Asymmetric Vascular Stent
Feasibility Study of a New Low-Porosity Patch-Containing Stent
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Background and Purpose—Intracranial aneurysm (IA) treatment through hemodynamic modification with novel stent designs is a burgeoning area of research. We present a feasibility study for a new low-porosity patch-containing stent designed to treat intracranial aneurysms. The device is deployed so the patch covers the aneurysm neck ensuring strong flow diversion away from the aneurysm while keeping a low probability of occlusion of perforating vessels.

Methods—We created 17 side-wall aneurysms in 6 dogs, 2 per carotid artery if animal size permitted. Twelve proximal aneurysms were treated with AVSs: 5 distal aneurysms were untreated, serving as controls against self-thrombosis; 7 treated aneurysms were fully-covered; and 5 were partially-covered. After 4 weeks, a final angiogram was performed and aneurysms were explanted. Angiograms acquired pre- and posttreatment and at 4-week follow-up were analyzed quantitatively using normalized time-density curves (NTDC). Cone-beam micro-CT and histological specimen analysis were then performed.

Results—Posttreatment, NTDC average peaks dropped to 45% of initial values for the partially-covered aneurysms and 78% for the fully-covered aneurysms. Cone-beam micro-CT imaging performed at 4 weeks posttreatment showed partial thrombosis in 4 of 5 partially-covered aneurysms and complete thrombosis in all fully-covered aneurysms. Histology revealed neointimal coverage of all asymmetrical patch regions and thrombus formation in both fully- and partially-covered aneurysms. Four-week follow-up was not done for 1 animal (2 controls, 2 treated) that expired because of groin hemorrhage and for another animal (1 aneurysm) with an occluded carotid.

Conclusions—We demonstrate aneurysmal blood flow diversion using a new low-porosity patch-containing asymmetrical vascular stent in a canine side-wall aneurysm model. Overall results are encouraging and support continued AVS development. (Stroke. 2008;39:2105-2113.)

Key Words: aneurysm ■ stent ■ canine model ■ time-density curve
of a side-wall aneurysm and also indicated drastic decreases in aneurysm-dome wall shear stress and vorticity. The benefit of using an AVS (over a fully covered stent) is that the nonpatch area of the stent has a high porosity (>80%), ensuring a low probability of perforator blockage. A study by Lopes et al showed that stents with porosities between 79% and 77.4% maintained patent perforators after an average of 10 months. The effect of the low-porosity patch on perforators is as yet unknown.

To further AVS development, we report an in vivo feasibility study of AVS treatment.

Methods

Aneurysm Creation
All procedures were approved by the Institutional Animal Care and Use Committee. Side-wall aneurysms were created in beagles (11±1 kg; [9.5, 12] mean±STD; range: minimum, maximum) using previously described techniques. Briefly, the common carotid artery was isolated with 2 aneurysm clips, an arteriotomy was made using a vascular punch, an end-to-side anastomosis (7'0 monofilament) was performed with harvested external jugular, and the aneurysm dome was tied off using a Braunamid suture. If animals were large enough, 2 aneurysms were created per artery, separated by a 10 parent vessel diameter distance. Aneurysms were matured for 4 weeks before stenting. Proximal aneurysms were treated with the AVS; distal aneurysms served as controls. Dogs were given oral aspirin (8 mg/kg, daily) following aneurysm creation.

AVS Creation and Deployment
Fine stainless-steel mesh woven cloth of 500×500 wires per inch, with a wire diameter of 25 μm and 25% porosity, was cut using a microfocal NdYag laser (Equilasers) synchronized with a computer-controlled X-Y stage. We defined porosity as the fraction of the open surface area to the total surface (solid+opened).

To determine patch dimensions, intersections of different cylinders with diameters ranging 3 to 4 mm and a sphere (10-mm diameter) were considered. The center-of-the-sphere to center-of-the-cylinder distance was 9 mm. The intersection formed an ellipse. We created patches based on 4 ellipse sizes with the following diameters: 12×10, 11×9, 10×8, and 9×7 mm (intraprocedurally, stents with each of the 4 above-mentioned patch sizes would be available; and we would choose the appropriate stent on the basis of the measurements generated from procedural digital subtraction angiogram [DSA] runs). We then deposited 100-μm platinum markers at the patch extremities to aid x-ray guiding positioning. The patches were then microwelded to commercially available 3- or 4-mm diameter Penta coronary stents (Guidant Corporation [now Abbott]) of high-porosity (85%; Figure 1a). Stents were then positioned and cramped, using a manual stent crimper (Model SC-200, Machine Solutions), onto a balloon-tipped catheter (Guidant Corporation).

To verify adequate flexibility for in vivo use, we measured longitudinal stiffness using a 3-point bend test at room temperature. Stiffness was calculated as the slope of the force-displacement curve. Stent bending force was measured using a force sensor and software provided by Vernier Software Technology. System stiffness increased only 21±0.04% after the addition of a low-porosity patch.

The most challenging aspect of deployment was maximizing stent rotational alignment to ensure patch coverage of the aneurysm orifice (Figure 1b). Care is taken to choose the image intensifier orientation that best visualizes the aneurysm neck. This position is chosen using the 3D geometry rendering. Once the appropriate angles are set, we acquire a roadmap. Under roadmap guidance, alignment is performed by stent catheter rotation in extremely small increments. To maximize rotation ability, the inflation device should not be connected. Additionally, the guide wire is retracted or advanced to avoid interference of the platinum tip with the AVS markers. After each rotation, the catheter is moved slightly back and forth to remove stored catheter tension. Once the stent markers indicated alignment with the aneurysm orifice (Figure 1b: side view), the stent-delivery balloon is inflated. Figure 1c provides radiographic images illustrating this process in a fully-covered aneurysm. In the undeployed state, extremity markers are situated at the aneurysm orifice whereas the middle markers are near overlapping. After deployment, the markers are easily visible demonstrating adequate positioning.

During the stenting procedure, the animals were given a 50 U/kg bolus dose of heparin. Also of note, the procedural flushes contained 1 U/mL of heparin.

Angiography and Time-Density Curves
Angiographic analysis was performed using time-density curves (TDCs) measured before stenting (initial), poststenting (final),
The percent difference (PPD) between NTDC peaks before and after treatment:

\[
P_{\text{PPD}} = \frac{P_i - P_f}{P_i} \times 100
\]

where \(P_i\) is the initial (before stenting) peak NTDC value and \(P_f\) is the final (after stenting) peak NTDC value. The peak percentage difference (PPD) provides an indication of aneurysm inflow reduction. Additionally, we evaluated contrast residence time in the aneurysm dome. Slow contrast clearing or gravitation-induced pooling is correlated to slow flow in certain aneurysm regions. A 4-tiered scale was used to describe aneurysm contrast residence: (1) no residence (N), no contrast left in the aneurysm after the angiographic run; (2) brief residence (B), noticeable aneurysm contrast clearing within <1 minute; (3) pooling or settling (P), contrast material was trapped inside the aneurysm for >1 minute; and (4) no contrast (NC), no contrast material entering the aneurysm.

Initial and post-stenting NTDCs were compared quantitatively, because only in these 2 instances were the physical conditions of data acquisition almost identical, i.e., the animal in the same position and with the same gantry orientation and the guiding catheter in the same position. Follow-up angiograms were evaluated semiquantitatively because acquisition specifics could not be exactly reproduced. At 4 weeks of follow-up, a similar 4-tiered grading system was used to characterize aneurysm contrast flow: (1) patent (PA), contrast completely filled the aneurysm; (2) partial filling (PF), contrast filled only the remnant aneurysm; (3) faint blush (FB), barely visible cloudy contrast diffusion; and (4) no contrast (NC), no contrast observed.

**Macro-Evaluation of Samples Using Cone-Beam Micro-CT**

Cone-beam (CB) micro CT was used to study the morphology of the treated aneurysms after extraction. After the 4-week follow-up angiogram, animals were euthanized with sodium pentobarbital (100 mg/kg, intravenous) and pressure perfused with 10% neutral buffered formalin. The aneurysms were then explanted and subjected to CB micro-CT. The CB micro-CT system has a high-resolution detector with 43-μm pixels and a 12-μm x-ray focal spot and therefore provides high-resolution analysis without the mechanical distortion associated with histological preprocessing of the stented vessel. Specimens were perfused with a 50% contrast-saline mixture, and projections were taken every 1 degree. CT slices were reconstructed using a standard Feldkamp-filtered backprojection algorithm. The CT slice images were used to measure low-porosity patch coverage of the aneurysm orifice as well as aneurysm thrombus formation. For partially-covered aneurysms, a midpoint CT-slice, taken perpendicular to the artery axis, was used to calculate the percentage of aneurysm orifice covered.

**Histology**

After CB micro-CT, aneurysms were fixed in 10% neutral-buffered formalin for a minimum of 48 hours. Samples were then passed through an increasingly graded series of ethanol solutions (70% to 100%) and embedded in methyl-methacrylate plastic (Polysciences). Using a Reichert Jung Polycut E sledge microtome fitted with a tungsten-carbide knife (Leica Microsystems), sections ranging from 30 to 50 μm in thickness were taken from the aneurysm core, with the cutting plane perpendicular to the parent artery longitudinal axis, allowing sections to include the aneurysm and the parent artery. Sections were stained with Multiple Stain Solution (Polysciences) and analyzed under light microscopy for stent tissue coverage and aneurysm thrombosis.

**Results**

**Aneurysm Creation**

We created 17 aneurysms in 6 dogs; 12 underwent treatment with the asymmetrical stents and 5 were kept as controls. Aneurysm dimensions are provided in the Table. The vascular and aneurysmal dimensions were vessel diameter (3.68 ± 0.53 [2.88, 4.62] mm), aneurysm dome height (9.65 ± 2.19 [5.44, 12.90] mm), neck size (6.29 ± 1.54 [3.73, 10.03] mm), and dome-to-neck ratio (1.60 ± 0.50 [0.76, 2.70]). There were no significant differences in aneurysm morphology between the partial- and fully-covered cohorts (Table).
Stent Deployment/Procedural Results

Five of 12 aneurysms treated with AVSs were partially covered. The 7 remaining treated aneurysms showed full coverage of the aneurysm neck with the patch. All partially-covered aneurysms occurred in the beginning of the study. As the study advanced, our technique improved; and in the last 5 interventions, we had 100% success with stent placement.

One dog with 4 aneurysms (controls #1, #2, and fully-covered #13, #14) expired on postoperative day 1, after femoral hemorrhagic complications. For aneurysm #16, we were unable to acquire a follow-up angiogram because of parent vessel occlusion. Excluding the 1 nonneurological procedural mortality, no animals experienced neurological decline.

Angiographic Analysis Results

All treated aneurysms had initial, final, and follow-up angiographic analysis. Four of 7 fully-covered aneurysms underwent complete angiographic analysis (initial, final, and follow-up).

Figure 3 demonstrates example NTDCs for 3 cases. The first is an untreated aneurysm; the second is a partially-covered aneurysm demonstrating residual filling with contrast at 4 weeks of follow-up; and the third is a fully-covered aneurysm, also showing complete occlusion at follow-up. NTDCs were evaluated by looking at peak-values before and after treatment and their ratios. The peak-values of these curves reflect aneurysm flow conditions and therefore AVS treatment effects. Distal untreated aneurysms demonstrated no significant changes in curve parameters before and after proximal aneurysms treatment (Table). The PPD were as follows: (0.4 ± 3.20%; [−4, 17]) for control aneurysms, (45 ± 24.95% [20, 81]) for partially-covered aneurysms, and (78 ± 21% [42, 100]) for fully-covered aneurysms. The differences between cohorts’ PPD were highly statistically significant (Figure 3, bottom). Before intervention, all aneurysms demonstrated a qualitative grade of no residence. After intervention, controls demonstrated no residence, partially-covered aneurysms demonstrated brief residence (4/5) and pooling (1/5), and fully-covered aneurysms demonstrated pooling (5/7) and no contrast observed (2/7).

At the 4-week follow up, only controls were qualitatively graded as patent. Four partially-covered aneurysms were graded partial filling and one, #8, as a faint blush. Two fully-covered aneurysms, #14 and #17, were graded as no contrast, and two, #11 and #12, were graded as faint blushing. One fully-covered aneurysm, #16, suffered parent vessel occlusion at the 4-week follow up.

CB Micro-CT Scanning Results

CB micro-CT was used to evaluate stent placement relative to aneurysm neck, as well as thrombus formation. Midpoint CT slices (fully-covered, partially-covered, and an untreated aneurysm) are shown in Figure 4. In control aneurysms, CT scans demonstrated patent aneurysm domes, with no indica-

### Table. Summary of Aneurysm Geometry and Flow Results

<table>
<thead>
<tr>
<th>Stent Placement</th>
<th>Geometry Results</th>
<th>Flow Results</th>
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<tbody>
<tr>
<td></td>
<td>Vessel (mm)</td>
<td>Dome (mm)</td>
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<tr>
<td>Controls</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3.42±0.41</td>
<td>9.98±2.91</td>
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<tr>
<td>2</td>
<td>2.1±1.9</td>
<td>6.7±6.7</td>
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<td>3</td>
<td>6.5±5.6</td>
<td>2.5±7.04</td>
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<tr>
<td>4</td>
<td>3.90±0.30</td>
<td>9.37±2.5</td>
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<tr>
<td>5</td>
<td>3.90±0.30</td>
<td>9.37±2.5</td>
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<tr>
<td>Partial coverage</td>
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<tr>
<td>6</td>
<td>3.90±0.30</td>
<td>9.37±2.5</td>
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<tr>
<td>7</td>
<td>12.6±3.76</td>
<td>6.1±100</td>
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<tr>
<td>8</td>
<td>2.1±0.8</td>
<td>4.1±2.4</td>
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<td>9</td>
<td>8.4±1.6</td>
<td>5.1±1.00</td>
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<td>10</td>
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<td>Full coverage</td>
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<td>11</td>
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<tr>
<td>12</td>
<td>12.6±3.76</td>
<td>6.1±100</td>
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<tr>
<td>13</td>
<td>2.1±0.8</td>
<td>4.1±2.4</td>
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<tr>
<td>14</td>
<td>8.4±1.6</td>
<td>5.1±1.00</td>
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<td>16</td>
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<tr>
<td>Average values</td>
<td>3.68±0.53</td>
<td>9.65±2.19</td>
</tr>
</tbody>
</table>

*Aneurysms 1, 2, 13, and 14 were created in the dog lost because of internal femoral bleeding.
†Aneurysm 16: the vessel was occluded at follow-up.
P<sub>i</sub> is the initial peak-value of the NTDC before treatment, P<sub>f</sub> is the final peak-value after treatment, and PPD is the percent difference between the 2 values (equation 6). Contr. Res. indicates contrast residual; N, none; B, brief; P, pooling; NC, no contrast; PA, patent aneurysm; PF, partial filling FB, faint blush; N/A, not applicable.
tion of thrombosis. Four partially covered aneurysms, #6, #7, #8, and #10, had 35% to 50% aneurysm orifice coverage. More than 70% of the aneurysm orifice was covered in the remaining partially-covered aneurysm, #9. In the fully-covered aneurysms, no contrast was seen entering the aneurysm dome, despite the faint blush observed in 2 aneurysms’ angiograms. Vessel lumens were patent in 4 of the 5 fully-covered aneurysms without indication of hyperplasia.

Figure 3. NTDCs shown for the 3 result categories, from top to bottom: control aneurysm; partially-covered aneurysm; and fully-covered aneurysm. Image from left to right are for the 3 angiograms: initial (immediately pretreatment), final (immediately posttreatment, except for the control), follow-up (4 weeks posttreatment). These frames are snapshots acquired just after the contrast bolus arrived at the aneurysm location. The histogram at the bottom gives results of the peak percent difference (PPD) obtained after treatment of the proximal aneurysms with AVS for all 3 cases: control (untreated), partially-covered, and fully-covered.
Histology Results

Representative photomicrographs for the 3 aneurysm categories are shown in Figure 5. In case #11 (upper left), the aneurysm orifice is fully-covered; in case #10 (lower left), partially-covered; and in case #5 (upper right), a control is shown. Both the fully- and partially-covered aneurysms (#5, #10) show new tissue growth surrounding the stent struts and asymmetrical patch. Smooth muscle cells and collagen extend from the patch region into the aneurysm, forming moderately organized connective tissue. Progressing from the patch toward the vessel lumen, smooth muscle cells are depositing extracellular matrix to create a new intimal layer (black arrows in magnified views). In the fully-covered aneurysm, this new tissue seals the entire aneurysm neck and the dome is filled with unorganized and organized thrombus. The spaces are likely a result of shrinkage of thrombus during the dehydration steps of processing. New tissue growth in the partially-covered specimen is located in the area behind the patch (black arrow in case #10 in Figure 5). Untreated aneurysms show no new tissue growth at the aneurysm neck and no thrombus in the dome, confirming the cone beam–micro-CT results.

Discussion

Aneurysm geometry demonstrated no statistically significant differences between control, partially-covered, and fully-covered groups.

DSA analysis using NTDCs demonstrates a radical reduction in aneurysm contrast flow, which is unmatched in previous reports of stent-treated aneurysms. These results suggest that an aneurysm orifice must be ≥70% covered with a ≤25% porosity material to achieve aneurysm thrombosis and endothelialization within 4 weeks. Of note, we did not include aneurysms treated with standard stent designs, as different groups have extensively evaluated such stents. For instance, measurements by...
Sadasivan et al demonstrated a reduction in TDC peak of approximately 13%.

To compensate for variable experimental conditions, such as contrast dilution and rate of contrast injected, tissue attenuation, and x-ray imaging parameters, we normalized TDCs to the total amount of injected contrast. The total amount injected was found using an image-based technique. We found extreme variations of up to 3 orders of magnitude in the absolute value of the normalization constant. Despite these variations, the initial NTDC peaks data for all 17 aneurysms remained in the smaller range from 0.8 to 12.6% (Table). This is secondary to the side-wall geometry of the aneurysms, where aneurysm flow is shear, rather than inertially driven and is therefore lower than comparably-sized aneurysms on curved vessels. Further evaluation of AVS treatment of aneurysms in curved vessels and at bifurcations is needed.

In fully-covered aneurysms, very little contrast material was observed entering aneurysm. In cases #14 and #17, no contrast was visualized in the aneurysm; whereas in the 5 other fully-covered aneurysms, contrast flow was extremely limited. The NTDC peaks were between 42% and 81% less than before stenting. After contrast entered the aneurysm, the flow could be described as a slow cloudy diffusion (faint blush), followed by very long pooling (lasting indefinitely—beyond the time constraints of the procedure). This slow clearance is indicative of exceedingly low flow. Under these conditions, gravitational forces became dominant, causing the heavier contrast material to settle in the aneurysm. This process, referred to as “pooling” or “settling,” is an indication of successful flow diversion from the aneurysm.

For partially covered aneurysms, the maximum PPD ranged between a minimum 20% and maximum 81%. In 4 of 5 cases, contrast clearance was relatively brisk, suggesting that the aneurysmal flow was still strong. In 1 partially-covered aneurysm with 70% orifice coverage, there was a marked increase in contrast residence.

On histological examination, all aneurysms with >40% reduction in PPD and demonstration of contrast pooling, were entirely thrombosed. In contrast, those partially covered aneurysms with contrast reduction but without pooling did not fully thrombose. The rapid clearance of contrast in the uncovered portions of those aneurysms (#6, #7, #9, and #10) indicated significant blood flow, which obviated full thromboses. At 4-week follow-up, all 4 nonpooling partially-covered aneurysms were partially thrombosed, whereas the one partially-covered aneurysm, #8, which demonstrated pooling completely thrombosed. Of note, although all covered aneurysms were fully thrombosed, in one case, #16, the parent vessel was occluded as well. Interestingly, intraprocedural angiography demonstrated severe vasospasm pre- and posttreatment in this vessel. To comply with the approved study protocol, we did not use vasospasm-treating medications. With adequate vasospasm treatment, it is possible that this complication may have been avoided.

The most challenging aspect of stent deployment is appropriate alignment with the aneurysm neck. Longitudinal patch localization (along the axis of the artery) provided no difficulty, as we could identify the patch position at all times; but rotational patch alignment was tedious at times. Importantly, this improved dramatically with experience. We initially experienced unanticipated technical difficulties in rotational stent alignment secondary to balloon inflation (only 2 of 6 early stents with complete coverage). Typically, a deployment balloon is folded in 3 flaps before crimping the stent. As the balloon inflates, the flaps unfold causing stent rotation. We therefore began minimizing balloon folding as much as possible; and in the second half of the study, we achieved almost complete success in correct stent deployment (5 of 6 stents with complete coverage). It is likely that future accuracy improvements can be achieved should self-expanding materials replace the balloon-expandable design. The fate of associated perforators could not be evaluated using this model, and this is an important reason why further animal work is necessary. Nonetheless, a potential benefit of using an AVS (versus a fully-covered stent) is that the nonpatch area of the stent has a high porosity (≈80%), ensuring a low probability of perforator blockage. In the study performed by Lopes et al, 77.4% to 79% porosity stents maintained patent perforators after an average of 10 months. The effect of the low-porosity patch on perforators is as yet unknown, but it is our hope that future work will better define this potential risk of AVS utilization.

We present a rigorous quantitative, as well as qualitative, analysis of a new endoluminal flow-diverting technique using an asymmetrical-design stent containing a low-porosity patch. We demonstrate significant flow alteration in 100% of treated aneurysms, with 67% achieving complete or near-complete flow arrest. This was accomplished with no occurrences of clinically relevant stroke and 1 nondevice-specific death (fatal groin hemorrhage). Additionally, there was a substantial learning curve that, once surmounted, would likely result in significantly better occlusion rates given further investigation. Even so, these data compare favorably to recent literature examining the treatment of experimental aneurysms with an endoluminal flow-disrupting device.

Concern may exist for the delayed nature of thromboses in AVS-treated aneurysms when dealing with subarachnoid hemorrhage (SAH) patients. As short-term rehemorrhage is a significant concern in this population, the AVS may not be the ideal therapy for these patients, particularly given the need for antiplatelet therapy. However, the AVS may greatly improve complete obliteration rates when stent assistance is used for primary coiling. Additionally, computational fluid dynamics calculations and particle image velocimetry done in phantoms indicate an immediate reduction in dome shear stress and dynamic pressure (2 orders of magnitude) with AVS placement. These changes may, in themselves, suffice to prevent rehemorrhage—although such postulation is, as of yet, purely speculative. These facts may support the usage of the AVS even in SAH; however, further in vivo evaluation is certainly needed.

Although these results are exciting, they are only preliminary investigations into this treatment modality. Our low-porosity patch resulted in a 20% increase in stent longitudinal stiffness. We envision the eventual use of more flexible materials in clinical cases where geometry could be far more complicated. Additionally, as discussed above, stent deploy-
ment can also be greatly improved. Furthermore, improvements in AVS distal rotational alignment may be achievable by indirect means such as magnetic catheter steering. It should also be noted that this study uses a relatively simple canine lateral aneurysm model. This model was chosen because of the size and navigable vessel geometry of the animal. Concerns included the need for a femoral vessel of sufficient size to accommodate a 7-French introducer sheath as well as the probable learning curve associated with any new technology (as shown in our results). However, on the basis of the observations and experience gained from this study, we are improving our methods of stent preparation and delivery to a point that we can use a 5- or 6-French introducer sheath and are beginning to generate preliminary data in a rabbit elastase aneurysm model.

Efforts will also need to be made to translate these successes to application for terminal or bifurcation aneurysms, which may require Y-stenting techniques; however, these data overall provide substantial proof of the concept and strongly encourage future endeavors in the development of asymmetrical stent technologies.

Conclusions

In this feasibility study, we showed the initial results of treatment of IAs in a canine aneurysm model with a new AVS. Our in vivo results, in conjunction with current state-of-the-art x-ray imaging resolution and catheter development, indicate that such an approach is possible in the near future. The current design is appropriate for lateral aneurysms, and work is in progress to extend the applicability to a larger variety of aneurysm geometries, such as bifurcation aneurysms. Further studies in more representative vessel morphologies, such as the rabbit elastase model, are in progress, and initial results have been already presented. It appears probable that the AVS may become a valued tool in the aneurysm treatment armamentarium.

Appendix

Calculations and quantities used to derive the NTDC for the aneurysms are indicated in Figure 2. We first calculated the total amount of contrast material entering the aneurysm ROI by integrating over the entire ROI as a function of time, t, for each frame,

\[
NTDC(t) = \frac{\int \int \left( Bckg - PI_{ROI} \right) dL}{N} \times 100
\]

where \( PI_{ROI} \) represents the individual pixel intensity, \( Bckg \) is the average background value, and the double integral indicates summation of all the pixels contained in the ROI area.

The normalization constant, \( N \), will be equal with the total mass of material passing through a vessel cross-section integrated over the entire run, multiplied with the velocity:

\[
N = V_{bolus} \int_0^T \left( \int_{L_{scan}} \left( Bckg - PI_{scan} \right) dL \right) dT
\]

For each frame, we numerically integrated along the line \( L_{scan} \) in Figure 2, the difference between the background and the individual pixels \( PI_{scan} \) to obtain the contrast passing thought the vessel, and we also integrate over time (entire sequence).

\[ V_{bolus} \] is the velocity of the bolus which is obtained by dividing the vessel path-length, \( \Delta D \), between locations \( L_1 \) and \( L_2 \), by the transit time, \( T_{transit} \), of the bolus between the 2 points indicated in Figure 2 using a bolus-peak tracking method.\(^{(4)}\)

\[
V_{bolus} = \frac{\Delta D}{T_{transit}}
\]

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We thank Hussain Rangwala for the schematics of the stent displayed in Figure 1a and the results of the 3-point stiffness check and Peter Bush for expertise and equipment used in the histology evaluations.

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