ACCULINK™ Carotid Stent System

Information for Prescribers

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

TABLE OF CONTENTS

CAUTION:

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

1.0 DEVICE DESCRIPTION

The ACCULINK™ Carotid Stent System (ACCULINK™ System) includes a self-expanding nickel-titanium stent pre-mounted on an over-the-wire delivery system. 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 guidewire 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 and Markers

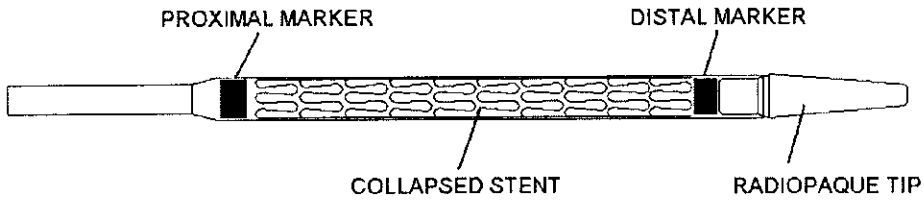


Figure 2. Handle Detail

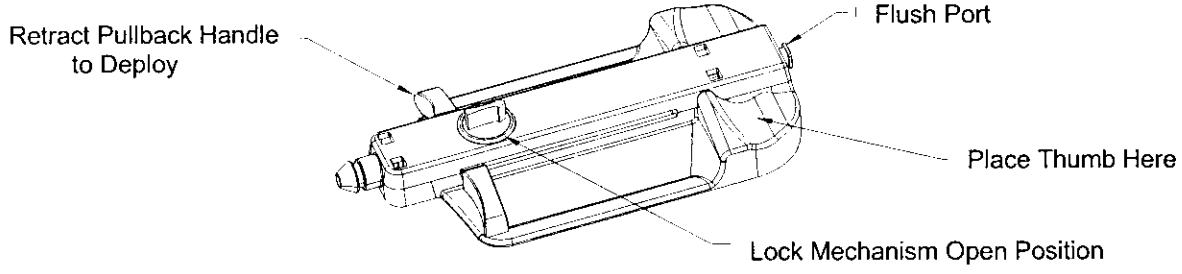
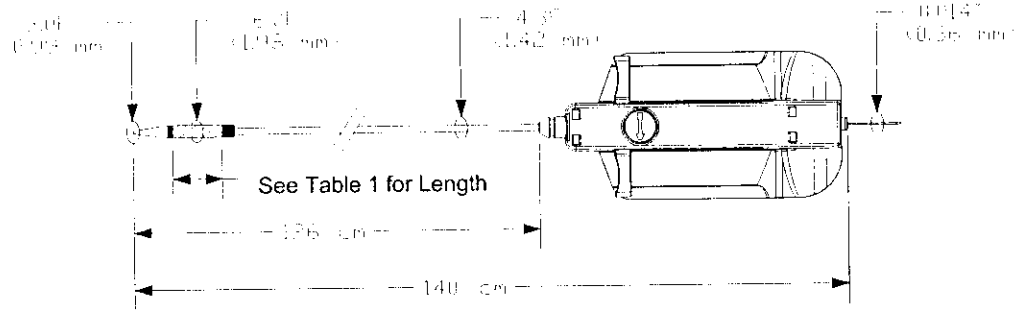


Figure 3. Delivery System Schematic



The 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 ACCULINK™ Carotid Stent System is compatible with either an 8F guiding catheter (minimum inner diameter (I.D.) 0.085" / 2.2 mm) or a 6F introducer sheath (minimum I.D. 0.085" / 2.2 mm). It is also compatible with Guidant carotid embolic protection systems.

Table 1. 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. 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 ACCULINK™ Carotid Stent System, used in conjunction with Guidant carotid embolic protection systems, is indicated for the treatment of patients at high risk for adverse events from carotid endarterectomy (See Section 7.0 of these instructions) who require carotid revascularization and meet the criteria outlined below.

1. Patients with neurological symptoms and ≥50% stenosis of the common or internal carotid artery by ultrasound or angiogram **OR** patients without neurological symptoms and ≥80% stenosis of the common or internal carotid artery by ultrasound or angiogram, **AND**

2. Patients must have a reference vessel diameter within the range of 4.0 mm and 9.0 mm at the target lesion.

3.0 CONTRAINDICATIONS

The 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 ACCULINK™ Carotid Stent System for their intended uses, contraindications, and potential complications.

The safety and efficacy of the ACCULINK™ Carotid Stent System have not been demonstrated with embolic protection systems other than the Guidant embolic protection systems.

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 ACCULINK™ Carotid Stent System have NOT yet been established in patients with the characteristics noted below.

Patient Characteristics:
- Patients at low to moderate risk for adverse events from carotid endarterectomy.
- 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 percutaneous transluminal angioplasty (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 in not possible.

- Risk of distal embolization may be higher if the 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 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.

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 is used, allow and maintain adequate distance between the filter and the stent delivery system or deployed stent to avoid potential entanglement. If filter basket entanglement or basket detachment occurs, surgical conversion or collapsing the basket with a second stent should be considered.

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 ACCULINK™ Carotid Stent System to verify that the device has not been damaged in shipment. Do not use damaged equipment.

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 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

The 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 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.

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 MRI safe 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 2.0W/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 2.0W/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-risk surgical patients and non-surgical patients with lesions in the internal carotid artery, in three separate clinical trials. A total of 581 registry 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.

Tables 3 and 4 present the adverse events reported for registry patients enrolled in each 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. Events are categorized by body system and are defined as follows:

- Non-stroke neurological includes events such as visual / speech disturbances, confusion, seizure, weakness, and TIA.
- 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.
- Access site complications include events such as bruising, hematoma, and bleeding.
- Vascular includes events such as peripheral arterial disease and deep vein thrombosis.
- Hemodynamic includes events such as hypo- and hypertension, syncope, and dizziness.
- Bleeding includes events such as non-access site bleeding, anemia up to 30 days, and GI bleed up to 30 days.
- Blood dyscrasia includes events such as anemia later than 30 days, and thrombocytopenia.
- Respiratory includes events such as pneumonia, embolism, chronic obstructive pulmonary disease (COPD), and respiratory failure.
- Gastrointestinal includes events such as nausea, ulcer, bowel obstruction, and GI bleed later than 30 days.
- Genitourinary includes events such as urinary tract infection and prostatic hyperplasia.
- Infection includes events such as laryngitis, sepsis, and endocarditis.
- Metabolic includes events such as diabetes, electrolyte imbalance, and renal failure.
- Musculoskeletal includes events such as pain, fractures, and joint replacements.

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

Table 3. Serious Adverse Events Summary, ≤ 30 days

Event Categories[1,2]	ARCHeR 2 (N=278) n	%	ARCHeR 3 (N=145) n	%	P value[3]	ARCHeR 1 (N=158) 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

[1]Patients may have had multiple events and therefore can be counted in more than one category / subcategory of event. Counts represent the number of patients who have experienced one or more events.
[2]Three of the reported adverse events were related to device failures / malfunctions. The three are described below in footnotes 5 – 7.
[3]Because 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 ARCHeR 2 and ARCHeR 3.
[4]Two 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 this table. The events are included as strokes in the composite endpoints.
[5]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.
[6]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.
[7]The 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).
[8]The 3 miscellaneous adverse events reported in the ARCHeR 1 study were bladder tumor, headache, and rash.

Table 4. Serious Adverse Events Summary, Up to 365 Days[1]

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

[1]Data >30 days for ARCHeR 3 is not available because not all subjects have completed 1-year follow-up.
[2]Patients may have had multiple events and therefore can be counted in more than one category / subcategory of event. Counts represent the number of patients who have experienced one or more events.
[3]None of the adverse events reported in the period 31 – 365 days were related to device failures / malfunctions.
[4]The 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. Cause of Death[1]

Events	ARCHeR 1		ARCHeR 2		ARCHeR 3	
	n	%	n	%	n	%
0 – 30 days[2]	**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 days[3]	**N=154**		**N=272**		**N/A[4]**	
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		

[1]None of the reported deaths were due to a device malfunction or failure.
[2]Of the deaths 0 – 30 days, 5 were considered device or procedure related: 3 strokes, 2 cardiac.
[3]Of the deaths 31 – 365 days, 1 was considered device or procedure related: 1 stroke.
[4]Data >30 days for ARCHeR 3 is not available because not all subjects have completed 1-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 ACCULINK™ Carotid Stent System should be reported immediately to Guidant Corporation, Customer Service, at (800) 227-9902. If outside the USA, call (951) 914-4669.

7.0 CLINICAL STUDIES

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 (≥50% stenosis) and asymptomatic (≥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 6.

Table 6. 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 independent neurologist and patient assessment at 24 hours, 30 days, 6 months, 12 months (every 6 months thereafter for ARCHeR 1and 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)		

[1]Attainment of final result, <50% residual stenosis covering an area no longer than the original lesion, using the ACCULINK™ System as described in the protocol.
[2]Device delivered, placed, and retrieved as described in the protocol.
[3]ACCULINK™ device / procedure success without death, emergency endarterectomy, repeat PTA / thrombolysis of the target vessel, stroke, or MI within seven days of the procedure.
[4]Data collection for the ARCHeR 3 study is not complete beyond 30 days. Secondary endpoints have not been evaluated.

[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.

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.

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

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 6, 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 (≥50% stenosis) and asymptomatic (≥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 ≥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 ≥80% by angiography, using NASCET methodology to determine degree of stenosis.

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

- 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 ≥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.
  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) FEV_1 <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 7 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 7. 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	

[1]Patients evaluated may have one or more of the evaluations listed: neurological, ultrasound, or clinical.
[2]Other 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 8. All reported angiographic data on the treated lesions are based on measurements obtained by a centralized angiographic core laboratory.

Table 8. Baseline Patient Demographics

Demographics and Medical History	ARCHeR 2 N=278	ARCHeR 3 N=145	P value[1]	ARCHeR 1 N=158
Age				
Mean ± SD	70.48± 9.38 (278)	71.13± 9.40 (145)	0.499	69.21± 9.65 (158)
Range (min, max)	(45.29, 92.67)	(38.94, 88.78)		(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 (276)	14.84± 7.82 (142)	0.707	16.17± 7.45 (157)
Range (min, max)	(0.00, 56.51)	(3.57, 43.81)		(4.72, 50.37)
Minimum Lumen Diameter (MLD, mm)				
Mean ± SD (N)	1.35± 0.56 (276)	1.21± 0.53 (142)	0.013	1.37± 0.64 (156)
Range (min, max)	(0.10, 3.57)	(0.00, 3.03)		(0.10, 3.15)
Percent Diameter Stenosis (%DS)				
Mean ± SD (N)	69.93±10.86 (276)	73.04±10.13 (142)	0.005	72.62±10.99 (156)
Range (min, max)	(31.03, 95.95)	(47.40, 100.0)		(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)

[1]Statistical 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 6 for the three studies were evaluated and categorized as either safety or efficacy endpoints.

Table 9 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 10 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 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 $p<0.05$).

[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.

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 9. ARCHeR Pivotal Trials - Safety Assessment Event Rates (≤ 30 days)

Event Categories[1]	ARCHeR 2 (N=278) n	%	ARCHeR 3 (N=145) n	%	P value[2]	ARCHeR 1 (N=158) 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
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

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

[2]Two 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.

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

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

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

[6]Three 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.

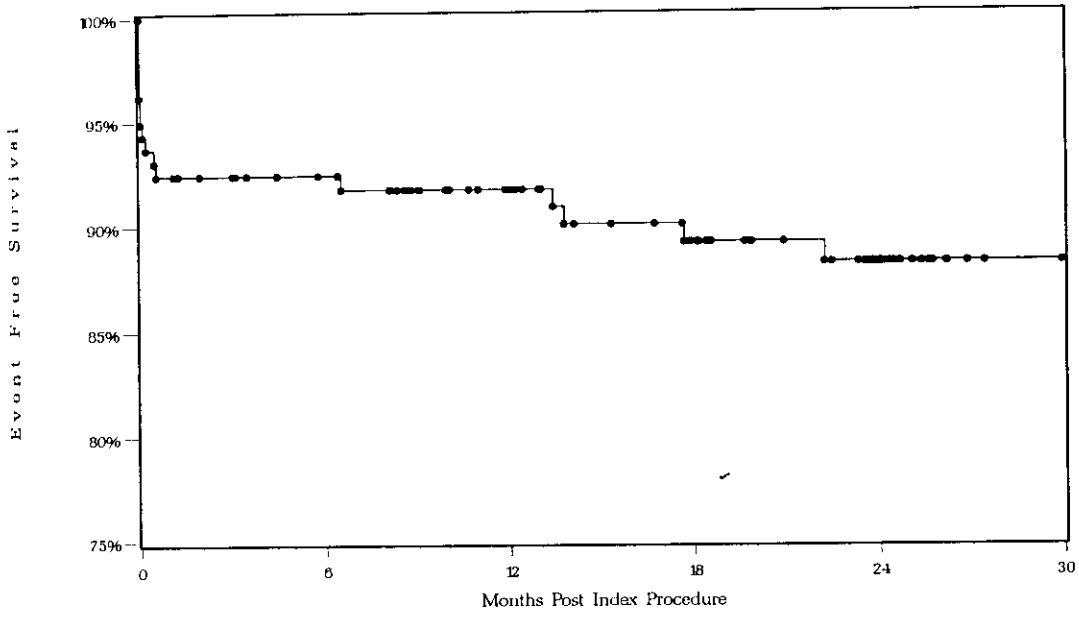
One emergent intervention in the ARCHeR 3 study resulted when the RX ACCUNET™ Filter Basket became entangled with the deployed stent and detached from the guidewire during the retrieval attempt. The physician opted to stent the basket in place in the artery. No additional adverse events related to this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

Table 10. ARCHeR Pivotal Trial Results – Efficacy Assessment Event Rates

Events	ARCHeR 2 n/N	%	ARCHeR 3 n/N	%	P value	ARCHeR 1 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

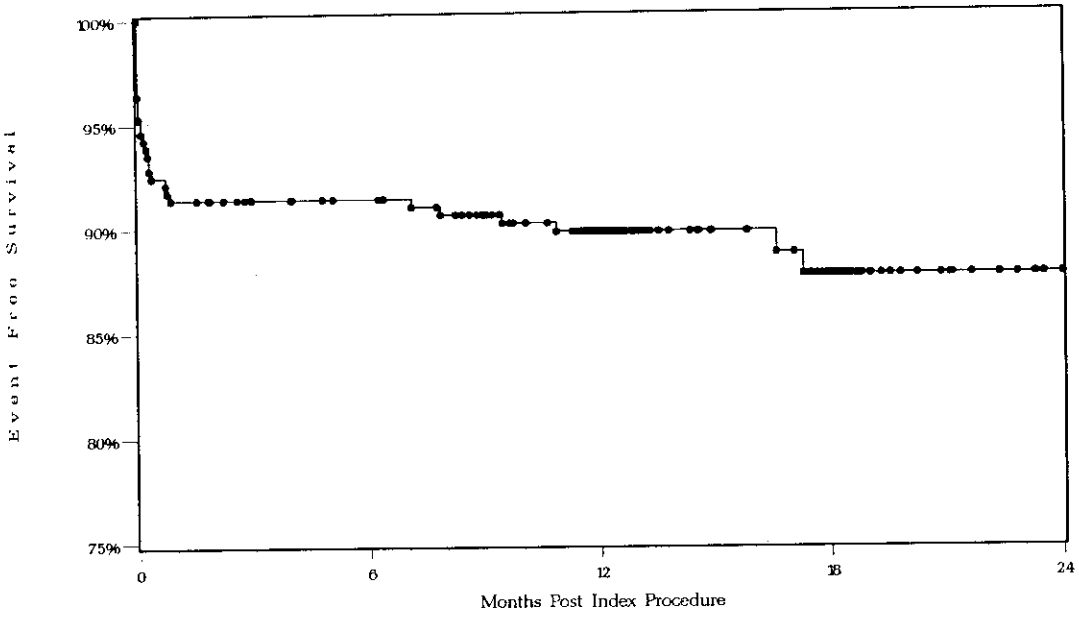
[1] Estimated via Kaplan-Meier analysis.
[2] 95% 1-sided confidence interval by normal approximation, using Peto's formula for the Kaplan Meier standard error.
[3] Device delivered, placed, and retrieved as described in protocol.
[4] Stent successfully deployed and residual stenosis < 50% following stent 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 10mm 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%

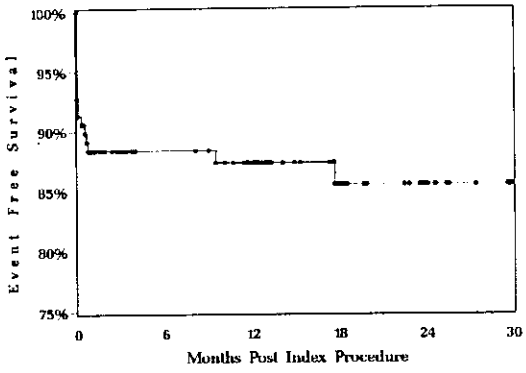
Figure 5. ARCHeR 2 Study, Freedom from composite endpoint of Stroke, Death, and MI within 30 days and Ipsilateral Stroke between days 31 and 730



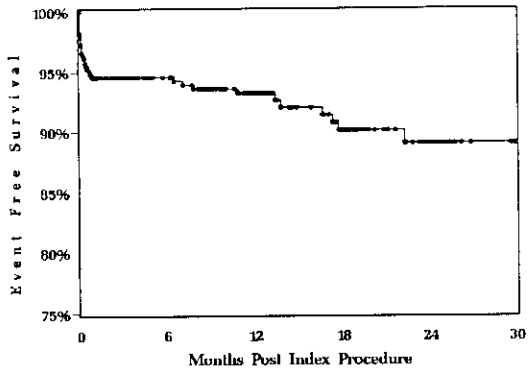
Months After Index Procedure	0	1	3	6	12	24
# At Risk	278	268	254	246	231	164
# Events	10	24	24	24	28	30
% Event Free	96.4%	91.4%	91.4%	91.4%	89.8%	87.7%

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

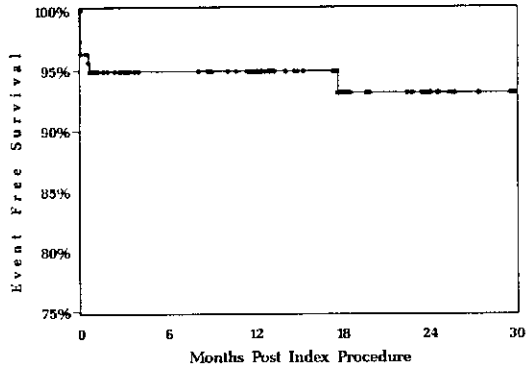
A. Symptomatic patients, freedom from composite of all Death or Stroke <30days, and Ipsilateral Stroke days 31-910



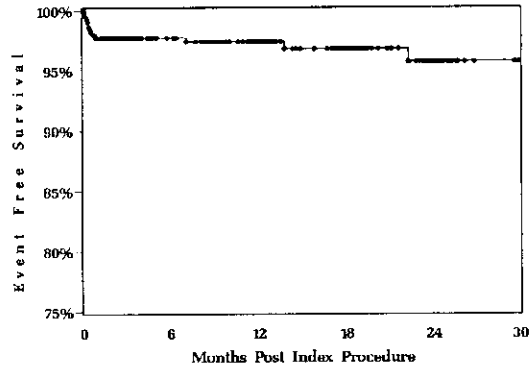
B. Asymptomatic patients, freedom from composite of all Death or Stroke <30days, and Ipsilateral Stroke days 31-910



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



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



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 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 I.D. 0.085" / 2.2 mm. Guiding catheter should not exceed 90 cm length.
- ≥ 0.096" (2.44 mm) Rotating Hemostatic Valve (RHV) (optional). This device is compatible with the Guidant COPILOT® Bleedback Control Valve. (Ensure all ancillary devices are also compatible with a bleedback control valve.).
- Balloon dilatation catheter (optional)
- Guidant carotid embolic protection system with a 0.014" guide wire (optional)
- 1,000 u/500 cc heparinized normal saline (HepNS)
- Two to three 10-20 cc syringes

CAUTION: The 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 11 and 12 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 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 11. 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 12. 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 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 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 distally near the stent.

3. While holding the distal tip of the delivery system, gently remove the distal mandrel by twisting and pulling as illustrated in Figure 7.

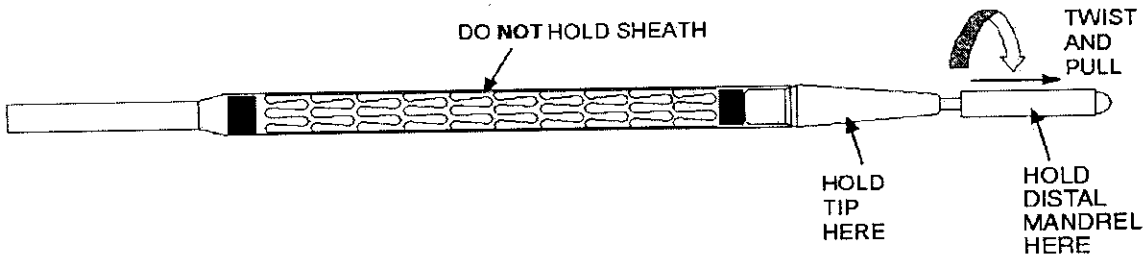
   CAUTION: Do not hold the sheath or stent during mandrel removal.

   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.

4. Continue flushing after mandrel removal. If the distal mandrel does not remove easily or flush solution is not observed exiting at the distal end of the sheath, do not use the device.

5. Keep the device lying flat to avoid kinking in the shaft.

Figure 7: Distal Mandrel Removal



(Hold the tip to remove the distal mandrel.)

8.6.2 Embolic Protection System Preparation

The ACCULINK™ Carotid Stent System is indicated for use in conjunction with a Guidant carotid embolic protection system. 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 is used, allow for and maintain adequate distance between the filter and the stent delivery system or deployed stent to avoid potential entanglement. If filter basket entanglement or basket detachment occurs, surgical conversion or collapsing the basket with a second stent should be considered.

8.6.3 Lesion Preparation

WARNING: Maintain the patient's ACT at > 250 seconds throughout 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 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: 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.

   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.

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

2. Advance the delivery system over the guide wire up to the lesion site. Use the radiopaque markers to locate the stent.

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

3. If applicable, ensure that the RHV remains OPEN and that bleedback is observed. If the Guidant COPILOT® device or sheath is used, no bleedback will be 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 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 8.

5. 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 re-advancing the handle. Relock 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.

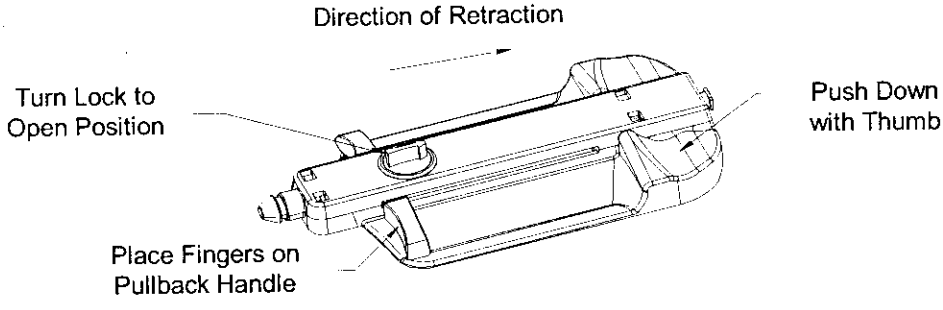
   CAUTION: When more than one stent is required to cover the lesion, or if there are multiple lesions, the distal lesion should be stented first, followed by stenting of the proximal lesion. Stenting in this order obviates the need to cross the proximal stent for placement of the distal stent, and reduces 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 5mm). 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.

Figure 8: 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 expended 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 Guidant ACCULINK™ Carotid Stent System is packaged with a Patient Implant Card for the patient that contains specific information about the Guidant 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, the carotid stent implant procedure, and the ACCULINK™ Carotid Stent System and ACCUNET™ Embolic Protection System is available from Guidant upon request. Please contact Customer Service at 1-800-227-9902 to obtain copies.

The Instructions for Use booklet is available on the Guidant website at www.guidant.com/ifu/. The Patient Guide is also available at www.guidant.com/patient/.

10.0 HOW SUPPLIED

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

Contents: One (1) ACCULINK™ Carotid Stent System.

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

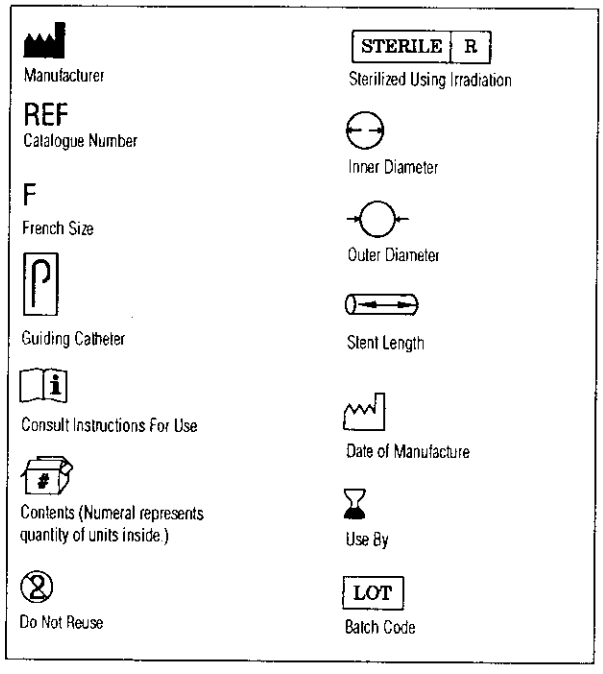
11.0 PATENTS

This product and its use are protected by one or more of the following patents: United States 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; 6131,266; 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.

Guidant Corporation
Santa Clara, CA 95054-2807 USA

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

Graphical Symbols for Medical Device Labeling



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.

Table of Contents

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™ System) 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

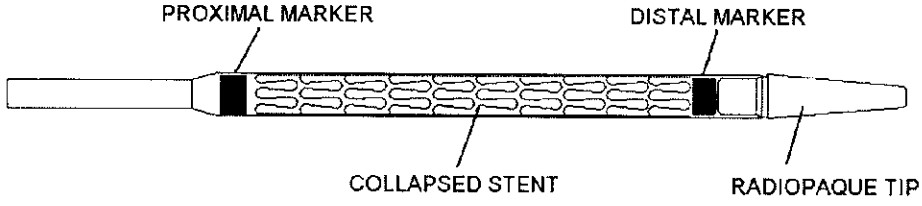


Figure 2. Handle Detail

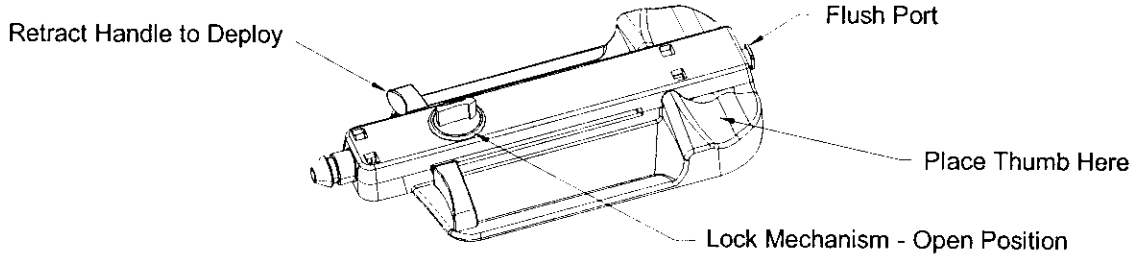
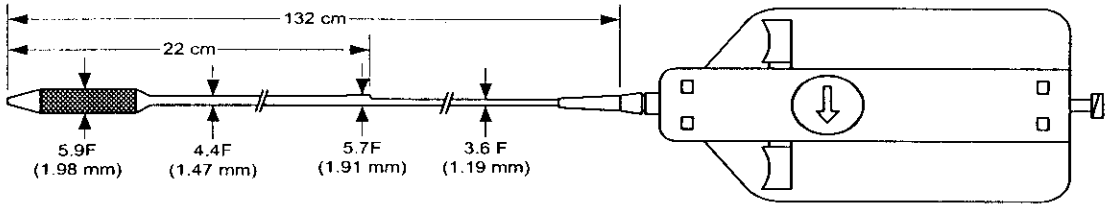


Figure 3. Delivery System Schematic



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 8F guiding catheter (min. ID 0.085" / 2.2mm) or a 6F introducer sheath (min. ID 0.085" / 2.2mm). It is also compatible with Guidant carotid embolic protection systems.

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 Guidant carotid embolic protection systems, is indicated for the treatment of patients at high risk for adverse events from carotid endarterectomy (See Section 7.0 of these instructions) who require carotid revascularization and meet the criteria outlined below.

1. Patients with neurological symptoms and ≥50% stenosis of the common or internal carotid artery by ultrasound or angiogram **OR** patients without neurological symptoms and ≥80% stenosis of the common or internal carotid artery by ultrasound or angiogram, **AND**

2. Patients must have a reference vessel diameter within the range of 4.0 mm and 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 the Guidant embolic protection systems.

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 at low to moderate risk for adverse events from carotid endarterectomy.
- 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 in 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.

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 is used, allow for and maintain adequate distance between the filter and the stent delivery system or deployed stent to avoid potential entanglement. If filter basket entanglement or basket detachment occurs, surgical conversion or collapsing the basket with a second stent should be considered.

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.

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 MRI safe 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 2.0W/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 2.0W/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-risk surgical patients and non-surgical patients with lesions in the internal carotid artery, in three separate clinical trials. A total of 581 registry 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.

Tables 3 and 4 present the adverse events reported for registry patients enrolled in each 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. Events are categorized by body system and are defined as follows:

- Non-stroke neurological includes events such as visual / speech disturbances, confusion, seizure, weakness, and TIA.
- 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.
- Access site complications include events such as bruising, hematoma, and bleeding.
- Vascular includes events such as peripheral arterial disease and deep vein thrombosis.
- Hemodynamic includes events such as hypo- and hypertension, syncope, and dizziness.
- Bleeding includes events such as non-access site bleeding, anemia up to 30 days, and GI bleed up to 30 days.
- Blood dyscrasia includes events such as anemia later than 30 days, and thrombocytopenia.
- Respiratory includes events such as pneumonia, embolism, chronic obstructive pulmonary disease (COPD), and respiratory failure.
- Gastrointestinal includes events such as nausea, ulcer, bowel obstruction, and GI bleed later than 30 days.
- Genitourinary includes events such as urinary tract infection and prostatic hyperplasia.
- Infection includes events such as laryngitis, sepsis, and endocarditis.
- Metabolic includes events such as diabetes, electrolyte imbalance, and renal failure.
- Musculoskeletal includes events such as pain, fractures, and joint replacements.

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

Table 3. Serious Adverse Events Summary, ≤ 30 days

Event Categories[1,2]	ARCHeR 2 (N=278) n	%	ARCHeR 3 (N=145) n	%	P value[3]	ARCHeR 1 (N=158) 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

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

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

[3]Because 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 ARCHeR 2 and ARCHeR 3.

[4]Two 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 this table. The events are included as strokes in the composite endpoints.

[5]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.

[6]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.

[7]The 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).

[8]The 3 miscellaneous adverse events reported in the ARCHeR 1 study were bladder tumor, headache, and rash.

Table 4. Serious Adverse Events Summary, Up to 365 Days[1]

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

[1]Data >30 days for ARCHeR 3 is not available because not all subjects have completed 1-year follow-up.
[2]Patients may have had multiple events and therefore can be counted in more than one category / subcategory of event. Counts represent the number of patients who have experienced one or more events.
[3]None of the adverse events reported in the period 31 – 365 days were related to device failures / malfunctions.
[4]The 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. Cause of Death[1]

Events	ARCHeR 1		ARCHeR 2		ARCHeR 3	
	n	%	n	%	n	%
0 – 30 days[2]	**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 days[3]	**N=154**		**N=272**		**N/A[4]**	
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		

[1]None of the reported deaths were due to a device malfunction or failure.
[2]Of the deaths 0 – 30 days, 5 were considered device or procedure related: 3 strokes, 2 cardiac.
[3]Of the deaths 31 – 365 days, 1 was considered device or procedure related: 1 stroke.
[4]Data >30 days for ARCHeR 3 is not available because not all subjects have completed 1-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 Guidant Corporation, Customer Service, at (800) 227-9902. If outside the USA, call (951) 914-4669.

7.0 CLINICAL STUDIES

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 (≥50% stenosis) and asymptomatic (≥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 6.

Table 6. 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 independent neurologist and patient assessment at 24 hours, 30 days, 6 months, 12 months (every 6 months thereafter for ARCHeR 1and 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)		

[1]Attainment of final result, <50% residual stenosis covering an area no longer than the original lesion, using the ACCULINK™ System as described in the protocol.
[2]Device delivered, placed, and retrieved as described in the protocol.
[3]ACCULINK™ device / procedure success without death, emergency endarterectomy, repeat PTA / thrombolysis of the target vessel, stroke, or MI within seven days of the procedure.
[4]Data collection for the ARCHeR 3 study is not complete beyond 30 days. Secondary endpoints have not been evaluated.

[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.

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.

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

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 6, 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 (≥50% stenosis) and asymptomatic (≥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 ≥ 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 ≥ 80% by angiography, using NASCET methodology to determine degree of stenosis.

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

- 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 ≥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.
  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) FEV_1 <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 7 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 7. 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	

[1]Patients evaluated may have one or more of the evaluations listed: neurological, ultrasound, or clinical.
[2]Other 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 8. All reported angiographic data on the treated lesions are based on measurements obtained by a centralized angiographic core laboratory.

Table 8. Baseline Patient Demographics

Demographics and Medical History	ARCHeR 2 N=278	ARCHeR 3 N=145	P value[1]	ARCHeR 1 N=158
Age				
Mean ± SD Range (min, max)	70.48± 9.38 (278) (45.29, 92.67)	71.13± 9.40 (145) (38.94, 88.78)	0.499	69.21± 9.65 (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) Range (min, max)	14.55± 7.14 (276) (0.00, 56.51)	14.84± 7.82 (142) (3.57, 43.81)	0.707	16.17± 7.45 (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)

[1]Statistical 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 6 for the three studies were evaluated and categorized as either safety or efficacy endpoints.

Table 9 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 10 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 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.

---

[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.

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 9. 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
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

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

[2]Two 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.

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

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

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

[6]Three 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.

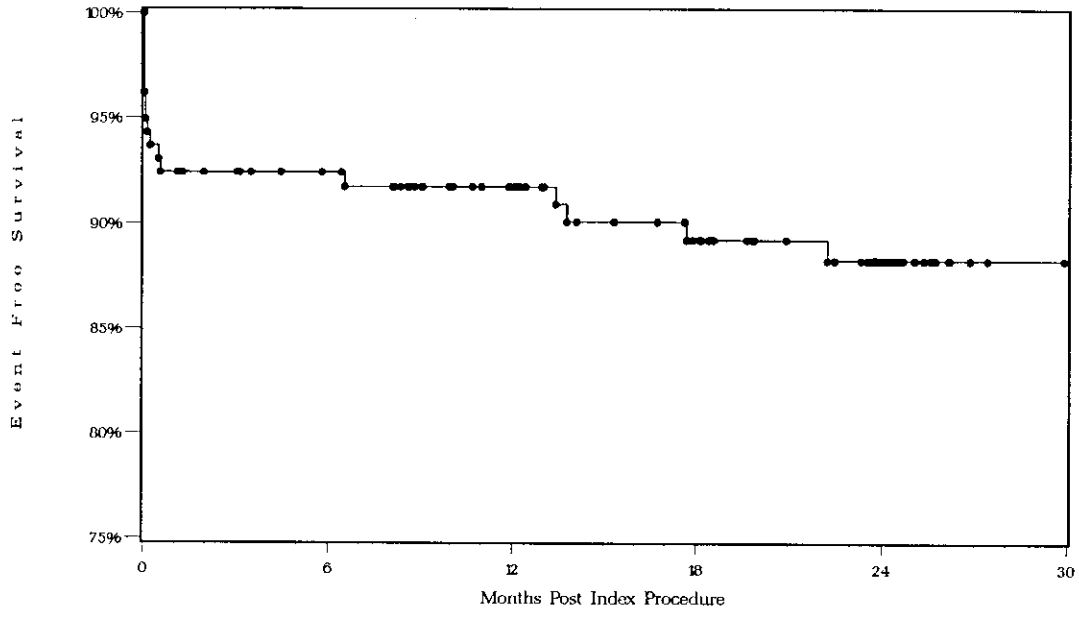
One emergent intervention in the ARCHeR 3 study resulted when the RX ACCUNET™ Filter Basket became entangled with the deployed stent and detached from the guidewire during the retrieval attempt. The physician opted to stent the basket in place in the artery. No additional adverse events related to this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

Table 10. ARCHeR Pivotal Trial Results – Efficacy Assessment Event Rates

Events	ARCHeR 2 n/N	%	ARCHeR 3 n/N	%	P value	ARCHeR 1 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

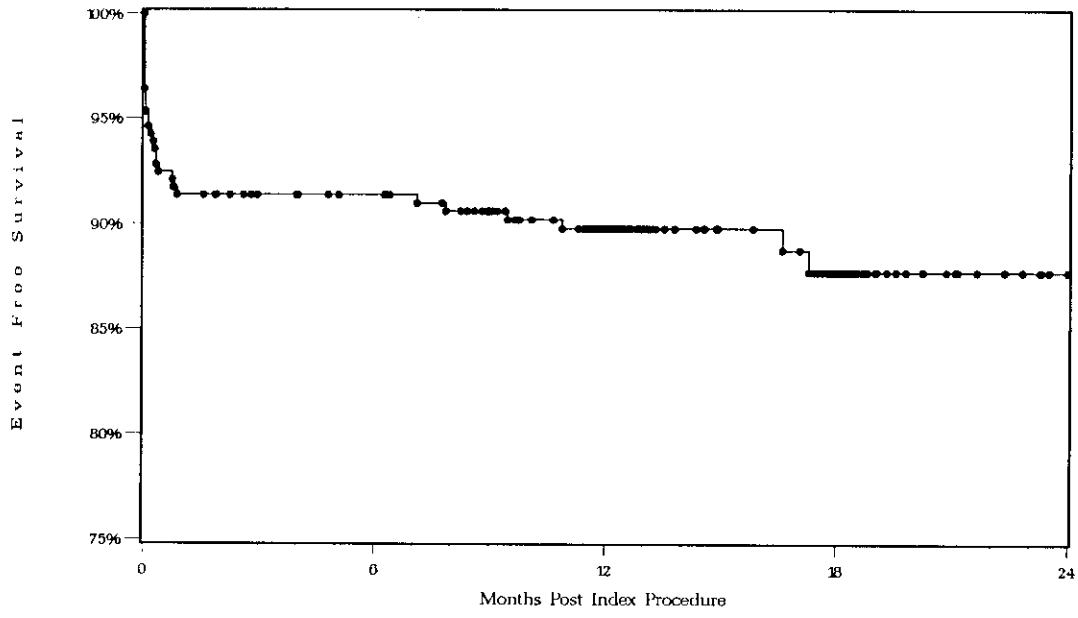
[1] Estimated via Kaplan-Meier analysis.
[2] 95% 1-sided confidence interval by normal approximation, using Peto's formula for the Kaplan Meier standard error.
[3] Device delivered, placed, and retrieved as described in protocol.
[4] Stent successfully deployed and residual stenosis < 50% following stent 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 10mm 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%

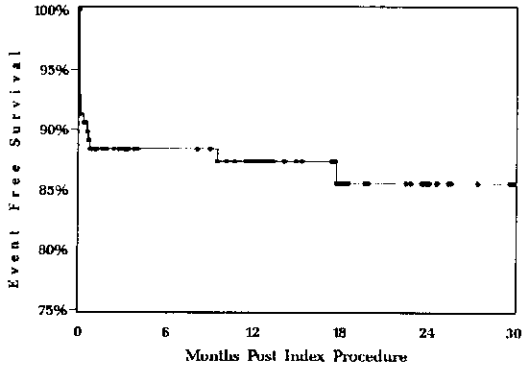
Figure 5. ARCHeR 2 Study, Freedom from composite endpoint of Stroke, Death, and MI within 30 days and Ipsilateral Stroke between days 31 and 730



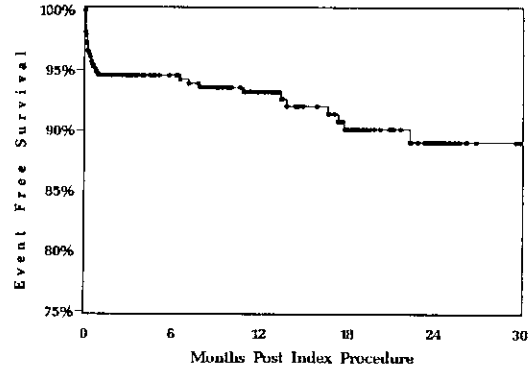
Months After Index Procedure	0	1	3	6	12	24
# At Risk	278	268	254	246	231	164
# Events	10	24	24	24	28	30
% Event Free	96.4%	91.4%	91.4%	91.4%	89.8%	87.7%

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

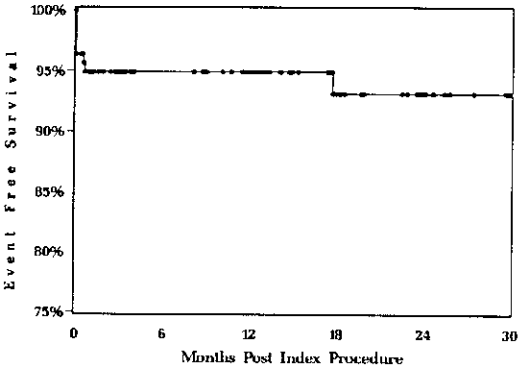
A. Symptomatic patients, freedom from composite of all Death or Stroke <30days, and Ipsilateral Stroke days 31-910



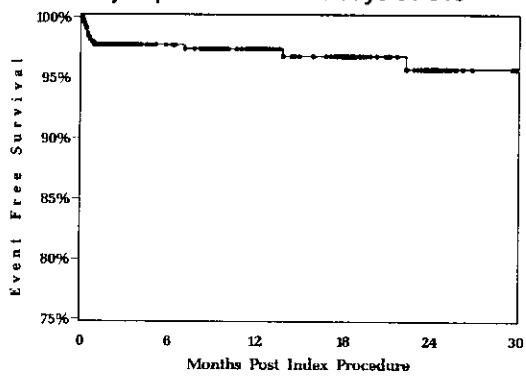
B. Asymptomatic patients, freedom from composite of all Death or Stroke <30days, and Ipsilateral Stroke days 31-910



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



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



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)
- Guidant carotid embolic protection system with a 0.014" guide wire
- 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 11 and 12 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 11. 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 12. 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 7.

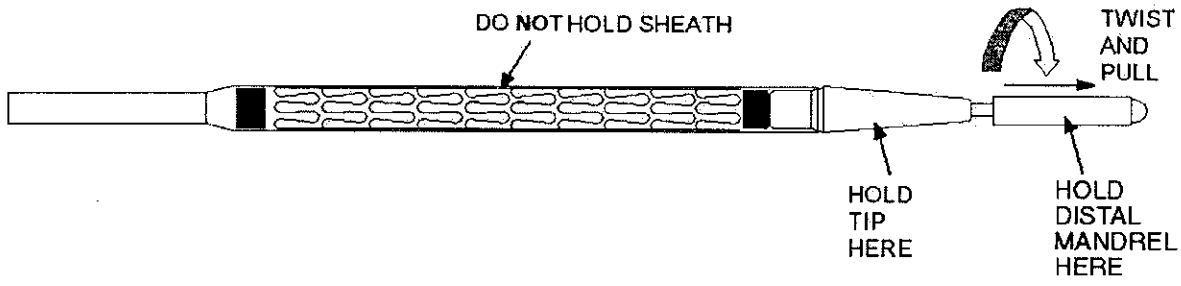
   CAUTION: Do not hold the sheath or stent during mandrel removal.

   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.

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 7: 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 a Guidant carotid embolic protection system. 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 is used, allow for and maintain adequate distance between the filter and the stent delivery system or deployed stent to avoid potential entanglement. If filter basket entanglement or basket detachment occurs, surgical conversion or collapsing the basket with a second stent should be considered.

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.

   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.

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 8.

   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.

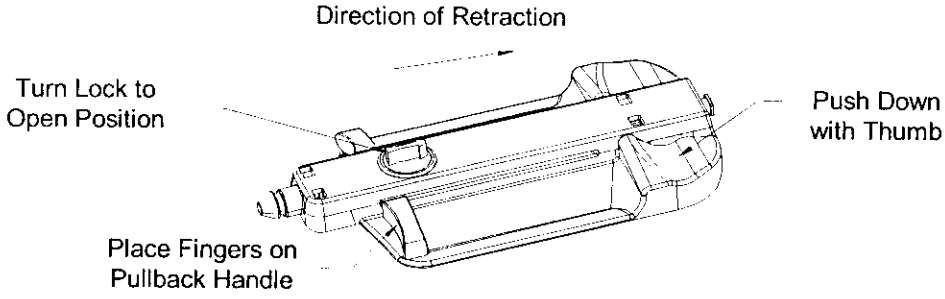
   CAUTION: When more than one stent is required to cover the lesion, or if there are multiple lesions, the distal lesion should be stented first, followed by stenting of the proximal lesion. Stenting in this order obviates the need to cross the proximal stent for placement of the distal stent, and reduces 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 5mm). 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.

Figure 8: 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 Guidant RX ACCULINK™ Carotid Stent System is packaged with a Patient Implant Card for the patient that contains specific information about the Guidant 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 Guidant upon request. Please contact Customer Service at 1-800-227-9902 to obtain copies.

The Instructions for Use booklet is available on the Guidant website at www.guidant.com/ifu/. The Patient Guide is also available at www.guidant.com/patient/.

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

This product and its use are protected by one or more of the following patents: United States 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.

Guidant Corporation
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