Pedro Lylyk, M.D.
Departments of Neurosurgery and Interventional Neuroradiology, Clínica Sagrada Familia; Clínica Adventista Belgrano; and Fundación Lucha contra las Enfermedades Neurológicas de la Infancia, Buenos Aires, Argentina

Carlos Miranda, M.D.
Departments of Neurosurgery and Interventional Neuroradiology, Clínica Sagrada Familia; Clínica Adventista Belgrano; and Fundación Lucha contra las Enfermedades Neurológicas de la Infancia, Buenos Aires, Argentina

Rosana Ceratto, M.D.
Departments of Neurosurgery and Interventional Neuroradiology, Clínica Sagrada Familia; Clínica Adventista Belgrano; and Fundación Lucha contra las Enfermedades Neurológicas de la Infancia, Buenos Aires, Argentina

Angel Ferrario, M.D.
Departments of Neurosurgery and Interventional Neuroradiology, Clínica Sagrada Familia; Clínica Adventista Belgrano; and Fundación Lucha contra las Enfermedades Neurológicas de la Infancia, Buenos Aires, Argentina

Esteban Scrivano, M.D.
Departments of Neurosurgery and Interventional Neuroradiology, Clínica Sagrada Familia; Clínica Adventista Belgrano; and Fundación Lucha contra las Enfermedades Neurológicas de la Infancia, Buenos Aires, Argentina

Hugh Ramirez Luna, M.D.
Departments of Neurosurgery and Interventional Neuroradiology, Clínica Sagrada Familia; Clínica Adventista Belgrano; and Fundación Lucha contra las Enfermedades Neurológicas de la Infancia, Buenos Aires, Argentina

Aaron L. Berez, M.D.
Chestnut Medical Technologies, Inc., Menlo Park, California

Quang Tran, B.S.M.E., M.B.A.
Chestnut Medical Technologies, Inc., Menlo Park, California

Peter K. Nelson, M.D.
Departments of Neurosurgery and Neuroradiology, New York University, New York, New York

David Fiorella, M.D., Ph.D.
Departments of Neurosurgery and Neuroradiology, Barrow Neurological Institute, Phoenix, Arizona

Reprint requests:
David Fiorella, M.D., Ph.D., Department of Endovascular Neurosurgery, Barrow Neurological Institute, 2910 North 3rd Avenue Phoenix, AZ 85013.
Email: david.fiorella@bnaneuro.net

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CURATIVE ENDOVASCULAR RECONSTRUCTION OF CEREBRAL ANEURYSMS WITH THE PIPELINE EMBOLIZATION DEVICE: THE BUENOS AIRES EXPERIENCE

OBJECTIVES: The Pipeline embolization device (PED) (Chestnut Medical Technologies, Inc., Menlo Park, CA) is a new microcatheter-delivered endovascular construct designed to achieve the curative reconstruction of the parent arteries giving rise to wide-necked and fusiform intracranial aneurysms. We present our initial periprocedural experience with the PED and midterm follow-up results for a series of 53 patients.

METHODS: Patients harboring large and giant wide-necked, nonsaccular, and recurrent intracranial aneurysms were selected for treatment. All patients were pretreated with dual antiplatelet medications for at least 72 hours before surgery and continued taking both agents for at least 6 months after treatment. A control digital subtraction angiogram was typically performed at 3, 6, and 12 months.

RESULTS: Fifty-three patients (age range, 11–77 years; average age, 55.2 years; 48 female) with 63 intracranial aneurysms were treated with the PED. Small (n = 33), large (n = 22), and giant (n = 8) wide-necked aneurysms were included. A total of 72 PEDs were used. Treatment was achieved with a single PED in 44 aneurysms, with 2 overlapping PEDs in 17 aneurysms, and with 3 overlapping PEDs in 2 aneurysms. The mean time between the treatment and last follow-up digital subtraction angiogram was 5.9 months (range, 1–22 months). Complete angiographic occlusion was achieved in 56%, 93%, and 95% of aneurysms at 3 (n = 42), 6 (n = 28), and 12 (n = 18) months, respectively. The only aneurysm that remained patent at the time of the 12-month follow-up examination had been treated previously with stent-supported coiling. The presence of a preexisting endoluminal stent may have limited the efficacy of the PED reconstruction in this aneurysm. No aneurysms demonstrated a deterioration of angiographic occlusion during the follow-up period (i.e., no recanalizations). No major complications (stroke or death) were encountered during the study period. Three patients (5%), all with giant aneurysms, experienced transient exacerbations of preexisting cranial neuropathies and headache after the PED treatment. All 3 were treated with corticosteroids, and these symptoms resolved within 1 month.

CONCLUSION: Endovascular reconstruction with the PED represents a safe, durable, and curative treatment of selected wide-necked, large and giant cerebral aneurysms. The rate of complete occlusion at the time of the 12-month follow-up examination approached 100% in the present study. To date, no angiographic recurrences have been observed during serial angiographic follow-up.

KEY WORDS: Aneurysm, Endovascular, Pipeline embolization device, Segmental arterial disease

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ABBREVIATIONS: ISS, in-stent stenosis; **mRS**, modified Rankin Scale; **PED**, Pipeline embolization device; **PITA**, Pipeline for the Intracranial Treatment of Aneurysms

Endovascular treatment of intracranial aneurysms has evolved substantially over the past 2 decades, transitioning from an investigational therapy into routine clinical practice and ultimately emerging as the treatment of

choice for many lesions. Randomized clinical trials such as the International Study of Subarachnoid Aneurysm Treatment (18) and the Barrow Ruptured Aneurysm Trial (17) have established the advantages of endovascular treatment in selected clinical scenarios.

Despite this tremendous evolution in endovascular therapy, some important limitations remain, particularly in the treatment of wide-necked, large and giant, or "nonsaccular" fusiform aneurysms. These lesions can frequently be difficult to reconstruct with coils, even when they are used with the commercially available self-expanding intracranial stents (Neuroform; Boston Scientific, Natick, MA; Enterprise; Cordis Neurovascular, Warren, NJ; LEO and LEO Plus; Balt Extrusion, Montmorency, France). Endovascular treatments of such lesions frequently fail to produce complete aneurysm occlusion. Even when complete or near-complete occlusion has been achieved after the initial embolization, these aneurysms remain prone to coil compaction and recanalization, and they frequently recur, requiring 1 or more retreatments (8, 18, 19, 29).

To date, endovascular therapy has been almost exclusively focused on filling the aneurysm sac with embolic material, i.e., "endosaccular" treatment. This strategy is very effective for the treatment of most narrow-necked aneurysms that arise from a "focal defect" in the parent artery wall (involving <25% of the parent artery circumference). However, endosaccular occlusion does not address the remaining circumference of the diseased parent artery that gives rise to the aneurysm. In larger, more dysplastic-appearing aneurysms, the demarcation between the normal artery and diseased vessel becomes less distinct. For this reason, the endosaccular strategy is often ineffective in treating wide-necked or fusiform aneurysms that arise from a larger, more diffuse, "segmental defect" in the parent vessel.

These segmental defects are only addressed with an "endoluminal" strategy that achieves circumferential parent vessel reconstruction. This effect has been achieved to some extent using the commercially available balloon-expandable (14, 15, 33) and self-expanding stents (2–4, 9, 11, 13, 16). However, the existing intracranial stents have very limited metal surface area coverage (6.5%–9% for self-expanding stents and 12%–16% for balloon mounted stents) and, thus, their ability to elicit remodeling of the parent artery is limited. In most aneurysms, these devices are inadequate to achieve occlusion by themselves, and aggressive endosaccular coil embolization in concert with endoluminal reconstruction is required to reliably achieve a durable result.

The Pipeline embolization device (PED) (Chestnut Medical Technologies, Inc., Menlo Park, CA) represents the first endovascular construct specifically engineered to function as a stand-alone device for the endovascular reconstruction of a segmentally diseased parent vessel. The PED is a self-expanding, microcatheter-delivered, cylindrical mesh device composed of 48 individual cobalt chromium and platinum strands. The device has 30% to 35% metal surface area coverage when fully deployed (7).

The initial experience with the PED has shown it to be effective in achieving the curative anatomic reconstruction of large segmental vascular defects, which give rise to the wide-necked, large and giant, or nonsaccular aneurysms that have traditionally presented the greatest challenge to existing endovascular and open vascular neurosurgical treatment strategies (5–7, 20). We present periprocedural outcomes and midterm angiographic follow-up results for a series of 53 patients with 63 wide-necked aneurysms that were treated with the PED.

PATIENTS AND METHODS

Patient Population and Selection

The present study is a prospective, all-inclusive case series of patients undergoing treatment with the PED for wide-necked (defined as aneurysms with a dome-to-neck ratio of <2 or a neck size ≥4 mm) saccular aneurysms, nonsaccular aneurysms, large and giant aneurysms, and aneurysms for which previous treatment attempts failed. Between March 2006 and June 2008, 53 patients (mean age, 55.2 years; age range, 11–77 years; 48 female and 5 male) harboring 63 aneurysms were treated.

Because the PED is an investigational device, its application in this series of patients was always prospectively approved either on a case-by-case basis as compassionate use (initial experience), within the context of the Pipeline for the Intracranial Treatment of Aneurysms (PITA) trial (a multicenter, single arm, nonrandomized trial) (20), or within the context of the post-PITA Buenos Aires registry (single-center registry) by our institutional ethics committees in accord with local regulations. Written informed consent was obtained from every patient. All aneurysms were treated electively after the appropriate institutional regulatory clearance had been secured, and the informed consent was obtained. Six of the patients (with 6 treated aneurysms) included in the present series were also included in the PITA trial.

Antiplatelet Medication Regimen

Patients were pretreated with 75 mg of clopidogrel and 325 mg of aspirin at least 72 hours before PED treatment. Dual antiplatelet medication was maintained for at least 6 months after the procedure. Intravenous heparin was administered during the procedure to maintain an activated clotting time between 250 to 300 seconds. Heparinization was not reversed at the conclusion of the procedure.

PED

The PED is a flexible, microcatheter-delivered, self-expanding, endovascular "stent-like" construct engineered specifically for the treatment of cerebral aneurysms (Fig. 1). The device consists of a braided mesh cylinder composed of 48 individual platinum and cobalt chromium microfilaments. The stent is mounted in a recess on a flexible delivery wire and is front-loaded via an introducer and delivered through a standard 0.027-inch internal diameter microcatheter (Mass Transit; Cordis Neurovascular, Warren NJ; Renegade Hi-Flo; Boston Scientific).

Procedure

All treatments were performed under general anesthesia and via the transfemoral approach. In those procedures in which coils were introduced into the aneurysm, either the coiling was done before placement of the PED, or the microcatheter was placed within the saccular component of the aneurysm and "jailed" by placing the PED construct across the aneurysmal segment. With this jailing or parallel technique, coiling is subsequently performed through the jailed microcatheter after the PED construct has been placed. After coiling is completed, the

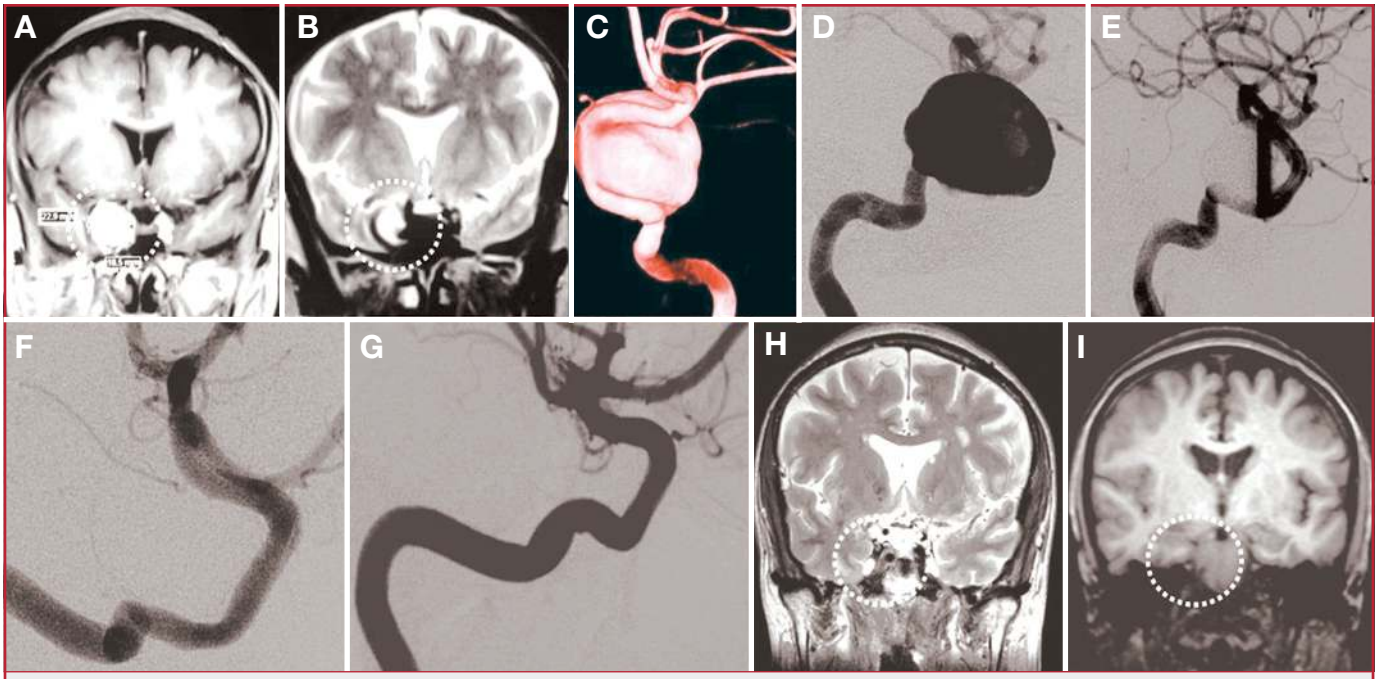

FIGURE 1. *A 58-year-old woman with a giant right cavernous segment internal carotid artery (ICA) aneurysm presented with a right sixth nerve palsy. Postcontrast coronal T1-(**A**) and T2-weighted (**B**) magnetic resonance imaging (MRI) scans demonstrating the giant aneurysm arising from the right ICA, impressing upon the medial aspect of the right temporal lobe. Shaded surface display from a three-dimensional (3D) rotational angiogram (**C**) and conventional angiogram in the lateral projection (**D**) demonstrating a long segmental defect arising from the posterior wall of the ICA. **E**, angiogram immediately after reconstruction with the Pipeline embolization device (PED) showing that contrast medium flow has been diverted from the aneurysm sac into the cerebrovasculature. Contrast material within the aneurysm is static, forming a dependent contrast level or "eclipse sign." Follow-up angiograms at 1 month (**F**) and 6 months (**G**) showing anatomic remodeling of the ICA with complete occlusion of the aneurysm. Coronal T2-weighted (**H**) and precontrast T1-weighted (**I**) MRI scans showing complete resolution of the mass effect from the aneurysm. Dotted circles in A, B, H, and I indicate the location of the aneurysm.*

microcatheter is easily removed by gently retracting it from the aneurysm. The removal of the microcatheter did not disrupt the PED construct in any of the aneurysms.

All PEDs were deployed following a standard procedure. First, the microcatheter was manipulated under high-magnification fluoroscopic roadmap control across the aneurysm neck. The PED, mounted on a delivery wire and constrained within a sheath, was then inserted into the rotating hemostatic valve and introduced into the hub of the microcatheter. By pushing the delivery wire, the PED was advanced through the length of the microcatheter and into position for deployment. The PED delivery wire was then held in place while the microcatheter was carefully retracted to initiate deployment. Through a combination of forward pressure on the delivery wire and retraction of the microcatheter, the device was deployed, expanding to come free of the delivery microwire. When constrained within a microcatheter, the PED is elongated 2.5 times its maximally expanded deployed configuration. This foreshortening must be taken into account during the positioning and deployment of the construct.

Procedural Assessment and Follow-up Examination

Technical success was defined as PED deployment with complete coverage of the aneurysm neck, preserved patency of the parent artery, and no clinically evident adverse events. Posttreatment clinical follow-up was performed at the time of discharge. Concurrent clinical and angiographic follow-up was performed at 1, 3, 6, and 12 months after the treatment. Neurological examinations were performed by an independent neurologist.

Aneurysm sizes are provided as the single greatest dimension. Only the portion of the aneurysm opacified by contrast agent was measured. Regions of the aneurysm that were occluded by preexisting embolization coils or intraluminal thrombus were not included in the largest dimensional measurement. Vessel wall defects were classified as focal if less than 25% of the circumference of the parent artery was involved by the aneurysm neck and segmental if more than 25% of the circumference of the parent vessel wall was involved.

Follow-up angiography was performed in the standard projections as well as in the working angle for PED placement. The primary angiographic end point was complete aneurysm occlusion. Any residual filling of the aneurysm was characterized as incomplete occlusion.

RESULTS

Patient Characteristics

Over a 26-month study period (March 2006 to May 2008), 53 patients (average age, 55.2 years; age range, 11–77 years) with 63 aneurysms were treated with the PED. The clinical presentations of the patients are documented in Table 1. At the time of treatment, 30 patients (56%) had a modified Rankin Scale (mRS) score of 0, 12 patients (23%) had a score of 1, and 11 patients

TABLE 1. Clinical presentation

Presentation	No.	%
Incidental	25	47.2
Headache	6	11.3
Previous subarachnoid hemorrhage	7	13.2
Mass effect	4	7.5
Visual deficit	5	9.4
Cranial nerve palsy	6	11.3
Total	53	100.0

TABLE 2. Aneurysm location

Aneurysm location	No.	%
Internal carotid artery		
Cavernous	11	17.4
Carotid cave	5	7.9
Parophthalmic	9	14.2
Superior hypophyseal	5	7.9
Ophthalmic	13	20.6
Posterior communicating	10	15.8
Anterior choroidal	1	1.5
Carotid terminus	1	1.5
Posterior circulation		
Posterior inferior coronary artery	1	1.5
Vertebral	4	6.3
Vertebrobasilar junction	1	1.5
Basilar	2	3.1
Total	63	100.0

(21%) had a score of 2. Among the 11 patients with an mRS of 2, 3 presented with previous subarachnoid hemorrhage, 3 with mass effect, 3 with cranial nerve palsy, and 2 with visual deficits (Fig. 1).

Lesion Characteristics: Location and Size

The locations of the aneurysms treated are listed in Table 2; 55 (87.3%) involved the anterior circulation and 8 (12.7%) involved the posterior circulation. According to the International Study of Unruptured Intracranial Aneurysms (32) size classification, 33 (52%) aneurysms were small (<10 mm), 22 (35%) were large (10–25 mm), and 8 (13%) were giant (>25 mm) (32). The mean aneurysm size was 11.1 mm (range, 3.5–30 mm). Fifty-five (87%) aneurysms were saccular, and 8 others (13%) were nonsaccular (circumferential, fusiform, or dissecting morphology). According to our classification system, 94% of the aneurysms arose from segmental defects of the artery, whereas 6% arose from focal defects. The 4 aneurysms arising from focal defects were either large (n = 3) or giant (n = 1) and were located within the anterior circulation.

Lesion Characteristics: Previous Treatment

Of the 63 lesions treated, 40 (63%) were de novo unruptured aneurysms (Fig. 1), whereas 23 (37%) were previously treated and subsequently recanalized (Fig. 2). Of the previously treated aneurysms, 16 were unruptured and 7 had previously ruptured. Previous treatments included coiling alone in 14 patients, stent-supported coiling in 6 patients, surgical clipping in 2 patients, and stent monotherapy in 1 patient. The indications for PED placement (Table 3) were categorized as saccular aneurysm with a dome/neck ratio of less than 2 (n = 32 [51%]), large or giant size (n = 4, 6%), fusiform/dissecting morphology (n = 8 [12%]), and failure of previous treatment (endovascular or surgical; n = 19, [31%]).

PED Treatment

Forty-four aneurysms (70%) were treated with a single PED, 17 (27%) were treated with 2 PEDs, and 2 (3%) were treated with 3 PEDs. In 4 of the aneurysms (6%) in which a single PED was used for treatment, embolization coils were also used. During treatment of the remaining 59 lesions (94%), the PED was used as a stand-alone device without embolization coils. All aneurysms arising from focal defects in the parent artery were treated with a single device.

PED deployment was technically successful 97% of the time (70 of 72 devices deployed). In 1 procedure, the proximal aspect of the PED was inadvertently deployed into the aneurysm, and an Alligator retrieval device (Chestnut Medical Technologies, Inc.) was used to retract and reposition the device across the aneurysm neck. In a second procedure, the distal tip of the PED delivery wire became engaged within the deployed PED and fractured. The fractured distal aspect of the wire was secured into a stable position against the vessel wall by the deployed PED. Neither of these technical complications resulted in a clinically evident complication. In all patients (100%), the PEDs were ultimately deployed in an acceptable position across the targeted aneurysm.

No major (stroke or death) clinically evident periprocedural (within 30 days) complications were encountered during the study period. Minor complications occurred in 6 of 53 patients (11%). Five patients developed hematomas at the femoral puncture site. One patient developed a rash from a reaction to the contrast material. Three patients (5%) initially presenting with IIIrd and VIth cranial nerve palsies owing to giant carotid cavernous aneurysms developed headache and exacerbation of their cranial nerve palsies during the first postoperative week. All 3 were treated with a course of steroids. Two recovered to their pretreatment baseline over the next month, and the third ultimately improved in comparison to the pretreatment status.

Angiographic Results: Immediate and Follow-up

At the conclusion of the treatment, only 5 of 63 (8%) aneurysms showed complete angiographic occlusion. All lesions that were completely occluded immediately after PED placement were small (<10 mm) aneurysms for which previous

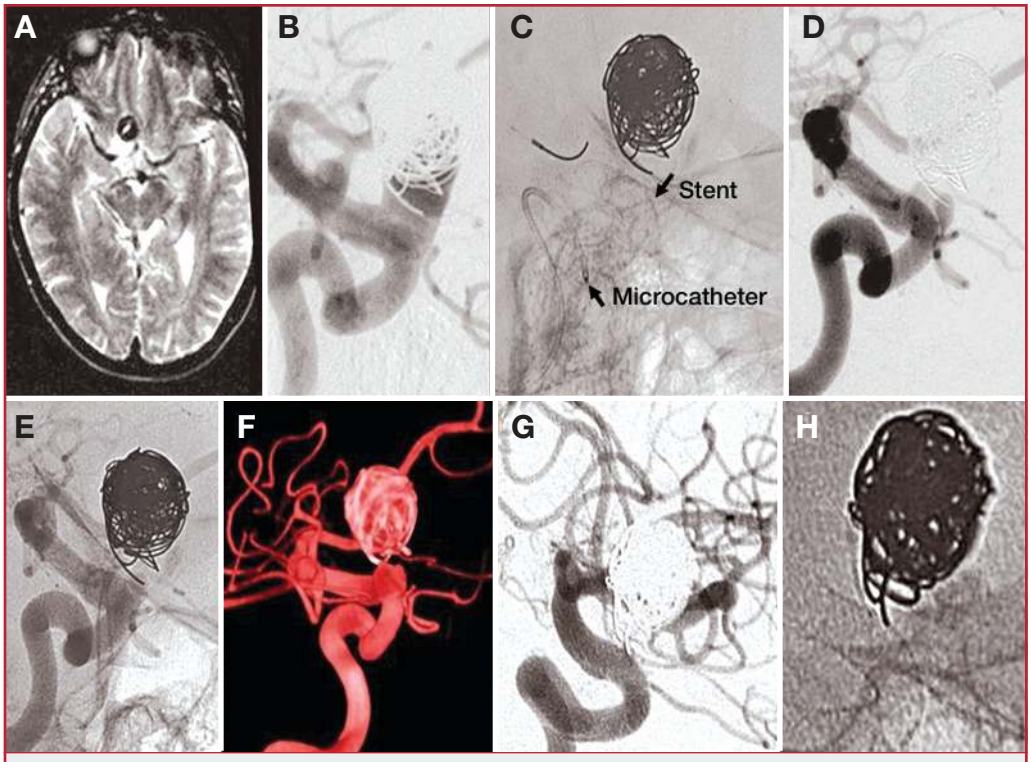

FIGURE 2. *A 59-year-old woman initially presented with a symptomatic unruptured large right carotid-ophthalmic artery aneurysm arising from a segmental defect in the vessel. The aneurysm was initially treated with coil embolization.* **A**, *axial T2-weighted MRI showing the signal void corresponding to the dome of the aneurysm with mass effect upon the inferior medial aspect of the right frontal lobe.* **B**, *lateral angiogram obtained 1 year after the original treatment showing coil compaction and a large amount of residual filling of the aneurysm.* **C**, *native image immediately after PED reconstruction showing the construct in place across the aneurysm neck ("stent," arrow), the 0.027-inch internal diameter (ID) delivery catheter (microcatheter) within the proximal cavernous segment of the internal carotid artery and the PED delivery wire within the proximal middle cerebral artery more distally. Subtracted angiogram (***D***) and native (***E***) and reconstructed (***F***) 3D rotational angiograms at the 3-month follow-up examination showing minimal residual filling in the region of the aneurysm neck only. Subtracted (***G***) and native (***H***) angiograms in the working projection at the 12-month follow-up examination demonstrating anatomic reconstruction of the parent artery and complete aneurysm occlusion. This case demonstrates the rate at which progressive thrombosis and vascular remodeling occur after PED reconstruction.*

TABLE 3. Indications for stent placement

Indication	No. (%) of aneurysms	No. of stents
De novo aneurysms		
Saccular, dome/neck ratio >2	32 (51%)	33
Saccular (large/giant), dome/neck ratio <2	4 (6%)	4
Nonsaccular	4 (6%)	6
Recurrent aneurysms (retreatments)		
Nonsaccular	4 (6%)	7
Saccular	19 (31%)	22
Total	63 (100%)	72

therapy had not failed (i.e., de novo lesions). Although residual filling was noted in the remaining aneurysms, the transit of contrast material into and out of, the aneurysm was markedly slowed, and the initial inflow jet was disrupted. During the capillary and venous phases of the angiogram, the newly reconstructed parent artery could often be visualized as a negative defect surrounded by contrast material. This negative defect is created as unopacified inflow quickly clears the contrast material from the lumen of the reconstructed parent artery, which then stands out in relief against the more static contrast material that is retained within the aneurysm sac (Fig. 3). Contrast material could often be seen layering within the dependant portion of the larger aneurysms, forming an eclipse sign on subtracted images, which typically persisted into the late venous phase (Fig. 4).

One-, 3-, 6-, and 12-month angiographic follow-up results were available for 51, 42, 28, and 18 aneurysms, respectively. The average angiographic follow-up period was 5.9 months. By 6 months, 93% (26 of 28) of the aneurysms had progressed to complete occlusion. Of the 18 aneurysms studied at 12 months, 17 (94.4%) had progressed to complete occlusion (Figs. 5 and 6; Table 4). The sole aneurysm with residual filling after 12 months was a giant, circumferential, fusiform basilar aneurysm treated with 2 PEDs. This lesion had recurred after stent-supported coil embolization before PED treatment. It is possible that the preexisting stent may have impaired the wall apposition of the PED construct in this patient.

Of the 38 vessels with 3-month angiographic follow-up, 3 (8%) showed mild (25%–50%) in-stent stenosis (ISS), 2 (5%) showed moderate (50%–70%) ISS, and 2 (5%) showed severe (>70%) ISS. Three of these cases of ISS resolved to some extent by the 6-month follow-up angiogram, with 1 of the mild cases resolving completely, 1 of the moderate stenoses regressing to mild ISS, and 1 case of the severe stenoses regressing to moderate ISS. All cases of ISS were asymptomatic and, thus, none were treated.

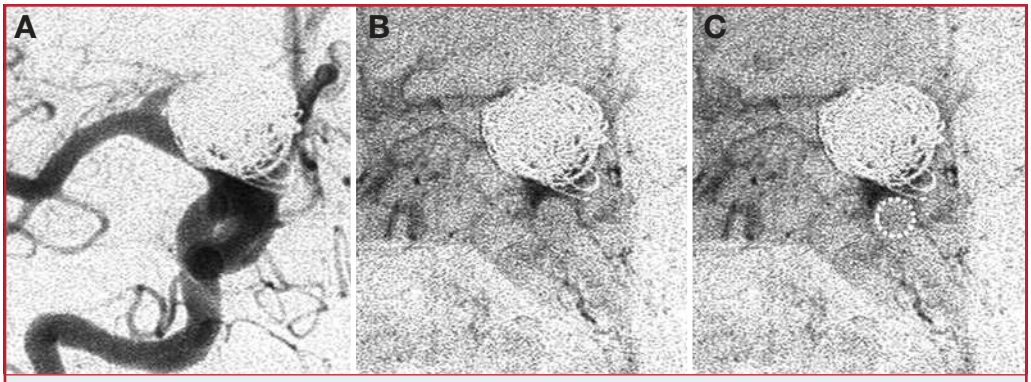

FIGURE 3. *Negative defect of reconstructed parent artery after PED reconstruction. Immediately after placement of a single PED, the A-plane image intensifier was positioned to demonstrate the PED in a "down-the-barrel" projection.* **A**, *angiogram during the early arterial phase demonstrating opacification of the reconstructed parent artery as well as the saccular component of the wide-necked aneurysm. The aneurysm incorporates the entire superior circumference (almost 180 degrees) of the supraclinoid internal carotid artery.* **B**, *late capillary phase image showing the reconstructed parent artery as a negative defect, surrounded by contrast material retained within the saccular wide-necked aneurysm.* **C**, *dotted circle demarcating the negative defect of the reconstructed lumen. It would be nearly impossible to completely reconstruct a segmental defect of this extent with coils alone.*

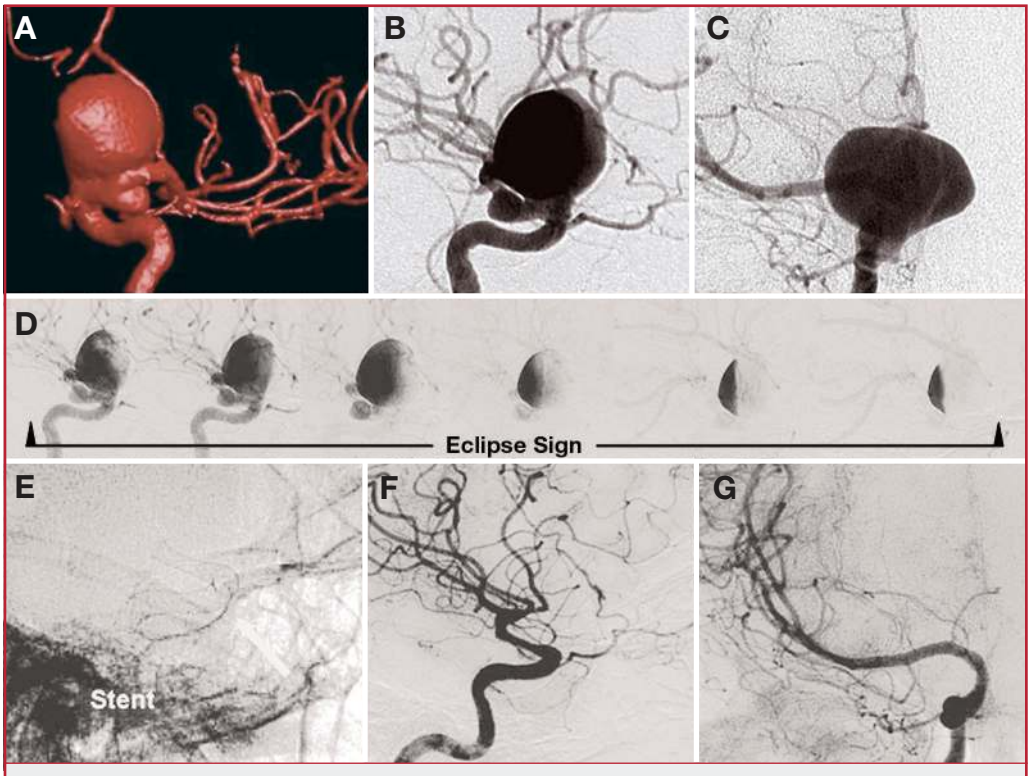

FIGURE 4. *A 57-year-old woman presenting with right amaurosis fugax. Reconstructed image from a 3D rotational angiogram (***A***) and conventional subtracted angiographic images in the lateral (***B***) and posteroanterior (PA) (***C***) projections showing a giant right carotid-ophthalmic segment and smaller posterior wall supraclinoid segment aneurysms.* **D**, *serial subtracted angiographic frames spanning from the arterial to the late venous phase showing the hemodynamic changes after PED reconstruction with dependent stasis of contrast material within the aneurysms forming the "eclipse sign."* **E**, *native image in the lateral projection showing the PED construct conforming to the configuration of the reconstructed supraclinoid internal carotid artery. Subtracted lateral (***F***) and PA (***G***) projections from a follow-up angiogram at 6 months showing anatomic reconstruction of the artery and complete aneurysm occlusion.*

Clinical Results

Thirty-nine patients have had at least 3 months of clinical follow-up, and 17 have had 1 full year of follow-up. No patients have experienced delayed deterioration in their clinical status after the 30-day periprocedural period. Two of the 12 patients with an initial mRS score of 2 improved to a score of 1 at the 6-month clinical follow-up. Scores for all patients with an initial mRS score of 1 or 0 were unchanged at 3 to 6 months of follow-up.

DISCUSSION

The most important findings of the present study are the following: 1) the PED reproducibly elicits curative endovascular reconstruction of selected intracranial aneurysms; 2) aneurysm treatment with the PED is safe; 3) aneurysm treatment with the PED is durable; 4) preexisting endoluminal constructs can potentially limit the efficacy of the PED; and 5) primary endovascular reconstruction represents a fundamental paradigm shift in the technique of endovascular aneurysm treatment.

Endovascular therapy has emerged as an accepted and, in some cases, preferred treatment for cerebral aneurysms. However, the technique has the major shortcomings of incomplete treatment and questionable long-term durability. These shortcomings have led to persisting reservations about the technology despite the results of large, randomized, multicenter trials demonstrating its superiority to surgical clipping in selected patients (23).

In most reported series, only a minority of aneurysms treated by coil embolization are ultimately cured angio-

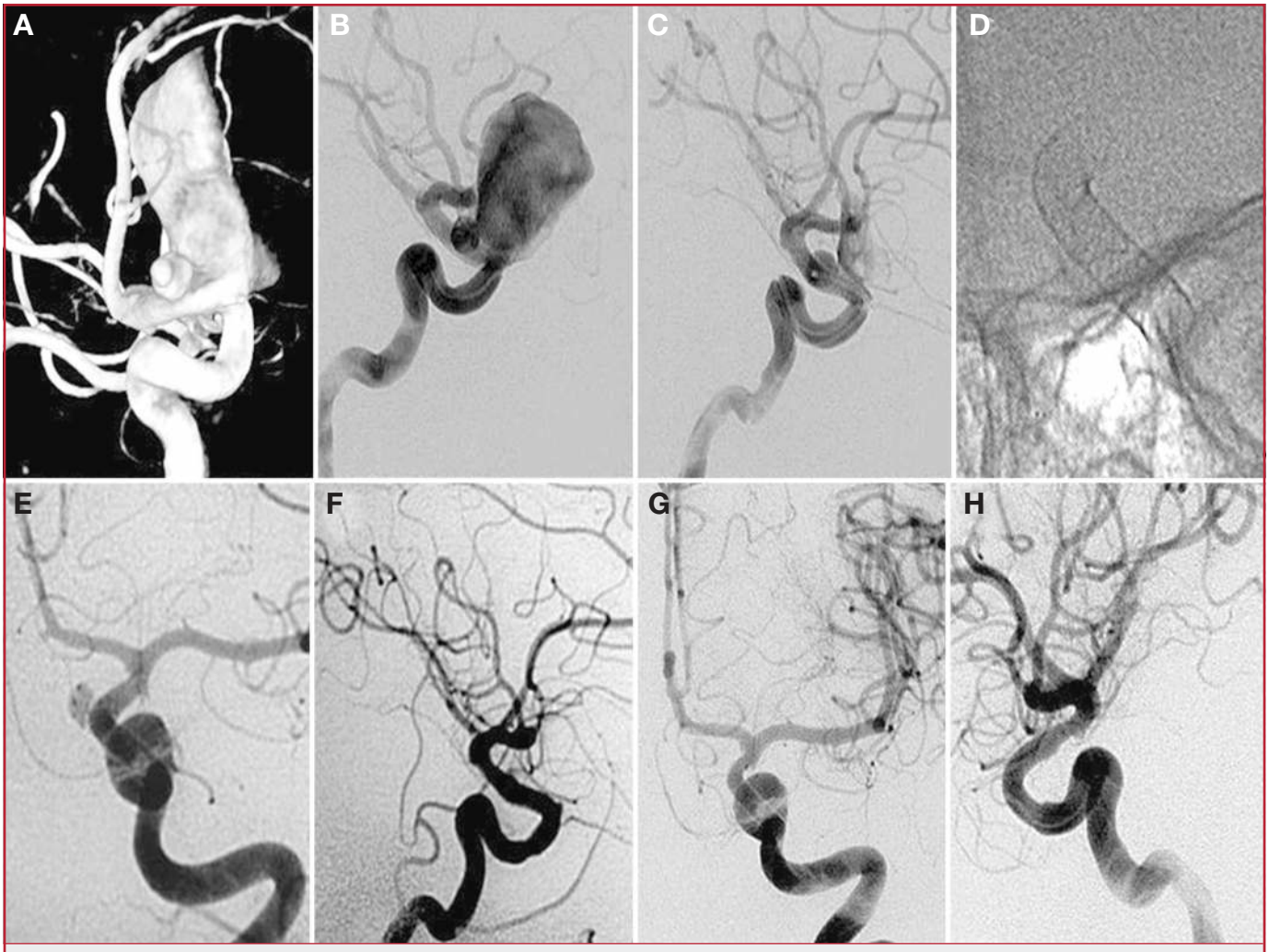

FIGURE 5. *A 55-year-old woman presenting with a VIth nerve palsy. Reconstructed image from a 3D rotational angiogram (A) and lateral subtracted angiogram (B) showing the giant left carotid-ophthalmic segment and small superior hypophyseal aneurysms. C, subtracted image in the lateral projection showing markedly reduced flow into both aneurysms. D, native transorbital oblique image of the PED in position within the left supraclinoid internal carotid artery spanning the origins of both carotid aneurysms. Follow-up subtracted angiograms in the transorbital (E) and lateral (F) projections at 20 days showing complete occlusion of the giant carotid-ophthalmic aneurysm with persistent patency of the smaller, more distal superior hypophyseal artery aneurysm. Three-month follow-up digital subtraction angiograms in the transorbital (G) and lateral (H) projections showing anatomic remodeling of the parent artery with complete occlusion of both aneurysms. This patient demonstrates that the anatomic location, configuration, and regional flow phenomena of the parent artery-aneurysm complex (more than aneurysm size) may dictate the rate at which thrombosis occurs in some instances.*

graphically. Raymond et al. (24) reported a 38.3% rate of complete angiographic occlusion at the 12 month follow-up evaluation in a series of 353 consecutive coiled aneurysms. Kole et al. (12) reported a 19% rate of complete occlusion in a series of 131 coiled aneurysms with long-term angiographic follow-up (mean, 18 months). In the International Subarachnoid Aneurysm Trial, a 66% rate of complete angiographic occlusion was observed in a cohort largely (91%) composed of small aneurysms (18). These rates of occlusion are even lower in selected subgroups such as large, giant, wide-necked, and nonsaccular aneurysms.

The recent Cerebral Aneurysm Rerupture After Treatment study (10) provides evidence that, at least for ruptured aneurysms, it is critical to achieve complete angiographic obliteration to provide adequate protection from subsequent hemorrhage. In that study, ruptured aneurysms were followed after either surgical or endovascular treatment to assess the incidence of rehemorrhage. Although the overall hemorrhage risk was very low after coiling (1.3 rehemorrhages per 100 person-years), the risk of rebleeding increased drastically with decreasing levels of aneurysm occlusion (0.6 rehemorrhages per 100 person-years for completely occluded aneurysms versus 15

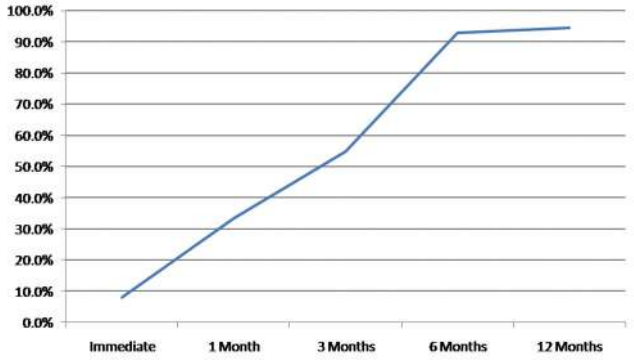

FIGURE 6. *Rate of complete angiographic occlusion during the follow-up period (ordinate: percentage of aneurysms with follow-up showing complete angiographic occlusion; abscissa: time in months). Whereas few aneurysm occluded immediately after the placement of the PED construct, nearly all lesions progressed to angiographic cure over the following 6 to 12 months. This progression should be taken into account during PED reconstruction procedures, in that the placement of multiple overlapping devices to achieve immediate angiographic occlusion is not necessary in the majority of patients and, depending on the anatomic location, may lead to increased complications.*

TABLE 4. Rate of complete occlusion at angiographic follow-up examination

Aneurysm size	Complete occlusion rate				
	Immediate	1 mo	3 mo	6 mo	12 mo
Small	5/33	11/30	14/22	8/14	9/9
Large	0/22	3/15	6/14	8/9	7/7
Giant	0/8	4/6	3/5	4/5	1/2

rehemorrhages per 100 person-years for partially occluded lesions). Moreover, several investigators have demonstrated that incomplete aneurysm obliteration with coils contributes to instability of treatment, with progressive coil compaction and aneurysm recurrence with time that can be associated with a need for repeated treatments, bleeding, or death (1, 12, 24).

The PED differs fundamentally from these predicate endovascular technologies in that PED reconstruction reproducibly elicits an angiographic cure of selected intracranial aneurysms. In the present series, more than 90% of the lesions treated with PED progressed to complete occlusion by the 6-month follow-up evaluation (Figs. 1–5). This level of efficacy is even more remarkable when one considers the types of lesions comprising the present series—large, giant, wide-necked, and nonsaccular aneurysms and aneurysms for which previous treatment had failed.

Similar results were achieved during the multicenter, single-arm PITA study, in which a series of 31 aneurysms (average size, 11.5 mm; average neck size, 5.8 mm) were treated with the PED with a 93% rate of complete occlusion at the 6-month follow-up examination (20). Six of the aneurysms included in the present series were also incorporated into the PITA data set. Thus, the PED establishes a new benchmark for the treatment of cerebral aneurysms—complete aneurysm occlusion—that has not been reliably achieved by prior endovascular therapies.

Aneurysm Treatment With the PED Is Safe

In a series of 246 patients with unruptured aneurysms treated with Guglielmi detachable coils, Murayama et al. (19) reported a 5.3% rate (13 of 246) of procedural morbidity and mortality. The vast majority of the lesions included in the series of Murayama et al. were amenable to coiling without the use of an adjunctive balloon (self-expanding intracranial stents were not available during this time). In contrast, the majority of aneurysms treated in the present series would have required the use of 1 or more adjunctive devices to accomplish an endosaccular embolization. Thus, one would expect that treatment with conventional endovascular techniques would result in a much higher rate of periprocedural morbidity and mortality than that reported by Murayama et al. However, despite the complexity of the lesions included in the present series, no major clinical adverse events were encountered during either PED reconstruction or the subsequent clinical follow-up period. These data provide preliminary support for the hypothesis that the PED presents not only a more definitive treatment of selected complex intracranial aneurysms, but also a potentially safer treatment as well.

The safety profile of the PED may be attributed to several aspects of the treatment strategy. First, the delicate saccular component of the aneurysm does not have to be catheterized, and no coils or other materials are directly introduced into the aneurysm during treatment. Thus, the risk of procedural perforation is much lower. Second, the PED can be used as a stand-alone therapy (as it was in 70% of the patients in the current series), considerably simplifying the entire procedure, particularly for the types of complex aneurysms included in the present series. In the majority of the present patients, definitive aneurysm occlusion was accomplished in one step with the deployment of a single PED across the aneurysmal segment. If conventional devices had been used, these large and complex aneurysms would typically have required not only the introduction of numerous embolization coils, but also periodic repositioning of the microcatheter and coils within the aneurysm, as well as the manipulation of 1 or more adjunctive devices (temporary occlusion balloons or stents) within the parent artery.

Aneurysm Treatment With the PED Is Durable

Owing to the random distribution of coils within an aneurysm and the tendency of the individual coil strands to break the aneurysm up into multiple small compartments, the best packing densities that can be routinely achieved with conventional embolization coils (with or without adjunctive devices) ranges between 30% and 40% in experimental silicone models and between 20% and 30% in clinical human aneurysm treatments (21, 22, 25–28). The rates are much lower for large and giant aneurysms and for aneurysms with wide necks (31). Thus, the majority (70%–80%) of the volume within coiled aneurysms is not filled with embolic material.

Not only are aneurysms difficult to pack densely with coils, but contiguously bridging the entire aneurysm neck with coils is also extremely difficult, particularly if the aneurysm is wide-necked, incorporating a significant percentage of the circumference of the parent vessel (i.e., a segmental defect). In these situations, even with the most meticulous technique, there are invariably gaps between coils in the region of the defect. These gaps allow persistent inflow and impair the endothelialization and neointimal growth over the aneurysm neck, which are ultimately required to achieve complete angiographic occlusion and durable, curative embolization.

These technical limitations of coiling are manifest as poor durability of the immediate posttreatment result. Raymond et al. (24) observed a recanalization rate of 33.6% for all treated aneurysms. This recurrence rate was considerably higher for large (50.6%) and wide-necked (52.3%) aneurysms. Similarly, Murayama et al. (19) reported recanalization rates of 35.3% and 59.1% for large and giant aneurysms, respectively. In addition, once aneurysms recur and require retreatment, they frequently recur a second time, with a repeat recurrence rate of 48.6% (24). For these reasons, patients who undergo aneurysm therapy are consigned to a schedule of serial imaging follow-up. Although much of this follow-up can now be performed noninvasively with magnetic resonance imaging (30), follow-up angiography is often required. In many patients, one or more retreatments may be necessary to maintain adequate aneurysm occlusion. When considered cumulatively, these serial imaging evaluations and retreatments add significantly to patient inconvenience and the overall cost associated with endovascular treatment.

In the present series, no treated lesions demonstrated recanalization during an average of 5.9 months of follow-up. Moreover, no patient treated with a PED to date has demonstrated any deterioration in the angiographic appearance during serial follow-up (PKN, personal communication, 2008). Considering the mechanism by which aneurysm occlusion occurs with the PED, it is difficult to hypothesize a mechanism by which recanalization or recurrence could occur after endoluminal reconstruction of the parent artery and complete aneurysm occlusion have been successfully achieved.

Preexisting Endoluminal Constructs Can Potentially Limit the Efficacy of the PED

The only aneurysm in the current series that did not progress to complete occlusion at 1 year of follow-up had been previously coiled with an adjunctive self-expanding stent. Indwelling endoluminal constructs (e.g., Neuroform and Enterprise) represent important potential impediments to the efficacy of the PED. These devices may impair the apposition of the PED construct to the wall of the parent artery, setting up the potential for "endoleaks" around the outside of the construct, which can maintain patency of the aneurysm sac and disrupt the overgrowth of a homogeneous, contiguous layer of neointima and neoendothelium over the surface of the construct. In addition, the presence of these devices can significantly complicate the navigation of the delivery catheter into position and the actual deployment of the PEDs, potentially increasing the technical difficulty and risks associated with the reconstruction.

Given the availability of the PED in the near future, operators may take these issues into consideration before electively treating complex aneurysms with 1 or more conventional self-expanding intracranial stents. This caution is particularly true for unruptured, asymptomatic, or minimally symptomatic extradural aneurysms that are not likely to be cured with conventional endovascular procedures (e.g., large, giant, wide-necked, and circumferential aneurysms) and for those aneurysms that pose significant technical challenges to treatment with conventional devices (e.g., nonsaccular aneurysms). Treating these patients with conventional devices may preclude the ability to achieve a curative constructive treatment with the PED in the future. In addition, the complexity of the endovascular procedures using conventional devices may expose the patients to significantly higher procedural risks than would PED reconstruction. The same consideration should be given before elective deconstruction of a parent artery-aneurysm complex that may be amenable to constructive treatment with the PED.

Primary Endovascular Reconstruction Represents a Paradigm Shift in Endovascular Therapy

During endosaccular aneurysm coiling, the operator is obligated to achieve as dense a filling of the aneurysm as possible with embolic material with the goal of achieving complete aneurysm occlusion at the time of the initial procedure. Although some aneurysms can improve angiographically (e.g., progressively thrombosis) after coil embolization, a significant proportion (as discussed above) recur, and, thus, the operator typically views the immediate postembolization result as the angiographic baseline that will either remain stable or progressively deteriorate with time. In addition, a number of studies have demonstrated that aneurysm packing density is inversely related to the risk of future aneurysm recurrence (27, 28).

The technique of PED reconstruction differs fundamentally from the operator's perspective. The curative reconstruction that is induced by the PED construct occurs over a period of weeks to months. Thus, the actual procedural technique and expected angiographic findings are different from those for traditional endosaccular aneurysm occlusion techniques. Residual filling at the conclusion of the reconstruction procedure is the rule, although the pattern of inflow is usually dramatically different after PED placement. In particular, the transit of contrast material into the aneurysm is usually transformed from an organized inflow jet to a disorganized "wash in" of contrast material during the arterial and early capillary phase of angiography. The contrast material in the aneurysm becomes static and typically persists into the late venous phase of angiography. This retained contrast material within the aneurysm often surrounds the reconstructed parent artery, which demonstrates normal arterial phase wash out of contrast material. This reconstructed neo-artery then appears as a negative defect (Fig. 3) during the capillary phase of angiography, surrounded by retained intra-aneurysmal contrast material. In larger aneurysms this intra-aneurysmal stasis is also evidenced by a persistent dependant layering of contrast material

within the aneurysm sac (the "eclipse sign") (Figs. 1 and 4). These angiographic findings indicate a marked disruption of aneurysm inflow and predict the progression of these lesions to angiographic occlusion (Figs. 1 and 4).

It is important for the operator to recognize these signs and expect residual filling at the immediate conclusion of the procedure. Attempts to completely obliterate flow at the time of the original procedure by placing a number of telescoping PED devices could hypothetically result in an unnecessary compromise of the luminal diameter of the parent artery, an increase in the thromboembolic risk associated with an increased volume of foreign material within the parent artery or occlusion of eloquent regional perforating or branch arteries. In addition, it is important to recognize that if aneurysm patency persists into follow-up, placement of an additional telescoping PED as part of a staged treatment represents a straightforward procedure.

PED Limitations

Many aneurysms that are among the most technically challenging to treat and most resistant to standard endovascular approaches with the highest rates of immediate treatment failure, incomplete treatment, and recanalization could hypothetically be easily treated and ultimately constructively cured with the PED. This principle applies to many large, giant, wide-necked, nonsaccular, and recurrent aneurysms.

At the same time, there are anatomic locations and clinical scenarios that pose significant challenges to PED reconstruction. The PED, as an endoluminal construct, requires dual antiplatelet prophylaxis to maintain patency. For this reason, acute subarachnoid hemorrhage represents a relative contraindication to PED reconstruction. The efficacy of a flow-diverting construct for the treatment of bifurcation aneurysms has not, to date, been evaluated. It is not known whether reconstruction of a single limb of a major vascular bifurcation would provide flow redirection that is sufficient to elicit aneurysm occlusion without creating physiologically significant flow compromise within the contralateral (nonreconstructed) limb. Aneurysms arising from vascular segments with eloquent perforators or branch vessels represent a potential limitation; however, when applied judiciously in these locations, the existing experience suggests that the patency of these vessels can be preserved (5). However, in the setting of baseline perforator compromise, e.g., in atheromatous, dolichoectatic vessels, PED reconstruction would probably not be as well tolerated. Finally, as mentioned above, preexisting intraluminal constructs, may impair PED reconstruction.

CONCLUSIONS

Endovascular reconstruction with the PED represents a safe, durable, and curative treatment of selected wide-necked, large, and giant cerebral aneurysms. Although there are limitations with respect to the clinical scenarios and anatomic locations in which the device can be effectively used, for those aneurysms amenable to treatment, PED reconstruction appears to represent an optimal treatment modality.

Disclosures

Aaron L. Berez, M.D., and Quang Tran, B.S.M.E., M.B.A., are stockholders in and employees of Chestnut Medical Technologies, Inc. Peter K. Nelson, M.D., is a stockholder in Chestnut Medical Technologies, Inc. The other authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

1. Campi A, Ramzi N, Molyneux AJ, Summers PE, Kerr RS, Sneade M, Yarnold JA, Rischmiller J, Byrne JV: Retreatment of ruptured cerebral aneurysms in patients randomized by coiling or clipping in the International Subarachnoid Aneurysm Trial (ISAT). **Stroke** 38:1538–1544, 2007.
2. Fiorella D, Albuquerque FC, Deshmukh VR, McDougall CG: Usefulness of the Neuroform stent for the treatment of cerebral aneurysms: Results at initial (3–6-mo) follow-up. **Neurosurgery** 56:1191–1202, 2005.
3. Fiorella D, Albuquerque FC, Deshmukh VR, Woo HH, Rasmussen PA, Masaryk TJ, McDougall CG: Endovascular reconstruction with the Neuroform stent as monotherapy for the treatment of uncoilable intradural pseudoaneurysms. **Neurosurgery** 59:291–300, 2006.
4. Fiorella D, Albuquerque FC, Han P, McDougall CG: Preliminary experience using the Neuroform stent for the treatment of cerebral aneurysms. **Neurosurgery** 54:6–17, 2004.
5. Fiorella D, Kelly ME, Albuquerque FC, Nelson PK: Curative reconstruction of a giant mid-basilar trunk aneurysm with the Pipeline embolization device. **Neurosurgery** (in press).
6. Fiorella DK, Kelly ME, Turner RD, Lylyk P: Endovascular treatment of cerebral aneurysms. **Endovascular Today** June, 53–65, 2008.
7. Fiorella D, Woo HH, Albuquerque FC, Nelson PK: Definitive reconstruction of circumferential, fusiform intracranial aneurysms with the pipeline embolization device. **Neurosurgery** 62:1115–1121, 2008.
8. Friedman JA, Nichols DA, Meyer FB, Pichelmann MA, McIver JI, Toussaint LG 3rd, Axley PL, Brown RD Jr: Guglielmi detachable coil treatment of ruptured saccular cerebral aneurysms: Retrospective review of a 10-year single-center experience. **AJNR Am J Neuroradiol** 24:526–533, 2003.
9. Higashida RT, Halbach VV, Dowd CF, Juravsky L, Meagher S: Initial clinical experience with a new self-expanding nitinol stent for the treatment of intracranial cerebral aneurysms: The Cordis Enterprise stent. **AJNR Am J Neuroradiol** 26:1751–1756, 2005.
10. Johnston SC, Dowd CF, Higashida RT, Lawton MT, Duckwiler GR, Gress DR: Predictors of rehemorrhage after treatment of ruptured intracranial aneurysms: The Cerebral Aneurysm Rerupture After Treatment (CARAT) study. **Stroke** 39:120–125, 2008.
11. Kis B, Weber W, Berlit P, Kühne D: Elective treatment of saccular and broad-necked intracranial aneurysms using a closed-cell nitinol stent (Leo). **Neurosurgery** 58:443–450, 2006.
12. Kole MK, Pelz DM, Kalapos P, Lee DH, Gulka IB, Lownie SP: Endovascular coil embolization of intracranial aneurysms: Important factors related to rates and outcomes of incomplete occlusion. **J Neurosurg** 102:607–615, 2005.
13. Lee YJ, Kim DJ, Suh SH, Lee SK, Kim J, Kim DI: Stent-assisted coil embolization of intracranial wide-necked aneurysms. **Neuroradiology** 47:680–689, 2005.
14. Lylyk P, Ceratto R, Hurvitz D, Basso A: Treatment of a vertebral dissecting aneurysm with stents and coils: Technical case report. **Neurosurgery** 43:385–388, 1998.
15. Lylyk P, Cohen JE, Ceratto R, Ferrario A, Miranda C: Endovascular reconstruction of intracranial arteries by stent placement and combined techniques. **J Neurosurg** 97:1306–1313, 2002.
16. Lylyk P, Ferrario A, Pasbón B, Miranda C, Doroszuk G: Buenos Aires experience with the Neuroform self-expanding stent for the treatment of intracranial aneurysms. **J Neurosurg** 102:235–241, 2005.
17. McDougall CG: Barrow ruptured aneurysm trial: One year results. Presented at the American Association of Neurological Surgeons Annual Meeting, Chicago, Illinois, April 26–May 1, 2008.
18. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, Holman R: International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: A randomized trial. **J Stroke Cerebrovasc Dis** 11:304–314, 2002.

19. Murayama Y, Nien YL, Duckwiler G, Gobin YP, Jahan R, Frazee J, Martin N, Viñuela F: Guglielmi detachable coil embolization of cerebral aneurysms: 11 years' experience. **J Neurosurg** 98:959–966, 2003.
20. Nelson PK: Pipeline for the intracranial treatment of aneurysms (PITA) trial. Presented at the International Stroke Conference, New Orleans, Louisiana, February 20–22, 2008.
21. Piotin M, Iijima A, Wada H, Moret J: Increasing the packing of small aneurysms with complex-shaped coils: An in vitro study. **AJNR Am J Neuroradiol** 24:1446–1448, 2003.
22. Piotin M, Mandai S, Murphy KJ, Sugiu K, Gailloud P, Martin JB, Rüfenacht DA: Dense packing of cerebral aneurysms: An in vitro study with detachable platinum coils. **AJNR Am J Neuroradiol** 21:757–760, 2000.
23. Raja PV, Huang J, Germanwala AV, Gailloud P, Murphy KP, Tamargo RJ: Microsurgical clipping and endovascular coiling of intracranial aneurysms: A critical review of the literature. **Neurosurgery** 62:1187–1203, 2008.
24. Raymond J, Guilbert F, Weill A, Georganos SA, Juravsky L, Lambert A, Lamoureux J, Chagnon M, Roy D: Long-term angiographic recurrences after selective endovascular treatment of aneurysms with detachable coils. **Stroke** 34:1398–1403, 2003.
25. Slob MJ, van Rooij WJ, Sluzewski M: Coil thickness and packing of cerebral aneurysms: A comparative study of two types of coils. **AJNR Am J Neuroradiol** 26:901–903, 2005.
26. Slob MJ, van Rooij WJ, Sluzewski M: Influence of coil thickness on packing, re-opening and retreatment of intracranial aneurysms: A comparative study between two types of coils. **Neurol Res** 27 [Suppl 1]:S116–S119, 2005.
27. Sluzewski M, van Rooij WJ, Slob MJ, Bescós JO, Slump CH, Wijnalda D: Relation between aneurysm volume, packing, and compaction in 145 cerebral aneurysms treated with coils. **Radiology** 231:653–658, 2004.
28. Tamatani S, Ito Y, Abe H, Koike T, Takeuchi S, Tanaka R: Evaluation of the stability of aneurysms after embolization using detachable coils: Correlation between stability of aneurysms and embolized volume of aneurysms. **AJNR Am J Neuroradiol** 23:762–767, 2002.
29. Vallee JN, Aymard A, Vicaut E, Reis M, Merland JJ: Endovascular treatment of basilar tip aneurysms with Guglielmi detachable coils: Predictors of immediate and long-term results with multivariate analysis 6-year experience. **Radiology** 226:867–879, 2003.
30. Wallace RC, Karis JP, Partovi S, Fiorella D: Noninvasive imaging of treated cerebral aneurysms, part I: MR angiographic follow-up of coiled aneurysms. **AJNR Am J Neuroradiol** 28:1001–1008, 2007.
31. Wehman JC, Hanel RA, Levy EI, Hopkins LN: Giant cerebral aneurysms: Endovascular challenges. **Neurosurgery** 59 [Suppl 3]:S125–S138, S3–S13, 2006.
32. Wiebers DO, Whisnant JP, Huston J 3rd, Meissner I, Brown RD Jr, Piepgras DG, Forbes GS, Thielen K, Nichols D, O'Fallon WM, Peacock J, Jaeger L, Kassell NF, Kongable-Beckman GL, Torner JC: Unruptured intracranial aneurysms: Natural history, clinical outcome, and risks of surgical and endovascular treatment. **Lancet** 362:103–110, 2003.
33. Zenteno MA, Murillo-Bonilla LM, Guinto G, Gomez CR, Martinez SR, Higuera-Calleja J, Lee A, Gomez-Llata S: Sole stenting bypass for the treatment of vertebral artery aneurysms: Technical case report. **Neurosurgery** 57 [Suppl 1]:E208, 2005.

COMMENTS

Lylyk et al. are to be recognized for a significant advancement in endovascular aneurysm treatment. They describe the advantages of their design in increasing metal contact with the parent vessel and reconstructing a lumen in both the coronal and sagittal planes. Traditional stents have a metal surface of 6% to 9%, or 12% to 16% for self-expanding and balloon-expanding stents, as compared with the Pipeline embolization device (PED) (Chestnut Medical Technologies, Inc., Menlo Park, CA), which has a 30% to 35% metal surface coverage.

The authors describe progressive obliteration of the aneurysm through subsequent parent vessel remodeling. In their series of 53 patients, this occurred with complete cure in 52 cases over a period of 12 months. In only 1 patient did a failure of aneurysm occlusion occur; this was attributed to the prior placement of a self-expanding stent. This resulted in an "endoleak" with persistent filling of the aneurysm, owing to lack of apposition and occlusion of the region between the stent and the parent artery. It is important that these cases represented the most challenging of aneurysms, with 22 large, 8 giant, and only 33 small aneurysms. Of note, 19 patients required multiple stents; 17 patients received 2 stents, and 2 patients received 3 stents. No anterior or middle cerebral artery aneurysms were treated in this series, and the basilar artery aneurysm that was treated was in the basilar trunk. Of the 38 vessels with angiographic follow-up at 3 months, 7 vessels demonstrated variable in-stent stenosis (3 mild, 2 moderate, and 2 severe, with >70% luminal compromise). All cases of in-stent stenosis were asymptomatic, and 3 of the 7 cases resolved over 6 months, with only 1 severe case persisting at the 6-month follow-up.

The immediate angiographic findings show that the PED, as a stand-alone device, produces progressive flow redirection, not occlusion. This results in decreased inflow, from a jet to a to-and-fro eddy current, that eventually leads to aneurysm thrombosis. Therefore, delayed occlusion occurs at 3, 6, and 12 months, with a clot build-up in the aneurysm. Immediate angiographic findings include an "ellipse" of subtracted stagnant contrast medium at the aneurysm neck entry zone. No reported cases of excessive clot burden were reported.

This work represent a significant paradigm shift in the future treatment of complex aneurysms. More time and experience will be required to identify the as yet unidentified long-term effect of these stents, yet the transition of a stand-alone stent has evolved. No longer is a stent being considered as a buttress for coils but as a scaffold to reshape the diseased parent artery. This addresses the inherent problem with coils, which is filling a hole rather than closing it. It is hoped that this device will add durability to endovascular treatments and avoid recurrence, regrowth, and the delayed compaction of coils into a thrombus or pseudocapsule. Important limitations include antiplatelet therapy, delayed aneurysm occlusion, and limited experience at branching vessels. The test of time will be the final arbiter of success, as the preliminary results of this group are very encouraging.

Rocco A. Armonda
Bethesda, Maryland

The authors report the Buenos Aires experience in treating 53 patients (63 aneurysms) with the PED. Not only are the results impressive (95% complete angiographic occlusion at 12 months and no major complications), but this represents a paradigm shift in the treatment philosophy for endovascular therapy for aneurysms. Previous and current endovascular treatments for aneurysms have aimed at endosaccular occlusion, and this study represents a shift toward flow redirection and parent vessel reconstruction. The experience, skill, and expertise of the operators of this group may be a factor in the impressive results reported here; however, the concept that a flow-redirecting stent would lead to curative vessel reconstruction is substantiated by previous animal studies (1).

The PED represents a true advancement in the endovascular treatment of aneurysms, however, it is not a panacea. The authors had no strokes in their experience, but perforating or other branch vessels that may be incorporated at the neck of an aneurysm may be at risk for occlusion as the aneurysm thromboses after placement of the device. Flow redirection may not be sufficient in some cases. Four of the aneurysms required coiling in addition to the PED. The PED may not be appropriate in patients with acutely ruptured aneurysms, because of the risks of antiplatelet therapy in the setting of subarachnoid hemorrhage, which have been documented by other groups (2). There may be cases that do not occlude after placement of 1 or more PEDs, or there may be aneurysm recurrences, requiring further therapy. If this occurs,

the tight mesh of the PED will block access to the aneurysm for any further endovascular therapy, such as coiling or liquid embolics, if needed.

This Buenos Aires experience with the PED is an important contribution to our field. I believe that the change in treatment philosophy will lead to the introduction of further flow directors and other devices that will advance our treatment of aneurysms.

Brian L. Hoh
Gainesville, Florida

1. Kallmes DF, Ding YH, Dai D, Kadirvel R, Lewis DA, Cloft HJ: A new endoluminal, flow-disrupting device for treatment of saccular aneurysms. **Stroke** 38:2346–2352, 2007.
2. Tumialán LM, Zhang YJ, Cawley CM, Dion JE, Tong FC, Barrow DL: Intracranial hemorrhage associated with stent-assisted coil embolization of cerebral aneurysms: A cautionary report. **J Neurosurg** 108:1122–1129, 2008.

In this study, Lylyk et al. report their preliminary experience in 53 patients harboring 63 intracranial aneurysms treated with the Pipeline device. All of the treated aneurysms had a wide neck. Although the majority were small aneurysms, several large aneurysms and a few giant aneurysms were treated as well. Thirty-seven percent of the treated aneurysms had recanalized after prior endovascular treatment. The authors' results show that placement of a PED across the aneurysm's neck is both feasible and safe. No major complications directly related to deployment of the device were encountered. More importantly, after deployment of the device, progressive obliteration of the target aneurysm was noted, and no recanalizations were observed. Midterm angiographic follow-up revealed a 10% incidence of moderate or severe stenosis at the level of the stented segment. All of the stenoses were asymptomatic, and some improved over time.

This is a landmark study that outlines the potential of this new generation of endovascular devices. Over the years, it has been exciting to follow the development of these devices from a theoretical concept (1, 4), to animal studies (2, 3, 6), and eventually to clinical application. In the early 1990s, Wakhloo et al. (6) and Geremia et al. (2) theorized that sole stent placement across an intracranial aneurysm could modify intra-aneurysmal hemodynamics and promote intraluminal aneurysm thrombosis, and they showed the potential of this approach in animal studies. However, early intracranial stents were difficult to navigate and, because of their low porosity, did not result in significant modification of the intra-aneurysmal hemodynamics (4, 5). The PED represents a further evolution of intracranial stents, and, by virtue of the high density of its struts, it induces hemodynamic changes, eventually leading to intra-aneurysmal thrombosis.

The results reported by Lylyk et al. are preliminary. Only a few patients had a follow-up of 1 year or longer. Several questions remain unanswered: Is this a definitive treatment? Is there a risk of long-term recurrences? What is the long-term effect on vessel patency after placement of the Pipeline device? Which aneurysms are best suited for this approach? What is the fate of perforating vessels crossed by the device? It is hoped that data from the Pipeline for the Intracranial Treatment of Aneurysms trial will answer most of these questions. In the meantime, I share with caution the authors' enthusiasm for this device, which, undoubtedly, can open a new chapter in the evolution of endovascular treatment of intracranial aneurysms.

Giuseppe Lanzino
Rochester, Minnesota

1. Aenis M, Stancampiano AP, Wakhloo AW, Lieber BB: Modeling of flow in a straight stented and nonstented side wall aneurysm model. **J Biochem Eng** 119:206–212, 1997.
2. Geremia G, Haklin G, Brennecke L: Embolization of experimentally created aneurysms with intravascular stent devices. **AJNR Am J Neuroradiol** 15:1223–1231, 1994.
3. Kallmes DF, Ding YH, Dai D, Kadirvel R, Lewis DA, Cloft HJ: A new endoluminal, flow-disrupting device for treatment of saccular aneurysms. **Stroke** 38:2346–2352, 2007.
4. Lieber BB, Stancampiano AP, Wakhloo AK: Alteration of hemodynamics in aneurysm models by stenting: Influence of stent porosity. **Ann Biomed Eng** 25:460–469, 1997.
5. Wakhloo AK, Lanzino G, Lieber BB, Hopkins LN: Stents for intracranial aneurysms: The beginning of a new endovascular era? **Neurosurgery** 43:377–379, 1998.
6. Wakhloo AK, Schellhammer F, de Vries J, Haberstroh J, Schumacher M: Self-expanding and balloon-expandable stents in the treatment of carotid aneurysms: An experimental study in a canine model. **AJNR Am J Neuroradiol** 15:493–502, 1994.

The main goal of traditional endovascular treatment for intracranial aneurysms has been endosaccular aneurysm embolization with parent vessel preservation. The success of this strategy is limited if the aneurysm is fusiform, large/giant, or wide-necked. Therefore, these aneurysms have remained as "primary surgical" aneurysms treated with either direct surgical reconstruction or bypass. In contrast to the traditional endovascular approach, the new PED aims to cure aneurysms by endovascular reconstruction of the parent vessel, even without endosaccular embolization. Thus, the PED could be thought of almost as an "endovascular equivalent" to the surgical clip ("extravascular" parent vessel reconstruction).

In the current study, Lylyk et al. report their initial periprocedural experience with the PED. Data were collected prospectively. The authors treated 63 intracranial aneurysms, 30 of which were large (22 aneurysms) or giant (8 aneurysms). Mean time to last follow-up angiogram was 5.9 months. Complete angiographic occlusion was achieved in 56% of aneurysms at 3 months, 93% at 6 months, and 95% at 12 months, suggesting progressive aneurysm thrombosis to be ultimately the mechanism of "cure." There were no major complications. Three patients (5%) experienced a transient worsening of their preexisting symptoms.

Lylyk et al. achieved impressive success with the PED, which is apparently a breakthrough in aneurysm therapy. We look forward to further reports of short- and long-term results with the PED in the near future on a worldwide basis.

Erik F. Hauck
L. Nelson Hopkins
Buffalo, New York