

Treatment of vasospasm with a 480-nm pulsed-dye laser

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✓ Laser energy at a wavelength of 480 nm was applied in 1- μ sec pulses of 3 to 10 mJ to two models of vasospasm. Rabbit common carotid arteries (CCA's) were constricted chronically by the application of human blood within a silicone sheath. Peak vasospasm developed 24 to 48 hours later, and persisted for up to 6 days. Endovascular laser treatment was delivered to 40 CCA's via a 200- μ m diameter silica quartz fiber introduced through the femoral artery. The CCA caliber increased from 60% of the pre-vasospasm control diameter to a minimum post-laser diameter of 83% of control. No instances of laser-induced perforation or of arterial thrombosis were observed for up to 60 days after treatment. Prophylactic laser application to nine normal vessels was able to attenuate the development of vasospasm if blood was applied immediately thereafter (88% vs. 59% of control diameter, $p < 0.02$), but not if blood was applied 7 days later. Studies in 16 normal CCA's established that there was a considerable margin between the laser energy required to induce dilatation and that which caused perforation, providing that the fiber remained relatively central within the artery. Morphological examination demonstrated focal loss of endothelial cells immediately after laser application, followed approximately 7 days later by the development of areas of intimal hyperplasia. Only minimal changes were observed in the medial or adventitial layers.

In a second study, the basilar artery of seven dogs was constricted chronically by two intracisternal injections of autologous blood 3 days apart. Five dogs received endovascular laser treatment 7 or 10 days after the first injection, when basilar artery diameter was reduced to a mean of 61% and 77% of control, respectively. Immediately following treatment, basilar artery diameter increased to 104% and 102% of resting diameter, respectively. Both untreated and laser-treated arteries were smaller than the control diameter at 30 days (80% and 82%, respectively), but in each group the vasodilatory response to hypercapnia was preserved.

These findings indicate that 1- μ sec laser pulses are well tolerated by systemic and cerebral arteries in two different animal models, and suggest that the 480-nm pulsed-dye laser may have an application for the treatment or prophylaxis of cerebral vasospasm.

KEY WORDS • pulsed-dye laser • vasospasm • common carotid artery • basilar artery • subarachnoid hemorrhage • rabbit • dog

PULSED-DYE lasers have been used increasingly to treat a variety of medical conditions. These include the eradication of port-wine stains,^{2,5} the fragmentation of urinary calculi,¹⁸ the ablation of atheromatous plaques,^{13,14} and thrombolysis following experimental myocardial infarction.⁸ This type of laser has several important features. First, depending upon the dye selected, laser emission can be varied throughout the visible spectrum and matched to the absorption peak of the target tissue. Second, energy can be delivered by single optical fibers. Third, because the pulse

duration is generally shorter than the thermal relaxation time of neighboring tissues, heat-induced injury to surrounding structures is minimized.¹

Recent reports from our laboratory have demonstrated that the pulsed-dye laser may be of benefit in the treatment of vasospasm. Intravascular delivery of low pulse energies induces sustained dilatation in rabbit femoral arteries constricted acutely by a variety of pharmacological agents,⁷ and in isolated dog basilar artery segments constricted by superfusion with hemolysate.¹⁶ Extravascular irradiation of rabbit basilar

artery constricted *in vivo* either by superfusion with hemolysate, or by a "two-hemorrhage" subarachnoid hemorrhage (SAH) protocol, is similarly effective.¹⁶ However, our previous studies have not permitted us to assess the duration of dilatation or to determine long-term effects on the arterial wall.

Intracranial arteries differ fundamentally in structure from extracerebral vessels, principally because they have no more than a rudimentary adventitia. A chronic model of cerebral vasospasm clearly would be the most appropriate manner in which to study the long-term effects of laser treatment on vasospasm. Unfortunately, the smallest laser fiber available to us initially was slightly too large and inflexible to permit catheterization of an intracranial artery in spasm. For this reason we elected first to undertake a pilot study using an extracerebral vessel.

Materials and Methods

Chronic Vasospasm in Rabbit Common Carotid Artery

New Zealand White rabbits of either sex, each weighing 2 to 3 kg, were anesthetized with ketamine hydrochloride, 30 mg/kg, and 4% halothane by inhalation. Following endotracheal intubation, anesthesia was maintained with 1% to 2% halothane. End-tidal CO₂ was maintained between 35 and 45 mm Hg. Systemic blood pressure was monitored in selected animals via a brachial or femoral artery catheter. Bilateral common carotid artery (CCA) angiography was obtained with Renografin-60 as the contrast material following selective catheterization via a Tracker-18 catheter introduced via the femoral artery.* The Tracker catheter was then removed and the femoral artery ligated.

Both CCA's were exposed through a midline cervical incision. All loose areolar tissue investing the vessels was excised. Silicone tubing with an internal diameter of 2.6 mm was divided into 3-cm lengths and copper wire markers were attached to each end. The sleeves were stored in 70% isopropanol until use; one sleeve was placed around each CCA. The space between the artery and the tube was filled with fresh nonheparinized human blood, after which the animals were allowed to recover.

The rabbits were reanesthetized 24 to 48 hours later, and angiography was repeated as before. In the rare event that spasm was not evident, blood application was repeated and the animals were reassessed 24 hours later. The rabbits were divided into five groups: a control group, a laser-treated group; a sham-treated group; a group with laser prophylaxis; and a group with laser vessel perforation.

Control Group. The time course of untreated vasospasm was established by serial angiography in 15

CCA's from 13 rabbits. The silicone sleeves were removed after 7 days. In nine animals, the left CCA was excised at the time of cuff removal, and angiography was then repeated 30 and 60 days later.

The ability of vessels with vasospasm to relax in the presence of a vasodilator was assessed angiographically in a further six CCA's 24 hours after blood application. Papaverine, 30 mg, was diluted to 2 ml with saline, and warmed to 37°C. Following carotid angiography, papaverine was infused continuously via the Tracker catheter over a 5-minute period, and angiography was repeated 10 minutes later.

Laser Treatment Group. Twenty-four to 48 hours after the induction of spasm, 40 CCA's from 32 rabbits received endovascular laser therapy from a 1- μ sec pulsed-dye laser at a wavelength of 480 nm.† The tip of the Tracker-18 catheter was positioned in the proximal CCA. A polytetrafluoroethylene (PTFE)-coated fused silica quartz fiber with a 200- μ m diameter and a fire-polished ball tip (spot size 0.6 to 1.1 mm) was inserted into the Tracker-18 catheter and advanced coaxially under fluoroscopic control to the most distal extent of the spasm. Laser light was delivered to the quartz fiber at a range of pulse energies between 4.7 and 10 mJ (pulse-pulse variation < 10%) and a repetition rate of 2 Hz. The fiber was withdrawn progressively into the catheter during treatment, at a rate of approximately 1 mm/sec, until the entire area under the cuff was irradiated. Angiography was then repeated. If no dilatation was observed, treatment was repeated at a higher pulse energy. If only modest enlargement was seen, laser treatment was repeated using the same parameters.

Animals were allowed to recover after laser treatment. The silicone cuffs remained *in situ* for the first 7 days. Serial angiography was performed as before at intervals for up to 60 days. In seven rabbits the contralateral CCA was excised shortly after laser dilatation, and angiograms were obtained 30 and 60 days later.

Sham-Treated Group. The effect of Tracker catheter and laser fiber insertion was determined in five vessels. Angiograms and morphological studies were obtained immediately after 200- μ m fiber insertion, and at varying intervals thereafter.

Laser Prophylaxis Group. In nine rabbits, laser energy of 7 to 10 mJ (20 to 50 pulses/cm of vessel) was applied unilaterally to a 4-cm length of normal CCA. Silicone sheaths and human blood were applied to the irradiated region either immediately thereafter (five vessels) or 7 days later (four vessels). Angiography was obtained simultaneously from left and right CCA's 24 hours after blood application, via a catheter placed in the aortic arch.

* Tracker-18 catheter manufactured by Target Therapeutics, San Jose, California.

† Dymed Spectrum Series 3010 pulsed-dye laser manufactured by Dymed Corp., Marlborough, Massachusetts.

Pulsed-dye laser treatment of vasospasm

Perforation Study Group. The threshold for laser perforation was determined in 16 normal CCA's. The vessels were exposed and kept moist by intermittent irrigation with Ringer's solution. A 200- μ m diameter quartz fiber was inserted into the artery as before, but was kept static within the vessel so that laser energy was applied to a single focus. The threshold for perforation was established at varying pulse energies when the fiber tip was placed either centrally within the vessel, adjacent to but not touching the wall, or indenting the artery. The position of the ball tip was verified by observation through an operating microscope. Irradiation was discontinued if perforation had not occurred by the 200th pulse.

Rabbits were sacrificed by pentobarbital sodium overdose. The brains were removed, sectioned at 5-mm intervals, and stained with 4% 2-3-5 triphenyltetrazolium chloride (TTC). The CCA's were excised after *in situ* perfusion through the ascending aorta with 1% glutaraldehyde solution containing 100 mM sodium cacodylate buffer at a pH of 7.4. The arteries were subjected to light microscopy (after hematoxylin and eosin and/or elastin staining) and/or transmission electron microscopy.

Dog "Two-Hemorrhage" SAH Model

Seven adult mongrel dogs, each weighing 20 to 35 kg, were anesthetized with 2.5% thiamylal sodium and ventilated mechanically with a dual-phase respirator.‡ End-tidal CO₂ was maintained at 40 mm Hg.§ The head was fixed in a stereotactic frame and left vertebral angiography was obtained via a No. 6.5 French catheter introduced from the femoral artery.|| The dogs were subjected to a "two-hemorrhage" SAH protocol as described previously.¹⁷ In brief, the occipitonal area was shaved and the head flexed acutely. The cisterna magna was punctured with a No. 19 needle. After withdrawal of 3 ml clear cerebrospinal fluid, 3 ml of fresh autologous nonheparinized blood was injected slowly into the subarachnoid space over 1 to 2 minutes. The stereotactic frame was removed and the animal was placed 30° head down for 20 minutes to promote pooling of blood in the basal cistern. Three days later a second hemorrhage was induced in a manner similar to the first.

In two animals, the time course of untreated vasospasm was established for up to 30 days by serial angiography. The remaining five dogs received endovascular laser treatment either 7 or 10 days after the first SAH. Following vertebral angiography, the left anterior spinal artery was catheterized with a Tracker-18 catheter. The tip was positioned, where possible, as far as the

bifurcation of the anterior spinal artery. A 125- μ bare fused silica quartz fiber (spot size 0.6 to 0.7 mm), with a platinum marker at the tip, was inserted into the catheter and manipulated as far into the basilar artery as possible. The catheter was then withdrawn into the vertebral artery, leaving the fiber *in situ*. An energy of 3 mJ was applied to the quartz fiber at a repetition rate of 2 Hz. Approximately 20 pulses/cm were applied to the basilar and anterior spinal arteries as the fiber was withdrawn progressively into the vertebral artery. Angiography was repeated immediately after treatment and at intervals for up to 60 days.

The animals were sacrificed by exsanguination under anesthesia, and perfusion through the left vertebral artery with buffered 1% glutaraldehyde solution at pH 7.4. The basilar artery was excised for morphological examination.

Data Collection and Analysis

All vessel diameters were measured angiographically using a $\times 7$ magnifying loupe. The x-ray source and film were kept at a fixed distance from the animal. The diameter of the rabbit CCA was measured at five points in the region under the silicone sleeve, while the diameter of the dog basilar arteries was measured at eight points throughout the laser-treated area (or equivalent area in the case of the two control studies).

Values are expressed as mean \pm standard deviation. Student's t-test, paired or unpaired as appropriate, was used to determine statistical significance. P values of < 0.05 were considered significant.

Results

Rabbit Common Carotid Artery Model

Control Group. The CCA diameter was uniform throughout the segment under study (mean diameter 1.93 ± 0.2 mm). The induction of bilateral CCA spasm was tolerated well, with a mortality rate of less than 8%. Vasospasm developed within 24 hours in more than 94% of the CCA's, and was generally more severe in younger animals. Arterial constriction reached a maximum at 24 and 48 hours, when vessel caliber was reduced to a minimum of 60% (1.15 ± 0.2 mm) and 53% (1.15 ± 0.2 mm) of control diameter, respectively. Vessel caliber enlarged progressively thereafter, was 80% (1.54 ± 0.4 mm) of control by 72 hours, and had returned to near-normal diameter 6 days after blood application.

Intracarotid injection of 30 mg papaverine over 5 minutes resulted in transient hypotension, but blood pressure in every case was normal at the time of repeat angiography. Arterial diameter increased by 11% in the segment of the artery in spasm (1.54 ± 0.2 mm vs. 1.33 ± 0.2 mm) and by 14% in normal CCA proximal to the segment in spasm (2.06 ± 0.2 mm vs. 1.8 ± 0.1 mm).

Carotid arteries in spasm exhibited the morphological characteristics of vasculopathy. An acute inflammatory

‡ Dual-phase respirator manufactured by Harvard Apparatus, South Natick, Massachusetts.

§ CO₂ monitor manufactured by Accucap, Datascope Corp, Paramus, New Jersey.

|| Catheter manufactured by Cook Co., Bloomington, Indiana.

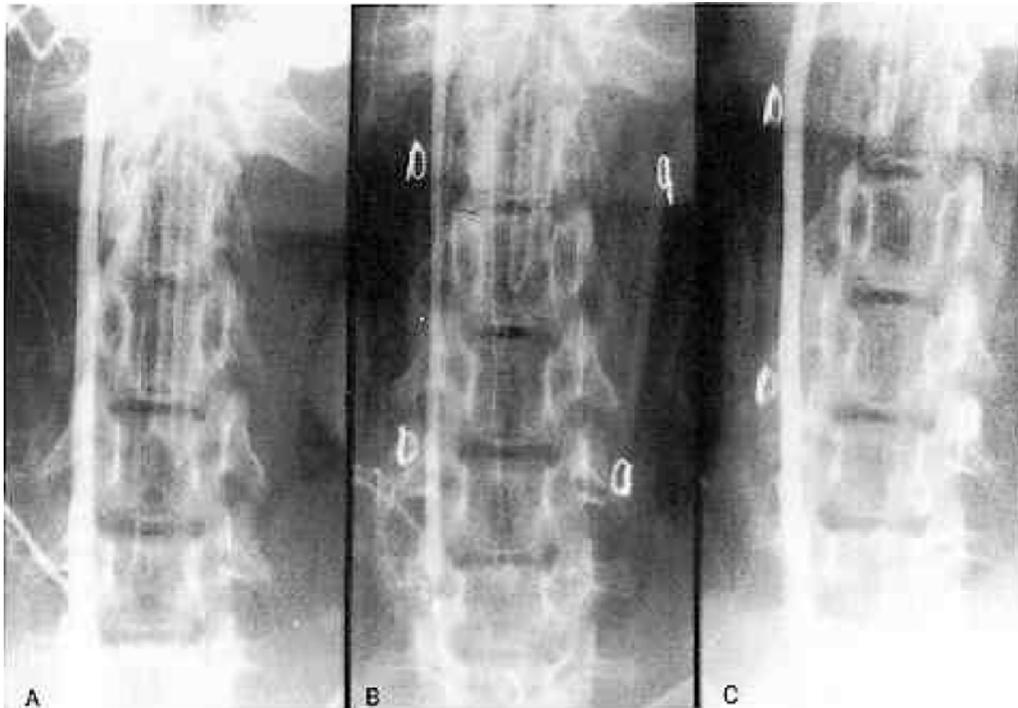


FIG. 1. Rabbit right common carotid artery arteriograms. A: Control group artery. B: Artery 24 hours after induction of vasospasm. The ends of the silicone sleeves are marked with copper wire. C: Artery immediately after laser treatment.

infiltrate was present in almost all cases within 24 to 48 hours of blood application, but the arteries appeared normal at 30 days. Erythrocytes were seen routinely within the adventitia of constricted vessels.

After ligation of the contralateral vessel, CCA diameter increased by 22% over a period of 60 days (2.37 ± 0.2 mm vs. 1.95 ± 0.2 mm), but no histological abnormalities were seen in these arteries.

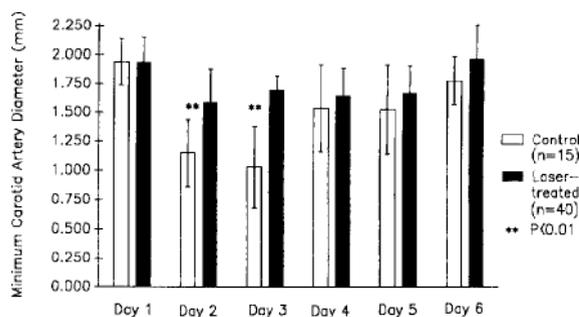


FIG. 2. Time course of treated and untreated vasospasm in rabbit common carotid arteries constricted chronically by the application of human blood within a silicone sleeve impregnated with 70% isopropanol. *Open bars* represent untreated vessels and *solid bars* indicate vessels treated on Day 2 with endovascular therapy from a 1- μ sec pulsed-dye laser (480 nm). Minimum arterial caliber in the region under the sleeve is given in both groups. Data are expressed as mean \pm standard deviation. n = number of arteries.

Laser Treatment Group. Intravascular pulsed-dye laser irradiation dilated the constricted CCA's in all 40 experiments. In one additional case (the fourth in the series), the CCA was perforated during insertion of the quartz fiber. In the remainder, between 15 and 64 pulses/cm of vessel at an energy ranging from 4.7 to 10 mJ were required to increase caliber from a peak spasm diameter of 60% of control (1.15 ± 0.29 mm) to a minimum post-laser diameter of 83% of control (1.59 ± 0.29 mm, $p < 0.001$) (Fig. 1). No more than three treatments were required for any single artery. The time course of treated and untreated vasospasm is shown in Fig. 2. Some return of constriction was observed in 50% of CCA's 48 to 72 hours after treatment, although at each stage vessels remained larger than in the untreated control group. Repeat constriction was seen only in arteries in which complete dilatation was not achieved initially. There were no instances of laser-induced perforation or of arterial thrombosis. Sixty days after laser treatment, the CCA diameter was a maximum of 11% larger than the untreated areas of the same vessel. Even after ligation of the contralateral CCA, there was no excessive dilatation of the laser-treated segment (maximum 6% larger than the untreated portion of the same artery: 2.6 ± 0.03 mm vs. 2.45 ± 0.02 mm).

Light microscopic examination of paraffin-embedded transverse sections, stained with hematoxylin and eosin or elastin, demonstrated that laser treatment was

Pulsed-dye laser treatment of vasospasm

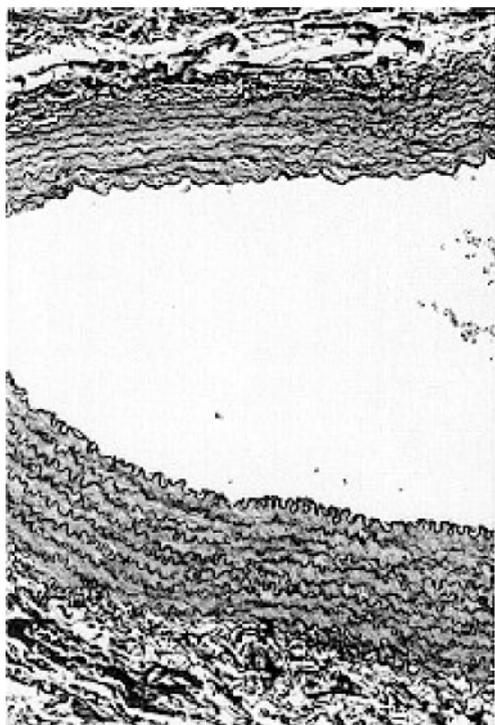


FIG. 3. Transverse section of a rabbit common carotid artery 24 hours after endovascular laser dilatation. While some parts of the vessel wall (top) exhibit loss of endothelial cells and stretching of the media and adventitia, other parts of the artery appear normal (bottom). Elastin. $\times 115$.

asymmetrical in every case. Large segments of the vessel circumference were often little different from control, while in other areas there was loss of endothelial cells immediately after treatment (Fig. 3). No disruption of the medial or adventitial cell layers was observed, although patchy loss of smooth-muscle cell nuclei was seen occasionally a few days after treatment. Intramural



FIG. 4. Transverse section of rabbit common carotid artery 60 days after laser dilatation. Intimal hyperplasia is evident in this segment of vessel, although the majority of the artery appeared normal. H & E, $\times 120$.

hematomas and dissections did not occur. Small patches of intimal hyperplasia, up to five cells in thickness, developed approximately 5 to 7 days after treatment and were present in almost all specimens by 60 days (Fig. 4). Regenerated endothelial cells were often cuboidal rather than flat, and were associated with intimal smooth-muscle proliferation. Similar findings were seen by electron microscopy. While in some areas there was complete loss of endothelial cells after dilatation, the opposite side of the vessel at the same point usually appeared normal (Fig. 5). Surprisingly, few platelets and erythrocytes were adherent to denuded areas.

A solitary laser-induced complication occurred when the quartz fiber became unbonded from its PTFE sheath. During treatment, only the PTFE covering was withdrawn into the Tracker catheter, while the fiber itself remained static within the artery. The entire dose

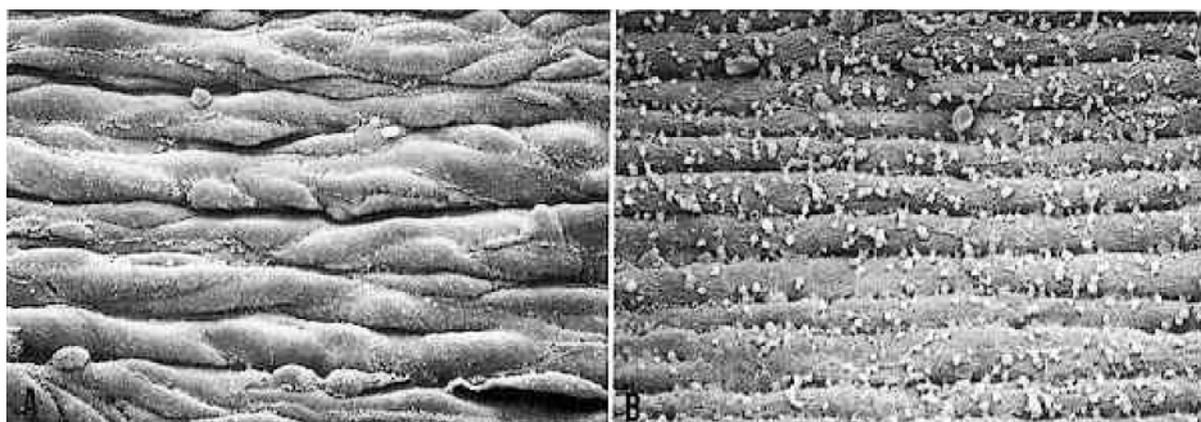


FIG. 5. Scanning electron micrographs showing opposite walls of a rabbit common carotid artery immediately after laser dilatation. *Bar* = $10 \mu\text{m}$. A: Normal endothelium. B: There is a loss of endothelial cells, with platelet adhesion to the internal elastic lamina.

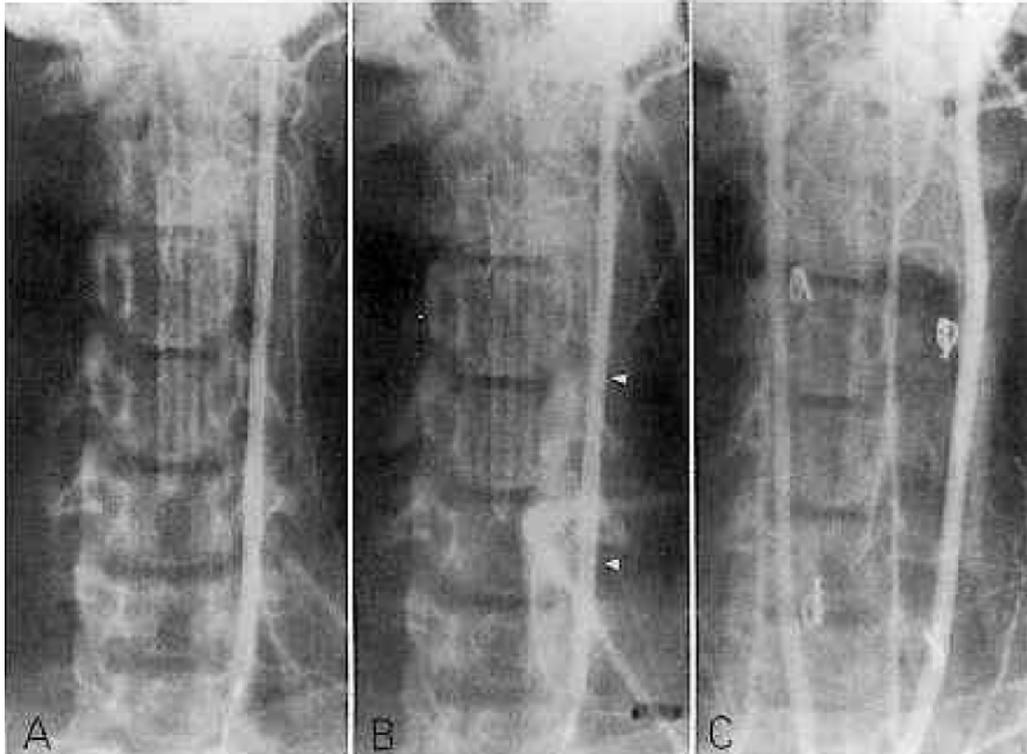


FIG. 6. Angiograms showing results of laser prophylaxis. A: Control vessels. The common carotid arteries (CCA's) were of the same caliber, therefore only the left is shown. B: Immediately after laser irradiation of the left CCA to the area marked by arrows. Silicone sleeves and blood were applied immediately. C: Arch aortogram 24 hours later showing considerably more spasm on the untreated side.

for the 3.5-cm segment of vessel was delivered to a focal point (spot size approximately 1 mm). A small saccular aneurysm (0.6 mm in diameter) developed immediately in the vessel, but did not enlarge over the ensuing 60 days.

No neurological complications attributable to laser treatment were seen, and no infarcts were visible in

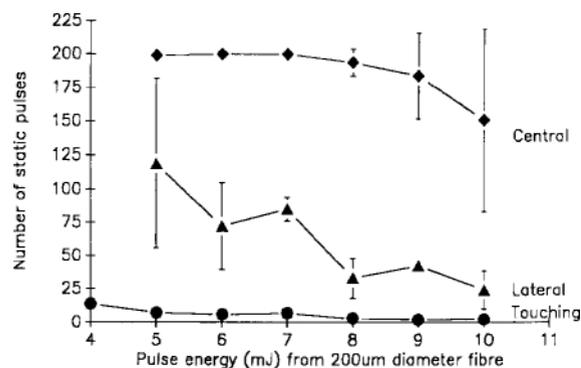


FIG. 7. Results of perforation studies in 16 normal rabbit common carotid arteries. Varying pulse energies were applied via a 200- μ m fiber which was fixed either centrally within the artery, adjacent to but not touching the wall, or indenting the vessel. Application was discontinued if perforation had not occurred by the 200th pulse. Results are expressed as the mean \pm standard deviation.

brains serially sectioned and stained with TTC. However, two control and three laser-treated rabbits were sacrificed prematurely because of the development of foot drop related to multiple femoral artery cannulations.

Sham-Treated Group. Sham laser treatment of five CCA's increased spasm immediately by an average of 15%, but this resolved within 20 minutes and subsequent caliber did not differ significantly from control arteries. In no instance was dilatation seen after insertion of the fiber or Tracker catheter. Scanning electron microscopic examination of these arteries demonstrated some immediate asymmetrical loss of endothelial cells but, unlike laser-treated vessels, intimal hyperplasia did not develop later.

Laser Prophylaxis Group. Laser irradiation of normal CCA's (7 to 10 mJ, 20 to 50 pulses/cm of vessel) did not alter the angiographic appearance of the vessel. The severity of vasospasm was significantly less in arteries in which blood was applied immediately after laser pretreatment (88% vs. 59% of control diameter; $p < 0.02$) (Fig. 6). However, laser pretreatment had no significant effect on the severity of spasm if blood was applied 1 week later.

Perforation Study Group. Because laser-induced perforations usually bled only momentarily, it was pos-

Pulsed-dye laser treatment of vasospasm

sible in most cases to perform multiple studies on different segments of the same artery. The threshold for perforation was dependent on both the pulse energy and the relationship between the fiber tip and the arterial wall. While at an energy of 8 mJ, 200 pulses rarely caused perforation if the fiber was centrally placed; lateral placement at the same pulse energy required an average of 33 ± 15 pulses to cause perforation, and if the fiber indented the artery only four \pm one pulses. The results of these studies are shown in Fig. 7.

Intravascular Treatment of Dog Basilar Artery

The "two-hemorrhage" protocol resulted in severe vasospasm in all dogs. Basilar artery diameter was reduced to $61\% \pm 10\%$ of control at 7 days, and $77\% \pm 8\%$ at 10 days. Laser treatment was attempted 7 days after induction of spasm in three dogs. In one it was possible to insert the quartz fiber tip to the mid-basilar region, while in the other two only the junction of the anterior spinal and basilar arteries was reached. The final two dogs were catheterized 10 days after the first SAH and, in both, the fiber was inserted to within 1 cm of the basilar apex. Laser treatment increased mean basilar and/or anterior spinal artery diameter to $104\% \pm 2\%$ and $102\% \pm 2\%$ of control at 7 and 10 days, respectively (Fig. 8).

Two dogs died immediately after laser dilatation; one was sacrificed electively and the other did not recover from anesthesia and died 2 hours later. In the second animal, which was treated 7 days after induction of vasospasm, great difficulty was encountered in negotiating the bifurcation of the anterior spinal artery to enter the basilar artery. Catheterization failed on one side of "the diamond," but was successful on the other. At postmortem examination, it was found that the entire laser-treated segment had dilated uniformly, but that the side of failed catheterization had perforated about 0.5 cm from the bifurcation.

No neurological deficit was apparent in the three surviving laser-treated dogs. In these animals, and in both controls, the basilar artery diameter at 30 days was smaller than the pre-vasospasm state ($80\% \pm 6\%$ and $82\% \pm 0.5\%$, respectively). However, in both groups, the vasodilatory response to hypercapnia (PaCO_2 70 mm Hg) was preserved (104% and 90% of basal diameter, respectively) (Fig. 9).

Morphological examination of the basilar artery immediately after laser treatment showed uniform loss of endothelial cells but, as with the rabbit model, there was little adhesion of red cells or platelets to denuded areas and no injury to smooth muscle. Sixty days after dilatation, vessels appeared normal throughout and, in particular, there was no evidence of intimal hyperplasia.

Discussion

This study demonstrates that the 480-nm 1- μ sec pulsed-dye laser is able to dilate both systemic and cerebral arteries in chronic spasm. Immediately after

laser application the diameter of rabbit CCA's was increased from 60% to 83% of control values, and dog basilar artery from 61% to 104%. Arteries remained larger than untreated control vessels for as long as vasospasm persisted. Laser pretreatment of normal rabbit CCA's attenuated the development of immediate vasospasm (88% vs. 59%), but not if spasm was induced 7 days later. Dilatation was well tolerated by both types of artery. There were no instances of laser-induced perforation, arterial thrombosis, or embolic complications. The only aneurysm to develop in experiments on 40 rabbit CCA's and five dog basilar arteries followed an accidental over-treatment.

Morphological examination has shown that laser dilatation results frequently in patches of endothelial injury. However, the presence of lesser changes in control animals suggests that this occurs in part as a consequence of catheterization. Only minimal injury is caused to the medial and adventitial layers.

Chronic Vasospasm in Rabbit Carotid Artery

Although systemic arteries differ in structure from intracranial vessels, chronic vasospasm still can be induced. Heterologous blood was contained within a silicone sheath to reduce the rate of resorption, and the tubing was impregnated with isopropanol to induce a slow rate of hemolysis. Peak spasm developed 24 to 48 hours later and persisted for up to 6 days. The response to intra-arterial papaverine was almost identical to that reported in dog basilar artery following experimental SAH.^{10,17} This model therefore fulfills the basic criteria for vasospasm: namely, chronicity, resistance to pharmacological vasodilators, and evidence of vasculopathy.

Laser Treatment of Systemic Vasospasm

Dilatation followed laser application in all experiments. Although overall the degree of dilatation achieved with the rabbit CCA model was less than that for the dog basilar artery study, this was the result of a different treatment strategy. In early rabbit experiments only the minimum energy necessary to cause any significant dilatation was applied. However, once it became apparent that injury to the vessel wall was minimal, treatment was continued in the remaining experiments until near-normal arterial caliber was restored.

Morphological Studies

Histological examination of CCA's demonstrated that morphological changes were asymmetrical in every case. This is thought due to the rigidity of the 200- μ m fiber and the curve at the origin of each CCA, which caused displacement of the fiber tip to one side of the artery. This has two consequences. First, the degree of injury caused to parts of the vessel wall is likely to be greater than necessary to cause complete dilatation. Indeed, in a small number of arteries examined no evidence of endothelial injury was seen, indicating that

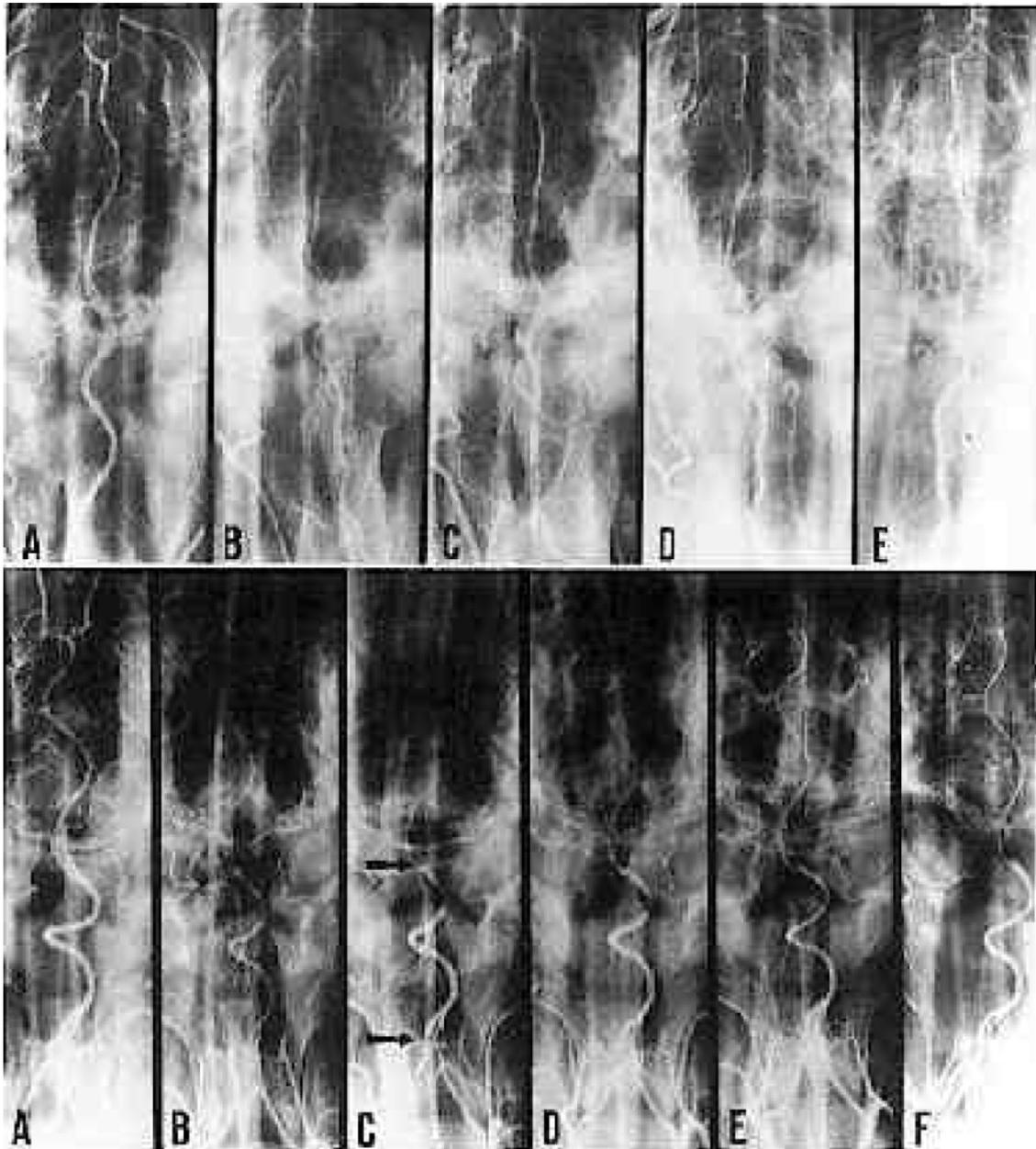


FIG. 8. Serial left vertebral angiograms. *Upper:* Studies in a dog that received endovascular laser treatment to the basilar artery 10 days after induction of vasospasm. A: Control study. B: Study before laser application. C: Study immediately after laser. The distal 1 cm of the basilar artery was not treated for fear that the fiber tip might perforate the basilar apex. D: Study 30 days later, PaCO₂ 40 mm Hg. E: Study at the same time as D with a PaCO₂ of 70 mm Hg. The vasodilatory response to hypercapnia is preserved. *Lower:* Results of endovascular dilatation of the anterior spinal and proximal basilar artery in a dog 7 days after induction of vasospasm. The caliber of treated and untreated portions of the same vessel is contrasted. A: Control study. B: Study before laser application. C: Study immediately after laser application to area between arrows. D: Study 24 hours later. E: Study 48 hours after laser dilatation. F: Study 4 days after treatment.

vascular damage is not an invariable consequence of laser therapy. Possible causes of endothelial cell loss are thermomechanical ablation⁶ or cavitation-mediated damage. Second, asymmetrical morphological changes may explain why repeat constriction was observed in

some vessels 48 to 72 hours after treatment. This occurred only in cases in which normal vessel caliber was not restored after laser treatment. Morphological examination of one such artery demonstrated that spasm recurred only on the under-treated side of the artery.

Pulsed-dye laser treatment of vasospasm

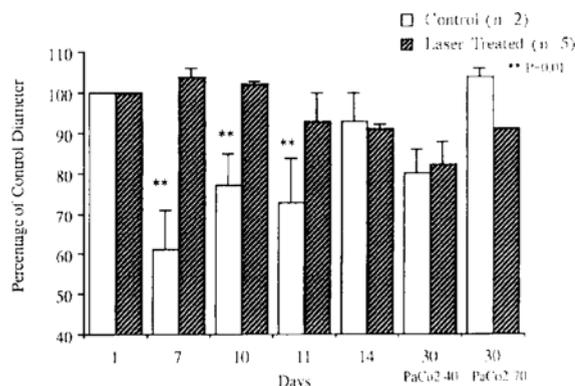


FIG. 9. Time course of untreated vasospasm (open bars) and following endovascular laser therapy (solid bars) 7 or 10 days after induction of chronic vasospasm in seven dogs by intracisternal injection of autologous blood 3 days apart. Data are expressed as mean \pm standard deviation.

Vasospasm Prophylaxis

Laser pretreatment of normal CCA's attenuated the development of immediate vasospasm, but not if spasm was induced 7 days later. This suggests that the laser effect may be relatively short-lived. However, because the artery appeared normal both before and after pretreatment, the laser energy administered was necessarily empirical, and it is possible that administration of a higher dose might have proved more effective.

Perforation Studies

Delivery of excessive energy to the rabbit CCA resulted in endothelial denudation, intramural hemorrhage, thermal debris, dissection, aneurysm formation, or perforation. The risk of perforation was dependent on both the pulse energy and, more important, the distance from the fiber tip to the vessel wall. There was a considerable margin between the energy necessary to induce dilatation and that which caused perforation at pulse energies within the therapeutic range, providing that the fiber was not placed near or touching the arterial wall. The demonstration that only a few pulses are necessary to cause perforation if the fiber indents the arterial wall has important implications for treatment. Laser energy should never be applied during advancement of the fiber, because of the high probability that perforation will occur when a tortuous segment of artery is encountered. For this reason, the fiber was inserted to the most distal extent of spasm, and treatment administered during fiber withdrawal into the catheter.

Laser Treatment of Cerebral Vasospasm

The canine two-hemorrhage SAH model is not ideal to study pulsed-dye laser treatment of vasospasm for two reasons. First, the dog basilar artery is formed not directly from the vertebral arteries but by the union of four anterior spinal arteries, and it is often very tortuous. Second, the smallest catheter that will deliver the

laser fiber has an external diameter of 1.3 mm, whereas the dog basilar artery in spasm is only approximately 0.9 mm. Catheterization is necessarily traumatic. In no dog treated 7 days after induction of vasospasm was it possible to insert the fiber to the basilar apex and, in one case, the anterior spinal artery was perforated during the attempt.

Results of laser treatment in the canine model were very similar to those in the rabbit CCA. Laser treatment restored the basilar artery to its prespasm diameter, and no long-term complications were observed. Although the arterial diameter was less than control values 30 and 60 days after treatment, this was true also for the control group, suggesting that this was a consequence of the SAH protocol. In both groups, the vasodilatory response to hypercapnia was preserved.

The morphological appearance of laser-treated dog basilar artery was similar to that of treated rabbit CCA. Focal loss of endothelial cells occurred immediately after treatment, but was not accompanied by large aggregations of platelets or red cells. Damage to the internal elastic lamina and media was negligible. However, the laser effect was much more uniform, and intimal hyperplasia did not occur as a late complication.

Mechanism of Dilatation

While the precise mechanism by which arteries are dilated has not been established, it is likely to be due to rapid vessel expansion caused by the enlargement and/or subsequent collapse of a cavitation bubble generated by erythrocyte microvaporization.⁴ The procedure merits comparison with balloon angioplasty, which has been used with some success in the treatment of cerebral vasospasm.^{9,12,20} Endothelial injury is also a complication of this procedure, and may result in progressive intimal smooth-muscle proliferation.^{3,19} Persistent and generalized loss of endothelium-dependent relaxation may occur.¹⁹ However, endothelial injury is not universal after pulsed-dye laser dilatation, and the degree of injury and subsequent intimal proliferation seen in rabbit CCA is considerably less than that observed after moderate balloon injury to rabbit iliac artery.¹⁹ The latter may be of importance since experiments have shown that endothelial dysfunction may persist after regrowth.^{15,19} Furthermore, lipid accumulates preferentially in areas of intimal thickening covered by regenerated endothelium, and may predispose to atherosclerosis.¹¹

Conclusions

These findings suggest that 480-nm 1- μ sec laser pulses may be of benefit not only in the treatment of established cerebral vasospasm, but also as a prophylactic measure in patients at high risk of developing this complication after aneurysmal SAH. Further work is required to optimize the delivery of laser energy to the vessel wall, in order to maximize vasodilatation while at the same time minimizing the risk of endothelial injury.

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