Flow Diversion of Giant Curved Sidewall and Bifurcation Experimental Aneurysms with Very-Low-Porosity Devices

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Key words
- Animal model
- Experimental aneurysm
- Flow diverter
- Giant aneurysm
- Stent deformation

Abbreviations and Acronyms
cSW: Curved sidewall
EwB: Endwall bifurcation
FDs: Flow diverters
FSS: Free segment of the stent

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OBJECTIVE: **Flow diverters (FDs) are increasingly used to treat difficult intracranial aneurysms. The objective of this study was to test whether treatment challenges posed by giant curved sidewall (cSW) and endwall bifurcation (EwB) aneurysms can be overcome with the use of very-low-porosity devices.**

METHODS: **Large and giant EwB (n = 12) and cSW aneurysms (n = 5) were constructed in 17 dogs. EwB aneurysms were treated with 48 (n = 4), 64 (n = 4), or two overlapping 64-wire low-porosity devices (n = 4), whereas all cSW aneurysms were treated with single 64-wire devices. Angiographic results were recorded immediately and at 12 weeks before euthanasia. Pathologic specimens were photographed and neointimal coverage of devices measured and scored.**

RESULTS: **By 12 weeks, 1 of 12 EwB and 1 of 5 cSW aneurysms were occluded. All other aneurysms were patent. Device-related arterial stenoses occurred in 13 of 17 animals, hemodynamically significant in two. All branches jailed by the FDs remained patent. There was a significant correlation between angiographic scores and the degree of neointima formation on the device (Rho = 0.527; $P = 0.04$). Failures of aneurysm occlusion could be explained by holes, sometimes barely visible, in the neointima that formed over FDs.**

CONCLUSION: **Low-porosity FDs fail to reliably occlude experimental giant EwB and cSW aneurysms.**

INTRODUCTION

Flow diverters (FDs) are increasingly used to treat large or giant aneurysms, and more recently, bifurcation aneurysms (2, 12). The optimal device porosity and pore density that will successfully occlude all aneurysms while sparing jailed branches, if it exists, remains unknown. Optimal FD characteristics may vary from one case to another, depending on aneurysm size, type, and flow patterns.

Previous studies in a modular carotid aneurysm model have shown that FDs made from 36 braided wires are capable of occluding straight lateral wall aneurysms but fail when implanted across curved sidewall or bifurcation aneurysms (4). Increasing the number of metallic filaments (from 36 to 48 and 64 wires), thus increasing pore density and decreasing pore size and porosity, or multiplying devices (2 × 64-wire FDs) in an overlapping fashion could, at least in theory, overcome the challenges posed by such difficult aneurysms. The present work explored devices of decreasing porosity and increasing pore density in the treatment of challenging giant curved sidewall (cSW) and endwall bifurcation (EwB) aneurysm models. Our hypotheses were that (1) decreasing FD porosity would lead to occlusion of cSW aneurysms and; (2) the EwB aneurysms could not successfully be occluded with FDs without jeopardizing the branch jailed by the device. Experimental results did not confirm our hypotheses: low porosity-flow diversion could not achieve reliable occlusion of these difficult aneurysms, no matter what device or combination of devices was used.

MATERIALS AND METHODS

In Vitro Studies

The 2 FDs that were used (48- and 64-wire braided devices) are stent-in-stent constructions made of an outer high-porosity stent (LVIS; Microvention Inc., Tustin, California, USA) and an inner low-porosity FD made of either 48 or 64 braided wires. FDs were placed into 3.5-mm diameter straight glass tubes, magnified, and photographed with an overlaid 1 × 1 mm² reference square. The square area occupied by the metal struts within the reference square was subtracted from the total square area to give the porosity. The pore density was the number of pores within the reference square. Six different portions of the device were photographed and mean values recorded. The same procedure was repeated with devices inserted in a 90-degree curved

glass tube with a radius of curvature of 10 mm. Curved devices were photographed orthogonal to the apex of the convex curvature.

The ends of the various FD or FD constructs were then placed in two silicone tubes of identical diameter, allowing the mid-portion of the stent to expand and react to manipulations, bent 90 degrees, and photographed, paying attention to the metallic density of the stent struts (Figure 1).

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- to 10-kg beagles under general anesthesia, as previously described (4, 11), with some modifications. To summarize, in 17 animals, the left external jugular vein was used to create a large or giant vein pouch aneurysm on the right carotid artery, using a side-to-side anastomosis (13) and the left carotid artery was divided and anastomosed to the right carotid artery, on the carotid wall opposite to the aneurysm ostium. In 12 animals, to form a bifurcation aneurysm, a clip was placed on the innominate artery proximal to the subclavian artery, to produce a "subclavian steal," effectively routing blood down as well as up the right common carotid artery, thus forming the two branches of a T-bifurcation. In five other animals, cSW aneurysms were formed in the same manner, except instead of clipping the innominate artery, the right carotid artery was occluded immediately proximal to the anastomosis. Two types of aneurysms were thus constructed: EwB and 90-degree cSW (Figure 2).

Endovascular Treatment

Four days before endovascular treatment, animals were premedicated with acetylsalicylic acid 81 mg daily, along with a loading dose of 150 mg of clopidogrel, followed by 37.5 mg daily. Endovascular treatment was performed 4–6 weeks after surgical construction of the aneurysm through a coaxial microcatheter system introduced by a percutaneous transfemoral approach. EwB aneurysms were treated with a single (n = 4) 48-wire device, a single (n = 4) or double overlapping (n = 4) 64 wire FDs, and all cSW aneurysms (n = 5) were treated with a single 64-wire FD, which were gifts from Microvention Inc. The nominal lengths of the devices ranged from 34 to 44 mm in a 3.5-mm vessel. Clopidogrel therapy was discontinued 10 days after stent implantation, whereas ASA 81 mg per day was continued until euthanasia.

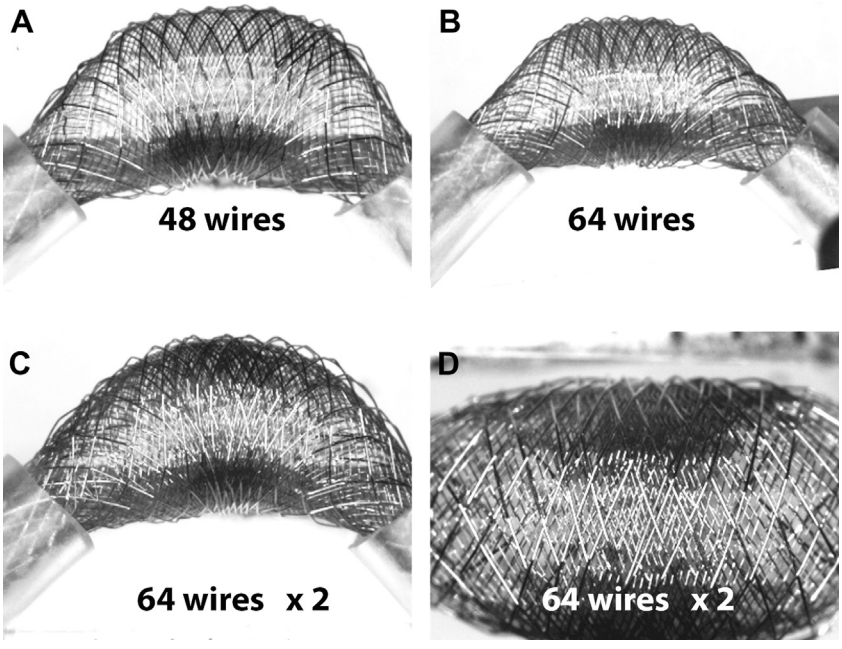

Figure 1. In vitro photographs of (**A**) 48-wire, (**B**) 64-wire, and (**C**) double overlapping 64-wire flow diverters. (**D**) Magnified view of double 64-wire device, showing the high metallic density of these constructs.

Angiography

Transfemoral angiography was performed in all animals immediately before and after FD deployment, at 2–4 weeks, and immediately before euthanasia at 3 months. To prevent femoral hematomas on dual antiplatelet therapy, all punctured femoral arteries were ligated. Angiographic results were scored by 2 experienced observers (T.D. and J.R.), who used a previously published system modified from Kamran et al. (8). A score of 0 indicated no change in the volume of the aneurysm after treatment, 1 indicated residual contrast filling more than 50% of the pretreatment aneurysm volume, 2 indicated residual contrast filling less than 50% of the pretreatment aneurysm volume, 3 indicated residual filling confined to the neck region, and 4 indicated no residual filling (complete occlusion). Angiographic scores were dichotomized into incomplete occlusion (scores 0, 1, 2) and complete or near-complete occlusion (scores 3, 4). The patency of arterial branches also was assessed, and stenoses, if present, were calculated using 1 − N/D, where N = diameter at most stenosed region, and D = diameter of the distal normal artery.

Euthanasia and Pathology

Euthanasia by barbiturate overdose was performed at 3 months. After fixation in 10% formalin, the carotid artery aneurysm construct was opened longitudinally. The "free" segment of the stent, or FSS (3), was photographed using a computerized imaging system (Vision PE, Clemex Technologies, Montreal, Canada). For each ex vivo aneurysm, we attempted to determine the amount of neointimal coverage of the device, which was calculated by taking 1 minus the surface area of the biological material divided by the total FD surface area. Selected samples of tissue coverage over areas of interest were