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Combined Use of Stents and Coils to Treat Experimental Wide-Necked Carotid Aneurysms: Preliminary Results

Istvan Szikora, Lee R. Guterman, Kristin M. Wells, and L. N. Hopkins

PURPOSE: To develop a new technique to treat wide-necked side-wall aneurysms, combining the implantation of intraarterial stents with the endosaccular placement of coils. **METHODS:** Bilateral side-wall aneurysms were surgically created on the carotid arteries of four dogs. In each animal, Guglielmi detachable coils were introduced into one of the aneurysms after implantation of a balloon-expandable Strecker stent within the parent artery, adjacent to the aneurysm orifice. The contralateral aneurysms were treated with coils alone. **RESULTS:** In two dogs, one of the stented and both nonstented aneurysms remained partially open for 4 weeks after subtotal packing with coils. In another two dogs, tight aneurysm packing with coils resulted in complete occlusion of all four aneurysms. Bulging of the coil mass resulted in 30% to 75% narrowing of the nonstented parent arteries. At 4 and 5 weeks, significant stenosis resulting from reactive hyperplasia was observed in all stented carotid arteries. **CONCLUSION:** Based on these preliminary results, we conclude that Guglielmi detachable coils can be introduced into an aneurysm cavity through Strecker stents. The stents allow tighter packing of wide-necked aneurysms by preventing coils from migrating or bulging into the parent arteries.

Index terms: Aneurysm, intracranial; Aneurysm, embolization; Aneurysm, therapeutic blockade; Interventional instrumentation, coils; Interventional instrumentation, stents; Interventional neuro-radiology, experimental; Animal studies

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Surgical clipping of giant intracranial aneurysms is technically difficult and carries a relatively high risk. The endovascular approach has gained wide acceptance as a treatment alternative for surgically inaccessible cases. However, wide-necked giant aneurysms are a challenge even for endovascular methods.

Conventional techniques attempt to exclude the aneurysm from the intracranial circulation by filling the sac with different thrombogenic devices. Since Serbinenko's first publication (1), a number of patients have been treated by endosaccular occlusion with different detachable balloons (2-4). Complete occlusion of giant aneurysms is difficult; recurrence has been reported after partial treatment (4). The most recent advance, Guglielmi detachable coils (Target Therapeutics, Fremont, Calif), permits placement and retrieval of long platinum coils into and out of the aneurysm cavity (5, 6). The Guglielmi detachable-coil system has proved less successful for the treatment of wide-necked aneurysms (7) because of resultant migration or bulging of coils into the parent artery through the large orifice of the aneurysm. Direct sacrifice of the parent artery by detachable balloon occlusion frequently remains the treatment of choice for aneurysms of the internal carotid artery.

The placement of stents (cylinders constructed of fine wire mesh) across the orifice of an aneurysm, a novel approach, attempts to restore lam-

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inar flow to the lumen of the parent artery while excluding the entry of blood into the aneurysmal cavity. Although several laboratories have reported good results in animals when treating experimental aneurysms with tantalum stents, previous experiments performed in our laboratory indicate that tantalum stents do not provide angiographic obliteration of experimental wide-necked aneurysms: four of seven aneurysms thrombosed partially and one thrombosed completely (Guterman LR, Szikora I, Wells KM, Hopkins LN, Treatment of Lateral Wall Vein Graft Aneurysms with Stents and Stents with Coils in Canines, presented at the 43rd Annual Meeting of the Congress of Neurological Surgeons, Vancouver, British Columbia, Canada, 1993). To develop a method to treat giant aneurysms with large orifices, we combined intraarterial implantation of tantalum stents and endosaccular packing with electrically detachable platinum coils.

Methods

Aneurysm Creation

Bilateral side-wall vein-graft aneurysms were created in four mongrel dogs following a technique first described by German and Black (8), under a protocol approved by our institution's Animal Care Committee. All procedures were performed under sterile conditions and with general anesthesia. The common carotid arteries were exposed on both sides of the neck. A 5-mm arteriotomy was performed with a number 11 blade. A 5-mm vascular punch was used to enlarge the arteriotomy. A 7-mm portion of a previously removed segment of the external jugular vein was sewn to the arteriotomy using 7-0 prolene suture. The distal end of the vein graft was closed with 7-0 prolene suture.

Aneurysm patency was confirmed 3 weeks after surgery by transfemoral digital subtraction angiography (Fig 1) using an OEC-Diasonics Series 9000 C-arm image intensifier with a neurovascular software supplement (OEC-Diasonics, Salt Lake City, Utah). The aneurysms were treated from 26 to 126 days after the surgical procedure. No spontaneous aneurysm thrombosis was observed during this follow-up period; therefore, we did not use an untreated aneurysm as an internal control. The shortest and longest diameters of the aneurysms were measured in two views by digital subtraction angiography. An angioplasty balloon catheter was placed within the parent artery adjacent to one of the aneurysms in each animal as described below. The length of the balloon, indicated by radiopaque markers, was measured in the same views either by fluoroscopy or on road-map angiograms. The magnification factor was then calculated while comparing this measurement with the real length of the balloon. Aneurysm volumes were calculated as prolate spheroids, using the appropriate geometric formula ($V = 4/3 \pi \times A/2 \times B/2 \times C/2$, where A,

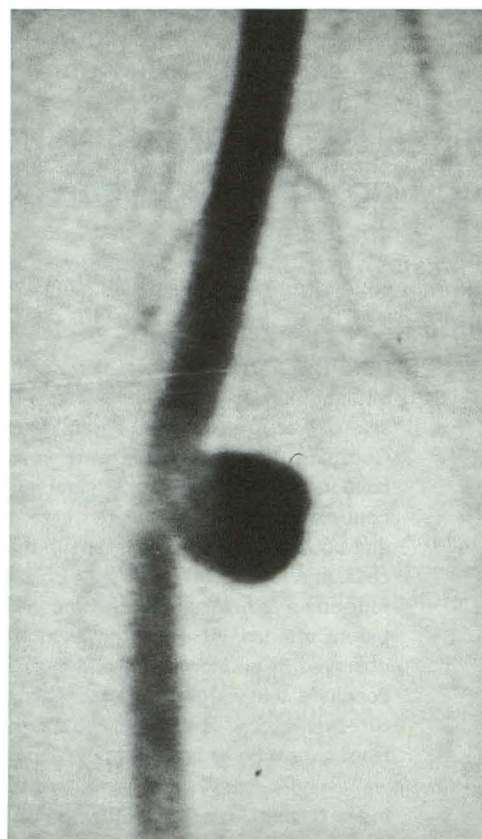


Fig. 1. Digital subtraction angiography 120 days after surgery shows a patent giant aneurysm.

B, and C are the largest diameters of the aneurysms in three orthogonal planes).

Stent Implantation

One aneurysm in each animal was treated by placing a balloon-expandable tantalum stent (Strecker stent, Medi-Tech, Watertown, Mass) within the parent artery, adjacent to the aneurysm orifice. In one dog, a coronary Strecker stent, measuring 4.5 mm in diameter and 25 mm in length (ie, 4.5/25 mm), constructed from 0.07-mm tantalum wire, was used. The stent was mounted on a 3.2-F, 6-atm maximum-inflation pressure angioplasty balloon catheter (Medi-Tech). This procedure was performed without systemic heparinization, and the dog was followed up for 1 month before further treatment.

In the remaining three dogs, 5/33-mm, 0.1-mm wire, peripheral Strecker stents were used with a 5-F, 6- or 12-atm maximum-inflation pressure angioplasty balloon catheter as a delivery system (Fig 2). Stent implantation was followed by endosaccular coil placement 1 hour later. These three animals received intravenous injection of 1000 U of heparin before placement of the stent delivery catheter to avoid thrombotic complications during the lengthy intra-arterial manipulation.

To study the flow dynamics within the aneurysm cavity before and after stent implantation, a Tracker-18 micro-

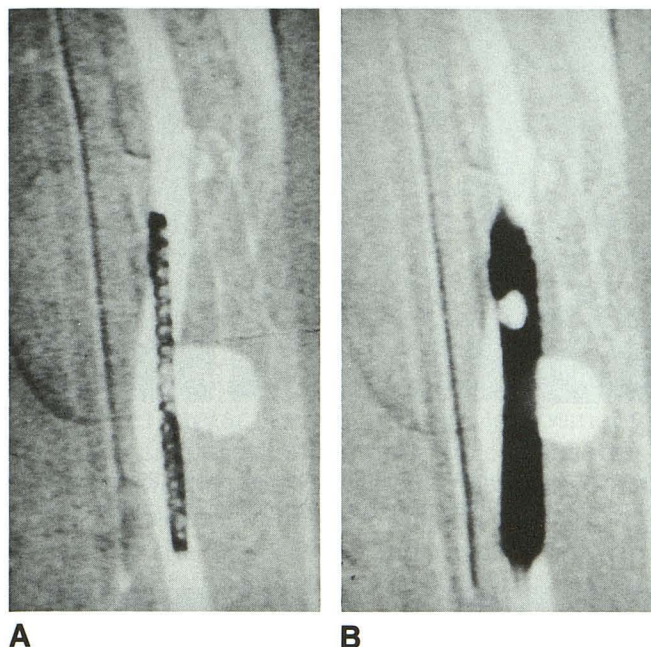


Fig. 2. A, Digital subtraction road-map angiography, lateral view. A 5/33-mm peripheral Strecker stent (Medi-Tech) is placed adjacent to the orifice of the aneurysm.

B, The stent is expanded by inflation (12 atm) of the angioplasty balloon.

catheter (Target Therapeutics) was advanced into the aneurysmal sac, and contrast material was injected into the inflow and outflow tract and within the dome of the aneurysm (Figs 3A and 3B). This study was performed before stenting, as well as 2 weeks and 1 month after stenting in one animal (Figs 3C and 3D) and 1 hour after stent implantation in the remaining subjects. Placement of the Tracker catheter through the mesh of the stent was relatively easy in each case and involved introducing a Taper-16 or Seeker-16 guide wire (Target Therapeutics) into the aneurysm cavity and easing the catheter over the wire.

Coil Packing

After the patency of the stented aneurysms was confirmed by digital subtraction angiography, Guglielmi detachable coils were delivered through the stent into the aneurysm cavity with a Tracker-18 Guglielmi detachable coil microcatheter (Fig 4A). During the same session, the contralateral aneurysms were treated with coils alone. The animals were divided into two groups. In two animals (group A), attempts were made to occlude the aneurysm cavities with Guglielmi detachable coils without compromising the lumen of the parent arteries on both sides (Fig 4B). In two animals (group B), Guglielmi detachable coils were placed into the aneurysm cavities as tightly as possible—regardless of the hemodynamic consequences. Coil placement continued until the aneurysm cavities no longer could accommodate coil mass (Fig 4C).

After the procedure, anticoagulation was reversed with 10 mg of intravenous protamine sulfate in the three animals

receiving intravenous heparin before treatment. One animal in group B was killed in 6 hours to serve as a pathologic control. The other three subjects were followed up with digital subtraction angiography for 4 to 5 weeks and then killed.

Specimen Preparation

The common carotid arteries were removed and fixed in 10% phosphate-buffered formaldehyde (Fisher Scientific, Fair Lawn, NJ). The stented carotid arteries were opened longitudinally along the walls opposite the aneurysm orifices. Gross pathologic examination of the portions of the carotid arteries covered by the stents was done. The stents were carefully removed using a surgical dissecting microscope. Special care was taken to save all tissue covering the inner surfaces of the stents. The diameters of the aneurysm orifices were measured, and the areas of the orifices were determined by the appropriate formula for a circle or an ellipse ($r^2 \times \pi$ or $A/2 \times B/2 \times \pi$). The tissue layers covering the stents were removed from the struts of the stents and sectioned perpendicular to the main axes of the arteries.

Using microscissors, an approximately 3-mm-thick horizontal cross-sectional slice was made across the body of each aneurysm and the portion of the carotid artery adjacent to the orifice. Under microscopy, pieces of the coils were carefully removed from the mass of thrombus. The nonstented aneurysms were prepared similarly but without opening the carotid arteries.

Cross-sectional cuts of the portions of the stented arteries proximal to the stents and of the segments covered by the stents were also made. The nonstented carotid arteries were sectioned proximal to the aneurysms.

All sections were embedded in paraffin and stained with hematoxylin and eosin.

Results

Postsurgical Follow-Up

Digital subtraction angiography obtained immediately before endovascular treatment displayed bilateral, large, patent aneurysms in all animals. Aneurysm volumes varied between 132 and 485 mm³, as determined by digital subtraction angiography. We attribute the differences in aneurysm volume to the surgical technique and to variations in venous anatomy of dogs. Although the lengths of the vein pouches were identical in all cases (7 mm), the diameters of the external jugular veins varied considerably among the animals. Measurements of aneurysm orifices were obtained from the best available projection on digital subtraction angiography. The longitudinal diameters of the orifices ranged from 5 to 6 mm. This was consistent with the surgical tech-

Fig. 3. Characteristic flow pattern within the aneurysm cavity.

A and B, Digital subtraction angiography, lateral view, before treatment (animal 1, group A). A Tracker-18 Guglielmi detachable-coil microcatheter is advanced into the aneurysm cavity (*arrowhead*, microcatheter tip). A, Contrast material injection demonstrates inflow tract (*arrow*) within the distal aspect of the aneurysm and vortex flow within the center of the aneurysm cavity (*small arrow*). B, Microcatheter tip (*arrowhead*) positioned into the dome of the aneurysm. The outflow zone (*arrow*) is visualized.

C and D, Digital subtraction angiography 2 weeks after stent placement (animal 1, group A). C, Microcatheter tip is advanced into the distal aspect of the orifice (*arrowhead*) through the mesh of the stent (*small arrows*). Contrast injection shows the inflow zone (*arrow*) and vortex flow. D, Microcatheter tip is placed within the proximal portion of the aneurysm (*arrowhead*). The outflow tract is well visualized (*long arrow*). The mesh of the stent is indicated by a *small arrow*.

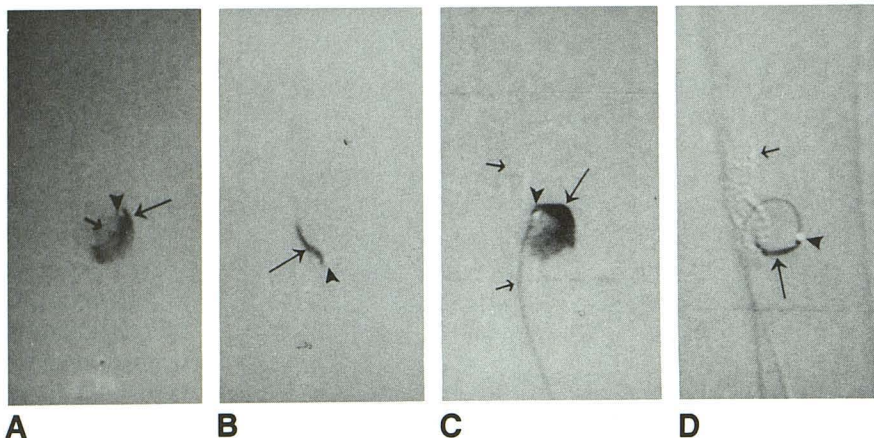
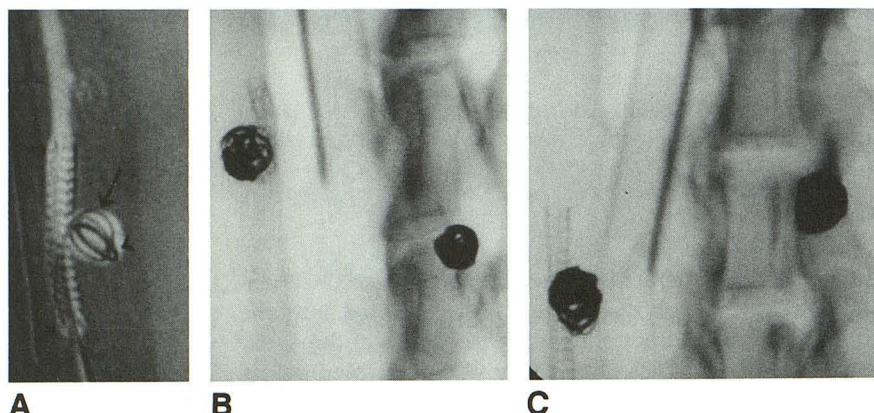


Fig. 4. Aneurysm packing with Guglielmi detachable coils.

A, Digital subtraction road-map angiography demonstrates a 5/33-mm stent adjacent to the orifice of the aneurysm (*small arrows*) and a Tracker-18 Guglielmi detachable-coil microcatheter advanced into the aneurysm cavity (*arrowhead*, catheter tip). A Guglielmi detachable coil (8 mm in diameter, 40 cm in length) is being delivered into the lumen of the aneurysm (*arrow*).

B and C, Plain x-ray film of the neck after treatment displays subtotal packing of the aneurysms with platinum coils on both sides (B) and tight packing bilaterally (C).



nique, in which a 5-mm vascular punch was used for arteriotomy.

Stent Implantation

In the first animal, treated by a 0.07-mm wire coronary stent without heparinization, approximately one third of the aneurysm lumen was angiographically obliterated immediately after stent placement (Figs 5A and 5B). Five minutes after stent placement, the angiographic appearance of the aneurysm had returned to normal. One week later, digital subtraction angiography revealed an aneurysm cavity identical to the pre-treatment image (Fig 5C). Angiographic evaluation of flow in the aneurysm cavity at 2 weeks and 4 weeks after treatment revealed a characteristic inflow and outflow tract (Figs 3C and 3D). In one animal, treated by a 0.1-mm wire peripheral stent after systemic heparinization, slow flow and irregular filling of the aneurysm were observed immediately after stenting. No changes of

the aneurysm fillings were observed in the remaining two dogs after stent treatment (Figs 6A and 6B).

Coil Packing

In group A, subtotal aneurysm packing with coils resulted in approximately 90% angiographic occlusion of both nonstented aneurysms and one stented aneurysm (Table 1). The second stented aneurysm was completely obliterated. Residual filling was observed either in a neck remnant or within the aneurysm dome (Figs 7A and 7B). Repeat angiography was performed at 2 and 4 weeks. There were no changes in the angiographic appearance of the coiled or stented and coiled aneurysms. No evidence of coil remodeling or migration was seen. The coil masses did not bulge into the lumens of the parent vessels on either the stented or the nonstented sides. One month after treatment, angiography revealed a hemodynamically insignificant narrowing of the

stented portion of the carotid arteries, reducing the lumen by approximately 35% (Figs 7C and 7D).

In group B, angiography performed immediately after treatment displayed 100% occlusion of both coiled and stented and coiled aneurysms in both animals (Table 2). On the stented sides, coils were not evident within the lumens of the parent vessels. The coil masses had not bulged through the orifices into the lumina of the parent vessels (Fig 8A). In the nonstented aneurysms, angiography obtained after reversal of heparinization with protamine sulfate revealed hemodynamically significant stenosis of the carotid arteries, resulting in slow flow in the distal carotids. The coil masses were seen bulging through the orifices of the aneurysms and resulted in 75% narrowing of the lumens of the carotid arteries adjacent to the aneurysms (Fig 8B). After 4 weeks, the aneurysms remained completely obliterated in one dog. On the stent and coil side, hemodynamically insignificant stenosis narrowed the stented portion of the lumen of the parent artery by 35% to 40% as determined using digital subtraction angiography images in two orthogonal views (Fig 8C). The coil mass in the nonstented aneurysm still bulged into the lumen of the vessel, but normal flow had been restored in the parent artery (Fig 8D). Residual coil was not observed in the lumen of the vessel. In the second dog in this group, the coil mass on the nonstented side bulged through the orifice of the aneurysm, effecting a 50% compromise in the parent vessel lumen. Through this vessel, the rate of flow was unchanged. This animal was killed 6 hours after placement of the stent and coils.

Pathology

After removing stents from the common carotid arteries, the diameters of the ostia of the aneurysms were measured and found to range between 6 and 8 mm. The areas of the ostia were calculated and varied from 28.27 to 37.69 mm². A dense fibrous proliferation was observed covering the inner surfaces of the stents in all but the one animal killed early. The thickness of this smooth tissue layer inside the stent was relatively uniform and varied between 0.3 and 0.5 mm. Because of the preparation technique, in which the carotid arteries were opened longitudinally, we could not measure the true luminal diameters of the parent arteries adjacent to the aneurysms. However, we do not believe that these measurements would provide an accurate estimation of the stenosis, which resulted either from fibrous proliferation or from bulging of the coil mass, because shrinking during fixation probably affects the stented and nonstented portions of the vessel differently.

Cross-sections of the aneurysms displayed coils embedded in masses of thrombus. In all subtotally occluded aneurysm cavities, the masses of thrombus were partially black and fragile, whereas the remainder was white, solid, fibrous tissue. The aneurysm cavities that were completely occluded angiographically were entirely filled by solid masses of white fibrous tissue, consistent with organizing thrombus. Black, fragile masses of thrombus were observed within both aneurysms removed from the animal killed early. The lumens of all stented carotid arteries were clearly spared adjacent to the aneurysm orifices, although the actual diameters could not be meas-

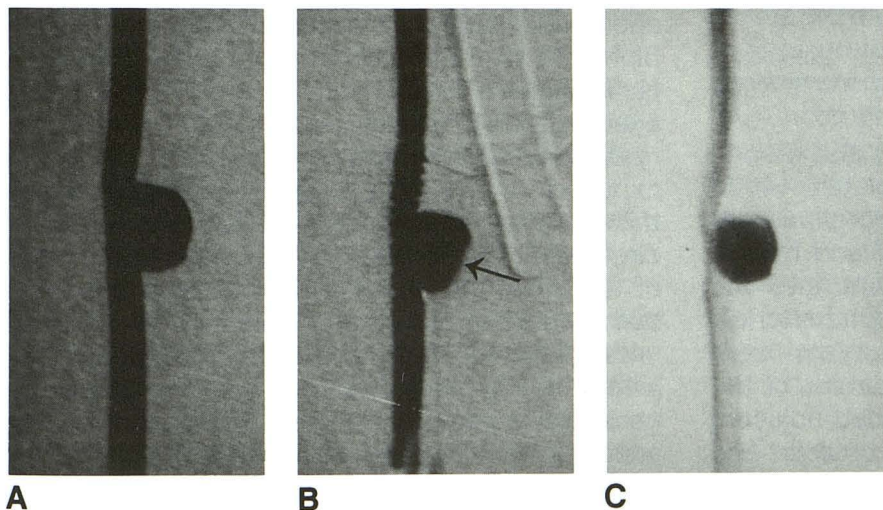


Fig. 5. Transient, mild alteration of flow within the aneurysm after stent placement.

A, Digital subtraction angiography, lateral view, before treatment.

B, Immediately after stent placement, approximately one third of the aneurysmal sac is not visualized (arrow).

C, One week after stenting, the angiographic appearance is identical to the pre-treatment image.

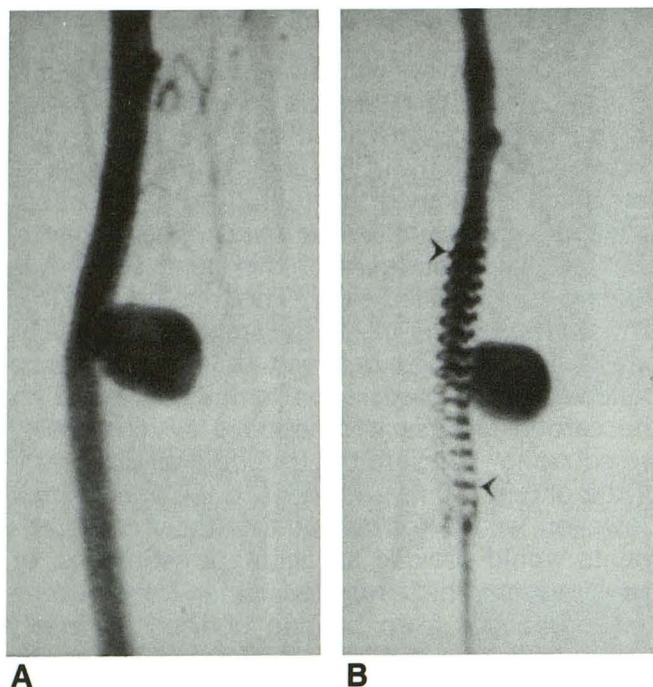


Fig. 6. Unchanged aneurysm filling after stent implantation. A, Digital subtraction angiography, lateral view, before treatment. B, Immediately after stent implantation (arrowheads indicate stent), aneurysm filling is unchanged.

TABLE 1: Results of group A: subtotal packing of aneurysms using Guglielmi detachable coils with and without previous stent implantation

	Complete Occlusion	Incomplete Occlusion	Stenosis Caused by Coil Bulging	Stenosis Caused by Intimal Proliferation
Immediate				
Coils alone	0	2	0	0
Stent and coils	1	1	0	0
After 4 weeks				
Coils alone	0	2	0	0
Stent and coils	1	1	0	30%–50%

ured, as mentioned above. The coils and associated thrombi were contained completely within the aneurysm cavities, and no bulging was observed through the orifices. The coil and thrombus mass protruded to some extent into the lumen of each of the nonstented carotid arteries. In those specimens in which the aneurysms were tightly packed with coils alone, the lumina of the carotid arteries were virtually occluded adjacent to the orifices by bulging masses of coils and thrombi. We attribute this in part to the shrinking of the specimens during fixation, which affected

the parent arteries more than the tightly packed aneurysm cavities.

Histologic analysis of the sections of partially occluded aneurysms (either stented or nonstented) under light microscopy displayed mixtures of organizing thrombi, amorphous fibrin material, and large areas containing intact red blood cells outside the newly formed capillaries within the organizing thrombi. The cavities corresponding to the removed coils were surrounded by a few foreign-body giant cells. The sections of completely occluded aneurysms were entirely filled by organizing thrombi displaying several newly formed small blood vessels.

Endothelial cells seemed to cover the luminal surfaces of the thrombus masses within the completely occluded nonstented aneurysms. We could not study reendothelialization of the orifices of the stented aneurysms, because the intimal layers were removed from these specimens along with the stents.

The wall of the stented portion of the carotid artery of the animal killed early was stretched and the endothelial surface flattened. The intima and the media were compressed around the artery. Deep impressions left by the stent struts could be seen. The internal elastic lamina was poorly identified. In the remaining specimens, sections of the tissue covering the inner surfaces of the implanted stents displayed fibrous proliferations that were approximately three to four times thicker than the diameters of the cavities from which the struts of the stents (0.07 to 0.1 mm) were removed.

Discussion

The treatment of giant cerebral circulation aneurysms with wide necks is associated with a high rate of morbidity and mortality. Microsurgical placement of metal alloy clips across the aneurysm neck is technically difficult. The aneurysm volume and associated mass effect make exposure of the neck arduous, especially when the aneurysm arises from vessels of the posterior circulation. Calcifications in the vessel or the neck of the aneurysm make clip placement treacherous. Ectatic aneurysmal segments of the parent vessel adjacent to the aneurysm orifice may tear when the clip blades are closed on the aneurysm neck. Perforating vessels arising adjacent to the aneurysm orifice can be trapped between the blades of the clip, which may result in occlusion and infarction. Successful deployment of an

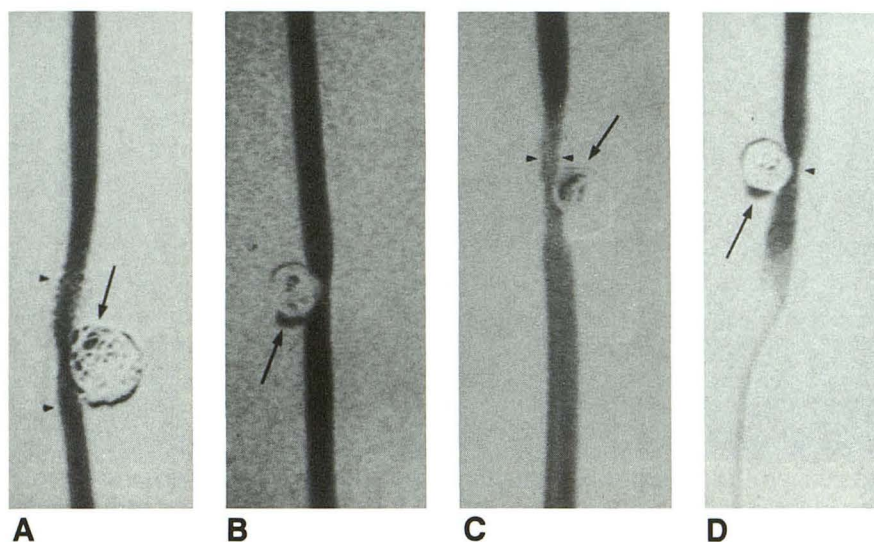


Fig. 7. Results of subtotal aneurysm packing using Guglielmi detachable coils with and without previous stent implantation (animal 1, group A).

A, Digital subtraction angiography immediately after subtotal aneurysm packing with Guglielmi detachable coils through a stent (arrowheads) shows residual aneurysm filling within the inflow zone (arrow).

B, Residual filling (arrow) within the dome of the contralateral aneurysm treated with coils alone.

C, Digital subtraction angiography 4 weeks later demonstrates unchanged filling (arrow) within the stented and coiled aneurysm. The stented portion of the lumen of the carotid artery is narrowed by approximately 35% (arrowheads).

D, Unchanged residual flow (arrow) within the nonstented aneurysm 4 weeks after treatment. Coil bulging into the lumen of the parent artery is not seen. The mild stenosis of the carotid artery adjacent to the aneurysm neck (arrowhead) is related to surgery and postoperative scar tissue formation. Note the circular appearance of this stenosis.

TABLE 2: Results of group B: tight packing of aneurysms using Guglielmi detachable coils with and without previous stent implantation

	Complete Occlusion	Incomplete Occlusion	Stenosis Caused by Coil Bulging	Stenosis Caused by Intimal Proliferation
Immediate				
Coils alone	2	0	50%–75%	0
Stent and coils	2	0	0	0
After 4 weeks ^a				
Coils alone	1	0	75%	0
Stent and coils	1	0	0	50%

^a One animal was killed earlier.

aneurysm clip results in apposition of the circumference of the aneurysm neck and complete isolation from the circulating blood in the parent vessel. Laminar flow is restored to the lumen of the parent vessel. As a result, endothelial cells can cover the defect in the vessel and permanently occlude the aneurysm orifice.

Endovascular treatment of wide-necked cerebral circulation aneurysms has had limited success. Although microcatheter access to the aneurysm cavity is easily attained, complete occlusion of the aneurysm cavity, resulting in restoration of laminar flow within the lumen of the parent vessel, has been difficult to achieve. Silicone or latex balloons rarely fill the aneurysm cavity completely. For complete occlusion of the cavity to occur, these devices require thrombus to occupy

the defects between the balloon and the aneurysm wall.

Detachable coils are soft and conform to the aneurysm cavity without difficulty, yet complete occlusion of wide-necked aneurysms has been achieved only in 11% to 15% of cases in a recently published series (7). Coils do not completely fill the aneurysm and rely on thrombus formation to fill the imperfections between coil mass and aneurysm cavity. In aneurysms with large orifices, as the coils are delivered from the microcatheter tips, the secondary structures of the coils are not contained within the aneurysm cavities. The resulting bulge of the coil mass into the lumen of the parent vessel can result in thrombosis and infarction. Even complete angiographic obliteration after coil treatment does not ensure permanent occlusion (9).

The protective effect of partial treatment against aneurysm rupture is not yet established (10). Incomplete occlusion of the aneurysm cavity has been postulated to provide some protection from bleeding (11), protecting the dome from the forces generated by the impact of the central stream. Unfortunately, partial treatment of the aneurysm neck does not restore laminar flow to the lumen of the parent vessel. As a result, the shear stress generated at the junction between the aneurysm neck and the parent vessel remains. This shear stress can result in dissection and rupture of the aneurysm dome. Recurrence of an incompletely thrombosed aneurysm has been found in 17% of aneurysms treated by

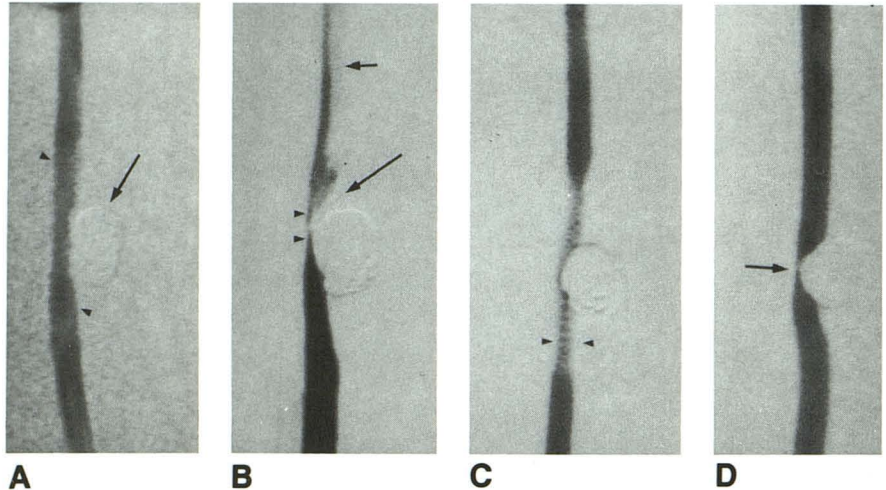
Fig. 8. Results of tight aneurysm packing with Guglielmi detachable coils after stent implantation (animal 3, group B).

A, Digital subtraction angiography demonstrates complete obliteration of the aneurysm immediately after stent implantation (*arrowheads*) and coil packing (*arrow*). The coil mass does not bulge into the parent vessel lumen.

B, Nonstented aneurysm on the contralateral side. Digital subtraction angiography shows complete occlusion of the aneurysm. The coil mass is bulging into the parent vessel lumen, resulting in 75% stenosis (*arrowheads*) and irregular filling, indicating slow flow (*small arrow*) of the distal carotid artery. A small portion of a coil is seen within the parent artery, distally to the aneurysm (*arrow*).

C, Digital subtraction angiography, oblique view, 5 weeks after treatment, demonstrates permanent occlusion of the stented aneurysm and approximately 35% stenosis of the stented portion of the parent artery (*arrowheads*). Note that on this oblique view, the aneurysm partially overlaps the carotid artery.

D, Digital subtraction angiography, oblique view, of the nonstented aneurysm; coil mass is still narrowing the lumen of the parent vessel (*arrow*), but the flow within the artery returned to normal. The aneurysm is completely obliterated.



detachable balloons (4). Rerupture of partially treated aneurysms also has been reported (7, 12, 13).

Complete thrombosis of a partially occluded aneurysm cavity could be facilitated if the magnitude and direction of the central blood-flow stream can be redirected away from the orifice, resulting in stasis within the aneurysm lumen. Strother et al (14) studied in detail the flow patterns within different kinds of experimental aneurysms. The flow within the body of a side-wall aneurysm consists of three distinct territories: a distinct inflow stream entering the lumen at the distal aspect of the neck, an outflow zone corresponding to the proximal edge of the orifice, and vortex flow within the center of the sac. We found similar results in our experiments (Fig 3). Graves et al (15) concluded that modification of the flow within a side-wall aneurysm, either by blocking the inflow tract with coils or balloons, or by displacement of the inflow track from its characteristic location, can lead to thrombosis of the aneurysm cavity.

Stent technology to treat cerebral circulation aneurysms offers a new alternative for isolating the aneurysm cavity from the blood flow in the parent vessel. The concept of intravascular stenting as an adjunct to intraluminal angioplasty was first proposed by Dotter and Judkins in 1964 (16), and results of the initial experiments with the percutaneous introduction of an intravascular supporting device were reported by Dotter in 1969 (17). Since 1983, different stent designs

have been introduced and tested both experimentally and clinically (18–24). Stents currently used are designed to prevent elastic recoil of the dilated portion of an artery and to compress plaque and intimal dissection against the vessel wall. Stents become covered by endothelial layers during a period of 4 to 6 weeks after implantation providing a smooth, nonthrombogenic surface (25). If categorized by delivery technique, stents may be regarded as balloon expandable (Palmaz, Strecker, and Gianturco-Robin) and self-expanding (Wall and Gianturco Z). Regardless of the design, the stent should resist radial force, afford a high expansion ratio, and offer low thrombogenicity. In general, stents that expose less surface area of metal to the internal surface of the vessel are less thrombogenic.

Significant clinical experience has been gained using stents for peripheral angioplasty within the past decade. Clinical trials using the Palmaz, Strecker, and Wall stents disclosed an initial technical and angiographic success rate of more than 90% for atherosclerotic disease of the iliac artery and angiographic patency rates from 70% to 85% at 6 to 18 months for atherosclerotic disease of the femoropopliteal region. Using the Palmaz and Wall stents, 60% and 80% of stented renal arteries remained open at 6 months, respectively (26). The Palmaz-Schatz stent has been used extensively for coronary artery atherosclerotic disease with a reported restenosis rate of 20% to 25% at 6 months (21, 27). Although the incidence of acute and subacute stent thrombosis can be

successfully reduced by systemic anticoagulant therapy (27, 28), late restenosis continues to limit the long-term success rate of intracoronary stenting. Late restenosis is related to a cellular proliferation within the vessel wall, stimulated by interactions between platelets adherent to the damaged intima, macrophages, endothelial cells, and smooth-muscle cells (28). The implantation of stents may induce this process either by initial intimal damage, resulting from inflation of the delivery balloon, or by continuous barotrauma, induced by an expanded self-expandable stent (28).

Intraluminal endoprostheses of different designs have been used experimentally to exclude abdominal aortic aneurysms from the circulation (29). Devices included a polyurethane graft with a metal wire frame (30), Gianturco stents covered by porous nylon grafts (31), and Dacron grafts attached to Palmaz stents. The latter device was also used to treat human abdominal aortic aneurysms (32). Stents covered by porous nylon have successfully excluded aneurysms from the circulation. A renal artery, originating from the portion of the aorta, covered by such a stent remained patent, but histology revealed ischemic changes in the kidney supplied by the stent-covered artery (31). Scanning electron microscopy demonstrated endothelialization of the portion of the Palmaz stent and the Dacron graft that were in direct contact with the arterial wall, but not the segment of the graft bridging over the aneurysm itself (32).

The treatment of intracranial aneurysms represents a different issue, because unlike aortic aneurysms, the majority of cerebral aneurysms are saccular rather than fusiform. In addition, the inadvertent occlusion of small-diameter side branches, arising in the vicinity of the aneurysm, may result in catastrophic consequences. Furthermore, most intracranial circulation aneurysms are located at bifurcations instead of on the lateral walls of arteries. However, the treatment of side-wall saccular aneurysms by placing intraluminal prostheses seems technically feasible. Theoretically, reconstruction of the lumen of the parent vessel should redirect the blood flow away from the aneurysm cavity. Presently available stents were designed for implantation in atherosclerotic segments of vessels after angioplasty. Existing designs attempted to maximize vessel patency and to prevent thrombosis of side branches and of the parent vessel lumen. It seems illogical to assume that these devices would serve

to thrombose irreversibly the aneurysm cavity when placed adjacent to the orifice of an aneurysm. Rather than occlude the orifice, some stents could alter the inflow dynamics at the aneurysm orifice.

In theory, the intraarterial implantation of a stent may lead to aneurysm thrombosis in four different ways. First, the portion of the stent placed across the distal aspect of the aneurysm orifice may block the inflow stream, resulting in stasis and subsequent thrombosis. Second, the presence of a fine mesh structure (stent) adjacent to the neck of the aneurysm may modify the characteristic flow pattern while displacing the inflow stream from its original track. This may result in aneurysm thrombosis (15). Third, the stent struts, covering the orifice of the aneurysm, represent a certain area of metal wires reducing the actual area of the orifice. It is known from the observations of Black and German (33) and the work of Geremia et al (34) that experimental side-wall aneurysms will not remain patent unless the sizes of the orifices exceed critical proportions of the volume of the sacs. Stents may induce aneurysm thrombosis by changing the ratio of aneurysm orifice-to-aneurysm cavity volume. Finally, the placement of tantalum stents into carotid arteries results in a dense fibrocellular reaction that causes a 40% to 50% reduction in the cross-sectional diameters of the vessels. This fibrous hyperplasia could lead to occlusion of the aneurysm orifice.

Successful treatment of experimental side-wall aneurysms by implantation of stents adjacent to the aneurysm orifices has been reported. In 1991 Geremia et al reported near-complete occlusion of experimental carotid artery aneurysms in three mongrel dogs by placing Wall stents (Schneider, Minneapolis, Minn) adjacent to the aneurysm orifices (Geremia GK, Granato D, Raju S, Termin P, Charletta D, Embolization of Experimentally Created Aneurysms with Intravascular Stent Devices, presented at the 29th Annual Meeting of the American Society of Neuroradiology, Washington, DC, 1991). One year later, Geremia et al reported complete occlusion of aneurysms using the same model and devices (Geremia GK, Haklin M, Charletta D, et al, Embolization of Experimentally Created Aneurysms with Intravascular Stent Devices, presented at the 30th Annual Meeting of the American Society of Neuroradiology, St. Louis, Mo, 1992). In another presentation, Geremia et al reported patency of side branches that came in contact with the stent (Geremia GK, Kim

TW, Haklin M, Brennecke L, Douglass J, Intravascular Stents: Effects on Branching Vessels Originating from a Stent Containing Parent Artery, presented at the 30th Annual Meeting of the American Society of Neuroradiology, St. Louis, Mo, 1992). Wakhloo et al reported complete occlusion of three of five experimental aneurysms after treatment with balloon-expandable tantalum stents (Strecker stent, Medi-Tech) and of all 10 aneurysms treated with nitinol stents (Medi-Tech) (35). They found up to 40% stenosis of the carotid artery after tantalum stent deployment and up to 15% reduction of lumen diameter after intraarterial placement of nitinol stents resulting from neointimal proliferation. Turjman et al (36) reported 100% occlusion of five side-wall canine carotid aneurysms after treatment with Strecker stents.

In a previous series of experiments, we placed stents in seven canine carotid arteries harboring wide-necked aneurysms using 5/33-mm (six animals) and 4.5/25-mm (one animal) balloon-expandable Strecker stents (Guterman LR, Szikora I, Wells KM, Hopkins LN, Treatment of Lateral Wall Vein Graft Aneurysms with Stents and Stents with Coils in Canines, presented at the 43rd Annual Meeting of the Congress of Neurological Surgeons, Vancouver, British Columbia, Canada, 1993). Of seven aneurysms, two remained open, one was completely occluded initially and reopened in 1 week, three thrombosed partially, and one thrombosed completely. Three carotid arteries harboring two of the partially occluded and the one completely obliterated aneurysms thrombosed 1 week after stent placement. We found no progressive thrombosis after partial occlusion but rather reopening of initially occluded aneurysms. In contrast to previously published data, we concluded that the flow changes induced by tantalum stents do not result in permanent thrombosis of experimental wide-necked aneurysms.

In the present study, we did not attempt to compare the capability of different stent designs to occlude aneurysms, or to assess the histologic changes, including intimal proliferation, induced by the device. The purpose of this study was to prove the feasibility of a technique that combines intraluminal grafting with endosaccular packing. We chose the commercially available Strecker balloon-expandable stent, which was reportedly successfully used to occlude side-wall aneurysms by other investigators (35, 36). In our experience, the intraarterial implantation of a Strecker stent

failed to occlude or displace the inflow stream in all four cases (Figs 3A and 3C). In these experiments, the aneurysm volume ranged from 132 to 483 mm³. We attribute the differences in volume to the surgical technique used to create the aneurysms. Gross pathologic measurement of the orifice found the diameter to be larger than 6 mm in each case, and the area of the orifice ranged from 28.27 to 37.69 mm². The highest ratio between the aneurysm cavity volume and orifice area was 17.08, significantly less than the ratio of 23.6 that is critical to permanent thrombosis, according to Black and German (15). The struts of the Strecker stent do not cover enough area adjacent to the aneurysm orifice to increase this ratio above the critical level, because permanent thrombosis did not occur after stent placement. Although a dense neointimal proliferation resulted in stenosis of the parent vessel, neointimal proliferation did not occlude the stent mesh at the orifice. In one animal, a Tracker-18 microcatheter was advanced into the aneurysm cavity through the mesh of the stent 2 weeks and 1 month after stent treatment (Figs 3C and 3D).

Our previous experiments concluded that placement of a tantalum Strecker stent adjacent to the aneurysm orifice does not result in complete thrombosis. Therefore, we attempted to exploit the potential benefit of intraarterial stents as a device to reconstruct the lumina of the parent vessels adjacent to wide-necked aneurysms and to retain thrombogenic material in the aneurysm cavities. Initially, we felt that augmented perturbations of the inflow and outflow tract induced by stent placement might lead to aneurysm thrombosis. We theorized that placement of a few coils would be sufficient to induce aneurysm thrombosis. To test this hypothesis, we attempted to alter the inflow tract in the aneurysm without providing tight packing of the aneurysm cavity.

In group A, one stented aneurysm was incompletely occluded by subtotal packing (Fig 7A). After 28 days, the aneurysm failed to thrombose (Fig 7C). This failure indicates that alteration of the flow pattern within the sac would not result in thrombosis. We conclude that perturbing the inflow and outflow tracts does not result in thrombosis.

In group B, the tight packing of the aneurysm cavity resulted in complete obliteration of all stented and nonstented aneurysms (Fig 8A). In the nonstented aneurysms, tight packing of the

aneurysm cavities resulted in bulging of the coil masses into the lumina of the parent vessels. We were unable to measure the true luminal diameters of the parent arteries on the specimens and calculate the real magnitudes of the stenoses produced by bulging of the coil masses. However, histopathologic findings clearly confirmed that stents effectively prevented coils from protruding into the lumina of the parent arteries. The rough surfaces of the protruding coils and the associated hemodynamically significant stenosis of the lumen of the parent vessel could act as surfaces for thrombosis and sources of emboli. In the canine model, the stenosis induced by the coil mass remained, but flow in the lumen of the parent vessel returned to normal (Fig 8D). We do not feel this phenomena would occur in humans and attribute this to the variation in clotting factors between humans and canines.

This study was not designed to elucidate the possible complications of stents. Whether stents may serve as a source of emboli during the early period after implantation remains unknown. Reendothelialization of the inner surface of the stent (25) may prevent thromboembolic complications a few weeks after implantation. Previous studies suggest that early stent thrombosis can be successfully avoided by systemic anticoagulation (27, 37). Anticoagulation also may prevent the complication of distal embolization.

The inclination of tantalum stents to induce fibrous hyperplasia, which results in vessel stenosis, significantly limits their possible clinical application within the intracranial circulation. In our study, intimal proliferation produced an approximately 0.3- to 0.5-mm-thick neointimal layer covering the surface of the stents, resulting in a 35% to 40% reduction in the diameter of the parent artery. Such extensive narrowing of an intracranial artery is clearly undesirable. We attribute the magnitude of stenosis to the particular stent device used. The histologic findings in the stented carotid artery from the animal killed early indicate severe damage to the arterial wall induced by the inflation of the stent-delivery balloon. The injury caused by balloon inflation may initiate the process of intimal proliferation (28). The results of Wakhloo et al (35) indicate that stents of different designs and materials produce less intimal reaction and associated vessel stenosis.

The ultimate goal of intracranial aneurysm treatment is complete exclusion of the aneurysm cavity from the circulation. This may be achieved

either by surgical clipping of the neck or by endovascular treatment that induces permanent thrombosis of the aneurysm cavity. For this treatment to be irreversible, reendothelialization must occur at the aneurysm neck. In our experiment, histopathologic analysis revealed the formation of organized thrombi that filled the entire aneurysm cavities only in those aneurysms that were completely occluded by tight packing with coils. Endothelial cells covered the luminal surfaces of the thrombus masses within the nonstented, completely occluded aneurysms. However, reendothelialization of the orifices cannot be confirmed without serial sections to demonstrate that the entire areas of the orifices were covered by newly formed endothelia. Thin serial sections through the aneurysms that contained stents and coils proved cost-prohibitive and technically infeasible. In addition, the endothelia were removed along with the stents from the stented arteries. More sophisticated histopathologic techniques are being developed to examine the aneurysm orifices in stented and coiled aneurysms.

We conclude that Guglielmi detachable coils can be advanced into an aneurysm cavity through the mesh of an expanded Strecker stent. Our preliminary results indicate that tantalum stents do not promote complete aneurysm thrombosis—even if the aneurysmal sac is almost completely packed with coils. These results should be confirmed by further experiments with more aneurysms in a larger animal series. However, this study shows that the combined use of intra-arterial stenting and endosaccular packing with coils is a feasible new treatment for wide-necked aneurysms, allowing tight packing of the aneurysm cavity without compromising the lumen of the parent artery. The use of different occlusion devices and embolic materials combined with intraarterial stenting is currently under evaluation in our laboratory.

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