

Balloons in Endovascular Neurosurgery: History and Current Applications

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The use of balloons in the field of neurosurgery is currently an essential part of our clinical practice. The field has evolved over the last 40 years since Serbinenko used balloons to test the feasibility of occluding cervical vessels for intracranial pathologies. Since that time, indications have expanded to include sacrificing cervical and intracranial vessels with detachable balloons, supporting the coil mass in wide-necked aneurysms (balloon remodeling technique), and performing intracranial and cervical angioplasty for atherosclerotic disease, as well as an adjunct to treat arteriovenous malformations. With the rapid expansion of endovascular technologies, it appears that the indications and uses for balloons will continue to expand. In this article, we review the history of balloons, the initial applications, the types of balloons available, and the current applications available for endovascular neurosurgeons.

KEY WORDS: Aneurysms, Balloon test occlusion, Balloons, Cervical atherosclerosis, Intracranial stenosis, Onyx

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The field of endovascular neurosurgery has been expanding rapidly. With expansion of the endovascular tools and techniques, the indications also have been expanding. At the beginning, balloons were the only available techniques; latter coils, embolic agents, and stents were introduced. Balloon technology also has expanded from the noncompliant latex balloons to now compliant single- and double-lumen balloons. Smaller balloons are available, making distal navigability into distal territories a reality. Newer-generation balloons are compatible with liquid embolic agents, making such treatment easier. In this article, we present the chronological evolution of balloons and expand on their indications and clinical results, including the most recent literature.

ABBREVIATIONS: **BRT**, balloon remodeling technique; **BTO**, balloon test occlusion; **CAS**, carotid artery stenting; **CCF**, carotid cavernous fistulas; **CEA**, carotid endarterectomy; **CPD**, cerebral protection device; **DMSO**, dimethyl sulfoxide; **FDA**, Food and Drug Administration; **ICA**, internal carotid artery; **MCA**, middle cerebral artery; **PTA**, percutaneous transluminal angioplasty; **SAMMPRIS**, Stenting vs Aggressive Medical Management for the Prevention of Recurrent Stroke; **TBA**, transluminal balloon angioplasty

BALLOON TEST OCCLUSION

The concept of using balloons to treat cerebrovascular lesions was inspired by a 1959 May Day celebration in Moscow's Red Square. While watching children use tether lines to manipulate helium balloons, Fedor Serbinenko, a Russian neurosurgeon, began to envision small balloons moving through tortuous arteries.¹ Serbinenko's research with endovascular balloons appeared in the Russian literature in 1971 and in the English literature in 1974 in the *Journal of Neurosurgery*.² In these articles, he described several applications for endovascular balloons, including a novel technique for diagnostic temporary arterial occlusion known as balloon test occlusion (BTO). He reported the temporary occlusion of 304 arteries of the extracranial and intracranial vasculature with a complication rate of only 0.7%.

At the time, parent artery sacrifice had been used to treat complex cerebrovascular lesions for decades; however, identifying patients with sufficient collateral circulation to tolerate the procedure remained a challenge. Existing methods of preliminary test occlusion included manual compression of the carotid artery, which lacked sensitivity and specificity, and invasive temporary clamping of the parent artery. Using latex and silicone balloons he manufactured in a small laboratory, Serbinenko developed an alternative

method for testing cerebrovascular reserve in which balloons filled with contrast material were attached to endovascular catheters and flow-directed under fluoroscopic evaluation into the target parent vessel.² The internal carotid artery (ICA) was accessed via direct puncture of the common carotid artery, and the vertebral arteries were accessed via either transfemoral catheterization or percutaneous puncture of the cervical vertebral artery.

BTO remains the current foundation for temporary arterial test occlusion. Some of the indications for BTO include pseudoaneurysms; cranial and cervical neoplasms with vascular involvement; traumatic arterial injury, infection, or neoplasm; carotid-cavernous fistulas (CCFs); and giant aneurysms with complex anatomies that preclude surgical clipping or embolization. The procedure is performed by temporary occluding the ICA just distal to the carotid bulb or the proximal vertebral artery with an inflated balloon with the patient awake. For the anterior circulation, a 20-minute BTO is sufficient, whereas a 30-minute BTO is recommended for the posterior circulation. If the patient develops a neurological deficit at any point during the occlusion, the balloon is deflated and the test is terminated immediately. Patients who fail the standard clinical BTO examination have 100% likelihood of developing ischemic compromise after proximal artery sacrifice unless extracranial to intracranial bypass is first performed.³⁻⁵

A variety of adjunctive methods that increase the sensitivity and specificity of BTO for identifying patients for whom parent artery sacrifice is unsafe have been described. In addition to monitoring the patient neurologically, regional cerebral blood flow during BTO may be evaluated directly using radioactive xenon with external probes,^{6,7} stable xenon-enhanced computed tomography (CT),^{3,8} technetium-99m hexamethylpropyleneamine oxime single photon emission CT,⁹ or [15O]-labeled H₂O positron emission tomography.¹⁰ Other indirect indicators of regional cerebral blood flow have also been used, including perfusion CT and magnetic resonance (MR) imaging, angiography of collateral vessels,^{7,11} measurement of arterial stump pressure,^{4,8,12} electroencephalogram,¹³ and transcranial Doppler ultrasonography.⁶ Finally, provocative hypotension with an acetazolamide challenge yields a more sensitive assessment of cerebrovascular reserve^{14,15} (Figure 1). MR-based computerized model simulations for predicting cerebral blood flow before and after various revascularization procedures were also developed and validated in a small subset of patients.¹⁶ Selective BTO for intracranial vessels, that is, posterior cerebral artery or anterior cerebral artery, could be performed to access collateral flows in case of distal intracranial giant aneurysms before sacrifice (Figure 2).

Complications related to the BTO vary, depending on the method of cerebral blood flow analysis, but are generally comparable to those observed with cerebrovascular catheter angiography and include vessel dissection and thromboembolic stroke. Mathis et al³ published a series of 500 cases of BTO of the ICA in which the procedural BTO complication rate was 1.6% and the incidence of permanent neurological deficit was 0.4%. Tarr et al¹⁷ performed 300 BTOs with xenon CT and reported a 1.7% neurological complication rate, including a 0.33%

occurrence of permanent neurological deficit. In contrast, Segal et al¹⁸ performed 56 BTOs with single-photon emission computed tomography and reported no complications. The authors attributed this difference to the fact that with single-photon emission computed tomography, unlike xenon CT, the balloon can be inflated under fluoroscopic guidance, which helps to avoid overinflation, which might cause intimal injury.⁸

As endovascular technology has progressed, several different types of balloon catheters have been used for BTO. The Swan-Ganz catheter was low cost, could be introduced without an exchange wire, and came with a relatively compliant latex balloon. Additionally, the double-lumen configuration enabled pressure measurements and contrast injection beyond the point of balloon occlusion. The tip of the catheter was formed over steam into a common cerebral configuration and flow-guided into position.¹⁹ Also popular were the 5F and 7F Meditech balloon catheters (Boston Scientific, Watertown, Massachusetts). These catheters had latex balloons and a double lumen but could be placed into the ICA over a 0.025-in exchange wire.^{20,21} The drawback of the 7F Meditech balloon system was that it produced significantly more radial vessel wall pressure on the vessel if the balloon was overinflated, thus increasing the risk of vessel injury. Finally, the smaller and more compliant nondetachable silicone balloon (Target Therapeutics, Fremont, California) was also used in patients with arterial narrowing or vessel tortuosity; however, this system required a 7.3F introductory guiding sheath and only had a single lumen.¹⁹ The Meditech and nondetachable silicone balloons are no longer commercially available. Other guide catheter-mounted balloons include the Concentric balloon guide catheter (Stryker Neurovascular, Fremont, California) and Cello balloon guide catheter (eV3-Covidien, Neurovascular, Irvine, California). Both balloons are compliant 10 × 10-mm silicone balloons mounted on the distal tip of an 8F (Concentric and Cello) or (Concentric) 9F guide catheter. Both balloons were developed to provide flow reversal during mechanical clot retrieval in the treatment of acute stroke.

In the United States, currently available balloons include the HyperGlide and HyperForm balloons (eV3, Neurovascular), the Ascent occlusion balloon catheter (Codman Neurovascular, Raynham, Massachusetts), and the Scepter balloon (Microvention, Tustin, California). All of these devices are approved by the Food and Drug Administration (FDA) for use in the neurovasculature. The HyperGlide and HyperForm devices consist of a single-lumen catheter and a nondetachable, low-pressure balloon. The HyperForm is the more compliant of the two. A 0.010-in microguidewire is positioned distal to the balloon catheter to occlude the central lumen and to allow the balloon to inflate through catheter side holes. The HyperGlide is available with 4- and 5-mm-diameter balloons, and the HyperForm is available with 4- and 7-mm-diameter balloons. Both the Ascent and the Scepter consist of a compliant balloon and a coaxial, dual-lumen shaft that permits passage of a guidewire through the central lumen and balloon inflation through the outer, independent lumen. Thus, they can be inflated without occluding the

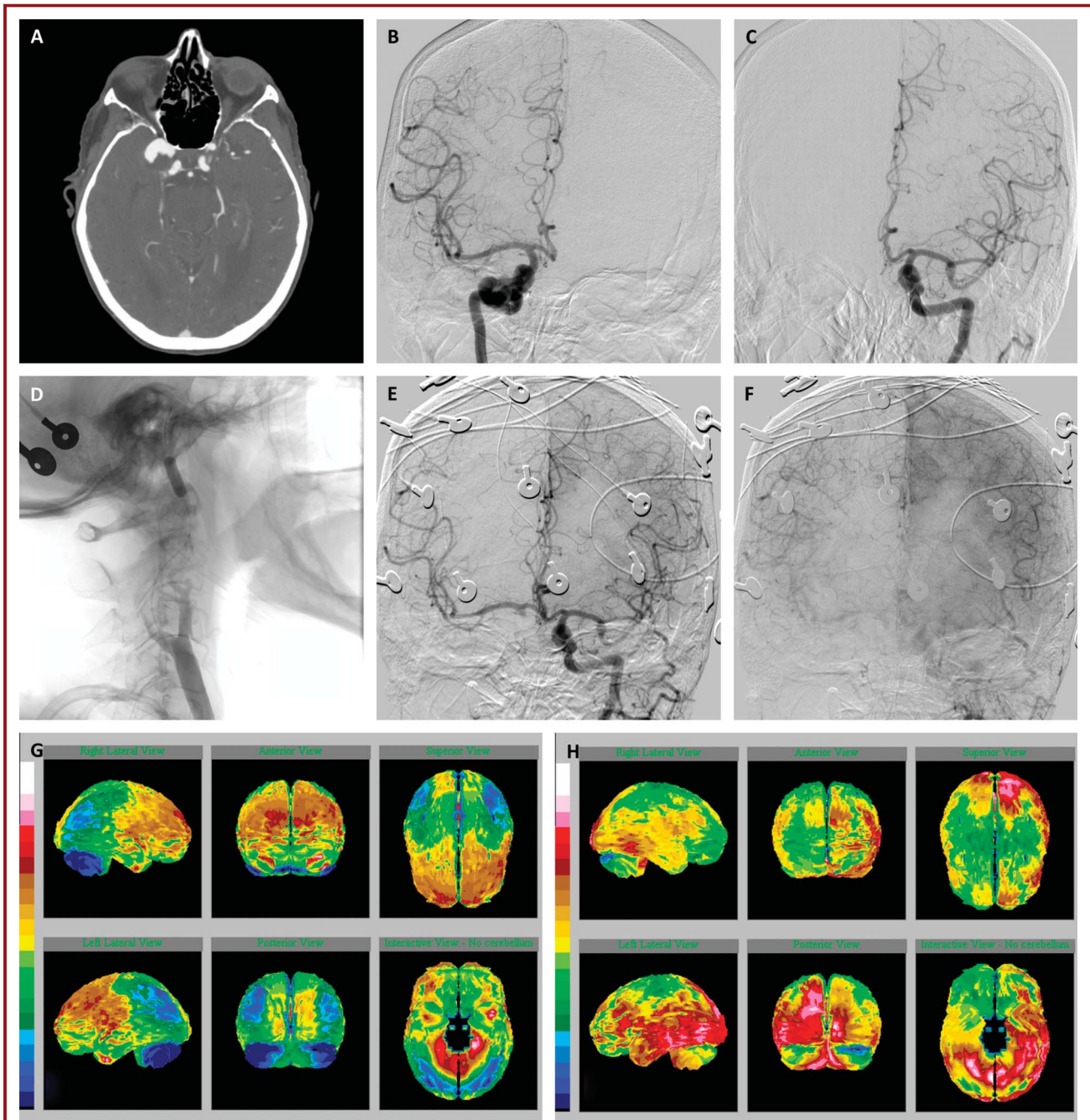


FIGURE 1. Balloon test occlusion (BTO) for a giant, cavernous, partially thrombosed internal carotid artery (ICA) aneurysm. **A**, computed tomographic angiography in a patient with recent ophthalmoplegia symptoms showing a partially thrombosed giant aneurysm within the cavernous ICA segment. Digital subtraction angiography of the right (**B**) and left (**C**) anteroposterior ICA showing the partially thrombosed giant aneurysm within the cavernous ICA segment. **D**, right common carotid artery angiogram (unsubtracted angiogram) during the BTO, demonstrating flow arrest within the ICA. The balloon (HyperForm 7 × 7 mm) is inflated with contrast within the upper cervical ICA region. **E**, early arterial left ICA angiogram demonstrating cross-flow of blood from the left ICA to the right middle cerebral artery (MCA). There is no opacification of the cavernous right ICA aneurysmal segment. **F**, late venous phase of the left ICA injection demonstrating a 4-second delay in venous filling between the 2 cerebral hemispheres, indicating a decrease in perfusion within the right MCA region. **G**, baseline cortical surface map of a single-photon emission computed tomography (SPECT) scan performed before the BTO. **H**, cortical surface map of a SPECT scan with ^{99m}Tc-hexamethylpropylene amine oxime injected during the hypotensive challenge of the BTO. This demonstrates a difference in cerebral perfusion between the 2 cerebral hemisphere. There is differential drop in perfusion in the right MCA territory; this is reduced compared with the baseline SPECT scan.

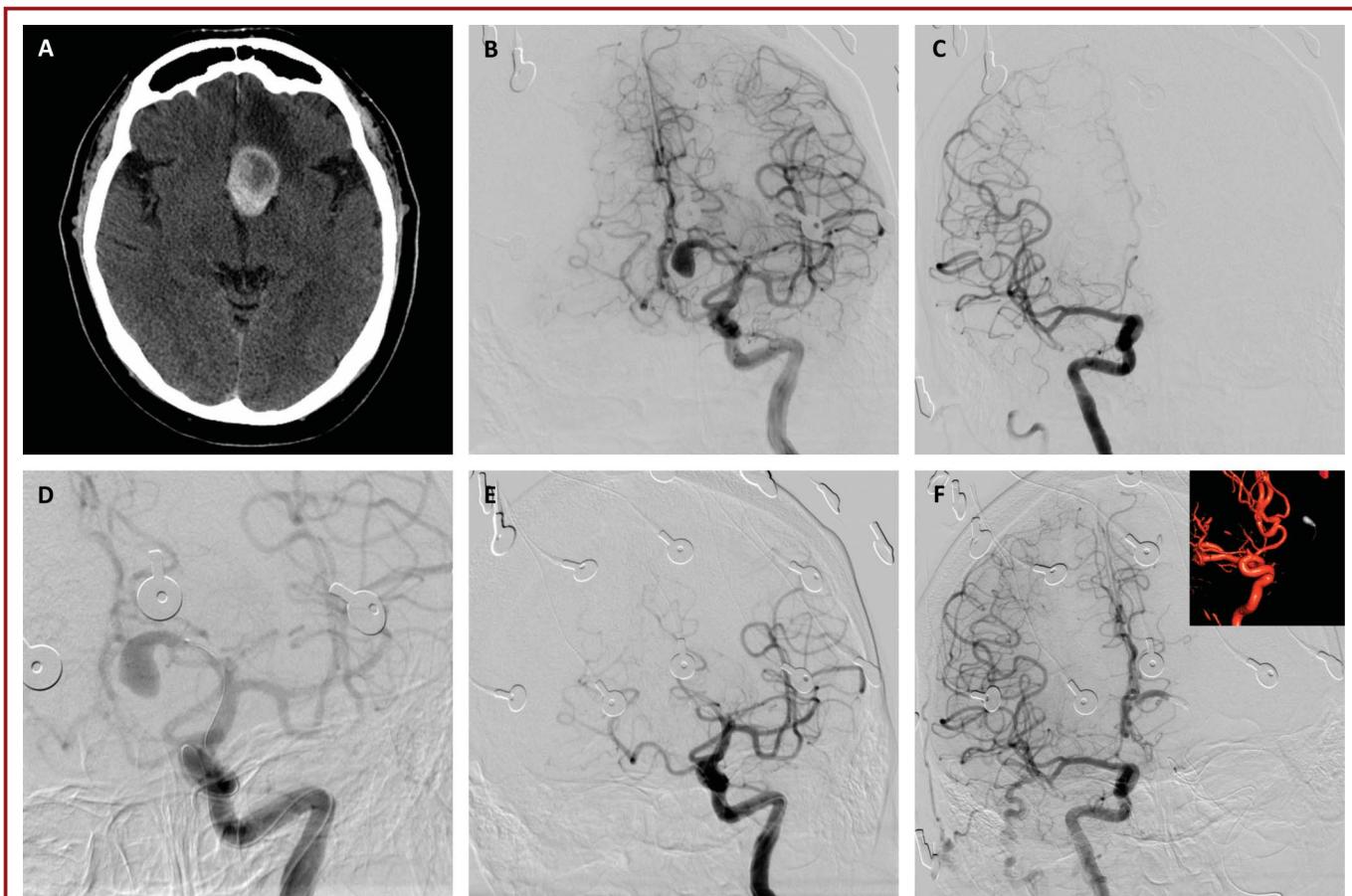


FIGURE 2. **A**, computed tomographic scan of the brain showing a midline, giant, partially thrombosed aneurysm with surrounding brain edema. Digital subtraction angiography of the left (**B**) and right (**C**) internal carotid artery (ICA) showing partial filling of a left A1 segment from the aneurysm; the right A1 is hypoplastic. **D**, a HyperForm balloon (3 × 7 mm) navigated into the left A1 segment as part of the selective balloon test occlusion (BTO). The patient is monitored neurologically and by electroencephalography. **E**, left ICA injection confirming the flow arrest into the left A1 segment with the inflated balloon. **F**, right ICA injection showing adequate filling of both anterior cerebral arteries from the small hypoplastic A1. The patient had no neurological changes during the BTO. Top right, 3-dimensional rotational angiography of the right ICA during the BTO confirming the filling of both anterior cerebral arteries. The left A1 was sacrificed endovascularly, resulting in thrombosis of the aneurysm. The patient remained neurological intact.

lumen with a guidewire. The Ascent balloon is available in 2 forms, a semicompliant form (4 × 10 mm, 4 × 15 mm) and supercompliant form (6 × 9 mm, 4 × 7 mm). However, the supercompliant Ascent balloon is less compliant than the HyperForm balloon. The Scepter balloon is available in 2 forms: the Scepter-C (compliant) and the Scepter-XC (extracompliant). This maintains a compliance similar to that of the HyperGlide/HyperForm balloon family. The Scepter-C is available in 4-mm diameter and lengths of 10, 15, and 20 mm. The Scepter-XC is available only in 4 × 11 mm. Both the Ascent and the Scepter balloons provide easier navigability (compared with HyperForm/HyperGlide balloons) since they can be navigated over a 0.014-in rather than a 0.010-in microwire. In Europe, the Baltacci²² (BALT, Montmorency, France) has also been used successfully for BTO.²³ The balloon is made of compliant latex that is

attached to a flow-dependent catheter. This device is compatible with a 0.009-in guidewire, but the guidewire is not required. Available balloon diameters are 4 to 6 mm. All of these devices are marketed for balloon remodeling of intracranial aneurysms and are discussed in more detail in the section on balloon remodeling technique (BRT).

DETACHABLE BALLOONS

Shortly after developing BTO, Serbinenko developed a method for permanent occlusion of the cervical and intracranial arteries. After floating a balloon without an end hole to the target vessel, the balloon was severed by the cutting edge of the arterial introduction needle. Subsequently, Serbinenko developed latex balloons with a valve mechanism that allowed balloon detachment by placing

traction on the delivery microcatheter. He used this technique for permanent (deconstructive) cervical and intracranial arterial occlusions and occlusion of CCFs with endoluminal reconstruction of the carotid artery. In his preeminent 1974 publication, Serbinenko² reported 2 deaths in 162 cases of permanent arterial occlusions, both after basilar artery catheterization.

In 1975, Debrun et al^{24,25} developed a latex tie-on detachable balloon for the treatment of neurovascular CCF and intracranial fistulas (Figure 3). These balloons are fashioned from a latex sleeve that the surgeon manually ligates over a coaxial microcatheter using a latex thread. Once the balloon is detached, the thread forms a self-sealing valve. The balloon is detached by pulling out the microcatheter to which the balloon is tied. Because the balloon is tied to the microcatheter, the risk of premature detachment is minimal. Additionally, the tightness with which the surgeon ties the balloon to the microcatheter can be adjusted to achieve different levels of detachment strength. The disadvantage is that these balloons require experience and greater manual dexterity to prepare, and many young surgeons are not trained to work with these balloons.

Subsequently, latex and silicone detachable balloons with internal valves were developed with various modifications.²⁶ These balloons are easier to use than the tie-on detachable balloons, but the risk of premature detachment is higher. These balloons are tied to the microcatheter tip and detached with a second coaxial catheter. Unfortunately, today's market for small, compliant detachable balloons is so small that almost all companies no longer manufacture them.²⁷ Detachable silicone balloons manufactured by Target Therapeutics were approved by the FDA for carotid occlusion and CCF obliteration but were discontinued in 2002.²⁸ The latex Gold Valve balloon produced by Nycomed (Ingenor, France) is not approved by the FDA for use in the United States but is used elsewhere all over the world. The Gold Valve balloon is commercially available in 4 sizes that are not

numbered according to size. The number 12 is the largest and is inflated with 2 mL contrast solution. It is most easily advanced with a 10F guiding catheter but can also advance through a 9F with some friction. The number 9 holds 1 mL contrast; the number 16 holds 0.7 mL; and the number 17 holds 0.5 mL.

When these balloons are used to occlude native arteries or vascular malformations, there are relative advantages and disadvantages of latex vs silicone balloons.²⁹ Latex Gold Valve balloons are less expensive than silicone balloons and are more distensible. In terms of inflation profiles, a single latex balloon may be inflated to a sufficient size to close the fistula; however, latex is stiffer and requires more force to inflate and is more likely to rupture during inflation. The greater pliability of silicone results in a more predictable inflation profile. In addition, although latex is impermeable, silicone balloons are semipermeable and must be inflated with isotonic solutions such as metrizamide or visipaque. A theoretical disadvantage of latex balloons is the prevalence of latex allergies. However, although fatal allergic reactions associated with rectal latex balloons inserted during barium enemas have been reported,³⁰ there is no clinical evidence that latex balloons can cause allergic reactions when placed in the cerebral vasculature.³¹

Another important difference is the relative thrombogenicity and mobility of each type of balloon. The vascular obstruction and irritation caused by the balloon stimulates the development of a hemostatic plug that develops into an organized thrombus. Eventually, a scar develops that is attached to the vessel wall, which ultimately keeps the balloon in place. The balloon should remain inflated and in place for approximately 1 week to guarantee fibrous attachment to the vascular wall and permanent occlusion of the target vessel.³¹ Latex balloons are less likely to migrate immediately after placement both because the latex creates more friction with the vessel wall and because latex more rapidly induces endothelialization and thrombus formation.³² Electron

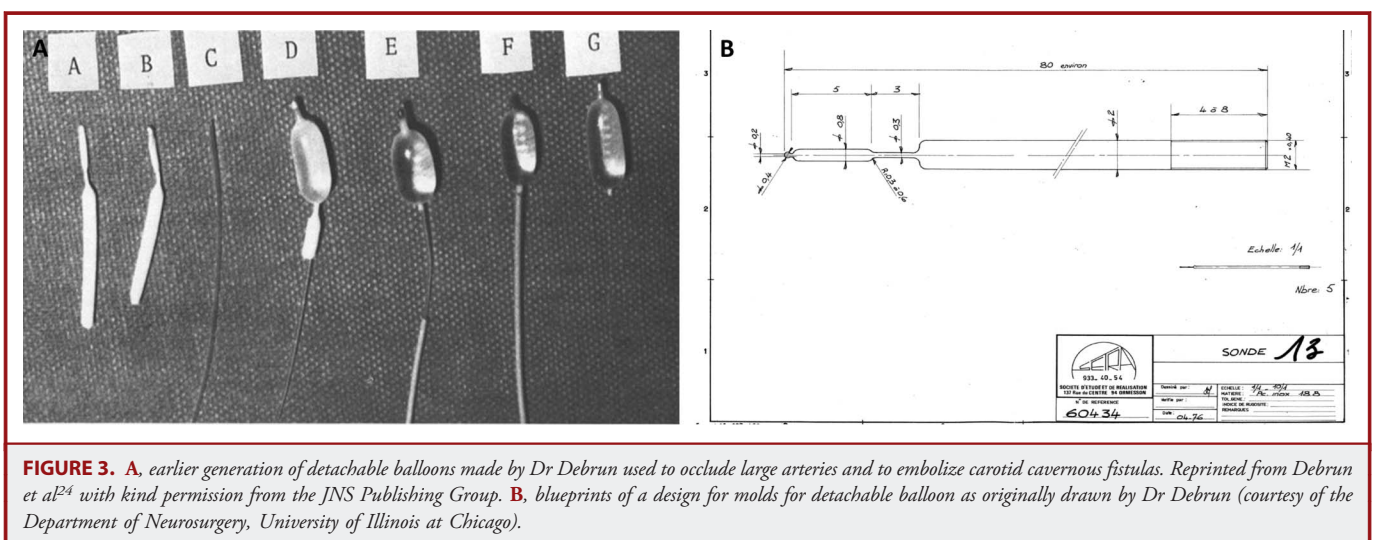


FIGURE 3. A, earlier generation of detachable balloons made by Dr Debrun used to occlude large arteries and to embolize carotid cavernous fistulas. Reprinted from Debrun et al²⁴ with kind permission from the JNS Publishing Group. B, blueprints of a design for molds for detachable balloon as originally drawn by Dr Debrun (courtesy of the Department of Neurosurgery, University of Illinois at Chicago).

microscopy of the surface of type of balloon reveals that whereas silicone is smooth and homogeneous, latex is rough with numerous craters. The irregular surface of latex likely promotes turbulent flow and thrombosis.³⁰ Thus, although latex balloons tend to deflate spontaneously within 2 to 3 weeks of placement, thrombosis and fibrosis have probably already occurred.³¹ In contrast, silicone balloons typically remain inflated for months but are more mobile.^{30,31} Thus, latex balloons may be more effective when complete arterial closure is desired, whereas silicone balloons may be less likely to generate potentially embolic surface thrombus and thus may be a safer choice when adjacent arterial flow must be preserved.

Detachable balloons are used primarily for the treatment of direct CCFs (Figure 4)^{24,26} and hunterian occlusion of giant intracranial aneurysms,^{29,33,34} the former being more technically challenging (Figure 5). The balloon is navigated to the cavernous sinus, at which point a sharp deflection of the course of the balloon is seen as it passes through the ostium. The balloon may

also vibrate in the turbulence of the fistula flow.³⁵ The balloon tends to pass easily through high-flow fistulas; however, occlusion of smaller fistulas may require a second, nondetachable balloon placed in the parent ICA adjacent to the fistula to push the balloon into the cavernous sinus.³⁶ In this regard, the sizes of the fistula and cavernous sinus are important technical considerations. The fistula must be smaller than an inflated balloon but large enough to permit passage of the deflated balloon. Meanwhile, the cavernous sinus must be sufficiently large to accommodate the inflated balloon. A large fistula coupled with a small cavernous sinus may result in retraction of the inflated balloon into the ICA.³⁷ Once in place, the balloon is inflated until the fistula is occluded, at which point it may be detached by a number of methods. A second coaxial sleeve may be used to push the balloon off the delivery catheter²⁶; however, this method may be impeded by poor tracking of the sleeve and the inability to push the balloon into place. Simple inflation and gentle traction on the delivery catheter are also done²⁶; however, there is the risk

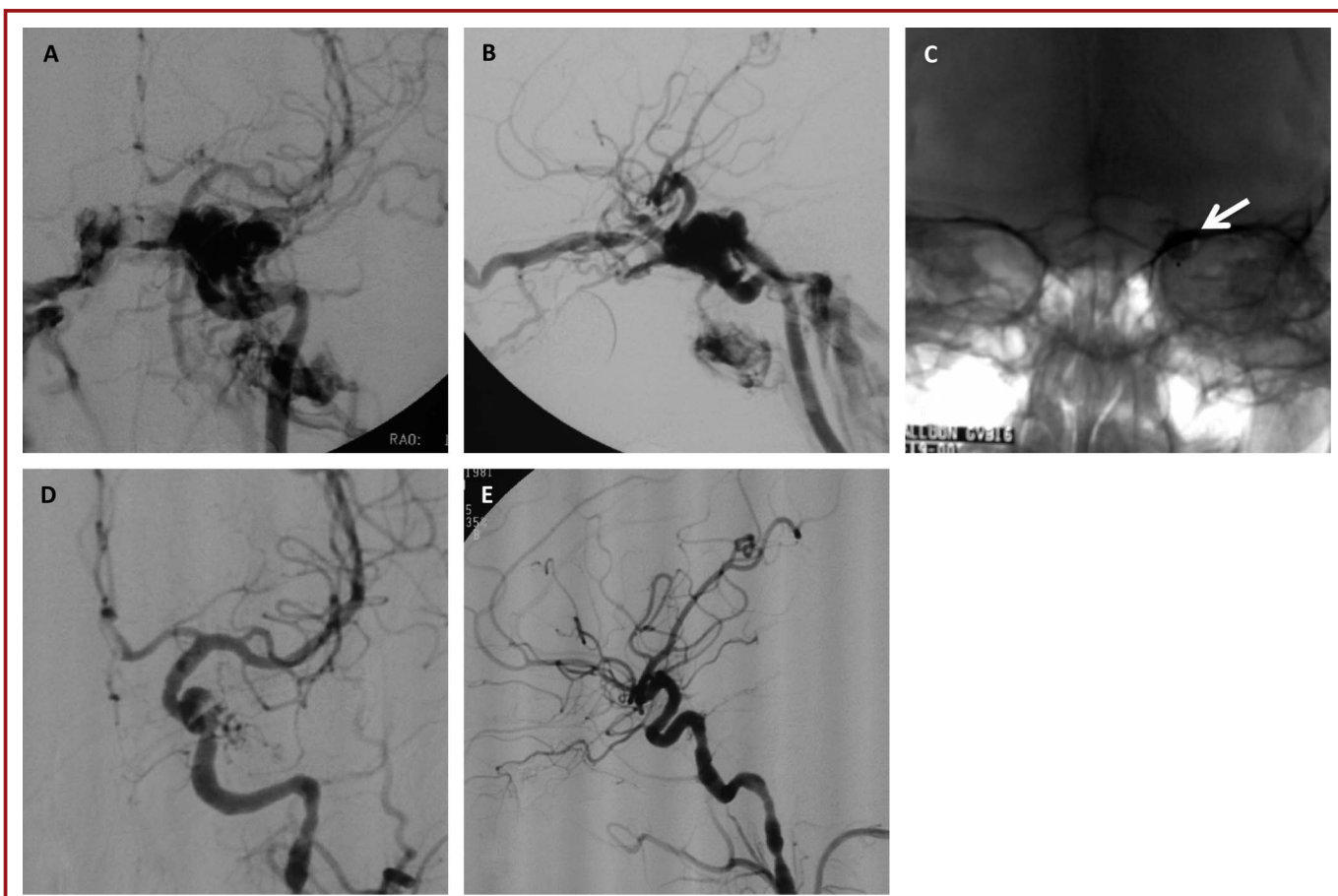


FIGURE 4. A, left internal carotid artery (ICA) angiogram (anteroposterior) and lateral (B) demonstrating a direct carotid cavernous fistula (CCF) with severe venous congestion and retrograde cortical venous reflux. C, fluoroscopic imaging after detachable balloon placement in the cavernous sinus (arrow). D, right ICA angiogram (anteroposterior) and lateral (E) after embolization of the CCF with detachable balloon showing no evidence of any early venous drainage.



FIGURE 5. **A**, right internal carotid artery (ICA) angiogram (anteroposterior) and lateral **(B)** showing a direct carotid cavernous fistula and early opacification of both cavernous sinuses with no antegrade flow beyond the cavernous sinus. Because the patient had no neurological symptoms with no contribution from the right ICA, no balloon test occlusion was performed before sacrifice of the ICA. **C**, fluoroscopic view of the neck showing the placement of 3 detachable balloons (arrows) in the cervical ICA and into the cavernous sinus. **D**, right common carotid artery angiogram confirming complete occlusion of the right ICA with no reconstitution of the cavernous fistula from the external carotid artery. **E**, contralateral left ICA (LICA) injection. Both hemispheres are filling from the left ICA injection. No retrograde filling of the fistula is seen.

of balloon migration at the time of detachment. An alternative method described by Masaryk et al³⁸ entails using a second nondetachable balloon to stabilize placement of the first balloon at the time of detachment. The second balloon is maximally reinflated within the carotid while traction is placed on the detachable balloon, thus eliminating any risk of the detachable balloon migrating into the arterial circulation. Recently, Wang et al³⁹ described 8 patients with direct CCFs treated with a combination of detachable balloons and Willis covered stents (MicroPort, Shanghai, China): 2 patients treated with detachable balloons and coils and 1 patient treated with detachable balloons, Willis covered stent, and coils.

Successful occlusion of the direct CCF with patency of the ICA is achieved in 80% to 88% of cases.⁴⁰⁻⁴² The carotid usually must be sacrificed when the communication is so large that the balloon bulges through the tear and occludes or severely narrows the ICA lumen. Rarely, the tear is too small to permit passage of the

balloon, in which case the ICA must be sacrificed. However, permanent occlusion of the ICA is not a bad result if the patient has sufficient cerebrovascular reserve.

A variety of complications may be encountered. Premature detachment of the balloon is infrequent. The risk of premature detachment is highest when the size of the balloon approximates the size of the artery.⁴³ In 5% of cases, movement or deflation of the balloon results in incomplete closure of the fistula, which is usually remedied by a second treatment. In the event that the cavernous sinus cannot be reentered with a balloon, it is recommended that a repeat angiogram be performed 1 week later, during which time many cases will evolve into complete closure or become amenable to a second treatment.⁴³ Note that deflation of the balloon before formation of a hemostatic plug may allow venous pouches or false aneurysms to form, which can silently enlarge to 4 or 6 cm without producing mass effect symptoms.⁴³ Ocular palsy may occur in as many as 25% of cases

as a result of compression by the balloon of the cranial nerves within the wall of the cavernous sinus; however, the vast majority of these paralyzes resolve within 6 months after treatment.⁴⁴ Normal pressure breakthrough phenomenon has been observed in a fast-flow fistula, thus necessitating staged closure of the fistula.³² In rare cases, the ICA is completely occluded, but the fistula is incompletely closed and fills from distal retrograde flow into the ICA. If the patient is asymptomatic, these cases can be observed for spontaneous closure. Otherwise, surgical clipping of the ICA or endovascular coiling of the leak via the posterior circulation is indicated. In the event that the balloon does not completely occlude the fistula but occludes the posterior venous drainage, anterior venous drainage through the superior ophthalmic vein is increased, resulting in severe proptosis and chemosis. This requires urgent closure of the fistula through the arterial or venous route. Additional complications include cerebral ischemia (3%), cerebral infarction (4%), and permanent neurological damage (3%).⁴⁵ Because detachable balloons are not available in the United States, coils and embolic agents have been used to transvenously occlude CCF and for arterial sacrifice.⁴⁶

INTRACRANIAL ANEURYSMS

Balloon Remodeling Technique

Although Serbinenko's 1974 article focused primarily on temporary and permanent occlusion of major cerebral vessels, he also reported 2 cases in which the cavities of arterial aneurysms were occluded by balloons.² The first was a basilar tip aneurysm, and the second was a giant aneurysm at the origin of the posterior communicating artery. Balloon embolization was subsequently popularized in the 1970s and 1980s; however, the technique had several drawbacks. Placement of balloons inside aneurysms without the aid of a guidewire is challenging, and the early endovascular balloons lacked sufficient compliance to conform to complex aneurysmal shapes. In addition, the aneurysm could have a ball-valve effect, resulting in reaccumulation of blood

inside the aneurysm.^{24,26,47} The technique went out of favor after the advent of detachable coils.

The use of balloons in the treatment of intracranial aneurysms was revived in France in 1997 by Moret, who developed the BRT.⁴⁸ The technique was brought to the United States by Aletich et al,⁴⁹ who published their experience with BRT at the University of Illinois at Chicago in the *Journal of Neurosurgery* in 2000. Wide-necked aneurysms are challenging to embolize with detachable coils because the absence of an anatomic barrier between the aneurysm and parent artery allows the coils to herniate into the parent artery. In addition, loose coil packing often results in a neck remnant from which the aneurysm may recur. To address these issues, the BRT uses an inflated balloon to temporarily occlude the neck of the aneurysm during coil placement. This not only prevents coil herniation but also forces the coil to assume the 3-dimensional shape of the aneurysm, which results in denser coil packing^{48,49} (Figure 6).

BRT has several additional advantages that have prompted some authors to suggest that BRT be attempted, if possible, for all aneurysms, regardless of neck size.^{50,51} First, the balloon conforms to the shape of the parent vessel, which better delineates the neck of the aneurysm and adjacent vessels. Thus, vessels branching from the aneurysm neck are protected during coiling. Second, inflation of the balloon across the entrance of vessels to be avoided eases microcatheter navigation. Third, BRT does not usually necessitate intraprocedural or postprocedural antiplatelet therapy, which increase the risk of rebleeding from external ventricular catheters.⁵² Because of the possible risk of thromboembolic complications associated with BRT, some institutions elect to place the patients preprocedurally on antiplatelet therapy. Finally, the balloon may be used to control parent vessel blood flow during management of intraprocedural hemorrhage.⁵³

Initially, BRT was performed with latex balloons because they were the only type of balloon available.^{48,49} However, the stiffness of these balloons prohibited safe positioning of the balloon microcatheter in tortuous access vessels.^{48,49,54-56} Latex balloons

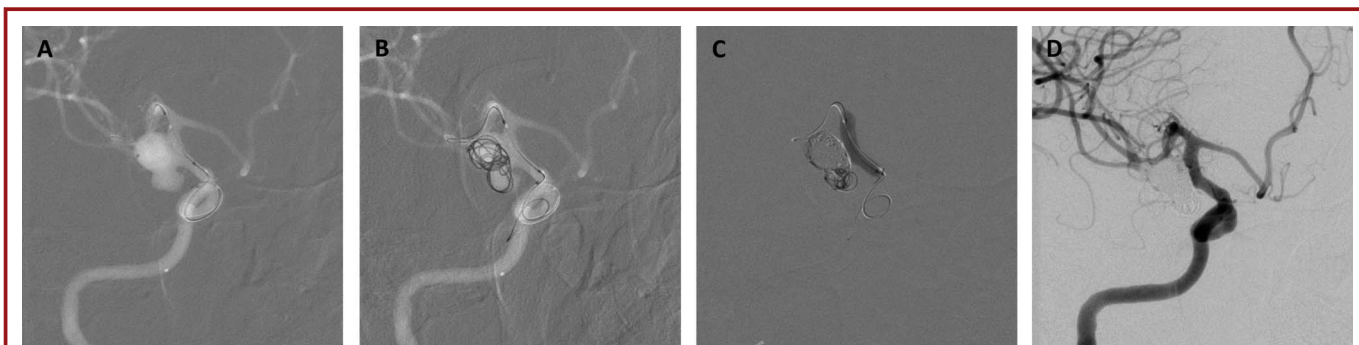


FIGURE 6. Patient with a ruptured right wide-necked bilobed posterior communicating artery aneurysm. **A**, road map with a working projection at the beginning of coiling. A HyperGlide balloon (4 × 20 mm) is placed across the right neck in the internal carotid artery (ICA). **B**, road map after placement of the first coil and deflation of the balloon. The framing coil fills both compartments of the aneurysm. **C**, further coiling of the aneurysm. The coils are filling the smaller compartment. The balloon is still inflated. **D**, digital subtraction angiography after coiling. The aneurysm appears to be well secured, with no coils herniating into the parent vessel.

were replaced with more compliant silicone and Silastic balloons such as the Solstice, Endeavor, and nondetachable silicone balloons. The Solstice was a pliable, distally occluded balloon manufactured by Microinterventional Systems (Fremont, California). It was approved by the FDA for neurovascular applications. Its over-the-wire configuration enabled precise balloon placement across the neck of ICA aneurysms and provided stability during inflation. However, the only size available was 3.5 mm, which created technical problems. The Solstice needed to be overinflated to occlude the ICA at the level of the aneurysm neck. In some cases, even the overinflated balloon failed to adequately seal the aneurysm neck, allowing coil prolapse. Overinflation also increased the risk of balloon failure either by rupture or by loss of the ability of the wire to occlude the distal lumen, preventing inflation. In addition, the balloon was stiff distally, which made it difficult to navigate through tortuous vessels, even with the guidewire.⁴⁹ Medtronic Inc (Minneapolis, Minnesota) acquired Microinterventional Systems in 1995; later, the Solstice was removed from the market.⁵⁷ Overinflation of the balloon carries a risk of intimal injury, and the benefit of such a maneuver should always be weighed against the risk of possible injury.

The Endeavor and nondetachable silicone balloons, manufactured by Target Therapeutics, were nondetachable, silicone balloons without end holes. Although these balloons were approved by the FDA in 1990 for use in the neurovasculature, they have not been available in the United States since the late 1990s. These low-pressure balloons were extremely pliable and exerted minimal pressure on the vessel wall during inflation. In addition, the 2F shaft facilitated navigation through tortuous vessels. However, the balloons needed to be flow-directed into position, thus limiting precise placement and allowing migration during inflation. Additionally, the pliability allowed coil prolapsed into the parent artery even if complete occlusion was attained. Finally, the tendency of the microcatheter to kink severely limited the use of the balloon in the treatment of ophthalmic, paraphthalmic, and paraclinoid aneurysms.⁴⁹

Currently available balloons for balloon remodeling differ in shape (from oblong to round), compliance, and tractability. The indications of each balloon are defined by the shape of the aneurysm and its relationship with the arterial wall. The HyperGlide and HyperForm (eV3) represent the next generation of neurovascular balloons.^{51,58,59} Both consist of a single-lumen catheter fitted with a nondetachable, low-pressure balloon. A 0.010-in Xpedion microguidewire is positioned distal to the balloon catheter to occlude the central lumen and to allow the balloon to inflate through catheter side holes. The guidewire also facilitates accurate positioning across the aneurysm neck. The HyperGlide is oblong and is available in diameters of 4 and 5 mm and lengths of 10, 15, 20, and 30 mm. It is used primarily for balloon remodeling of wide-necked sidewall aneurysms. Positioning the guidewire past the distal tip of the catheter perfectly stabilizes the balloon in front of the neck of the aneurysm during inflation and deflation. The most suitable locations are the ICAs and vertebral arteries.

The round, more compliant HyperForm is used when the balloon must conform to complex bifurcation aneurysms. The HyperForm bulges into the bifurcating vessels of bifurcation aneurysms, even if the tip of the balloon is directed into one of the bifurcation branches. In addition, the HyperForm protects branches originating from the aneurysm neck by forming nodes that bulge into the origins of these vessels and similarly conforms to and protects arterial branches adjacent to the aneurysm neck.⁵⁸ The great suppleness and compliance of the HyperForm also allow it to be used in small arteries (eg posterior inferior cerebellar artery, posterior cerebral artery, anterior communicating artery).⁵⁹ The HyperForm is available as 3-, 4-, and 7-mm-diameter balloons. Longer (20-mm length) and smaller (3-mm diameter) sizes came to market recently, which increased their use in more difficult vasculatures such as the M2 and anterior cerebral artery branches.

The HyperGlide and HyperForm must be properly prepped before use. The device comes with an uncurved 0.010-in hydrophilic Xpedion guidewire. The preferred contrast solution consists of a >50/50 mixture of 300 mg/mL iodinated contrast with saline to enable safe visualization. Higher concentrations of contrast may cause poor balloon deflation.⁶⁰

Several other technical considerations must be kept in mind with these balloons. Inflation is pressure dependent rather than volume dependent. The diameter of the balloon is controlled via a 1- or 3-mL syringe filled with 50/50 contrast in normal saline solution attached to the Y connector. Overinflation of the balloon is generally unnecessary to seal the neck of the aneurysm and is discouraged because of the risk of damage to the arterial wall.⁶⁰ Additionally, withdrawal of the guidewire to deflate the balloon while the balloon catheter is inside the vessel may aspirate blood into the balloon. Thrombus formation may then prevent further balloon deflation. Finally, if the inflation of the balloon cannot be validated on fluoroscopy or if any doubt exists, the balloon must be withdrawn immediately and checked. Possible reasons the balloon is unable to be visualized include improper filling with saline instead of contrast solution or refluxed blood preventing contrast solution from entering. Thus, if the balloon may be inflated but not visualized, continued inflation may lead to vessel rupture.⁶⁰

Other remodeling balloons that are currently commercially available in the United States include the Ascent occlusion balloon catheter (Micrus Endovascular Corp, San Jose, California), the Scepter balloon catheter (Microvention), and the Sentry balloon catheter (Target/Boston Scientific, Fremont, California). The Ascent was approved by the FDA in August 2008 for neurovascular and peripheral applications. The Scepter balloons were approved for use in the United States by the FDA in June 2012. Both balloons feature a unique coaxial, dual-lumen design that allows the use of a single catheter. The central guidewire lumen is sufficiently large to accommodate a 0.014-in guidewire and to deliver 0.010- and 0.018-in-diameter coils. It is surrounded by an outer parallel noncommunicating lumen for contrast. This independent contrast lumen provides consistent visibility

regardless of guidewire position. The outer lumen is also used to inflate the balloon; thus, unlike other single-lumen balloon catheters, the balloon can be inflated without occluding the lumen with a guidewire. Both Ascent and Scepter balloons are available in 2 versions. The less compliant version offers longitudinal coverage and minimal slipping for the treatment of sidewall aneurysms, and the more compliant version conforms to bifurcation lesions. The Ascent 4-mm-diameter balloons (semicompliant) are available in lengths of 7, 10, or 15 mm. The Ascent 6 × 9-mm (super-compliant) balloon is also available. The Scepter-C is available in 4-mm diameter and lengths of 10, 15 and 20 mm. The Scepter-XC is available only in 4 × 11 mm. Recently, Pukenas et al⁶¹ and Lassaro et al⁶² reported institutional experience with large wide-necked intracranial aneurysms that underwent BRT coil embolization with the Ascent balloon catheter without complications. Similarly, Scepter balloons have been used safely with BRT.⁶³ Both balloons provide an additional potential advantage during BTO when the same balloon microcatheter can be used to deploy coils and Onyx while the balloon is still inflated, thus lowering the risk of further embolization.⁴⁶ The Sentry balloon catheter is not approved by the FDA for neurovascular applications and was used primarily for coiling of sidewall aneurysms before the advent of the more compliant HyperGlide.⁶⁴⁻⁶⁶ The Sentry is a low-pressure balloon that features a single-lumen design with an ultralow distal profile (0.86 mm) to facilitate navigation through tortuous vasculature. It is available in lengths of 10 and 15 mm, both of which achieve inflated outer diameters of 3.5 mm.

Three additional devices are available only in Europe: the Copernic, Eclipse, and Baltacci manufactured by BALT. The Copernic is a low-pressure balloon with compliancy similar to that of the HyperGlide. It is compatible with a 0.012-in microguidewire and is available in diameters of 3 to 5 mm with lengths of 10 to 30 mm. The Eclipse is designed for use with BRT to treat bifurcation and terminal aneurysms. This compliancy of the Eclipse is similar to that of the HyperForm. It is available in balloon diameters of 4 to 6 mm with lengths of 7 to 20 mm. The Baltacci, a compliant latex balloon, is marketed for remodeling of basilar and middle cerebral artery (MCA) bifurcation aneurysms. Although it is attached to a flow-dependent catheter, it is compatible with a 0.009-in guidewire. Two models are available. The Baltacci B1 is available in diameters of 4 to 6 mm and lengths of 6 to 9 mm. The Baltacci B2 is available in diameters of 4 to 6 mm and lengths of 12 to 18mm.

The objective of BRT is to achieve complete and stable occlusion of the aneurysm because incomplete packing may lead to recurrence caused by coil compaction.^{67,68} Studies evaluating the efficacy of BRT have reported incomplete occlusion rates (<95% occlusion) ranging from 0% to 12%.^{48-51,55,69} The safety of BRT was once controversial because the risk of thromboembolic complications is theoretically increased by the presence of 2 microcatheters in the parent vessel, the temporary occlusion of the parent artery, repeated balloon inflations and deflations, and the substantial amount of packing material exposed to the bloodstream.^{66,70} However, the results of several large series have confirmed the safety of BRT.^{50,51,59,71-73} A 2008

meta-analysis published by Shapiro et al⁷⁴ included 23 articles with data on 867 conventional coiling and 273 BRT procedures for thromboembolism analysis. The authors concluded that aneurysm coiling with BRT was not associated with a statistically significantly increased risk of thromboembolism compared with conventional coiling methods. For perforation analysis, 21 articles with data on 993 conventional coiling and 170 BRT procedures were included. The reported perforation incidence using BRT for subarachnoid hemorrhage cases was $1.7 \pm 9.4\%$ and $1.8 \pm 2.1\%$ in non-subarachnoid hemorrhage cases; however, the number of studies that reported outcomes for both conventional coiling and BRT was too low for statistical analysis. In 2009 and 2010, Pierot et al^{69,75} published their data from the Aneurysms Treated by Endovascular Approach and the Clinical and Anatomic Results in the Treatment of Ruptured Intracranial Aneurysms series, respectively.

The data for the Aneurysms Treated by Endovascular Approach series was collected from 27 institutions and included 325 patients treated with conventional coiling and 222 patients treated with BRT. The Clinical and Anatomic Results in the Treatment of Ruptured Intracranial Aneurysms series included 768 ruptured aneurysms, of which 608 were treated with conventional coiling and 160 were treated with BRT. In both series, BRT was performed in all aneurysm locations; however, there were disproportionately fewer anterior communicating artery and anterior cerebral artery aneurysms because only first-generation remodeling balloons were available at the time of the study, which were difficult to navigate into the anterior arterial complex. For unruptured aneurysms, the overall complication rate was 10.8% for standard coiling and 11.7% for BRT. For ruptured aneurysms, complications occurred in 17.4% of standard coiling and 16.9% of BRT cases. The incidence of intraoperative rupture was not statistically significant between the BRT and standard coiling groups (3.2% vs 2.2%). Recently, Cekirge et al⁵¹ published a study that included 864 MCA, distal anterior cerebral artery bifurcation, and anterior communicating artery aneurysms treated using the BRT with the HyperForm balloon. The reported complication rate was 3.6%, which comprised a 1.9% incidence of thromboembolic complications and 1.7% incidence of hemorrhagic complications. This series suggests that BRT does not carry additional risk even in the small distal anterior circulation vessels. The authors also noted that the HyperForm balloon was useful for controlling intraoperative rupture. The overall mortality rate resulting from procedural complications was 1.4% in this series. Still, a randomized study comparing the safety of BRT with simple coiling has yet to be performed.

Shapiro et al⁷⁴ in their meta-analysis excluded several publications that found an increased complication risk associated with BRT because the authors did not report thromboembolic complications and procedural ruptures and transient and permanent complications separately. In their series of 1811 aneurysms, Henkes et al⁷⁰ reported a complication rate of 38.5% with coiling, although the details of the complications were not reported. However, it should be noted that BRT was used in only 1.4% of their cases, which averages 5 BRT cases per author in

10 years. Another study by Sluzewski et al⁶⁶ found a statistically higher incidence of clinically significant complications associated with BRT compared with conventional coiling (14.1% vs 3%). Again, however, of the 827 aneurysms treated, BRT was performed in only 8.6% of the cases. Thus, the results of these studies likely reflect inexperience with the technique. Additionally, the balloons used in these series were the BALT B1 balloon glued to a No. 1.8 microcatheter, the Endeavor, the Solstice, and the Sentry, none of which is as compliant as the HyperForm balloon.

Several variations of this technique are worthy of mention. The double-balloon remodeling technique was developed to treat aneurysms in which the aneurysmal neck involves 2 branches at the bifurcation of the parent arteries. Separate balloons are used on each side of the branching site to protect the branching arteries and to seal the aneurysm neck. This technique has been used successfully to treat an aneurysm incorporating both trunks of the MCA, a large aneurysm of the anterior communicating artery,⁷⁶ and a basilar bifurcation aneurysm with both posterior cerebral arteries branching from its base.⁷⁷ The double-balloon trapping technique uses 1 balloon placed across the neck of the aneurysm to “trap” a second balloon within the aneurysm. Kelly et al⁷⁸ used this technique to treat a superior cerebellar artery aneurysm incorporating the origin of the superior cerebellar artery. Finally, balloon remodeling has also been used in combination with the multicatheter technique to treat complex MCA aneurysms with good angiographic results with a relatively low mortality and morbidity.⁷⁹ In 2- and 3-catheter techniques, 2 or 3 coils are deployed sequentially or through prepositioned microcatheters without detachment to form a coil basket that preserves the parent artery or incorporated branch.^{80,81} A balloon can be used in combination with this technique to protect the parent artery while 2 catheters in the aneurysm sac are used to make the coil basket.

Balloon-Assisted Onyx-500 Aneurysm Treatment

Onyx (eV3) is a liquid embolic agent consisting of ethylene vinyl alcohol copolymer dissolved in dimethyl sulfoxide (DMSO) and mixed with tantalum for fluoroscopic visualization. Onyx HD-500 is a high-viscosity version of this material that is designed specifically for the treatment of intracranial aneurysms. When injected into an aneurysm, Onyx precipitates to form a spongy polymer cast, which sets over approximately 10 minutes with diffusion of the solvent DMSO. Similar to BRT, the balloon is inflated across the aneurysmal neck during Onyx injection to prevent intra-aneurysmal blood flow and extravasation of Onyx. The balloon also shapes the cast with a concave border at the aneurysm sac–parent vessel interface, which helps reestablish normal parent vessel flow dynamics.⁸² The HyperGlide, HyperForm, Scepter, and BALT remodeling balloons are DMSO compatible (Figure 7).

Onyx also has several advantages compared with coils as an embolic agent, particularly in the treatment of wide-necked aneurysms. First, Onyx fills the entire volume of the aneurysm lumen, whereas coils fill <30%. Second, Onyx is more likely to

obliterate the small inflow zone, which results in better angiographic results. Third, the Onyx cast is unlikely to compact, which is the most common cause of coil recanalization. Fourth, Onyx is more readily subtracted from digital subtraction angiography than coils, which is critically important if the aneurysm overlaps the parent artery on the best working view.⁸³ Theoretical disadvantages of balloon-assisted Onyx embolization are similar to those of BRT. It is frequently not possible to navigate the balloon through tortuous anatomy, and balloon occlusion of arteries distal to the circle of Willis is generally not tolerated because of the lack of collateral flow. Disadvantages of Onyx compared with coils are that Onyx cannot be retrieved after injection and that extravasating liquid Onyx can spread along the parent artery wall and occlude adjacent perforating arteries.⁸⁴

The largest study of the safety and efficacy of balloon-assisted Onyx embolization was the Cerebral Aneurysm Multicenter Europe Onyx trial.⁸⁴ This prospective, observational study performed in 20 European centers included a series of 123 aneurysms, 79 of which were large or giant. Twelve-month follow-up showed complete occlusion in 79% of cases, subtotal occlusion in 13%, and incomplete occlusion in 8% of cases. Other authors have reported recanalization rates of 0% in small aneurysms and 0% to 36% in large or giant aneurysms. By comparison, reported recanalization rates after coil embolization are 14.7% to 23% for nongiant aneurysms^{85,86} and up to 90% for giant aneurysms.⁸⁷ It should be noted, however, that in the early experience with Onyx, many surgeons only sealed the orifice of the aneurysm rather than completely filling the aneurysm volume. This practice was discontinued because of the “onion skin” effect, which occurs when blood dissects between the nonadhesive Onyx cast and the vessel wall, leading to recanalization. This is prevented by the current practice of filling the entire aneurysm dome. The incidence of permanent neurological morbidity reported in the Cerebral Aneurysm Multicenter Europe Onyx trial at follow-up was 8.2%. Permanent complication rates from other studies range from 0% to 9%, which is comparable to that for coil embolization.^{83,88-90} Delayed parent vessel occlusion is the most common significant complication. The risk is greater when the material spills into the parent artery or when there is extensive reconstruction of the parent vessel in very wide-necked aneurysms. The risk of delayed occlusion has been decreased by more aggressive antiplatelet therapy before and after the procedure with aspirin and clopidogrel, as well as the introduction of longer balloons, denser Onyx HD 500 with better visibility, and the Quick Stop syringe (Micro Therapeutics, Inc, Irvine, California).⁸⁴ The use of Onyx HD 500 has decreased recently, with evidence suggesting progressive adjacent parent vessel stenosis,⁹¹ and with more aneurysms being treated with flow diverters.⁹²

Balloon-Assisted Onyx Treatment for Vascular Malformations

The use of Onyx in preoperative embolization of intracranial arteriovenous malformations and dural arteriovenous fistulas has

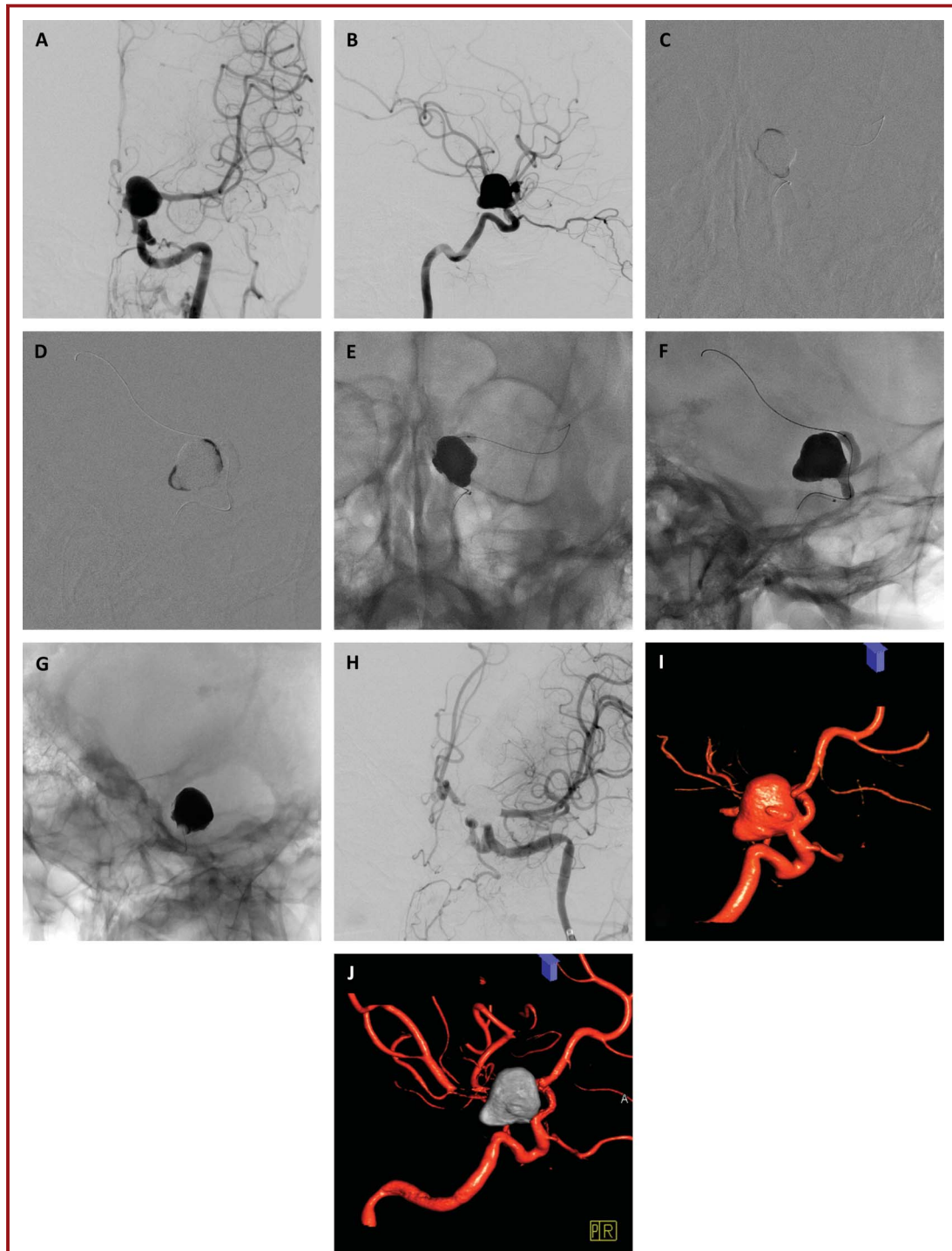


FIGURE 7. Digital subtraction angiography of the left internal carotid artery (ICA), anteroposterior (A) and lateral (B), showing a large left supraclinoid ICA aneurysm with fusiform dilatation of the parent ICA segment. The aneurysm was treated with Onyx-500. C and D, road map during Onyx injection with the balloon inflated in the left ICA. The new Onyx cast appears dark on the subtracted road map. E and F, fluoroscopic images before balloon deflation. The Onyx cast fills the aneurysm down to the aneurysm neck. G, fluoroscopic image after balloon removal. The Onyx cast has a crescent appearance around the aneurysm neck, reconstructing the parent ICA vessel. H, left ICA after Onyx embolization. No aneurysm remnant is seen. Before (I) and after (J) 3DRA showing the Onyx cast filling the entire volume of the aneurysm.

expanded in the last decade. The conventional method of injecting the Onyx is through a DMSO-compatible microcatheter. Before the Onyx penetrates the nidus of the arteriovenous malformation/arteriovenous fistula, an initial proximal plug is necessary, a process that can be time-consuming and often results in extensive proximal reflux. Recently, a new dual-lumen complement balloon (Scepter, Microvention) was used by several groups.^{93,94} The advantage of this balloon microcatheter is that it is 0.014-in microwire compatible, is DMSO safe, and is easy to navigate with a flexible coaxial double-lumen design. It comes in 2 forms, the Scepter-C (compliant) and the Scepter-XC (extracompliant). This maintains a compliance similar to that of the HyperGlide/HyperForm balloon family while adding easier navigability because it can be navigated over a 0.014-in rather than 0.010-in microwire. The advantage of this dual balloon is that the inflation of the balloon in the feeder vessels will avoid the need to form a proximal plug

and avoid proximal migration of the Onyx into the proximal feeding vessel. The proximal Onyx plug was not necessary with the balloon-assisted technique; there was no need for repeated balloon inflation and deflation during the embolization. This also resulted in a faster procedure with less fluoroscopy time⁹³⁻⁹⁵ (Figure 8).

Balloon-Assisted Stent Treatment

Balloon-assisted stent treatment is another method for treating wide-necked aneurysms. It is especially useful for treating circumferential and fusiform aneurysms with preservation of the parent artery, which cannot be accomplished with balloon remodeling or stenting alone.^{50,54,96,97} The technique has also been used successfully to coil blood blisterlike aneurysms of the ICA.⁹⁸ During the first stage of the procedure, a stent is placed across the entire parent vessel-aneurysm complex for parent vessel

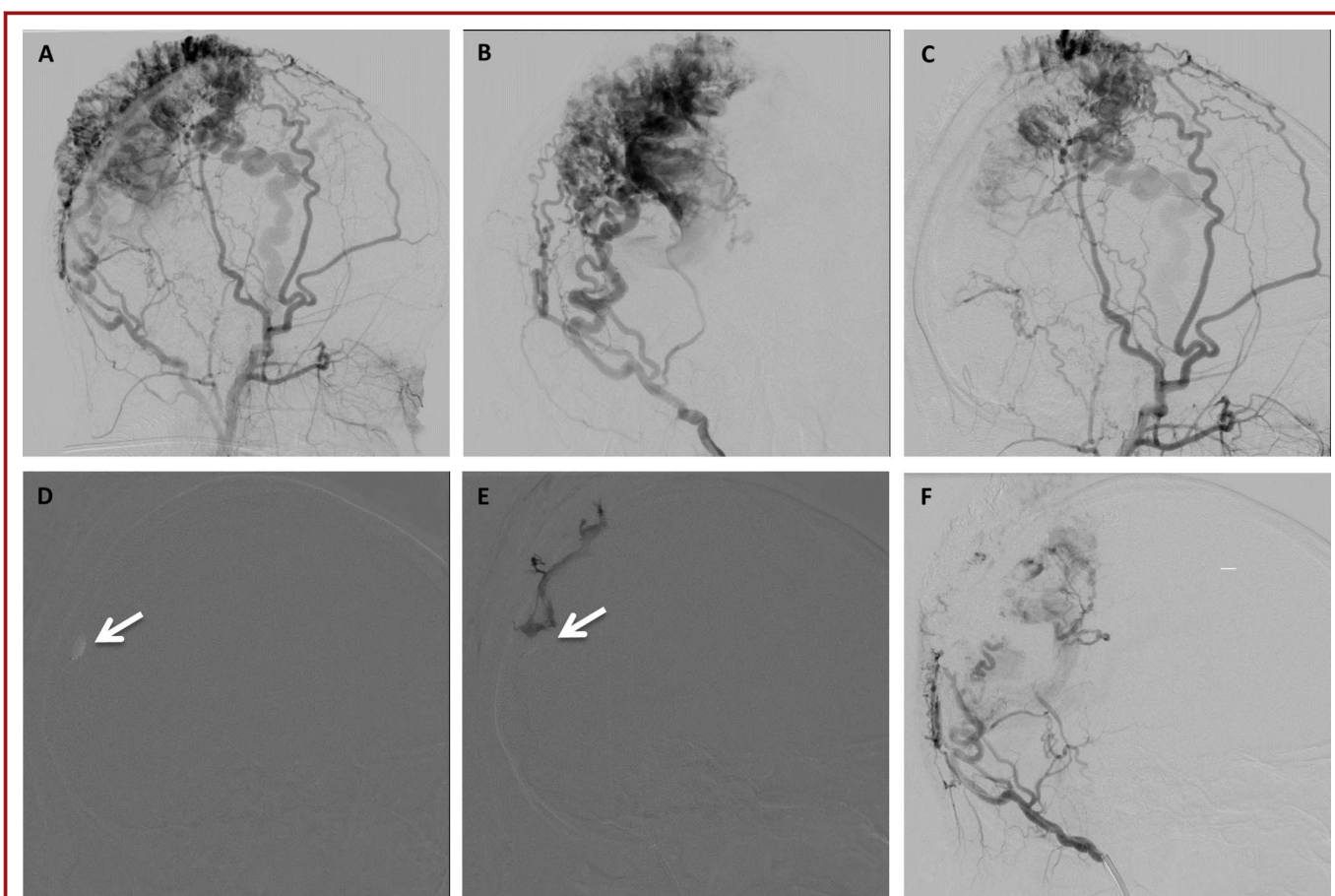


FIGURE 8. Digital subtraction angiography (DSA) of the left external carotid artery (ECA; **A**) in a patient who presented during pregnancy with expanding scalp mass and recurrent scalp bleeding. Selective angiography of the left occipital artery (**B**) and superficial temporal artery (**C**) demonstrating a large scalp arteriovenous malformation (AVM) with complex venous drainage. **D**, road map with contrast used to inflate a Scepter (4 × 11 mm) balloon. The balloon was positioned in the distal left occipital artery feeding vessel of the AVM (arrow). The inner lumen of the balloon was used to inject Onyx-18 into the AVM nidus. **E**, saved road map during Onyx injection. No Onyx reflux is seen proximal to the inflated balloon (arrow). **F**, DSA of the left occipital artery after Onyx injection into AVM nidus. A second embolization session was performed through the left superficial temporal artery, followed by surgical resection and scalp reconstruction.

reconstruction. In the second stage, the balloon is inflated within the stent to demarcate and protect the reconstructed parent vessel lumen during coil placement. There are 2 variations of this technique. Although some surgeons will perform the second stage of the procedure immediately,⁹⁶ others prefer to delay the second stage 6 to 8 weeks.⁵⁴ This delay allows the stent to become partially endothelialized, which may decrease the risk of stent migration during balloon catheter manipulation within the stent. Additionally, a second stent may be placed after embolization, which “tacks up” any coils that may have partially prolapsed into the parent vessel despite balloon protection.^{54,98}

Proper anticoagulation with aspirin and clopidogrel is critical. The circumferential nature of the aneurysm typically permits only partial (85%) occlusion. Consequently, the embolization coils frequently remain exposed to the column of flow within the parent vessel where they represent an intravascular nidus for clot formation. Typically, clopidogrel and aspirin are used and heparinization is not reversed at the termination of the procedure. However, dual antiplatelet therapy and systemic anticoagulation increase the risk of intracranial hemorrhage and possibly rebleeding from a ruptured aneurysm.^{54,99}

The safety and efficacy of the balloon-in-stent technique have been demonstrated only in small series. Fiorella et al⁵⁴ treated 7 patients with this technique, including 3 with ICA aneurysms, 3 with basilar trunk or basilar apex aneurysms, and 1 with a fusiform vertebral artery aneurysm. Partial aneurysm occlusion (75%-90%) was achieved in 5 cases, and nearly complete (>95%) occlusion was achieved in 2 cases. There were no immediate or delayed complications related to the procedures. Suh et al⁹⁶ successfully treated 20 fusiform aneurysms using this technique with no procedure-related complications. After a mean follow-up of 12.3 months, there were no instances of parent artery occlusion or aneurysm recanalization. Finally, Lubicz et al⁹⁷ treated 11 patients with circumferential or fusiform aneurysms. Asymptomatic ICA dissection occurred in 2 patients. At the 12-month follow-up, minor recanalization was seen in 2 patients. The majority of these cases were performed with the HyperGlide balloon catheter. The Sentry balloon was also used. Balloons can also be used as part of neck-sealing technique across the neck of large and giant aneurysms to allow a second microcatheter (for stenting) to be navigated distal to the aneurysm.^{100,101} In 2011, the FDA approved the use of Pipeline Embolization Device for the treatment of large intracranial aneurysms. In a small portion of those patients, incomplete opening of the Pipeline Embolization Device might occur. Balloons were used to anchor the Pipeline Embolization Device into the parent vessel¹⁰² or to dilate it after deployment (personal experience).

CEREBRAL VASOSPASM

Clinically symptomatic cerebral vasospasm occurs in approximately 30% of cases of aneurysmal subarachnoid hemorrhage and is a contributing cause of morbidity and mortality for these patients.¹⁰³ First-line medical treatment consists of hypertension,

hypervolemia, and hemodilution (“triple H” therapy) and calcium channel blockers.¹⁰⁴ However, if medical treatment is ineffective or not tolerated, transluminal balloon angioplasty (TBA) may be used to directly dilate the spastic artery and to restore distal blood flow (Figure 9). Intra-arterial drug infusion, which is used in conjunction with or as an alternative to TBA, is not the subject of this article.

Although the specific mechanism of action responsible for the effects of TBA is not completely understood, animal and human autopsy studies have identified several pathophysiological vascular changes that take place. Physical changes in the vessel wall include tearing of collagen fibers, straightening of the internal elastic lamina, thinning of the tunica media, and stretching of the smooth muscle cells.^{105,106} Functional changes include a dramatic decrease in tissue responsiveness to both vasoconstrictors and vasodilators.¹⁰⁶ These changes account for the durable therapeutic effect of TBA.¹⁰⁷⁻¹¹⁰

TBA is generally restricted to cerebral vessels >2 mm. Typical locations of TBA in the anterior circulation include the supraclinoid ICA and M1 segment of the MCA and are amenable to TBA. TBA may also be performed in the posterior communicating, A1, M2, and P1 arteries; however, the smaller vessel diameter increases the risk of vessel rupture.^{111,112} However, the posterior inferior cerebellar artery, anterior inferior cerebellar artery, and P2, A2, and M3 arterial branches are generally inaccessible.¹¹³ With the smaller version of HyperForm balloons, distal vessels (ie, A2, M3, and P2) have been angioplastied.¹¹⁴ In the posterior circulation, the vertebral and basilar arteries are amenable to TBA.

A variety of balloons have been used for TBA. In 1984, Zubkov et al¹¹⁵ first reported the use of TBA for the treatment of vasospasm after aneurysmal subarachnoid hemorrhage using a flow-directed latex balloon. In 1990, Higashida et al¹¹⁶ developed a low-pressure, semipermeable silicone balloon that reduced the risk of endothelial damage. In addition, the overinflated balloon increased lengthwise rather than in diameter, thus providing an additional safety mechanism against vessel rupture. This balloon was used in the first large clinical series of TBA for the treatment of subarachnoid hemorrhage–induced vasospasm published by Eskridge et al.¹¹⁷ Although it was not a guidewire-directed system, a wire could be introduced into the balloon to deflect the direction of the balloon tip.¹¹⁸

Over the following decade, flow-directed balloons were replaced by low-pressure over-the-wire balloons. In 1999, the STEALTH balloon microcatheter developed by Target Therapeutics was used by Eskridge et al¹¹¹ to access and perform TBA on vasospastic A1 segments. Although the STEALTH had a higher inflation pressure than previously used balloons, Eskridge et al cleverly mitigated the risk of vessel rupture by replacing the occlusive wire supplied with the STEALTH with a nonocclusive, hydrophilic guidewire. The STEALTH was inflated with a tip-occluding guidewire controlled by a manual balloon insufflations device and deflated by withdrawing the guidewire and releasing the balloon contents through the end hole. The nonocclusive, hydrophilic

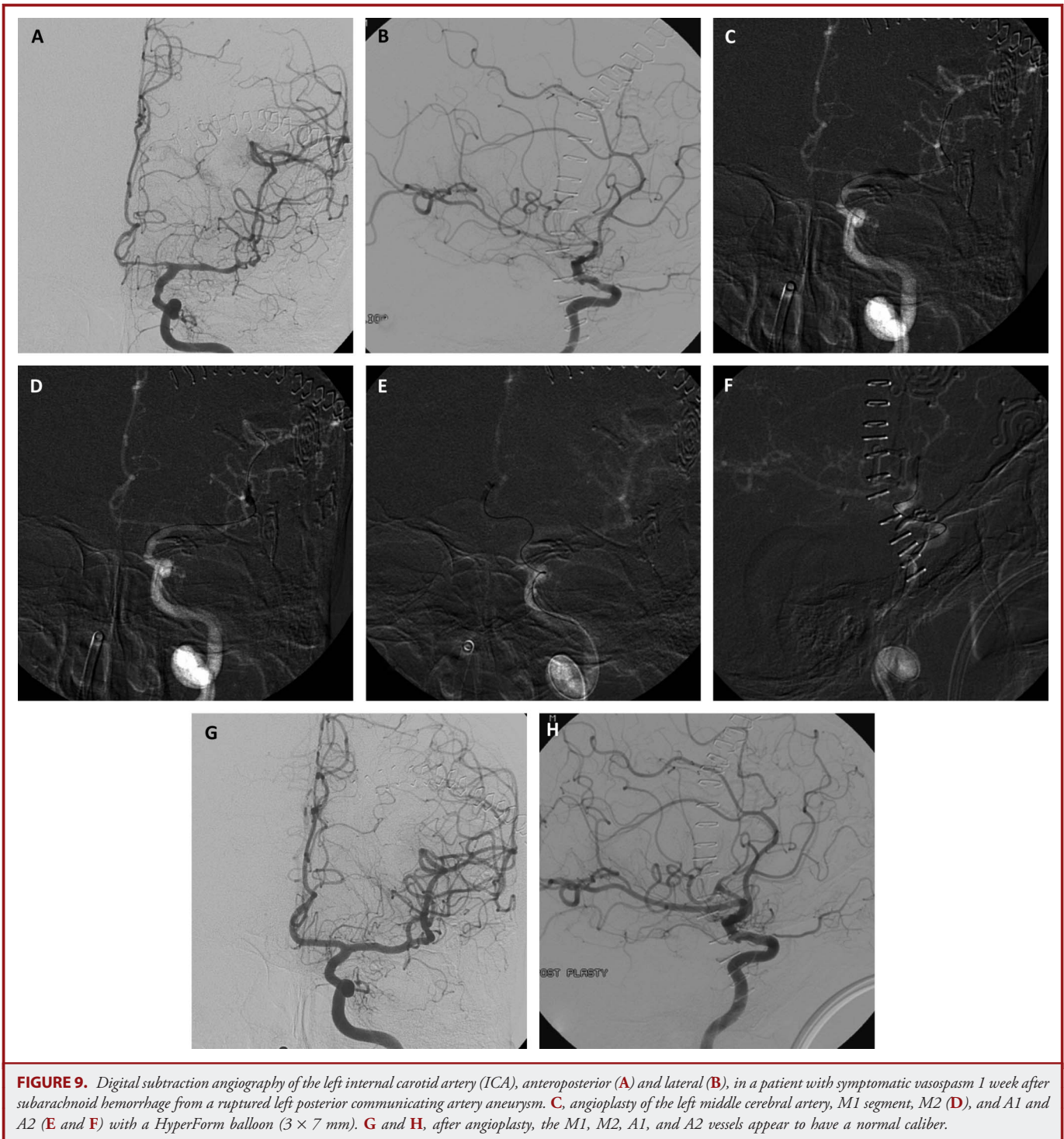


FIGURE 9. Digital subtraction angiography of the left internal carotid artery (ICA), anteroposterior (A) and lateral (B), in a patient with symptomatic vasospasm 1 week after subarachnoid hemorrhage from a ruptured left posterior communicating artery aneurysm. C, angioplasty of the left middle cerebral artery, M1 segment, M2 (D), and A1 and A2 (E and F) with a HyperForm balloon (3 × 7 mm). G and H, after angioplasty, the M1, M2, A1, and A2 vessels appear to have a normal caliber.

guidewire transformed the STEALTH into a calibrated-leak balloon, thus limiting the high pressure applied by the balloon to the vessel wall. The hydrophilic guidewire also improved balloon navigation across stenotic A1 segments and provided support for

the balloon across the acute bend of the A1 segment during balloon inflation. Still, the STEALTH was relatively stiff, which made navigation through the numerous genua of the ICA challenging. The STEALTH is no longer commercially available.

Several other low-pressure, over-the-wire devices consisting of softer semipermeable silicone or elastomer membrane balloons mounted on a single-lumen catheter were subsequently introduced. These included devices approved for the neurovasculature such as the Cirrus/Solstice (Microinterventional Systems), Commodore (Cordis Corporation; Miami Lakes, Florida), and Equinox (Micro Therapeutics, Inc) balloon catheters, which are no longer commercially available.¹¹² The Sentry balloon catheter discussed previously is not approved by the FDA for use in the neurovasculature, but it is still commercially available and has been used for TBA. The primary limitation of these devices is that they lacked the flexibility to be steered into small, tortuous vessels. Additionally, the balloons were not available in small enough sizes to be used in the distal vasculature. For example, the smallest available outer diameter of the Sentry balloon is 3.5 mm. Because it is difficult to inflate a balloon to a diameter less than its designed maximum, using these balloons for TBA in the distal vasculature carries too great a risk of vessel rupture. Thus, until recently, TBA was usually reserved for larger, proximal vessels, and smaller, more tortuous, more distal vessels were not mechanically treated.

The newest permutations of these balloons are the HyperGlide and HyperForm (eV3), which are specifically designed to access more distal intracranial vasculature with the aid of a 0.010-in Xpedion guidewire. The HyperGlide is available in 4-mm diameter and lengths of 10, 15, 20, and 30 mm. The HyperForm is available in 4- or 7-mm diameters and 7-mm length. As previously noted, inflation diameter is calibrated to the volume of contrast solution injected rather than insufflations pressure. Thus, although the 4-mm diameter of these balloons exceeds the average 2- to 3-mm diameter of the A1 segment, partial inflation can be quickly stopped once these compliant balloons begin to conform to the vessel lumen, thus helping to decrease the risk of vessel rupture. Smaller balloon diameters will be coming to the market in the near future and will improve the safety and ability to access the A1 segment and more distal segments in other territories, potentially including A2 and M2. More recently, the Scepter-C balloon is being used for treatment of TBA over a more steerable microwire (0.014 in) with no increased morbidity.¹¹⁹ There appears to be no difference between the compliant and the noncompliant balloons in preventing recurrence or for the need for reangioplasty in patients treated for cerebral vasospasm.¹²⁰

There is a lack of randomized clinical studies that have assessed the effect of TBA on outcome; however, several retrospective studies have demonstrated clinical improvement rates of 31% to 92% after TBA.¹²¹⁻¹²⁶ In 2005, Hoh and Ogilvy¹²⁶ published a meta-analysis that included 530 patients and found an overall clinical improvement of 62% after TBA. In addition, a population study of 9534 patients from 70 medical centers found that treating aneurysmal subarachnoid hemorrhage-induced vasospasm with TBA reduced in-hospital mortality by 16%.¹²² Recently, Jestaedt et al¹²⁷ reported that the rate of infarction was significantly lower in vascular territories treated with TBA compared with territories not treated with TBA (38% vs 7%).

Regarding the timing of TBA, a prospective nonrandomized study by Rosenwasser et al¹²⁵ showed that TBA performed within 2 hours of the onset of vasospasm resulted in a higher rate of clinical improvement (90% vs 40%). Given the durable pathophysiological effects of TBA, prophylactic therapy has been considered. A 1999 study of prophylactic TBA on 13 patients with Fisher grade III aneurysmal subarachnoid hemorrhage resulted in no incidents of cerebral vasospasm; however, 1 patient died of arterial rupture during TBA.¹²⁸ More recently, a phase II study of prophylactic TBA in patients with Fisher grade III subarachnoid hemorrhage did not show a significant difference in Glasgow Outcome Scale score but demonstrated a trend toward fewer patients developing vasospasm or needing therapeutic TBA.¹²⁹

Although TBA is an effective treatment, the benefits must be weighed against the risk of complications that can be devastating.^{112,117,125,127,129} The most serious complication of TBA is arterial rupture, which can occur when the balloon is oversized relative to the vessel diameter. This occurred in only 1.1% of the cases reported by Hoh and Ogilvy.¹²⁶ Overall, vessel rupture is reported in 4% of cases.^{117,124,130} If no angiographic study is available that demonstrates the normal diameter of the vessel before the onset of vasospasm, the diameter unfortunately must be estimated from anatomic assumptions. Congenitally hypoplastic arteries commonly found in the A1 and P1 segments must be avoided because they can be easily overdilated and rupture. Additionally, critical spasm may result in insufficient distal vascular opacification to correctly position the catheter. For example, projecting the balloon tip into a proximal lenticulostriate perforator rather than an M2 segment will likely rupture the former vessel on inflation.¹¹³ Other complications include unprotected aneurysm rerupture, thromboembolism, arterial dissection, branch occlusion, hemorrhagic infarction, and hematoma at the vascular access site.¹³¹⁻¹³³ The risk of thrombotic complications, especially in patients recovering from subarachnoid hemorrhage, is reduced by heparinization to an activated clotting time of 200 to 250 seconds throughout the procedure unless contraindicated. Ensuring that the balloon is completely deflated before catheter manipulation will prevent shearing forces leading to arterial dissection.^{113,134}

CEREBROVASCULAR ATHEROSCLEROSIS

Ischemic stroke is the third leading cause of morbidity and mortality in the United States, with about 800 000 strokes and 300 000 transient ischemic attacks per year,¹³⁵ the majority of which are due to extracranial and intracranial atherosclerotic disease.¹³⁶⁻¹³⁸ Percutaneous transluminal angioplasty (PTA) of high-grade atherosclerotic lesions was first reported in the peripheral vasculature in 1964¹³⁹ and soon become an established treatment modality in the peripheral, coronary, renal vasculature. In contrast, cerebrovascular PTA has gained slower acceptance because of technical difficulties and concerns about disastrous complications. However, in the last 20 years, PTA and

stenting of the extracranial vessels has been established as an alternative to surgical repair, and the feasibility and safety of intracranial PTA and stenting are currently under serious investigation.

The mechanism of PTA involves longitudinal fracture of the atherosclerotic plaque and stretching of the media and adventitia. Dilatation also causes desquamation of endothelial cells and histological damage proportional to the diameter and duration of balloon inflation.^{140,141} PTA almost always causes areas of medial dissection and plaque separation, especially after dilatation of calcified lesions¹⁴⁰; however, the cardiology literature reports a low incidence of acute occlusion at the angioplasty site secondary to dissection because the orientation of most plaques fractures is in the direction of arterial flow.¹⁴² After the procedure, endothelialization and surface remodeling result in healing of most dissection planes within 1 month.¹⁴³

Certain physical principles apply to PTA regardless of anatomic site. The dilating force generated by the balloon is proportional to the balloon pressure, balloon diameter, and surface area of contact with the vessel wall¹⁴⁴; therefore, at a given inflation pressure, larger-diameter balloons generate more radial force than smaller balloons. However, note that larger-diameter balloons also rupture at lower pressures than smaller balloons because wall tension is proportional to the radius of the balloon (the Laplace law).¹⁴⁵ The force transmitted to the treated vessel also depends on the character of the stenosis. High-grade stenosis and longer lesions experience greater radial force than low-grade stenoses. Conversely, less pressure is required to treat residual stenosis than to treat high-grade stenosis in the same-diameter vessel.¹⁴⁶

In contrast to endovascular balloons designed for other procedures, angioplasty balloons used to dilate atherosclerotic lesions are noncompliant and inflate to a predictable maximum diameter. The original angioplasty balloons were made of polyvinyl chloride; however, the compliance of this material increased with multiple inflations and burst at relatively low pressures. Newer balloon materials include polyethylene, polyethylene terephthalate, and nylon-reinforced polyurethane. Polyethylene balloons can sustain higher inflation pressures and are less prone to tearing or perforation in calcified plaques. Polyethylene terephthalate is the least compliant material that allows low-profile, high-pressure balloons; however, this material is more susceptible to perforation in calcified plaques. Nylon-reinforced polyurethane produces relatively noncompliant balloons with high burst pressures.¹⁴⁷

Examples of high-pressure angioplasty balloons used for angioplasty of atherosclerotic extracranial vessels include the Aviator (Cordis Corporation) and Viatrac 14 Plus (Guidant Corp; Indianapolis, Indiana).¹⁴⁸ The Aviator was first approved by the FDA in November 2001 for dilatation of stenosis in the major lower extremity arteries, renal arteries, and arteriovenous dialysis fistulas. The balloon is made of DURALYN. It generates a nominal filling pressure of 10 atm and a rated burst pressure of 14 atm. Available balloons range from 4 to 5.5 mm in diameter and 15 to 40 mm in length. The tapered (<0.90 mm) distal

catheter tip facilitates crossing of tight lesions, and the 3.3F shaft features a dual lumen that enables rapid monorail exchange. One lumen is used for inflation of the balloon with contrast medium, and the second lumen, located only in the distal shaft, accommodates a 0.14-in-diameter guidewire. The low profile of the device may reduce the risk of plaque disruption and embolization when crossing atherosclerotic stenoses. In 2007, Cordis launched the Aviator Plus, which is approved for the added indication of carotid angioplasty and is available in balloon diameters up to 7 mm. The Viatrac 14 Plus was FDA approved in January 2008 for the dilatation of stenosis in the peripheral vasculature and arteriovenous dialysis fistulas, but it has been used in the carotid arteries. The high-pressure balloon has a nominal filling pressure of 8 atm and a rated burst pressure of 14 atm. Available balloon diameters range from 4 to 7 mm. The low-profile shaft has a design similar to the Aviator. Other coronary balloons available include the TREK balloons (Abbot Vascular, Abbott Park, Illinois), which vary in diameter from 1.2 to 5 mm, and the Sprinter balloons (Medtronic).

For concentric calcified plaques and in-stent restenosis, a cutting balloon such as the Ultra2 Monorail (Boston Scientific, Fremont, CA) may be more effective. This device features a noncompliant balloon fitted with 3 microsurgical atherotomes mounted longitudinally on its surface. These microsurgical blades create controlled dissections within stenotic lesions, thus reducing the resistance of the lesion to expansion. Consequently, less force is required to expand the vessel, which may result in less trauma to the vessel wall than conventional balloon angioplasty. This device was designed and approved by the FDA in June 2003 for complex coronary lesions. It is available in lengths of 6 and 15 mm and diameters from 2.0 to 4.0 mm. The nominal pressure of the balloon is 6 atm, and the rated burst pressure is 10 atm. Both over-the-wire and monorail versions are available.

Cutting balloons were introduced initially for the treatment of coronary in-stent stenosis, for which they have demonstrated procedural advantages, higher success rates, and lower rates of retreatment.^{149,150} The use of cutting balloons in carotid stenosis has been reported in multiple small institutional series¹⁵¹⁻¹⁵³ with a relatively good short-term patency.

For many years, angioplasty of the vertebral ostium and intracranial vessels was performed with compliant balloons designed for coronary interventions because the low profile of these devices permitted navigation through the tortuous cervicocranial vessels.¹⁵⁴ The earliest intracranial angioplasties used the STEALTH (Target Therapeutics) or Stratus (Medtronic, Inc/Microinterventional Systems) balloon systems.¹⁵⁵⁻¹⁵⁹ Other devices used with success include the Open-Sail (Guidant, Diegem, Belgium), Predator XL or Ninja (Cordis Corp), and Ranger (Boston Scientific). Most commonly used, however, was the Maverick PTCA balloon catheter manufactured and distributed by Boston Scientific. Both over-the-wire and monorail versions are available; however, the former generally provides greater tracking capability, particularly through tortuous vessels. The tip is made from a nylon-like material that is extremely

resilient and flexible, enabling navigation through the tortuous intracranial anatomy. It is available with a 9-mm-long balloon that is easier to maneuver and causes less vessel straightening on inflation. Available balloon diameters are 1.5 to 4 mm. The coaxial shaft enables the use of a 0.014-in microguidewire through the inner lumen, whereas the outer lumen is used for inflation.

Recently, the Gateway PTA Balloon Catheter (Boston Scientific), designed specifically for intracranial use, was approved as a humanitarian use device by the FDA. The Gateway was developed from the platform of the Maverick balloon catheter with additional hydrophilic coating to enhance intracranial navigability. The inflation pressure of the semicompliant balloon is approximately 6 atm. The balloon is available in diameters of 1.5 to 4 mm and lengths of 10, 15, and 20 mm. The manufacturer recommends that the balloon be undersized to 80% of the target vessel diameter to minimize the risk of vascular trauma.

In Europe, the Cristal balloon manufactured by BALT is marketed for intracranial angioplasty and valvuloplasty. This device is mechanically similar to the Gateway. To cover a wide variety of procedures, >180 Cristal balloon sizes are available, ranging from 2 to 40 mm. Custom sizes can also be manufactured on request. The intracranial models range in size from 2.5 × 7 to 4.5 × 21 mm. The working pressure of the balloon is 10 atm.

High-pressure balloons must be sized conservatively because when oversized they generate sufficient radial force to easily rupture the vessel wall. Balloon size is estimated from the diameter of the normal vessel just distal to the lesion. If the normal diameter of the vessel is uncertain, smaller-diameter balloons should be used initially to avoid overdilatation. Predilatation of the ICA is usually performed with 2- to 4-mm balloons, and a 5- to 6-mm balloon is used for in-stent dilatation. In the intracranial vasculature, the use of undersized balloons and slow balloon inflation has reduced the incidence of complications such as intimal dissection, thrombosis, recoiling, and vessel rupture.¹⁶⁰ Balloon diameters of 2.0 to 2.5 mm are usually appropriate. Balloon length should also be kept to a minimum to optimize trackability.¹⁴⁵

Extracranial Carotid Artery Stenosis

About 20% of strokes are secondary to carotid stenosis.¹³⁷ In 1980, the first atherosclerotic stenosis in a symptomatic patient was treated endovascularly.¹⁶¹ The technique was rarely used before the 1990s because of the poor long-term patency of the carotid artery and concerns about inducing periprocedural embolic strokes. Patency duration has been increased with the addition of intraluminal stents, and over the past 10 years, technical success for carotid artery stenting (CAS) has improved to >97%.¹⁶² In patients with CAS, selective angiography of the nontarget and target carotid arteries is performed to assess collateral circulation and to confirm the diagnosis, respectively. Frequently, an embolic cerebral protection device (CPD) may then be deployed in the ICA distal to the stenosis. The stent is advanced across the stenotic lesion and deployed, followed by

angioplasty with a noncompliant balloon. Less than 30% residual stenosis is generally considered acceptable¹⁶³ (Figure 10).

Several large randomized trials comparing the outcomes of CAS and carotid endarterectomy (CEA) have recently been completed.¹⁶⁴⁻¹⁷⁰ The first such study was the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy trial in 2004 that demonstrated noninferiority of CAS with the use of a CPD compared with CEA.¹⁶⁴ The cohort consisted of both symptomatic and asymptomatic patients, and the trial found a lower 30-day and 1-year morbidity and mortality in the CAS group. The majority of this risk reduction was due to a lower incidence of myocardial infarction after CAS. Consequently, the FDA approved CAS for the treatment of symptomatic carotid artery stenosis.¹⁷¹ However, subsequent studies have been less encouraging. The nonrandomized Endarterectomy vs Angioplasty in Patients with Symptomatic Severe Carotid Stenosis trial was discontinued prematurely because of the high rate of periprocedural complications after CAS.^{168,172} Similarly, the International Carotid Stenting Study included >1700 symptomatic patients and reported a higher 120-day risk of stroke and death after CAS.¹⁶⁹ A nonrandomized substudy of the International Carotid Stenting Study observed a higher incidence of new ischemic lesions identified on MR imaging in the CAS group as well.

Although CEA remains safer than CAS in terms of 30-day stroke and death rates,^{165,166,168-170,173-176} the efficacy of CAS may be comparable to that of CEA for midterm prevention of ipsilateral stroke.^{165,166,168-170,173-180} Recently, the Carotid Revascularization vs Endarterectomy Trial compared CAS and CEA in >2500 symptomatic and asymptomatic patients with severe stenosis.¹⁷⁰ After a median follow-up period of 2.5 years, the rates of ipsilateral stroke were comparable in each group. Therefore, given the midterm comparability of CAS and CEA, CAS may be an attractive option for select patients with a low risk of 30-day complications.

The risk of stroke or death after CAS is related to a variety of factors. In terms of lesion morphology, 30-day stroke or death is increased for ICA stenoses that are longer than 10 mm, calcified, or located near the ostium. Emboli are more likely to dislodge from longer plaques that often require multiple dilatations and longer stents.¹⁸¹ Studies have also verified a significant correlation between operator experience and outcome.¹⁸² The American Heart Association guidelines for secondary prevention of stroke stipulate that CAS is a reasonable option when performed by surgeons, with established periprocedural morbidity and mortality rates of 4% to 6%, similar to reported rates of CEA.¹⁸³ Patients who cannot tolerate reversal of cerebrovascular flow because of incomplete interhemispheric collateral circulation are poor candidates for CAS.¹⁷¹ Notably, octogenarians are at a significantly higher risk of periprocedural stroke and death.¹⁸⁴ This finding may be due to unfavorable arterial anatomy and unstable plaque morphology in elderly patients.¹⁸⁵

Embolization during carotid PTA has been an ever-present concern; however, the role of cerebral CPDs remains controversial. Systematic reviews of nonrandomized case series have shown that

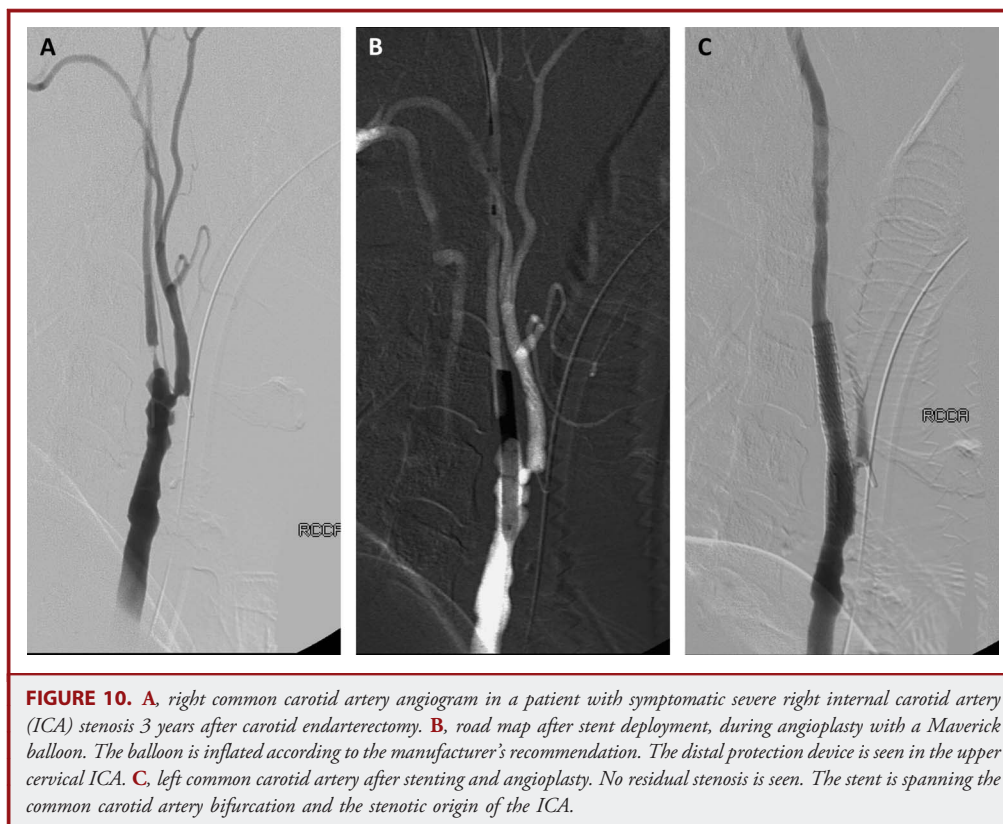


FIGURE 10. **A**, right common carotid artery angiogram in a patient with symptomatic severe right internal carotid artery (ICA) stenosis 3 years after carotid endarterectomy. **B**, road map after stent deployment, during angioplasty with a Maverick balloon. The balloon is inflated according to the manufacturer's recommendation. The distal protection device is seen in the upper cervical ICA. **C**, left common carotid artery after stenting and angioplasty. No residual stenosis is seen. The stent is spanning the common carotid artery bifurcation and the stenotic origin of the ICA.

CPD decreases the incidence of thromboembolic complications.^{181,186} Investigators in the Endarterectomy vs Angioplasty in Patients with Symptomatic Severe Carotid Stenosis trial stopped unprotected CAS early as a result of a nearly quadrupled 30-day stroke rate without CPD.¹⁸⁰ Consequently, in 2004, consensus opinion advocated the use of CPDs, declaring that randomized trials would be unethical.^{187,188} However, the efficacy of CPDs may simply be due to corresponding advances in stenting technique, refinement of patient selection criteria, and increased experience with stenting.¹⁸¹ The Stent-Protected Angioplasty vs Carotid Endarterectomy trial did not show a significant protective effect from CPDs,¹⁶⁵ and the International Carotid Stenting Study and Carotid Revascularization vs Endarterectomy Trial lead-in phase showed more imaging lesions in patients treated with CPDs.^{179,182} A 2008 prospective randomized trial by Barbato et al¹⁸⁹ found that CPDs did not reduce the prevalence of periprocedural ischemic lesions. Three types of CPDs have been developed: devices for distal occlusion, proximal occlusion, and distal filtration.¹⁹⁰ However, a recent meta-analysis did not find any significant difference in the risk of procedural stroke with regard to the type of CPD.¹⁸¹

Extracranial Vertebral Artery Stenosis

About 25% of all strokes involve the posterior circulation¹³⁶; however, the association between posterior circulation strokes

and vertebral artery stenosis is less well defined than the relationship between anterior circulation stroke and carotid stenosis. The proximal vertebral artery is the most frequent site of vertebral artery stenosis.^{191,192} Although these lesions are usually clinically insignificant as a result of the patency of the contralateral vertebral artery and collateral flow, bilateral occlusive disease of the extracranial vertebral arteries can lead to vertebrobasilar insufficiency.¹⁹³ In 1 study, 20% of patients with symptomatic vertebrobasilar ischemia had >50% stenosis of the proximal vertebral artery, and about half of these patients also had contralateral lesions.¹⁹⁴ Another study showed that patients with a history of posterior circulation transient ischemic attack have a 25% to 29% prevalence of stroke during 5- to 6-year follow-up.¹⁹⁵ The rate of recurrence is as high as 18% despite warfarin or aspirin therapy,¹⁹⁶ and surgical treatments such as carotid-vertebral transposition, endarterectomy, and bypass surgery are associated with significant morbidity.¹⁹⁷⁻¹⁹⁹ Thus, endovascular management of these lesions is a viable option (Figure 11).

Balloon angioplasty of the extracranial vertebral artery was first described in the 1980s.^{200,201} Stenting began in the 1990s to maintain vessel patency.²⁰² Treatment of extracranial vertebral stenosis with balloon-expandable stents has since been described in several case series with high technical success rates.²⁰²⁻²¹²

The incidence of major periprocedural complications reported in the literature is 0% to 3.4%.¹⁶³ The most serious immediate

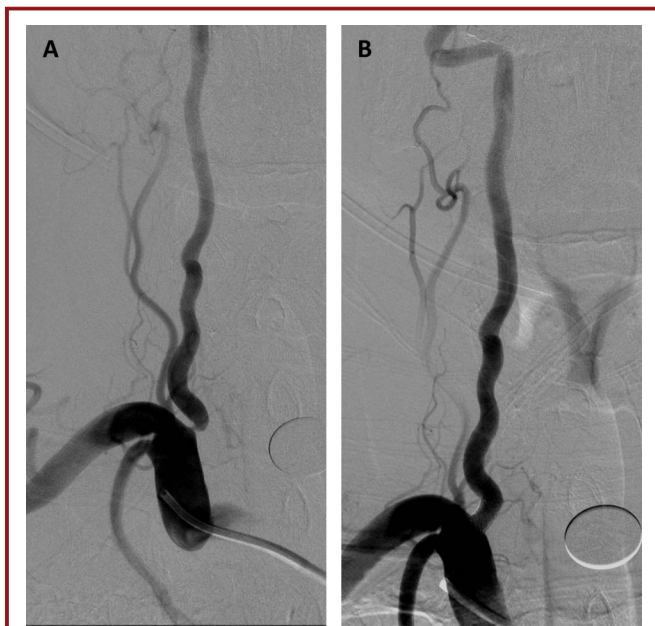


FIGURE 11. **A**, right subclavian artery angiogram demonstrating severe stenosis of the origin of the right vertebral artery in a patient with multiple posterior circulation transient ischemic attack symptoms. **B**, right subclavian artery angiogram after deployment of balloon mounted stent (coronary stent). The stent is deployed as the balloon is inflated at the origin of the right vertebral artery.

complication is distal embolism.²⁰³ The incidence of periprocedural posterior transient ischemic attacks is 0% to 4.8%²¹³; however, the incidence of periprocedural high-intensity lesions on diffusion-weighted imaging is significantly higher.^{203,214} Consequently, some authors recommend using embolic protection devices during vertebral artery stenting as opposed to balloon protection.^{208,209,215}

Data regarding the prognosis after extracranial vertebral stenting are limited but encouraging. The literature suggests that the risk of stroke in the posterior circulation is <1% during the midterm follow-up.^{205,206} However, in-stent restenosis remains a long-term concern.²⁰²⁻²⁰⁷ The reported incidence of restenosis varies widely from 0% to 63% among various studies.^{202-205,216} Recently, drug-eluting stents to prevent in-stent restenosis have been advocated.^{210-212,217} Factors that may be predictive on in-stent restenosis are diabetes mellitus and longer lesion length.²¹⁸ Because the arterial wall of the vertebral ostium has a tough muscular ring, moderate overdilation may be accomplished with minimal added risk of vessel rupture and may be an effective modality for preventing restenosis.²⁰³ Appropriate positioning of stents may be another important point to ensure safe stent placement and to prevent restenosis. The stent should completely cover the ostium and should not protrude into the subclavian artery at the proximal side of the ostium.²⁰³ Because the stent has to partially extend into the subclavian artery, accessing that stent may be problematic in cases of restenosis.

Recently, a new ostial balloon has been used to facilitate angioplasty at that location. The Ostial Flash balloon catheter (Ostial Corp, Mountain View, California) was designed with 2 overlapping separate balloons. The proximal balloon is a compliant one (dilates within the subclavian artery) and noncompliant balloon (for angioplasty of the stenosis). Early experience with this Ostial balloon has been encouraging, with successful catheterization of the stenosis and angioplasty of the ostial stenosis.²¹⁹

Data comparing extracranial vertebral artery stenting with optimal medical management are lacking. The Carotid and Vertebral Artery Transluminal Angioplasty Study randomized 16 patients to vertebral artery PTA and stenting or medical management; however, the study lacked sufficient power to generate meaningful conclusions.¹⁶⁶ A large randomized controlled trial comparing the long-term risk of stroke associated with extracranial vertebral artery stenosis after the best medical treatment with PTA and stenting is still needed; however, vertebral PTA and stenting can be considered an emerging therapy for patients with symptomatic vertebral artery stenoses who have failed best medical management.

Intracranial Stenosis

Atherosclerotic intracranial stenosis accounts for 8% to 10% of ischemic events.¹³⁸ Intracranial PTA is inherently more dangerous than in other parts of the body because of the fragility of intracranial arteries, which have few media and muscular layers, are difficult to access, have disastrous consequences of vessel rupture, and carry a risk of distal embolization.²²⁰⁻²²³ However, patients with symptomatic intracranial stenoses have a 10% to 50% annual risk of recurrent stroke,^{224,225} and medical therapy reduces this risk only to 10% to 38%.^{224,226-228} Furthermore, options for patients who fail antithrombotic therapy are limited. The prospective Warfarin-Aspirin Symptomatic Intracranial Disease trial failed to demonstrate a higher efficacy of warfarin compared with aspirin for stroke and death prevention in patients with intracranial stenosis $\geq 50\%$, except for a slight benefit seen in patients with basilar artery stenosis, and anticoagulation was shown to significantly increase the risk of cerebral hemorrhage.^{227,229} These results, as well as recent advances in microcatheter and balloon technology that permit easier access to intracranial vessels, have led to renewed enthusiasm for intracranial PTA and stenting.

Intraoperatively, glycoprotein IIb/IIIa inhibitors have been shown to decrease morbidity and mortality in coronary stenting²³⁰; however, these studies have not been replicated for the cerebrovasculature. The balloon is positioned so that the center of the balloon dilates the site of most critical stenosis. Additional dilatation may be necessary to achieve residual stenosis of <30%. A stent may then be deployed with the assistance of a high-pressure balloon that firmly embeds it within the plaque. After the procedure, aspirin is continued indefinitely and clopidogrel is discontinued after 6 weeks to 3 months.^{231,232} Several small

single-center series have been published showing progressive technical improvement of intracranial PTA.^{217,233-241} Reported rates of periprocedural complications range from 0% to 14.7%.^{217,232-241} The incidence of complications such as intimal dissection, thrombosis, recoiling, and vessel rupture has declined through the use of undersized balloons and slow balloon inflation.¹⁶⁰

Intracranial angioplasty with stenting has recently become technically feasible and available in several stroke centers worldwide. Low-profile, balloon-premounted coronary stents were previously used; however, the Wingspan stent system, which is

specifically designed for intracranial vessels, has recently been approved by the FDA as a humanitarian use device. This Wingspan is self-expanding and adapts to the shapes of target vessels. Early studies are encouraging, with reported periprocedural risk of stroke or death of 4.5% to 14.7%^{232,242-247}; however, several issues must still be evaluated. Lawson et al²⁴⁹ reported acute intraprocedural thrombus formation within 20 minutes after stent placement in 14.6% of cases. They recommend serial angiography every 10 minutes for at least 30 minutes after Wingspan placement to detect acute thrombosis.²⁴⁸ This complication is likely due to plaque rupture during angioplasty

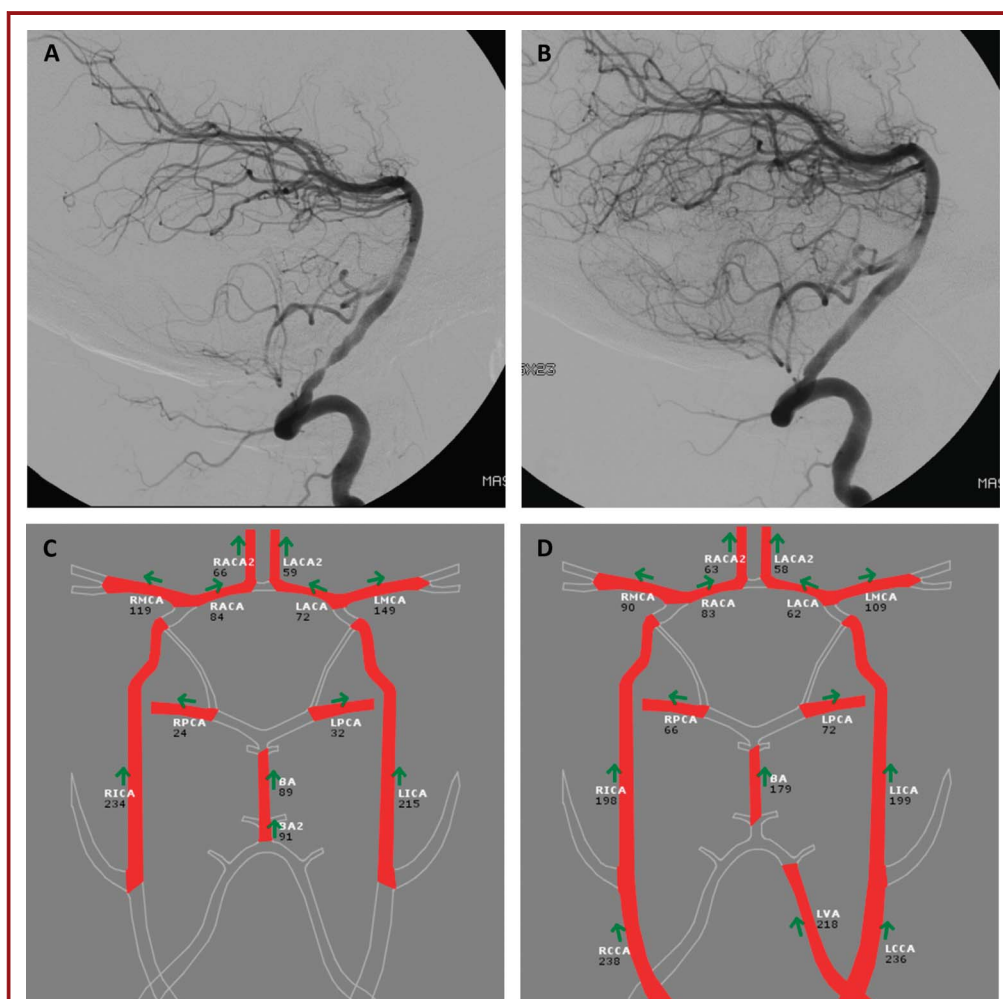


FIGURE 12. **A**, left vertebral artery (VA) angiogram showing severe stenosis of the intracranial portion of the left VA in a patient with a contralateral right VA occlusion. Patient presented with progressive symptoms despite maximal medical therapy. **B**, left VA angiogram after angioplasty and stenting using a Gateway balloon and Wingspan stent. No residual stenosis is seen after angioplasty/stenting. **C** and **D** quantitative magnetic resonance angiography flow map (NOVA, VasSol, River Forest, Illinois). The flow within the left VA increased from 91 to 218 cm^3/min after angioplasty and stenting, indicating adequate flow restoration of flow within the posterior circulation. BA, basilar artery; LACA, left anterior cerebral artery; LICA, left internal carotid artery; LMCA, left middle cerebral artery; LPCA, left posterior cerebral artery; RACA, right anterior cerebral artery; RICA, right internal carotid artery; RMCA, right middle cerebral artery; RPCA, right posterior cerebral artery.

with release of intrinsic factor²⁴⁹; however, whether acute thrombosis occurs despite antiplatelet therapy is unclear. One hypothesis debated in the interventional cardiology literature is the role of aspirin or clopidogrel resistance in some patients.²⁵⁰ In addition, in-stent restenosis was observed in 25% to 30% of lesions in prospective Wingspan registries,^{244,246} half of which were more extensive than the original lesions.²⁵¹ Treatment of in-stent restenosed lesions did not produce durable results.²⁵² The mechanism of in-stent stenosis is also not well understood but may be related to intimal injury during stent expansion and vascular wall shear stress produced by deformation of vessel geometry.²⁵³

Recently, the Stenting vs Aggressive Medical Management for the Prevention of Recurrent Stroke (SAMMPRIS) trial was published. This prospective, National Institutes of Health-funded, multicenter clinical trial randomized patients to either intracranial stenting plus medical therapy or medical therapy alone and compared the safety and effectiveness of each treatment in preventing stroke, heart attack, or death in patients who have had a stroke or transient ischemic attack secondary to intracranial stenosis. Patients were enrolled in the study for up to 30 days after a stroke in an area supplied by a stenotic artery (70%-99%) or intensive medical therapy consisting of aspirin 325 mg and clopidogrel 75 mg daily for 90 days after the stroke, followed by lifelong aspirin. The results showed that the aggressive medical management was superior to PTA and stenting. The 30-day rate of stroke or death was 14.7% in the PTAS and 5.8% in the medical management group (Figure 12).

Previous studies of balloon angioplasty alone have demonstrated high technical and long-term success compared with stenting.^{156,220,254-256} A multicenter study that included 95 primary angioplasty procedures and 98 intracranial stents placements showed no difference in survival at 2 years between the 2 groups.²⁵⁷ In a recent meta-analysis that included >2300 procedures, technical success was reported in 80% of primary angioplasty procedures compared with 95% of stenting procedures.²⁵⁷ The incidences of stroke and mortality were comparable between the 2 groups during a 1-month period. However, these studies were not randomized; therefore, the results were probably biased because treatment modality was likely based on angiographic and clinical criteria. In the period after the SAMMPRIS trial, submaximal angioplasty procedures were offered for selected patients with acute symptomatic ischemic events, with an event-free survival similar to that of the medical arm in the SAMMPRIS trial.^{258,259}

CONCLUSION

As the field of endovascular neurosurgery continues to evolve, newer technology will continue to evolve. It is essential to understanding the evolution of balloons, their potential applications, and related operative nuances. Currently, more than a dozen balloons are available for use. The indications for such technology are rapidly expanded, and often the expertise for its use is lacking. This article is presented to highlight some of those nuances that are not often published and are needed for younger physicians.

Disclosure

Dr's Alaraj and Aletich are consultants for Codman Neurovascular. The other authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

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