Anthem

# Clinical UM Guideline

**Subject:** Carotid, Vertebral and Intracranial Artery Stent Placement with or without Angioplasty
**Guideline #:** CG-SURG-76
**Status:** Reviewed
**Publish Date:** 09/27/2023
**Last Review Date:** 08/10/2023

## Description

This document addresses extracranial (cervical) carotid, vertebral and intracranial artery stent placement with or without angioplasty. Extracranial carotid artery angioplasty with stenting (CAS) or without stenting has been investigated as a minimally invasive alternative to the current standard of care, that being carotid endarterectomy (CEA). CAS can be performed percutaneously (that is, passage of a balloon catheter into the lesion via a femoral or brachial artery, followed by dilatation of the blocked segment and stent placement) or through a small incision in the neck (that is, transcarotid artery revascularization [TCAR]). TCAR employs a flow reversal system to provide continuous embolic protection throughout the CAS procedure for extracranial carotid artery stenosis. Similarly, angioplasty and stenting has been investigated as an alternative treatment for individuals with symptomatic intracranial artery and extracranial vertebrobasilar artery stenosis, since these conditions portend a poor prognosis even with medical therapy, and surgical intervention is associated with considerable morbidity.

## Clinical Indications

**Medically Necessary:**

**Extracranial Stent Placement with or without Angioplasty:**

Extracranial carotid artery stent placement with or without angioplasty is considered **medically necessary** for individuals who meet EITHER A or B of the following criteria **and** can be safely treated by this approach **and** who have no angiographically visible intraluminal thrombus:

A. Symptomatic stenosis equal to or greater than 50%, **or** asymptomatic stenosis equal to or greater than 80%; **and**
   **One or more** of the following conditions which put the individual at a high risk or unsuitable for surgery:
   1. Congestive heart failure (NYHA Class III/IV) or left ventricular ejection fraction less than 30%; **or**
   2. Open heart surgery needed within the next 6 weeks; **or**
   3. Recent myocardial infarction (greater than 24 hours and less than 4 weeks); **or**
   4. Severe chronic obstructive pulmonary disease; **or**
   5. Unstable angina (CCS class III/IV); **or**
   6. Inability to move the neck to a suitable position for surgery; **or**
   7. Tracheostomy.

   **or**
B. Symptomatic stenosis equal to or greater than 50%, **or** asymptomatic stenosis equal to or greater than 80%; **and**
   **One or more** of the following conditions:
   1. Contralateral laryngeal nerve palsy; **or**
   2. Existence of lesions distal or proximal to the carotid bulb and bifurcation of the common carotid; **or**
   3. Pseudoaneurysm; **or**
   4. Radiation-induced stenosis following previous radiation therapy to the neck or radical neck dissection; **or**
   5. Restenosis after carotid endarterectomy (CEA); **or**
   6. Severe tandem lesions that may require endovascular therapy; **or**
   7. Stenosis secondary to arterial dissection; **or**
   8. Stenosis secondary to fibromuscular dysplasia; **or**
   9. Stenosis secondary to Takayasu arteritis; **or**
   10. Stenosis that is surgically difficult to access (for example, high bifurcation requiring mandibular dislocation); **or**
   11. Stenosis associated with contralateral carotid artery occlusion; **or**
   12. Inability to move the neck to a suitable position for surgery; **or**
   13. Tracheostomy.

*Note:* If, in exceptional circumstances, extracranial carotid artery angioplasty is performed without stent placement, the above medically necessary criteria must still be met.

**Intracranial Stent with or without Angioplasty:**

Percutaneous intracranial artery stent placement with or without angioplasty is considered **medically necessary** as part of the treatment of individuals with an intracranial aneurysm when **ALL** of the following criteria are met:

A. Surgical treatment is not appropriate or attempted surgery was unsuccessful; **and**
B. Standard endovascular techniques (coiling) are inadequate to achieve complete isolation of the aneurysm because of anatomic considerations which include, but are not limited to:
   1. wide-neck aneurysm (4 mm or more); **or**
   2. sack-to-neck ratio less than 2:1.

**Not Medically Necessary:**

Carotid artery angioplasty and stent placement (CAS) is considered **not medically necessary** when the above criteria are not met, including but not limited to, the following conditions:

A. Complete occlusion (100% stenosis) of the relevant carotid artery; **or**
B. Severe symptomatic carotid stenosis in individuals not meeting the criteria above; **or**
C. Symptomatic stenosis less than 50% of the relevant carotid artery; **or**
D. Asymptomatic stenosis less than 80% of the relevant carotid artery; **or**
E. Carotid stenosis with angiographically visible intraluminal thrombus; **or**
F. A stenosis that cannot be safely reached or crossed by endovascular approach.

Percutaneous stent placement with or without associated percutaneous angioplasty is considered**not medically necessary** when used in the treatment of stenosis of:

A. Vertebral arteries; **or**
B. Intracranial arteries.

Percutaneous stent placement with or without associated percutaneous angioplasty is considered**not medically necessary** when used in the treatment of aneurysm of:

A. Vertebral arteries; **or**
B. Intracranial arteries, except when the criteria above are met.

Percutaneous angioplasty of the intracranial arteries when performed without associated stent placement is considered**not medically necessary.**

## Coding

*The following codes for treatments and procedures applicable to this guideline are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.*

*Extracranial*
**When services may be Medically Necessary when criteria are met:**

| | |
|---|---|
| **CPT** | |
| 37246 | Transluminal balloon angioplasty (except lower extremity artery(ies) for occlusive disease, intracranial, coronary, pulmonary, or dialysis circuit), open or percutaneous, including all imaging and radiological supervision and interpretation necessary to perform the angioplasty within the same artery; initial artery [when specified as angioplasty of cervical carotid artery] |
| 37215 | Transcatheter placement of intravascular stent(s), cervical carotid artery, open or percutaneous, including angioplasty, when performed, and radiological supervision and interpretation; with distal embolic protection |
| 37216 | Transcatheter placement of intravascular stent(s), cervical carotid artery, open or percutaneous, including angioplasty, when performed, and radiological supervision and interpretation; without distal embolic protection |
| **ICD-10 Procedure** | |
| 037H04Z-037N44Z | Dilation of carotid artery with drug-eluting intraluminal device [right or left, common, internal or external, by open, percutaneous or percutaneous endoscopic approach; includes codes 037H04Z, 037H34Z , 037H44Z, 037J04Z, 037J34Z, 037J44Z, 037K04Z, 037K34Z, 037K44Z, 037L04Z, 037L34Z, 037L44Z, 037M04Z, 037M34Z, 037M44Z, 037N04Z, 037N34Z, 037N44Z] |
| 037H0DZ-037N4DZ | Dilation of carotid artery with intraluminal device [right or left, common, internal or external, by open, percutaneous or percutaneous endoscopic approach; includes codes 037H0DZ, 037H3DZ, 037H4DZ, 037J0DZ, 037J3DZ, 037J4DZ, 037K0DZ, 037K3DZ, 037K4DZ, 037L0DZ, 037L3DZ, 037L4DZ, 037M0DZ, 037M3DZ, 037M4DZ, 037N0DZ, 037N3DZ, 037N4DZ] |
| 037H0ZZ-037N4ZZ | Dilation of carotid artery [right or left, common, internal or external, by open, percutaneous or percutaneous endoscopic approach; includes codes 037H0ZZ, 037H3ZZ, 037H4ZZ, 037J0ZZ, 037J3ZZ, 037J4ZZ, 037K0ZZ, 037K3ZZ, 037K4ZZ, 037L0ZZ, 037L3ZZ, 037L4ZZ, 037M0ZZ, 037M3ZZ, 037M4ZZ, 037N0ZZ, 037N3ZZ, 037N4ZZ] |
| **ICD-10 Diagnosis** | |
| I63.031-I63.039 | Cerebral infarction due to thrombosis of carotid artery |
| I63.131-I63.139 | Cerebral infarction due to embolism of carotid artery |
| I63.231-I63.239 | Cerebral infarction due to unspecified occlusion or stenosis of carotid arteries |
| I65.21-I65.29 | Occlusion and stenosis of carotid artery |
| I72.0 | Aneurysm of carotid artery (common) (external) (internal, extracranial portion) |
| I77.3 | Arterial fibromuscular dysplasia (fibromuscular hyperplasia of carotid artery) |
| Z93.0 | Tracheostomy status |

**When services are Not Medically Necessary:**
For the procedure codes listed above when criteria are not met or for all other diagnoses not listed; or when the code describes a procedure or situation designated in the Clinical Indications section as not medically necessary.

**When services are also Not Medically Necessary:**

| | |
|---|---|
| **CPT** | |
| 0075T | Transcatheter placement of extracranial vertebral artery stent(s), including radiologic supervision and interpretation, open or percutaneous; initial vessel |
| 0076T | Transcatheter placement of extracranial vertebral artery stent(s); including radiologic supervision and interpretation, open or percutaneous; each additional vessel |
| **ICD-10 Procedure** | |
| 037P34Z-037Q44Z | Dilation of vertebral artery with drug-eluting intraluminal device [right or left, by percutaneous or percutaneous endoscopic approach; includes codes 037P34Z, 037P44Z, 037Q34Z, 037Q44Z] |
| 037P3DZ-037Q4DZ | Dilation of vertebral artery with intraluminal device [right or left, by percutaneous or percutaneous endoscopic approach; includes codes 037P3DZ, 037P4DZ, 037Q3DZ, 037Q4DZ] |
| 037P3ZZ-037Q4ZZ | Dilation of vertebral artery [right or left, by percutaneous or percutaneous endoscopic approach; includes codes 037P3ZZ , 037P4ZZ, 037Q3ZZ, 037Q4ZZ] |
| **ICD-10 Diagnosis** | |
| | All diagnoses |

*Intracranial*
**When services may be Medically Necessary when criteria are met:**

| | |
|---|---|
| **CPT** | |
| 61635 | Transcatheter placement of intravascular stent(s), intracranial (eg, atherosclerotic stenosis), including balloon angioplasty, if performed |
| **ICD-10 Procedure** | |
| 037G34Z-037G44Z | Dilation of intracranial artery with drug-eluting intraluminal device [by approach, includes codes 037G34Z, 037G44Z] |
| 037G3DZ-037G4DZ | Dilation of intracranial artery with intraluminal device [by approach; includes codes 037G3DZ, 037G4DZ] |
| **ICD-10 Diagnosis** | |
| I60.00-I60.9 | Nontraumatic subarachnoid hemorrhage [ruptured cerebral aneurysm] |
| I67.1 | Cerebral aneurysm, nonruptured |
| Q28.2 | Arteriovenous malformation of cerebral vessels |
| Q28.3 | Other malformations of cerebral vessels |

**When services are Not Medically Necessary:**
For the procedure codes listed above when criteria are not met or for all other diagnoses not listed; or when the code describes a procedure or situation designated in the Clinical Indications section as not medically necessary.

**When services are also Not Medically Necessary:**
For the following procedure codes; or when the code describes a procedure designated in the Clinical Indications section as not medically necessary.

| | |
|---|---|
| **CPT** | |
| 61630 | Balloon angioplasty, intracranial (eg, atherosclerotic stenosis), percutaneous |
| 61640 | Balloon dilatation of intracranial vasospasm, percutaneous; initial vessel |
| 61641 | Balloon dilatation of intracranial vasospasm, percutaneous; each additional vessel in same vascular family |
| 61642 | Balloon dilatation of intracranial vasospasm, percutaneous; each additional vessel in different vascular family |
| **ICD-10 Procedure** | |
| 037G3ZZ | Dilation of intracranial artery, percutaneous approach |
| 037G4ZZ | Dilation of intracranial artery, percutaneous endoscopic approach |
| **ICD-10 Diagnosis** | |
| | All diagnoses |

## Discussion/General Information

**Extracranial Carotid Artery Angioplasty with Stent Placement (CAS) for Treatment of Atherosclerotic Stenosis of the Extracranial Carotid Arteries:**

Currently, carotid endarterectomy (CEA) is considered the established “gold standard” procedure for individuals with symptomatic and significant carotid artery stenosis. However, this is an invasive procedure associated with well-defined, (albeit acceptable) complications including the possibility of nerve injuries. A percutaneous endovascular approach to carotid artery lesions has been attractive, particularly since this technique has been applied successfully in other areas of the vascular tree including the coronary and lower limb circulation. However, unlike coronary or iliac angioplasty, occlusion of the carotid artery may not be amenable to emergency surgical correction. Serious embolic complications including stroke and death remain an issue.

The majority of published data represent prospective uncontrolled studies with a number of variables including candidate selection criteria, type of stent used, and use or non-use of an embolic protection device. Initial studies reported higher complication rates for stroke and/or death than with CEA (10-12% for CAS versus 5.8% for CEA). More recent studies, however, including two randomized studies, suggest similar major complication rates for the two procedures, together with similar restenosis rates. However, the two randomized studies were performed at a single institution by a particularly experienced operator and consisted of relatively small sample sizes. Also, in other studies, issues related to candidate selection, inconsistent use of stents and protection devices and short follow-up indicate the need for further larger scale, longer term, randomized, controlled studies comparing CAS with CEA to determine the relative efficacy and complication rates of these procedures. The multi-center Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) randomized 504 mostly symptomatic subjects with 70% carotid artery stenosis to receive endovascular treatment or CEA. There was no difference in the rates of death or stroke at 30 days, and 3-year follow-up showed no difference in the rate of stroke. This trial has been criticized, however, because the rate of stroke or death was higher than that reported in other randomized trials of CEA. Also, residual restenosis was more frequent with the endovascular approach than CEA (14% versus 4% respectively). However, it should be noted that only 22% of participants in this trial received stents. Two earlier randomized trials of carotid stenting were stopped early because of inferior outcomes, which were thought to be related to earlier stent designs and inexperience with the technique.

Brown, the principal investigator of CAVATAS and CAVATAS-2 (an ongoing international study), in an editorial in the American Journal of Medicine (2004) wrote, “There is, therefore, a need for further randomized trials of CAS with protection devices compared with CEA to establish convincingly the value of CAS.” Brown further stated:

> Although the early results of CAS with protection devices appear encouraging, there are no long term data to rival that available from the carotid surgical trials. Hence, caution argues that stenting should continue to be seen as an experimental procedure and carried out only in the context of randomized clinical trials.

Currently, there are multi-center, randomized, controlled studies in progress in Europe and the United States. Results of two trials, the SPACE trial (Stent Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy) and the EVA-3S trial (Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis) are now available. The SPACE trial was a randomized non-inferiority trial that provided outcomes data at 30 days, which failed to prove the non-inferiority of CAS, compared to conventional CEA. However, the authors state that the results do not justify widespread use in the short term of CAS, and outcomes at 6-24 months are awaited (Ringleb, 2006). Published results of the EVA-3S trial reported finding that, for symptomatic subjects with carotid stenosis of 60% or more, the rates of death and stroke at 30 days and 6 months following surgery were lower for CEA, compared with CAS (Mas, 2006).

Four-year follow-up results of the EVA-3S trial found that the safety of stenting needs to be improved for individuals with symptomatic

carotid stenosis. This multicenter, randomized trial compared the safety of CAS with CEA. Participants were eligible for the EVA-3S study if they were 18 years or older, had a transient ischemic attack (TIA) or a nondisabling stroke (or retinal infarct) within 120 days before enrollment, and had an atherosclerotic stenosis of 60% to 99% of the symptomatic carotid artery. The study enrolled 527 subjects who were randomly assigned to undergo CEA (n=262) or CAS (n=265). The primary endpoint was the rate of any periprocedural stroke or death within 30 days postprocedure; the EVA-3S trial was terminated early because of a higher 30-day risk of stroke or death in the CAS group. The main secondary endpoint was a composite of any periprocedural stroke or death and any nonprocedural ipsilateral stroke during 4 years of follow-up.

Results of the 4 years of follow-up of the EVA-3S data found the cumulative probability of periprocedural stroke or death and nonprocedural ipsilateral stroke was higher with CAS than with CEA (11.1% versus 6.2%; hazard ratio [HR], 1.97; 95% confidence interval [CI], 1.06 to 3.67; p=0.03). The HR for any periprocedural disabling stroke or death or any nonprocedural fatal or disabling ipsilateral stroke was 2.00 (CI, 0.75 to 5.33; p=0.17). A hazard function analysis showed the 4-year differences in the cumulative probabilities of outcomes between stenting and CEA were largely accounted for by the higher periprocedural (within 30 days of the procedure) risk of stenting compared with CEA. After the periprocedural period, the risk of ipsilateral stroke was low and similar in both treatment groups. The authors concluded that for individuals with symptomatic carotid stenosis, CAS is not as safe an alternative as CEA, although CAS is as effective as CEA for prevention of middle-term ipsilateral stroke (Mas, 2008).

Yadav and colleagues reported on results of the SAPPHIRE trial (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) in October 2004. This trial included 334 participants classified as “high risk,” based on the presence of neurological symptoms and a greater than 50% stenosis of the common or internal carotid artery or who were asymptomatic with greater than 80% stenosis, who were randomized to CEA or CAS. Of the 167 subjects randomly assigned to stenting, 159 received the assigned treatment. Of the 167 assigned to surgery, 151 received the assigned treatment. All participants also had one or more medical or surgical comorbid conditions that placed them at high risk for CEA. Exclusion criteria for the trial included history of a bleeding disorder, along with other criteria. The technique employed the Cordis Corporation’s PRECISE™ Nitinol Stent System with the ANGIOGUARD™ Embolic Capture Guide-wire System. At 1 year, superior results were reported for the CAS group, measured by a composite endpoint of major adverse events including all-cause death, stroke, and myocardial infarction (12% for CAS vs. 20% for CEA). The authors concluded that among individuals with severe carotid artery stenosis and coexisting conditions, CAS with the use of an embolic-protection device is not inferior to CEA. Additional information on results of the SAPPHIRE trial were subsequently reported which indicated that, among subjects at high surgical risk, CAS was associated with less health status impairment during the initial 2-week post-surgical recovery period than CEA-treated subjects. However, these differences in quality of life measures resolved by 1 month post-procedures, and no other differences between the two treatment groups in health-related quality of life were noted (Stolker, 2010).

Most authors currently writing in the literature are of the opinion that CEA, a proven effective long-term surgical approach, remains the gold standard of interventional care, and they do not advocate the widespread practice of CAS with stenting as an alternative, at this time, particularly in those who are not at high risk for CEA. This includes the short-term results of a multicenter, open, randomized, controlled trial, the International Carotid Stenting Study (ICSS), which enrolled only symptomatic subjects within 1 year and carotid artery stenosis of 50% or greater; 853 participants were randomized to CAS and 857 to CEA. Randomization procedures effectively concealed allocation to investigators; study subjects were unblinded, and embolic protection devices were recommended, but not required. The investigators acknowledged that the follow-up data was insufficient to examine the primary endpoint, that is, 3-year rates of fatal or disabling stroke; only the 30-day morbidity, as reflected by stroke, death, or myocardial infarction (a secondary endpoint) was reported. In per-protocol analyses, the 30-day stroke and death rate was 3.4% and 7.4% following CEA and CAS, respectively. While 30-day stroke and death rates were not specifically reported in an intention-to-treat analysis, the corresponding estimated rates were 3.4% and 6.8%. There were few periprocedural myocardial infarctions (MIs)—3 in the stenting arm (0.4%) and 5 following CEA (0.6%). These preliminary ICSS results are noted to be consistent with two previously reported large randomized controlled trials enrolling similar symptomatic subjects (SPACE, EVA-3S). The authors also noted that within the ICSS results, CAS was not performed with periprocedural (30-day) stroke and death rates sufficiently low (that is, less than 6%) to achieve a net clinical benefit and CAS was inferior to CEA (Ederle, 2010).

Preliminary results were published for the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST), which is a large, ongoing, randomized, controlled trial with blinded endpoint adjudication, sponsored by the National Institute of Neurological Disorders and Stroke (NINDS) and the National Institutes of Health (NIH). The primary aim is to compare the outcomes of CAS with those of CEA among subjects with symptomatic or asymptomatic extracranial carotid stenosis. Trial participants were considered to be symptomatic if they had had a TIA, amaurosis fugax, or minor nondisabling stroke involving the study carotid artery within 180 days before randomization. Eligibility criteria were stenosis of 50% or more on angiography, 70% or more on ultrasonography, or 70% or more on computed tomographic angiography (CTA) or magnetic resonance angiography (MRA) if the stenosis on ultrasonography was 50 to 69%. Eligibility was extended in 2005 to include asymptomatic subjects, for whom the criteria were stenosis of 60% or more on angiography, 70% or more on ultrasonography, or 80% or more on CTA or MRA if the stenosis on ultrasonography was 50 to 69%. Subjects were excluded if they had had a previous stroke that was sufficiently severe to confound the assessment of endpoints. Trial participants from 108 centers in the U.S. and Canada included 2502 subjects over a median follow-up period of 2.5 years. Total numbers were 1262 received CAS, and 1240 underwent CEA. Participants were not randomly assigned to a treatment group until the operators performing both the CAS and CEA procedures had been certified, which included 224 interventionalists who were certified after satisfactory evaluation of their endovascular experience, CAS results, and participation in both hands-on training and a lead-in phase of training.

Preliminary results among subjects with symptomatic or asymptomatic carotid stenosis indicated that the risk of the composite primary outcome of stroke, MI, or death did not differ significantly in the two treatment groups. However, it was noted that there was a higher risk of stroke in the CAS group and a higher risk of MI in the CEA group during the periprocedural period. These countervailing effects during the periprocedural period resulted in similar rates of the primary outcomes, because the rates of events after the periprocedural period were similar in the two groups. The authors acknowledge that the differential results for MI and stroke offer opportunities for improvement in the training of surgeons and interventionalists performing CAS procedures, expanded knowledge and experience with stent designs and embolic protection devices, as well as better informed candidate selection, especially amongst those over 70 years of age. The authors note that candidate selection may require attention to age for either procedure, due to the association between older age and increased risk for adverse events. This interaction between age and treatment efficacy was detected at approximately 70 years of age. The effects of advanced age on the differences between CAS- and CEA-treated groups were seen in the SPACE trial results, as well as in these early CREST results where younger participants had slightly better outcomes with CAS and older persons had a better outcome with CEA. The trial investigators speculated that mechanisms underlying the increased risk with CAS in the very elderly (age over 70) probably include vascular tortuosity and severe vascular calcification. It is generally considered that these preliminary results (mean follow-up of 2.5 years) lack sufficient detail for firm conclusions and are viewed as consistent with the growing body of evidence examining outcomes of CAS, in comparison to CEA, that indicate the need for further robust study. The absence of comparison with current best medical therapy is another significant limitation of CREST (Brott, 2010). Silver published final results of the CREST in 2011 which reflected that, although the participating interventionalists performing CAS were highly selected, periprocedural death/stroke rates following CAS exceeded those for CEA: in symptomatic subjects 5.6% versus 2.4%, respectively

(the lowest rate for CAS reported in any trial); in asymptomatic subjects 2.6% versus 1.4%, respectively. The relative risk (RR) for periprocedural death/stroke in the symptomatic group was 1.89 (95% CI, 1.11 to 3.21) and in the asymptomatic group was 1.85 (95% CI, 0.79 to 4.34). The trial had limited power to detect a difference between procedures in the asymptomatic group (Silver, 2011). Additional meta-analyses have generally found that restenosis is more common following CAS than CEA (Bangalore, 2011; Economopoulos, 2011; Murad, 2011).

Ten-year results of the CREST trial were published in 2016 which found that among 2502 subjects, there was no significant difference in the rate of the primary composite endpoint between the stenting group (11.8%; 95% CI, 9.1 to 14.8) and the CEA group (9.9%; 95% CI, 7.9 to 12.2) over 10 years of follow-up (hazard ratio [HR] 1.10; 95% CI, 0.83 to 1.44). With respect to the primary long-term endpoint, postprocedural ipsilateral stroke over the 10-year follow-up occurred in 6.9% (95% CI, 4.4 to 9.7) of subjects in the stenting group and in 5.6% (95% CI, 3.7 to 7.6) of those in the CEA group. The rates did not differ significantly between groups (HR 0.99; 95% CI, 0.64 to 1.52). No significant between-group differences with respect to either endpoint were detected when symptomatic and asymptomatic subjects were analyzed separately. Results of the CREST trial were underpowered to determine whether CEA and CAS with embolic protection were equivalent, according to symptomatic status (Brott, 2016).

In August 2004, the U.S. Food and Drug Administration (FDA) granted Premarket Approval (PMA) to Guidant Corporation's two stent systems (the ACCULINK™ Carotid Stent System and the RX ACCULINK™ Carotid Stent System), which are used in conjunction with two carotid embolic protection systems (the ACCUNET™ and the RX ACCUNET™ Embolic Protection Systems, Guidant Corp., Santa Clara, CA) for the treatment of individuals considered to be at high risk for adverse events from CEA who require carotid revascularization and meet the following criteria:

1. Persons with neurological symptoms and equal to or greater than 50% stenosis of the common or internal carotid artery by ultrasound or angiogram OR persons without neurological symptoms and equal to or greater than 80% stenosis of the common or internal carotid artery by ultrasound or angiogram; AND
2. Individuals must have a reference vessel diameter within the range of 4.0 mm and 9.0 mm at the target lesion.

As part of this approval, Guidant agreed to conduct long-term follow-up of subjects in the studies it submitted to the FDA and conduct another post approval study including 1000 newly enrolled participants. The data submitted to the FDA, on which its approval was based, were from three prospective, non-randomized, multicenter, single arm trials known as ARCHeR 1, 2 and 3 (ACCULINK for Revascularization of Carotids in High Risk Patients) enrolling a total of 581 subjects who were considered either high risk for CEA or not surgical candidates for current surgical options (CEA) and who were symptomatic with a 50% or greater carotid artery stenosis, or asymptomatic with an 80% or greater stenosis. The ARCHeR results were published in 2006 (Gray, 2006). The primary composite endpoint of 30-day combined incidence of death, stroke and MI plus 1-year incidence of ipsilateral stroke was 9.6%. This was compared to 14.4% for historical surgical controls involving similar high surgical risk populations. Target lesion revascularization at 1 and 2 years was 2.2% and 2.9% respectively. These studies suggested that CAS may be safe and effective in a subset of individuals who are not candidates for CEA. In 2006, Guidant Corporation's vascular intervention and endovascular business was acquired by Abbott Vascular Solutions, Inc. (Temecula, CA).

On September 6, 2005, the FDA granted PMA approval to the Xact™ Carotid Stent System (Abbott Vascular Solutions, Inc.) for use in conjunction with the Abbott Emboshield® Embolic Protection System for very similar indications to the ACCULINK and RX ACCULINK devices.

Several additional carotid stent and embolic protection systems have been granted PMA approvals by the FDA as substantially equivalent to the RX ACCULINK and Xact device systems including, but not limited to: the Protégé® GPS™ and Protégé® RX Carotid Stent Systems used with the SpiderRX™ Embolic Protection Device (ev3 Inc., Plymouth, MN), which received FDA approval in January 2007. This CAS system was evaluated via the Carotid Revascularization with ev3 Inc. Arterial Technology Evolution (CREATE) Trial. The NexStent® Carotid Stent and Monorail® Delivery System (Endotex Interventional Systems, Inc., Cupertino, CA) received FDA clearance in October 2006. It is also compatible with the FilterWire EZ™ Embolic Protection System (Boston Scientific Corporation, San Jose, CA). FDA clearance for the FilterWire EZ Embolic Protection System, as well as for the two associated CAS systems, was based on a prospective, nonrandomized multicenter clinical trial (Carotid Artery Revascularization using the Boston Scientific EPI FilterWire EX and the EndoTex NExStent [CABERNET]). These devices received FDA clearance for similar indications to the prior approved devices.

CAS appears to be a reasonable option for select individuals who are poor surgical candidates, for reasons of either anatomy or comorbidities, and who otherwise meet the criteria for revascularization. However, CEA remains the gold standard procedure for those who are not at high risk for this procedure. A report from the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology (Chaturvedi, 2005) commented that there are several important areas for further investigation pertaining to CAS, including the role of cerebral hemodynamics in risk stratification for individuals with carotid stenosis.

In 2012, the Blue Cross Blue Shield Association published a Technology Evaluation Center (TEC) Assessment update on Angioplasty and Stenting of the Cervical Carotid Artery with Embolic Protection of the Cerebral Circulation. This report concluded that amongst individuals selected because of medical comorbidities and/or unfavorable anatomy, there is generalizable and applicable evidence that CAS is performed with periprocedural death/stroke rates exceeding 3% for asymptomatic and 6% for symptomatic subjects and, therefore, not accompanied by net clinical benefit. At present, the use of CAS with embolic protection of the cerebral circulation for individuals with carotid artery stenosis does not meet the TEC criteria (2012).

In 2011, the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American Stroke Association, American Association of Neuroscience Nurses, American Association of Neurological Surgeons, American College of Radiology, American Society of Neuroradiology, Congress of Neurological Surgeons, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of NeuroInterventional Surgery, Society for Vascular Medicine, and Society for Vascular Surgery issued Guidelines on the Management of Patients with Extracranial Carotid and Vertebral Artery Disease. The following recommendations are excerpted:

> Class I:
> CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is reduced by more than 70% as documented by noninvasive imaging or more than 50% as documented by catheter angiography and the anticipated rate of periprocedural stroke or mortality is less than 6% (Evidence Level: B).
>
> Class IIa:
> It is reasonable to choose CEA over CAS when revascularization is indicated in older patients, particularly when arterial patho-anatomy is unfavorable for endovascular intervention (Evidence Level: B).

> It is reasonable to choose CAS over CEA when revascularization is indicated in patients with neck anatomy unfavorable for arterial surgery (Evidence Level: B) (Brott, 2011).

Although there are few studies dealing with the effect of CAS on symptomatic carotid stenosis due to fibromuscular dysplasia, there are few treatment options for this population. In addition, the rarity of the condition also makes it unlikely that studies with moderate to large sample sizes will be conducted in the near future. Consequently, angioplasty with or without stenting remains an important treatment option for these individuals and has been successfully carried out in the practice community. Regarding use of CAS in asymptomatic disease, the American Heart Association/American Stroke Association (AHA/ASA) issued Guidelines for the Primary Prevention of Stroke in 2011, in which it was noted that advances in optimal medical therapy have resulted in uncertainty about the need for, and benefit of, CEA or CAS in the asymptomatic subgroup with carotid artery stenosis. The findings in this document conclude that more data are needed to compare long-term outcomes following CEA and CAS in asymptomatic individuals with carotid artery stenosis (Goldstein, 2011). Another updated guideline, the Society for Vascular Surgery Guidelines for Management of Extracranial Carotid Disease, concurs with the AHA/ASA guidance regarding asymptomatic disease (Ricotta, 2011).

In 2016, results of a prospective multi-center trial were published, the Asymptomatic Carotid Trial (ACT) I which compared CAS with embolic protection and CEA in subjects 79 years of age or younger who had severe carotid stenosis of the carotid artery bifurcation, caused by atherosclerotic disease, and were asymptomatic, (that is, no history of stroke, transient ischemic attack [TIA], or amaurosis fugax in the 180 days before enrollment). Notably, participants in the ACT I trial were not considered to be at high risk for surgical complications. This manufacturer-sponsored study enrolled subjects who were randomly assigned in a 3:1 ratio to undergo CAS with embolic protection (stenting group) or CEA (endarterectomy group). The trial was designed to enroll 1658 subjects but was halted early, due to slow enrollment, after 1453 individuals underwent randomization. However, trial participants were followed for up to 5 years post-procedure. The primary composite endpoint of death, stroke, or MI within 30 days after the procedure or ipsilateral stroke within 1 year was tested at a noninferiority margin of 3 percentage points. Results were reported that reflected that CAS was noninferior to CEA with regard to the primary composite endpoint (event rate, 3.8% and 3.4%, respectively; p=0.01 for noninferiority). The rate of stroke or death within 30 days was 2.9% in the CAS group and 1.7% in the CEA group (p=0.33). From 30 days to 5 years after the procedure, the rate of freedom from ipsilateral stroke was 97.8% in the CAS group and 97.3% in the CEA group (p=0.51), and the overall survival rates were 87.1% and 89.4%, respectively (p=0.21). The cumulative 5-year rate of stroke-free survival was 93.1% in the CAS group and 94.7% in the CEA group (p=0.44). The authors concluded that CAS was noninferior to CEA with regard to the rate of the primary composite endpoint at 1 year. In analyses that included up to 5 years of follow-up, there were no significant differences between study groups in the rates of non-procedure-related stroke, all stroke, and survival (Rosenfield, 2016).

There is limited evidence concerning the net benefit of angioplasty and stenting for vertebral arteries, and large well-designed trial results are not available at this time.

**Intracranial Artery Stent Placement with or without Angioplasty for the Treatment of Intracranial Arterial Stenosis:**

Through Humanitarian Device Exemptions (HDEs), the FDA has cleared the following intracranial stent systems: the NEUROLINK® Intracranial Stent System (Guidant Corp., Menlo Park, CA) in August 2002 and the Wingspan Stent System™ with Gateway™ PTA Balloon Catheter (Stryker Neurovascular, Fremont, CA) in August 2005. The NEUROLINK System is indicated for the treatment of individuals with recurrent intracranial stroke caused by atherosclerotic disease refractory to pharmacotherapies, in intracranial vessels ranging from 2.5 to 4.5 mm in diameter with greater than or equal to 50% stenosis that are accessible to the stent system. The Wingspan Stent System is indicated for improving cerebral artery lumen diameter in individuals with intracranial atherosclerotic disease, refractory to pharmacotherapies, in intracranial vessels with 70-99% stenosis that are accessible to the system. On August 8, 2012 the FDA announced the indications for use and labeling for the Wingspan System *have changed to limit the use of Wingspan to:*

> A narrow, select group of patients and conditions. These changes are based on analysis of the original HDE clinical study, data from studies performed after the HDE approval was granted, and data from a clinical trial called the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) study. After reviewing the available safety information, the FDA believes that a very specific group of patients with severe intracranial stenosis and recurrent stroke, despite continued medical management, who have not had any new symptoms of stroke within the 7 days prior to planned treatment with Wingspan, may benefit from the use of the device. The agency's assessment of benefits and risks for this device considered that these patients are at serious risk of life-threatening stroke and have limited alternative treatment options (FDA, 2012).

On April 25, 2019 the FDA posted a new Safety Communication warning that the off-label use of the Wingspan Stent System can increase the incidence of stroke or death. The federal watchdog said that it received results from a mandated post-market surveillance study, the WEAVE study (Wingspan StEnt System PostmArket SurVEillance) that showed, "There is a significantly higher incidence of stroke or death within 72 hours for patients who underwent a procedure with the Wingspan stent outside its specific indications." Data in the study came from 198 subjects at 24 clinical sites in the U.S. Of the 198 individuals enrolled in the WEAVE study, 152 met the FDA-approved indications for use. Results from the study indicate that subjects who met the FDA-approved indications had a 1.3% risk of death, 1.3% risk of stroke without death, a 2.6% combined rate of stroke or death, and a 97.4% rate of freedom from stroke or death. Subjects who did not meet the FDA-approved indications had a 4.3% rate of death, a 19.6% rate of stroke without death, and a combined 23.9% rate of stroke or death, with only a 76.1% freedom from stroke or death, prompting the issuance of this FDA warning. No change to the 2012 labeling was recommended at this time. "Based on the WEAVE study results and other available safety information, a very specific group of patients, consistent with the current FDA-approved indications and patient selection criteria listed above, may benefit from use of Wingspan" (FDA, 2019).

The SSYLVIA trial (Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries) was a multicenter, non-randomized prospective feasibility study using the NEUROLINK Intracranial Stent System. It included 61 symptomatic subjects who had suffered a TIA or stroke attributable to a single arterial stenosis of at least 50%. Following stent placement, the stroke rate within 30 days was 6.6%, and 30 day to 12 month stroke rate was 7.3%. At 6 months, the restenosis rate (of greater than 50% stenosis) was 32.4% for intracranial stents and 42.9% for extracranial vertebral stents. The investigators acknowledged, "Currently there is no proven benefit of this procedure relative to medical therapy" (SSYLVIA, 2004).

The Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial was intended to compare percutaneous transluminal angioplasty and stenting (PTAS) to intensive medical therapy among subjects with 70-99% stenosis. This large trial was sponsored by the Medical University of South Carolina, in collaboration with the National Institutes of Health (NIH) and the National Institute of Neurological Disorders and Stroke (NINDS). The primary outcome measure was to determine whether intracranial stenting (with the Wingspan stent) with intensive medical therapy is superior to medical therapy alone for preventing secondary stroke in high-risk subjects with symptomatic stenosis of a major intracranial artery. Recruitment took place at 50 sites in the U.S. with a target enrollment of 764 participants. However, this study was halted early in 2011, due to a higher rate of adverse events in the angioplasty/stenting group (NCT00576693).

Subsequent further analysis of the SAMMPRIS data have concurred with the preliminary findings noting that the 30-day rate of stroke

or death was 14.7% in the PTAS group (nonfatal stroke 12.5%; fatal stroke 2.2%) and 5.8% in the medical management group (nonfatal stroke 5.3%; non-stroke-related death 0.4%; p=0.002). Beyond 30 days, stroke in the same intracerebral territory occurred in 13 subjects in each group. The probability of the occurrence of a primary endpoint event over time differed significantly between the 2 treatment groups (p=0.009), with 1-year rates of the primary endpoint of 20.0% in the PTAS group and 12.2% in the medical management group. The investigators concluded that, in individuals with intracranial arterial stenosis, aggressive medical management was superior to PTAS with the use of the Wingspan stent system, both because the risk of early stroke after PTAS was high and because the risk of stroke with aggressive medical therapy alone was lower than expected (Chaudhry, 2011; Chimowitz, 2011; Derdeyn, 2014; Qureshi, 2012; Siddiq, 2012).

Another randomized controlled trial of intracranial stenting plus medical therapy vs. medical therapy alone, the CASSISS trial (China Angioplasty & Stenting for Symptomatic Intracranial Severe Stenosis) of subjects with transient ischemic attack or ischemic stroke due to symptomatic severe intracranial atherosclerotic stenosis, resulted in no significant difference in the risk of stroke or death within 30 days or stroke in the qualifying artery territory beyond 30 days through 1 year. The authors concluded that, “Despite efforts to reduce perioperative complication rates by vetting of surgeons and sites and refining patient selection, the findings nonetheless demonstrated no clinical benefit from the addition of stenting to medical therapy for the treatment of symptomatic severe intracranial atherosclerotic stenosis.” (Gao, 2022)

In 2009, the American Heart Association Council on Cardiovascular Radiology and Intervention, Stroke Council, Council on Cardiovascular Surgery and Anesthesia, Interdisciplinary Council on Peripheral Vascular Disease, and Interdisciplinary Council on Quality of Care and Outcomes Research issued a scientific statement on Indications for Intracranial Endovascular Neuro-interventional Procedures. The recommendation related to endovascular treatment of symptomatic intracranial stenosis was noted as Class IIb with Level of Evidence C (usefulness/effectiveness is unknown/unclear). The level of evidence was the same for use of angioplasty and stenting in the treatment of acute ischemic stroke (Meyers, 2009). These findings align with results of a pilot study, the Stent-Assisted Recanalization in Acute Ischemic Stroke Trial (SARIS) which was a prospective, single-arm trial that investigated the safety and efficacy of primary stent deployment (with the Wingspan System) for revascularization in 20 individuals with acute stroke. The 1-month mortality rate was 25% which, according to the authors, suggested the possibility of benefit of intracranial stenting in acute stroke treatment. However, no robust conclusions could be drawn from this small (n=20), non-randomized, single center study and additional larger trials are needed (Levy, 2009).

In 2012, standards of practice recommendations were published on behalf of the Society of Neuro Interventional Surgery, which were based on assessment of available evidence from an updated literature review which extracted published literature from 2000 to 2011 regarding the treatment of symptomatic intracranial atherosclerotic disease (ICAD). Evidence was evaluated and classified according to American Heart Association (AHA)/American Stroke Association standards with recommendations developed which were based on guidelines for evidence based medicine proposed by the American Academy of Neurology (AAN), the Stroke Council of the AHA and the University of Oxford, Centre for Evidence Based Medicine (CEBM). This evidence-based assessment identified 59 publications and noted that the SAMMPRIS study is the only prospective, randomized, controlled trial currently available (which was given an AHA level B designation, AAN class II and CEBM level 1b). The Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial arteries (SSYLVIA) trial was a prospective, non-randomized study with the outcome assessment made by a non-operator study neurologist, (which allowed an AHA level B, AAN class III and CEBM level 2 rating). The remaining studies were uncontrolled or did not have objective outcome measurement, (and were classified as AHA level C, AAN class IV and CEBM level 4 rating). These investigators concluded that medical management with combination aspirin and clopidogrel for 3 months and aggressive risk factor modification should be first line therapy for individuals with symptomatic ICAD. Endovascular angioplasty, with or without stenting, is a possible therapeutic option for selected subjects with symptomatic ICAD and may be considered in subjects with symptomatic 70-99% intracranial stenosis when aggressive maximal medical therapy has failed. However, further studies are necessary to define appropriate selection criteria and the best therapeutic approach for various subsets of affected individuals (Hussain, 2012).

In 2013, the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Peripheral Vascular Disease, and Council on Clinical Cardiology issued Guidelines for the Early Management of Patients with Acute Ischemic Stroke which contain two new recommendations that concur with the other specialty medical society guidance regarding extracranial and intracranial artery angioplasty and stenting as a treatment of acute ischemic stroke as follows:

> The usefulness of emergent intracranial angioplasty and/or stenting is not well established. These procedures should be used in the setting of clinical trials (Class IIb; Level of Evidence C);
>
> The usefulness of emergent angioplasty and/or stenting of the extracranial carotid or vertebral arteries in unselected patients is not well established (Class IIb; Level of Evidence C). Use of these techniques may be considered in certain circumstances, such as in the treatment of acute ischemic stroke resulting from cervical atherosclerosis or dissection (Class IIb; Level of Evidence C). Additional randomized trial data are needed (Jauch, 2013).

**Intracranial Artery Stent Placement with or without Angioplasty for the Treatment of Intracranial Arterial Aneurysms:**

The International Study of Unruptured Intracranial Aneurysms (ISUIA) trial assessed 4060 subjects with unruptured aneurysms, recording the natural history of those who had no surgery and evaluating morbidity and mortality associated with repair of unruptured aneurysms by surgical clipping or endovascular repair. Over a 5-year period, 18% of the 1692 trial participants who did not receive endovascular or surgical treatment died due to intracranial hemorrhage. Outcomes were much better for the 451 subjects who received endovascular therapy and the 1917 individuals who received surgical clipping with death rates of 1.8% and 1.5%, respectively (Wiebers, 2003).

The largest clinical series describing use of stents in treating intracranial aneurysms was published in 2010 reporting on a series of 1137 subjects (1325 aneurysms) treated between 2002 and 2009. In this series, 1109 individuals with aneurysms (83.5%) were treated without stents (coiling) and 216 (16.5%) were treated with stents (15 balloon-expandable and 201 self-expandable stents). Stents were delivered after coiling in 55% (119/216) and before coiling in 45% (97/216) of the cases. Permanent neurological procedure-related complications occurred in 7.4% (16 of 216) of the procedures with stents versus 3.8% (42 of 1109) in the procedures without stents (logistic regression p=0.644; odds ratio [OR], 1.289; 95% CI, 0.439-3.779). Procedure-induced mortality occurred in 4.6% (10 of 216) of the procedures with stents versus 1.2% (13 of 1109) in the procedures without stents (logistic regression p=0.006; OR, 0.116; 95% CI, 0.025-0.531). Thus far, the authors have followed 53% (114 of 216) of individuals with aneurysms treated with stents and 70% (774 of 1109) of individuals with aneurysms treated without stents, with angiographic recurrence in 14.9% (17 of 114) of stent-treated subjects versus 33.5% (259 of 774), of subjects treated with coiling without stenting (p<0.0001; OR, 0.3485; 95% CI, 0.2038-0.5960). Based on this series, the authors concluded that use of stents was associated with a significant decrease of angiographic recurrences, but with more lethal complications compared with coiling without stents (Piotin, 2010). Additional small studies note the need for additional data to further define the technical challenges in stent deployment, the durability of endovascular stent grafting for intracranial aneurysms and the exact role of this treatment (Biondi, 2007; Mocco, 2009; Wajnberg, 2009).

Santillan published results of the Safety and Efficacy of Neuroform3 for Intracranial Aneurysm Treatment (SENAT) trial that included

79 subjects harboring wide-necked intracranial aneurysms who were treated using the Neuroform3 stent. The stenting procedure failed in 2 subjects. Therefore, 77 individuals harboring 79 intracranial aneurysms were included for analysis. Subject and aneurysm characteristics, progression of aneurysm occlusion, and occurrence of complications were analyzed with follow-up imaging that included digital subtraction angiography (DSA) or MRA. Overall, complete aneurysm occlusion was observed in 42.4% of the cases immediately after treatment and progressed to 96.5% at 7-year follow-up. The mean angiographic follow-up time was 25.8 months (range, 0-84 months). Eleven aneurysms (14%) were retreated. Sixty-eight subjects (88.3%) had a favorable clinical outcome with a modified Rankin Scale (mRS) ≤ 1; 3 subjects (3.9%) had an mRS of 2 and 5 (6.5%) did not have a clinical follow-up. The mean clinical follow-up time was 45.4 months (range, 3-92 months). One subject (1.3%) died from a procedure-related hemorrhage. The authors concluded that the Neuroform3 stent-assisted coil embolization of wide-necked intracranial aneurysms prevents hemorrhage and provides a high rate of aneurysm occlusion at long-term follow-up (Santillan, 2011).

In 2007, the ENTERPRISE™ Vascular Reconstruction Device and Delivery System (Cordis Neurovascular, Inc., Miami Lakes, FL) also received HDE designation clearance from the FDA for:

> Use with embolic coils for the treatment of wide-neck, intracranial, saccular or fusiform aneurysms arising from a parent vessel with a diameter of ≥ 3 mm and ≤ 4 mm. Wide-neck is defined as having a neck width ≥ 4mm or a dome-to-neck ratio < 2.

Although cleared by the FDA, the clinical effectiveness of these intracranial stent systems has not been clearly established. Preliminary findings, on which the FDA clearances were based, need further validation in large randomized controlled trials. On April 6, 2011 the FDA announced its clearance of another device for repair of wide neck aneurysms, the Pipeline Embolization Device™ (ev3, Inc. Menlo Park, CA) which includes a flow-diverting stent and is for use in the endovascular treatment of large wide-necked intracranial aneurysms in the cavernous and paraclinoid regions of the internal carotid artery (FDA, 2011).

Additional recent research reports on studies using angioplasty/stenting devices and endovascular coils to repair intracranial aneurysms. There is some evidence demonstrating improved short-term outcomes when compared to medical therapy alone (Fiorella, 2007; Lylyk, 2005; Molyneux, 2009; Murayama, 2003; Pierot, 2010; Raja, 2008; Timaran, 2009), however, this evidence is mostly in the form of case reports. There is much interest in the use of stents, in addition to endovascular coils, when presented with aneurysms with challenging anatomy where conventional surgical options are not effective, for example wide-necked aneurysms. Clinical feedback has been consistent regarding the selective use of stents, as part of endovascular treatment of intracranial aneurysms in these rare situations. Based on the results from these case series, use of stent devices to supplement coil therapy of an aneurysm is appropriate with wide-neck aneurysms (4 mm or more) or when the sack-to-neck ratio is less than 2:1. However, the current evidence does not demonstrate the safety or efficacy of percutaneous angioplasty procedures without stent placement for the treatment of intracranial aneurysms (Piotin, 2010).

Another device, the Woven Endobridge (WEB®) Aneurysm Embolization System (Sequent Medical™ Inc. [MicroVention, Inc.] Aliso Viejo, CA) received FDA premarket approval for use at the middle cerebral artery (MCA) bifurcation, internal carotid artery (ICA) terminus, anterior communicating artery (AComm) complex, or basilar artery apex for the endovascular treatment of adults with saccular, wide neck, bifurcating intracranial aneurysms with dome diameter from 3 mm to 10 mm and either neck size of 4 mm or greater or a dome-to-neck ratio greater than 1 and less than 2. One-year follow-up data from the WEB Intrasaccular Therapy Study (WEB-IT), which was a prospective non-randomized pivotal study, was used to base FDA approval on (Arthur, 2019) subject to results of a 5-year post-approval study (FDA, P170032; 2018). Further study is needed with randomized controlled trials and longer outcomes data (Lv, 2018; Tau, 2018; Zhang, 2020).

**Intracranial Artery Stent Placement with or without Angioplasty for the Treatment of Intracerebral Vasospasm associated with Subarachnoid Hemorrhage (SAH):**

In March 2005, the FDA granted an HDE clearance to the CoAxia NeuroFlo™ catheter for, “The treatment of cerebral ischemia caused by symptomatic vasospasm following aneurysmal subarachnoid hemorrhage (SAH). The device can be secured by either surgical or endovascular intervention for those who have failed maximal medical management.” The CoAxia NeuroFlo catheter (CoAxia, Inc., Maple Grove, MN) is a multi-lumen device with two balloons mounted near the tip. The balloons can be inflated or deflated independently for controlled partial obstruction of aortic blood flow. It is assumed that the obstruction created by the inflated balloons will reduce blood flow to the lower part of the body while increasing blood volume to the upper part of the body, including the brain, without significant increase in pressure. The increase in cerebral blood volume presumably drives blood flow into the penumbra, restoring circulation and improving chances of recovery. This procedure has not exhibited significant cardiac, cerebral, or renal complications in clinical trials. The CoAxia NeuroFlo catheter is inserted through an introducer sheath through the femoral artery, and balloons are placed on either side of the renal arteries. The infra-renal (IR) balloon is inflated first to 70% occlusion. It is recommended that the supra-renal (SR) balloon be inflated to 70% occlusion about 5 minutes later. Inflation of both balloons should be maintained for 40 minutes. Balloon inflation may be modified over this period, based on blood pressure. The balloons should then be sequentially deflated, SR then IR, and removed. Treatment with the CoAxia NeuroFlo catheter is recommended only after subjects have failed or are ineligible for medical therapy (FDA, 2005).

Additional small studies of intracranial endovascular angioplasty continue to reflect some benefit for individuals with vasospasm associated with SAH. However, the outcomes data is limited and shows significant complication rates. Further investigation is warranted (Abruzzo, 2012; Jestaedt, 2008; Jun, 2010; Khatri, 2011; Murai, 2005; Turowski, 2005; Velat, 2011; Zwienenberg-Lee, 2008).

**Description of Technology**

Traditionally, surgical treatment has been with open CEA. The carotid artery is exposed through an incision, and the atherosclerotic plaque causing the narrowing is removed surgically. Recently, CAS emerged as an alternative to open surgery. While carotid angioplasty has been performed alone, currently this procedure typically includes the placement of a stent, in order to prevent restenosis. However, in certain conditions of fibromuscular dysplasia and in situations where stent placement is technically not feasible, angioplasty alone may be performed.

Stent implantation is a supplement to angioplasty, in which a balloon introduced via a catheter is inserted through a blockage and expanded to enlarge the vessel, allowing restoration of blood flow. This procedure involves the permanent placement of a mechanical device within blocked arteries or veins, in order to compress the obstructive material and to support the vessel wall, preventing both constriction and further blockage. Insertion of an embolic protection device may accompany stent placement. This device consists of a small wire mesh or basket that is used to capture any embolic debris that may dislodge from the lesion, in order to prevent the debris from reaching the brain or other intracranial areas. Such devices are purported to further decrease the neurologic event risk from CAS.

In 2007, a consensus document on carotid stenting was released by the American College of Cardiology Foundation/Society for Cardiovascular Angiography and Interventions/Society for Vascular Medicine and Biology/Society of Interventional Radiology/American Society of Interventional & Therapeutic Neuroradiology (ACCF/SCAI/SVMB/SIR/ASITN). This document states

that:

> CAS is viewed as a reasonable alternative to CEA, particularly in subjects at high risk for CEA, and use of EPDs (embolic protection devices) seems to be important in reducing risk of stroke… At the present time, the evidence is insufficient to support CAS in asymptomatic high-risk subjects who have less than 80% stenosis or in those who are not at high-risk for surgery (Bates, 2007).

In 2003, a collaborative panel of the Joint Standards of Practice Committee of the American Society of Interventional and Therapeutic Neuroradiology, the American Society of Neuroradiology, and the Society of Interventional Radiology developed quality improvement guidelines for the performance of cervical CAS. The document includes standards for qualifications and responsibilities of personnel, specifications of the procedure, equipment quality and control, documentation, thresholds, success and complication rates, quality control and improvement, safety, infection control, and candidate education concerns. Furthermore, the document outlines suggested inclusion criteria and relative and absolute contraindications for CAS (Barr, 2003).

Human Device Exemptions (HDEs) differ from the standard FDA approval process and are designed to allow the use of qualified devices without requiring the rigorous safety and efficacy testing required for standard device approvals. A humanitarian device is one that is intended to benefit individuals in the treatment and diagnosis of rare diseases or conditions that affect or are manifested in fewer than 4000 individuals in the United States per year. The goal of the HDE process is to allow the use of specific devices for indications where other alternatives are unavailable. A healthcare provider is responsible for obtaining Institutional Review Board approval before a humanitarian device with an exemption may be administered or implanted. For the NEUROLINK System, the Center for Devices and Radiological Health (CDRH) of the FDA determined that, based on the data submitted in the HDE, the NEUROLINK System will not expose recipients to an unreasonable or significant risk of illness or injury. The probable benefit to health from using the device outweighs the risks of illness or injury as follows:

> For the treatment of individuals with recurrent stroke attributable to atherosclerotic disease refractory to medical therapy in intracranial vessels ranging from 2.5 to 4.5 mm in diameter with greater than or equal to 50% stenosis that are accessible to the stent system.

The FDA issued an approval order on August 9, 2002.

*Proposed Benefits*

CAS is purported to decrease stenosis in carotid arteries with varying degrees of blockage. Theoretically, with blood flowing more freely through the artery, symptoms, such as TIA, are diminished or relieved completely, and the risk of stroke and associated neurological impairment is also greatly diminished. Although CEA provides the same advantages, CAS is a less invasive procedure and is promoted as an alternative to CEA particularly where an invasive procedure would lead to a high risk of complications. Studies show that the technical success of CAS ranges from about 96% to 100% and residual stenosis after CAS ranges from 2% to 15%. Percutaneous intracranial artery stent placement with or without angioplasty is also used in the treatment of intracranial aneurysms where certain clinical factors contribute to high risk for life threatening events and established surgical and medical management strategies are either contraindicated or ineffective.

*Possible Risks*

Risks from CAS include restenosis after implantation of the stent (generally uncommon). Non-neurologic complications (for example, slow heart rate, transient loss of consciousness) may occur during the procedure. Neurologic complications are generally due to embolic debris that dislodged from the site of the lesion either during or after the procedure and may lead to stroke and/or death. In recent studies, the overall postoperative neurologic complication rates for CAS of the extracranial carotids for the treatment of stenosis have ranged from about 0% to 10%.

Transcarotid artery revascularization (TCAR) was recently introduced as a novel CAS option that circumvents several of the high embolic-risk maneuvers found in transfemoral CAS and employs a flow reversal system that provides continuous embolic protection throughout the procedure. According to this review article, early results from this technique have shown low stroke/death rates comparable to CEA while maintaining the minimally invasive benefits of CAS. It is reported that TCAR has a strong potential to become the preferred method of performing CAS in the near future and may challenge CEA as the preferred carotid artery revascularization method (Liang, 2019).

On March 10, 2016 the ENROUTE® Transcarotid Neuroprotection System (Silk Road Medical, Inc. Sunnyvale, CA) was granted FDA 510(k) clearance as substantially equivalent to predicate devices for the following:

> The ENROUTE Transcarotid Neuroprotection System (ENROUTE Transcarotid NPS) is intended to provide transcarotid vascular access, introduction of diagnostic agents and therapeutic devices, and embolic protection during carotid artery angioplasty and stenting procedures for patients diagnosed with carotid artery stenosis and who have appropriate anatomy described below:
>
> - Adequate femoral venous access;
> - Common carotid artery reference diameter of at least 6 mm;
> - Carotid bifurcation is a minimum of 5 cm above the clavicle as measured by duplex Doppler ultrasound (DUS) or computerized axial tomography (CT) angiography or magnetic resonance (MR) angiography.

On May 18, 2015 the ENROUTE Transcarotid Stent System was granted PMA clearance for use in conjunction with the ENROUTE Transcarotid NPS for the following indications:

> For the treatment of patients at high risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below:
>
> 1. Patients with neurological symptoms and ≥ 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 vessel diameter of 4-9mm at the target lesion, AND
> 3. Carotid bifurcation is located at minimum 5 cm above the clavicle to allow for placement of the ENROUTE Transcarotid NPS (PMA P140026: FDA Summary of Safety and Effectiveness Data, 2015).
>
> Use of the ENROUTE Transcarotid Stent System is contraindicated in the following patients:
>
> 1. Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated.
> 2. Patients in whom the ENROUTE Transcarotid NPS is unable to be placed.
> 3. Patients with uncorrected bleeding disorders.

4. Patients with known allergies to nitinol.
5. Lesions in the ostium of the common carotid artery (FDA, 2015).

In 2020, early results of the post-approval study of TCAR were published. The ROADSTER 2 study (Reverse Flow used during carotid artery stenting procedure) followed the initial 30-day safety and efficacy study of TCAR (the ROADSTER study), which included 141 subjects considered high risk for CEA at 18 sites between November 2012 and July 2014. This study demonstrated acute device and technical success rates of 99% (140 of 141 subjects) and an all-stroke rate of 1.4% (2 of 141); stroke and death was 2.8% (4 of 141); and stroke, death and myocardial infarction (MI) was 3.5% (5 of 141). One subject (0.7%) experienced postoperative hoarseness from potential Xth cranial nerve injury (CNI), which completely resolved at the 6-month follow-up visit (Kwolek, 2015 NCT01685567).

The ROADSTER 2 study of 632 subjects with significant carotid artery disease was intended to evaluate the safety and efficacy of TCAR performed by a broad group of physicians with variable TCAR experience. The ROADSTER 2 study is a prospective, open label, single arm, multicenter, post-approval registry for subjects undergoing TCAR, which included individuals considered at high risk for complications from CEA with symptomatic stenosis ≥ 50% or asymptomatic stenosis ≥ 80%. The primary end point was procedural success, which encompassed technical success plus the absence of stroke, MI, or death within the 30-day postoperative period. Secondary end points included technical success and individual/composite rates of stroke, death, and MI. All trial participants underwent independent neurological assessments before the procedure, within 24 hours, and at 30 days after TCAR. An independent clinical events committee adjudicated all major adverse events. Between 2015 and 2019, 692 individuals (intent-to-treat population) were enrolled at 43 sites. Sixty cases had major protocol violations, leaving 632 subjects adhering to the FDA approved protocol (per-protocol population). The majority (81.2%) of operators were TCAR naïve before study initiation. Trial subjects underwent TCAR for neurological symptoms in 26% of cases, and all subjects had high risk factors for CEA (anatomic-related 44%; physiological 32%; both 24%). Technical success occurred in 99.7% of all cases. The primary end point of procedural success rate in the intent-to-treat population was 96.5% (per-protocol 97.9%). The early postoperative outcomes in the intent-to-treat population included stroke in 13 subjects (1.9%), death in 3 cases (0.4%), and MI in 6 individuals (0.9%). The composite 30-day stroke/death rate was 2.3%, and stroke/death/MI rate was 3.2%. In the per-protocol population, there were strokes in 4 subjects (0.6%), death in 1 case (0.2%), and MI in 6 individuals (0.9%) leading to a composite 30-day stroke/death rate of 0.8% and stroke/death/MI rate of 1.7%. The authors concluded that TCAR results in excellent early outcomes with high technical success combined with low rates of postprocedure stroke and death. It was noted that these results were achieved by a majority of operators new to this technology at the start of the trial. Adherence to the study protocol and peri-procedural antiplatelet therapy optimized these outcomes. Longer-term follow-up data are needed to confirm these early outcomes (Kashyap, 2020; NCT02536378).

As of Feb. 23, 2021 the FDA issued a Class II device recall for affected lots of the ENROUTE Transcarotid Stent System which is under investigation for the following:

> Action: On 01/13/2021, the firm sent an "URGENT: MEDICAL DEVICE RECALL" Notification via email to customers informing them that product complaints have been received where the tip/nose cone detached from the stent delivery system during use and it is possible the resulting patient harm can range from minor intervention required to retrieve the detached tip/nose cone to embolization or stroke if the device failure goes undetected.

According to the web site for the Society for Vascular Surgery (SVS), the following information is noted:

> Transcarotid Artery Revascularization (TCAR) is a clinically proven, minimally invasive procedure to treat carotid artery disease and help prevent future strokes. TCAR is unique in that blood flow is temporarily reversed during the procedure so that any bits of plaque that may break off are diverted away from the brain (SVS, 2021).

In an updated SVS guideline for management of extracranial cerebrovascular disease, the following is excerpted:

> Carotid endarterectomy (CEA) remains favored over transfemoral carotid artery stenting (TF-CAS) for most anatomically suited low/standard risk patients with indications for carotid revascularization. Transcarotid artery revascularization (TCAR) is a newer hybrid CAS procedure that places the stent through a small neck incision. In observational studies, TCAR had a lower risk of perioperative stroke compared with TF-CAS, and lower rates of myocardial infarction or cranial nerve injury compared with CEA. For these reasons, the SVS now considers TCAR preferable to TF-CAS or CEA in high surgical risk patients such as those with high-risk carotid or other anatomy, or unacceptably high medical risk (AbuRahma, 2021).

In 2020, Naazie and colleagues conducted a systematic review and meta-analysis of TCAR with dynamic flow reversal vs. transfemoral CAS (TFCAS) and CEA. Nine nonrandomized studies evaluating 4012 individuals who underwent TCAR were included. The overall 30-day risks after TCAR were stroke/death 1.89% (95% CI, 1.50, 2.37); stroke 1.34% (95% CI, 1.02, 1.75); death 0.76% (95% CI, 0.56, 1.08); MI 0.60% (95% CI, 0.23, 1.59); stroke/death/MI 2.20% (95% CI, 1.31, 3.69); and CNI 0.31% (95% CI, 0.12, 0.83). The failure rate of TCAR was 1.27% (95% CI, 0.32, 4.92). Two nonrandomized studies suggested that TCAR was associated with lower risk of stroke and death, as compared with TFCAS (1.33% vs. 2.55%; OR 0.52, 95% CI, 0.36, 0.74 and 0.76% vs. 1.46%; OR 0.52, 95% CI, 0.32, 0.84, respectively). Four nonrandomized studies suggested that TCAR was associated with a lower risk of CNI (0.54% and 1.84%; OR 0.52, 95% CI, 0.36, 0.74) than CEA, but no statistically significant difference in the 30-day risk of stroke, stroke/death, or stroke/death/MI. The authors concluded that among subjects undergoing TCAR with dynamic flow reversal for carotid stenosis the 30-day risk of stroke or death was low. The perioperative stroke/death rate of TCAR was similar to that of CEA while CNI risk was lower. Larger prospective studies are needed to account for confounding factors and provide higher certainty.

In 2019, the SVS Vascular Quality Initiative (VQI) reported results of the TCAR Surveillance Project (TSP), which was designed to evaluate the safety and effectiveness of TCAR in real-world practice. Data from the initial 646 subjects enrolled in the TSP from March 2016 to December 2017 were analyzed and compared with those of trial subjects who underwent TFCAS between 2005 and 2017. Individuals with tandem, traumatic, or dissection lesions were excluded. Multivariable logistic regression and 1:1 coarsened exact matching were used to analyze neurologic adverse events (stroke and transient ischemic attacks [TIAs]) and in-hospital mortality. Trial subjects in the two procedures were matched on age, ethnicity, coronary artery disease, congestive heart failure, prior coronary artery bypass graft or percutaneous coronary intervention, chronic kidney disease, degree of ipsilateral stenosis, American Society of Anesthesiologists class, symptomatic status, restenosis, anatomic and medical risk, and urgency of the procedure. The investigators noted that, compared with subjects undergoing TFCAS (n=10,136), those undergoing TCAR (n=638) were significantly older, had more cardiac comorbidities, were more likely to be asymptomatic, and less likely to have a recurrent stenosis.

The results showed that rates of in-hospital TIA/stroke, as well as of TIA/stroke/death were significantly higher in the TFCAS group, compared with the TCAR group (3.3% vs 1.9% [p=0.04] and 3.8% vs 2.2% [p=0.04], respectively). In both procedures, symptomatic individuals had higher rates of TIA/stroke/death, compared with asymptomatic subjects (for TCAR 3.7% vs 1.4% [p=0.06]; for TFCAS 5.3% vs 2.7% [p<0.001]). After multivariable adjustment, there was a trend for increased stroke or death rates in the TFCAS group, compared with the TCAR group but it was not statistically significant (2.5% vs 1.7%; p=0.25; odds ratio, 1.75, 95% CI, 0.85-3.62). However, the TFCAS group was associated with twice the odds of in-hospital adverse neurologic events and TIA/stroke/death, compared with the TCAR group (odds ratio, 2.10; 95% CI, 1.08-4.08; p=0.03), independent of symptom status. Coarsened exact matching showed similar results. These preliminary results of the VQI TSP demonstrated beneficial effects for TCAR compared with

TFCAS in real-world practice (Malas, 2019).

In 2020, a further comparative study was conducted of in-hospital outcomes for subjects undergoing TCAR and CEA from January 2016 to March 2018 using the SVS VQI TSP registry and the SVS VQI CEA database, respectively. The primary outcome was a composite of in-hospital stroke and death. A total of 1182 individuals underwent TCAR, compared with 10,797 subjects who underwent CEA. The individuals undergoing TCAR were older (median age, 74 vs 71 years; p<0.001) and more likely to be symptomatic (32% vs 27%; p<0.001); they also had more medical comorbidities, including coronary artery disease (55% vs 28%; p<0.001), chronic heart failure (20% vs 11%; p<0.001), chronic obstructive pulmonary disease (29% vs 23%; p<0.001), and chronic kidney disease (39% vs 34%; p=0.001). On unadjusted analysis, the TCAR group had similar rates of in-hospital stroke/death (1.6% vs 1.4%; p=0.33) and stroke/death/MI (MI; 2.5% vs 1.9%; p=0.16), compared with CEA. There was no difference in rates of stroke (1.4% vs 1.2%; p=0.68), in-hospital death (0.3% vs 0.3%; p=0.88), 30-day death (0.9% vs 0.4%; p=0.06), or MI (1.1% vs 0.6%; p=0.11). However, on average, the TCAR procedures were 33 minutes shorter than CEA (78 ± 33 minutes vs 111 ± 43 minutes; p<0.001). The subjects undergoing TCAR were also less likely to incur CNI (0.6% vs 1.8%; p<0.001) and less likely to have a postoperative length of stay > 1 day (27% vs 30%; p=0.046). On adjusted analysis, there was no difference in terms of stroke/death (odds ratio, 1.3; 95% CI, 0.8-2.2; p=0.28), stroke/death/MI (odds ratio, 1.4; 95% CI, 0.9-2.1; p=0.18), or the individual outcomes. The authors concluded that despite a substantially higher medical risk in those undergoing TCAR, the in-hospital stroke/death rates were similar between the TCAR and CEA groups. Further comparative studies with larger samples sizes and longer follow-up are needed to establish the role of TCAR in extracranial carotid disease management (Schermerhorn, 2020).

Available data from pre-clinical studies, prospective single-arm studies, and comparative analyses of registry data have demonstrated similar major outcomes from TFCAS and TCAR procedures for carotid stenosis, with lower adverse event rates from TCAR. Investigators have called for a well-controlled randomized trial with careful oversight to be prioritized to obtain level 1 evidence and further validate these preliminary findings (Lackey, 2020; Liang, 2020).

## Definitions

Angina pectoris: Chest pain that is typically severe and crushing. The individual experiences a feeling of pressure and suffocation just behind the breastbone (the sternum) caused by an inadequate supply of oxygen to the heart muscle.

Canadian Cardiovascular Society (CCS): This organization further defines anginal classes as follows:

Class I: Ordinary physical activity does not cause angina;
Class II: Slight limitation of ordinary activity;
Class III: Marked limitation of ordinary physical activity;
Class IV: Inability to carry on physical activity without discomfort.

Carotid arteries: Arteries originating from the aorta that pass through the neck flowing up to the brain. The carotid arteries and their subsequent branches supply approximately 80% of the brain's blood supply.

Carotid artery angioplasty with stent placement (CAS): This catheter-based procedure involves utilizing a percutaneous endovascular approach (from within the involved vessel) to access an area of vessel stenosis (obstruction). Balloons within the catheter are then sequentially inflated, in order to clear the stenosed lesion within the vessel with endoscopic removal of any atherosclerotic debris (or plaque) followed by deployment of a stent device which is permanently implanted within the stenosed section of vessel to ensure patency. This minimally invasive alternative to open surgery is proposed for treatment of carotid artery stenosis, as well as for treatment of aneurysms (area of vessel wall weakness) within the intracranial cerebral vascular system.

Carotid endarterectomy (CEA): This is a surgical procedure where the fatty build up in the wall of an artery is directly removed. This procedure is most typically done in the carotid artery when there is a severe or symptomatic narrowing of the vessel lumen.

Contralateral: This term refers to the opposite side of the body.

Endovascular coils (also referred to as coil embolization): This refers to a minimally invasive technique where an intracranial aneurysm (weakness in the wall of a vessel) is accessed endovascularly (from within the vessel with use of catheters) to insert small platinum coils. These coils are threaded through the catheter and deployed into the aneurysm to block blood flow into the aneurysm and prevent rupture of the aneurysm. Coil devices have received FDA clearance; the first was the Guglielmi® Detachable Coil (Boston Scientific, Corp., Fremont, CA) which was cleared under an Investigational Device Exemption (IDE) in 1995.

Fibromuscular dysplasia: This is a non-atherosclerotic, non-inflammatory disease of the blood vessels that most commonly affects the internal carotid and renal arteries. The condition is rare and the cause is unknown, although cigarette smoking and a history of hypertension may increase the risk. The severity of symptoms varies widely and may result in arterial stenosis, aneurysms, and dissection (separation of the layers of the vessel wall) that result in significant morbidity. Therapy may include drug therapy (to treat hypertension that results from renal artery involvement), surgical revascularization, and angioplasty.

Intracranial arteries: These arteries are located within the skull. The intracranial arteries are comprised of branches of the carotid and vertebral arteries that supply blood to the brain, (that is, the anterior, middle and posterior cerebral, vertebrobasilar or basilar).

Stenosis: A narrowing in a blood vessel such as an artery. This narrowing is usually caused by fatty deposits (atherosclerosis) in the vessel wall.

Vertebral arteries: These arteries are located at the back of the neck and originate from the subclavian arteries. The vertebral arteries and their subsequent branches supply approximately 20% of the brain's blood supply. Vertebral artery and intracranial artery stenosis have a poor prognosis and generally lead to neurological deterioration or death. Medical management is the treatment option most used. Surgical risks and complications are significant.

## References

**Peer Reviewed Publications:**


1. Abruzzo T, Moran C, Blackham KA, et al. Invasive interventional management of post-hemorrhagic cerebral vasospasm in patients with aneurysmal subarachnoid hemorrhage. J Neurointerv Surg. 2012; 4(3):169-177.
2. Abuzinadah AR, Alanazy MH, Almekhlafi MA, et al. Stroke recurrence rates among patients with symptomatic intracranial vertebrobasilar stenoses: systematic review and meta-analysis. J Neurointerv Surg. 2016; 8(2):112-116.
3. Alazzaz A, Thornton J, Aletich VA, et al. Intracranial percutaneous angioplasty for arteriosclerotic stenosis. Arch Neurol. 2000; 57(11):1625-1630.
4. Albuquerque FC, Fiorella D, Han P, et al. A reappraisal of angioplasty and stenting for the treatment of vertebral origin stenosis. Neurosurgery. 2003; 53(3):607-616.

5. ACST-2 Collaborative Group, Halliday A, Bulbulia R, Gray W, et al. Status update and interim results from the asymptomatic carotid surgery trial-2 (ACST-2). Eur J Vasc Endovasc Surg. 2013; 46(5):510-518.
6. Arthur AS, Molyneux A, Coon AL, et al. The safety and effectiveness of the Woven EndoBridge (WEB) system for the treatment of wide-necked bifurcation aneurysms: final 12-month results of the pivotal WEB Intrasaccular Therapy (WEB-IT) Study. J Neurointerv Surg. 2019; 11(9):924-930.
7. Bangalore S, Kumar S, Wetterslev J, et al. Carotid artery stenting vs. carotid endarterectomy: meta-analysis and diversity-adjusted trial sequential analysis of randomized trials. Arch Neurol. 2011; 68(2):172-184.
8. Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. N Engl J Med. 1998; 339(20):1415-1425.
9. Becske T, Kallmes DF, Saatci I, et al. Pipeline for uncoilable or failed aneurysms: results from a multicenter clinical trial. Radiology. 2013; 267(3):858-868.
10. Biondi A, Janardhan V, Katz JM, et al. Neuroform stent-assisted coil embolization of wide-neck intracranial aneurysms: strategies in stent deployment and midterm follow-up. Neurosurgery. 2007; 61(3):460-468.
11. Bowser AN, Bandyk DF, Evans A, et al. Outcome of carotid stent-assisted angioplasty versus open surgical repair of recurrent carotid stenosis. J Vascu Surg. 2003; 38(3):432-438.
12. Brahmanandam S, Ding EL, Conte MS, et al. Clinical results of carotid artery stenting compared with carotid endarterectomy. J Vasc Surg. 2008; 47(2):343-349.
13. Brooks WH, McClure RR, Jones MR, et al. Carotid angioplasty and stenting versus carotid endarterectomy for treatment of asymptomatic carotid stenosis: a randomized trial in a community hospital. Neurosurgery. 2004; 54(2):318-325.
14. Brott TG, Brown RD Jr, Meyer FB, et al. Carotid revascularization for prevention of stroke: carotid endarterectomy and carotid artery stenting. Mayo Clinic Proc. September, 2004; 79(9):1197-1208.
15. Brott TG, Hobson RW 2nd, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med. 2010; 363(1):11-23.
16. Brott TG, Howard G, Roubin GS, et al. Long-term results of stenting versus endarterectomy for carotid-artery stenosis. N Engl J Med. 2016; 374(11):1021-1031.
17. Brown MM. Carotid artery stenting – evolution of a technique to rival carotid endarterectomy. Am J Med. 2004; 116(4):273-275.
18. Bush RL, Lin PH, Bianco CC, et al. Carotid artery stenting in a community setting: experience outside of a clinical trial. Ann Vasc Surg. 2003; 17(6):629-634.
19. Caplan LR, Meyers PM, Schumacher HC. Angioplasty and stenting to treat occlusive vascular disease. Rev Neurol Dis. 2006; 3(1):8-18.
20. CAVATAS Investigators. Endovascular versus surgical treatment in patients with carotid stenosis in the carotid and vertebral artery transluminal angioplasty study (CAVATAS): a randomized trial. Lancet. 2001; 357(9270):1729-1737.
21. Chaturvedi S, Fessler R. Angioplasty and stenting for stroke prevention: good questions that need answers. Neurology. 2002; 59(5):664-668.
22. Chaudhry SA, Watanabe M, Qureshi AI. The new standard for performance of intracranial angioplasty and stent placement after Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis (SAMMPRIS) Trial. Am J Neuroradiol. 2011; 32(11):E214.
23. Chimowitz MI, Lynn MJ, Derdeyn CP, et al. Stenting versus aggressive medical therapy for intracranial arterial stenosis. N Engl J Med. 2011; 365(11):993-1003.
24. Cloud GC, Crawley F, Clifton A, et al. Vertebral artery origin angioplasty and primary stenting: safety and restenosis rates in a prospective series. J Neurol Neurosurg Psychiatry. 2003; 74(5):586-590.
25. Cloud GC, Markus HS. Vertebral artery stenosis. Curr Treat Options Cardiovasc Med. 2004; 6(2):121-127.
26. Compter A, van der Worp HB, Schonewille WJ, et al. Stenting versus medical treatment in patients with symptomatic vertebral artery stenosis: a randomized open-label phase 2 trial. Lancet Neurol. 2015; 14(6):606-614.
27. Cremonesi A, Manetti R, Setacci F, et al. Protected carotid stenting: clinical advantages and complications of embolic protection devices in 442 consecutive patients. Stroke. 2003; 34(8):1936-1941.
28. Curry TK, Messina LM. Fibromuscular dysplasia; when is intervention warranted? Semin Vasc Surg. 2003; 16(3):190-199.
29. de Havenon A, Sheth K, Johnston KC, et al. Acute ischemic stroke interventions in the United States and racial, socioeconomic, and geographic disparities. Neurology. 2021; 97(23):e2292-e2303.
30. Derdeyn CP, Chimowitz MI. Angioplasty and stenting for atherosclerotic intracranial stenosis: rationale for a randomized clinical trial. Neuroimag Clin N Am. 2007; 17(3):355-363.
31. Derdeyn CP, Chimowitz MI, Lynn MJ, et al.; Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis Trial Investigators. Aggressive medical treatment with or without stenting in high-risk patients with intracranial artery stenosis (SAMMPRIS): the final results of a randomized trial. Lancet. 2014; 383(9914):333-341.
32. Dietz A, Berkefeld J, Theron JG, et al. Endovascular treatment of symptomatic carotid stenosis using stent placement: long-term follow-up of patients with a balanced surgical risk/benefit ratio. Stroke. 2001; 32(8):1855-1859.
33. Doerfler A, Becker W, Wanke I, et al. Endovascular treatment of cerebrovascular disease. Curr Opin Neurol. 2004; 17(4):481-487.
34. Eckstein HH, Ringleb P, Allenberg JR, et al. Results of the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) study to treat symptomatic stenoses at 2 years: a multinational, prospective, randomized trial. Lancet Neurol. 2008; 7(10):893-902.
35. Economopoulos KP, Sergentanis TN, Tsivgoulis G, et al. Carotid artery stenting versus carotid endarterectomy: a comprehensive meta-analysis of short-term and long-term outcomes. Stroke. 2011; 42(3):687-692.
36. Ederle J, Dobson J, Featherstone RL, et al. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study) ICSS: an interim analysis of a randomized controlled trial. Lancet. 2010; 375(9719):985-997.
37. Fiorella D, Albuquerque FC, Han P, McDougall CG. Preliminary experience using the NeuroForm stent for the treatment of cerebral aneurysms. Neurosurgery. 2004; 54(1):6-17.
38. Fiorella D, Chow MM, Anderson M, et al. A 7-year experience with balloon-mounted coronary stents for the treatment of symptomatic vertebrobasilar intracranial atheromatous disease. Neurosurgery. 2007; 61(2):236-42; discussion 242-3.
39. Fiorella D, Levy EI, Turk AS, et al. US multicenter experience with the wingspan stent system for the treatment of intracranial atheromatous disease: periprocedural results. Stroke. 2007; 38(3):881-887.
40. Fox DJ Jr, Moran CJ, Cross DT 3rd, et al. Long-term outcomes after angioplasty for symptomatic extracranial carotid stenosis in poor surgical candidates. Stroke. 2002; 33(12):2877-2880.
41. Gable DR, Bergamini T, Garrett WV, et al. Intermediate follow up of carotid artery stent placement. Am J Surg. 2003; 185(3):183-187.
42. Gao P, Wang T, Wang D, et al. Effect of stenting plus medical therapy vs medical therapy alone on risk of stroke and death in patients with symptomatic intracranial stenosis (CASSISS). JAMA. 2022; 328(6):534-542.
43. Gasparis AP, Ricotta L, Cuadra SA, et al. High-risk carotid endarterectomy: fact or fiction. J Vasc Surg. 2003; 37(1):40-46.
44. Geyik S, Yavuz K, Yurttutan N, et al. Stent-assisted coiling in endovascular treatment of 500 consecutive cerebral aneurysms with long-term follow-up. Am J Neuroradiol. 2013; 34(11):2157-2162.

45. Gray WA Hopkins LN, Yadav S, et al. Protected carotid stenting in high-surgical risk patients: the ARCHeR results. J Vasc Surg. 2006; 44(2):258-269.
46. Gray WA, Yadav JS, Verta P et al. The CAPTURE registry: results of carotid stenting with embolic protection in the post approval setting. Catheter Cardiovasc Interv. 2007; 69(3):341-348.
47. Gress DR, Smith WS, Dowd CF, et al. Angioplasty for intracranial symptomatic vertebrobasilar ischemia. Neurosurgery. 2002; 51(1):23-29.
48. Gupta R, Schumacher HC, Mangla S, et al. Urgent endovascular revascularization for symptomatic intracranial atherosclerotic stenosis. Neurology. 2003; 61(12):1729-1735.
49. Gurm HS, Yadav JS, Fayad P, et al. Long-term results of carotid stenting versus endarterectomy in high-risk patients. N Engl J Med. 2008; 358(15):1572-1579.
50. Hanel RA, Levy EL, Guterman LR, Hopkins LN. Intracranial atherosclerotic disease: common, dangerous and treatable. Clin Neurosurg. 2005; 52:68-75.
51. Hartmann M, Jansen O. Angioplasty and stenting of intracranial stenosis. Curr Opin Neurol. 2005; 18(1):39-45.
52. Hasani Z, Keunen RWM, Tavy DLJ, et al. Safety and effectiveness of selective carotid angioplasty prior to cardiac surgery: A single-center matched case-control study. Interact Cardiovasc Thorac Surg. 2018; 26(5):834-839.
53. Higashida RT, Meyers PM. Intracranial angioplasty and stenting for cerebral atherosclerosis: new treatments are needed! Neuroradiology. 2006; 48(6):367-372.
54. Hobson RW 2nd. Carotid artery stenting. Surg Clin North Am. 2004a; 84(5):1281-1294, vi.
55. Hobson RW 2nd. Rationale and status of randomized controlled clinical trials in carotid artery stenting. Semin Vasc Surg. 2003a; 16(4):311-316.
56. Hobson RW 2nd. Update on the Carotid Revascularization Endarterectomy versus Stent Trial (CREST) protocol. J Am Coll Surg. 2002; 194(1 Suppl):S9-S14.
57. Hobson RW 2nd, Brott TG, Roubin GS, et al. Closure of the lead-in phase of CREST (Carotid Revascularization Endarterectomy vs. Stenting trial): 30-day and one year analysis. Stroke. 2008; 39(2):557.
58. Hobson RW 2nd, Howard VJ, Roubin GS, et al.; CREST Investigators. Carotid artery stenting is associated with increased complications in octogenarians: 30-day stroke and death rates in the CREST lead-in phase. J Vasc Surg. 2004b; 40(6):1106-1111.
59. Hobson RW 2nd, Lal BK, Chakhtoura E, et al. Carotid artery stenting: analysis of data for 105 patients at high risk. J Vasc Surg. 2003b; 37(6):1234-1239.
60. Howard G, Roubin GS, Jansen O, et al. Association between age and risk of stroke or death from carotid endarterectomy and carotid stenting: a meta-analysis of pooled patient data from four randomized trials. Lancet. 2016; 387(10025):1305-1311.
61. Hulsbergen AFC, Mirzaei L, van der Boog ATL, et al. Long-term durability of open surgical versus endovascular repair of intracranial aneurysms: A systematic review and meta-analysis. World Neurosurg. 2019; 132:e820-e833.
62. Iyer SS, White CJ, Hopkins LN, et al. Carotid artery revascularization in high-surgical-risk patients using the Carotid WALLSTENT and FilterWire EX/EZ: 1-year outcomes in the BEACH Pivotal Group. J Am Coll Cardiol. 2008; 51(4):427-434.
63. Jestaedt L, Pham M, Bartsch AJ, et al. The impact of balloon angioplasty on the evolution of vasospasm-related infarction after aneurysmal subarachnoid hemorrhage. Neurosurgery. 2008; 62(3):610-617.
64. Jiang H, Ni W, Xu B, et al. Outcome in adult patients with hemorrhagic moyamoya disease after combined extracranial-intracranial bypass. J Neurosurg. 2014; 121(5):1048-1055.
65. Jiang WJ, Yu W, Du B, et al. Outcome of patients with ≥70% symptomatic intracranial stenosis after wingspan stenting. Stroke. 2011; 42(7):1971-1975.
66. Jordan WD, Alcocer F, Wirthlin DJ, et al. High-risk carotid endarterectomy: challenges for carotid stent protocols. J Vasc Surg. 2002; 35(1):16-22.
67. Jun P, Ko NU, English JD, et al. Endovascular treatment of medically refractory cerebral vasospasm following aneurysmal subarachnoid hemorrhage. Am J Neuroradiol. 2010; 31(10):1911-1916.
68. Kadkhodayan Y, Rhodes N, Blackburn S, et al. Comparison of Enterprise with Neuroform stent-assisted coiling of intracranial aneurysms. AJR Am J Roentgenol. 2013; 200(4):872-878.
69. Kashyap VS, King AH, Foteh MI, et al. A multi-institutional analysis of transcarotid artery revascularization compared to carotid endarterectomy. J Vasc Surg. 2019; 70:123-129.
70. Kashyap VS, Schneider PA, Foteh M, et al. Early outcomes in the ROADSTER 2 study of transcarotid artery revascularization in patients with significant carotid artery disease. Stroke. 2020; 51(9):2620-2629.
71. Kastrup A, Groschel K, Krapf H, et al. Early outcome of carotid angioplasty and stenting with and without cerebral protection devices: a systemic review of the literature. Stroke. 2003; 34(3):813-819.
72. Katzen BT, Criado FJ, Ramee SR, et al. Carotid artery stenting with emboli protection surveillance study: thirty-day results of the CASES-PMS study. Catheter Cardiovasc Interv. 2007; 70(2):316-323.
73. Khatri R, Memon MZ, Zacharatos H, et al. Impact of percutaneous transluminal angioplasty for treatment of cerebral vasospasm on subarachnoid hemorrhage patient outcomes. Neurocrit Care. 2011; 15(1):28-33.
74. Kim Y, Sharrief A, Kwak MJ, et al. Underutilization of endovascular therapy in black patients with ischemic stroke: An analysis of state and nationwide cohorts. Stroke. 2022; 53(3):855-863.
75. Komotar RJ, Mocco J, Wilson DA, et al. Current endovascular treatment options for intracranial carotid artery atherosclerosis. Neurosurg Focus. 2005; 18(1):e5.
76. Kwolek CJ, Jaff MR, Leal JI, et al. Results of the ROADSTER multicenter trial of transcarotid stenting with dynamic flow reversal. J Vasc Surg. 2015; 62(5):1227-1234.
77. Lackey AR, Erben Y, Da Rocha Franco JA, et al. Transcarotid artery revascularization results in low rates of periprocedural neurologic events, myocardial infarction, and death. Curr Cardiol Rep. 2020; 22(1):3.
78. Lal BK, Hobson RW 2nd. Treatment of carotid artery disease: stenting or surgery. Curr Neurol Neurosci Rep. 2007; 7(1):49-53.
79. Levy EI, Horowitz MB, Koebbe CJ, et al. Transluminal stent-assisted angioplasty of the intracranial vertebrobasilar system for medically refractory, posterior circulation ischemia: early results. Neurosurgery. 2001; 48(6):1215-1223.
80. Levy EI, Siddiqui AH, Crumlish A, et al. First Food and Drug Administration-approved prospective trial of primary intracranial stenting for acute stroke -- SARIS (Stent-Assisted Recanalization in Acute Ischemic Stroke). Stroke. 2009; 40:3552-3556.
81. Liang P, Wu WW, Schermerhorn ML. Recent advances in the treatment of carotid artery disease. J Cardiovasc Surg (Torino). 2019; 60(3):345-353.
82. Luebke T, Aleksic M, Brunkwall J. Meta-analysis of randomized trials comparing carotid endarterectomy and endovascular treatment. Eur J Vasc Endovasc Surg. 2007; 34(4):470-479.
83. Lifante I, Hirsh JA, Selim M, et al. Safety of latest-generation self-expanding stents in patients with NASCET-ineligible severe symptomatic extracranial internal carotid artery stenosis. Arch Neurol. 2004; 61(1):39-43.
84. Lv X, Zhang Y, Jiang W. Systematic review of Woven EndoBridge for wide-necked bifurcation aneurysms: complications, adequate occlusion rate, morbidity, and mortality. World Neurosurg. 2018; 110:20-25.
85. Lylyk P, Vila JF, Miranda C, et al. Partial aortic obstruction improves cerebral perfusion and clinical symptoms in patients with symptomatic vasospasm. Neurol Res. 2005; 27 Suppl 1:S129-S135.

86. Malik AM, Vora NA, Lin R, et al. Endovascular treatment of tandem extracranial/intracranial anterior circulation occlusions: preliminary single-center experience. Stroke. 2011; 42(6):1653-1657.
87. Marks MP, Marcellus ML, Do HM, et al. Intracranial angioplasty without stenting for symptomatic atherosclerotic stenosis: Long-term follow-up. AJNR Am J Neuroradiol. 2005; 26(3):525-530.
88. Markus HS, Larsson SC, Kuker W, et al. Stenting for symptomatic vertebral artery stenosis: The Vertebral Artery Ischemia Stenting Trial. Neurology. 2017; 89(12):1229-1236.
89. Mas JL, Chatellier G, Beyssen B, et al.; EVA-3S Investigators. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. N Engl J Med. 2006; 355(16):1660-1671.
90. Mas JL, Trinquart L, Leys D, et al. EVA-3S Investigators. Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial: results up to 4 years from a randomized, multicenter trial. Lancet Neurol. 2008; 7(10):885-892.
91. McCabe DJ, Pereira AC, Clifton A, et al. Restenosis after carotid angioplasty, stenting or endarterectomy in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS). Stroke. 2005; 36(2):281-286.
92. Mocco J, Snyder KV, Albuquerque FC, et al. Treatment of intracranial aneurysms with the Enterprise stent: a multicenter registry. J Neurosurg. 2009; 110(1):35-39.
93. Molyneux AJ, Kerr RSC, Birks J, et al. Risk of recurrent subarachnoid hemorrhage, death or dependence and standardized mortality ratios after clipping or coiling of an intracranial aneurysm in the International Subarachnoid Aneurysm Trial (ISAT): long term follow-up. Lancet Neurol. 2009; 8(5):427-433.
94. Mukherjee D, Yadav JS. Percutaneous treatment for carotid stenosis. Cardiol Clin. 2002; 20(4):589-597.
95. Murad MH, Shahrour A, Shah ND, et al. A systematic review and meta-analysis of randomized trials of carotid endarterectomy vs. stenting. J Vasc Surg. 2011; 53(3):792-797.
96. Murai Y, Kominami S, Kobayashi S, et al. The long-term effects of transluminal balloon angioplasty for vasospasms after subarachnoid hemorrhage: analyses of cerebral blood flow and reactivity. Surg Neurol. 2005; 64(2):122-126; discussion 127.
97. Murayama Y, Nien YL, Duckwiler G, et al. Guglielmi detachable coil embolization of cerebral aneurysms: 11 years' experience. J Neurosurg. 2003; 98(5):959-966.
98. Naazie IN, Cui CL, Osaghae I, et al. A systematic review and meta-analysis of transcarotid artery revascularization with dynamic flow reversal versus transfemoral carotid artery stenting and carotid endarterectomy. Ann Vasc Surg. 2020; 69:426-436.
99. Naylor AR, Bolia A, Abbott RJ, et al. Randomized study of carotid angioplasty and stenting versus carotid endarterectomy: a stopped trial. J Vasc Surg. 1998; 28(2):326-334.
100. Paniagua D, Howell M, Strickman N, et al. Outcomes following extracranial carotid artery stenting in high-risk Patients. J Invasive Cardiol. 2001; 13(5):375-381.
101. Park ST, Kim JK, Yoon KH, et al. Atherosclerotic carotid stenoses of apical versus body lesions in high-risk carotid stenting patients. AJNR Am J Neuroradiol. 2010; 31(6):1106-1112.
102. Perler BA. Carotid endarterectomy: the "gold standard" in the endovascular era. J Am Coll Surg. 2002; 194(1 Suppl):S2-8.
103. Pierot L, Cognard C, Ricolfi F, et al.; CLARITY Investigators. Immediate anatomic results after the endovascular treatment of ruptured intracranial aneurysms: analysis in the CLARITY Series. AJNR Am J Neuroradiol. 2010; 31(5):907-911.
104. Piotin M, Blanc R, Spelle L, et al. Stent-assisted coiling of intracranial aneurysms: clinical and angiographic results in 216 consecutive aneurysms. Stroke. 2010; 41(1):110-115.
105. Powers WJ, Clarke WR, Grubb RL Jr, et al; COSS Investigators. Extracranial-intracranial bypass surgery for stroke prevention in hemodynamic cerebral ischemia: the Carotid Occlusion Surgery Study randomized trial. JAMA. 2011; 306(18):1983-1992.
106. Qureshi AI, Al-Senani FM, Husain S, et al. Intracranial angioplasty and stent placement after stenting and aggressive medical management for preventing recurrent stroke in intracranial stenosis (SAMMPRIS) trial: present state and future considerations. J Neuroimaging. 2012; 22(1):1-13.
107. Qureshi AI, Knape C, Maroney M, et al. Multicenter clinical trial of the NexStent coiled sheet stent in the treatment of extracranial carotid artery stenosis: immediate results and late clinical outcomes. J Neurosurg. 2003; 99(2):264-270.
108. Raja PV, Huang J, Germanwala AV, et al. Microsurgical clipping and endovascular coiling of intracranial aneurysms: a critical review of the literature. Neurosurgery. 2008; 62(6):1187-1202; discussion 1202-1203.
109. Reimers B, Schluter M, Castriota F, et al. Routine use of cerebral protection during carotid artery stenting: results of a multi-center registry of 753 patients. Am J Med. 2004; 116(4):217-222.
110. Ringleb PA, Allenberg J, Bruckmann H, et al.; SPACE Collaborative Group. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomized non-inferiority trial. Lancet. 2006; 368(9543):1239-1247.
111. Ringleb PA, Chatellier G, Hacke W, et al. Safety of endovascular treatment of carotid artery stenosis compared with surgical treatment: a meta-analysis. J Vasc Surg. 2008; 47(2):350-355.
112. Rockman CB, Su W, Lamparello, PJ, et al. A reassessment of carotid endarterectomy in the face of contralateral carotid occlusion: surgical results in symptomatic and asymptomatic patients. J Vasc Surg. 2002; 36(4):668-673.
113. Rosenfield K, Matsumura JS, Chaturvedi S, et al. Randomized trial of stent versus surgery for asymptomatic carotid stenosis. N Engl J Med. 2016; 374(11):1011-1020.
114. Roubin GS, New G, Iyer SS, et al. Immediate and late clinical outcomes of carotid artery stenting in patients with symptomatic and asymptomatic carotid artery stenosis. Circulation. 2001; 103(4):532-537.
115. Santillan A, Greenberg E, Patsalides A, et al. Long-Term Clinical and Angiographic Results of Neuroform Stent-Assisted Coil Embolization in Wide-Necked Intracranial Aneurysms. Neurosurgery. 2012; 70(5):1232-1237.
116. Shapiro M, Becske T, Sahlein D, et al. Stent-supported aneurysm coiling: a literature survey of treatment and follow-up. Am J Neuroradiol. 2012; 33(1):159-163.
117. Shawl FA. Carotid artery stenting: acute and long-term results. Curr Opin Cardiol. 2002; 17(6):671-676.
118. Sheriff F, Xu H, Maud A, et al. Temporal trends in racial and ethnic disparities in endovascular therapy in acute ischemic stroke. J Am Heart Assoc. 2022; 11(6):e023212.
119. Siddiq F, Memon MZ, Vazquez G, et al. Comparison between primary angioplasty and stent placement for symptomatic intracranial atherosclerotic disease: meta-analysis of case series. Neurosurgery. 2009; 65(6):1024-1033.
120. Silver FL, Mackey A, Clark WM, et al. Safety of stenting and endarterectomy by symptomatic status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST). Stroke. 2011; 42(3):675-680.
121. Slovut DP, Olin JW. Fibromuscular dysplasia. N Engl J Med. 2004; 350(18):1862-1871.
122. Spes CH, Schwende A, Beier F, et al. Short- and long-term outcome after carotid artery stenting with neuroprotection: single-center experience within a prospective registry. Clin Res Cardiol. 2007; 96(11):812-821.
123. SSYLVIA Study Investigators. Stenting of symptomatic atherosclerotic lesions in the vertebral or intracranial arteries (SSYLVIA): study results. Stroke. 2004; 35(6):1388-1392.
124. Steinbauer MG, Pfister K, Greindl M, et al. Alert for increased long-term follow-up after carotid artery stenting: results of a prospective, randomized, single-center trial of carotid artery stenting vs. carotid endarterectomy. J Vasc Surg. 2008; 48(1):93-98.
125. Stolker JM, Mahoney EM, Safley DM, et al.; SAPPHIRE Investigators. Health-related quality of life following carotid stenting

versus endarterectomy: results from the SAPPHIRE (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) trial. JACC Cardiovasc Interv. 2010; 3(5):515-523.
126. Tau N, Sadeh-Gonik U, Aulagner G, et al. The Woven EndoBridge (WEB) for endovascular therapy of intracranial aneurysms: Update of a systematic review with meta-analysis. Clin Neurol & Neurosurg. 2018; 166: 110–115.
127. Timaran CH, Veith FJ, Rosero EB, et al. Intracranial hemorrhage after carotid endarterectomy and carotid stenting in the United States in 2005. J Vasc Surg. 2009; 49(3):623-629.
128. Turowski B, du Mesnil de Rochemont R, Beck J, et al. Assessment of changes in cerebral circulation time due to vasospasm in a specific arterial territory: effect of angioplasty. Neuroradiology. 2005; 47(2):134-143.
129. van Haaften AC, Bots ML, Moll FL, de Borst GJ. Therapeutic options for carotid in-stent restenosis: review of the literature. J Vasc Interv Radiol. 2010; 21(10):1471-1477.
130. Velat GJ, Kimball MM, Mocco JD, Hoh BL. Vasospasm after aneurysmal subarachnoid hemorrhage: review of randomized controlled trials and meta-analyses in the literature. World Neurosurg. 2011; 76(5):446-454.
131. Veldeman M, Hollig A, Clusmann H, et al. Delayed cerebral ischemia prevention and treatment after aneurysmal subarachnoid hemorrhage: A systematic review. Br J Anaesth. 2016; 117(1):17-40.
132. Wajnberg E, de Souza JM, Marchiori E, et al. Single-center experience with the Neuroform stent for endovascular treatment of wide-necked intracranial aneurysms. Surg Neurol. 2009; 72(6):612-619.
133. Wang SK, Severance S, Westin GG, et al. Perioperative and 1-year transcarotid revascularization outcomes in symptomatic patients. J Vasc Surg. 2020; 72(6):P2047-2053.
134. Weinberg I, Beckman JA, Matsumura JS, et al. Carotid Stent Fractures are not associated with adverse events: Results from the ACT-1 Multicenter Randomized Trial (Carotid Angioplasty and Stenting versus Endarterectomy in Asymptomatic Subjects who are at standard risk for carotid endarterectomy with significant extracranial carotid stenotic disease). Circ. 2018; 137(1):49-56.
135. Wiebers DO, Whisnant JP, Huston J 3rd, et al., International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet. 2003; 362(9378):103-110.
136. Yadav JS, Wholey MH, Kuntz RE, et al.; Stenting and Angioplasty with Protection in Patients at High risk for Endarterectomy Investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 2004; 351(15):1493-1501.
137. Yaghi S, Khatri P, de Havenon A, et al. Peri-procedural stroke or death in stenting of symptomatic severe intracranial stenosis. J Neurointerv Surg. 2020; 12(4):374-379.
138. Yu W, Smith WS, Singh V, et al. Long-term outcome of endovascular stenting for symptomatic basilar artery stenosis. Neurology. 2005; 64(6):1055-1057.
139. Zaidat OO, Smith TP, Alexander MJ. Long-term outcome of endovascular stenting for symptomatic basilar artery stenosis. Neurology. 2005; 65(8):1340-1341.
140. Zhang SM, Liu LX, Ren PW, et al. Effectiveness, Safety and Risk Factors of Woven EndoBridge Device in the Treatment of Wide-Neck Intracranial Aneurysms: Systematic Review and Meta-Analysis. World Neurosurg. 2020; 136:e1-e23.
141. Zwienenberg-Lee M, Hartman J, Rudisill N, et al.; Balloon Prophylaxis for Aneurysmal Vasospasm (BPAV) Study Group. Effect of prophylactic transluminal balloon angioplasty on cerebral vasospasm and outcome in patients with Fisher grade III subarachnoid hemorrhage: results of a phase II multicenter, randomized, clinical trial. Stroke. 2008; 39(6):1759-1765.

**Government Agency, Medical Society, and Other Authoritative Publications:**

1. AbuRahma AF, Avgerinos EM, Chang RW, et al. Society for Vascular Surgery (SVS). Clinical Practice Guidelines for Management of Extracranial Cerebrovascular Disease. J Vasc Surg. 2022; 75:4S-22S.
2. Barr JD, Connors JJ 3rd, Sacks D, et al. Joint Standards of Practice Committee of the American Society of Interventional and Therapeutic Neuroradiology, the American Society of Neuroradiology, and the Society of Interventional Radiology. Quality improvement guidelines for the performance of cervical carotid angioplasty and stent placement. J Vasc Interv Radiol. 2003; 14(9 Pt 2):S321-S335.
3. Bates ER, Babb JD, Casey DE Jr, et al. American College of Cardiology Foundation Task Force; American Society of Interventional & Therapeutic Neuroradiology; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Society for Interventional Radiology (ACCF/SCAI/SVMB/SIR/ASITN). 2007 Clinical Expert Consensus Document on carotid stenting. Vasc Med. 2007; 12(1):35-83.
4. Bettman MA, Katzen BT, Whisnat J, et al. Carotid stenting and angioplasty: a statement for healthcare professionals from the Councils on Cardiovascular Radiology, Stroke, Cardio-Thoracic and Vascular Surgery, Epidemiology and Prevention, and Clinical Cardiology, American Heart Association. Circulation. 1998: 97(1): 121-123.
5. Blue Cross Blue Shield Association. Angioplasty and stenting of the cervical carotid artery with distal embolic protection of the cerebral circulation. TEC Assessment, 2004; 19(15).
6. Blue Cross Blue Shield Association. Angioplasty and stenting of the cervical carotid artery with embolic protection of the cerebral circulation. TEC Assessment, 2007; 24(1).
7. Blue Cross Blue Shield Association. Angioplasty and stenting of the cervical carotid artery with embolic protection of the cerebral circulation. TEC Assessment, 2012; 24(12).
8. Bonati LH, Lyrer P, Ederle J, et al. Percutaneous transluminal balloon angioplasty and stenting for carotid artery stenosis. Cochrane Database Syst Rev. 2012; (4):CD000515.
9. Brott TG, Halperin JL, Abbara S et al. 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS Guideline on the Management of Patients With Extracranial Carotid and Vertebral Artery Disease. Stroke. 2011; 42(8):e464-e540.
10. CaRESS Steering Committee. Carotid revascularization using endarterectomy or stenting systems (CaRESS) phase I clinical trial: one year results. J Vasc Surg. 2005; 42(2):213-219.
11. Centers for Medicare & Medicaid Services (CMS). National Coverage Determination. Available at: https://www.cms.gov/medicare-coverage-database/search.aspx. Accessed on July 19, 2023.
    - Percutaneous Transluminal Angioplasty. NCD #20.7. Medicare Coverage Database. Rockville, MD: CMS, December 9, 2009.
    - Vertebral Artery Surgery. NCD #20.1. Medicare Coverage Database. Rockville, MD: CMS. Effective date not posted.
12. Chaturvedi S, Bruno A, Feasby T, et al. Carotid endarterectomy–an evidence based review: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2005; 65(9):794-801.
13. Connolly ES Jr, Rabinstein AA, Carhuapoma JR, et al.; American Heart Association Stroke Council; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; Council on Cardiovascular Surgery and Anesthesia; Council on Clinical Cardiology. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2012; 43(6):1711-1737.

14. Connors JJ 3rd, Sacks D, Furlan AJ, et al. NeuroVascular Coalition Writing Group; American Academy of Neurology; American Association of Neurological Surgeons; American Society of Interventional and Therapeutic Radiology; American Society of Neuroradiology; Congress of Neurological Surgeons; AANS/CNS Cerebrovascular Section; Society of Interventional Radiology. Training, competency, and credentialing standards for diagnostic cervicocerebral angiography, carotid stenting, and cerebrovascular intervention: a joint statement from the American Academy of Neurology, American Association of Neurological Surgeons, American Society of Interventional and Therapeutic Radiology, American Society of Neuroradiology, Congress of Neurological Surgeons, AANS/CNS Cerebrovascular Section, and Society of Interventional Radiology. Radiology. 2005; 234(1):26-34.
15. Coward LJ, Featherstone RL, Brown MM. Percutaneous transluminal angioplasty and stenting for vertebral artery stenosis. Cochrane Database Syst Rev. 2005;(2):CD000516.
16. Cruz-Flores S, Diamond AL. Angioplasty for intracranial artery stenosis. Cochrane Database Syst Rev. 2006; (3):CD004133.
17. Diringer MN, Bleck TP, Claude Hemphill J, et al.; Neurocritical Care Society. Critical care management of patients following aneurysmal subarachnoid hemorrhage: Recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference. Neurocrit Care. 2011; 15(2):211-240.
18. Ederle J, Featherstone RL, Brown MM. Randomized controlled trials comparing endarterectomy and endovascular treatment for carotid artery stenosis: a Cochrane systematic review. Stroke. 2009; 40(4):1373-1380.
19. Eskey CJ, Meyers PM, Nguyen TN, et al. Indications for the performance of intracranial endovascular neurointerventional procedures: A scientific statement from the American Heart Association. Circ. 2018; 137(21):e661-e689.
20. Goldstein LB, Bushnell CD, Adams RJ, et al.; American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Epidemiology and Prevention, Council for High Blood Pressure Research, Council on Peripheral Vascular Disease, and Interdisciplinary Council on Quality of Care and Outcomes Research. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011; 42(2):517-584.
21. Higashida RT, Meyers PM, Connors JJ, et al. Intracranial angioplasty and stenting for cerebral atherosclerosis: a position statement of the American Society of Interventional and Therapeutic Neuroradiology, Society of Interventional Radiology and the American Society of Neuroradiology. AJNR Am J Neuroradiol. 2005; 26(9):2323-2327.
22. Higashida RT, Meyers PM, Phatouros CC, et al.; Technology Assessment Committees of the American Society of Interventional and Therapeutic Neuroradiology and the Society of Interventional Radiology. Reporting standards for carotid artery angioplasty and stent placement. J Vasc Interv Radiol. 2004; 15(5):421-422.
23. Hussain MS, Fraser JF, Abruzzo T, et al.; Society for NeuroInterventional Surgery. Standard of practice: endovascular treatment of intracranial atherosclerosis. J Neurointerv Surg. 2012; 4(6):397-406.
24. Jauch EC, Saver JL, Adams HP Jr, et al.; American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Peripheral Vascular Disease, and Council on Clinical Cardiology. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013; 44(3):870-947.
25. Jonas DE, Feltner C, Amick HR, et al. Screening for Asymptomatic Carotid Artery Stenosis: A Systematic Review and Meta-Analysis for the U.S. Preventive Services Task Force. Evidence Synthesis No. 111. AHRQ Publication No. 13-05178-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2014.
26. Kernan W, Ovbiagele B, Black HR, et al; American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014; 45(7):2160-236.
27. Liang P, Soden P, Wyers MC, et al. The role of transfemoral carotid artery stenting with proximal balloon occlusion embolic protection in the contemporary endovascular management of carotid artery stenosis. J Vasc Surg. 2020; 72(5):1701-1710.
28. Liapis CD, Bell PR, Mikhailidis D, et al.; ESVS Guidelines Collaborators. ESVS guidelines. Invasive treatment for carotid stenosis: indications, techniques. Eur J Vasc Endovasc Surg. 2009; 37(4 Suppl):1-19.
29. Luo J, Wang T, Yang K, et al. Endovascular therapy versus medical treatment for symptomatic intracranial artery stenosis. Cochrane Database Syst Rev. 2023; 2(2):CD013267.
30. Malas MB, Dakour-Aridi H, Wang GJ, et al. Transcarotid artery revascularization versus transfemoral carotid artery stenting in the Society for Vascular Surgery Vascular Quality Initiative. J Vasc Surg. 2019; 69(1):92-103.
31. Mazighi M, Tanasescu R, Ducrocq X, et al. Prospective study of asymptomatic atherothrombotic intracranial stenoses: the GESICA study. Neurology. 2006; 66(8):1187-1191.
32. Medical University of South Carolina. Stenting vs. Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS). National Library of Medicine (NLM) Identifier: NCT00576693. Last updated May 30, 2018. Available at: http://clinicaltrials.gov/ct2/show/study/NCT00576693?term=SAMMPRIS&rank=1#locn. Accessed on July 19, 2023.
33. Meyers PM, Schumacher HC, Higashida RT, et al. Indications for the performance of intracranial endovascular neurointerventional procedures: A scientific statement from the American Heart Association Council on Cardiovascular Radiology and Intervention, Stroke Council, Council on Cardiovascular Surgery and Anesthesia, Interdisciplinary Council on Peripheral Vascular Disease, and Interdisciplinary Council on Quality of Care and Outcomes Research. Circulation. 2009; 119(16):2235-2249.
34. Ricotta JJ, AbuRahma A, Ascher E, et al. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease. J Vasc Surg. 2011; 54(3):e1-e31.
35. Sacco RL, Adams R, Albers G, et al. AHA/ASA Guidelines. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: The American Academy of Neurology affirms the value of this guideline. Stroke. 2006; 37(2):577-617.
36. Salzler GG, Farber A, Rybin DV, et al. The association of Carotid Revascularization Endarterectomy versus Stent Trial (CREST) and Centers for Medicare and Medicaid Services Carotid Guideline publication on utilization and outcomes of carotid stenting among "high-risk" patients. J Vasc Surg. 2017; 66(1):104-111 e101.
37. Schermerhorn ML, Liang P, Dakour-Aridi H, et al. In-hospital outcomes of transcarotid artery revascularization and carotid endarterectomy in the Society for Vascular Surgery Vascular Quality Initiative. J Vasc Surg. 2020; 71(1):87-95.
38. Silk Road Medical. Post-approval study of Transcarotid Artery Revascularization in patients with significant carotid artery disease. NCT02536378. Last updated July 29, 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT02536378. Accessed on July 22, 2023.
39. Silk Road Medical. The ENROUTE Transcarotid Neuroprotection System (ENROUTE Transcarotid NPS) DW-MRI Evaluation (DW-MRI-US). NCT03982420. Last updated May 9, 2022. Available at: https://clinicaltrials.gov/ct2/show/NCT03982420. Accessed on July 22, 2023.
40. Steiner T, Juvela S, Unterberg A, et al.; European Stroke Organization. European Stroke Organization guidelines for the management of intracranial aneurysms and subarachnoid hemorrhage. Cerebrovasc Dis. 2013; 35(2):93-112.
41. Stenting and angioplasty with protection in patients at high risk for endarterectomy: 3-year results (SAPPHIRE: 3 year results).

ACC Cardiosource Review Journal. 2008; 17.
42. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). New device approval. Available at: https://www.fda.gov/medical-devices. Accessed on July 20, 2023.

    - NEUROLINK® System. H020002. Approved August 9, 2002.
    - Wingspan™ Stent System with Gateway™ PTA Balloon Catheter. H050001. Approved Aug. 3, 2005.
    - Xact® Carotid Stent System. P040038. Approved Sept. 6, 2005.

43. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Summary of Safety and Effectiveness Data (SSED). ACCULINK™ Carotid Stent system; RX ACCULINK™ Carotid Stent System. August 30, 2004. P040012. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf4/p040012b.pdf. Accessed on August 15, 2023.
44. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). New device approval Summary of Safety and Effectiveness. Protege® GPSTM Carotid Stent System Protege® RX Carotid Stent System. January 21, 2015. P060001/S020. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf6/p060001s020b.pdf. Accessed on July 22, 2023.
45. U.S. Food and Drug Administration (FDA). Use of the Stryker Wingspan Stent System outside of approved indications leads to an increased risk of stroke or death: FDA Safety Communication. April 25, 2019. Available at: https://www.fda.gov/news-events/fda-brief/fda-brief-fda-reminds-health-care-professionals-about-risks-wingspan-stent-system-after-study-shows. Accessed on July 22, 2023.
46. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). New device approval letter. March 30, 2005. CoAxia NeuroFlo™ Catheter. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf3/H030005a.pdf. Accessed on July 22, 2023.
47. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). New device approval letter. May 8, 2007. ENTERPRISE™ Vascular Reconstruction Device and Delivery System. H060001. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf6/H060001A.pdf. Accessed on July 22, 2023.
48. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). Medtronic Announces Voluntary Recall of its Pipeline™ Embolization Device, Alligator™ Retrieval Device, X-Celerator™ Hydrophilic Guidewire, Ultraflow™ and Marathon™ Flow Directed Micro Catheters. October 14, 2016. Available at: https://neuronewsinternational.com/medtronic-announces-voluntary-recall-of-its-pipeline-embolization-device-alligator-retrieval-device-x-celerator-hydrophilic-guidewire-ultraflow-and-marathon-flow-directed-micro-catheters/. Accessed on July 24, 2023.
49. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). New device approval letter. December 31, 2018. Woven Endobridge (WEB)® Aneurysm Embolization System. P170032. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170032A.pdf. Accessed on July 24, 2023.
50. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). ENROUTE™ Transcarotid Stent System P140026. May 18, 2015. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf14/P140026A.pdf. Accessed on July 24, 2023.
51. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). ENROUTE® Transcarotid Neuroprotection System K153485. March 10, 2016. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf15/K153485.pdf. Accessed on July 24, 2023.
52. U.S. Food and Drug Administration (FDA). Class 2 Device Recall ENROUTE Transcarotid Stent System. P140026. February 23, 2021. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfres/res.cfm?id=185523. Accessed on July 24, 2023.
53. van der Schaaf I, Algra A, Wermer M, et al. Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid hemorrhage. Cochrane Database Syst Rev. 2005;(4):CD003085.
54. Zaidat OO, Fitzsimmons BF, Woodward BK, et al. Effect of a balloon-expandable intracranial stent vs medical therapy on risk of stroke in patients with symptomatic intracranial stenosis: the VISSIT randomized clinical trial. JAMA. 2015; 313(12):1240-1248.
55. Zaidat OO, Klucznik R, Alexander MJ, et al. National Institutes of Health (NIH). Multi-center Wingspan Intracranial Stent Registry Study Group. The NIH registry on use of the Wingspan stent for symptomatic 70-99% intracranial arterial stenosis. Neurology. 2008; 70(17):1518-1524.

## Websites for Additional Information

1. American Heart Association/American Stroke Association. Information about stroke. Available at: http://www.strokeassociation.org/STROKEORG/. Accessed on July 19, 2023.
2. Society for Vascular Surgery (SVS). Transcarotid Artery Revascularization. Available at:https://vascular.org/patients/vascular-treatments/transcarotid-artery-revascularization#description. Accessed on July 19, 2023.

## Index

**The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.**

## History

| Status | Date | Action |
|---|---|---|
| Reviewed | 08/10/2023 | Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Discussion and References sections. |
| Reviewed | 08/11/2022 | MPTAC review. The Discussion and References sections were updated. |
| Reviewed | 08/12/2021 | MPTAC review. TCAR has been added to the Scope of this document. The Discussion, References and Index sections were updated. Updated Coding section to add ICD-10-PCS codes for open procedure. |
| Reviewed | 02/11/2021 | MPTAC review. The Discussion, References and Index sections were updated. Reformatted Coding section. |
| Revised | 02/20/2020 | MPTAC review. The NMN position statements for CAS and for percutaneous stent placement with or without associated percutaneous angioplasty for stenosis and aneurysm of vertebral or intracranial vessels were reformatted for clarification with no change to stance. The Discussion and References sections were updated. |
| Reviewed | 03/21/2019 | MPTAC review. References were updated. |
| New | 05/03/2018 | MPTAC review. Moved content of SURG.00001 Carotid, Vertebral and Intracranial Artery Stent Placement with or without Angioplasty to new clinical utilization management guideline document with the same title. The References section was updated. |

---