Clinical Policy Bulletin:
Angioplasty and Stenting of Extra-Cranial and Intra-Cranial Arteries

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Policy

Aetna considers percutaneous transluminal angioplasty of the extra-cranial carotid arteries, with or without stent implantation and embolic protection, medically necessary in symptomatic individuals with at least 50% stenosis of the carotid artery.

Aetna considers percutaneous transluminal angioplasty of the extra-cranial vertebral arteries, with or without stent implantation and embolic protection, medically necessary for persons with at least 50% stenosis of the vertebral artery who are symptomatic despite optimal medical treatment (e.g., antithrombotic agents, statins, and other risk factor modifications).

Aetna considers percutaneous transluminal angioplasty of the intracranial arteries medically necessary for the treatment of medically refractory symptomatic delayed cerebral ischemia (cerebral vasospasm) after aneurysmal subarachnoid hemorrhage. Aetna considers prophylactic percutaneous transluminal angioplasty of intracranial arteries after aneurysmal subarachnoid hemorrhage experimental and investigational.

Aetna considers percutaneous transluminal angioplasty, with or without stenting, of the intra-cranial arteries experimental and investigational for the prophylaxis or treatment of atherosclerotic stenosis of intracranial arteries and for all other indications because its effectiveness for these indications has not been established:

Aetna considers endovascular repair of wide-necked intracranial aneurysms using stent-assisted embolic coiling medically necessary for otherwise inoperable aneurysms.
Aetna considers extracranial-intracranial arterial bypass surgery for the treatment of ischemic cerebrovascular disease of the carotid or middle cerebral arteries, which includes the treatment or prevention of stroke, experimental and investigational because the effectiveness of this approach has not been established.

**Background**

**Angioplasty and Stenting of Extra-Cranial Arteries:**

Angioplasty and stenting of carotid and vertebral lesions represents a promising therapeutic option in patients at increased risk for surgical endarterectomy. Endarterectomy has several limitations. Among them, patients with severe coronary artery disease show a 3-fold increase in morbidity and mortality due to cardiac complications of the procedure. Similarly, the risk of endarterectomy is increased in patients with carotid lesions that, due to their anatomic location, are difficult to approach surgically. In addition, the risk of endarterectomy is increased in patients having previous cervical radiotherapy, previous endarterectomy, or lesions located or extending distally in the internal carotid artery.

There has been a high level of interest in treating extra-cranial carotid and vertebral stenoses with either angioplasty or stents. The relative technical ease of performing such procedures has attracted considerable attention in the clinical community. Such procedures are being performed in several academic medical centers. A prospective, randomized, controlled, multicenter clinical trial designed to compare these endovascular interventions with the "gold standard" of surgical carotid endarterectomy is currently being conducted.

Although a recent study found that among patients with severe carotid artery stenosis and co-existing conditions (symptomatic carotid-artery stenosis of at least 50% of the luminal diameter or an asymptomatic stenosis of at least 80%), carotid stenting with the use of an emboli-protection device is not inferior to carotid endarterectomy (Yadav et al, 2004), the editorial accompanying this study stated that the small sample size and the study end points prevent conclusions regarding the relative roles of endarterectomy and carotid artery stenting in the treatment of carotid artery stenosis. Physicians, industry sponsors, and regulatory agencies should insist on large scale, multi-center studies to ascertain the appropriate role of carotid artery stenting in patients in different clinical and anatomical subgroups.

Debette et al (2004) stated that carotid angioplasty and stenting is sometimes used as an alternative to surgery, despite the lack of evidence for its safety and effectiveness. These investigators concluded that carotid angioplasty and stenting can not be considered as a routine procedure and should be restricted to high-risk patients unfit for surgery. Additionally, a recent Cochrane review (Coward et al, 2004) on percutaneous transluminal angioplasty and stenting for carotid artery stenosis concluded that: "Data from randomised trials comparing endovascular treatment for carotid artery stenosis with carotid endarterectomy suggest that the two treatments have similar early risks of death or stroke and similar long term benefits. However, the substantial heterogeneity renders the overall estimates of
effect somewhat unreliable. Furthermore, two trials were stopped early because of safety concerns, so perhaps leading to an over-estimate of the risks of endovascular treatment. On the other hand, endovascular treatment appears to avoid completely the risk of cranial neuropathy. There is also uncertainty about the potential for re-stenosis to develop and cause recurrent stroke after endovascular treatment. The current evidence does not support a widespread change in clinical practice away from recommending carotid endarterectomy as the treatment of choice for suitable carotid artery stenosis. There is a strong case to continue recruitment in the current randomised trials comparing carotid stenting with endarterectomy”.

In a study on indications for intervention of atherosclerotic occlusive extra-cranial vertebral artery disease, Wehman et al (2004) reported that symptomatic patients with a single, causative extra-cranial atherosclerotic vertebral artery lesion that measures more than 50% stenosis by digital subtraction angiography receive treatment with angioplasty and stenting.

The Centers for Medicare and Medicaid Services (CMS) (2005) has determined that carotid artery stenting (CAS) with distal embolic protection is necessary for the following:

1. Patients who are at high risk for carotid endarterectomy and who also have symptomatic carotid artery stenosis greater than 70%. Medicare limits coverage to procedures performed using Food and Drug Administration (FDA)-approved CAS systems and embolic protection devices;
2. Patients who are at high risk for carotid endarterectomy and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B Investigational Device Exemption (IDE) clinical trials regulation, as a routine cost under Medicare’s clinical trials policy, or in accordance with the National Coverage Determination on CAS post-approval studies;
3. Patients who are at high risk for carotid endarterectomy and have asymptomatic carotid artery stenosis greater than 80%, in accordance with the Category B IDE clinical trials regulation, as a routine cost under Medicare’s clinical trials policy, or in accordance with the National Coverage Determination on CAS post-approval studies.

The Centers for Medicare and Medicaid Services defines patients at high risk for carotid endarterectomy as having significant co-morbidities and/or anatomic risk factors (i.e., recurrent stenosis and/or previous radical neck dissection), and would be poor candidates for carotid endarterectomy (CEA) in the opinion of a surgeon. For purposes of Medicare policy, significant co-morbid conditions include but are not limited to:

1. Congestive heart failure (CHF) class III/IV;
2. Contralateral carotid occlusion;
3. Left ventricular ejection fraction (LVEF) less than 30%;
4. Other conditions that were used to determine patients at high risk for CEA in the prior carotid artery stenting trials and studies, such as ARCHER, CABERNET, SAPPHIRE, BEACH, and MAVERIC II;
5. Previous CEA with recurrent stenosis;
6. Prior radiation treatment to the neck;
7. Recent myocardial infarction (MI);
8. Unstable angina.

According to CMS, symptoms of carotid artery stenosis include carotid transient ischemic attack (distinct focal neurological dysfunction persisting less than 24 hours), focal cerebral ischemia producing a non-disabling stroke (modified Rankin scale less than 3 with symptoms for 24 hours or more), and transient monocular blindness (amaurosis fugax). The Centers for Medicare and Medicaid Services excludes patients who have had a disabling stroke (modified Rankin scale greater than 3) from eligibility for coverage of a carotid artery stent.

A CMS Decision Memorandum (2005) states that the degree of carotid artery stenosis should be measured by duplex Doppler ultrasound or carotid artery angiography and recorded in the patient medical records. If the stenosis is measured by ultrasound prior to the procedure, then the degree of stenosis must be confirmed by angiography at the start of the procedure. The Centers for Medicare and Medicaid Services states that if the stenosis is determined to be less than 70% by angiography, then CAS should not proceed.

A CMS Decision Memorandum (2007) states that "for patients who are at high risk for CEA surgery with asymptomatic carotid artery stenosis greater than 80%, several case series or registry reports and post-approval studies have been published since our prior decision which provided restricted coverage for these patients. The basis of our restricted coverage in the prior decision was the undocumented natural history of asymptomatic stenosis on medical therapy (lack of a medical control group in past studies), the lack of long term data on CAS in these patients, and the lack of data on CAS performed outside the controlled trial setting. While the outcomes of asymptomatic carotid artery stenosis with optimal medical therapy remain unclear and unstudied, the published reports provide evidence regarding our other prior concerns. The observational studies by Halabi, Chaer, Park and Safian provided supporting evidence for CAS in patients with asymptomatic stenosis greater than 80%. The post-approval studies, CAPTURE and CASES-PMS, provided additional evidence on 30-day outcomes and some information on 1 year outcomes. The post-approval studies also showed that CAS outcomes were similar by provider volume (experience levels) and in settings outside clinical trials. Unlike the situation with symptomatic patients, there were no trials or studies that raised concerns about the safety of CAS in asymptomatic patients with stenosis greater than 80%.

"With the published reports since our prior decision, CMS finds that the evidence is sufficient to conclude that PTA with carotid artery stenting improves health outcomes for patients who are at high risk for CEA surgery and have asymptomatic carotid artery stenosis > 80%. With this, CMS proposes to remove the requirement that these procedures only be performed in a clinical trial or post approval study, based largely on the findings from CAPTURE and CASES-PMS. As with the currently covered indications, facilities performing CAS for this patient group must meet the facility requirements outlined in this NCD. As discussed above, CAS is not covered in the absence of distal embolic protection including those instances in which technical difficulties prevented deployment."

The CMS Decision Memorandum (2007) also states that for patients who are greater than 80 years of age, there is mounting evidence that the rate of death,
stroke and MI after CAS is higher than for patients less than 80 years. Stanziale and colleagues reported that octogenarians had a significantly higher rate of stroke, death or MI than nonoctogenarians (9.2% versus 3.4%, respectively; p = 0.024). Safian and colleagues reported data that showed patients greater than 75 years had higher adverse outcomes than patients less than 75 (7.6% versus 4.8%). CAPTURE showed that patients greater than 80 years of age had significantly higher rates of death, stroke or MI at 30 days than patients less than 80 years (9.4% versus 5.3%, respectively; statistically significant, p < 0.0001). SPACE found that patients greater than 75 years of age had a significantly higher rate of ipsilateral ischemic stroke and death at 30 days compared to patients greater than 75 (11.01% versus 5.92%; exceeding the non-inferiority margin). Outcomes by age were not specifically reported by Chae, Halabi, Mas and Park.

"The consistency of these findings across the trials and studies, observed in both symptomatic and asymptomatic patients, creates concerns for the safety of older patients undergoing CAS. This is also consistent with the recognition that patients > 80 years of age are at higher risk for CEA. These patients were specifically excluded from the NASCET and ACAS trials. This was also one of the high risk criteria in the SAPPHIRE trial for carotid revascularization in general. The higher incidence of adverse outcomes is particularly concerning for patients who have asymptomatic stenosis. In many of these patients, more harm than good would have come from the PTA and CAS procedure. Given the evidence, CMS proposes to continue the restriction that CAS for asymptomatic patients with stenosis > 80% and who are > 80 years of age be covered only in the setting of a clinical trial or post approval study for safety purposes. In addition, CMS proposes to expand this restriction to include symptomatic patients with stenosis > 70% and who are > 80 years of age".

Guidance from the National Institute for Health and Clinical Excellence (NICE, 2011) concludes that "current evidence on the safety of carotid artery stent placement for asymptomatic extracranial carotid stenosis shows well-documented risks, in particular the risk of stroke. The evidence on efficacy is inadequate in quantity. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research."

Guidance from NICE (2011) concluded that "current evidence on the safety and efficacy of carotid artery stent placement for symptomatic extracranial carotid stenosis is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance and audit or research. During the consent process, clinicians should ensure that patients understand the risk of stroke and other complications associated with this procedure. Clinicians should also ensure that patients understand the reasons for advising carotid artery stent placement rather than endarterectomy in their particular case."

Gurm et al (2008) reported on the long-term (3 years) results of carotid stenting versus endarterectomy in high-risk patients. The trial evaluated carotid artery stenting with the use of an emboli-protection device as compared with endarterectomy in 334 patients at increased risk for complications from endarterectomy who had either a symptomatic carotid artery stenosis of at least 50% of the luminal diameter or an asymptomatic stenosis of at least 80%. The pre-
specified major secondary endpoint at 3 years was a composite of death, stroke, or MI within 30 days after the procedure or death or ipsilateral stroke between 31 days and 1080 days (3 years). At 3 years, data were available for 260 patients (77.8 %), including 85.6 % of patients in the stenting group and 70.1 % of those in the endarterectomy group. The pre-specified major secondary endpoint occurred in 41 patients in the stenting group (cumulative incidence, 24.6 %; Kaplan-Meier estimate, 26.2 %) and 45 patients in the endarterectomy group (cumulative incidence, 26.9 %; Kaplan-Meier estimate, 30.3 %) (absolute difference in cumulative incidence for the stenting group, -2.3 %; 95 % confidence interval [CI]: -11.8 to 7.0). There were 15 strokes in each of the 2 groups, of which 11 in the stenting group and 9 in the endarterectomy group were ipsilateral. The authors concluded that in this trial of patients with severe carotid artery stenosis and increased surgical risk, no significant difference could be shown in long-term outcomes between patients who underwent carotid artery stenting with an emboli-protection device and those who underwent endarterectomy.

In a phase II multi-center, randomized, clinical trial, Zwienenberg-Lee et al (2008) examined the effect of prophylactic transluminal balloon angioplasty (pTBA) on cerebral vasospasm and outcome in patients with Fisher grade III subarachnoid hemorrhage. A total of 170 patients were enrolled in the study. Of these, 85 patients were randomized to the treatment group and underwent pTBA within 96 hours after subarachnoid hemorrhage. Main endpoints of the study included the 3-month dichotomized Glasgow Outcome Score (GOS), development of delayed ischemic neurological deficit (DIND), occurrence of transcranial Doppler (TCD) vasospasm, and length of stay in the ICU and hospital. The incidence of DIND was lower in the pTBA group (p = 0.30) and fewer patients required therapeutic angioplasty to treat DIND (p = 0.03). Overall, pTBA resulted in an absolute risk reduction of 5.9 % and a relative risk reduction of 10.4 % unfavorable outcome (p = 0.54). Good grade patients had absolute and relative risk reductions of respectively 9.5 % and 29.4 % (p = 0.73). Length of stay in ICU and hospital was similar in both groups. Four patients had a procedure-related vessel perforation, of which 3 patients died. The authors concluded that while the trial is unsuccessful as defined by the primary endpoint (GOS), proof of concept is confirmed by these results. Fewer patients tend to develop vasospasm after treatment with pTBA and there is a statistically significantly decreased need for therapeutic angioplasty. Prophylactic TBA does not improve the poor outcome of patients with Fisher grade III subarachnoid hemorrhage.

van Haaften et al (2010) evaluated published evidence on therapeutic options for in-stent re-stenosis (ISR) following CAS placement. A total of 20 studies were found, describing 100 interventions after carotid ISR in 96 patients. The interventions most performed were repeat percutaneous transluminal angioplasty (PTA; n = 54), repeat CAS placement (n = 31), and carotid endarterectomy with stent removal (n = 9). No peri-procedural complications were identified in any of the studies evaluated. Recurrent re-stenosis after intervention for ISR occurred in 12 of 84 cases (14 %). All 12 patients received tertiary treatment. Two patients developed a third recurrence and eventually disabling stroke, 1 of whom died. In the other 10 interventions, no further follow-up was described. The authors concluded that several treatment strategies for ISR after CAS placement have been reported, with acceptable short-term results. The quality of the currently available data is still limited by the variability of results and study designs. Thus,
no recommendation can be made for any specific therapy. This argues for better study design and more consistency of reporting standards.

**Angioplasty and Stenting of Intra-Cranial Arteries for the Treatment of Atherosclerotic Stenosis:**

Although atherosclerotic stenoses of the intra-cranial vessels are less frequent than those of the extra-cranial vessels, they are associated with a high risk for stroke that is the 3rd leading cause of death in the United States. Atherosclerotic stenosis of intra-cranial arteries is usually treated with medication (e.g., acetyl salicylic acid, clopidogrel, and ticlopidine). It has also been reported recently that cilostazol, a phosphodiesterase inhibitor, can prevent the progression of intra-cranial arterial stenosis (Kwon et al, 2005). When pharmacotherapies fail to improve symptoms, balloon angioplasty has been reported to be useful. However, this surgical procedure is associated with a significant risk of complications (e.g., acute occlusion or symptomatic dissection, re-stenosis, and stroke). It has also been reported that stenting could reduce the rate of re-stenosis following balloon angioplasty of intra-cranial arteries. However, the clinical benefit of balloon angioplasty, with or without stenting, has not been firmly established.

In a retrospective case series study, Lylyk et al (2005a) discussed their experience in the treatment of patients with symptomatic intra-cranial atherosclerotic stenoses that are refractory to medical therapy, and who underwent stent-assisted angioplasty (n = 104). Patient records were analyzed for location and degree of stenosis, regimen of anti-platelet agents, devices used, procedure-related complications and adverse events. Clinical (Modified Rankin Scale) and radiographical outcomes were obtained 24 hours, 1 month and 3 to 6 months after treatment. A total of 65 lesions (62.5%) were located in the posterior circulation. Mean stenosis was 75.4%. In all patients, the angiographical degree of stenosis was reduced to less than 30%. One stent was implanted in 66 patients (63%), and 2 or more in 38 patients (37%). Modified Rankin Scale was 1 to 2 in 67.5% of the cases, 3 to 4 in 25.9%, 5 in 2.8%, and 6 in 3.8%. Procedural morbidity was 5.7%, while procedural mortality was 3.8%. Angiographical follow-up was available in 58 patients (55.7%) and the rate of re-stenosis was 12.5%. These investigators concluded that in selected patients, endovascular revascularization of intra-cranial arteries by means of stent-assisted angioplasty is technically feasible, effective and safe.

In an uncontrolled study, Yu and associates (2005) reported their findings on 18 patients who underwent stenting for symptomatic basilar artery stenosis. There were 3 major peri-procedural complications (16.7%) without fatality. At a mean follow-up of 26.7 months, 15 patients (83.3%) had an excellent long-term outcome. Only 1 patient (5.6%) had moderate disability from recurrent stroke, and 2 patients died of medical illness at 30 and 36 months after stenting. There were several limitations in this case series report: (i) it is a retrospective study in which patients were stented empirically without standard inclusion and exclusion criteria creating possible selection bias, (ii) not every patient received maximal medical therapy before stenting, and (iii) these are single-center data, and may not be generalizable for reasons of referral and selection bias, neurointerventional physicians’ expertise, and multi-disciplinary care. These authors stated that because of the poor prognosis of symptomatic basilar artery stenosis found in
previous studies, prospective multi-center randomized controlled studies of endovascular basilar artery stenting are warranted despite the risk of major procedural complications.

In a retrospective study, Marks and colleagues (2005) assessed their findings on 36 patients with 37 symptomatic atherosclerotic intra-cranial stenoses who underwent primary balloon angioplasty. All patients had symptoms despite medical therapy. A total of 34 patients were available for follow-up (mean of 52.9 months, range of 6 to 128 months). Mean pretreatment stenosis was 84.2% before angioplasty and 43.3% after angioplasty. The peri-procedural death and stroke rate was 8.3% (2 deaths and 1 minor stroke). Two patients had strokes in the territory of angioplasty at 2 and 37 months following angioplasty. The annual stroke rate in the territory appropriate to the site of angioplasty was 3.36%, and for those patients with a residual stenosis of greater than or equal to 50% it was 4.5%. Patients with iatrogenic dissection (n = 11) did not have transient ischemic attacks or strokes after treatment. These investigators concluded that results of long-term follow-up suggest that intra-cranial angioplasty without stent placement reduces the risk of further stroke in symptomatic patients.

On the other hand, Hauth and colleagues (2004) found that angioplasty of intra-cranial arteries can be associated with life-threatening complications. These investigators ascertained the feasibility and safety of angioplasty or angioplasty and stenting of extra- and intra-cranial vertebral artery (VA) stenosis. In 16 consecutive patients (9 men, 7 women; mean age of 61 years, range of 49 to 74 years) 16 stenotic VAs were treated with angioplasty or angioplasty and stenting. Eleven stenoses were localized in V1 segment, 1 stenosis in V2 segment and 4 stenoses in V4 segment of VA. Fourteen VA stenoses were symptomatic, while 2 were asymptomatic. The etiology of the stenoses was atherosclerotic in all cases. Angioplasty was performed in 8/11 V1 and 2/4 V4 segments of the VA. In 3/11 V1 segments and 2/4 V4 segments of the VA, combined angioplasty with stenting were used. The procedures were successfully performed in 14/16 VAs (87%). Complications were asymptomatic vessel dissection resulting in vessel occlusion in 1/11 V1 segments and asymptomatic vessel dissection in 2/4 V4 segments of the VA. One patient died in the 24-hr period after the procedure because of subarachnoid hemorrhage as a complication following vessel perforation of the treated V4 segment. These authors concluded that angioplasty or angioplasty in combination with stenting of extra-cranial VA stenoses can be performed with a high technical success rate and a low complication rate. However, in intra-cranial VA stenosis the procedure is technically feasible but complications can be life-threatening. The durability and procedural complication rates of primary stenting without using pre-dilation in extra- and intra-cranial VA stenosis should be defined in the future. Moreover, in a review on vertebrobasilar disease, Savitz and Caplan (2005) noted that preliminary results of angioplasty or stenting of occlusive VA lesion in the neck reveal that re-stenosis is more common than with carotid artery stenting. The small diameter and angulation of the VA origin complicate endovascular treatment. Intra-cranial vertebral and basilar artery angioplasty and stenting have produced mixed results. It is also interesting to note that Boulos and colleagues (2005) stated that placement of intra-cranial and extra-cranial drug-eluting stent appears to be a safe alternative to the medical management of atherosclerotic disease of the vertebrobasilar and carotid systems. Moreover, these researchers concluded that further randomized studies are needed to
ascertain the safety and effectiveness of this procedure. These observations are in agreement with those of Gupta et al (2003), Doerfler et al (2004), Kim et al (2004), Komotar et al (2005), as well as Hartmann and Jensen (2005).

In a retrospective study (21 intra-cranial lesions in 18 patients), Gupta and associates (2003) reported that endovascular re-vascularization of intra-cranial vessels is technically feasible and may be performed successfully. However, peri-procedural complication and fatality rates in neurologically unstable patients are high. Endovascular re-vascularization was performed on 8 distal internal carotid artery lesions, 6 middle cerebral artery lesions, 4 intra-cranial VA lesions, and 3 basilar artery lesions. Re-canalization was complete in 5 arteries (Thrombolysis in Myocardial Infarction [TIMI] Grade III), partial in 14 arteries (TIMI Grade II), and complete occlusion (TIMI 0) developed in 1 artery. In a patient with a tight basilar stenosis, no angioplasty could be performed because of the inability to cross the stenosis with the guide wire. Major peri-procedural complications occurred in 9 (50 %) patients: intra-cranial hemorrhage in 3 (17 %), disabling ischemic stroke in 2 (11 %), and major extra-cranial hemorrhage in 4 (22 %). Three patients died: 1 from intra-cerebral hemorrhage and 2 from cardiopulmonary failure. These investigators suggested that patient selection, procedure timing, and peri-procedural medical management are critical factors to reduce peri-procedural morbidity and mortality.

In a review on endovascular treatment of cerebrovascular disease, Doerfler et al (2004) stated that angioplasty and stenting of intra-cranial atherosclerotic disease is feasible but remains a high-risk procedure, indicated only in highly selected patients. These investigators noted that advances in endovascular therapy have occurred in all areas of cerebrovascular disease. They further stated that to obtain maximal patient benefit, endovascular treatment should be performed as an interdisciplinary approach in high-volume centers; and concluded that long-term follow-up review is needed to clarify the overall role of endovascular treatment in the management of patients with cerebrovascular disease. Furthermore, Kim and associates (2004) stated that although stent-assisted angioplasty is an effective treatment for coronary and peripheral arterial disease, its effectiveness in intra-cranial arteriosclerotic disease has not been verified. They evaluated the radiographical and clinical outcome of stent-assisted angioplasty for symptomatic middle cerebral artery (MCA) stenosis (n = 14). Patients had symptomatic high-grade stenosis (greater than 60 %) on the proximal portion of the MCA, and had experienced either recurrent transient ischemic attacks (TIAs) resistant to medical therapy or one or more stroke attacks. Stent-assisted angioplasty was successfully performed in 8 of 14 patients without any serious complications and unsuccessful in 2 of 14 patients due to the tortuous curve of the internal carotid artery siphon. Four patients had complications: 2 had an arterial rupture (1 was rescued by an additional stent and balloon tamponade, the other patient died); the remaining 2 patients had thrombotic occlusion and distal thrombosis. Residual stenosis was less than 50 % in diameter in all patients. All 8 patients who underwent follow-up cerebral angiography had no re-stenosis. Follow-up single photon emission computed tomography demonstrated improved perfusion in the affected MCA territory in all subjects with TIA and in 1 of 3 stroke patients. Using the Modified Rankin Scale at follow-up, 4 of 5 TIA patients and 5 of 6 stroke patients were deemed functionally improved or having a stable clinical status. These authors concluded that although the re-stenosis rate in stent-assisted
angioplasty seems to be better than in primary balloon angioplasty as reported previously, the complication rate is still high. Elective stenting is an alternative therapeutic method for the prevention of secondary ischemic stroke in stroke patients with MCA stenosis, and seems to be a potentially effective but also hazardous therapeutic technique in patients with recurrent TIAs. These investigators concluded that the findings of this study indicate the need for randomized control studies of this intervention. In addition, long-term follow-up data and additional clinical experience are needed to determine the durability of this procedure.

In a review on endovascular treatment options for intra-cranial carotid artery atherosclerosis, Komotar et al (2005) stated that novel stent technology represents the beginning of innovative methods that will be employed by endovascular neurosurgeons to treat intra-cranial atherosclerosis. However, more clinical trials, especially those that compare stenting with the best medical management available are needed to ascertain the effectiveness and appropriateness of this technique. These investigators concluded that "angioplasty with stent placement carries risks along with a significant rate of restenosis; however, advancements in technology and methodology have begun to address these issues. In short, endovascular methods have revolutionized the treatment of this disease. With continued experience and a multidisciplinary approach in the evaluation of these patients, favorable outcomes may be achieved".

In a review on conventional, direct, and staged stenting for high-grade stenoses involving the posterior intra-cranial circulation, Levy and associates (2005) stated that for patients with high-grade posterior circulation intra-cranial stenoses involving the perforator-rich zones of the basilar artery, staged stenting may reduce procedure-related morbidity. A staged approach allows for plaque stabilization resulting from post-angioplasty fibrosis, which may protect patients from "snow-plowing," embolic shower of debris, or dissection. The authors noted that further clinical, in vivo, and histological investigation is warranted. In a review on recent advances in angioplasty and stenting of intra-cranial atherosclerotic stenosis, Hartmann and Jansen (2005) stated that "intracranial angioplasty with or without stenting is a promising treatment option. Patient selection, careful periprocedural medical management, and a highly skilled neuroendovascular surgeon are all required to perform the procedure with an acceptable risk. If stenting is to be shown to be a safe therapeutic alternative, prospective trials comparing stenting with optimal medical treatment need to be performed". Furthermore, a recent Cochrane review (Coward et al, 2005) concluded that there is currently inadequate evidence to evaluate the effectiveness of percutaneous transluminal angioplasty, with or without stenting, or primary stenting for the treatment of VA stenosis.

Through Humanitarian Device Exemptions (HDEs), the FDA approved 2 intra-cranial stent systems: (i) the Neurolink System (Guidant Corporation) in August 2002, and (ii) the Wingspan Stent System with Gateway PTA Balloon Catheter (Boston Scientific Corporation) in August 2005. The former is indicated for the treatment of patients with recurrent intra-cranial stroke caused by atherosclerotic disease refractory to pharmacotherapies, in intra-cranial 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 latter is indicated for improving cerebral artery
lumen diameter in patients with intra-cranial atherosclerotic disease, refractory to pharmacotherapies, in intra-cranial vessels with greater than or equal to 50% stenosis that are accessible to the system.

Although approved by the FDA, the clinical effectiveness of these two intra-cranial stent systems has not been clearly established. In a multi-center, non-randomized, prospective feasibility study, the Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSLYVIA) Study group (2004) assessed the Neurolink System for the treatment of patients with vertebral or intra-cranial artery stenosis. In 61 patients enrolled in this study, 43 (70.5%) intra-cranial arteries (15 internal carotid, 5 middle cerebral, 1 posterior cerebral, 17 basilar, 5 vertebral) and 18 (29.5%) extra-cranial VAs (6 ostia, 12 proximal to the posterior inferior cerebellar artery [PICA]) were treated. In the first 30 days, 4 patients (6.6%) had strokes and no deaths occurred. Successful stent placement was achieved in 58/61 cases (95%). At 6 months, stenosis of greater than 50% occurred in 12/37 (32.4%) intra-cranial arteries and 6/14 (42.9%) extra-cranial VAs, 4 in the vertebral ostia. Seven (39%) recurrent stenoses were symptomatic. Four of 55 patients (7.3%) had strokes later than 30 days, 1 of which was in the only patient not stented. These investigators concluded that the Neurolink System is associated with a high rate of successful stent deployment. Strokes occurred in 6.6% of patients within 30 days and in 7.3% between 30 days and 1 year. Although re-stenoses occurred in 35% of patients, 61% were asymptomatic, the authors stated that more studies involving the Neurolink System are warranted.

The FDA’s approval of the Wingspan Stent System was based on an international safety study of 45 patients who had a stroke caused by an intra-cranial lesion and for whom medical treatment failed to prevent another stroke. The device had a stent success rate of 100%, a procedural success rate of 97.7%, and a 4.4% incidence of death or stroke in the ipsilateral hemisphere of the brain as the lesion at 30 days post-procedure. The incidence of death or same hemisphere stroke at 6-month follow-up was 7.0% (Kofol and Donovan, 2005). This encouraging preliminary finding needs to be validated by further randomized controlled trials.

In March 2005, the FDA also granted a HDE to the CoAxia NeuroFlo catheter for the treatment of cerebral ischemia caused by symptomatic vasospasm following aneurysmal SAH. The NeuroFlo catheter is a multi-lumen device with 2 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 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 the patient’s blood pressure. The balloons should be sequentially...
deflated, SR then IR, and removed. Treatment with the NeuroFlo catheter is recommended only after patients have failed or are ineligible for medical therapy.

Llylyk et al (2005b) reported the findings of 24 selected patients with symptomatic vasospasm due to aneurysmal SAH treated by partial and transitory aortic obstruction with a novel device (NeuroFlo, CoAxia, MN). Aneurysms were secured by coils prior to the procedure. These researchers studied the adverse effects related to the aorta-obstructing device, and changes in cerebral blood flow (CBF) and neurological outcome. Mean flow velocity increased in both middle cerebral arteries over 15%, and the score in the NIH Stroke Scale decreased greater than or equal to 2 point in 20 patients (83%). During the procedure, 3 patients developed symptoms that were controlled. At 30 days follow-up, 3 patients had 6 points (unrelated death), 3 had 3 points, 6 had 1 point, and 12 had 0 points, in the modified Rankin scale. The authors concluded that partial aortic obstruction was safe, the CBF increased without inducing significant hypertension and the neurological defects improved in most of the patients. They stated that efficacy with a better level of evidence will be determined by a randomized study.

In an interim report of the Safety and Efficacy of NeuroFlo Technology in Ischemic Stroke (SENTIS) trial, Uflacker et al (2008) concluded that the NeuroFlo system so far proved to be safe enough for clinical use and seems to be promising in improving survival in the acute stroke population. However, this article was later retracted (2009).

In a Cochrane review on angioplasty for intra-cranial artery stenosis, Cruz-Flores and Diamond (2006) concluded that there is currently insufficient evidence to recommend angioplasty with or without stent placement in routine practice for the prevention of stroke in patients with intra-cranial artery stenosis. The descriptive studies showed that the procedure is feasible although it carries a significant morbidity and mortality risk. Evidence from randomized controlled trials is needed to evaluate the safety and effectiveness of angioplasty in preventing recurrent stroke. This is in agreement with the observation of Higashida and Meyers (2006) who stated that "at this time, patients with significant intracranial stenosis should receive counseling on the benefits and risks of revascularization therapy. Ultimately, determination of which patients should undergo revascularization procedures will require carefully planned, randomized clinical trials".

An assessment by the National Institute for Health and Clinical Excellence (NICE, 2007) concluded: "The evidence on clinical efficacy of endovascular stent insertion for intracranial atherosclerotic disease is currently inadequate and the procedure poses potentially serious safety concerns. Therefore, clinicians should collaborate to organise randomised studies of adequate size to compare endovascular stent insertion for intracranial atherosclerotic disease against best medical management. These studies should clearly define patient selection and be designed to provide outcome data based on follow-up of at least 2 years." The Specialist Advisors to NICE considered this procedure to be of uncertain safety with potential adverse effects including death, stroke, arterial dissection, vessel occlusion, vessel rupture, hemorrhage, restenosis and stent thrombosis.

The Centers for Medicare & Medicaid Services (CMS, 2008) re-considered their prior decision on intracranial PTA and stenting in November 2006, and announced...
their decision to maintain their position that this is a promising but unproven therapy. The Centers for Medicare & Medicaid Services reviewed 5 studies (Bose et al, 2007; Fiorella et al, 2007; Levy et al, 2007; Layton et al, 2008; Zaidat et al, 2008) published since their last review that presented data using the Wingspan stent system. The Centers for Medicare & Medicaid Services noted that the study by Bose et al (2007) presented data that was submitted to the FDA, and was considered in CMS' prior decision memorandum.

The Centers for Medicare & Medicaid Services observed that 3 of the new studies report on registry data; CMS noted that, as with all case series type studies, these studies are difficult to interpret without additional studies that reduce the possibility of inherent biases and substantiate the clinical findings. The studies by Fiorella et al (2007) and Levy et al (2007) presented data from the Wingspan registry of 78 patients. Zaidat and colleagues (2008) reported on the National Institutes of Health (NIH) Wingspan registry of 129 patients. The Centers for Medicare & Medicaid Services stated that various biases may have been factors in the observed differences in the registry data compared to the initial Wingspan study presented by Bose et al (2007). Levy and colleagues (2007) reported: “The ISR (in-stent restenosis) rate with the Wingspan stent is higher in our series than previously reported, occurring in 29.7 % of patients.” The Centers for Medicare & Medicaid Services found, in addition, that the lack of control groups and long term follow-up add to the uncertainty of clinical benefit. The CMS decision memorandum also expressed concern that Levy et al (2007) considers in-stent dissections to be “clinically silent,” particularly in view of their treatment with a second stent. The CMS decision memorandum also pointed out that concerns were also noted by Kallmes and Cloft (2008) who reported: “The overall restenosis rate in the study by Levy et al was 31 %, even though they excluded 4 cases of complete occlusion. Including those cases of complete occlusion would have increased the reported rate of restenosis by approximately 4 %.” The CMS decision memorandum also found that a higher restenosis rate (25 %) and adverse outcome rate (14 %) were also seen in the analysis by Zaidat and colleagues (2008), although the patients enrolled in the NIH registry had greater stenosis (70 to 99 %) compared to the other registry.

The Centers for Medicare & Medicaid Services concluded that “[g]iven the invasive nature of this treatment and the severe risks, as noted by Fiorella and colleagues, a well designed, well conducted randomized controlled trial is needed.” In supporting the need for a clinical trial, the CMS decision memorandum cited Derdeyn and Chimowitz (2007) who stated: “At present, however, there is no level 1 evidence to support angioplasty and stenting for patients who have symptomatic intracranial atherosclerotic disease. Case series suggest that the safety and stroke risk reduction of this procedure may provide a benefit, particularly with self-expanding stent technology. A randomized, controlled trial is needed to prove the efficacy of this therapy.” The CMS decision memorandum also cited Kallmes and Cloft (2008), who wrote: “We, the community of physicians, really have to continue to ponder what the real value of Wingspan is, and we must demand more data about safety and efficacy relative to other treatment options.”

The Centers for Medicare & Medicaid Services concluded that it “believes the evidence is promising and strongly encourages the development and completion of randomized controlled trials and currently covers PTA and stenting for the
treatment of intracranial artery stenosis greater than or equal to 50 percent in patients with atherosclerotic disease when furnished in accordance with the FDA-approved protocols governing Category B IDE clinical trials." The CMS decision memorandum noted that there is a newly funded clinical trial titled "Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS)" designed to determine health outcomes comparing optimal medical therapy to stenting and includes a 2-year mean follow-up. The Centers for Medicare & Medicaid Services stated that this randomized trial "is expected to provide solid evidence on this intervention."

Chimowitz et al (2011) stated that atherosclerotic intra-cranial arterial stenosis is an important cause of stroke that is increasingly being treated with percutaneous transluminal angioplasty and stenting (PTAS) to prevent recurrent stroke. However, PTAS has not been compared with medical management in a randomized trial. These investigators randomly assigned patients who had a recent TIA or stroke attributed to stenosis of 70 to 99 % of the diameter of a major intra-cranial artery to aggressive medical management alone or aggressive medical management plus PTAS with the use of the Wingspan stent system. The primary end-point was stroke or death within 30 days after enrollment or after a re-vascularization procedure for the qualifying lesion during the follow-up period or stroke in the territory of the qualifying artery beyond 30 days. Enrollment was stopped after 451 patients underwent randomization, because the 30-day rate of stroke or death was 14.7 % in the PTAS group (non-fatal stroke, 12.5 %; fatal stroke, 2.2 %) and 5.8 % in the medical-management group (non-fatal stroke, 5.3 %; non-stroke-related death, 0.4 %) (p = 0.002). Beyond 30 days, stroke in the same territory occurred in 13 patients in each group. Currently, the mean duration of follow-up, which is ongoing, is 11.9 months. The probability of the occurrence of a primary end-point event over time differed significantly between the two treatment groups (p = 0.009), with 1-year rates of the primary end-point of 20.0 % in the PTAS group and 12.2 % in the medical-management group. The authors concluded that in patients with intra-cranial 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.

In an editorial that accompanied the afore-mentioned study, Broderick (2011) noted that this is not the first trial that failed to show a benefit for intra-cranial re-vascularization. These failed trials provide some key lessons: (i) the challenges of intra-cranial re-vascularization are greater than those of extra-cranial re-vascularization, (ii) aggressive and attentive medical therapy is an effective approach to prevent stroke in high-risk patients, and (iii) the FDA and the Centers for Medicare and Medicaid Services (CMS) play critical roles in the advancement of cost-effective medicine. Moreover, they stated that new technology for preventing and treating stroke should be tested in trials that address clinical effectiveness and incorporate the best current medical management of stroke.

A systematic literature review of the Wingspan stent from the U.S. Food and Drug Administration (2012) concluded: "Currently available data demonstrate that with the use of the Stryker Wingspan stent system a decrease in stenosis levels can be achieved immediately and technical success of placement is generally high. However, in the only available RCT to date, use of the Stryker Wingspan stent
system presented a 30-day and 1-year risk of stroke or death which is about twice as high as that observed with aggressive medical care for the treatment of intracranial arterial stenosis. Across studies, immediate improvement in stenosis may not be maintained and ISR can occur. There is an array of acute complications (<72 hours post-procedure). In conclusion, we find evidence that the Stryker Wingspan stent system can be deployed successfully and can decrease stenosis levels following the procedure. However, data from randomized clinical trials demonstrating its ability to be used safely and effectively to decrease the risk of stroke or death are not available*.

Malik et al (2011) noted that acute ischemic stroke due to tandem occlusions of the extra-cranial internal carotid artery and intra-cranial arteries has a poor natural history. These investigators evaluated their single-center experience with endovascular treatment of this unique stroke population. Consecutive patients with tandem occlusions of the internal carotid artery origin and an intra-cranial artery (i.e., internal carotid artery terminus, M1 middle cerebral artery, or M2 middle cerebral artery) were studied retrospectively. Treatment consisted of proximal re-vascularization with angioplasty and stenting followed by intra-cranial intervention. End-points were re-canalization of both extra-cranial and intra-cranial vessels (Thrombolysis In Myocardial Ischemia greater than or equal to 2), parenchymal hematoma, and good clinical outcome (modified Rankin Scale less than or equal to 2) at 3 months. These researchers identified 77 patients with tandem occlusions. Re-canalization occurred in 58 cases (75.3 %) and parenchymal hematoma occurred in 8 cases (10.4 %). Distal embolization occurred in 3 cases (3.9 %). In 18 of 77 patients (23.4 %), distal (i.e., intra-cranial) re-canalization was observed after proximal re-canalization, obviating the need for distal intervention. Good clinical outcomes were achieved in 32 patients (41.6 %). In multi--variate analysis, Thrombolysis In Myocardial Ischemia greater than or equal to 2 re-canalization, baseline National Institutes of Health Stroke Scale score, baseline Alberta Stroke Programme Early CT score, and age were significantly associated with good outcome. The authors concluded that endovascular therapy of tandem occlusions using extra-cranial internal carotid artery re-vascularization as the first step is technically feasible, has a high re-canalization rate, and results in an acceptable rate of good clinical outcome. They stated that future randomized, prospective studies should clarify the role of this approach.

Jiang et al (2011) stated that there were limited data on the long-term outcome of patients with symptomatic intra-cranial atherosclerotic stenosis greater than or equal to 70 % after Wingspan stenting. Using these researchers' Wingspan cohort data and the data from the Warfarin and Aspirin for Symptomatic Intracranial Atherosclerotic Disease (WASID) as a historical control, they tested the hypothesis that stenting provided no benefit over anti-thrombotic therapy alone for these high-risk patients. Between January 2007 and February 2009, 100 consecutive patients with intra-cranial atherosclerotic stenosis greater than or equal to 70 % and symptoms within 90 days were enrolled into this prospective single-center Wingspan cohort study and followed-up until the end of February 2010. Stenosis was measured per the WASID criteria. One-year risk of primary end point (any stroke or death within 30 days and ipsilateral ischemic stroke afterward) was compared with that of ipsilateral ischemic stroke in the WASID patients with greater than or equal to 70% stenosis. The stent placement success rate was 99
All patients but 1 had clinical follow-up of greater than or equal to 12 months. During a mean follow-up of 1.8 years, 9 patients developed primary end point events (5 within 30 days and 4 afterward). The 1-year risk of the outcome events was lower than that in similar WASID patients: 7.3 % (95 % CI: 2.0 % to 12.5 %) versus 18 % (95 % CI: 13 % to 24 %; p < 0.05). The authors concluded that the clinical outcome of Wingspan stenting for high-risk intra-cranial atherosclerotic stenosis patients in this high-volume center study compares favorably with that of anti-thrombotic therapy alone. They stated that a randomized trial comparing medical therapy alone with medical therapy plus Wingspan stenting, conducted at high-volume centers, is needed to confirm the stenting benefit.

Qureshi et al (2012) noted that the results of prematurely terminated stenting and aggressive medical management for preventing recurrent stroke in intracranial stenosis (SAMMPRIS) due to excessively high rate of stroke and death in patients randomized to intra-cranial stent placement is expected to affect the practice of endovascular therapy for intra-cranial atherosclerotic disease. These investigators reviewed the components of the designs and methods SAMMPRIS trial and described the influence of those components on the interpretation of trial results. A critical review of the patient population included in SAMMPRIS was conducted with emphasis on "generalizability of results" and "bias due to cherry picking phenomenon". The technical aspects of endovascular treatment protocol consisting of intra-cranial angioplasty and stent placement using the Gateway balloon and Wingspan self-expanding nitinol stent and credentialing criteria of trial interventionalists were reviewed. The influence of each component is estimated based on previous literature including multi-center clinical trials reporting on intra-cranial angioplasty and stent placement. The inclusion criteria used in the trial ensured that patients with adverse clinical or angiographic characteristics were excluded. Self-expanding stent as the sole stent, technique of pre-stent angioplasty, peri-procedural anti-platelet treatment, and intra-procedural anti-coagulation are unlikely to adversely influence the results of intra-cranial stent placement. A more permissive policy toward primary angioplasty as an acceptable treatment option may have reduced the overall peri-procedural complication rates by providing a safer option in technically challenging lesions. The expected impact of a more rigorous credentialing process on peri-procedural stroke and/or death rate following intra-cranial stent placement in SAMMPRIS such as the one used in carotid re-vascularization endarterectomy versus stenting trial remains unknown. The authors concluded that the need for developing new and effective treatments for patients with symptomatic intra-cranial stenosis can not be undermined. The data support modification but not discontinuation of the approach to intra-cranial angioplasty and/or stent placement for intra-cranial stenosis. There are potential patients in whom angioplasty and/or stent placement might be the best approach, and a new trial with appropriate modifications in patient selection and design may be warranted.

In summary, although there is preliminary evidence that balloon angioplasty, with or without stenting, may be effective in treating symptomatic patients with intra-cranial stenoses, available data are mainly from retrospective case series. Randomized controlled studies are needed to ascertain the effectiveness of this technology compared to best medical care in preventing stroke in patients with intra-cranial stenosis that is symptomatic or asymptomatic. Other parameters that need to be addressed are: (i) the frequency of peri-procedural stroke (disabling
and non-disabling), death, and the combination of stroke and death, (ii) the frequency of other major peri-procedural complications that require additional therapy, prolonged hospital stay or death as well as minor complications (e.g., hematoma, wound infection, and nerve palsy), (iii) the frequency of stroke in the territory of the stenosed vessels, (iv) the frequency of re-stenosis in the involved vessels, and (v) the frequency of hospital resource use, including length of stay and frequency of re-admission.

Derdeyn et al (2014) noted that early results of the Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis (SAMMPRIS) trial showed that, by 30 days, 33 (14.7%) of 224 patients in the stenting group and 13 (5.8%) of 227 patients in the medical group had died or had a stroke (percentages are product limit estimates), but provided insufficient data to establish whether stenting offered any longer-term benefit. In this study, these researchers reported the long-term outcome of patients. They randomly assigned (1:1, stratified by center with randomly permuted block sizes) 451 patients with recent transient ischemic attack or stroke related to 70 to 99% stenosis of a major intracranial artery to aggressive medical management (anti-platelet therapy, intensive management of vascular risk factors, and a lifestyle-modification program) or aggressive medical management plus stenting with the Wingspan stent. The primary end-point was any of the following: stroke or death within 30 days after enrolment, ischemic stroke in the territory of the qualifying artery beyond 30 days of enrolment, or stroke or death within 30 days after a revascularization procedure of the qualifying lesion during follow-up. Primary end-point analysis of between-group differences with log-rank test was by intention-to-treat. During a median follow-up of 32.4 months, 34 (15%) of 227 patients in the medical group and 52 (23%) of 224 patients in the stenting group had a primary end-point event. The cumulative probability of the primary end-points was smaller in the medical group versus the PTAS group (p = 0.0252). Beyond 30 days, 21 (10%) of 210 patients in the medical group and 19 (10%) of 191 patients in the stenting group had a primary end-point. The absolute differences in the primary end-point rates between the 2 groups were 7.1% at year 1 (95% CI: 0.2 to 13.8%: p = 0.0428), 6.5% at year 2 (-0.5 to 13.5%; p = 0.07) and 9.0% at year 3 (1.5 to 16.5%; p = 0.0193). The occurrence of the following adverse events was higher in the PTAS group than in the medical group: any stroke (59 [26%] of 224 patients versus 42 [19%] of 227 patients; p = 0.0468) and major hemorrhage (29 [13%] of 224 patients versus 10 [4%] of 227 patients; p = 0.0009). The authors concluded that the early benefit of aggressive medical management over stenting with the Wingspan stent for high-risk patients with intracranial stenosis persists over extended follow-up. They stated that these findings provided support to the use of aggressive medical management rather than PTAS with the Wingspan system in high-risk patients with atherosclerotic intracranial arterial stenosis.

Abuzinadah et al (2014) conducted a systematic review and meta-analysis of studies reporting the rates of stroke recurrence or death (the primary outcome) in symptomatic intracranial vertebo-basilar stenosis with medical or endovascular treatment over a minimum follow-up period of 6 months. These researchers included all studies in any language indexed in MEDLINE or EMBASE, supplemented by bibliography searches and by contacting the authors. The secondary end-points were stroke recurrence, and basilar artery and vertebral artery stroke recurrence rates. A total of 23 studies (592 medical treatment
patients and 480 endovascular treatment patients) were included. The risk of combined stroke recurrence or death was 14.8 per 100 person-years (95 % CI: 9.5 to 20.1) in the medical group compared with 8.9 per 100 person-years (95 % CI: 6.9 to 11.0) in the endovascular group. The incidence rate ratio was 1.3 (95 % CI: 1.0 to 1.7). The stroke recurrence rate was 9.6 per 100 person-years (95 % CI: 5.1 to 14.1) in the medical group compared with 7.2 per 100 person-years (95 % CI: 5.5 to 9.0) in the endovascular group. The authors concluded that these findings showed that the risk of stroke recurrence or death or the risk of stroke recurrence alone was comparable between the medical and endovascular therapy groups. A small preventive effect of endovascular therapy may exist, particularly if the 30 day post-procedural risk is reduced.

Angioplasty and Stenting of Intra-Cranial Arteries for the Treatment of Cerebral Vasospasm after Aneurysmal Subarachnoid Hemorrhage:

Aneurysmal subarachnoid hemorrhage (SAH) is a common form of stroke. Frequently, a significant number of patients with this condition develop angioigraphical or clinical vasospasm with devastating consequences. The pathogenesis of cerebral vasospasm following SAH remains unclear despite extensive research. Due to the lack of a clear etiology, medical treatment is still largely limited to hypertensive-hypervolemic-hemodilution (triple-H) therapy, and calcium channel blockers (e.g., nimodipine). Cerebral vasospasm that has become refractory to maximal medical therapy can be treated with intra-arterial infusion of vasodilators (e.g. papaverine). Moreover, recent advent in the field of interventional neurology and the development of minimally invasive techniques has resulted in expansion of potential therapeutic approaches for cerebral vasospasm secondary to aneurysmal SAH (Kosty, 2005). Balloon angioplasty is being investigated as a treatment option in patients with vasospasm following aneurysmal SAH; however its effectiveness for this indication has yet to be established.

In a case reports study, Murayama et al (2003) assessed the safety and effectiveness of combined Guglielmi detachable coil (GDC) embolization and balloon angioplasty in a single session for the treatment of ruptured aneurysms associated with symptomatic vasospasm (n = 12). Patients underwent GDC aneurysm occlusion and balloon angioplasty (n = 6), intra-arterial papaverine infusion (n = 2), or both (n = 4) in a single session. In 9 patients, aneurysm coil occlusion was performed first. Complete GDC occlusion was achieved in 8 patients, a small neck remnant persisted in 3, and embolization was incomplete in 1 patient. In all subjects, angiographical improvement of cerebral vasospasm was obtained. In 1 subject, a thromboembolic complication occurred and was treated with urokinase. Clinical outcomes at discharge were good recovery in 6, moderate disability in 2, severe disability in 3, and death in 1. These researchers concluded that endovascular treatment can be the first therapeutic option for ruptured aneurysms associated with severe vasospasm on admission. It offers some advantages over surgery in this setting, but these are balanced by the risk of thromboembolism. This is in agreement with the observation of Wijdicks et al (2005) who noted in their review that balloon angioplasty is a durable means of alleviating arterial narrowing and preventing stroke in patients with symptomatic vasospasm following aneurysmal SAH. However, the procedure has risks, especially in inexperienced hands. Additionally, the timing of endovascular
intubation and use of inotropes in patients with cardiac dysfunction are unresolved issues.

In a review on cerebral vasospasm after SAH, Janjua and Mayer (2003) stated that the care management of this condition has evolved significantly over the past 10 years, with many new diagnostic modalities and promising treatments (e.g., balloon angioplasty) now available. These researchers concluded that clinical trials are needed to assess the effectiveness of these new techniques and to further define the optimal management of this often devastating complication following SAH. This is in agreement with the observation of Rabinstein and colleagues (2004). These investigators reviewed 81 consecutive patients with symptomatic cerebral vasospasm from aneurysmal SAH treated with percutaneous balloon angioplasty or selective intra-arterial papaverine infusion (105 procedures). Mean patient age was 54 years (range of 29 to 88 years). Twenty-nine patients (36%) presented with poor-grade (WFNS grade IV or V) SAH. Clinical deficits were global in 55 patients (70%), and angiographic vasospasm was diffuse in 53 (65%). Endovascular treatment consisted of transluminal angioplasty alone (18 procedures, 17%), intra-arterial papaverine infusion (65 procedures, 62%), or both (22 procedures, 21%). Unequivocal arterial dilatation was achieved in all but 2 patients, and major complications occurred in 2% of the procedures. Ten patients (12%) died in the hospital, and 36 (44%) recovered poorly. Permanent deficits attributable to cerebral vasospasm were present in 37 patients (52% of survivors). On multi-variate logistic regression analysis, advanced age and poor WFNS grade at presentation were predictive of poor clinical outcome. These authors stated that balloon angioplasty and intra-arterial papaverine are promising treatments for severe symptomatic vasospasm following SAH. They also noted that advanced age and poor clinical status (WFNS grade IV or V) at the time of SAH onset are predictive of poor clinical outcome despite endovascular treatment with balloon angioplasty or intra-arterial papaverine in patients with symptomatic vasospasm.

In a retrospective study, Turowski et al (2005) reported that in experienced hands, intra-cranial angioplasty is a feasible and safe option in a selected group of patients with severe (over 50% stenosis) symptomatic vasospasm following SAH. Cerebral circulation time is a surrogate parameter closely linked to cerebral perfusion. This study showed that not only stenosis but also changes in circulation time were obtained by angioplasty. A total of 20 angioplasties of 1 or 2 vessel segments were performed over 2 years in 18 consecutive patients with post-hemorrhagic vasospasm. In all patients, degree of stenosis and circulation time could be reduced by angioplasty. Clinical results were ranked according to Glasgow Outcome Scale. Imaging after 15/20 angioplasties showed no additional infarction. In 4/20 cases, computed tomography (CT) showed demarcation of infarction after angioplasty. In 1/20 cases of posterior circulation angioplasty, CT is not sensitive enough to exclude smaller infarctions.

In a clinical trial, Murai and associates (2005) examined the long-term effects of transluminal balloon angioplasty (TBA) on cerebral blood flow (CBF) and the functional properties of the arterial wall after aneurysmal SAH. A total of 12 patients underwent unilateral TBA. Xenon-enhanced CT was performed for an average of 18 days after TBA to measure CBF and cerebrovascular reactivity...
(CVR). Cerebral blood flow and CVR were compared between the side of TBA and the contralateral side. A total of 19 vascular territories were treated successfully with TBA in the subjects. Angiographical improvement of vasospasm was demonstrated in all 12 patients, and 9 (75%) patients showed neurological improvement. After TBA, global CBF was 35.1 +/- 8.2 mL/100 g per minute, with CBF on the side with TBA (37.8 +/- 10.3 mL/100 g per minute) being essentially the same as that on the other side (p = 0.0671, paired Student t test). Likewise, reactivity to acetazolamide did not differ significantly between sides (p = 0.0817). These investigators concluded that TBA increased proximal vessel diameters but showed no significant influence on CBF or CVR 3 weeks later. Benefits presumably were short-term, but the procedure was clinically safe.

Balloon angioplasty is also being used prophylactically for patients with cerebral vasospasm following SAH (Janjua and Mayer, 2003; Wu et al, 2004). A phase II clinical trial is ongoing at 5 centers comparing the outcomes of transluminal balloon prophylaxis with those of conventional medical management in patients with aneurysmal SAH who are at high risk for vasospasm (the Internet Stroke Center, 2004).

Velat et al (2011) reviewed randomized controlled trials (RCTs) and meta-analyses in the literature regarding the treatment and prevention of cerebral vasospasm following aneurysmal SAH. A literature search of MEDLINE, the Cochrane Controlled Trials Registry, and the National Institutes of Health/National Library of Medicine clinical trials registry was performed in January 2010 using predefined search terms. These trials were critically reviewed and categorized based on therapeutic modality. A total of 44 RCTs and 9 meta-analyses met the search criteria. Significant findings from these trials were analyzed. The results of this study were as follows: nimodipine demonstrated benefit following aneurysmal SAH; other calcium channel blockers, including nicardipine, do not provide unequivocal benefit; triple-H therapy, fasudil, transluminal balloon angioplasty, thrombolytics, endothelin receptor antagonists, magnesium, statins, and miscellaneous therapies such as free radical scavengers and anti-fibrinolytics require additional study. Tirilazad is ineffective. The authors concluded that there are many possible successful treatment options for preventing vasospasm, delayed ischemic neurologic deficits, and poor neurologic outcome following aneurysmal SAH; however, further multi-center RCTs are needed to determine if there is a significant benefit from their use. Nimodipine is the only treatment that provided a significant benefit across multiple studies.

An UpToDate review on “Treatment of aneurysmal subarachnoid hemorrhage” (Singer et al, 2013) states that “Angioplasty -- While balloon angioplasty of the basal cerebral blood vessels appears to be an effective treatment for treatment of cerebral vasospasm, it has not as yet been found to be a useful prophylactic approach. A phase II randomized trial of 85 patients found that prophylactic angioplasty was not associated with significant reductions in the incidence of delayed ischemia or vasospasm, nor with improved outcomes … Balloon angioplasty has become the mainstay of treatment at many centers for symptomatic focal vasospasm of the larger cerebral arteries which is refractory to hemodynamic augmentation, again despite an absence of clinical trial data …. Clinical vasospasm that persists despite hyperdynamic therapy may be treated by percutaneous intraarterial angioplasty or intraarterial administration of
vasodilators. There is limited data suggesting that their use improves clinical outcomes.

Guidelines from the American Academy of Neurology on subarachnoid hemorrhage (Connolly, et al., 2012) state: "Cerebral angioplasty and/or selective intra-arterial vasodilator therapy is reasonable in patients with symptomatic cerebral vasospasm, particularly those who are not rapidly responding to hypertensive therapy (Class IIa; Level of Evidence B).". The guidelines explain: Endovascular intervention is often used in patients who do not improve with hemodynamic augmentation and those with sudden focal neurological deficits and focal lesions on angiography referable to their symptoms. Interventions generally consist of balloon angioplasty for accessible lesions and vasodilator infusion for more distal vessels. Many different vasodilators are in use. In general, these are calcium channel blockers, but nitric oxide donors have been used in small series as well. Papaverine is used less frequently because it can produce neurotoxicity. The primary limitation of vasodilator therapy is the short duration of benefit. As with hemodynamic augmentation, there have been no randomized trials of these interventions, but large case series have demonstrated angiographic and clinical improvement." The guidelines recommend against stenting, stating that "Stenting of a ruptured aneurysm is associated with increased morbidity and mortality, and should only be considered when less risky options have been excluded (Class III; Level of Evidence C)."

Guidelines from the Neurocritical Care Society (Diringer, et al., 2011) state: "Endovascular treatment using intra-arterial vasodilators and/or angioplasty may be considered for vasospasm-related DCI [delayed cerebral ischemia] (moderate quality evidence-strong recommendation)." The guidelines state that "the timing and triggers of endovascular treatment of vasospasm remains unclear, but generally rescue therapy for ischemic symptoms that remain refractory to medical treatment should be considered. The exact timing is a complex decision which should consider the aggressiveness of the hemodynamic intervention, the patients’ ability to tolerate it, prior evidence of large artery narrowing, and the availability of and the willingness to perform angioplasty or infusion of intra-arterial agents (moderate quality evidence—strong recommendation)." The guidelines, however, recommend against prophylactic endovascular treatment. "The use of routine prophylactic cerebral angioplasty is not recommended (High quality Evidence—Strong Recommendation)." The guidelines explain: "Most studies are retrospective case series or comparison studies, with few prospective studies. Hence, the literature has demonstrated the feasibility, durability, and safety profile of intra-arterial vasodilator therapy and angioplasty, and the combination of the two, but has not demonstrated this for newer methods. The literature has not provided sufficient information regarding timing of the endovascular rescue therapy nor the optimum number of repeat treatments necessary. However, the single randomized controlled trial of prophylactic angioplasty, done early after SAH without the presence of angiographic arterial narrowing, suggested a lower risk of DCI, albeit at a risk of vessel rupture and death from the procedure and ultimately no difference in outcome [citing Zwienenberg-Lee, et al., 2008]. There are presently insufficient data to determine if intraarterial vasodilator therapy alone, or angioplasty alone, or a combination of treatments is superior to one another or superior to medical treatment alone."
By contrast, international guidelines from the European Stroke Organization on management of intracranial aneurysms and subarachnoid hemorrhage (Steiner, et al., 2013) have no recommendations for angioplasty or intra-arterial vasodilators.

In summary, while there is some preliminary evidence from retrospective case series studies that balloon angioplasty may be beneficial in treating cerebral vasospasm following aneurysmal SAH, its effectiveness in the prevention and treatment of this condition need to be verified by prospective, randomized, controlled trials.

Extracranial-Intracranial Arterial Bypass Surgery:

The Centers for Medicare & Medicaid Services' National Coverage Determination for “Extracranial-Intracranial (EC-IC) Arterial Bypass Surgery” (CMS, 1991) stated that “EC-IC arterial bypass surgery is not a covered procedure when it is performed as a treatment for ischemic cerebrovascular disease of the carotid or middle cerebral arteries, which includes the treatment or prevention of strokes. The premise that this procedure which bypasses narrowed arterial segments improves the blood supply to the brain and reduces the risk of having a stroke has not been demonstrated to be any more effective than no surgical intervention. Accordingly, EC-IC arterial bypass surgery is not considered reasonable and necessary within the meaning of §1862(a)(1) of the Act when it is performed as a treatment for ischemic cerebrovascular disease of the carotid or middle cerebral arteries”.

A study by the EC/IC Bypass Study Group (1985) failed to confirm the hypothesis that extracranial-intracranial anastomosis is effective in preventing cerebral ischemia in patients with atherosclerotic arterial disease in the carotid and middle cerebral arteries. To determine whether bypass surgery would benefit patients with symptomatic atherosclerotic disease of the internal carotid artery, the investigators studied 1377 patients with recent hemisphere strokes, retinal infarction, or transient ischemic attacks who had atherosclerotic narrowing or occlusion of the ipsilateral internal carotid or middle cerebral artery. Of these, 714 were randomly assigned to the best medical care, and 663 to the same regimen with the addition of bypass surgery joining the superficial temporal artery and the middle cerebral artery. The patients were followed for an average of 55.8 months. Thirty-day surgical mortality and major stroke morbidity rates were 0.6 and 2.5 per cent, respectively. The postoperative bypass patency rate was 96 per cent. Nonfatal and fatal stroke occurred both more frequently and earlier in the patients operated on. Secondary survival analyses comparing the two groups for major strokes and all deaths, for all strokes and all deaths, and for ipsilateral ischemic strokes demonstrated a similar lack of benefit from surgery. Separate analyses in patients with different angiographic lesions did not identify a subgroup with any benefit from surgery. Two important subgroups of patients fared substantially worse in the surgical group: those with severe middle-cerebral-artery stenosis (n = 109, Mantel-Haenszel chi-square = 4.74), and those with persistence of ischemic symptoms after an internal-carotid-artery occlusion had been demonstrated (n = 287, chi-square = 4.04).

Rodriguez-Hernandez et al (2011) stated that although most ischemic strokes are thrombo-embolic in origin and their management is endovascular or medical,
some are hemodynamic in origin and their management may be surgical. Extracranial-intracranial bypass with superficial temporal artery-to-middle cerebral artery (MCA) bypass, high-flow interposition grafts, and reconstructive techniques have been developed. Clinical indications and efficacy are controversial, and these researchers examined current practices. Bypass surgery is indicated for patients with athero-occlusive disease that results in chronic, low cerebral blood flow accompanied by episodes of ischemic symptoms. Specific diagnoses include: (i) internal carotid artery occlusion; (ii) MCA occlusion and, rarely, high-grade MCA stenosis; (iii) vertebra-basilar atherosclerotic steno-occlusive disease; (iv) vasculitis resulting in severe occlusive disease; and (v) moyamoya disease. Discouraging results from the Extracranial-Intracranial Bypass Trial demonstrated the importance of selecting surgical patients based on objective measures of hemodynamic insufficiency. Two such tests are xenon-enhanced computed tomography with acetazolamide challenge and positron emission tomography with measurement of oxygen extraction fraction. Perfusion computed tomography may be another, more practical test. Surgical series, systematic reviews of the literature, and 2 new RCTs that use these diagnostic techniques reveal contradictory results. Although they demonstrated that bypass surgery has a morbidity rate of less than 5 % and a patency rate of more than 95 %, they have not proven a clear benefit.

Powers et al (2011) tested the hypothesis that EC-IC bypass surgery, added to best medical therapy, reduces subsequent ipsilateral ischemic stroke in patients with recently symptomatic atherosclerotic internal carotid artery occlusion (AICAO) and hemodynamic cerebral ischemia. Patients with arteriographically confirmed AICAO causing hemispheric symptoms within 120 days and hemodynamic cerebral ischemia identified by ipsilateral increased oxygen extraction fraction measured by PET were included in this analysis. Of 195 patients who were randomized, 97 were randomized to receive surgery and 98 to no surgery. Follow-up for the primary end point until occurrence, 2 years, or termination of trial was 99 % complete. No participant withdrew because of adverse events. Anastomosis of superficial temporal artery branch to a MCA cortical branch for the surgical group was carried out. Antithrombotic therapy and risk factor intervention were recommended for all participants. Main outcome measures included: for all participants who were assigned to surgery and received surgery, the combination of (i) all stroke and death from surgery through 30 days after surgery, and (ii) ipsilateral ischemic stroke within 2 years of randomization; for the non-surgical group and participants assigned to surgery who did not receive surgery, the combination of (i) all stroke and death from randomization to randomization plus 30 days, and (ii) ipsilateral ischemic stroke within 2 years of randomization. The trial was terminated early for futility. Two-year rates for the primary end point were 21.0 % (95 % CI: 12.8 % to 29.2 %; 20 events) for the surgical group and 22.7 % (95 % CI: 13.9 % to 31.6 %; 20 events) for the non-surgical group (p = 0.78, Z test), a difference of 1.7 % (95 % CI: -10.4 % to 13.8 %). Thirty-day rates for ipsilateral ischemic stroke were 14.4 % (14/97) in the surgical group and 2.0 % (2/98) in the non-surgical group, a difference of 12.4 % (95 % CI: 4.9 % to 19.9 %). The authors concluded that among participants with recently symptomatic AICAO and hemodynamic cerebral ischemia, EC-IC bypass surgery plus medical therapy compared with medical therapy alone did not reduce the risk of recurrent ipsilateral ischemic stroke at 2 years.
Jacobs and Nichols (2014) stated that vascular cognitive impairment may be related to clinically apparent stroke, silent smaller strokes, or perhaps zones of incomplete infarction related to cerebral hypoperfusion. Flow limiting carotid stenosis or complete occlusion is associated with hemodynamic failure and poorer cognition. Improving CBF in such patients via re-vascularization procedures such as carotid endarterectomy, carotid stenting, EC-IC bypass surgery has inconsistently been associated with improved cognition.

CPT Codes / HCPCS Codes / ICD-9 Codes

CPT codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>35475</td>
<td>Transluminal balloon angioplasty, percutaneous; brachiocephalic trunk or branches, each vessel</td>
</tr>
<tr>
<td>36100</td>
<td>Introduction of needle or intracatheter, carotid or vertebral artery</td>
</tr>
<tr>
<td>37215</td>
<td>Transcatheter placement of intravascular stent(s), cervical carotid artery, open or percutaneous, including angioplasty, when performed, and radiological supervision and interpretation</td>
</tr>
<tr>
<td>37216</td>
<td>without distal embolic protection</td>
</tr>
<tr>
<td>37217</td>
<td>Transcatheter placement of intravascular stent(s), intrathoracic common carotid artery or innominate artery by retrograde treatment, open ipsilateral cervical carotid artery exposure, including angioplasty, when performed, and radiological supervision and interpretation</td>
</tr>
<tr>
<td>37218</td>
<td>Transcatheter placement of intravascular stent(s), intrathoracic common carotid artery or innominate artery, open or percutaneous antegrade approach, including angioplasty, when performed, and radiological supervision and interpretation</td>
</tr>
<tr>
<td>0075T</td>
<td>Transcatheter placement of extracranial vertebral artery stent(s), including radiologic supervision and interpretation, open or percutaneous; initial vessel</td>
</tr>
<tr>
<td>+ 0076T</td>
<td>each additional vessel (List separately in addition to code for primary procedure)</td>
</tr>
</tbody>
</table>

CPT codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>61630</td>
<td>Balloon angioplasty, intracranial (eg, atherosclerotic stenosis), percutaneous</td>
</tr>
</tbody>
</table>
61635  Transcatheter placement of intravascular stent(s), intracranial (eg, atherosclerotic stenosis), including balloon angioplasty, if performed

61640  Balloon dilatation of intracranial vasospasm, percutaneous; initial vessel

+ 61641  each additional vessel in same vascular family (List separately in addition to code for primary procedure)

+ 61642  each additional vessel in different vascular family (List separately in addition to code for primary procedure)

61711  Anastomosis, arterial, extracranial-intracranial (eg, middle cerebral/cortical) arteries

**Other HCPCS codes related to the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1725</td>
<td>Catheter, transluminal angioplasty, non-laser (may include guidance, infusion/perfusion capability)</td>
</tr>
<tr>
<td>C1726</td>
<td>Catheter, balloon dilation, non-vascular</td>
</tr>
<tr>
<td>C1727</td>
<td>Catheter, balloon tissue dissector, non-vascular (insertable)</td>
</tr>
<tr>
<td>C1874</td>
<td>Stent, coated/covered, with delivery system</td>
</tr>
<tr>
<td>C1875</td>
<td>Stent, coated/covered, without delivery system C1876</td>
</tr>
<tr>
<td></td>
<td>Stent, non-coated/non-covered, with delivery system</td>
</tr>
<tr>
<td>C1877</td>
<td>Stent, non-coated/non-covered, without delivery system</td>
</tr>
<tr>
<td>C1884</td>
<td>Embolization protective system</td>
</tr>
<tr>
<td>C1885</td>
<td>Catheter, transluminal angioplasty, laser</td>
</tr>
<tr>
<td>C2617</td>
<td>Stent, non-coronary, temporary, without delivery system</td>
</tr>
<tr>
<td>C2625</td>
<td>Stent, non-coronary, temporary, with delivery system</td>
</tr>
</tbody>
</table>

**ICD-9 codes covered if selection criteria are met:**

433.10,  Occlusion and stenosis of carotid artery with or without mention of cerebral infarction
433.11
433.20,  Occlusion and stenosis of vertebral artery with or without mention of cerebral infarction
433.21

**ICD-9 codes not covered if selection criteria are met:**

434.00 - Occlusion of cerebral arteries
434.91
Angioplasty and Stenting of Extra-Cranial and Intra-Cranial Arteries

435.0 - 437.9 Transient cerebral ischemia, acute, but ill-defined, cerebrovascular disease, and other and ill-defined cerebrovascular disease

852.0 - 852.19 Subarachnoid hemorrhage following injury with/without open intracranial wound [cerebral vasospasm after aneurysmal subarachnoid hemorrhage]

Other ICD-9 codes related to the CPB:

430 - 432.9 Subarachnoid hemorrhage, intracerebral hemorrhage, and other and unspecified intracranial hemorrhage

V58.63 Long-term (current) use of antiplatelets /antithrombotics

The above policy is based on the following references:

Angioplasty/Stenting of Extra-Cranial Arteries:


44. Moulton K, Argáez C. Carotid stenting versus carotid endarterectomy for the management of carotid artery atherosclerosis: Clinical and cost-
effectiveness and guidelines for use. Health Technology Inquiry Service (HTIS). Ottawa, ON: Canadian Agency for Drugs and Technologies in Health (CADTH); August 5, 2008.


Atherosclerotic Stenosis of Intra-Cranial Arteries:


Cerebral Vasospasm after Aneurysmal Subarachnoid Hemorrhage:

7. Internet Stroke Center at Washington University. BPAV. Balloon prophylaxis of aneurysmal vasospasm. Stroke Trials Registry. St Louis,

Extracranial-Intracranial Arterial Bypass Surgery:
