Chapter 14
Flow Diversion

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Until recently, at-risk patients with intracranial aneurysms were treated either with microsurgical reconstruction of the parent artery by aneurysm clipping or by endovascular approach, principally through deployment of detachable coils within the aneurysm sac (coil-endosaccular), a method more widely adopted following publication of results from the International Subarachnoid Aneurysm Trial [1, 2]. Although continuous innovation in coil design and coatings has broadened the initial complement of bare-platinum coils aimed at improved aneurysm packing and healing, the seemingly inescapable problem of aneurysm recurrence, and the undefined clinical implications of this phenomenon, as pertains to progressive aneurysm growth and rupture, has limited embrace of endosaccular approaches in providing definitive cure—particularly for complex cerebral aneurysms [2–4]—even when supported by other technical advances, such as adjunctive balloon assistance, to improve coil treatment of the aneurysm neck. Since 2007, an alternative endovascular approach, utilizing minimally porous endoluminal devices (MPEDs) or flow diverters (FDs) (targeting primary reconstruction of the affected parent vessel segment), has become increasingly pre-eminent in the repair of unruptured cerebral aneurysms.

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Emergence of Endoluminal Reconstructive Methods: Adjunctive Stent-Supported Coil Embolization

The feasibility of combined stent-supported aneurysm coiling was first established in an experimental aneurysm model [5] and subsequently confirmed by several case reports [6, 7] and small clinical series [8, 9]—documenting results initially with balloon-expandable stents and, following the introduction of Neuroform (Boston Scientific), Leo (Balt), and Enterprise (Codman), with self-expanding microstents.

Stent-Supported Coiling: Clinical Results

While early experience with *stent-supported coil-endosaccular* treatment of wide neck aneurysms was promising [8, 9], long-term angiographic evaluation of the synergy expected from such combined endovascular therapy has been less than altogether encouraging [9]. In a literature review of 39 articles reporting results from 1517 cases of stent-supported coiling, Shapiro et al. [10] found 45% of aneurysms to be completely occluded on initial posttreatment angiography and only 61% occluded on follow-up (Fig. 14.1). Ironically, although intended to support the

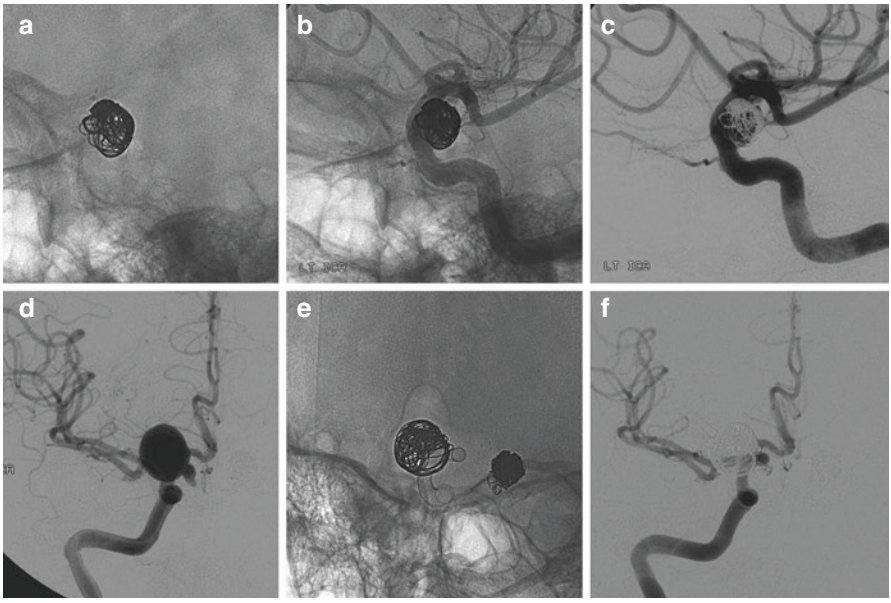

Fig. 14.1 Status post stent-assisted coiling of ruptured left paraophthalmic segment aneurysm with short-term recurrence 6 months post initial treatment (**a–c**). Mirror image right paraophthalmic aneurysm treated with Pipeline and coils, demonstrating complete occlusion 9 months later (**d–f**)

treatment of large and complex-neck aneurysms, small aneurysms account for the majority of aneurysms treated with adjunctive stenting [10]—suggesting tacit recognition for the utility of endoluminal devices at improving occlusion outcomes with coils in the general case.

Primary Endoluminal Technique

Insight into the potential for endoluminal directed aneurysm therapy soon followed commercialization of Neuroform, Enterprise, and Leo. In certain settings, it was observed that aneurysms treated exclusively by stenting alone, without coil placement (typically in the setting of a planned staged treatment or where overlapping stents were used to increase the metallic coverage of the aneurysm neck), occasionally underwent spontaneous thrombosis [11–13], presumably due to alterations in the intra-aneurysmal circulation imposed by the stent construct. With time dedicated minimally porous (higher coverage) endoluminal devices (MPEDs were developed to effect primary parent artery reconstruction without the necessity of aneurysm coils or other embolic materials.

Types of Endoluminal Devices

As of 2017, the Pipeline embolization device (Medtronic, Dublin, Ireland) remains the only endoluminal device cleared by the FDA for use in the United States. Other similar devices, such as the Silk (Balt Extrusion, Montmorency, France), Derivo (Acandis GmbH, Pforzheim, Germany), Flow Re-Direction Endoluminal Device (FRED) (MicroVention, Tustin, California), p64 Flow Modulation Device (Phenox, Bochum, Germany), and Surpass Intracranial Aneurysm Embolization System (Stryker Neurovascular Fremont, California), are approved for human use in Europe, parts of Asia, and Oceana. Since, to this point in time, the published literature predominantly describes the experience with Pipeline, the description below pertains to this device. Two alternative MPEDs, the Surpass Flow Diverter and the MicroVention Flow Redirect Intraluminal Device (FRED), are being evaluated in prospective trials in the United States as of 2017.

The PED is a self-expanding, cylindrically shaped, endovascular construct composed of 48 braided wire strands of cobalt-chromium and platinum-tungsten filaments, with every fourth strand woven into the construct composed of Pt-W to impart greater radio-opacity. The individual strands measure between 28 and 33 microns in diameter with no reported size difference between Co-Cr and Pt-W strands. The available device diameters range from 2.5 to 5.0 mm in 0.25 mm increments, with lengths ranging from 10 to 35 mm. All devices are designed to open approximately 0.25 mm beyond their nominal diameter when unopposed, such that the largest functional diameter would be around 5.25 mm. While a single PED

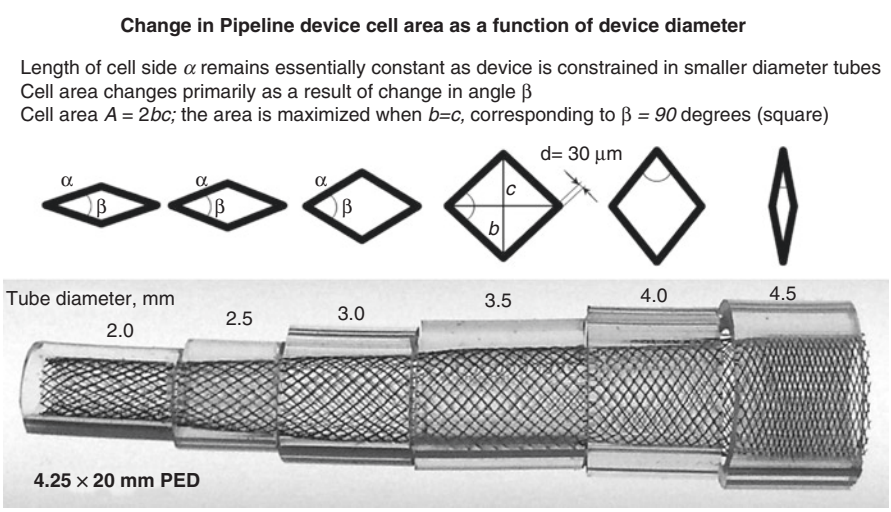

Fig. 14.2 Pipeline embolization device within transparent plastic tubes of predefined diameters. The arrangement demonstrates variation in porosity of the device depending on the diameter of the "vessel" within which it is implanted

provides 30–35% metal surface area coverage at nominal deployment in a straight conduit [12, 14, 15], multiple devices can be strategically telescoped within each other, overlapping devices to create a composite endovascular construct—either to increase the overall length of the construct or to selectively augment the degree of metal surface coverage over the aneurysm neck [12, 14, 15] (Fig. 14.2).

Various iterations of the device delivery system have been utilized, with the partially re-sheathable Pipeline Flex system currently in use throughout the world. As commercially available, the PED is mounted on a delivery microwire and constrained within a removable sheath. It is loaded into and delivered through a standard 0.027″ ID microcatheter (Fig. 14.3). Most anatomical locations accessible with a 0.027″ ID microcatheter can be reconstructed with the PED. A surface-modified device, utilizing a covalently bound phosphorylcholine surface treatment designed to reduce inherent implant thrombogenicity (the Pipeline Flex Embolization Device with Shield Technology), has been available in Europe and Australia since 2016. Both Pipeline Flex and Pipeline Shield are extremely flexible and conform to the native vascular anatomy with very little anatomical distortion regardless of regional tortuosity.

The incorporation of platinum strands allows the PED to be visible throughout its length when implanted in situ. This radio-opacity represents a significant working advantage when compared to previously available self-expanding intracranial stents, which are typically provided with more limited radio-opaque markings restricted to the device ends (Fig. 14.4). At the same time, PED constructs do not produce notable CT artifact, and CT angiography can be used as an effective noninvasive method to evaluate aneurysm treatment in follow-up. While fully MR compatible to 3.0 T, PED constructs (particularly those with overlapping devices) create enough local magnetic susceptibility to reduce signal generated by time-of-

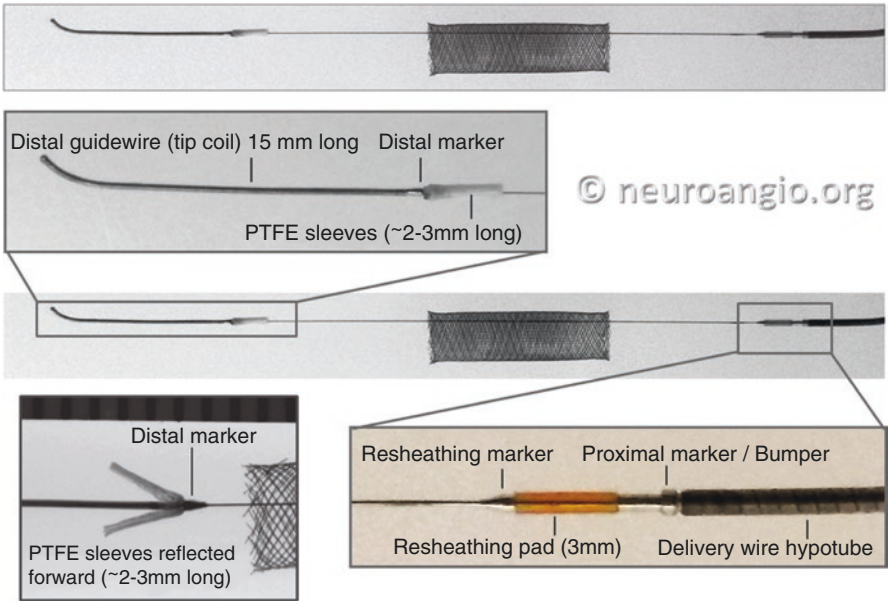

Fig. 14.3 Pipeline Flex embolization device and its delivery system components. (©neuroangio.org used with permission)

flight MR angiography techniques, thus giving the false impression of segmentally absent flow through the construct (Fig. 14.5). Contrast-based MRA sequences, while less sensitive to local susceptibility, nevertheless remain suboptimal for evaluation of the lumen within the implant.

Theoretical Basis of Parent Artery Reconstruction with Endoluminal Stent-Like Devices

As opposed to endosaccular directed therapies, reconstructive endoluminal techniques, like microsurgical clipping, target the arterial deficiency at the aneurysm neck and function to repair the abnormal, aneurysmal segment of the parent artery. This is achieved by implanting a metal scaffolding of sufficiently low porosity (small cell size) across the aneurysm neck to enable (1) thrombosis of the aneurysm and (2) neointimal overgrowth (repaving) of the vascular wall deficiency and any adjacent vessel dysplasia—recreating a structurally sound vascular segment while at the same time permitting uninterrupted perfusion of the parent artery and, ideally, any branch vessels arising adjacent to the lesion (that may be incidentally covered by the bridging devices).

Reconstruction of the deficient vascular segment is multifaceted, evolving over a period of weeks to months, and begins with the *uncoupling of momentum exchange*

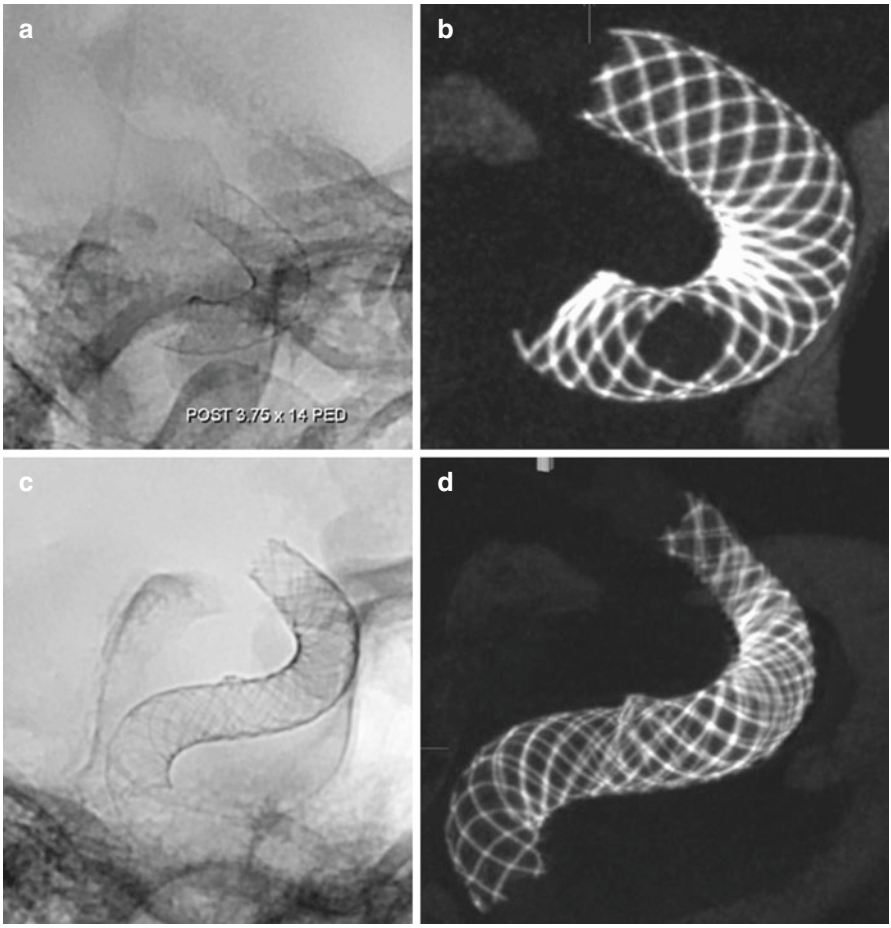

Fig. 14.4 Unsubtracted angiographic and Dyna-CT images of a single Pipeline device in situ (**a**, **b**), demonstrating excellent ability to visualize the construct, including its Pt-W braid with modern equipment. The same patient, following implantation of additional two devices, demonstrating substantial increase in metal coverage over the target anterior genu area (**c**, **d**)

between the parent artery and aneurysm [16–20]. This reduces intra-aneurysmal circulation (prolonging the intra-fundal circulation time)—thereby, contributing to conditions in which thrombosis of the aneurysm is favored. The reparative process is completed upon *neointimal overgrowth of the construct with subintimal incorporation of the stent into the parent vessel wall.* Where intra-aneurysmal flow is sufficiently reduced, gradual aneurysm thrombosis is facilitated, occluding the aneurysm fundus, leading ultimately to curative anatomical vascular repair (neointimal overgrowth of the aneurysm neck). The stages of these transitions [12] can be

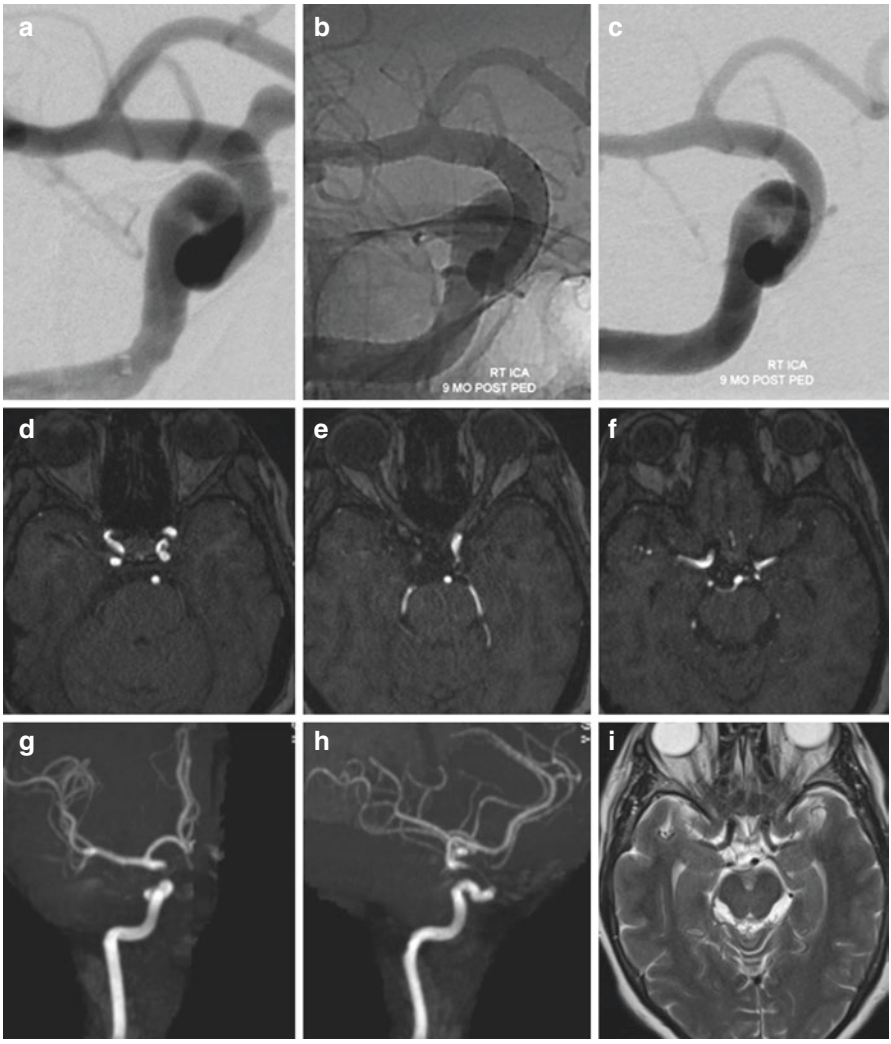

Fig. 14.5 (**a–i**): Right paraophthalmic aneurysm fully occluded following PED treatment. MRA shows typical intra-construct signal loss due to effects of magnetic shielding (**e**). While patency of the parent vessel can be inferred from presence of flow-related enhancement immediately proximal (**d**) and distal (**f**) to the device, as well as from presence of normal T2 flow void (**i**), the possibility of construct-related stenosis cannot be evaluated by TOF MRA methods

characterized as follows: (1) aneurysmal flow disruption, (2) intra-aneurysmal thrombosis, (3) neointimal overgrowth and endothelialization of the construct, and (4) resorption of intra-aneurysmal contents by scavenger cell-mediated processes—with resolution of aneurysmal mass effect.

The Issue of Perforator Branches

When deployed across an aneurysm neck, MPEDs act to reduce the convective component of exchange across the aneurysm neck—diminishing vortical circulation within the aneurysm and leading to intra-aneurysmal stasis and thrombosis. Flow into adjacent branch arteries, however, is governed by the regional cerebrovascular resistance and the arterial to venous pressure gradient across the vascular territory supplied by the index branch. Outside of complicating exigencies (such as parent or branch vessel vasospasm or the construct becoming acutely thrombosed), flow is maintained as long as the impedance across the construct remains significantly below the local cerebrovascular resistance of the jailed vascular territory. Under typical conditions, flow through the microvasculature is determined by various physiological parameters (the mean pressure gradient, cerebrovascular resistance, autoregulatory capacity of the irrigated territory, and intracranial pressure), and, from hemodynamic calculations, greater than 50% surface area coverage of the branch vessel orifice can be tolerated before the covering device begins to contribute significantly to runoff resistance and branch flow starts to diminish [21, 22]. This concept has been validated angiographically in humans, by examining the fate of ophthalmic arteries covered during the treatment of paraophthalmic segment aneurysms [23]. Moreover, histological evaluation of Pipeline 6 months after implantation into the rabbit aorta demonstrates an overgrowth of endothelium uniformly covering the construct [15], except at the orifices of covered branch vessels which present as rounded, funnel-like perforations of the neointimal covering [15, 24]. Thus, the constant flow through the branch vessel appears to inhibit neointimal overgrowth of the construct at branch vessel openings. Parenthetically, however, in vascular territories well supported by collateral pathways, subtle changes in resistance at the branch vessel orifice can lead to recruitment of collateral inflow—allowing arrest of anterograde flow into the index branch and altering the ultimate supply to a jailed vascular territory. Examples are seen frequently where MPEDs are used across the ophthalmic [23] and posterior communicating arteries, the A1 segment, and even anterior choroidal [25] or perforator branches, resulting in asymptomatic occlusion of the covered branches (Fig. 14.6).

Analyses of patients treated with the PED for large and giant ICA aneurysms with coverage of the ophthalmic artery have demonstrated predominance of excellent neuro-ophthalmological outcomes 6 months after the procedure, with very few new deficits, suggesting the possibility for deliberate cerebrovascular remodeling as a separate strategy (delayed mixed-deconstructive) for aneurysm treatment with MPEDs.

Benchmark Studies

Device Geometry

Although nominal metal coverage (reverse of porosity) of the device is listed as 30–35%, in practice, the porosity changes substantially depending on the configuration of the device (curvatures) and its diameter relative to the artery into which it is

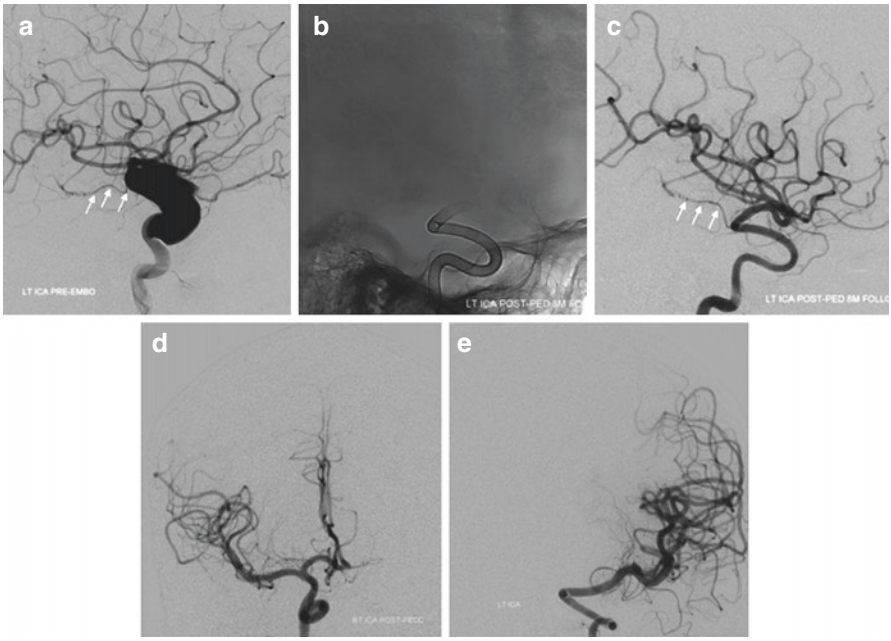

Fig. 14.6 (**a**–**e**): Giant intracranial left ICA aneurysm (**a**) successfully treated by multiple PEDs which required coverage of the left A1 segment, the anterior choroidal (hypoplastic), posterior communicating, and ophthalmic arteries. Eight months posttreatment, the aneurysm is closed. Both ophthalmic artery and A1 segment are no longer visualized, having undergone asymptomatic rearrangement of their supply from the external carotid system and the contralateral A1/ACOM, respectively. The anterior choroidal artery (white arrows), with lesser potential for collateral reconstitution, remains patent

placed. The porosity of any given device is determined by the area of the individual cell (pore) relative to that of its constituent braids (Fig. 14.1) and exhibits a parabolic relationship to the diameter of the device [26] (Fig. 14.7).

In keeping with its parabolic relationship to diameter, the degree of metal coverage falls quickly when the device is oversized relative to the parent artery, with minimized coverage values for all PED implants encountered with as little as 1 mm of oversizing (e.g., implantation of a 4 mm PED into a 3 mm vessel). Thus, in practice, coverage values of 30% are almost never achieved with a single implant—unless compression of the cell structure can be exerted across a very broad-necked aneurysm where the device is not constrained by the diameter of the parent vessel. In most cases, and particularly in large and giant aneurysms for which device was approved, multidevice coverage may be required to achieve the coverage necessary to reproduce the efficacy expected from the PUFS trial (median three devices/aneurysm) [27, 28]. Other reasons to use multiple devices include the overall construct stability imparted by overlapping devices in treating large fusiform aneurysms with long constructs and strategic considerations related to achieving differential coverage of adjacent branch vessels and the aneurysm neck and benefits derived from the use of shorter devices across complex aneurysms in tortuous anatomy where longer individual devices are susceptible to torsion (Fig. 14.8).When creating such constructs, it is advisable to overlap

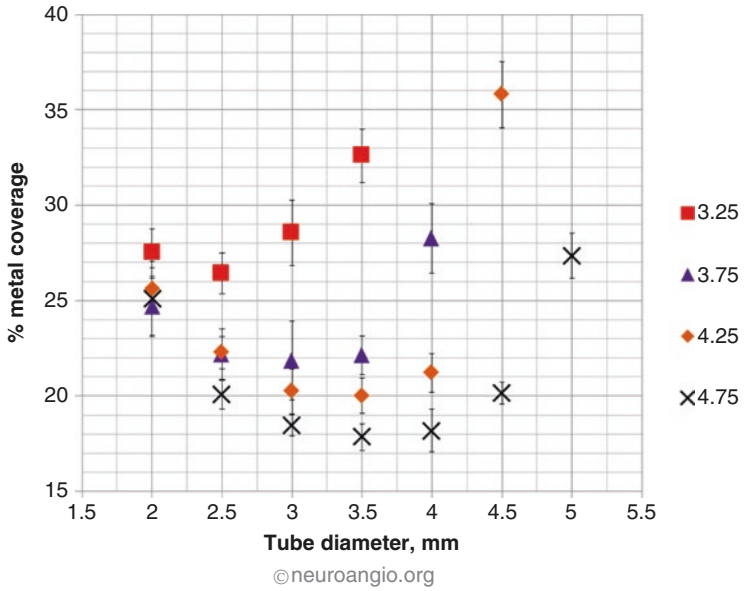

Fig. 14.7 Reverse parabolic relationship between % metal coverage and diameter of target vessel for PEDs of different nominal sizes. The degree of metal coverage steeply declines when any Pipeline device is implanted in a vessel of smaller caliber compared with its nominal size, reaching near-minimum values for as little as 1 mm of oversizing (e.g., implanting a 4 mm device in a 3 mm vessel). Extreme oversizing will eventually produce an increase in metal coverage. For all scenarios, nominally smaller diameter devices have relatively larger metal coverage values than larger diameter ones. For example, a single 4.75 mm device will likely have coverage values in the 20% or below range, while a 3.25 mm device, even when implanted in a 2.5 mm vessel, will still produce >25% coverage. (©neuroangio.org used with permission)

devices of progressively larger diameters in order to achieve a more uniform construct coverage, thereby avoiding extremes of near-perfect braid overlap which produce no effective increase in coverage. Thus, multicoverage does not simply produce a new coverage number—rather, it yields a range of coverage values. This range is widest when identical diameter devices are chosen and becomes progressively tighter when devices of increasingly different diameters are selected (Table 14.1).

Experience with the Pipeline Embolization Device

To date, the PED has been used to treat aneurysms in tens of thousands of patients. Robust evidence of its enduring effectiveness and safety has been provided by the recently concluded PUFS trial [27–29], extending observations available from several earlier single-center series [13, 30] and the PITA trial [31].

PUFS [27] was a single-arm trial of Pipeline for large (>10 mm), wide-necked (>4 mm) aneurysms, involving specifically defined segments of the internal carotid artery (petrous through hypophyseal segments) felt by the US FDA to be appropriate

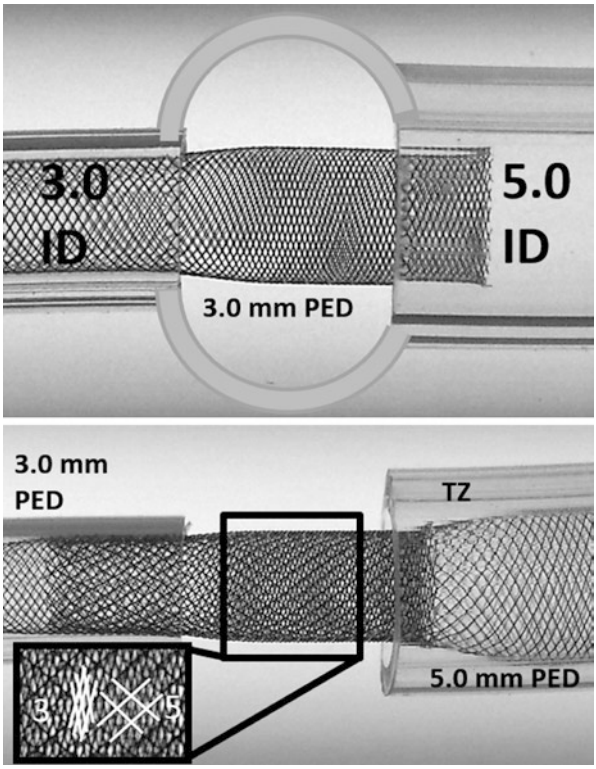

Fig. 14.8 A straightforward strategy for addressing landing zone mismatch using two devices, each appropriately sized to the parent artery. In (A), a 3.0 mm device is deployed from the 3.0 mm landing zone across the entire fusiform aneurysm. A 5.0 mm device is then telescoped into the 3.0 mm device, such that the transition zone TZ is shifted outside of the aneurysm, while the fusiform section is now double-covered. A third 5.0 mm device may be potentially placed across the transition zone TZ to increase coverage in this region

Table 14.1 Table of % metal coverage range achieved by using two overlapping PEDs in various diameter vessels

3 mm vessel	3.25	3.75	4.25	4.75
3.25	30–47%	30–40%	31–37%	34–37%
3.75		20–37%	30–37%	30–35%
4.25			21–35%	31–34%
4.75				20–36%
3.5 mm vessel	3.75	4.25	4.75	
3.75	24–41%	36–37%	33–34%	
4.25		22–36%	31–32%	
4.75			18–31%	
4 mm vessel	3.75	4.25	4.75	
3.75	38–46%	37–39%	36–37%	
4.25		21–35%	29–33%	
4.75			22–32%	
4.5 mm vessel	4.25	4.75		
4.25	36–57%	40–44%		
4.75		25–34%		

Employing devices of different diameter produces the most optimal narrow range of coverage values, minimizing the possibility of focal coverage deficiency

for the initial evaluation of the device. It incorporated a combined safety and efficacy endpoint, with efficacy defined as complete angiographic occlusion of the target aneurysm 180 days after treatment (without evidence of significant device-related stenosis or the use of adjunctive aneurysm implantables—such as coils and other stents). The use of a binary angiographic endpoint (occluded or not occluded) differentiates the PUFS from assorted trials of other endovascular aneurysm treatment devices, which traditionally have incorporated a gradient of occlusion in scoring treatment outcome. Enrollment in the PUFS trial was completed in August 2009 following treatment of 108 patients. Mean aneurysm size was 18.2 mm [22 aneurysms (20.4%) were giant (>25 mm)]. Mean neck size was 8.8 mm. The primary effectiveness endpoint of complete aneurysm occlusion (without device-related stenosis or adjunctive devices) at 6 months was achieved in 73.6% aneurysm, while 5.6% of patients experienced a major ipsilateral stroke or neurologic death. By 1 year, complete aneurysm occlusion was observed in 86.8% of aneurysms. Among the 76 aneurysms evaluated at 3 years angiographic follow-up, 93.4% were completely occluded [28]. At the 5-year conclusion of the PUFS trial [27], 95% of all aneurysms enrolled in the trial were completely occluded by follow-up angiography. There was no instance of aneurysm recanalization throughout the 5-year follow-up interval. The prevalence of major ipsilateral stroke or neurologic death was 5.6%, all occurring within 6 months. No additional adverse neurologic events were reported between 3 and 5 years posttreatment. These results have been supported by various single-center studies and meta-analyses reporting occlusion rates between 70% and 93% over intervals of 6–12 months.

Although impressive, considering the typical morphologies of aneurysms treated in these early studies, analysis of PED treatment failures [32] identified several independent predictors of incomplete aneurysm occlusion: fusiform morphology, decreasing dome to neck ratio, and the presence of previously implanted high-porosity stents in the aneurysmal segment. On an individual case basis, treatment failure tends to involve one of several common mechanisms: device mal-apposition, inadequate coverage, and the incorporation of a branch vessel(s) into the aneurysm fundus. Two of these features (device mal-apposition and inadequate coverage) potentially can be remedied by the operator at the time of treatment—mal-apposition by mechanical correction of an inadequately implanted device (angioplasty or J-wire modification) and, to address inadequate coverage of the aneurysm neck, the deployment of additional devices, either during the initial setting or at a later time (staged treatment). Moreover, various strategies (coil-assisted endoluminal treatment, staged occlusion of the aneurysm, and branch vessel run-off) may be employed to circumvent the effect of a fundal branch on treatment efficacy but require forethought in terms of therapeutic planning. The “Prospective study on Embolization of Intracranial Aneurysms with Pipeline” trial [33], sponsored by Medtronic to expand the US indications for the device, demonstrated 83.5% aneurysm occlusion at 12 months posttreatment, with a corresponding 2% morbidity/mortality rate, in unruptured wide-necked intracranial aneurysms

measuring ≤12 mm, located either in the ICA (up to the terminus) or in the vertebral artery proximal to and including the posterior inferior cerebellar artery (presented at the International Stroke Conference in 2017). In keeping with the overall smaller size of target aneurysms, fewer devices per aneurysm were required in PREMIER for 12-month occlusion rates comparable to PUFS (where a median of three devices/cases were used due to aneurysm complexity). Although conjecture, the substantially lower rate of complications in PREMIER, compared with PUFS and IntrePED [34], is likely due to evolving operator experience, the treatment of less complex target aneurysms, and the overall improvement in antiplatelet management.

Complications

In the initial PUFS communication, Becske et al. reported the primary safety endpoints of major ipsilateral stroke or neurologic death were encountered by 5.6% of patients enrolled. Subsequent meta-analyses, examining composite safety data from various trials and single-center series of flow diverter therapy (FDT), have reported morbidity and mortality rates ranging between 3–8% and 1.3–4%, respectively. Neurologically significant adverse events after PED therapy can be divided broadly into ischemic and hemorrhagic complications.

Ischemic Complications

Ischemic events reportedly complicate 2–3% of PED cases and may be attributed to in situ parent vessel (construct) thrombosis, emboli, or delayed ischemia resulting from device-related stenosis. Since publication of the PUFS trial and IntrePED registry [34], the rate of ischemic events appear to be falling [33], likely due to improved antiplatelet management (which at many centers includes some form of antiplatelet testing), increased operator experience, treatment of less complex aneurysms, and technical refinements facilitating safe, efficient device delivery (reducing the time of the procedure). Moreover, outside of the United States, availability of the surface-modified Pipeline Shield may contribute to fewer ischemic complications by lowering the intrinsic thrombogenicity of the phosphorylcholine-coated device. Beyond the acute stage, symptomatic device-related stenosis reportedly affects <1% of patients treated [27]. However, instances of asymptomatic delayed occlusion (beyond 1 year) may be observed in up to 5% of patients (particularly in those with giant fusiform aneurysms treated with long PED constructs), suggesting the necessity of continued surveillance and prolonged antiplatelet coverage for a subset of complex aneurysms (Fig. 14.9).

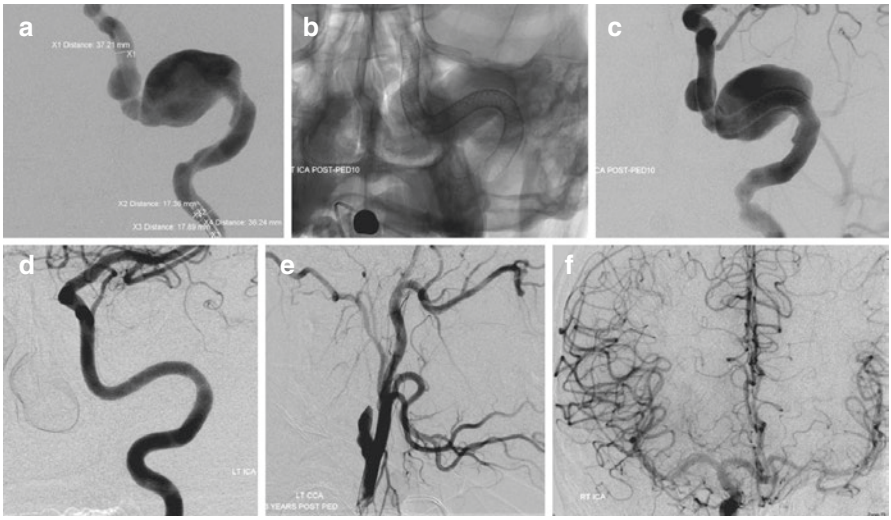

Fig. 14.9 Delayed occlusion of apparently successfully treated giant petrous/proximal cavernous segment aneurysm. Pre- (**a**) and immediate posttreatment (**b**, **c**) angiographic views. A 12-month posttreatment angiogram (**d**) shows apparent complete occlusion with no construct-related stenosis. A 3-year angiogram (**e**, **f**) shows parent vessel occlusion with asymptomatic collateral reconstitution of the left hemisphere

Hemorrhagic Complications

Hemorrhagic complications are observed in 2–3% of cases [27, 34] and include iatrogenic or spontaneous intraparenchymal bleeds and subarachnoid hemorrhage due to acute or delayed aneurysmal rupture.

Parenchymal hemorrhage after flow diversion is a rare but frequently devastating event, occurring with a frequency of 1–2% in most studies. Various mechanisms have been proposed, including subacute hemodynamic changes within the parent artery induced by implantation of the device across the aneurysm neck (reduction in Windkessel effect) and hemorrhagic conversion of ischemic lesions produced by periprocedural emboli (gas, thrombotic or related to foreign bodies). The association of emboli composed of hydrophilic coatings—originating from catheters used in the procedure—has been confirmed by autopsy of patients with fatal hemorrhages [35] and demonstrated by imaging to produce delayed inflammatory reactions (foreign body granulomas) in others [36] (Fig. 14.10). Typical parenchymal hemorrhages occur within 60 days of treatment and, given the ongoing use of dual antiplatelet regimens, are frequently massive and may be fatal. Management requires expertise in neurocritical care and vigilant antiplatelet monitoring to limit hemorrhage expansion while seeking to maintain device (and parent vessel) patency. Full antiplatelet reversal may be feasible when sufficient collaterals are present to permit asymptomatic occlusion of the parent artery with PED thrombosis.

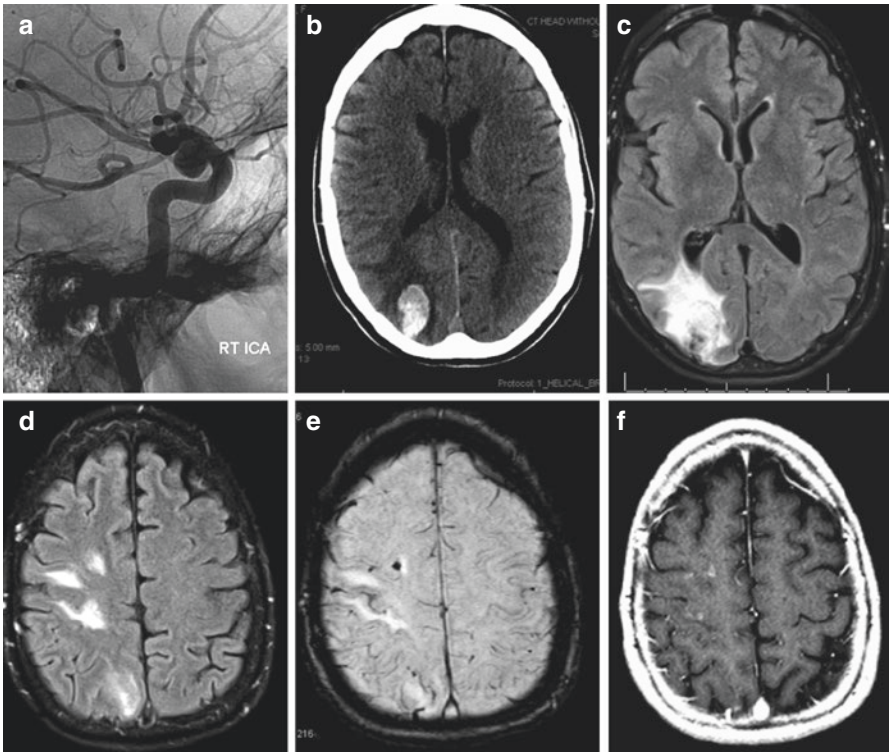

Fig. 14.10 (**a**–**f**) Right paraophthalmic aneurysm treated with PED. Two months post-procedure, the patient developed acute headache and quadrantanopia with a corresponding right occipital hemorrhage (**b**). MRI demonstrates extensive surrounding T2/FLAIR edema, as well as several other foci of edema (**d**), susceptibility (**e**), and enhancement (**f**) in the same hemisphere, characteristic of multiple foreign body emboli (hydrophilic catheter coating)

Delayed Aneurysm Rupture

The prevalence of delayed aneurysm rupture after FDT is estimated to be approximately 1% of cases (Fig. 14.11). While little is known about the etiology of such ruptures, several empirical observations are noteworthy. In a retrospective analysis, Kulcsar et al. [37] found 14 cases of delayed rupture among 1421 aneurysms treated by flow diversion therapy. The mean time to rupture was 60 days, with a median time of 9 days posttreatment. All ruptures occurred in aneurysms >10 mm diameter, with 13 of the 14 aneurysms characterized by diameters >19 mm. 12 of the 14 patients were newly symptomatic. Nine aneurysms were treated with a single device, four with two devices, and one with three devices. Of the 13 patients experiencing subarachnoid hemorrhage (one rupture resulted in a carotid-cavernous sinus fistula), 10 died, 2 remained in a vegetative state, and 1 clinically recovered.

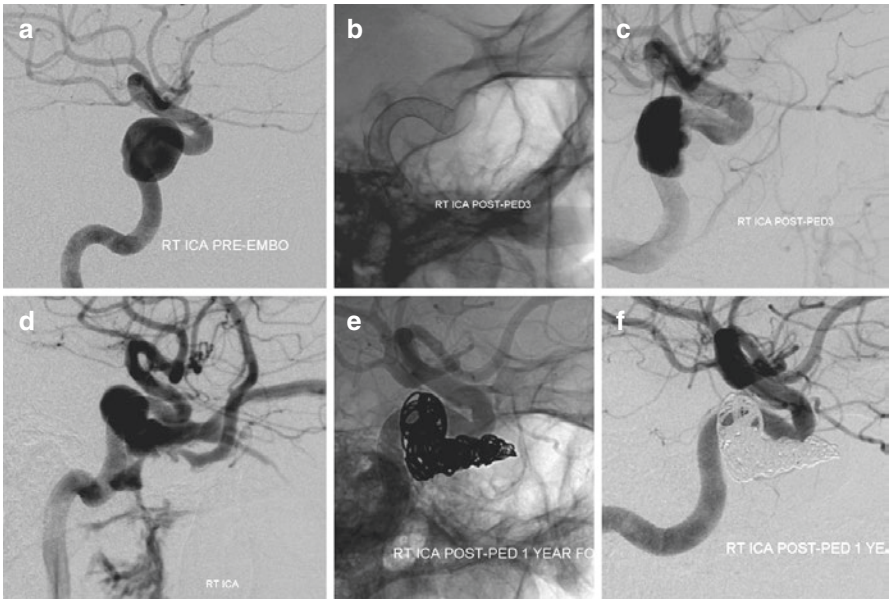

Fig. 14.11 Right cavernous aneurysm before (**a**) and after (**b**, **c**) PED treatment. A 6-month follow-up angiogram (**d**) shows aneurysm rupture with secondary direct carotid-cavernous fistula formation. The fistula was closed by transvenous coil embolization (**e**, **f**)

Parenthetically, although delayed aneurysmal rupture is a concern in FDT of large aneurysms and deservedly garnishes significant attention, delayed ruptures also have been observed after treatment of complex aneurysms by other means. In their report of the results with deconstructive treatment of giant and large internal carotid artery aneurysms with the excimer laser-assisted bypass technique, van Doormsal et al. [38] observed 1 fatal and 2 nonfatal postoperative aneurysm bleeds among 33 patients treated. Additionally, Heran et al. [39] reported 2 deaths from delayed aneurysm rupture (one at 1 month and the other at 5 months posttreatment) among 16 patients with large ophthalmic segment aneurysms undergoing coil-endosaccular embolization (with mostly incomplete angiographic occlusion). Collectively, these diverse instances of delayed rupture (all involving large aneurysms) suggest the presence of a fragile subset of complex aneurysms which are at near-term risk of hemorrhage—either spontaneously (accounting for the natural history risk of large aneurysm rupture) or after treatment by an immediately non-definitive intervention—which itself may independently contribute to the rupture risk. Recall that FDT and forms of deconstructive aneurysms treatment, where the lesion is not completely isolated proximally and distally from the circulation, are initially incomplete and require time to evolve into definitive cure.

Treatment Limitations

The advantages of FDT in providing durable, anatomically correct occlusion of large and giant cerebral aneurysms demonstrated in PUFS had led to much interest in the expanded use of these devices for the treatment of aneurysms beyond the ICA for which there currently are not acceptable treatment options.

Experience in the Posterior Fossa

Initial enthusiasm following the successful use of MPEDs to treat highly complex fusiform basilar aneurysms [40, 41] has been dampened by the high incidence of major ischemic and hemorrhagic complications when applied to a certain holobasilar, fusiform subset (Fig. 14.12) [42]. Increasingly, experience with posterior fossa

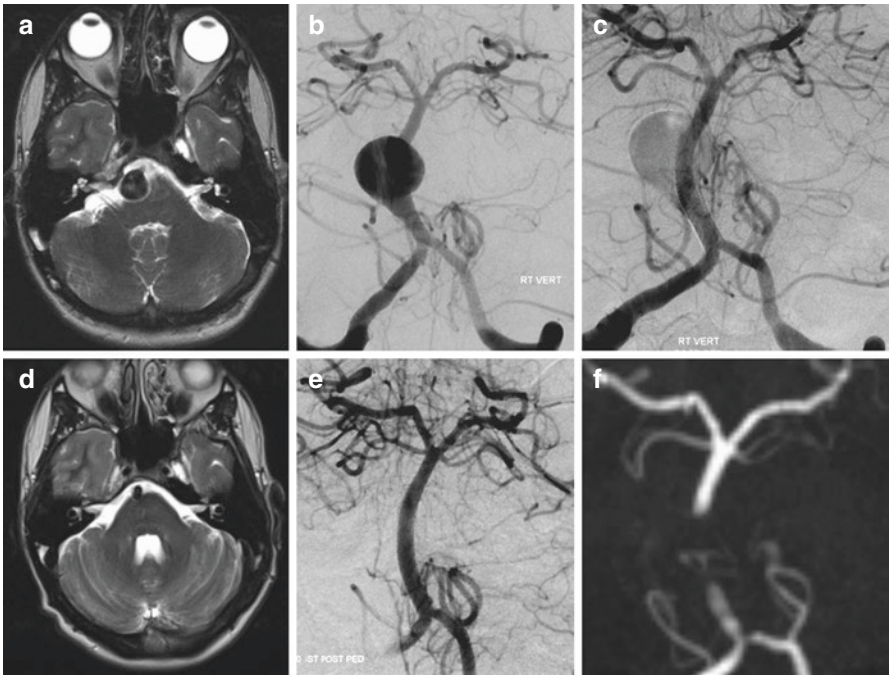

Fig. 14.12 Mid-basilar aneurysm presenting with a CNVI palsy, pre- (**a**, **b**) and immediately posttreatment (**c**) with overlapping PEDs. Delayed posttreatment MR (**d**), angiogram (**e**), and time-of-flight noncontrast MRA (**f**) demonstrating complete aneurysm occlusion with reduction in mass effect. The concurrent MRA shows typical effects of magnetic shielding within the pipeline construct, with robust flow-related enhancement immediately proximally and distally, thereby implying vessel patency

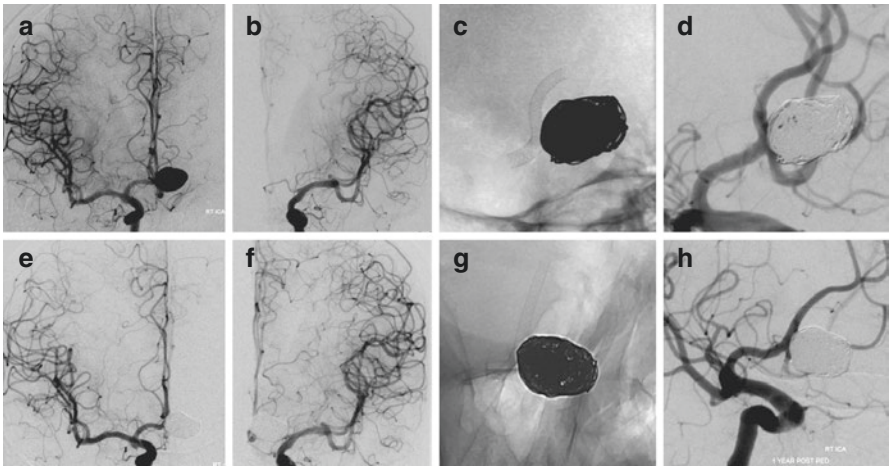

Fig. 14.13 (**a**–**h**): Large anterior communicating aneurysm with a dominant right A1 segment, treated by right A2 to A1 PED placement and coiling. Immediate posttreatment angiogram continues to demonstrate right A1 dominance (**d**). One year later, the aneurysm remains fully occluded. There has been interval hemodynamic rearrangement with right A1 role now limited to ipsilateral anterior cerebral artery support (**e**), while the left A1 has undergone compensatory enlargement and now supplies the entire distal left anterior cerebral artery territory (**f**)

aneurysms is leading to recognition of the heterogeneity of these lesions and providing insight into prognostic features indicating the likelihood of treatment success [43–45].

While recent results from the PREMIER trial [33] as well as the experience outside the United States support the use of MPEDs in the management of smaller, unruptured aneurysms, the application of these devices in the management of bifurcation aneurysms remains investigational (Fig. 14.13). Moreover, due to the time course of aneurysm occlusion after FDT and requirements for antiplatelet medications, their use in the setting of subarachnoid hemorrhage is likely to remain somewhat limited [46, 47]. Nevertheless, even in this setting, the adjunctive use of MPEDs—coupled with other embolic agents, either concomitantly or as part of a staged procedure—may find utility in aneurysmal SAH. For complex ruptured aneurysms, a strategy may involve coiling the aneurysm as completely as possible, with or without balloon assistance, in the acute setting—followed by staged MPED placement 2–4 weeks later—to reduce the likelihood of recanalization, once clinical issues related to the management of SAH (placement of an intraventricular drain for the treatment of hydrocephalus or subsequent angioplasty for treatment of SAH-associated vasospasm) have resolved and antiplatelet drugs may be more safely administered. Furthermore, MPEDs (coupled with acute induction of antiplatelet coverage) increasingly are assuming a primary role in the management of SAH resulting from rupture of blister aneurysms—particularly in settings where the parent vessel cannot be safely sacrificed due to poor collateral support (Fig. 14.14).

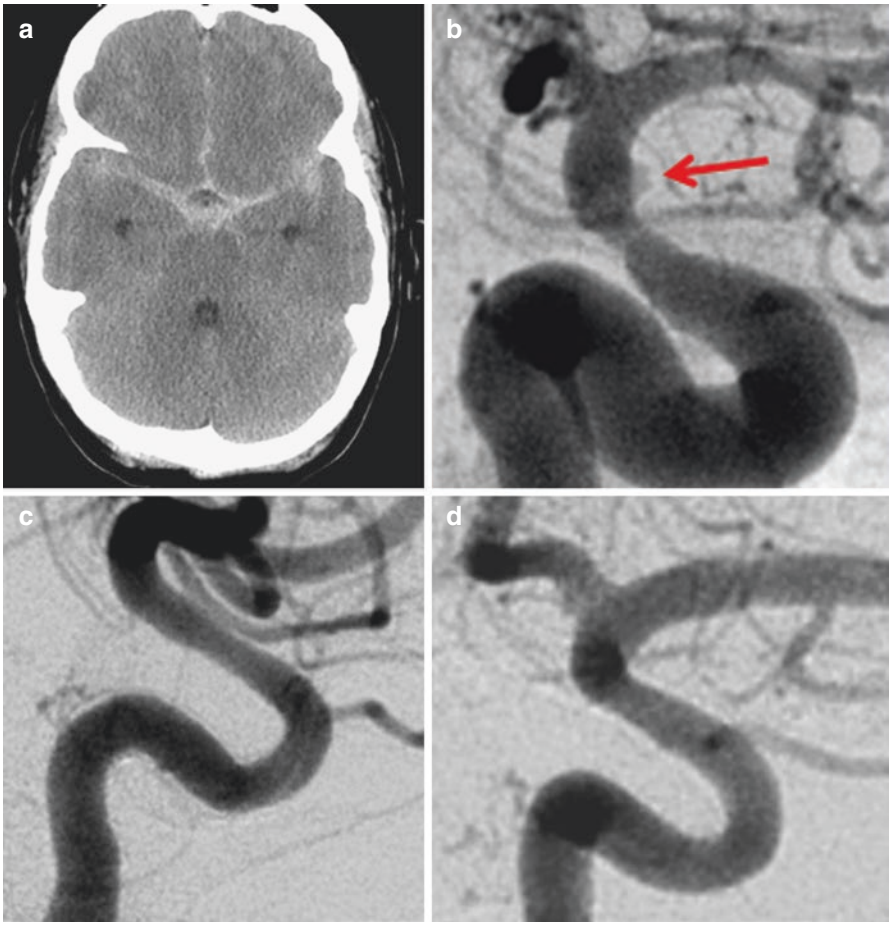

Fig. 14.14 (**a**–**d**): Dorsal wall blister aneurysm before (**b**) and 3 months following (**c**, **d**) Pipeline embolization. Three telescoped devices were used

Conclusions

As documented by the PUFS trial and various single and multi-institutional registries, FDT, in contrast to the often limited results of coil-endosaccular, offers high rates of complete and durable occlusion of large, complex-neck aneurysms, with comparatively lower rates of treatment-associated major morbidity and mortality [48–50], with the added benefit of relief from mass effect. Experience from the PREMIER trial and outside the Unites States suggests these benefits may be generalized to a larger population of cerebral aneurysms, and, thus, in the future will likely play an ever larger role in aneurysm treatment [46]. Nevertheless, several issues regarding their use will require additional experience and further evaluation:

the ideal number of devices (degree of coverage, critical porosity) necessary for definitive aneurysm occlusion, the necessity and duration of antiplatelet coverage, the role of antiplatelet testing, indications for adjunctive coiling, and the spectrum of aneurysm morphologies and locations preferentially addressed by FDT.

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