Difference [95% CI] ¹	CAS N = 1025	CEA N = 1073	Difference [95% CI] ¹
All Death, Stroke, and MI [95% Conf. Interval] ²	8.5% (9/106) [4.0%, 15.5%]	8.7% (9/103) [4.1%, 15.9%]	-0.2% [-7.9%, 7.4%]	5.5% (56/1021) [4.2%, 7.1%]	4.8% (51/1072) [3.6%, 6.2%]	0.7% [-1.2%, 2.6%]
Death	1	1	--	5	2	--
All Stroke	6	3	--	36	16	--
Major Stroke	2	0	--	4	2	--
Ipsilateral to Treated Hemisphere	2	0	--	4	2	--
Non-ipsilateral to Treated Hemisphere	0	0	--	0	0	--
Minor Stroke	4	3	--	32	14	--
Ipsilateral to Treated Hemisphere	4	3	--	29	11	--
Non-ipsilateral to Treated Hemisphere	0	0	--	3	3	--
MI	2	5	--	15	33	--
All Stroke and Death [95% Conf. Interval] ²	6.6% (7/106) [2.7%, 13.1%]	3.9% (4/103) [1.1%, 9.6%]	2.7% Assumptions not met	4.0% (41/1021) [2.9%, 5.4%]	1.7% (18/1072) [1.0%, 2.6%]	2.3% [0.9%, 3.8%]
Major Stroke and Death [95% Conf. Interval] ²	2.8% (3/106) [0.6%, 8.0%]	1.0% (1/103) [0.0%, 5.3%]	1.9% Assumptions not met	0.9% (9/1021) [0.4%, 1.7%]	0.4% (4/1072) [0.1%, 1.0%]	0.5% Assumptions not met

Note: Only includes the first occurrence of the most serious event for each subject.

¹By normal approximation.

²Clopper-Pearson exact confidence interval.

Table 22. CREST - Death, Stroke and MI within 30 Days -- Non-hierarchical Events by Octogenarian Status (PP Population)

Non-hierarchical Events	Octogenarian			Non-octogenarian		
	CAS N = 106	CEA N = 103	Difference [95% CI] ¹	CAS N = 1025	CEA N = 1073	Difference [95% CI] ¹
Death [95% Conf. Interval] ²	0.9% (1/106) [0.0%, 5.1%]	1.0% (1/103) [0.0%, 5.3%]	-0.0% Assumptions not met	0.5% (5/1021) [0.2%, 1.1%]	0.2% (2/1072) [0.0%, 0.7%]	0.3% Assumptions not met
All Stroke [95% Conf. Interval] ²	6.6% (7/106) [2.7%, 13.1%]	3.9% (4/103) [1.1%, 9.6%]	2.7% Assumptions not met	3.8% (39/1021) [2.7%, 5.2%]	1.7% (18/1072) [1.0%, 2.6%]	2.1% [0.7%, 3.5%]
Major Stroke [95% Conf. Interval] ²	2.8% (3/106) [0.6%, 8.0%]	1.0% (1/103) [0.0%, 5.3%]	1.9% Assumptions not met	0.7% (7/1021) [0.3%, 1.4%]	0.4% (4/1072) [0.1%, 1.0%]	0.3% Assumptions not met
Ipsilateral to Treated Hemisphere [95% Conf. Interval] ²	2.8% (3/106) [0.6%, 8.0%]	1.0% (1/103) [0.0%, 5.3%]	1.9% Assumptions not met	0.7% (7/1021) [0.3%, 1.4%]	0.3% (3/1072) [0.1%, 0.8%]	0.4% Assumptions not met
Non-ipsilateral to Treated Hemisphere [95% Conf. Interval] ²	0.0% (0/106) [0.0%, 3.4%]	0.0% (0/103) [0.0%, 3.5%]	0.0% Assumptions not met	0.0% (0/1021) [0.0%, 0.4%]	0.1% (1/1072) [0.0%, 0.5%]	-0.1% Assumptions not met
Minor Stroke [95% Conf. Interval] ²	3.8% (4/106) [1.0%, 9.4%]	2.9% (3/103) [0.6%, 8.3%]	0.9% Assumptions not met	3.1% (32/1021) [2.2%, 4.4%]	1.4% (15/1072) [0.8%, 2.3%]	1.7% [0.5%, 3.0%]
Ipsilateral to Treated Hemisphere [95% Conf. Interval] ²	3.8% (4/106) [1.0%, 9.4%]	2.9% (3/103) [0.6%, 8.3%]	0.9% Assumptions not met	2.8% (29/1021) [1.9%, 4.1%]	1.1% (12/1072) [0.6%, 1.9%]	1.7% [0.5%, 2.9%]
Non-ipsilateral to Treated Hemisphere [95% Conf. Interval] ²	0.0% (0/106) [0.0%, 3.4%]	0.0% (0/103) [0.0%, 3.5%]	0.0% Assumptions not met	0.3% (3/1021) [0.1%, 0.9%]	0.3% (3/1072) [0.1%, 0.8%]	0.0% Assumptions not met
MI [95% Conf. Interval] ²	1.9% (2/106) [0.2%, 6.6%]	6.8% (7/103) [2.8%, 13.5%]	-4.9% Assumptions not met	2.0% (20/1021) [1.2%, 3.0%]	3.1% (33/1072) [2.1%, 4.3%]	-1.1% [-2.5%, 0.2%]

Note: Only includes each subject's first occurrence of the event.

¹ By normal approximation.² Clopper-Pearson exact confidence interval.

Access site complication requiring treatment was a secondary endpoint. Access site complications are specific to the treatment received. For CAS, serious adverse events include sequelae related to groin site complications, often due to hematoma or bleeding. For CEA, access site complications are generally due to wound hematoma or bleeding, and infection. All of the adverse events for access site complications included in this section required additional medical treatment. Access site complications often led to prolonged or repeat hospitalization. The rate of access site complications requiring treatment was 1.1% (13/1157) in the CAS arm and 3.5% (43/1246) in the CEA arm. There was a statistically significant difference between the rates of access site complications in the CAS and CEA arms.

Table 23. CREST - Treatment Specific Access Site Complications

	CAS ¹ N = 1157	CEA ¹ N = 1246	Total N = 2403	Difference [95% CI] ²
Access Site Complication Requiring Treatment [95% Conf. Interval] ³	1.1% (13/1157) [0.6%, 1.9%]	3.5% (43/1246) [2.5%, 4.6%]	2.3% (56/2403) [1.8%, 3.0%]	-2.3% [-3.5%, -1.1%]

¹ Treatment was the first attempted treatment.

² By normal approximation.

³ Clopper-Pearson exact confidence interval

Table 24. CREST - Access Site Complications Requiring Treatment for CAS and CEA Subjects (N=2403)

Complications	CAS (N=13)	CEA (N=41)	Total (N=54)
Hematoma	5 (38.5%)	20 (48.8%)	25 (46.3%)
Bleeding	5 (38.5%)	5 (12.2%)	10 (18.5%)
Occlusion	2 (15.4%)	0 (0.0%)	2 (3.7%)
Pseudoaneurysm	1 (7.7%)	2 (4.9%)	3 (5.5%)
Infection	0 (0.0%)	7 (17.1%)	7 (12.9%)
Pain ¹	0 (0.0%)	4 (9.7%)	4 (7.4%)
Incision Site	0 (0.0%)	3 (7.3%)	3 (5.5%)

Note: One subject who had vessel occlusion subsequently reported bleeding and one subject who reported pain was ultimately treated for a wound hematoma are counted only once in this table.

¹ Site reported complication treated with narcotic pain medication

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Device success was based on the number of devices used in CAS procedures; more than one device may have been used for one subject thus the denominator was different from the Per-Protocol population.

Table 25. CREST - Acute Device Success

	CAS ¹ N = 1157
ACCUNET Success [95% Conf. Interval] ²	96.7% (1084/1121) [95.5%, 97.7%]
ACCULINK Success [95% Conf. Interval] ²	99.8% (1182/1184) [99.4%, 100.0%]

Note: ACCUNET success and ACCULINK success are counted per device.

Procedure and clinical success are calculated for subjects with only one study procedure attempted.

¹Treatment is the first attempted treatment if CAS and CEA were attempted.

²Clopper-Pearson exact confidence interval.

The CEA definition of 'procedure attempted' was subjects who received general or regional anesthesia in preparation for surgery; for CAS subjects, 'procedure attempted' was defined as the study embolic protection system or stent delivery system entering into a subject's vasculature during the procedure.

The procedure success rate for CAS subjects was 97.5% (1099/1127). Nine (9) out of 28 subjects had residual stenosis >50%.

The clinical success rate for CAS subject was 91.9% (1036/1127). Twenty-eight (28) out of 90 subjects did not achieve clinical success due to an unsuccessful procedure and 63 subjects had an endpoint event of DSMI within 30-days. One (1) subject with an endpoint event of DSMI also had a target lesion revascularization (TLR) within 30-days of the procedure.

The procedure success rate for CEA subjects was 93.6% (1100/1175). Procedure success was not attained for 75 subjects. This was due to cranial nerve injury, TIA, stroke, amaurosis fugax or other neurological complications.

The clinical success rate for CEA subjects was 89.8% (1055/1175). Clinical success was not attained for 120 subjects. This was due to 75 subjects who did not achieve procedure success and an additional 45 subjects who had an endpoint event of DSMI within 30-days.

Table 26. CREST - Procedure and Clinical Success (PP Population)

	CAS N = 1131	CEA N = 1176	Total N = 2307
Procedure Success [95% Conf. Interval] ¹	97.5% (1099/1127) [96.4%, 98.3%]	93.6% (1100/1175) [92.1%, 94.9%]	95.5% (2199/2302) [94.6%, 96.3%]
Clinical Success [95% Conf. Interval] ¹	91.9% (1036/1127) [90.2%, 93.4%]	89.8% (1055/1175) [87.9%, 91.5%]	90.8% (2091/2302) [89.6%, 92.0%]

Note: ACCUNET success and ACCULINK success are counted per device.

¹Clopper-Pearson exact confidence interval.

The data show that 5.2% (65/1246) of subjects had cranial nerve injury due to the CEA treatment; no subjects who received CAS reported this injury. The cranial nerve injury was considered unresolved in 3.5% (44/1246) of CEA subjects at 1 month and 2.0% (25/1246) of CEA subjects at 6 months post-procedure.

Table 27. CREST - Procedure-Related Cranial Nerve Injury Unresolved at 1 and 6 Months

	CAS ¹ N = 1157	CEA ¹ N = 1246	Total N = 2403	Difference [95% CI] ²
Procedure-related Cranial Nerve Injury	0.0% (0/1157) [0.0%, 0.3%]	5.2% (65/1246) [4.0%, 6.6%]	2.7% (65/2403) [2.1%, 3.4%]	-5.2% Assumptions not met
Unresolved at One Month [95% Conf. Interval] ³	0.0% (0/1157) [0.0%, 0.3%]	3.5% (44/1246) [2.6%, 4.7%]	1.8% (44/2403) [1.3%, 2.5%]	-3.5% Assumptions not met
Unresolved at Six Months [95% Conf. Interval] ³	0.0% (0/1157) [0.0%, 0.3%]	2.0% (25/1246) [1.3%, 2.9%]	1.0% (25/2403) [0.7%, 1.5%]	-2.0% Assumptions not met

¹Treatment was the first attempted treatment.

²By normal approximation.

³Clopper-Pearson exact confidence interval.

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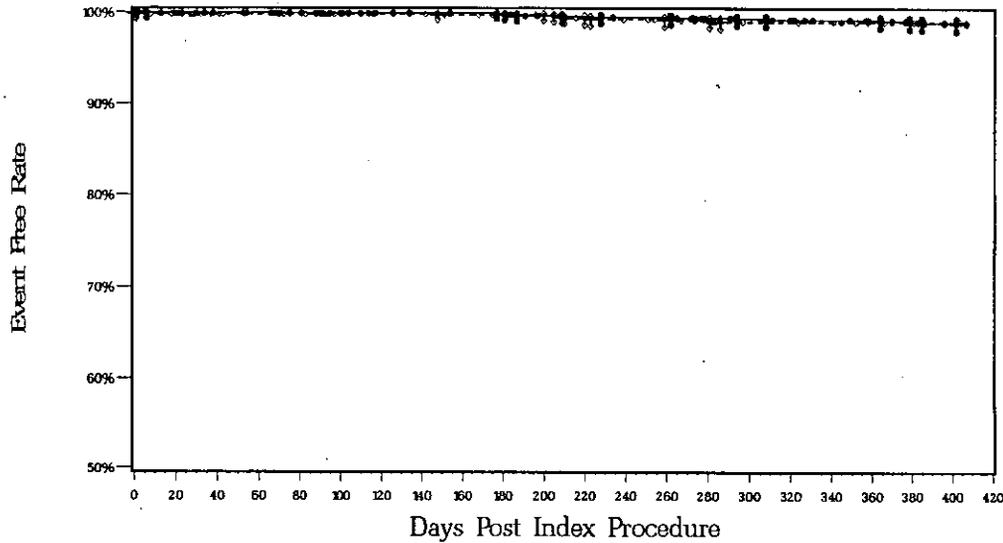
Target Lesion Revascularization (TLR) was determined to be clinically-driven in the CREST analysis when re-intervention of the target lesion was performed under either of the following circumstances:

- 1) The subject had a $\geq 50\%$ stenosis of the target lesion and had an ipsilateral stroke, TIA, or amaurosis fugax within 6 months prior to the TLR revascularization procedure.
- 2) The subject had a $\geq 80\%$ stenosis of the target lesion and did not have an ipsilateral stroke, TIA or amaurosis fugax within 6 months prior to the TLR revascularization procedure.

The freedom from clinically-driven TLR at 12 months by Kaplan-Meier analysis was 98.8% in the CAS arm and 99.0% in the CEA arm. The corresponding life tables to the survival curves indicate that the majority of clinically-driven TLR re-interventions occurred within 6 to 12 months post-procedure in both the CAS and CEA arms.

The Kaplan-Meier survival curves for the clinically-driven TLR in the CAS arm and the CEA arm at 12 months are comparable. The results demonstrate the long term durability of the CAS procedure compared to the conventional treatment with CEA in the standard surgical risk population requiring treatment for carotid stenosis.

Figure 10. CREST Freedom from Clinically-Driven Target Lesion Revascularization (TLR) at 12 Months (PP Population)



Solid line: CAS Subjects (n= 1131)
Dashed line: CEA Subjects (n= 1176)
Vertical bar: 95% Confidence Limit

Days Post Index Procedure	0	(0, 30]	(30, 180]	(180, 365]	(365, 407]
CAS					
Subjects at Risk	1131	1131	1119	1093	1060
Subjects Censored	0	11	25	25	1057
Number of Events	0	1	1	8	3
% Event Free	100%	99.9%	99.8%	99.1%	98.8%
% Standard Error	0.0%	0.1%	0.1%	0.3%	0.3%

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CEA					
Subjects at Risk	1176	1175	1164	1141	1110
Subjects Censored	0	10	22	22	1110
Number of Events	1	1	1	9	0
% Event Free	99.9%	99.8%	99.7%	99.0%	99.0%
% Standard Error	0.1%	0.1%	0.1%	0.3%	0.3%
Tests Between Groups	Test	Chi-Square	DF	p-value	
	Log-Rank	0.096	1	0.7568	
	Wilcoxon	0.080	1	0.7778	

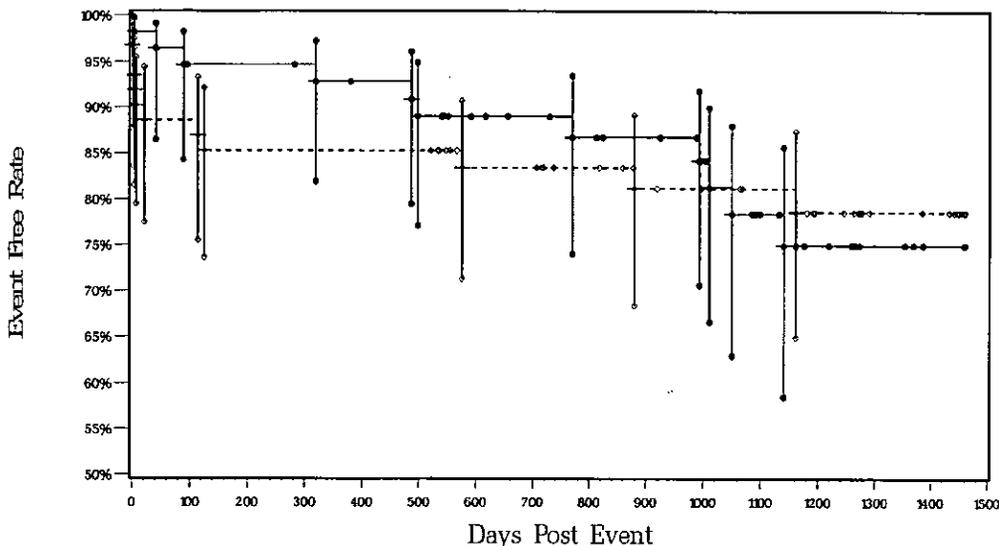
Note: Subjects at risk gives the number of subjects at risk of an event at the start of the interval, while subjects censored and number of events are the incremental counts of subjects censored or with events during the interval. The intervals are denoted as half-open bracket expression, where the start of interval 'i' is exclusive and the end of the interval 'j' is inclusive.

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Within the PP population, of subjects (N = 56) who experienced an MI within 30-days of their study procedure, there were 11 subjects who expired within 4 years, yielding an estimated freedom from death of 75.0% within 4 years, while the estimated freedom from death was 78.5% in those subjects who experienced a 30-day stroke (N = 62). The difference of estimated freedom from death between the two groups is not statistically significant.

Figure 11. CREST Comparison of Freedom from Death within Four Years between Subjects with a 30-Day MI versus 30-Day All Stroke (PP Population)



Solid line: MI Subjects (n= 56)
Dashed line: All Stroke Subjects (n= 62)
Vertical bar: 95% Confidence Limit

Days Post Event	0	(0, 365]	(365, 730]	(730, 1095]	(1095, 1461]
MI					
Subjects at Risk	56	56	50	40	25
Subjects Censored	0	2	8	11	24
Number of Events	0	4	2	4	1
% Event Free	100%	92.8%	89.0%	78.4%	75.0%
% Standard Error	0.0%	3.5%	4.2%	6.3%	6.9%
All Stroke					
Subjects at Risk	62	62	52	41	31
Subjects Censored	0	1	10	9	30
Number of Events	0	9	1	1	1
% Event Free	100%	85.3%	83.4%	81.1%	78.5%
% Standard Error	0.0%	4.5%	4.8%	5.2%	5.6%
Tests Between Groups	Test	Chi-Square	DF	p-value	

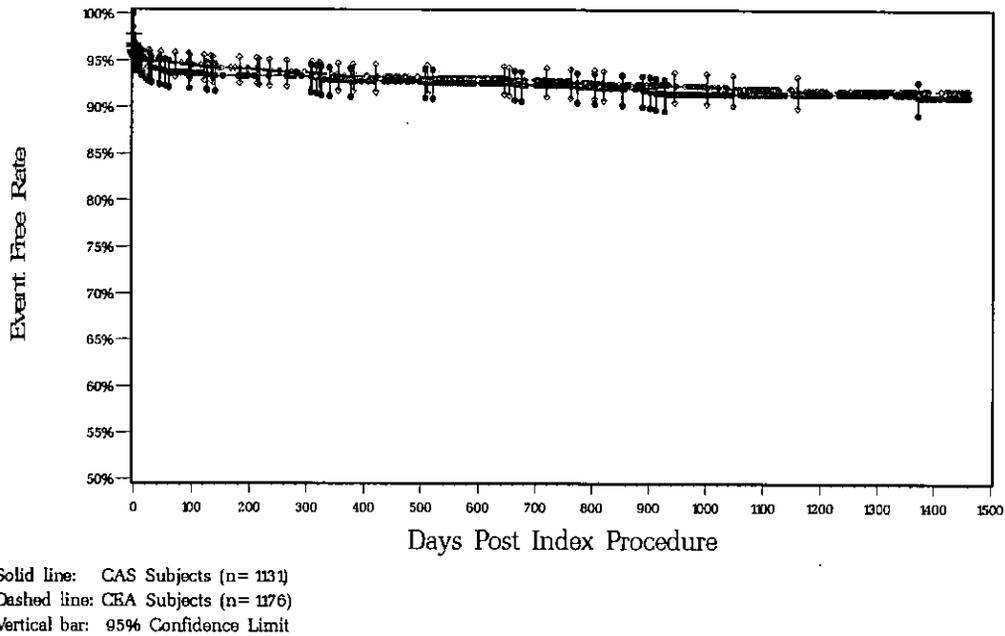
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	Log-Rank	0.001	1	0.9703	
	Wilcoxon	0.188	1	0.6648	

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At four years, the estimated freedom from endpoint events (DSMI within 30 days plus ipsilateral stroke between 31 days and 4 years) was 91.2% for the CAS subjects and 91.8% for the CEA subjects. The long-term durability and effectiveness of CAS has been confirmed to be consistent with conventional carotid endarterectomy in the population of standard surgical risk subjects with disease in the internal carotid artery.

Figure 12. Freedom from Death, Stroke and MI within 30 Days and Ipsilateral Stroke from 31 Days up to Four Years (PP Population)



Days Post Index Procedure	0	(0, 365]	(365, 730]	(730, 1095]	(1095, 1461]
CAS					
Subjects at Risk	1131	1094	1004	810	521
Subjects Censored	0	47	189	282	520
Number of Events	37	43	5	7	1
% Event Free	96.7%	92.9%	92.4%	91.5%	91.2%
% Standard Error	0.5%	0.8%	0.8%	0.9%	0.9%
CEA					
Subjects at Risk	1176	1150	1055	825	521
Subjects Censored	0	44	224	298	520
Number of Events	26	51	6	6	1
% Event Free	97.8%	93.4%	92.8%	92.0%	91.8%
% Standard Error	0.4%	0.7%	0.8%	0.8%	0.8%
Tests Between Groups					
	Test	Chi-Square	DF	p-value	
	Log-Rank	0.249	1	0.6176	
	Wilcoxon	0.286	1	0.5928	

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Of all subjects enrolled in CREST, 2140 were alive and had a follow-up visit at 12 months. 589 subjects had reached the 48-months follow-up time, were alive and had a follow-up visit as of the time of the data cut for this analysis. Table 28 delineates the follow-up visits at 12 and 48 months by study arm.

Table 28. Summary of Follow-Up Assessment

		CAS N=1262	CEA N=1240	Total N=2502
30 Days	Subjects Followed-up	1195	1170	2365
	Percent (Followed-up/Eligible)	95.9%	96.1%	96.0%
12 Months	Subjects Followed-up	1080	1060	2140
	Percent (Followed-up/Eligible)	90.6%	90.1%	90.3%
48 Months	Subjects Followed-up	306	283	589
	Percent (Followed-up/Eligible)	73.4%	71.5%	72.4%

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7.3 CAPTURE Post-Approval Study

The CAPTURE Study was a multi-center, prospective, registry study initiated after FDA's approval of the RX Acculink Carotid Stent System. The purpose of the study was to collect data on the RX Acculink System and RX Accunet Embolic Protection System when used by a broad group of physicians under commercial use conditions. In this study, patients were followed for 30 days after the procedure. The primary endpoint of the study was a composite of death, stroke, and myocardial infarction (DSMI) at 30 days. Additionally, all neurologic events and device-related adverse events were reported. A Clinical Events Adjudication Committee (CEAC) adjudicated all strokes and suspected strokes reported by participating clinical sites.

Specifically, the goals of the CAPTURE Study were to assess the following:

- To demonstrate that the RX Acculink Carotid Stenting System can be used safely by a broad group of physicians with varying levels of experience under commercial use conditions;
- To identify rare or unanticipated device-related adverse events; and
- To evaluate the adequacy of the RX Acculink Training Program.

Eligibility Criteria Summary

This report summarizes the data for the first 4331 patients enrolled at 144 clinical sites within the United States. Data is presented for 4225 evaluable patients in whom placement of an Acculink Stent with embolic protection was attempted in a carotid artery who completed 30-day follow-up or who experienced an endpoint (death or stroke or MI up to 30 days). These patients were enrolled in the CAPTURE Study from October 2004 through March 2006.

Baseline Patient Demographics

The baseline patient characteristics and angiographic lesion characteristics for the CAPTURE patients is presented in Table 29.

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Table 29. CAPTURE Patient Baseline Characteristics

	CAPTURE (N=4225)
Age (years)	
Mean \pm (SD)	72.7 \pm 9.1
Age \geq 80	23.4%
Gender	
Male	60.8%
Proportion of Symptomatic ¹ Patients	13.8%
Baseline Lesion & Vessel Characteristics	
Lesion Length (mm)	
Mean \pm SD	18.16 \pm 9.45
Percent Diameter Stenosis	
Mean \pm SD	85.34 \pm 8.41
Symptomatic ¹	83.25 \pm 11.99
Asymptomatic	85.66 \pm 7.68
Medical/Surgical Co-morbidities	
Hypertension ²	88.4%
Hypercholesterolemia ²	78.0%
Coronary Artery Disease	67.1%
Peripheral Vascular Disease	36.8%
Diabetes ²	34.9%
Current Smoker ²	21.0%
Pulmonary	19.0%
Congestive Heart Failure	16.3%
Arrhythmia	13.9%
Prior CEA	5.9%
Contralateral Occlusion of ICA	8.0%
Renal Failure	8.2%
Unfavorable Anatomic Conditions	11.4%

SD Standard Deviation

¹ TIA, Stroke or Amaurosis Fugax ipsilateral to the target lesion within 180 days of the procedure² Patients recorded as Unknown / Missing were taken out of denominator.**Results**

The primary endpoint of death (all cause), stroke, and MI at 30 days was 6.1% [95% C.I.:5.4%, 6.9%]. For composite event categories in Table 29, only the most serious event for each patient and only each patient's first occurrence of each event is included. For events labeled as non-hierarchical, patients who experience multiple events are counted in each event category.

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Table 30. CAPTURE – Event Rates (≤ 30 days)

	Percent of patients with Event (N=4225)
30-Day Primary Endpoint (Death, Stroke, MI) [95% Conf. Interval] ¹	6.1% [5.4%, 6.9%]
Death, Stroke [95% Conf. Interval] ¹	5.5% [4.8%, 6.2%]
Major Stroke, Death [95% Conf. Interval] ¹	2.6% [2.2%, 3.2%]
Death ² (all cause)	1.7%
Stroke ²	4.6%
Ipsilateral Major ²	1.5%
Ipsilateral Minor ²	2.3%
Non-Ipsilateral Major ²	0.2%
Non-Ipsilateral Minor ²	0.5%
Myocardial Infarction ²	0.9%

Data are presented hierarchically, except where indicated.

¹ Clopper-Pearson exact confidence interval

² Data presented non-hierarchically (therefore where applicable, the percentage of patients in subcategories do not sum to the total percentage for that category).

All physicians participating in the CAPTURE Study completed a Physician Training Program according to their level of carotid stenting experience prior to participating in the study. Primary endpoint data is presented in Table 31 for three levels of physician experience. Level 1 includes physicians with previous clinical trial experience using the RX Acculink and RX Accunet Systems in CAS procedures. Level 2 physicians had performed at least 10 CAS procedures prior to participation in CAPTURE. Level 3 physicians were experienced in carotid angiography and peripheral stenting but had little or no CAS experience.

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Table 31. CAPTURE – Event Rates by Physician Training Level (≤ 30 days)

	Physician Level 1 (N=339 pts)	Physician Level 2 (N=2798 pts)	Physician Level 3 (N=1088 pts)
All Death, Stroke, and MI* [95% Conf. Interval] ¹	5.9% [3.6%, 9.0%]	5.9% [5.1%, 6.9%]	6.7% [5.3%, 8.4%]
Death ² [95% Conf. Interval] ¹	0.3% [0.0%, 1.6%]	1.7% [1.2%, 2.2%]	2.0% [1.3%, 3.0%]
All Stroke ² [95% Conf. Interval] ¹	5.0% [2.9%, 7.9%]	4.4% [3.7%, 5.2%]	5.1% [3.8%, 6.5%]
Myocardial Infarction ² [95% Conf. Interval] ¹	0.9% [0.2%, 2.6%]	1.0% [0.6%, 1.4%]	0.8% [0.4%, 1.6%]

* Includes only the most serious event for each patient and includes only each patient's first occurrence of each event.

¹ Clopper-Pearson exact confidence interval.

² Data presented non-hierarchically (therefore where applicable, the number of patients in subcategories do not sum to the total number for that category).

Rare adverse events are defined to be device-related events occurring at a frequency of less than 0.1%. The following rare events were reported:

- Hyperperfusion Syndrome 0.05%
- Surgery (CEA) 0.02%
- In-Stent Thrombosis 0.02%
- Dissection/Occlusion 0.02%

A step-wise multivariate logistic regression analysis was conducted on CAPTURE data to explore potential predictors for DSMI, death and stroke, and stroke only within 30 days of the procedure. Two clinical variables, age and symptomatic status and two intra-procedural variables, pre-dilation without EPD and the use of multiple stents, appear to be significantly associated with higher endpoint event rates. It is not known from these data whether performing pre-dilation without EPD and/or using multiple stents represent the cause of the adverse outcomes or are markers for certain potentially high-risk lesion characteristics.

The CAPTURE study results obtained in a commercial environment for a large high-risk patient population are consistent with the results of the ARCHeR Study. These results have also demonstrated the adequacy of the Physician Training program.

8.0 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 stent placement should use this device.

WARNING: Do not use after the “Use By” date specified on the package. Assure that the device has been properly stored in a cool, dark, dry place prior to use.

WARNING: The RX Acculink Carotid Stent System is supplied STERILE and intended for single-use only. Do not use if the package is open or damaged. Do not reuse. Do not resterilize as this can compromise device performance and increase the risk of cross-contamination due to inappropriate reprocessing.

8.1 Materials Required

- 8F guiding catheter or 6F introducer sheath compatible with the vascular anatomy. Minimum guiding catheter / sheath size inner diameter (I.D.) 0.085” / 2.2 mm. Guiding catheter or sheath should not exceed 100 cm length.
- ≥ 0.096” (2.44 mm) Rotating Hemostatic Valve (RHV) (optional). The RX Acculink Carotid Stent System is **not** recommended for use with bleedback control hemostatic valves.
- Balloon dilatation catheter (optional)
- Abbott Vascular’s Accunet or Emboshield family of Embolic Protection Systems
- 1,000 u / 500 cc heparinized normal saline (HepNS) (sterile)
- Two to three 10-20 cc syringes

CAUTION: The RX Acculink System is not compatible with any guide wire larger than 0.014” (0.36 mm).

8.2 Periprocedural Care

During the ARChER clinical studies, when possible, aspirin 325 mg b.i.d and either clopidogrel 75 mg b.i.d. or ticlopidine 250 mg b.i.d. were started 48 hours prior to the procedure. After the procedure, either ticlopidine 250 mg b.i.d. or clopidogrel 75 mg daily for two to four weeks, and aspirin 325 mg daily for one month were prescribed, followed by aspirin 325 mg daily indefinitely, per physician discretion.

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 a stenotic 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

Stent ends should be sized between the 1.1:1 and 1.4:1 stent-to-artery ratio. See Tables 32 and 33 for stent sizes and diameters and recommended reference vessel diameters for straight and tapered stents. The shortest stent length consistent with total lesion coverage is optimal. Should adequate coverage by one stent be impossible, a second Acculink Stent may be used. The second stent should have the same internal diameter as the first stent deployed. If a tapered stent is used and a second stent is necessary, the second Acculink Stent should match the diameter of the adjacent tapered stent.

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

WARNING: Appropriate sizing of the stent to the vessel is required to reduce the possibility of stent migration.

Table 32. RX Acculink Carotid Stent System - Stent Diameters

Unconstrained Stent Diameter (mm)	Stent Length (mm)	Reference Vessel Diameter (mm)
5.0	20, 30, 40	3.6 – 4.5
6.0	20, 30, 40	4.3 – 5.4
7.0	20, 30, 40	5.0 – 6.4
8.0	20, 30, 40	5.7 – 7.3
9.0	20, 30, 40	6.4 – 8.2
10.0	20, 30, 40	7.1 – 9.1

Table 33. RX Acculink Carotid Stent System – Tapered Stent Diameters

Unconstrained Stent Diameter (mm)	Stent Length (mm)	ICA Reference Vessel Diameter (mm)	CCA Reference Vessel Diameter (mm)
6 – 8 Taper	30, 40	4.3 – 5.4	5.7 – 7.3
7 – 10 Taper	30, 40	5.0 – 6.4	7.1 – 9.1

8.5 Inspection Prior To Use

1. Inspect the temperature indicator on the inner pouch.

WARNING: Do not use if the temperature indicator is black.

2. Remove the RX Acculink System from its protective packaging. Remove the handle from the package prior to removing the shaft from the hoop. Lay the device flat. The shaft may kink if not handled carefully.

CAUTION: The delivery system has an internal hypotube. Take care to avoid unnecessary handling, which may kink or damage the delivery system. Do not use if device is kinked.

CAUTION: Carefully inspect the RX Acculink Carotid Stent System to verify that the device has not been damaged in shipment. Do not use damaged equipment.

3. Ensure that the distal mandrel remains within the inner lumen. Inspect the stent through the delivery system sheath to verify that it has not been damaged during shipment and that the stent does not overlap the proximal marker. Ensure that the stent is fully covered by the sheath.

CAUTION: Special care must be taken not to handle or in any way disrupt the stent on the delivery system. This is most important during catheter removal from packaging, mandrel removal, placement over guide wire, and advancement through an RHV and guiding catheter hub.

4. Read the specifications on the handle and verify that the stent is the correct diameter and length. Ensure that the lock mechanism on the handle is in the locked position. Do not use if any defects are noted.

CAUTION: Leave the safety lock closed until the stent is ready to deploy.

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

8.6 Preparation

8.6.1 Delivery System Preparation

CAUTION: Do not expose the delivery system to organic solvents (e.g. alcohol) as structural integrity and / or function of the device may be impaired.

1. Keep the distal mandrel in the guide wire lumen.
2. Fill a 10 cc syringe with heparinized normal saline, and inject the saline into the system through the flush port at the proximal end of the housing assembly. Flush until fluid is observed exiting the guide wire exit notch first.
3. Tightly pinch the guide wire exit notch. Vigorously flush until fluid is observed exiting at both the distal end of the sheath and at the mandrel. While holding the distal tip of the delivery system, gently remove the distal mandrel by twisting and pulling as illustrated in Figure 13.

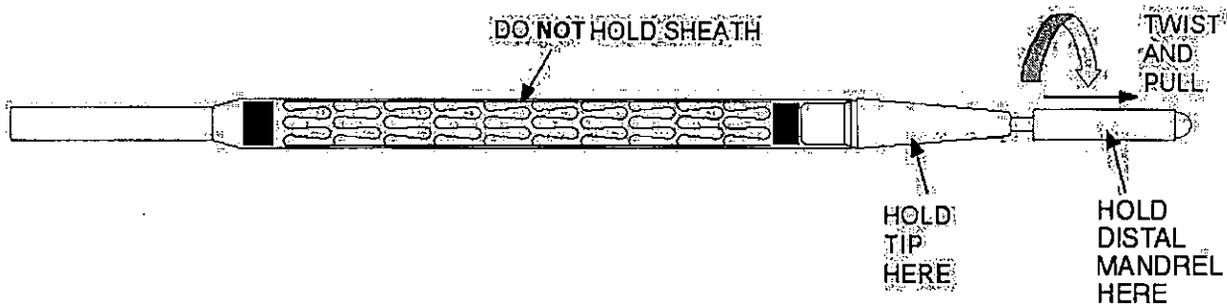
CAUTION: Do not hold the sheath or stent during mandrel removal.

CAUTION: Ensure the stent system is fully flushed with heparinized saline prior to use. Do not use the delivery system if flush is not observed exiting at the distal end of the sheath.

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4. Flush again after mandrel removal and observe fluid exiting the distal tip. If the distal mandrel does not remove easily, do not use the device.
5. Keep the device lying flat to avoid kinking in the shaft.

Figure 13. Distal Mandrel Removal



(Hold the tip to remove the distal mandrel.)

8.6.2 Embolic Protection System Preparation

The RX Acculink Carotid Stent System is indicated for use in conjunction with Abbott Vascular's AccUNET or Emboshield family of Embolic Protection Systems. Please refer to the Instructions for Use included with the embolic protection system for information on device preparation and placement.

WARNING: If a filter-based embolic protection system (EPS) is used, allow for and maintain adequate distance between the RX Acculink and the EPS to avoid potential filter engagement with the RX Acculink tip and / or filter entanglement with the deployed stent. If filter engagement and / or entanglement or filter detachment occurs, surgical conversion or additional catheter based intervention may be required.

8.6.3 Lesion Preparation

WARNING: Maintain the patient's ACT at > 250 seconds throughout RX Acculink Carotid Stent System usage to prevent thrombus formation on the device.

CAUTION: 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.

CAUTION: The RX Acculink Carotid Stent System must be used with a guiding catheter or introducer sheath to maintain adequate support of the 0.014" guide wire throughout the procedure.

CAUTION: Use with bleedback control hemostatic valves is not recommended.

CAUTION: When catheters are in the body, they should be manipulated only under fluoroscopy. Radiographic equipment that provides high quality images is needed.

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

1. If needed, pre-dilate the lesion with an appropriate size balloon dilatation catheter to a minimum opening of 2.5 mm.

WARNING: Caution should be used if pre-dilating the lesion without embolic protection as this may increase the risk of an adverse outcome.

Note: If no pre-dilatation is performed, there must be a minimum luminal opening of 2.5 mm to enable passage of the stent delivery system.

2. Maintain the guide wire position and withdraw the balloon dilatation catheter.

8.7 Delivery Procedure

1. After the pre-dilatation catheter has been removed, backload the delivery system onto the 0.014" (0.36 mm) guide wire. The guide wire will exit approximately 22 cm from the distal tip.

Note: If using a sheath with a hemostatic valve, the funnel introducer should be placed onto the RX Acculink delivery system prior to backloading onto the guide wire.

CAUTION: For best device performance, the guide wire exit notch should remain within the guiding catheter or sheath.

CAUTION: The delivery system is not designed for use with power injection. Use of power injection may adversely affect device performance.

2. Secure the guide wire and sheath position using one hand. Use the other hand to advance the delivery system over the guide wire to the lesion site. Use the radiopaque markers to locate the stent position.

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

Maintain adequate distance between the radiopaque tip of the RX Acculink and the proximal end of the EPS to avoid tip engagement with the EPS.

3. If applicable, ensure that the RHV remains OPEN and that bleedback is observed.

8.8 Stent Deployment

WARNING: 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.

CAUTION: Do not attempt to pull a partially expanded stent back through the guiding catheter or sheath; dislodgement of the stent from the delivery system may occur.

1. Place the handle on a stable surface or on the patient's leg. If using a sheath with a hemostatic valve, slide the funnel introducer forward along the shaft of the system and insert it into the valve opening.

2. Confirm the stent position angiographically.
3. Turn the safety lock counter-clockwise to the deployment position, symbolized by an open padlock icon . The arrow on the lock will point in the direction the handle will move. Ensure that the RHV remains OPEN. Remove any slack from the delivery system and reconfirm the stent position.
4. Adjust the position of the stent, if necessary. The device is designed to be deployed using one hand. Position the thumb in the textured proximal groove and place two fingers on the pullback handle as shown in Figure 14.

Ensure that the guide wire and sheath do not move during deployment. Immobilize the guide wire and RHV or sheath by holding them in place with your other hand.

CAUTION: Prior to stent deployment, remove all slack from the delivery system.

6. While pressing down with the thumb to avoid any forward motion, retract the handle to deploy the stent in the artery.

Note: If significant resistance is encountered during handle-pullback before the stent is deployed, re-lock the handle and remove the system.

7. Once the stent is deployed, re-advance the sheath by advancing the handle. Re-lock the delivery system before removal into the guiding catheter / sheath. Then remove the delivery system from the patient.
8. The stent can be post-dilated with a dilatation catheter to ensure good stent apposition and facilitate crossing with other interventional devices. Do not expand the stent past its labeled unconstrained maximum diameter.

CAUTION: When more than one stent is required to cover the lesion, or if there are multiple lesions, the distal lesion should be stented first, followed by stenting of the proximal lesion. Stenting in this order obviates the need to cross the proximal stent for placement of the distal stent, and reduces the chance of dislodging stents that have already been placed.

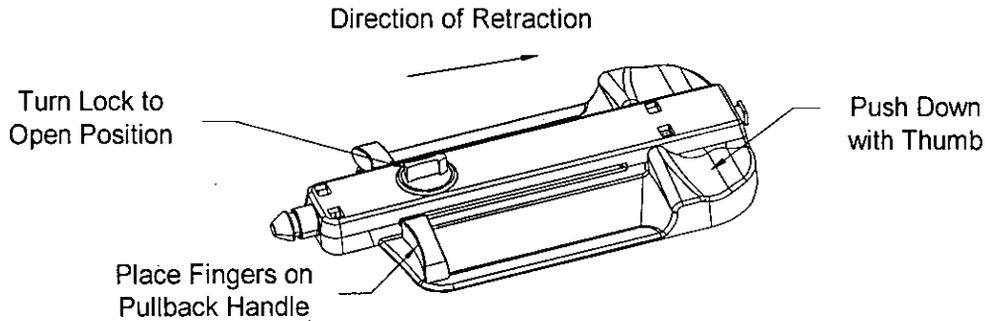
CAUTION: If overlap of sequential stents is necessary, the amount of overlap should be kept to a minimum (approximately 5 mm). In no instance, should more than 2 stents ever overlap.

CAUTION: Care must be exercised when crossing a newly deployed stent with other interventional devices to avoid disrupting the stent geometry and placement of the stent.

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

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Figure 14. Deployment Demonstration



*With the guide position fixed, deploy with one hand.
PUSH DOWN on the thumb groove and retract the pullback handle.*

8.9 Post-Stent Placement

1. Following stent placement, an angiogram should be performed to confirm vessel patency and percent stenosis remaining in the vessel lumen.

WARNING: The stent may cause a 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.

2. Upon completion of the angiogram, the embolic protection system should be removed according to the instructions for use supplied with the device.
3. Patients should be put on an appropriate regimen of anticoagulants / antiplatelets such as that described in Section 8.2.

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

WARNING: The long-term performance (> 3 years) of the Acculink Carotid Stent has not been established.

9.0 PATIENT INFORMATION

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

A Patient Guide, which includes information on carotid artery disease and the carotid stent implant procedure using embolic protection, is available from Abbott Vascular upon request. Please contact Customer Service at 1-800-227-9902 to obtain copies.

The Instructions for Use booklet is available on the Abbott Vascular website at www.abbottvascular.com/ifu/.

10.0 HOW SUPPLIED

Sterile: This device is sterilized with electron beam radiation. Non-pyrogenic.

Contents: One (1) RX Acculink Carotid Stent System, one (1) funnel introducer.

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

11.0 PATENTS AND TRADEMARKS

This product and / or its use are covered by one or more of the following United States Patents: 5,421,955; 5,421,955 B1; 5,514,154; 5,603,721; 5,728,158; 5,735,893; 5,759,192; 5,780,807; 6,056,776; 6,131,266; 6,325,824; 6,375,676; 6,468,302; 6,485,511; 6,537,311; 6,569,193; 6,582,460; 6,599,296; 6,695,862; 6,709,454. Other U.S. patents pending. Foreign patents issued and pending.

RX Acculink is a registered trademark of the Abbott Group of Companies.

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Abbott Vascular
Santa Clara, CA 95054-2087 USA

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

Graphical Symbols for Medical Device Labeling

 Manufacturer	 Sterilized using irradiation
 Catalogue number	 Inner diameter
 French size	 Outer diameter
 Guiding catheter	 Stent length
 Consult instructions for use	 Date of manufacture
 Contents (numeral represents quantity of units inside)	 Use by
 Do not reuse	 Batch code