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Title

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METHODS

Laser-Assisted Thermal Angioplasty in Human Peripheral Artery Occlusions: Mechanism of Recanalization

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Recanalization of completely occluded superficial femoral or popliteal arteries was attempted in 18 patients with use of an Argon laser-mediated thermal probe. The length of the occluded segments varied between 0.5 and 26.0 cm, but 67% of the occlusions were >9 cm long. The initial success rate was 67%. Arterial perforation occurred in six patients but was not associated with major complications.

To study the mechanism of the laser-mediated thermal probe, thermal recanalization was performed on 11 human arterial segments in vitro obtained after amputation, and mechanical recanalization was performed in vitro in 10 human peripheral arteries with use of a guide wire and catheter technique. An additional four arteries were studied with the laser probe as a non-heated mechanical device.

Both the mechanical and thermal devices appear to follow a similar pathway through a complete obstruction. These studies suggest that the thermal probe burns through soft fibrous tissue but is mechanically deflected away from hard fibrocalcific plaque. The probe then advances along the plane between the intimal plaque and the media for a variable length before perforating through the adventitia.

These observations suggest that the major mechanism of thermal probe recanalization may be a mechanical process. It appears that thermal probe devices do not inherently seek the true lumen of an occluded artery and that better guidance systems need to be developed.

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After several reports (1-5) of the use of laser energy to ablate atherosclerotic plaque in vitro, the first human percutaneous attempt to remove atheroma from a stenotic artery was performed with argon laser irradiation (6). However, control of the delivery of argon laser energy through a bare fiber is difficult with fluoroscopic guidance (7). Several other methods have been developed to address the problem of laser energy control (8,9). Sanborn et al. (10) and Cumberland et al. (11) used an argon laser to rapidly heat the metal capped tip of an optic fiber probe to produce laser-mediated thermal recanalization of atherosclerotic arteries in patients. Abela et al. (12) studied a

delivery system that uses a sapphire lens in the center of the terminal metal cap, which allows both thermal energy and laser light to interact with the tissue. Although these techniques have been effective in recanalizing chronic, completely occluded arteries, there is a significant incidence of arterial perforation. Moreover, if this method of laser angioplasty is to be safely applied to the coronary circulation (13,14), it is important to understand its mechanism of action (15).

The purpose of the current study was to identify the factors that predispose to the success or failure of percutaneous laser-mediated thermal recanalization of occluded human peripheral arteries. In addition, in vitro experiments were performed on human coronary and peripheral artery segments obtained from amputated legs to understand the mechanism of action of the laser-heated probe and its mechanical and thermal interaction with atherosclerotic occlusions. In these in vitro studies, recanalization with the laser-heated probe was compared with recanalization attempts with a standard mechanical method with use of a multipurpose catheter or angioplasty balloon catheter over a guide wire.

Methods

Clinical Studies

Patient selection. There were 26 patients with complete occlusion of the superficial femoral or popliteal artery who were considered possible candidates for this study. Eight of the 26 patients were excluded because their peripheral angiograms demonstrated that there was no entry site into the proximal superficial femoral artery at its origin with the common femoral artery. Neither the length of the complete obstruction nor the angiographic appearance of the distal end of the occlusion was used as a criterion to exclude patients. The age of the 18 patients in this study ranged from 53 to 72 years (mean 66). All of the patients had symptoms of claudication in one or both legs that began 6 months to 5 years before their participation in this study. Six of the patients had pain at rest and one patient had gangrene of his toes and faced imminent amputation. Most of the patients were self-referred and requested to be entered into this study because they did not want to undergo peripheral bypass surgery. Two patients had prior balloon angioplasty or bypass surgery but not to the artery that was currently considered for laser recanalization. Baseline clinical evaluation, including Doppler-measured systolic occlusion pressure in the leg and arm, was performed in all 18 patients. The patients signed the institution's consent protocol for human experiments.

Laser angioplasty procedure. The affected artery was entered by a percutaneous anterograde puncture of the common femoral artery. A guide wire was used to selectively enter the superficial femoral artery and an 8.5F introducing sheath was inserted. Baseline digital and cine-film angiograms were obtained. Laser-mediated thermal recanalization was attempted with use of the technique personally demonstrated to me by T. Sanborn and described by Cumberland et al. (11). The catheter delivery system was the Laserprobe (Trimedyne Inc.), which consists of a 300 μm quartz optical fiber and a metal cap (1.5 to 2.0 mm diameter) that is attached to the end of the fiber.

The laser probe was advanced under fluoroscopic control to the level of the complete obstruction. An argon laser (Laser-Ionics or Trimedyne Optilase) was then turned on at 10 to 12 W. The probe was not moved for 3 s to permit the temperature of the tip to attain its maximum (approximately 200°C). The laser probe was then gently advanced against the leading edge of the atherosclerotic obstruction. After the probe was advanced 3 to 5 cm into the obstruction, the laser was turned off and the probe was moved back and forth rapidly to prevent adherence of the probe with tissue as it cooled down. The probe was then removed and contrast medium (Hexabrix) was injected through the introducing sheath to determine whether progress had been made or a perforation of the artery had occurred. The laser probe was then reinserted and the thermal recanalization process was continued until either the entire occluded segment was traversed with the laser probe fiber or perforation occurred.

If successful recanalization was accomplished with the laser probe, a 0.035 in. (0.09 cm) guide wire was inserted through a 6F multipurpose catheter and passed through the channel to the distal end where the artery reconstituted. The superficial femoral artery was dilated with a 5 or 6 mm diameter balloon, 5 to 10 cm in length. If the occlusion involved a more distal vessel such as the tibial artery, a 2 to 3 mm coronary artery balloon dilation catheter was used with an 0.018 in. (0.05 cm) coronary guide wire. After balloon dilation, peripheral angiograms were obtained with use of digital and cine film techniques. In four patients after balloon dilation, an angioscope (American Edwards) was inserted through the introducer sheath to visualize the internal vascular topography.

In Vitro Studies

Tissue selection. Segments of human atherosclerotic arteries were obtained at autopsy or from patients who had surgical amputation of the leg for symptoms of claudication with gangrene. The arteries were dissected from the leg and stored in cold saline solution. After transport to the laboratory, the arteries were cut into segments 2 to 10 cm in length and placed in a quick drying latex mold to add external support to the segments and thereby simulate the vessel in situ. Angiograms were performed on these segments to document the presence of complete occlusion. To ensure that the in vitro model did not predispose to arterial perforation because the arterial segment had been dissected free from supporting tissues, a second set of recanalization procedures was performed on four completely occluded peripheral arteries in situ. In these studies, the entire leg from two patients was brought to the laboratory after amputation. The anterior and posterior tibial artery was identified and an introducing cannula was positioned in the proximal end. An angiogram was performed to document complete occlusion.

Laser angioplasty protocol. In nine arterial segments and two arteries in situ, the laser probe was inserted and thermal recanalization was performed under fluoroscopic control according to the following protocol. First, the probe was placed within the lumen of the arterial segment and the tip was heated by an argon laser at 10 to 12 W of power. The laser probe was kept stationary for 2 to 3 s to permit the tip to heat up. Forward pressure was then applied gently to the probe such that the tip could be observed just to begin to bend under fluoroscopy. The laser probe was kept activated with gentle pressure applied for 5 s as it pressed against the obstruction. Intermittently, the catheter was pulled back and forth as it probed the obstruction with the laser activated. The laser was kept activated for a maximum of 10 s in any one continuous attempt. The laser procedure was completed

Figure 1. Femoral angiograms: **A,** A 10 cm long completely occluded left superficial femoral artery showing reconstitution of the distal portion from collateral vessels of the femoral profundus artery. **B,** The result after laser recanalization and balloon dilation. The proximal residual dissection was created by the balloon dilation. The laser probe was not used over the portion of the artery that developed the dissection.
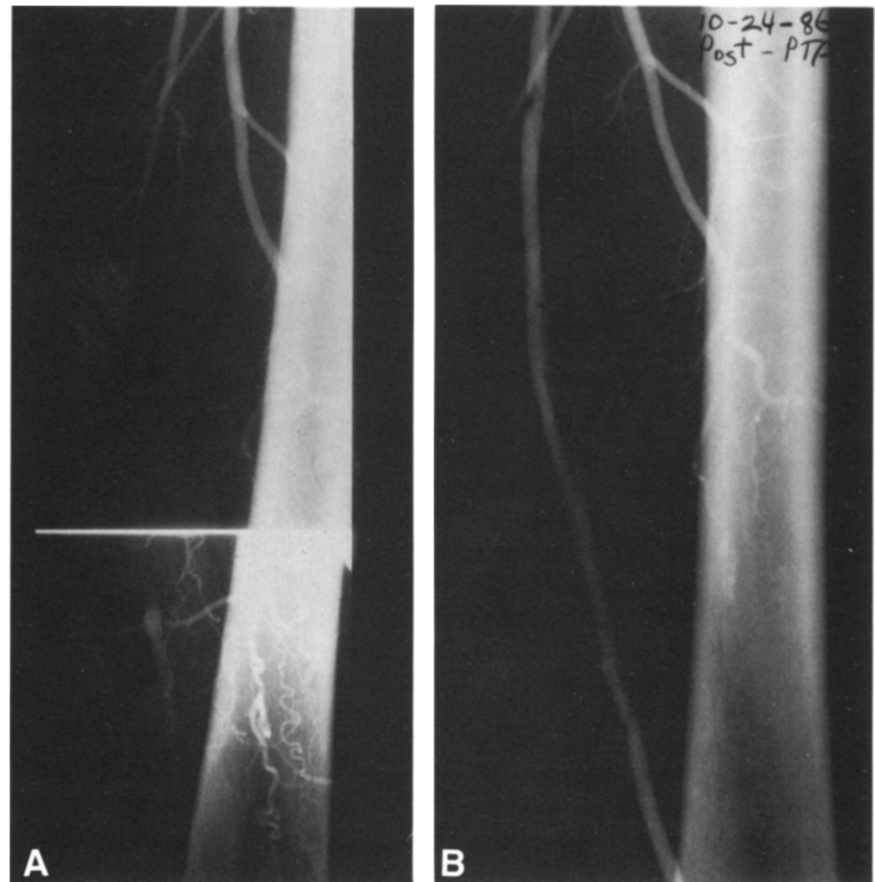
when either the laser probe passed through the distal end of the arterial segment or the external wall of the artery was perforated.

In eight other isolated arterial segments and in two in situ arteries, mechanical recanalization was attempted with a 6F multipurpose catheter and an 0.035 in. (0.09 cm) guide wire or with a balloon dilation catheter. In another four arterial segments, the laser probe was used as a mechanical device in a manner similar to the use of a guide wire. The probe was not heated during the process of recanalization in these four arteries.

The course of the laser probe or guide wire was determined by two methods. One third of the arteries were dissected longitudinally to observe the tract created during the recanalization process. In the other arteries, a 3-0 silk suture was tied to the distal end of the guide wire or the laserprobe after completion of the procedure. This suture was pulled back through the created lumen and kept in place during preparation for histology. The suture material was visible within the sections and distinguished the path of the laser probe or catheter from the natural lumen or artifactual clefts.

Results

Clinical Studies

Successful results. In the 18 patients, there were 12 primary successful procedures (67%). A successful procedure was defined as one in which the occluded segment was recanalized and anterograde flow through the length of the artery was visualized during angiography (Fig. 1). The mean baseline Doppler audible systolic occlusion pressure ankle/arm index was 0.62 ± 0.10 before laser and balloon angioplasty and 0.86 ± 0.05 after the procedure in the 12 patients who had an initially successful result.

The measurements of the length of the completely occluded segments and the diameter of the nondilated segment of the arteries are shown in Figure 2. The mean length of the totally occluded artery was 10.9 ± 7.2 cm (range 0.5 to 26.0). The mean diameter of the apparently normal segment was 4.4 ± 1.2 mm. The mean diameter of the narrowest segment after successful laser and balloon dilation was 4.0 ± 1.4 mm.

The variables that appeared to affect the results were the length of the obstruction, vessel tortuosity and dense calcifications in the plaque. Table 1 shows the success of the laser recanalization as a function of the length of the completely
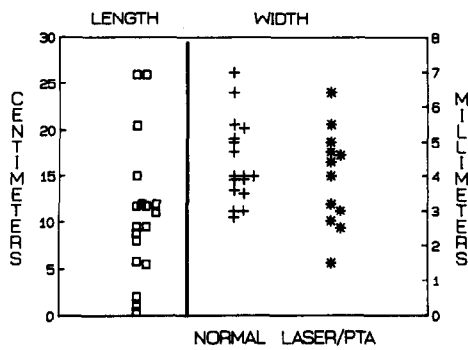
Figure 2. Length of obstructions and diameters post-laser angioplasty in 18 patients: the length of the completely occluded segments are displayed on the left panel (**open boxes**). The graph on the right shows the diameter of the presumed normal portion of the artery (**crosses**) compared with the diameter achieved after successful thermal recanalization and balloon dilation (**asterisks**). The mean diameter after successful angioplasty (laser/PTA) was not significantly different from the mean diameter in the presumed normal section.

occluded segment measured from the baseline angiogram. Calcium was present within the superficial femoral artery in 14 (78%) of the 18 patients by visual assessment of the scout film. Of the six patients who developed arterial perforation, calcium was present in five (83%). The size of the artery diameter distal to the occlusion did not affect the immediate outcome, however, poor distal runoff predisposed to reocclusion.

Reocclusion. Early reocclusion occurred in two patients with a long obstruction and poor runoff or intimal disruption. In one of these two patients, collateral vessels did not completely disappear after recanalization and dilation. Figure 3 demonstrates the angiographic and angioscopic images from a patient who had extensive disease throughout the superficial femoral artery with a complete occlusion 15 cm in length. The angioscope revealed a large flap of tissue that protruded into the lumen of the artery. The angioscopic images were more revealing than the angiograms for the extent of intimal and plaque disruption that occurred after the balloon dilation. Although the patient initially had a successful laser and balloon angioplasty, the artery reoccluded within 1 week after the procedure. During a second attempt at dilation, organizing thrombus was removed
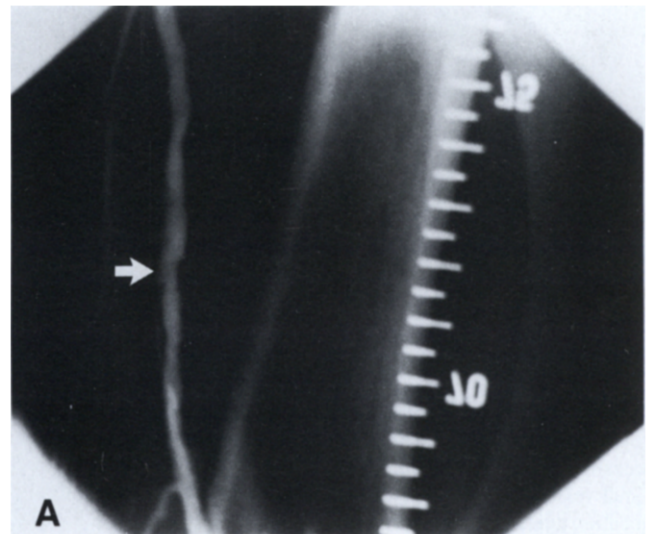
Table 1. Laser Angioplasty Success as a Function of Lesion Length

Length of Total Occlusion (cm)	Success	Failure
>10	5	4
<10	7	2
	p = NS	

Figure 3. **A,** Angiogram of a superficial femoral artery obtained after Laserprobe recanalization and balloon dilation of a 15 cm long complete occlusion. Although there is angiographic evidence of plaque disruption (**arrow**), there was good flow through the artery. **B,** The image obtained through an angioscope from the section of the artery at the position demonstrated by the arrow. There is a large flap of atheroma plaque protruding into the lumen. Although the angiogram reveals evidence for plaque disruption, the extent of the dissection and the topographic significance of the flap formation is only appreciated from the angioscopic image.

through a catheter from the arterial segment where the tissue flap had been observed.

Adverse effects. The procedure was well tolerated in all patients. The major complaint was the length of time required to lie on the X-ray table. Six patients experienced a transitory burning sensation when the activated laser probe was left in place against the atheroma for >10 s. A small, localized hematoma occurred in two patients who had an

arterial perforation, and they were kept in the hospital an extra day for observation.

Arterial perforation. During these procedures, the occluded artery was perforated by the laser probe in six cases. In one of the six, the artery was later successfully recanalized by mechanical methods; after the balloon dilation, there was no angiographic evidence of the perforation. In the other five patients, the procedure was terminated after the perforation because the probe preferentially sought out the newly created false lumen. In two of the six patients, perforation resulted in a small (1 to 2 mm diameter) arteriovenous fistula. This fistula was sealed with catheter-directed placement of Gelfoam and coiled springs. Although perforation precluded further percutaneous attempts at recanalization, the patients did not have any clinical sequelae and could proceed to elective surgical bypass. A longer-term complication of the procedure occurred in one patient. In this patient, a 26 cm long occlusion was at first successfully recanalized. However, one of the collateral vessels from the proximal superficial femoral artery was occluded as a result of the balloon dilation. In this patient, the artery reoccluded with thrombosis 1 week later and the patient's symptoms were exacerbated because of the diminished collateral blood flow.

In Vitro Studies

Recanalization was attempted by one of the three methods in 25 occluded human atherosclerotic peripheral and coronary artery segments.

Mechanical recanalization with guide wires. In 8 of 10 arterial segments, the guide wire did not remain within the central intimal plaque. On histologic and gross specimen analysis, the path of the guide wire was observed to deflect around the fibrocalcific plaque and advance in a plane between the intima and media (Fig. 4). From this peri-intimal plane, the guide wire perforated through the media and adventitia in two arteries.

Thermal recanalization. In 10 of the 11 arteries studied with the heated thermal probe, the probe deflected off the fibrocalcific atheroma and advanced in the plane between the intimal plaque and the internal elastic membrane adjacent to the media rather than advancing through the center of the plaque (Fig. 5). This action occurred whether the isolated artery segment or the artery in situ was used. The thermal probes advanced through the central portion of the plaque in only one artery. In the other 10 cases, the thermal probe perforated the arterial wall.

Mechanical recanalization with the non-heated probe. In all four arterial segments where the laser probe was used as a nonheated mechanical device, the nonheated probe was deflected from the plaque and advanced within the plane between the intima and media. There was one arterial

perforation when the laser probe was used as a nonheated device.

Discussion

Clinical studies. To interpret the results of our clinical study, it is necessary to understand the varying degrees of difficulty of the arterial occlusions that were attempted. For instance, 12 (67%) of the 18 patients had a completely occluded segment that was 9 to 26 cm long. The success rate would be expected to be low with use of a traditional guide wire and catheter approach to mechanically create a new lumen through such a long occlusion. This patient selection bias is not surprising because the majority of these patients were self-referred because they were not considered appropriate for balloon angioplasty and they did not want to undergo surgery. Despite a high percentage of relatively long occluded segments, the laser probe was used successfully in 12 (67%) of the 18 patients to recanalize the segment. Given the type of patients studied, we consider this to be an acceptable result, especially in view of the minor effects of the complications.

Although they did not reach statistical significance, the factors that appeared to affect the outcome of these procedures included the length of the complete occlusion, the tortuosity of the vessel and the extent of calcium in the occlusion. Although the laser probe fiber is flexible, it is difficult to make sharp directional changes. As a result, the probe needs to be aligned coaxially with the occluded vessel. This procedure is demanding because there is no contrast within the occluded segment of the vessel to delineate its course. Perforations also tended to occur when the obstruction was very firm and resisted gentle pressure from the heated tip for >7 s.

In addition to the immediate outcome of the laser procedure, other factors affect the long-term results such as the quality of the runoff in the distal vessels. The presence of diffuse disease in the tibio-peroneal arteries establishes a setting of diminished blood flow that increased the risk of thrombosis after the procedure. One marker of an adequate result is the disappearance of collateral blood vessels to the distal artery.

In vitro studies. The results from the in vitro studies suggest a mechanism of laser-assisted recanalization that may explain the high incidence of perforation in our clinical cases. Although one explanation of this high rate may be the effect of an unavoidable learning curve for any new method, a recent report (16) by an experienced interventional radiology group demonstrated similar results to ours. These experiments in human arteries suggest that both guide wires and thermal probes follow a similar course when they create a new channel in an artery (17–19). It was very uncommon for either device to penetrate the central portion of a hard atheroma. Rather, both devices usually deflected around
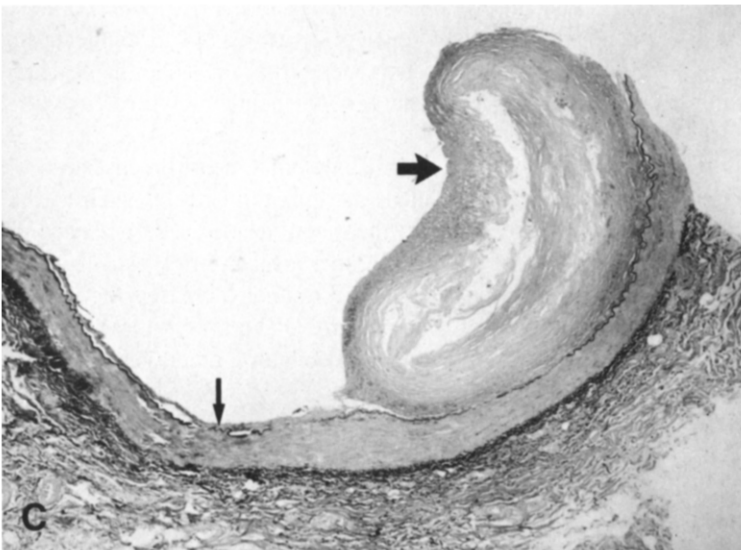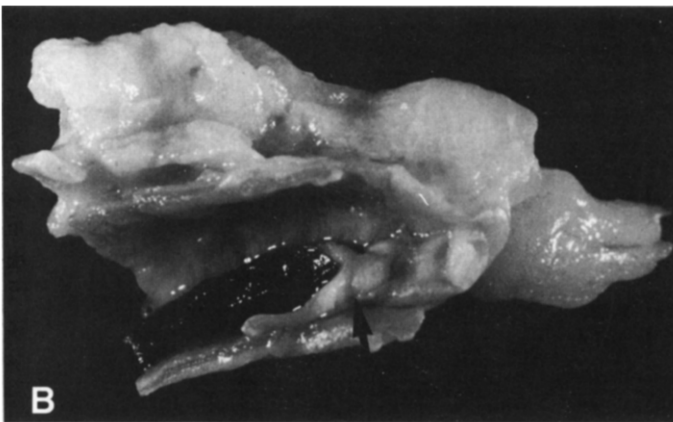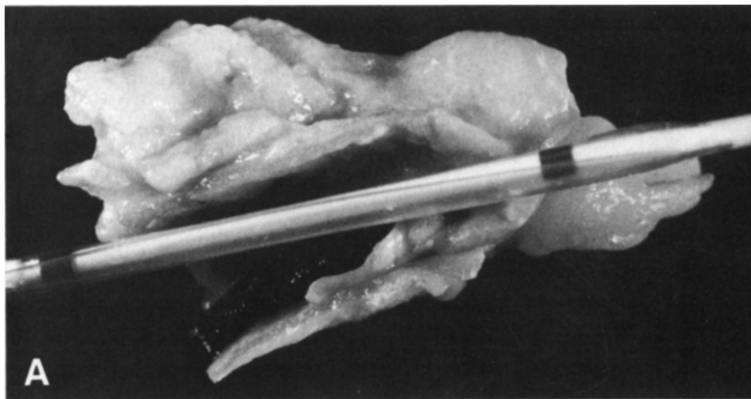
Figure 4. This completely occluded arterial segment was recanalized with an 0.018 in. (0.05 cm) guide wire and a 3.0 mm diameter angioplasty balloon. The artery was opened longitudinally before histologic section. A, The path of the balloon is demonstrated. B, With the balloon removed, the obstruction was noted to consist of a pre-existent thrombus that funneled into a fibro-theromatous plaque that occluded the artery. The guide wire did not pass through the clot or the central atheroma but was observed at the periphery of the plaque. C, This histologic cross section was taken at the level of the arrow in Figure 4B. The guide wire and balloon were deflected from the central atheroma occlusion and advanced along a plane that was just central to the internal elastic membrane (thin arrow) but was still within the intima. The inflation of the balloon indented the atheroma laterally from its side (thick arrow) and stretched the external arterial circumference.

firm atherosclerotic plaque and entered a plane between the intima and media, proximal to the internal elastic lamina. From this position, the guide wire, nonheated probe or the probe heated by the laser may successfully reenter the distal lumen where the atheroma plaque is thinner, or they may continue to be deflected and perforate the external arterial wall. The observation that the nonheated probe functioned in a similar manner to the guide wire and the probe when heated with the laser suggests that a similar mechanism of action may occur with all of the devices. It appears that the
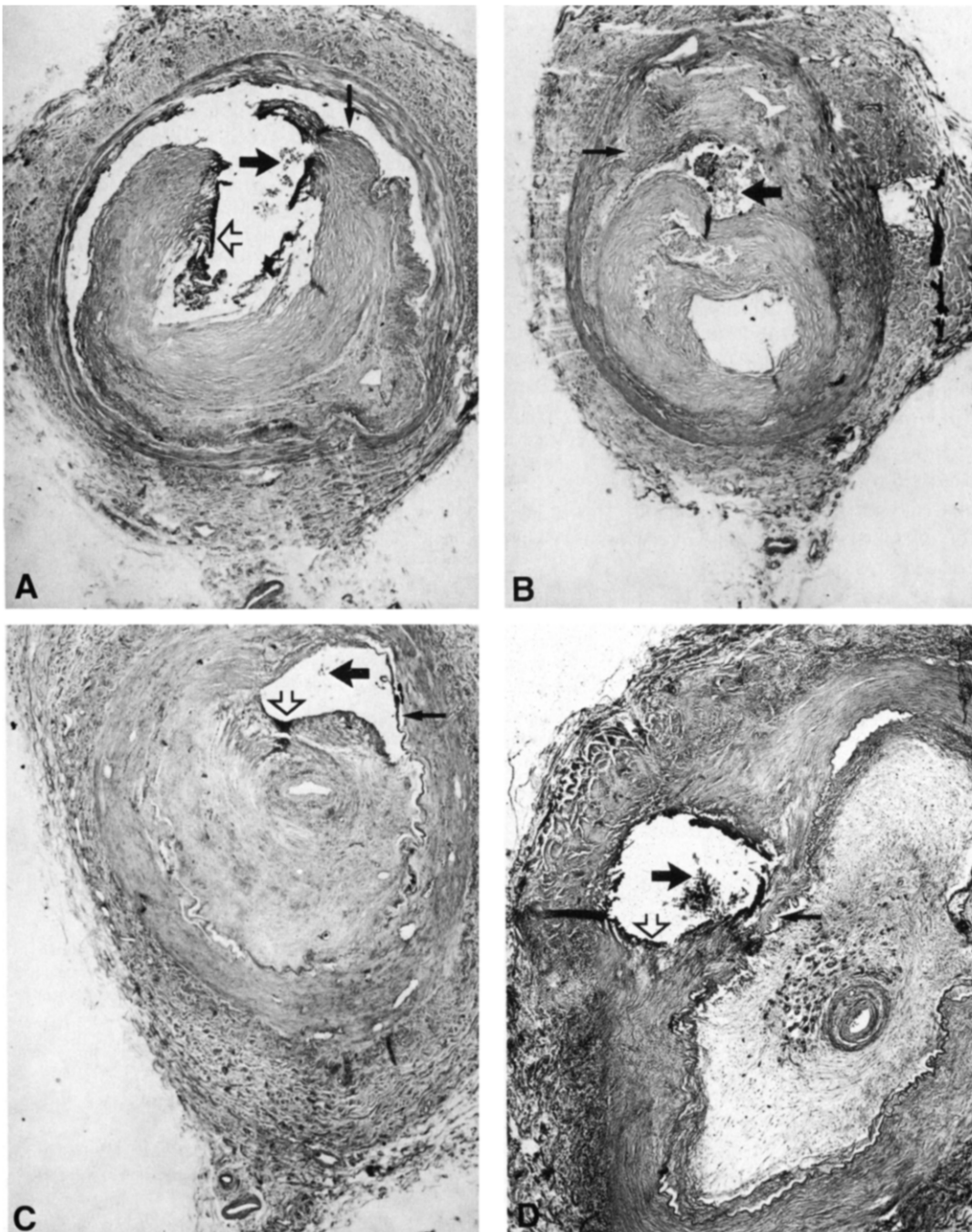
Figure 5. The path of the laser probe is demonstrated in this sequence of slides from the proximal to the distal end of an 8 cm long completely occluded arterial segment. **A,** The laser probe has burned a new lumen into the central portion of the atheroma as documented by the residual suture material **(thick arrow).** The burned tissue is seen as the darker stained material **(open arrow).** The thermally created channel lies within the internal elastic membrane **(thin arrow).** **B,** (1 cm more distal), the channel created by the laser probe is still within the intima but lies outside of the native lumen. The new channel lies within a portion of atheroma that appears less dense than the central fibrous tissue. The silk thread fibers **(thick arrow)** are well within the internal elastic membrane **(thin arrow).** **C,** (3 cm more distal than A), the lumen created in the atheroma by the laser probe is still within the intima, however, the pathway now is adjacent to the internal elastic membrane **(thin arrow).** The silk fibers **(thick arrow)** are within a lumen that is different from the remaining central native lumen. Thermal effect is noted at the open arrow. **D,** (5 cm distal to the position in A), the Laserprobe channel has crossed the internal elastic membrane **(thin arrow)** and is within the media. A circumferential burning effect is noted (open arrow). Silk thread fibers **(thick arrow)** document the laser probe path.

thermal probe is more likely to perforate the artery than the mechanical guide wire once it is in the plane between the intima and media because of the high temperature that is directly applied to the relatively thin media.

The higher incidence of perforation in the in vitro studies may be due to the smaller diameter of the tibio-peroneal arteries that were used and the greater extent of calcification compared with the incidence of perforation in the superficial femoral arteries of the clinical cases. The numerical perforation rate in the in vitro model is not of primary concern. The purpose of the present study was to attempt to understand the mechanism of successful recanalization or perforation both with traditional mechanical techniques and the newer thermal method. The justification for using as our model human peripheral atherosclerotic occlusions is that they consist of hard fibrocalcific disease that has developed over many years and more closely resemble the obstructions encountered in vivo compared with the animal model of atheroma, which is made of soft, fat-laden cells and is very different from the pathologic features of human disease.

Conclusions. The results of this study confirm initial reports (10,11) that laser-assisted thermal angioplasty is useful in reestablishing a patent lumen in long, completely occluded peripheral arteries that might otherwise require bypass surgery. The previously reported incidence of perforation (11) was significantly lower than ours, which might be explained by our selection of patients and the average length of obstruction. Our experimental observations may help to explain what occurs clinically in human atherosclerotic obstructions when a thermal probe is applied. If the obstruction is filled with thrombus or soft atheroma, the heated probe can burn through the tissue relatively easily. However, when the obstruction is a hard, fibrocalcific plaque, the probe may be deflected and burn through the intimal plaque, advance between the plaque and the media and either reenter the lumen distally or perforate externally. These observations indicate that physicians need to be cautious with thermal recanalization devices because they do not inherently seek the true lumen of the artery. In addition, these studies suggest that the major mechanism of thermal probe recanalization may be a mechanical process. To test this hypothesis, a randomized clinical trial comparing standard mechanical methods and the laser-heated thermal probe is required.

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