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## ORIGINAL RESEARCH

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# Flow Diverters Can Occlude Aneurysms and Preserve Arterial Branches: A New Experimental Model

**BACKGROUND AND PURPOSE:** FDs are new intracranial stents designed to occlude aneurysms while preserving flow to jailed arterial branches. We tested this fundamental principle in a new aneurysm model.

**MATERIALS AND METHODS:** Canine lateral wall aneurysms, featuring a branch located immediately opposite the aneurysm, were created in 16 animals to study the effects on aneurysm or branch occlusion using single HP stents (n = 4), 2 overlapping HP stents (n = 4), or an FD (n = 8). Two other animals, in which an efferent arterial branch was anastomosed to the aneurysm fundus, were also treated with FDs. Angiographic results after deployment, at 2 weeks, and at 3 months were scored using an ordinal scale. The metal porosity of the FSS and the amount of FSS neointima formation was determined by postmortem photography.

**RESULTS:** FDs led to better angiographic occlusion scores compared with HP stents (P = .026). FDs were significantly more likely to occlude the aneurysm than the branch (P = .01). When the branch was switched to originate from the aneurysm fundus, the FDs became ineffective (0/2). Neointimal closure of the aneurysm ostium was significantly better with FDs than with single or double HP stents (P = .039). Angiographic occlusion correlated with metallic porosity and neointimal tissue coverage (Spearman P = -0.81; P = .001).

**CONCLUSIONS:** In this study, flow diverters occluded lateral wall aneurysms more readily than branches. Metal device porosity strongly influenced the occlusion rate.

**ABBREVIATIONS:** ASA = aspirin; CCA = common carotid artery; CFD = computational fluid dynamics; FD = flow diverters; FSS = free segment of stent; HP = high-porosity

Low diverters are the latest, most promising new endovascular devices used to treat intracranial aneurysms. Despite the increasing clinical use of these novel devices, there is a paucity of preclinical studies to establish the foundations underlying the way they succeed, or fail, to safely occlude aneurysms. One fundamental problem is that, for the same device (assuming uniform construction), we intend for the FD to effectively occlude the aneurysm yet maintain patency of any jailed branches or perforators. While CFD studies suggest that this can be readily accomplished, <sup>1</sup> in vivo models able to test, in a head-to-head fashion, whether implanted devices can occlude aneurysms, yet spare arterial branches, are needed.

Using a new canine model, we address the following questions: When both an aneurysm and a branch are covered by

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the same device in the same conditions, can an FD lead to aneurysm occlusion while respecting branch patency? If this differential effect can be shown, what happens in vivo to the segment of the device covering the aneurysm compared with the one covering the branch? Are these findings caused by flow patterns? Are FDs superior in terms of occlusion rates compared with HP stents in lateral wall aneurysms? Finally, can the effects of FDs be reproduced by using 2 overlapping HP stents?<sup>2</sup>

#### **Materials and Methods**

#### **Definitions**

We define the effective portion of the stent as the FSS—the portion of the stent not apposed to the wall of the parent vessel. In a simple linear lateral wall model, the FSS is the portion of the stent that covers the ostium of the aneurysm. To assess the diverging biologic effects of FDs on aneurysms or arterial branches, we have designed a new model to simultaneously study, in the same animal and biologic environment, 2 free segments of stent of the same device: the aneurysm FSS that faces the aneurysm ostium and the diametrically opposed branch FSS that faces the ostium of a large branch (Fig 1). Angiographic occlusion and neointima formation on each isolated FSS can thus be studied separately—a task that cannot be accomplished with other models.

#### Surgical Aneurysm Creation

Protocols for animal experimentation were approved by the Institutional Animal Care Committee in accordance with guidelines of the Canadian Council on Animal Care. All procedures were performed in 7–10 kg beagles under general anesthesia. In the first 16 animals,

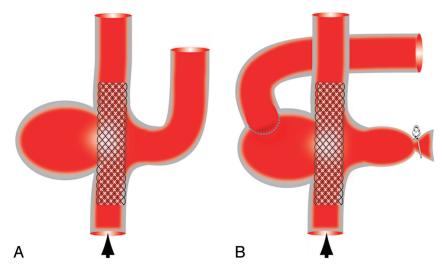


Fig 1. A, Experimental canine model featuring a branch immediately opposite a lateral wall aneurysm, allowing the direct comparison of aneurysm with branch occlusion rates. B, Variant of model, where efferent branch is anastomosed to aneurysm fundus to test the effect of arterial flow patterns on aneurysm occlusion.

Table 1: Characteristics of devices						
	Nominal Porosity (%)	Pore Density (Full Pores/mm²)	Maximum Full Pore Size (mm²)			
HP stent (4.5 $\times$ 30 mm)	89 ± 1.5	$0.6 \pm 0.5$	0.616			
Double overlapping HP stents (4.5 $ imes$ 30 mm)	$75.8 \pm 1.2$	$2.3 \pm 2.1$	0.371			
FD (3.75 $\times$ 27 mm)	$72.4 \pm 3.1$	$5.6 \pm 1.4$	0.078			

Note: - Measurements in 3.5-mm straight glass tubes.

through a midline vertical cervical incision, the left external jugular vein was harvested, inverted to remove potential valvular obstructions, and placed in heparinized saline until vein pouch creation. The pretracheal fascia was divided to obtain access to both carotid arteries. The left CCA was mobilized, temporary clips applied, and the distal CCA divided and tunneled behind the esophagus. The carotid artery was then made to adopt a natural lie, where it meets the opposite right carotid artery at a 90° angle. Temporary clips were then placed on the right CCA, and a 5-mm arteriotomy created on the medial surface opposite the transected left CCA ostium. The left carotid artery was anastomosed to the right CCA using a continuous 7.0 Prolene suture (Ethicon, Cincinnati, Ohio). After completion of the first anastomosis, a second arteriotomy was created directly opposite the first (on the lateral segment of the right CCA). The harvested vein segment was then sutured to the lateral arteriotomy in an end-to-side configuration with 7.0 Prolene, and the distal segment of the vein closed with a permanent vascular clip to form the aneurysm fundus. Temporary clips were then removed, and any sites of bleeding were repaired with sutures. The incision was then closed in multiple layers over Penrose drains, which were typically left for 24-48 hours.

#### Creation of an Arterial Branch Originating from the Venous Aneurysm

In 2 additional animals, to demonstrate the effects of efferent arterial blood flow, a modification to the previously described surgical construct was made. Before removal of the temporary clips, the left CCA was transected approximately 1 cm distal to the anastomosis. The remaining left CCA arterial stump was closed with a permanent vascular clip to interrupt efferent blood flow from the branch. Then, a 5-mm venotomy was created on the superior aspect of the vein pouch aneurysm, and the transected left CCA was swung over and anastomosed to the venous aneurysm, thereby creating an efferent outflow tract from the vein pouch aneurysm (Fig 1B).

#### Endovascular Treatment

Endovascular treatment was performed at least 4 weeks after surgical aneurysm construction, through a coaxial microcatheter system introduced by a percutaneous transfemoral approach. Animals were treated with an HP stent (n = 4), 2 overlapping HP stents (n = 4), or a single FD (n = 8) (MicroVention, Aliso Viejo, California). The animals with modified aneurysms, with an efferent branch originating from the venous pouch, were also treated with a single FD (n = 2). The nominal lengths of all devices ranged from 26-46 mm in a 4-mm vessel. All devices were deployed in a linear configuration (from the distal right CCA to the proximal right CCA) to bridge both the aneurysm neck and left CCA branch origin. The characteristics of stents and flow diverters are summarized in Table 1.

#### Antiplatelet Regimen

The first 3 animals were premedicated only with ASA. All 3 were found to have carotid thrombosis 2 weeks after FD implantation. These animals were excluded from analyses. The antiplatelet regimen was subsequently modified: 325 mg of ASA and 75 mg of clopidogrel were administered for 4 days before stent implantation. Clopidogrel therapy was discontinued 10 days poststent implantation, while 325 mg of ASA per day was continued until sacrifice. This regimen was empirically determined, as validated tests of platelet activities for canines do not exist.

#### Angiography

Transfemoral angiography was performed in all animals immediately before and poststent deployment, at 2 weeks, and immediately before sacrifice (12-14 weeks). To prevent femoral hematomas on dual antiplatelet therapy, all punctured femoral arteries were surgically exposed through a small linear incision and ligated. Angiographic results were scored using a system modified from Kamran et al.<sup>3</sup> A score of 0 indicated no change in aneurysm volume with treatment; 1, residual contrast filling more than 50% of the pretreatment aneurysm volume; 2, residual contrast filling less than 50% of the pretreatment aneurysm volume; 3, residual filling confined to the neck region; and 4, no residual filling (complete occlusion).

The patency of the arterial branch was also assessed, and stenoses, if present, were graded as greater or less than 50%, using the formula 1-N/D, where N= diameter at most stenosed region and D= diameter of the distal normal artery.

#### Sacrifice, Photography, and Pathology

Euthanasia by barbiturate overdose was performed at 12–14 weeks. After fixation in 10% formalin, the carotid artery aneurysm construct was opened longitudinally and photographed using a computerized imaging system (Vision PE; Clemex Technologies, Montreal, Canada).

For each ex vivo aneurysm FSS, 2 porosities were determined. First, the metallic porosity, corresponding to the porosity of the entire FSS, was determined by measuring the total surface area of the stent struts, using transillumination techniques to resolve the biologic material from the metal. Areas were measured by tracing each structure, by hand for each digitized photograph, and the total area calculated. The final porosity was calculated by adding the contributions of the traced areas of neointima or thrombus covering the stent or FD. The same procedure was used to assess the branch FSS, whenever possible. Selected representative samples of tissue coverage over areas of interest were biopsied under the operating microscope. Biopsy specimens were stained with hematoxylin and eosin and Movat pentachrome, followed by immunohistochemistry with smooth muscle cell alphaactin and endothelial Factor VIII. Two complete specimens were dehydrated in a graded series of ethanol and embedded in methyl methacrylate, leaving the devices in situ. After polymerization, 2- to 3-mm transverse sections were sectioned through the proximal and distal ends of the FDs and from the aneurysm FSS. The sections were ground to a thickness of 46-51 microns using linear grinding technology (EXAKT Technologies, Oklahoma City, Oklahoma), polished, and stained with toluidine blue and basic fuchsin.

#### **Statistics**

Comparisons between groups were made using the Kruskal-Wallis test for nonparametric data. When results were found to be significant, groups were compared in a  $2 \times 2$  fashion using Mann-Whitney tests with the Bonferroni correction. Comparisons between aneurysm and branch occlusion rates were made with the Wilcoxon test. Correlations between nonparametric data were studied with Spearman rank correlation coefficient ( $\rho$ ). All analyses were carried out with SPSS version 19 (SPSS, Chicago, Illinois), with a threshold for significance of P=.05.

#### **Results**

The surgical and endovascular procedures were well tolerated. All aneurysms were patent before endovascular treatment. Results are summarized in Table 2.

#### Angiographic Results

Choice of endovascular treatment strategy led to significantly different aneurysm occlusion rates (P = .015), with FDs being more effective than HP stents (P = .026), which never occluded the aneurysm. FDs were significantly more likely to occlude the aneurysm than the branch (P = .01). When the branch was switched to originate from the aneurysm fundus,

Table 2: Angiographic and pathologic results at 12 weeks postimplantation of endovascular HP and FD stents

		Angiography	Pathology	
Device	Animal	Occlusion Score	Metallic Porosity (%)	Final Porosity (%)
HP stent	1	0	72	28
	2	0	68	7
	3	0	85	7
	4	0	87	10
Double overlapping HP stents	5	2	76	1
	6	2	64	6
	7	3	60	2
	8	0	70	15
Flow diverters	9	2	18	2
	10	4	28	2
	11	4	33	1
	12	2	17	1
	13	4	41	1
Flow diverters	14 <sup>a</sup>	0	44	2
	15 <sup>a</sup>	0	47	8

<sup>&</sup>lt;sup>a</sup> Model with efferent branch anastomosed to aneurysm fundus.

the FDs became ineffective (0/2). None of the jailed branches became occluded, but 5/13 showed  $\geq$ 50% stenoses. The animals with arteries that became stenotic were distributed across treatment groups.

#### Pathology Results

FDs covered more of the aneurysm ostium with metal struts than single or double overlapping HP stents (P=.043). Neointimal closure of the aneurysm ostium was significantly better with FDs than with single or double HP stents (P=.039). Increased metallic strut coverage of the aneurysm correlated strongly with angiographic occlusion rates ( $\rho=-0.69$ ; P=.009) and with neointimal closure of the aneurysm ostium ( $\rho=-0.81$ ; P=.001). The 2 animals with branches anastomosed to the aneurysm had no tissue found within the aneurysm fundus at pathology. For all other aneurysms, despite angiographic branch permeability, there was a substantial amount of neointimal coverage of the branch FSS in all cases.

#### **Discussion**

We have demonstrated that in optimal conditions, FDs can occlude aneurysms yet leave branches patent. This differential effect of the endovascular device is due to blood flow patterns, as it is reversed by anastomosing an arterial branch to the aneurysm fundus. Aneurysm occlusion is caused by neointimal closure of the FD pores and is correlated to the amount of metal surface coverage over the aneurysm ostium. We observed that aneurysm closure does not occur when the device porosity is too high. However, the most appropriate metallic surface coverage is difficult to predict because of device deformation that occurs across the aneurysm FSS. When the devices failed to occlude the aneurysms, it was caused by gaps or leaks in the neointimal coverage of the aneurysm FSS. Although branches were patent in all cases, extensive neointimal coverage of the struts bridging the branch ostia were found, which were sometimes mixed with thrombus, raising concerns regarding the safety of this application in humans.

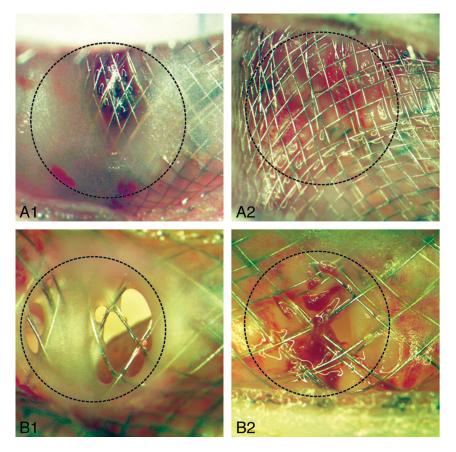


Fig 2. Macroscopic en-face photography of aneurysm (A1) and branch ostium (A2), 3 months after treatment with FD stent compared with aneurysm (B1) and branch ostium (B2) of animals treated with double overlapping HP stents. Angiographic branch patency was maintained in all cases, despite a substantial amount of neointimal coverage of the branch orifice.

#### A New Model

Preclinical studies using a rabbit elastase model have previously shown that experimental aneurysms can be occluded with FDs, while sparing the subclavian branches or lumbar artery origins, at 6 months postdeployment. <sup>4,5</sup> In the rabbit, the pores of the FD facing the aneurysm ostium were found to be fully closed by neointima, at least in cases of success, while neointimal closure was partial, minimal, or absent where the device bridged arterial branch ostia. <sup>4,5</sup> However, the arterial branch and aneurysm ostia are not tested under the same conditions in the elastase model, and because these depend on the animal's anatomy, they cannot be modified at will.

The model we present is a variant of our original bifurcation aneurysm model, <sup>6</sup> which allows FDs to be studied in different configurations, with or without the influence of an adjacent branch. The present variant, designed to compare aneurysm and branch occlusion rates in a head-to-head fashion, also provides optimal conditions for a device to successfully occlude an aneurysm: The FSS is oriented to both close the anatomic neck of the aneurysm as well as to normalize parent vessel blood flows.

#### The Role of Blood Flow Patterns in Preserving Patency

The first significant finding from this study is that a branch FSS of equivalent size and in equivalent anatomic circumstances did not become occluded despite being jailed by the lowest porosity FD stent (Fig 2). That branches and aneurysms behave differently after stent placement has been suggested by many investigators. <sup>1,4,5,7-10</sup> The most likely explanation for

maintained branch patency, while the aneurysm becomes occluded, would be that efferent blood flow prevents the stasis required for thrombosis and occlusion to occur. The animals with branch outflows anastomosed to the aneurysm fundus demonstrate that angiographic observations and pathologic results at the level of the respective FSS can be reversed: The branch FSS (now converted into an arterial aneurysm) became fully occluded with neointima, while the aneurysm FSS now showed large leaks (Fig 3). The aneurysms remained unchanged at 3 months. The measured metallic porosities for these 2 animals were admittedly slightly higher (range 44%-47%) than for the FD-treated aneurysms without branches (range 18%-41%), which suggests that perhaps the greater amount of open space may have contributed to the maintained patency of these aneurysms. However, the aneurysms treated with double overlapping HP stents were found to have at least 50% aneurysm occlusion in 3/4 animals, with metallic porosities ranging from 60%-76%, whereas the aneurysms with branches had no changes, with metallic porosities ranging from 44%-47%, suggesting that the presence of an arterial blood flow pattern was a more significant factor in maintaining the aneurysm patency than the metallic porosity.

These findings confirm a previous observation in a giant fusiform model, in which the presence of patent branches was suggested to explain the failure of the FD strategy. <sup>11</sup> Clinically, this finding has consequences for situations where aneurysms and branches share an FSS, because the presence of efferent flow through the stented branch may maintain aneurysm patency.

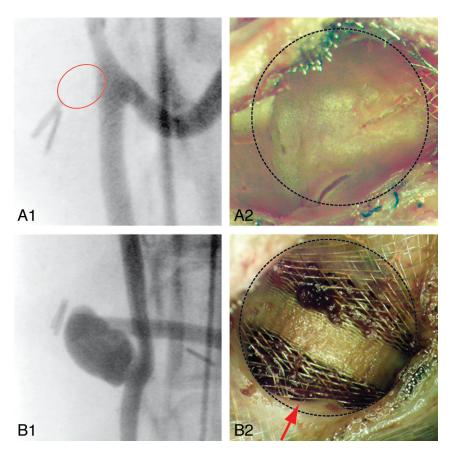


Fig 3. Three-month angiographic and pathologic comparison of flow diverter treatment with (A) lateral wall aneurysm and (B) lateral wall aneurysm with efferent branch flow from the aneurysm fundus. Note complete occlusion of aneurysm (A1) with full neointimal closure of the FSS (A2). When an arterial outflow is present, the aneurysm remains patent (B1) with incomplete neointimal closure or leaks (B2, arrow) in the FSS.

#### Stent and FD Porosities

A second important finding of this study is the relationship between porosity and success in aneurysmal closure. The characteristics of the FSS in terms of porosity and pore density determine the potency of the FD strategy. FFD studies support the notion that a less porous FSS (lower porosity, higher pore density devices) will have a more substantial effect on disrupting blood flow. One way that clinicians have increased a flow-disrupting strategy using high-porosity low-pore density stents is to use these in a multiple, overlapping fashion, thus increasing the amount of metal coverage of the aneurysm ostium with each sequential stent added. The potential effect of multiple conventional stents has not been studied experimentally in vivo, however.

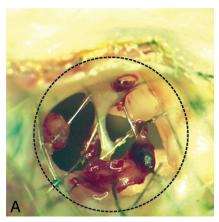
The porosity/pore density at which a conventional stent becomes a flow diverter has not been defined. This designation would admittedly be arbitrary, though perhaps a formal definition of a flow diverter, recognized by the community, could be established when a device is able to occlude a standard lateral wall aneurysm in a standardized animal model.

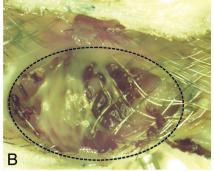
By conserving the same basic stent structure across groups, we were able to demonstrate that the key differentiating feature that permits the FD stent, but not a porous stent, to occlude the aneurysm is the decreased porosity and increased pore density of the flow-diverting stent (Fig 4). The use of an intermediate group, with double overlapping stents, suggests that the effect may be graded. It is important to remember that these results were obtained when FDs were in optimal condi-

tions to deflect flow (a lateral wall disposition) and to close the aneurysm ostium (the device can fully isolate the aneurysm neck from the parent vessel), as opposed to more demanding conditions, such as bifurcation aneurysms. Although the porosity and pore density of a stent can be studied and quantified on a bench top, the use of double overlapping stents creates uncertainty in terms of how the mesh of the individual stents will cover each other after deployment in vivo, with a range of possible metal porosity values for the final FSS. Perhaps more importantly, there are substantial differences between nominal porosities and actual effective porosities in vivo, once the stent or the FD adapts to local anatomy. The porosities listed in Table 2 represent the average porosity of the entire FSS in each case, as the FSS may undergo deformation after deployment, thus influencing final results. A porosity lower than 75% seems to suffice to obtain success, at least in the model studied. However, the FSS porosity required to occlude aneurysms while maintaining branch patency may depend on multiple factors, and a general rule, if it exists, remains unknown.

#### Neointima Formation on Aneurysm or Branch FSS

A third important result of this study is that there was consistently more neointima on the aneurysm FSS than on the branch FSS. While this is, in principle, reassuring, a large amount of neointimal tissue, sometimes mixed with less mature thrombotic material, did form at the ostia of branches covered by the stents or FDs. While all branches were patent,





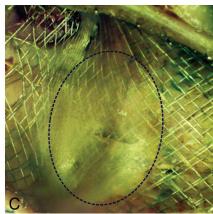


Fig 4. Comparison of pathologic outcomes after aneurysm treatment with (A) a single HP stent, (B) double overlapping HP stents, or (C) an FD stent, showing increasing neointima formation with decreasing porosity.

this finding ought to be a concern for clinicians, certainly given the known risk to jailed perforators.<sup>12</sup>

The model described here allows the translation of the differential effects exerted by the same device on aneurysm and branch patency rates into biologic differences at the level of the neointima forming over the aneurysm compared with the branch FSS. It may also prove useful to study the requirements for, and effects on, biologic processes of the antiplatelet medications that seem necessary for safe implantation. While we have not performed a systematic comparison, the occurrence of repeated carotid thrombosis with FD use (when animals were not treated with a double antiplatelet regimen) was a first for our laboratory. This may signal that FDs may be more thrombogenic than other types of intracranial stents.

#### Limitations of the Study

The present study introduces a new model that will necessitate standardization and validation. The number of animals studied is small. Confirmation by other laboratories would be welcome. FDs that were used are prototypes and results may not apply to clinically available devices. The aneurysms were surgical constructions and canine biology significantly differs from human biology. Extrapolation to human applications should always be prudent.

#### **Conclusions**

In this study, aneurysms were more likely than branches to become occluded after treatment with an FD. Aneurysm occlusion rates were correlated with metallic porosity and neointimal closure of the aneurysm FSS in this linear, lateral wall model.

#### References

- 1. Appanaboyina S, Mut F, Lohner R, et al. Computational modeling of blood flow in side arterial branches after stenting of intracranial aneurysms. *Int J Comut Fluid Dyn* 2008;22:669–76
- Benndorf G, Herbon U, Sollmann WP, et al. Treatment of a ruptured dissecting vertebral artery aneurysm with double stent placement: case report. AJNR Am J Neuroradiol 2001;22:1844–48
- Kamran M, Yarnold J, Grunwald IQ, et al. Assessment of angiographic outcomes after flow diversion treatment of intracranial aneurysms: a new grading schema. Neuroradiology 2011;53:501–08
- Kallmes DF, Ding YH, Dai D, et al. A new endoluminal, flow-disrupting device for treatment of saccular aneurysms. Stroke 2007;38:2346–52
- Kallmes DF, Ding YH, Dai D, et al. A second-generation, endoluminal, flowdisrupting device for treatment of saccular aneurysms. AJNR Am J Neuroradiol 2009;30:1153–58
- Naggara O, Darsaut TE, Salazkin I, et al. A new canine carotid artery bifurcation aneurysm model for the evaluation of neurovascular devices. AJNR Am J Neuroradiol 2010;31:967–71
- Lieber BB, Stancampiano AP, Wakhloo AK. Alteration of hemodynamics in aneurysm models by stenting: influence of stent porosity. Ann Biomed Eng 1997;25:460–69
- Ionita CN, Paciorek AM, Hoffmann KR, et al. Asymmetric vascular stent: feasibility study of a new low-porosity patch-containing stent. Stroke 2008;39:2105–13
- Ionita CN, Paciorek AM, Dohatcu A, et al. The asymmetric vascular stent: efficacy in a rabbit aneurysm model. Stroke 2009;40:959–65
- Lopes DK, Ringer AJ, Boulos AS, et al. Fate of branch arteries after intracranial stenting. Neurosurgery 2003;52:1275–78, discussion 1278–79
- 11. Darsaut TE, Bing F, Salazkin I, et al. **Testing flow diverters in giant fusiform** aneurysms: a new experimental model can show leaks responsible for failures. *AJNR Am J Neuroradiol* 2011;32:2175–79
- 12. Kulcsár Z, Ernemann U, Wetzel SG, et al. **High-profile flow diverter (Silk)** implantation in the basilar artery: efficacy in the treatment of aneurysms and the role of the perforators. *Stroke* 2010;41:1690–96