Effects of Endothelial Injury on the Rate of Thrombus Organization in Canine Carotid Arteries Occluded with Microcoils

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Summary

Thrombus organization in canine carotid arteries occluded with platinum microcoils was studied to determine if endothelial injury created with a Xenon Chloride Excimer Laser (XEL) could accelerate endovascular fibrosis.

Ten common carotid artery stumps were created in ten dogs. Each of four stumps were schematically divided into four longitudinally contiguous injury zones (thermal ablation injury, non-ablative injury, proximal and distal non-injury zones) to test the effects of ablative and non-ablative injury and to establish a set of internal controls that would account for proximity to circulating blood at the ostium of the occluded artery. Following XEL irradiation of the endothelium through an arteriotomy, each stump was embolized with microcoils. Four control stumps were subjected to sham laser procedures, and embolized in an identical fashion. Two additional stumps were embolized in the absence of sham surgery. Angiographic, gross and histologic analysis was performed after four weeks. Specimens of freshly clotted whole blood mixed with microcoils were used as an additional control.

In irradiated stumps and non-irradiated stumps (sham and embolization only), angiography revealed no evidence of coil compaction

or recanalization. In all irradiated stumps the thermal ablation zone contained fibrous tissue and neovascularity without unorganized thrombus. The other zones in the irradiated stumps were indistinguishable from each other and from all zones in the non-irradiated sham stumps, containing primarily unorganized thrombus. Stumps embolized in the absence of sham surgery were filled with material that was grossly and microscopically identical to specimens of freshly clotted whole blood containing microcoils.

The results indicate that thermal ablation injury of the endothelium accelerates thrombus organization in canine carotid arteries occluded with platinum microcoils.

Introduction

Recent reports have indicated a cerebral aneurysm recurrence rate of 14% within six to twelve months of coil embolization therapy^{1,2}. Factors that likely contribute to aneurysm recurrence include coil compaction, and lysis of unstable endoaneurysmal thrombus¹⁻³. In large, wide neck cerebral aneurysms, the fibrous organization of thrombus is a slow process that may take more than two months³⁻⁶. Thrombus organization into a mature, fibrous endovascu-

Figure 1 B) Technique of laser irradiation and coil embolization. Following closure of the arteriotomy, a 6 french guide catheter (curved black arrow) is introduced into the open end of the CCA stump, and the distal ostium of the stump is cinched down around the tip of the catheter with a temporary ligature. A tracker 18 microcatheter (long straight black arrows) is directed proximally through the guide catheter and the stump is progressively occluded from proximal to distal with microcoils (short straight black arrows) by incrementally withdrawing the microcatheter. C) Technique of laser irradiation and coil embolization. Following removal of both catheters, the distal end of the stump is suture ligated, and the proximal clip is removed to reestablish flow. Proximal Non-Injury Zone (PNIZ), Distal Non-Injury Zone (DNIZ).

lar scar may prevent aneurysm recurrence by mechanically stabilizing the endoluminal coil mass, and permanently sealing the aneurysmal ostium with a stable connective tissue matrix that is resistant to lysis and recanalization.

Efforts to address cerebral aneurysm recurrence have focused on the development of bioactive embolization devices intended to promote endovascular healing, and fibrous organization of thrombus⁷⁻¹¹. Clinical and experimental studies have shown that some mechanisms of vascular injury promote intensified and accelerated endovascular healing responses^{12,13}. This was first observed experimentally in animal models of balloon catheter injury, and clinically as restenosis after angioplasty and stenting^{12,13}. Although these examples represent forms of mechanical injury, experimental studies and clinical experience have both suggested that the healing response of the arterial wall is non-specific¹⁴⁻¹⁶.

The ability of endothelial injury to promote endovascular healing was recently illustrated in a study of canine vein pouch aneurysms embolized with P^{32} ion implanted microcoils¹⁷. The beta emitting P^{32} coils prevented recanalization of embolized aneurysms and promoted formation of a thick neointimal covering over the necks of embolized aneurysms¹⁷. Although the mechanism of this effect remains unproven, the dosimetry profile of the P^{32} device is consistent

with the creation of local endothelial injury. Consequently, the results support the hypothesis that endothelial injury promotes endovascular healing processes.

Lasers enable the production of highly focused, spatially defined endothelial injuries, with limited surface penetration of the target tissue. Prior studies of endothelial laser irradiation have demonstrated vascular healing responses consisting of myointimal proliferation, identical to the response observed in arteries subjected to balloon catheter injury¹⁵. Other studies have shown dose dependent smooth muscle cell proliferation following laser irradiation of the arterial endothelium¹⁸. The purpose of our study is to determine if endothelial injury, created with a XeCl pulse excimer laser, could promote and accelerate the organization of luminal thrombus in arteries occluded with microcoils.

Methods

All study protocols were approved by the Institutional Animal Care and Use Committee in accordance with National Institute of Health guidelines. All surgical and angiographic procedures were performed under general endotracheal anesthesia. Premedication was administered in the form of subcutaneous morphine sulfate (2 mg/Kg). Anesthetic induction was achieved by intravenous injection of diazepam

Figure 2 A) Pathology of thermal ablation injury. Endoluminal surface of a canine common carotid artery viewed en-face (original magnification x 16). The arterial lumen is opened along a longitudinal incision and the edges are tacked back by dissection pins. A subacute thermal ablation injury harvested 48 hours after creation, as part of the preliminary dosimetry study, demonstrates a large halo of subintimal hemorrhage extending beyond the boundaries of the irradiated endothelial surface. B) Pathology of thermal ablation injury. Longitudinal section of an acute thermal ablation injury harvested immediately after creation, as part of the preliminary dosimetry study, shows sharply circumscribed crater edges and microdissections extending into the arterial wall (hematoxylin and eosin; original magnification x 10).

(0.7 mg/Kg), ketamine (10 mg/Kg), and atropine (0.016 mg/Kg). Following oral endotracheal intubation, animals were mechanically ventilated. Anesthetic maintenance was accomplished by the administration of inhaled isoflurane. All subjects underwent planned sacrifice on the angiography table by pentobarbital overdose (324 mg/Kg). Including the seven dogs used for preliminary laser dosimetry studies, a total of 17 dogs were used for this study. All subjects were healthy adult female mongrel dogs weighing 25-30 Kg.

Laser applications were performed using a 1.5 mm (O.D.) end firing laser catheter coupled to a XeCl ($\lambda = 308$ nm) pulse excimer laser (Spectranetics Incorporated, Boulder, CO).

Coil embolization procedures were performed using Guglielmi Detachable Coils (Boston Scientific, Natick, MA). Prior to embolisation, the microcoils were disconnected from their delivery wires by dividing them from their junction zone with wire cutters. The coils were deployed by pushing them through microcatheters with a 0.018" guidewire. This manipulation eliminated the need for electrolysis and substantially reduced the overall time required for each embolization procedure.

Preliminary Laser Dosimetry Studies

The pulse fluence threshold for thermal ablation injury (the pulse fluence below which no

thermal ablation of tissue was observed) was empirically determined to be 17 $\text{mj}/\text{mm}^2/\text{pulse}$ from a preliminary *in vivo* dosimetry study conducted on the endothelium of normal canine carotid arteries. A total of 112 endothelial lesions were created in seven dogs (16 lesions/dog). In each dog, a set of B lesions were created using a pulse repetition rate (PRR) of 40/s, an exposure time of five seconds, and a series of eight different pulse fluences ranging from 5-60 $\text{mj}/\text{mm}^2/\text{pulse}$. A second set of eight lesions were created in each dog with a PRR of 25/s, using the same eight pulse fluences and an exposure time of five seconds. Consequently, there were 14 sample lesions (two from each dog), representing each of the eight pulse fluences studied, seven with a PRR of 25/s and seven with a PRR of 40/s.

Endothelial lesions were created by surgically isolating the right common carotid artery (CCA) of each dog between temporary clips, and irradiating spatially contiguous stations along the length of the artery through a longitudinal arteriotomy. The distance between the tip of the laser catheter and the endothelial surface was controlled with a ball valve tip guide wire. Thermal ablation injury was said to be present if there was instantaneous cavitation of target tissue upon irradiation. Thermal ablation injuries were evident immediately after endothelial irradiation as sharply circumscribed intimal craters or perforations. For a given pulse fluence, changing the PRR from 25/s to 40/s did not influence the thermal ablation effect in the pulse fluence range examined. At pulse fluences $\geq 20 \text{ mj}/\text{mm}^2/\text{pulse}$ thermal ablation injuries were created in 100% of irradiated specimens. Arterial wall perforations did not occur at pulse fluences below 60 $\text{mj}/\text{mm}^2/\text{pulse}$.

Creation of Common Carotid Artery Stumps, Laser Irradiation and Coil Embolization

Ten dogs were divided into three experimental treatment groups. Group 1, the laser treatment group, consisted of four dogs. In each of these dogs, the endothelium of the CCA stump was irradiated with a laser prior to embolization. Group 2, the sham control group, consisted of four dogs in which the CCA stumps were treated with sham laser procedures prior to coil embolization. Group 3, the non-sham control group, consisted of two dogs with CCA stumps

B

that were embolized with microcoils in the absence of sham laser surgery.

In all three groups, a 7 french sheath was placed in the right femoral artery, and the right CCA was surgically isolated through a midline neck incision following the intravenous administration of heparin.

In group 1 (laser treatment) dogs, a temporary clip was applied to the proximal end of the isolated CCA segment and the distal end was divided proximal to a suture ligature. The CCA lumen was then opened by extending a 3 cm longitudinal arteriotomy from the distal free edge of the proximal stump toward the CCA origin. The edges of the arteriotomy were tacked back with sutures to expose the luminal surface of the CCA en-face. The endothelial surface of the CCA stump was bathed in saline, and schematically divided into four contiguous endothelial injury zones along the longitudinal axis of the construct, each one centimeter long (proximal non-injury zone, alpha zone, beta zone, distal non-injury zone). A unique en-

endothelial injury protocol was then applied to each zone (figure 1). Thermal ablation injury was created in each alpha zone by uniformly irradiating the endothelial surface with a pulse fluence of 20 mJ/mm²/pulse, a PRR of 40/s, and a 5 s exposure time. Phototoxic injury was created in each beta zone by uniformly irradiating the endothelial surface with a pulse fluence of 12 mJ/mm²/pulse, a pulse rate of 25/s, and a 5 s exposure time. The proximal and distal non-injury zones were used as internal controls, and the endothelial surfaces were not irradiated. The arteriotomy incision extended across the alpha, beta and distal non-injury zones. The proximal non-injury zone was not violated by the arteriotomy incision to provide a series of internal controls that would reveal the effect of arteriotomy on tissue responses to coil embolization, through comparison to the distal non-injury zone. In the alpha and beta zones, the target tissue was irradiated by manually aiming the active end of the laser catheter directly at the target tissue. In each zone of target tissue, the PRR, pulse fluence and exposure time were kept constant. The distance between the tip of the laser catheter and the endothelial surface of the target tissue was precisely controlled by employing a ball valve tip guide wire as a centering device, and spacer. When the laser irradiation procedure was completed, the arteriotomy was sutured closed with 100 prolene suture. A 6 french guide catheter was then introduced into the distal open end of the CCA stump, and the distal ostium of the stump was cinched down around the tip of the catheter with a temporary ligature. The stump was distended, by infusing saline into the guide catheter. A tracker 18 microcatheter was directed through the guide catheter into the proximal end of the stump, up to the proximal clip, under fluoroscopic guidance. The stump was then progressively occluded from proximal to distal, by delivering platinum microcoils through the microcatheter under fluoroscopy and incrementally withdrawing the microcatheter. Following removal of both catheters, the distal end of the stump was suture ligated, and the proximal clip was removed to reestablish flow.

In group 2 (sham control) dogs, right CCA stumps were created as described above for group 1 (laser treatment) dogs. Sham laser procedures and embolizations were performed us-

ing the same technique applied to group 1 dogs. Sham laser surgeries were performed with an inactive laser catheter (uncoupled from laser) and ball valve tip guidewire.

In group 3 (non-sham control) dogs, right CCA stumps were fashioned by double suture ligating the distal right CCA and dividing it between ligatures.

A 6 french guide catheter, introduced through the transfemoral sheath, was then placed in the proximal right CCA stump of each dog under fluoroscopic guidance and perfused with saline. Under fluoroscopic guidance, a tracker 18 microcatheter was then advanced through the guide catheter and used to embolize the right CCA stump from distal to proximal with microcoils.

In all three groups, digital subtraction angiography (DSA) was performed through the 7 french transfemoral sheath, with a 6 french catheter positioned in the brachiocephalic artery or right CCA. Sixty to ninety cm of coil was used to occlude each stump (Group 1: 60 cm for stump 1, 60 cm for stump 2, 63 cm for stump 3, and 90 cm for stump 4. Group 2: 60 cm for stump 1, 70 cm for stump 2, 60 cm for stump 3, and 68 cm for stump 4. Group 3: 60 cm for stump 1 and 70 cm for stump 2).

After four weeks, DSA was repeated in all three groups. Following the intravenous administration of heparin, each right CCA stump was surgically isolated, perfusion fixed with paraformaldehyde, excised and sectioned for histologic processing.

Histology Methods

Half of the stumps in each group were divided into longitudinal sections and the remaining half were divided into trans-axial sections. Portions of each lesion were subjected to dissection under the surgical microscope. The remaining tissue was embedded in methacrylate and divided into histologic sections that were stained with mineralized bone stain and toluidine blue. Samples of platinum microcoils suspended in freshly clotted whole blood, obtained from each dog prior to sacrifice were fixed in paraformaldehyde and processed in identical fashion to use as a reference in subsequent examinations.

The microscopic features of unorganized thrombus in our experimental system were es-

tablished by examining the samples of freshly clotted whole blood mixed with coils. Persistent unorganized thrombus was defined as a large (occupying an entire high power field) cluster of densely packed erythrocytes within an amorphous hemosiderin stained fibrinous matrix (identical in appearance to what was found on examination of freshly clotted whole blood containing microcoils). Four tissue sections prepared from each type of lumen (alpha zone, beta zone, proximal non-injury zone, distal non-injury zone, group 2 sham control, group 3 non-sham control) were each examined for the presence of unorganized thrombus within the central region of the lumen. The central region was defined as the region circumscribed by a radius equal to one third of the true cross-sectional radius of the lumen. A specimen was said to contain unorganized thrombus if it was detected on any of the four representative tissue sections.

Statistical Analysis

The Fisher Exact Test was used to compare the alpha and beta zone lumina to the control lumina, with the presence of unorganized thrombus at four weeks post-embolization as the test variable. The lumina of both proximal and distal non-injury zones in group 1 (laser treatment) CCA stumps, and group 2 (sham control) CCA stumps were used as controls in the analysis.

The statistical significance of the difference in the average coil packing per stump (total coil in centimeters/CCA stump) between group 1 and group 2 was determined using a two-tailed Student's *t* test.

Results

Arteriography

In all three groups, immediate post-embolization arteriography revealed complete occlusion of the distal 3 cm of CCA stump packed with microcoils and persistent filling of the non-embolized CCA proximal to the coil mass (figure 3). Arteriograms performed four weeks post-embolization demonstrated partial internal thrombosis and occlusion of the CCA lumen proximal to the coil packed segment and no evidence of coil compaction in all CCA stumps.

Figure 3 Arteriography. Right carotid arteriogram obtained immediately after coil embolization demonstrates $\geq 90\%$ occlusion of a sham CCA stump, with uniform coil packing throughout. Black arrowheads indicate the right common carotid artery stump. White arrow indicates the rachio-cephalic artery, and black arrow indicates right subclavian artery.

Gross and Histologic Examination

Grossly, group 3 lumina, which were embolized in the absence of surgical arteriotomy or laser irradiation, were filled with gelatinous red thrombus containing loosely suspended loops of microcoils, identical in appearance and consistency to freshly clotted whole blood containing coils. In each case, the thrombus-coil mass was easily removed from the stump lumen, and the coils were easily separated from the thrombus associated with them (figure 4C).

Microscopically, there was no difference between the material in group 3 (non-sham control) lumina and freshly clotted whole blood containing coils. The coil matrix consisted of large numbers of densely packed erythrocytes and occasional macrophages in a loose fibrous network stained with hemosiderin.

Group 1 alpha lumina, which were subjected to thermal ablation injuries prior to embolization, were uniformly filled with highly cellular, fibrous connective tissue that blended into the

A

B

Figure 4 Gross pathology. A) Trans-axial cross-section through the alpha zone of a common carotid artery stump four weeks after laser irradiation and coil embolization (original magnification x 10). Endoluminal coils (straight white arrows) are encased in fibrous scar tissue (curved black arrows) and granulation tissue (curved white arrows). The lumen (border indicated by black arrowheads) is deformed into an eccentric configuration due to scar tissue contraction. B) Trans-axial cross-section through the distal non-injury zone of a common carotid artery stump 4 weeks after laser irradiation and coil embolization (original magnification x 10). Endoluminal coils (straight white arrows) are suspended in unorganized red thrombus (curved white arrows). Note that the rounded configuration of the lumen (borders indicated by black arrowheads) is preserved. C) Group 3 right common carotid artery stump 4 weeks after coil embolization (original magnification x 16). The arterial lumen has been opened along its longitudinal axis, and a mass of red thrombus intermixed with coils has been removed.

arterial wall and engulfed the endoluminal coils (figures 4A,5A). The endovascular scar was extensively penetrated by neovascularity, which was most dense in the peri-sutural region. No evidence of unorganized thrombus was found in any of the tissue sections prepared from the alpha lumina (table 1).

The distal non-injury zone lumina and beta zone lumina from group 1 (laser treatment) as well as group 2 (sham control) lumina all had similar endoluminal tissue content. In the central region, these lumina contained unorganized thrombus (figure 4B and 5B). Peripherally, granulation tissue was found asymmetrically concentrated in the region of the suture line.

The proximal non-injury zone lumina from group 1 (laser treatment) were uniformly filled

with unorganized thrombus, identical to group 3 lumina and freshly clotted whole blood containing coils.

Statistical Analysis

No statistically significant difference in the average coil packing per CCA stump (total coil in centimeters/CCA stump) was found between the treatment (n = 4) and sham (n = 4) groups using a two-tailed Student's t test ($\alpha = 0.005$, $t = 0.48$). The alpha lumina (n = 43) were distinguished from all of the control lumina (distal non-injury zone n = 4, proximal non-injury zone n = 4, sham lumina n = 4) by the absence of unorganized thrombus at four weeks post-embolization. For each of the three treatment-

Figure 5
Histopathology.
A) Trans-axial cross-section through the alpha zone of a common carotid artery stump four weeks after laser irradiation and coil embolization (toluidine blue; original magnification x 40). The lumen is filled with connective tissue (collagen fibers indicated by straight black arrows) that is penetrated by neovascularity (black arrowheads).
B) Longitudinal cross-section through the central region of a sham lumen shows poorly organized clot stained with hemosiderin. The arrows indicate multinucleate giant cells (toluidine blue; original magnification x 40). Black arrowheads indicate erythrocytes.

control comparisons, this difference was found to be statistically significant using the Fisher Exact Test ($p = 0.014$). In contrast, all of the beta lumina contained persistent thrombus within the central region, and were therefore not significantly different from control groups.

Discussion

The results of this work indicate that thermal ablation injury of the endothelium created with a XeCl pulse excimer laser accelerates organization of endoluminal thrombus, and promotes formation of mature endovascular scar tissue in coil embolized arterial stumps. In arterial stump segments treated by thermal ablation of the endothelium prior to embolization, thrombus was completely replaced by mature fibrous connective tissue within four weeks. In contrast, control arterial stump segments deprived of laser irradiation demonstrated no significant thrombus organization after four weeks.

Phototoxic endothelial injuries, which involve a combination of photothermal and photochemical insults, did not promote endovascular fibrosis. Instead, persistence of unorganized thrombus was discovered. This may reflect the inhibitory effect of ultraviolet radiation on cell proliferation¹⁹. Although irradiation of the luminal surface of arteries with pulse energies below the ablation threshold can cause lethal damage to endothelial cells, the damaged cells may remain in place initially, and desquamate in delayed fashion. If the endothelium of the laser-injured vessel initially remains intact, there may be less platelet adhesion to the surface of the artery prior to coil embolization. Furthermore, heat dependent coagulation and denaturation of collagen and elastin in the arterial wall may cause damage to the extracellular matrix which impairs cell adhesion and migration in response to injury²⁰.

When pulse energies above the thermal ablation threshold are used, irradiated endothelial cells are vaporized, leaving the collagenous matrix of the arterial wall directly exposed to circulating platelets²¹. Extracellular matrix proteins underlying the irradiated tissue volume remain chemically unaltered²¹. Adhesion of activated platelets to exposed collagen probably leads to the subsequent release of Platelet Derived Growth Factor (PDGF). The cellular elements in the tissue underlying the laser injury

were never exposed to ultraviolet radiation, and are able to normally participate in the healing process. In addition, thermal ablation injury is characterized by mechanical disruption of the connective tissue matrix of the arterial wall due to explosive vapor bubble formation²¹. This results in microdissections and fissures that contain mural thrombus, rich in activated platelets bearing PDGF (figure 2). PDGF, a potent mitogen, and key mediator in the proliferative response of the arterial wall to injury, may be one of the factors responsible for the effects of thermal ablation injury in our study²². This conclusion is supported by a previous study, which demonstrated that platelet extract enhances healing responses in experimental aneurysms embolized with collagen sponges²³.

In our experiment, we employed a simple model consisting of a canine CCA stump. CCA stumps differ morphologically and histologically from human cerebral aneurysms. It is conceivable that our experimental lesions might have a more robust response to injury than a cerebral aneurysm, since they retain all the elements of a normal arterial wall. Previous studies, however, have suggested that cerebral aneurysms possess a full repertoire of responses to injury, similar to those of the normal arterial wall²⁴. In the present study, a selectively higher peripheral concentration of granulation tissue and invariable central location of residual unorganized thrombus in embolized CCA stumps indicate a centripetal pattern of healing. These findings are similar to what is observed in human cerebral aneurysms and suggest a common mechanism of endovascular healing³⁻⁶.

Raymond et Al demonstrated that embolized peripheral canine arteries, unlike embolized peripheral porcine arteries, have a propensity toward recanalization that is similar to embolized human cerebral aneurysms²⁵. In our model, we demonstrated that endovascular occlusion with platinum microcoils results in the formation of unorganized thrombus that persists for at least four weeks post-embolization. This is consistent with the slow rate of endoluminal thrombus organization that occurs in large human cerebral aneurysms, and experimental canine vein pouch aneurysms^{3-6,25}.

Other investigators have used lasers to perform external photocoagulation of surgically exposed aneurysms in humans and experimen-

tal animals²⁶⁻²⁸. Those studies demonstrated fibroblastic obliteration and neoendothelialization of laser photocoagulated aneurysmal ostia within three to six weeks.

The tissue condensing and welding effects of laser photocoagulation were responsible for ostial closure, and fibrosis in these cases^{21,29,30}. It is unlikely that endothelial injury played a significant role in these studies, since the tissue was subjected to external irradiation. The first attempt to perform endovascular thermocoagulation of aneurysms was reported by O'Reilly et al³¹. This group used a continuous wave endovascular argon laser to heat steel caps deployed inside the necks of experimental vein pouch aneurysms.

The vascular tissue was not directly irradiated. In these experiments, the aneurysmal tissue contracted around the steel caps and underwent progressive fibrosis. Photocoagulation and thermocoagulation injuries are essentially pure thermal processes^{21,29,30}. The photocoagulation effect was not a significant consequence of tissue irradiation in our study. As discussed above, thermal ablation does not result in significant heating of tissue outside the vaporization volume and phototoxic injuries produced in this study were not sufficient to result in photocoagulation.

In arteries and arterial lesions embolized with microcoils, thrombus fills the vast majority of space within the occluded lumen³². If the provisional matrix formed by this thrombus undergoes lysis, a significant portion of the luminal space may re-establish continuity with the circulation. Although this process is variably dependent on a number of local haemodynamic and biological factors, the presence of an endothelial lining is essential for the process of recanalization since all vascular tissues must possess a physiologically active endothelium to maintain luminal patency.

The endothelium passively promotes lumen recanalization since it constitutes a surface that resists the formation of thrombus by flowing blood³³. This is achieved mainly through membrane expression of thrombomodulin and local release of prostacyclin (PGI₂)³⁴. The endotheli-

um also produces surface bound heparin sulfate, which binds liver derived anti-thrombin III (ATIII) and accelerates ATIII mediated thrombin inactivation³⁵. The endothelium actively participates in lumen recanalization by local secretion of serine proteases which include urokinase and tissue plasminogen activator³⁶. Raymond et al described a paradigm of post-embolization aneurysm healing in which the aneurysmal endothelium acts to preserve luminal integrity and promote recanalization³⁷. In a recently published study, these investigators demonstrated that the endothelium is instrumental in the persistence and progression of luminal remnants after embolization of experimental aneurysms³⁷.

The results of their study suggest that an intact endothelium interferes with effective endovascular healing after embolization, and that absence of an endothelial lining promotes obliteration of the adjacent luminal space. Their results are consistent with the findings of the present study and support our conclusion that endothelial ablation enhances endovascular healing processes after coil embolization, perhaps by a mechanism involving the interaction of circulating blood elements with sub-endothelial tissue.

Conclusions

Our results suggest that endothelial injury may reduce the possibility of lumen recanalization after coil embolization. Future efforts to design more durable endovascular cerebral aneurysm therapies should consider mechanisms of endothelial injury as a means to limit recanalization.

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