Endovascular Advances in the Treatment of Cerebral Aneurysms

An overview of the development of new neuroendovascular techniques and technology for the treatment of cerebral aneurysms.

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The first description of neuroendovascular surgical techniques dates back to 1904, when Dawbarn described open access to the external carotid artery for embolization of tumors of the head and neck with paraffin particles.[1] Actual catheterization of intracranial vessels was first described by Luessenhop and Velasquez in 1964.[2] A decade later, Serbinenko ushered in the era of neurointervention when he published on the treatment of more than 300 patients with direct carotid-cavernous fistulas and cerebral aneurysms using detachable and nondetachable balloons.[3] The detachable balloon became the first widely accepted device specifically designed for intracranial use.

The development of guidewire-supported microcatheters in the 1980s paved the way for detachable coil embolization of cerebral aneurysms.[4-6] This development allowed for the precise delivery of coils within the aneurysm and adjustment of these coils in the event of suboptimal positioning. Through years of refinement in neuroendovascular technologies, cerebral aneurysm coiling is now a widely accepted treatment option and is oftentimes preferred over microsurgical clip ligation. The development of adjunctive devices and techniques (eg, stent-assisted coiling, balloon-assisted coiling) further jettisoned endovascular strategies to the forefront of aneurysm treatment.

Subsequently, flow-diverting stents were introduced as a "stand-alone" treatment for cerebral aneurysms. Higher metal surface area (30%–50%) decreased porosity, resulting in the ability to direct bulk blood flow away from the aneurysm sac while maintaining parent vessel and adjacent perforator patency. In a delayed fashion, with endothelialization along the flow-diverter interstices, the aneurysm would eventually thrombose, functionally reconstructing the parent vessel.[7] Flow-diverting stents transformed the treatment of carotid artery and giant aneurysms, which traditionally had been managed with fairly complex open surgical trapping and bypass techniques. They have also permitted the endovascular treatment of aneurysms that were considered uncoilable. The long-term effectiveness of treatment of these aneurysms was recently reported in the 3-year follow-up of the Pipeline for Uncoilable or Failed Aneurysms trial, which demonstrated complete occlusion in 93.4% of aneurysms and no recanalization of previously completely occluded aneurysms.[8]

The field of endovascular neurosurgery continues to evolve. In this article, we summarize a few of the latest concepts and devices currently in clinical studies for the endovascular treatment of cerebral aneurysms. Although new stents, coils, and balloons with iterative improvements are being developed, this article focuses on novel neuroendovascular technology with unique designs.

INTRASACCULAR DEVICES

Woven EndoBridge

Introduced in 2011, the Woven EndoBridge (WEB) device (Sequent Medical, Inc.) was designed to mimic the effect of intraluminal flow-diverting stents but are placed completely within the aneurysm sac as a stand-alone therapy.[9,10] It is composed of a braided nitinol wire that holds the device in a globular shape. Similar to flow-diverting stents, the wire mesh structure provides between 35% and 45% neck metal coverage and yields a "stent-like" adherence to the inside of the aneurysm sac. It spans the ostium of the aneurysm, disrupt-

ing flow at the aneurysm neck. The device is delivered through the Via microcatheter (Sequent Medical, Inc.). It is fully retrievable, and the detachment system is electrothermal.

The initial multicenter clinical experience with the WEB device consisted of 21 aneurysms treated at three European centers.[11] Technical success was achieved in 20 cases; one inadvertent detachment with a successful retrieval occurred. One patient (4.8%) experienced transient clinical worsening due to a thromboembolic event that resolved at 3 months. This study consisted of only short-term follow-up (2–8 months), and adequate occlusion was observed in 80% of cases.

More recently, Asnafi et al performed a systematic review and meta-analysis of 565 patients with 588 aneurysms (22% ruptured aneurysms) treated with the WEB device.[12] Treatment failure occurred in 3% of cases. The initial adequate occlusion rate was 59%, increasing to 85% at 7 months. There was no difference in the occlusion rate between ruptured and unruptured aneurysms at follow-up (85% vs 84%; $P = .89$). Thromboembolic complications occurred in 8%, with no difference between patients with ruptured and unruptured aneurysms (2%; $P = .35$).

These results compare favorably with stent-assisted coiling. Recent meta-analyses have reported a stent-assisted coiling occlusion rate of 73% and periprocedural morbidity of 8% to 12%.[13-15] These results hold promise for a currently elusive endovascular solution to ruptured wide-necked aneurysms because the WEB device does not require dual antiplatelet therapy. Additional experience and follow-up with this device is needed and is currently being collected.

Artisse Intrasaccular Device

The Artisse intrasaccular device (Medtronic; formerly known as the Luna aneurysm embolization device) is a self-expanding, braided ovoid implant made from a double layer of nitinol wire mesh (Figure 1). Similar to the WEB device, it is designed to create flow disruption across the mesh from the parent artery to the aneurysm, and similarly, there is no need for dual antiplatelet therapy.

Use in rabbit models has demonstrated high rates of complete occlusion, with 10 of 15 aneurysms demonstrating complete occlusion within 30 minutes of device implantation and at 1-month follow-up.[16] Early human experience in 15 patients includes one aneurysm perforation and one thromboembolic complication.[17] Immediate complete occlusion was observed in one patient, and near-complete occlusion was present in nine patients. Follow-up at 6 months was available
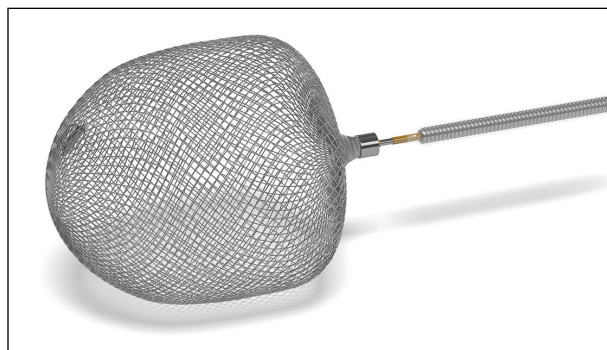

Figure 1. The Artisse intrasaccular device.

for four patients and demonstrated complete occlusion in two patients and neck remnants in two patients. Larger studies are currently being planned.

Medina Embolization Device

The Medina embolization device (Medtronic) is a novel design consisting of a core wire and outer memory alloy filaments that are shaped into petals that lie along the axis of the structure (Figure 2). As the device is deployed, it deforms to fill the space within the aneurysm. The filament petal design is intended to form broader loops that fill the aneurysm dome and ostium, creating a stable structure and distributing the forces acting on the aneurysm wall. The Medina embolization device was designed to treat any saccular aneurysm at any location.
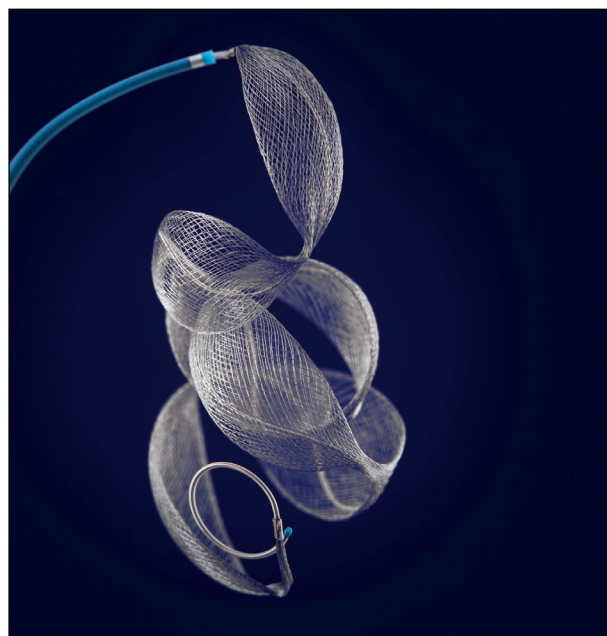
Figure 2. The Medina embolization device.

Early clinical experience with this novel embolization system has been encouraging.[18] In a series of nine patients, there were no technical failures. There were no peri- or postprocedural clinical complications. Three patients underwent follow-up angiography at 1 month, and all demonstrated > 95% aneurysm occlusion. Another report of 15 patients with greater follow-up (11 patients), showed acceptable occlusion (Raymond–Roy class 1 or 2) in 10 patients; one patient had an enlarging neck remnant.[19] Larger multicenter and longer-term studies are being planned.

BIFURCATION SUPPORT DEVICES

PulseRider

The PulseRider device (Codman Neuro) is intended as an adjunct scaffold device to be used with detachable coils, specifically for the treatment of wide-necked bifurcation aneurysms. The open-cell frame preserves luminal patency and flow through the parent vessel bifurcation while minimizing exposed intraluminal metal exposure, such as that seen with Y-configuration stenting (Figure 3).[20] An additional benefit over Y-configuration stenting is that it does not require the sometimes-challenging catheterization of the bifurcation branch vessels or catheterization through stent interstices.

Perioperative results have been encouraging in a small international series of 15 patients with wide-necked bifurcation aneurysms.[20] One treatment failure occurred due to suboptimal positioning of the PulseRider device. One thromboembolic event occurred when thrombus formed at the limbs of the device. Immediate control angiography demonstrated adequate aneurysm occlusion in all patients. At 1-month follow-up, no neurologic impairment was noted. Similar results were reported by Mukherjee et al, who experienced one thromboembolic event and Raymond–Roy class 1 occlusion in all 10 of their cases.[21]

pCONus Device

The pCONus device (phenox GmbH) is a stent-like, neck-bridging device designed to assist coil embolization of wide-necked bifurcation aneurysms. This nitinol device has four distal loops (petals) that radially flare and is crossed by a nylon net meant to support the coil mass (Figure 4). The proximal stent-like shaft creates 5% surface metal coverage. The pCONus device is delivered through a 0.021- or 0.027-inch microcatheter via electrolytic detachment and is fully retrievable.

The initial experience with the pCONus device consisted of 28 patients (nine ruptured aneurysms) and
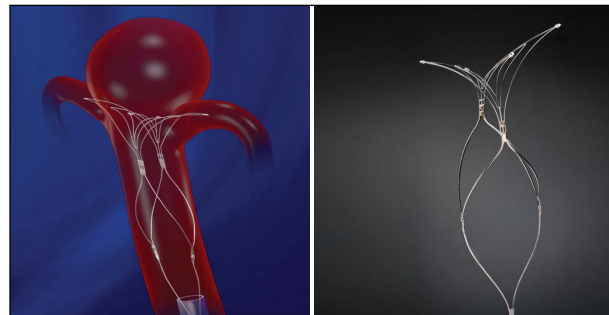
Figure 3. The PulseRider device.

was published in 2014.[22] There were no treatment-related failures, and no coil protrusion into the parent vessel was observed. One thromboembolic complication occurred without clinical consequence. On immediate control angiography, Raymond–Roy class 1 or 2 occlusion was achieved in 61% of patients. At a mean follow-up of 7.5 months, Raymond–Roy class 1 or 2 occlusion was observed in 86%, with nine aneurysms showing an improvement of at least 1 point on the Raymond–Roy classification scale. Similar results were reported in a more recent study with longer follow-up.[23] Raymond–Roy class 1 or 2 occlusion was seen in 95% on the immediate control angiography. At 1 year, adequate occlusion was present in all patients as evaluated by MRI.

The pCONus device also has demonstrated safety and efficacy in the treatment of acutely ruptured aneurysms.[24] In 21 patients with ruptured aneurysms, there were no deployment failures. Immediate control angiography demonstrated Raymond–Roy class 1 or 2 occlusion in 62%. One thromboembolic complication and one aneurysm perforation occurred.
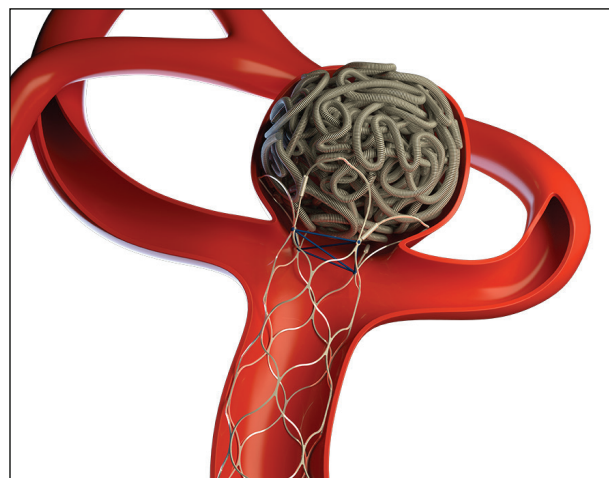
Courtesy of phenox GmbH.

Figure 4. The pCONus bifurcation aneurysm implant.
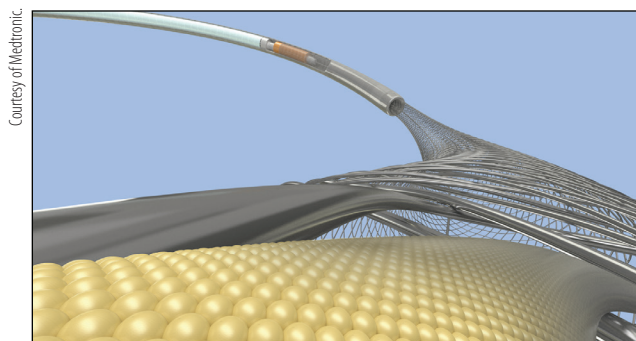
Courtesy of Medtronic.

Figure 5. The Pipeline Flex with Shield technology.

Pipeline Flex With Shield Technology

The Pipeline device (Medtronic; formerly developed by Covidien) was introduced in 2008 and remains the only approved flow-diverter stent in the United States. The second-generation Pipeline Flex debuted in 2014, with a stiffer delivery wire and polytetrafluoroethylene sleeves instead of a capture coil. Although recent data suggest that treatment of ruptured cerebral aneurysms with flow diversion (and the necessary antiplatelet therapy) may be safe, this strategy remains controversial.[25] The Pipeline Flex with Shield technology was designed to address this limitation and is currently under study in the United States.

The Shield technology is surface modification in which a synthetic phosphorylcholine is covalently bonded to the strands comprising the Pipeline device (Figure 5). In thrombogram testing, the peak thrombin was significantly lower using this technology compared to the Pipeline Flex device, which suggests a lower thrombogenicity.

Preliminary experience with the Pipeline Flex with Shield technology has been encouraging.[26] In a small series of 10 patients, there were no technical failures. None of the patients were preloaded with antiplatelet therapy; however, single antiplatelet therapy was started after the second week. One patient experienced stent occlusion at 1-week follow-up. An international, multicenter observational cohort (NCT 02719522) assessing the performance of this device is currently enrolling patients.

CONCLUSION

Endovascular cerebral aneurysm treatment continues to demonstrate considerable recent innovation using novel designs and concepts. Many of these novel devices represent new solutions to commonly encountered challenges, including device delivery, thrombogenicity, safety, and occlusion durability. ∎

1. Dawbarn RHM. The starvation operation for malignancy in the external carotid area. Its failures and successes. JAMA. 1904;17:792-795.
2. Luessenhop AJ, Velasquez AC. Observations on the tolerance of the intracranial arteries to catheterization. J Neurosurg. 1964;21:85-91.
3. Serbinenko FA. Balloon catheterization and occlusion of major cerebral vessels. J Neurosurg. 1974;41:125-145.
4. Richling B. History of endovascular surgery: personal accounts of the evolution. Neurosurgery. 2006;59(5 suppl 3):S30-38; discussion S3-13.
5. Guglielmi G, Vinuela F, Dion J, Duckwiler G. Electrothrombosis of saccular aneurysms via endovascular approach. Part 2: preliminary clinical experience. J Neurosurg. 1991;75:8-14.
6. Guglielmi G, Vinuela F, Sepetka I, Macellari V. Electrothrombosis of saccular aneurysms via endovascular approach. Part 1: electrochemical basis, technique, and experimental results. J Neurosurg. 1991;75:1-7.
7. Liou TM, Li YC. Effects of stent porosity on hemodynamics in a sidewall aneurysm model. J Biomech. 2008;41:1174-1183.
8. Becske T, Potts MB, Shapiro M, et al. Pipeline for uncoilable or failed aneurysms: 3-year follow-up results [published online October 14, 2016]. J Neurosurg.
9. Ding YH, Lewis DA, Kadirvel R, et al. The Woven EndoBridge: a new aneurysm occlusion device. AJNR Am J Neuroradiol. 2011;32:607-611.
10. Klisch J, Sychra V, Strasilla C, et al. The Woven EndoBridge cerebral aneurysm embolization device (WEB II): initial clinical experience. Neuroradiology. 2011;53:599-607.
11. Pierot L, Liebig T, Sychra V, et al. Intrasaccular flow-disruption treatment of intracranial aneurysms: preliminary results of a multicenter clinical study. AJNR Am J Neuroradiol. 2012;33:1232-1238.
12. Asnafi S, Rouchaud A, Pierot L, et al. Efficacy and safety of the Woven EndoBridge (WEB) device for the treatment of intracranial aneurysms: a systematic review and meta-analysis [published online August 11, 2016]. AJNR Am J Neuroradiol.
13. Feng MT, Wen WL, Feng ZZ, et al. Endovascular embolization of intracranial aneurysms: to use stent(s) or not? Systematic review and meta-analysis. World Neurosurg. 2016;93:271-278.
14. Phan K, Huo YR, Jia F, et al. Meta-analysis of stent-assisted coiling versus coiling-only for the treatment of intracranial aneurysms. J Clin Neurosci. 2016;31:15-22.
15. Zhao B, Yin R, Lanzino G, et al. Endovascular coiling of wide-neck and wide-neck bifurcation aneurysms: a systematic review and meta-analysis. AJNR Am J Neuroradiol. 2016;37:1700-1705.
16. Kwon SC, Ding YH, Dai D, et al. Preliminary results of the Luna aneurysm embolization system in a rabbit model: a new intrasaccular aneurysm occlusion device. AJNR Am J Neuroradiol. 2011;32:602-606.
17. Piotin M, Sourour N, Biondi A, et al. The Luna aneurysm embolization system for treatment of intracranial aneurysms. J Neurointerv Surg. 2012;4:A16.
18. Turk AS, Maia O, Ferreira CC, et al. Periprocedural safety of aneurysm embolization with the medina coil system: the early human experience. J Neurointerv Surg. 2016;8:168-172.
19. Aguilar Perez M, Bhogal P, Martinez Moreno R, et al. The medina embolic device: early clinical experience from a single center [published online August 2, 2016]. J Neurointerv Surg.
20. Bartolini B, Blanc R, Pistocchi S, et al. "Y" and "X" stent-assisted coiling of complex and wide-neck intracranial bifurcation aneurysms. AJNR Am J Neuroradiol. 2014;35:2153-2158.
21. Mukherjee S, Chandran A, Gopinathan A, et al. PulseRider-assisted treatment of wide-necked intracranial bifurcation aneurysms: safety and feasibility study [published online September 30, 2016]. J Neurosurg.
22. Aguilar-Perez M, Kurre W, Fischer S, et al. Coil occlusion of wide-neck bifurcation aneurysms assisted by a novel intra- to extra-aneurysmatic neck-bridging device (pCONus): initial experience. AJNR Am J Neuroradiol. 2014;35:965-971.
23. Ulfert C, Pfaff J, Schonenberger S, et al. The pCONus device in treatment of wide-necked aneurysms: technical and midterm clinical and angiographic results [published online September 16, 2016]. Clin Neuroradiol.
24. Perez MA, Bhogal P, Moreno RM, et al. Use of the pCONus as an adjunct to coil embolization of acutely ruptured aneurysms [published online July 13, 2016]. J Neurointerv Surg.
25. Chalouhi N, Zanaty M, Whiting A, et al. Treatment of ruptured intracranial aneurysms with the pipeline embolization device. Neurosurgery. 2015;76:165-172; discussion 172.
26. Habboub H. Can flow-diverters be used in acute SAH? Presented at World Live Neurovascular Conference 2016; May 27–29, 2016; Shanghai, China.

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