Evolution of cerebral revascularization techniques

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As a leading cause of death and disability in patients across the world, stroke is a problem that plagues both neurosurgeons and neurologists alike. Whether a result of atherosclerosis, moyamoya disease, or a complication in the treatment of a complex intracranial aneurysm, cerebrovascular occlusion can have devastating effects on patients. For nearly half a century neurosurgeons have searched for safer, more effective ways to increase the amount of blood flow to ischemic brain tissue. From the first extracranial–intracranial bypasses to the recent technological advancements seen with endovascular therapy, cerebral revascularization techniques have been constantly evolving. Over the years cerebral ischemia has gone from a condition that was previously considered surgically untreatable, to a condition with several viable options for prevention and treatment. In this paper the authors discuss the historical evolution of treatment for cerebrovascular occlusive disease. (DOI: 10.3171/FOC/2008/24/2/E3)

Abbreviations used in this paper: ACA = anterior cerebral artery; BMS = bare metal stent; CCA = common carotid artery; EC-IC = extracranial–intracranial; ELANA = excimer laser-assisted nonocclusive anastomosis; ICA = internal carotid artery; MCA = middle cerebral artery; PTA = percutaneous transluminal balloon angioplasty; SSYLVIA = Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries; STA = superficial temporal artery; TIA = transient ischemic attack.
complex intracerebral aneurysms alike. After this development, additional techniques designed to shunt blood to ischemic brain became increasingly prevalent. In 1974 Spetzler and Chater described the anastomosis of the occipital artery to the MCA in patients in whom the STA was unsuitable for bypass. Several years later a technique using the middle meningeal artery to bypass flow to the MCA was described by Nishikawa and colleagues.  

In addition to the increasing use of in situ bypass grafts pioneered by Yaşargil and Donaghy, several groups demonstrated the use of high-flow bypass grafts using saphenous vein or radial artery grafts to a variety of recipient vessels. Eight years after the work of Woringer and Kunlin was published, Lougheed and colleagues again used the saphenous vein to perform a CCA to ICA bypass. In 1978, Story et al. used a saphenous vein graft to shunt blood from the CCA to the MCA in a patient with TIAs. Shortly thereafter Spetzler and colleagues also reported using the saphenous vein to bypass blood flow to the MCA; however, they chose the ipsilateral subclavian artery as the proximal anastomotic vessel. Eventually, these techniques used for the anterior circulation were applied to the posterior circulation. In 1982 Sundt and colleagues first reported the treatment of vascular disease in the posterior circulation with vein grafts, and Sekhar and colleagues later reported using vein grafts for EC-IC vertebral artery reconstruction and for bypass from the ICA to the basilar artery.

Although these new procedures became more prevalent initially for the treatment of intracranial cerebroocclusive disease, their success was merely anecdotal. Finally, in 1985, the results of the International Cooperative EC/IC Bypass Study were released. This study was a 71-center, randomized prospective study initiated to determine whether STA–MCA anastomosis reduces the risk of ipsilateral ischemic stroke in these types of patients. Another significant advancement in EC-IC bypass surgery has been the ELANA, a modification of prior bypass techniques, described by Tulloken and colleagues. This technique allows EC-IC bypass without temporary occlusion of the recipient vessel by using an excimer laser/catheter system, potentially reducing the incidence of ischemia-related complications associated with vessel occlusion. The first case report of the application of this technique in humans was published in 1993; an epigastric artery was used to bypass blood flow from the STA to the ICA in a patient with bilateral carotid occlusion. In addition to its use in cerebroocclusive disease, this technique was later applied to the bypass of large intracranial aneurysms.
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and as such later studies were published that encompassed all applications of ELANA. In the biggest case series yet, Tulleken and colleagues\(^\text{62}\) reported on 40 patients who underwent ELANA for EC-IC bypass. The authors concluded that a small subset of patients with severe atherosclerotic disease was at a higher risk for graft failure, including graft disconnections, and as such should not be considered good candidates for the procedure.\(^\text{62}\) They did find, however, that the procedure appeared to be effective and well tolerated in the majority of patients. Ultimately, the ELANA procedure has great potential in the treatment of intracranial occlusive disease, however there are limited long-term follow-up data, and no existing trials that directly compare the technique with more conventional bypass techniques.

The advancements achieved with cerebral revascularization via direct bypass have also significantly affected the treatment of moyamoya disease. Extracranial–intracranial bypass was first used to treat moyamoya disease by Kikuchi and Karasawa in 1973,\(^\text{28}\) and was followed shortly by the reports of Krayenbuhl et al. in 1975,\(^\text{12,28}\). In 1983, Ishii and colleagues\(^\text{23}\) treated a 30-year-old woman with moyamoya disease by using a cephalic vein graft to bypass the STA to the ACA. The patient had a history of a large hemispheric stroke, and thus the surgery was performed on the contralateral side in an attempt to prevent future strokes.

**Indirect Revascularization**

Although the direct bypass of occluded intracranial blood vessels is often considered the most effective way to restore adequate blood flow to the distal cerebral vasculature, it is not always feasible. In patients in whom the graft vessels are too small, or in whom the ischemic brain may not be able to accommodate a high-flow bypass graft, other options must be sought. In these cases indirect methods are often the only option the neurosurgeon has available to revascularize the ischemic brain. In 1942 Kredel\(^\text{11}\) became the first surgeon to report placing a temporalis muscle flap over the surface of the brain in an attempt to induce collateral circulation. Thirty-five years later, Karasawa and colleagues\(^\text{25}\) used the temporalis muscle to revascularize cortical MCA branches in moyamoya patients, a procedure they called encephalomyosynangiosis. His group later described his treatment of moyamoya disease with an omental transplant, in which he anastomosed gastroepiploic vessels with the STA.\(^\text{26}\) Shortly thereafter, Spetzler and colleagues\(^\text{32}\) described a procedure in which collateral formation was induced by suturing the adventitia of the STA to the underlying arachnoid mater. A variation of this was later described by Matsushima and colleagues,\(^\text{41}\) a procedure they called encephaloduroarteriosynangiosis. Although these various procedures were shown to be effective in inducing collateral vessel growth in the MCA territory, they were less effective in treating lesions in the ACA and posterior circulation. However, in 1989 Endo and colleagues\(^\text{10}\) reported on their success in inducing the growth of collateral vessels in the ACA territory by creating bur holes and opening the dura mater. These techniques, or variations on them, are still in use today, most notably in patients with moyamoya disease.

**Endovascular Treatment**

Endovascular technologies, developed in the realm of coronary and peripheral vascular disease have, through adaptation, yielded a proliferation of noninvasive strategies for the management of intracranial atherosclerosis. This propagation has been tempered by the challenges the tortuous, small-caliber intracranial vasculature poses; however, the more recent development of neurovascular-specific devices has provided further augmentation.

**Percutaneous Transluminal Balloon Angioplasty**

To appropriately trace the progression of endovascular intervention for atherosclerotic disease one must begin with its origin, signified by the publication of Sundt et al.\(^\text{58}\) who described the use of balloon PTA for the management of basilar artery stenosis. In the 2 patients described in their study, surgical exposure of the vertebral artery was necessary for access, and in 1 patient, transient deficits attributable to occlusion of a basilar perforating vessel occurred. Further advancement in this area proceeded slowly due to fear of complications including vessel rupture, perforating vessel obstruction, distal embolization, and acute arterial occlusion.\(^\text{9,10}\) Subsequent publications concerning intracranial lesions were limited to case reports and small case series with minimal follow-up. Additionally, several larger series were published concerning the brachiocephalic system, including cases of vertebrobasilar disease, such as that of Higashida and colleagues in 1993.\(^\text{21}\) Of the 42 lesions they treated, only 3 involved the intracranial vasculature. Two of these were treated with a newer PTA balloon system, and 1 required operative exposure of the vertebral artery for access. The former were treated with good results and continued to do well on long-term follow-up; however, the patient requiring a concomitant operation suffered a pontine stroke and died 6 weeks after the procedure. Given these results and the limitations imposed by the size and flexibility of catheter systems, the authors concluded that only patients in whom maximal medical therapy had failed should be considered for PTA. Gress and colleagues\(^\text{15}\) expounded on this work, publishing their experience in the percutaneous management of vertebrobasilar ischemia from 1986 to 1999. Twenty-five lesions were treated in as many patients, resulting in a decrease in stenosis of > 40% in all. The overall risk associated with the procedure was quite significant, however, at 28%, with a 16% risk of disabling stroke or death. Not surprisingly, the rate of complications decreased over time with the surgeons’ attainment of experience and improvements in technology that allowed navigation of the vessels without associated vascular trauma.

This positive effect of experience on outcome was well illustrated in the retrospective series reported by Connors and Wojak.\(^\text{6}\) The authors described the changes in technique that occurred over 3 distinct periods. In the first a balloon of similar size, but slightly smaller than the target vessel was used, and inflation was rapid. Seven of 8 patients (87.5%) treated in this manner improved clinically, with 50% experiencing silent dissection. Subsequently, 12 patients were treated with balloons that approximated, but were at times larger than the target vessel, with very rapid dilation. Only 1 patient treated with this protocol was com-
pletely without complication; 3 (25%) experienced silent dissections, 5 (41.7%) had dissections with associated thrombus formation requiring urokinase, 1 had dissection with immediate occlusion, and another suffered an occlusion after an attempt to recross the treatment site. Two of these patients had a periprocedural stroke, 1 died, and 10 patients (83.3%) were reported to have had a good outcome. The final stage in this technical evolution was marked not only by a change in technique, but by the use of a smaller microcatheter and the routine use of an abciximab infusion. During this time period, the authors used undersized balloons and a long period of dilation (2–5 minutes). Seven (14%) of the 50 patients who underwent treatment had subsequent dissections, with only 2 requiring urokinase. Sudden vessel occlusion and stroke did not occur in any patient; however, there were 2 TIA’s, 1 vessel perforation, 1 instance of hemorrhagic conversion, and 1 postprocedural intraparenchymal hematoma. A good outcome, defined as stable or improved neurological status and resolution of symptoms was achieved in 98% of patients with only 1 periprocedural death (due to vessel perforation). One might suspect that this latter technique with its accompanying suboptimal angiographic result would be plagued by residual stenosis and restenosis; contrarily, only 16% had > 50% residual stenosis, with none > 70%, and only 8% had restenosis; all of these patients were successfully treated.

In addition to technical refinements, the accumulation of experience has also led to the development of a classification system based on angiographic appearance for risk stratification. Mori et al., in their report of 42 patients treated with balloon PTA, assigned patients, prior to treatment, into 1 of 3 groups: type A, lesions 5 mm long or smaller that are concentric or moderately eccentric and less than totally occlusive; type B, lesions 5–10 mm in length that are extremely eccentric or totally occluded, and less than 3 months old; type C, lesions that are > 10 mm long, excessively tortuous or angulated (> 90°), or totally occluded, and at least 3 months old. After PTA, patients were assessed both clinically and angiographically to survey for restenosis. Clinically successful angioplasty was achieved in 92, 86, and 33% of patients with lesion types A, B, and C, respectively. Furthermore, the cumulative risk of ipsilateral stroke, death, or bypass surgery was 8, 26, and 87%, respectively (p < 0.0001). The overall cumulative rates of stroke or bypass surgery were 14% at 1 year and 33% at 2 years. This information has provided clinicians with an additional means of facilitating proper patient selection for percutaneous intervention.

Although the above series demonstrate a significant improvement in periprocedural complication and mortality rates, the long-term efficacy of PTA for intracranial atherosclerosis has yet to be adequately assessed, a necessity in clarifying the benefit of treatment over natural history. Marks et al. reported the outcome of 23 patients after a mean follow-up of almost 3 years. Twenty-one (91.3%) of the 23 patients were treated successfully, with 1 patient not having a lesion amenable to intervention and another experiencing vessel rupture and periprocedural death. Of the 21, 1 had a stroke within the vascular territory of the treated vessel and 2 patients suffered strokes in another distribution, yielding an annual stroke rate of 3.2 and 4.8%, respectively. Subsequently, Wojak et al. elaborated on their earlier work, reporting the outcomes in 60 consecutive patients with 71 lesions; however, this population included patients treated with stenting in addition to angioplasty (26.2%). During an average follow-up of 62.5 months, the authors achieved a 90.5% procedural success rate, with a 4.8% rate of stroke or death. Twenty-three (27.4%) of the treated lesions had subsequent restenosis, occurring, on average, within 5 months. Only 5 patients presented with recurrent symptoms, the others were discovered on routine follow-up, and 13 were suitable for retreatment. Overall, the annualized stroke rate was 1.8%, with a 3.0% rate of stroke and death from all causes. Although representing a mixed population, this study still demonstrates an improvement in the natural history of intracranial atherosclerosis. Additionally, it highlights an important advance in the endovascular management of this disease, the use of vascular stents to treat lesions that cannot be appropriately managed with angioplasty alone.

**Bare Metal Stents**

Intracranial stent placement for the purpose of treating atherosclerotic disease was first reported for the anterior circulation by Feldman et al. in 1996, with the successful treatment of a 69-year-old patient who presented with TIAs secondary to right ICA stenosis. This was followed first by other accounts of anterior circulation interventions and then, in 1999, by case reports involving the posterior circulation, beginning with Phatourou et al. in March of that year. The impetus for this progression was a desire to combat restenosis, both from immediate rebound after angioplasty and from long-term intimal hyperplasia. Fiorilla and associates recently published their experience with BMSs in the treatment of atherosclerotic disease of the vertebrobasilar system. Forty-four patients (in the majority of whom medical therapy had failed) with 47 lesions underwent intervention with 95.7% technical success and 26.1% periprocedural complications and death. The average rate of stenosis was reduced from 82.5 to 10% after stent placement. Of the patients available for follow-up at or beyond 6 months, there was a 12.5% rate of in-stent restenosis or occlusion, with 15% experiencing recurrent signs of ischemia. Although performed with some success, these procedures continued to be plagued by the limitations of use of the vertebrobasilar system. Patients with only 1 periprocedural death (due to vessel perforation) and 1 instance of hemorrhagic conversion, and 1 postprocedural intraparenchymal hematoma. A good outcome, defined as stable or improved neurological status and resolution of symptoms was achieved in 98% of patients with only 1 periprocedural death (due to vessel perforation). One might suspect that this latter technique with its accompanying suboptimal angiographic result would be plagued by residual stenosis and restenosis; contrarily, only 16% had > 50% residual stenosis, with none > 70%, and only 8% had restenosis; all of these patients were successfully treated.

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Self-Expanding Stents

The next phase in the evolution of cerebral revascularization techniques has been the introduction of self-expanding stents specific to the cerebrovasculature. Both Bose et al. and Fiorella et al. explored the utility of the Wingspan stent system (Boston Scientific/Target), a nitinol microstent, in 2007. The goal of this innovation is to allow improved navigation while minimizing vascular trauma, to avoid the higher inflation pressures associated with balloon-mounted stents, and to prevent the in-stent restenosis associated with BMSs. Fiorella et al. attempted to treat 82 lesions in 78 patients, of whom 54 had > 70% stenosis. The stenosis was reduced from a preprocedural level of 74.6 to 27.2%, with a 6.1% incidence of major complications, including 4 deaths. Bose et al. placed stents in 45 patients demonstrating a similar reduction in the luminal diameter of the vessel, 74.9 to 28% at 6 months, with a 10.0% risk of death from any cause. These results would suggest that the radial force concomitant to the Wingspan Stent was sufficient to prevent the high rates of in-stent restenosis seen in SYLVIA; however, studies with long-term follow-up remain sparse.

Levy and associates have published their continued experience with the Wingspan System in an effort to better address these risks. They found that over a mean duration of approximately 6 months, 29.7% of the 84 lesions had in-stent restenosis of 50% or greater; however, 76% of these patients remained asymptomatic. Further analysis revealed there to be a significant difference between the occurrences of this phenomenon in the anterior (42%) versus the posterior (13.3%) circulation. Continued work, as reported by Turk et al., has provided for better characterization of this unexpected finding. This investigation revealed that those patients less than 55 years old were more likely to experience in-stent restenosis (45.2 versus 24.2%); however, 79.5% of lesions in this group were located in the anterior circulation, as compared to only 50.5% in the older group (p < 0.0010). Further analysis of anterior lesions in the younger cohort demonstrated that an ICA location, specifically the supraclinoid segment, was particularly prone to in-stent restenosis (88.9%). If reproducible, this represents a significant contribution to the literature concerning management, as these lesions seem to be poorly suited to stent placement. Not only are they more likely to undergo restenosis, but also they are more often symptomatic (60%). Given this and the existence of previous reports yielding lower rates of restenosis after PTA for anterior circulation lesions (14.3 versus 42.5%), there should be considerable reluctance to utilize stent placement in this area until there is further investigation. Turk and colleagues suggest that perhaps these supraclinoidal lesions represent a different pathophysiological entity, more akin to inflammatory arteriopathy than atherosclerotic disease.

Another more recent application of self-expanding stents in intracranial circulation is their use in the treatment of acute stroke. Building on their previous experience with BMSs, Levy et al. recently reported on the feasibility of using this technology to achieve recanalization after failure of thrombolitics. Eighteen patients with 19 lesions underwent stent placement in the setting of acute stroke, with this representing the initial mechanical maneuver in 6. This intervention was technically successful in all cases, with angiographically desirable results obtained in 79%. There were no periprocedural complications; however, 7 in-hospital deaths occurred subsequent to disease progression or associated complications. With such a limited patient population, it is difficult to ascertain the effect of this intervention on outcome. It appears, however, that women who demonstrate improvement 24 hours after stroke onset are more likely to have a favorable clinical course. At the least this demonstrates the feasibility of stent deployment in the setting of an acute thrombus resistant to thrombolitics.

Drug-Eluting Stents

Another recent novelty in the treatment of this disease is the adaptation of coronary drug-eluting stents to the intracranial circulation, again with the perceived benefit of reducing the significant restenosis seen with both PTA and BMS. Abou-Chebl et al. reported their early experience with 8 patients using both Cypher (Cordis Corp.) and Taxus (Boston Scientific, Inc.) stents. The mean rate of stenosis was reduced to 2.5% from 84.4% without significant complications. Over the follow-up period (~ 11 months), no patient had significant restenosis or required additional revascularization procedures. Several other small series of early experiences have also been published, reporting similar rates of stentoeic improvement and low periprocedural complications. The largest of these, by Gupta et al., describes the treatment of 62 lesions, 18 of which were in the extracranial ICA. Ninety-five percent of the devices were delivered successfully, with a reduction in the degree of mean stenosis from 83 to 12% and only 2 periprocedural complications. Over the course of follow-up (median 4 months), 5% of those with intracranial disease had restenosis > 50%.

Although these results are appealing, there are a multitude of issues yet to be addressed. First, there exists the concern that the placement of drug-eluting stents within the cranial vault will lead to neuronal toxicity. This has yet to be substantiated either in research in animals or in the small number of trials in human patients that have been reported in the literature, but the duration of follow-up is at present insufficient to be determinant. Second, and more disconcerting, is the potential for late stent thrombosis that has been demonstrated in the cardiovascular use of these devices. Several of these studies have demonstrated a 2- to 5-fold increase in the rate of late stent thrombosis compared with BMSs, and in fact, the risk with sirolimus-eluting stents may remain constant for up to 4 years. This finding relegates patients to long-term and potentially lifelong treatment with antithrombotic medication, exposing them to significant risk should these be interrupted, and potentially increasing the risk of hemorrhagic complications.

Conclusions

Cerebroocclusive disease has long represented a significant source of disability and death, and with the limited success of medical management, there exists an impetus for the development of a surgical solution. Throughout the last 70 years there has been a proliferation of options for such management, beginning in the 1940s with development of techniques for indirect revascularization. This evolution,
accompanied by the attainment of technical expertise has made it possible to alter the natural history of this disease. Concerning surgical bypass, although early investigations did not reveal benefit, further analysis revealed population-specific efficacy, and improvements in preoperative patient selection have lead to a resurgence in the use of these procedures. Concurrent with this has been the exponential growth of endovascular modalities, first through adaptation of cardiovascular and peripheral vascular technology and then more recently with the emergence of cerebrovascular-specific devices. Although these advances have revolutionized the treatment of cerebroocclusive disease, there is an urgent need for continued research.

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