Editorial

Laser Angioplasty
What Has Been Learned From Experimental Studies and Clinical Trials?

Timothy A. Sanborn, MD

“Today, many have not yet seen how advances in technology are transforming our lives. . . . New laser techniques could revolutionize heart bypass surgery . . . reduce hospital costs dramatically and hold out new promise for saving human lives.” President Ronald Reagan, State of the Union Address, February 6, 1985.

Viewing the field of laser angioplasty in 1988, we see a tremendous variety of approaches in different stages of experimental and clinical investigation (Table 1). For those who do not follow the field closely, it must be quite confusing to understand where this “Star Wars” approach to cardiology stands. For those in the laser field, perhaps it is time to define precisely what we wish to accomplish with lasers and to be specific in our terminology. Originally, the phrase “laser angioplasty” described the intravascular use of lasers (light amplification by stimulated emission of radiation) and was used to draw similarities to the recognized and established procedure of balloon angioplasty. However, the actual in vivo mechanisms of action or the pathophysiological effects of various laser devices on obstructive vascular diseases remain to be elucidated. More specific terms would improve the understanding of the technique and better define its role in relation to existing balloon angioplasty. Alternative terms have been used to describe potential cardiovascular uses and pathophysiological effects of laser energy and include 1) laser recanalization before balloon angioplasty, consisting of laser vaporization or removal of atherosclerotic material or laser thermal compression of occluded tissue and 2) laser sealing of intimal dissections after balloon angioplasty.

Laser Recanalization

While balloon angioplasty has been very successful in the treatment of high grade stenoses and relatively acute totally occluded vessels, one of its limitations has been in the treatment of chronic total occlusions where the ability to cross the occlusion is difficult or impossible. In these situations, laser recanalization has been proposed as a means of crossing lesions to allow for subsequent successful balloon angioplasty. Presently, this recanalization is defined angiographically; we are only beginning to understand the actual pathophysiological mechanism of laser recanalization and to determine how much is true laser vaporization of atherosclerotic material and how much is attributable to catheter dilation or laser thermal compression of occluded tissue.

Clinical results with bare fiberoptics. As with balloon angioplasty, to investigate the safety and efficacy of laser recanalization, this procedure was attempted in peripheral vessels first before considering coronary application. In the early phase of laser angioplasty investigation, several clinical trials were initiated with bare argon laser fiberoptics. In these studies, a variety of laser powers and pulse durations were used with both antegrade and retrograde laser delivery through total or subtotal femoropopliteal occlusions before balloon angioplasty. Improvement on angiography was only noted in one half to two thirds of patients after delivery of laser energy. Further, despite the fact that the fiberoptics were positioned coaxially in the center of the arterial lumen inside angiographic or balloon catheters and the fact that the fiberoptics were withdrawn through previously recanalized lesions in the majority of cases, there still was a 13–18% incidence of vessel wall perforation. Thus, the key limitations in these early clinical series of laser recanalization were inadequate channels and difficulty controlling the narrow laser beam.
as it exited from the fiberoptic. In the future, regardless of the laser wavelength used (argon, Nd: YAG, excimer, or carbon dioxide), similar problems of vessel perforation will undoubtedly remain as long as a narrow beam of laser energy is used. Currently, modified fiberoptic tips have demonstrated the greatest promise in laser recanalization.

Modified fiberoptic tips: Experimental results with the argon laser probe. The first, but certainly not the last, modified laser delivery system to demonstrate a high incidence of successful laser recanalization with a low incidence of vessel perforation is an argon laser-heated metallic-capped fiberoptic device (Laserprobe-PLR, Tridedyne, Santa Ana, California). Three in vivo experimental studies have now been published that demonstrate not only improved safety and efficacy of this laser-heated probe compared with bare fiberoptics\textsuperscript{3,4} but also less restenosis than conventional balloon angioplasty.\textsuperscript{5} First, in a series of 24 atherosclerotic rabbit iliac artery stenoses,\textsuperscript{3} angiography revealed greater widening of luminal stenoses in animals treated with the laser probe device as compared with a standard fiberoptic system. More important, while perforation of the vessel wall occurred frequently with the fiberoptic fiber, only one mechanical perforation occurred in 12 animals treated with the laser probe.

Histology in the acute phase revealed striking differences with these two fiberoptic systems. With direct laser radiation from the bare fiberoptic, a typical localized laser "crater" was noted along one side of the vessel wall with charring and considerable thrombus formation. On histological cross sections of eccentric lesions, the major portion of the atherosclerotic lesion was often "missed" by the narrow laser beam. In contrast, those vessels treated with the laser-heated metallic probe showed histological evidence of thermal injury distributed evenly around the entire luminal circumference with no charring and thinner, flatter thrombus formation. These histological data suggest that circumferential rather than localized distribution of energy is a factor in these improved results. The rounded metal cap was also beneficial in reducing mechanical perforation. These results were confirmed in a series of postmortem human coronary arteries xenografts transplanted into the canine femoral artery.\textsuperscript{4}

Recent follow-up angiographic and histological studies in the rabbit model demonstrated better long-term patency with laser thermal angioplasty in comparison with conventional balloon angioplasty.\textsuperscript{5} While the immediate enlargement of the angiographic luminal diameter was similar for both procedures, the vessels treated with 1.5–2.0-mm laser probe devices had less angiographic restenosis and a significantly larger angiographic mean luminal diameter than those treated with balloon angioplasty. On histological study 4 weeks after the laser procedure, there was a larger lumen, minimal thrombosis or smooth muscle cell proliferation, and a thin neointima covered with a fibrous cap. In contrast, those vessels treated with balloon angioplasty demonstrated evidence of previous fracture and dissection of the vessel wall\textsuperscript{5} with more of a fibrocellular proliferative response and ongoing thrombus formation (Figure 1). Morphometric analysis of these histological cross sections confirmed a significantly larger luminal area after laser thermal angioplasty compared with balloon angioplasty.

Thus, laser thermal angioplasty was associated with less restenosis and produced a significantly larger mean luminal diameter and mean luminal area than conventional balloon angioplasty. The differences in the pathophysiology of these techniques is probably responsible for these observations. That is, with laser recanalization of these high-grade stenotic lesions, there is partial laser vaporization or removal of atherosclerotic material and, perhaps more important, a smoother, less-thrombogenic surface is left behind compared with balloon angioplasty. Whether there is an additional thermal effect on the arterial wall that inhibits platelet accumulation or smooth muscle cell proliferation is another intriguing concept.

Clinical laser probe recanalization. After demonstrating the safety and efficacy of this device in

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<td>Spectral region</td>
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<td>Visible</td>
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<td>Wavelength (nm)</td>
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<td>488,514</td>
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<td>Delivery systems</td>
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FIGURE 1. Panel A: Cross section of a patent rabbit iliac vessel 4 weeks after laser thermal angioplasty demonstrating minimal fibrocellular proliferative response and a thin, condensed fibrous cap. Panel B: Histological section 4 weeks after balloon angioplasty revealing moderate fibrocellular proliferation caused by the dilation, which partially fills the lumen and obliterates the prior dissection planes between the neointimal flaps and the media (Verhoff–Van Gieson elastin stains; magnification, ×40). Reproduced with permission of Sanborn TA et al (Circulation 1987;75:1281–1286) and the American Heart Association.

Experimental animals, a clinical trial was initiated to investigate its role in performing percutaneous laser thermal angioplasty as an adjunct to balloon angioplasty in patients with severe peripheral vascular disease. The initial aims were twofold: first, to demonstrate the safety of this laser device and, second, to determine whether this procedure could add to conventional balloon angioplasty by increasing the initial success rate in peripheral artery total occlusions and recanalizing occlusions in which balloon and guide-wire techniques had failed. In an initial study, laser recanalization was achieved in 50 of 56 (89%) femoropopliteal and iliac artery occlusions. From a previous assessment of the angiogram or gentle probing of the proximal origin of the occlusion with a guide wire, the lesions were subjectively classified as “easy” (17 lesions) or “difficult” (21 lesions) to cross by conventional angioplasty methods. Eighteen occlusions were classified as “impossible” either because previous angioplasty attempts had failed (11 occlusions) or because they were considered unsuitable for conventional angioplasty (seven occlusions). All 17 easy, 19 of 21 difficult, and 14 of 18 impossible occlusions were successfully recanalized. Because there were two acute recurrences in the first 24 hours, the overall initial clinical success rate was 86%. These results compare favorably to recent clinical success rates of 72–78% for conventional balloon angioplasty of femoropopliteal occlusions.

In this initial series, the perforation rate was less than 2%, and this one perforation was attributed to
excessive mechanical pressure within a hard calcified occlusion rather than thermal perforation. In February 1987, based on similar results in 219 patients treated in 10 medical centers, the laser probe device was approved by the FDA for clinical use in peripheral arterial lesions considered difficult or impossible to treat by conventional means.

Other modified tips. With the success of this elliptical-shaped laser-heated probe, a variety of other tip modifications are now being developed to avoid the problems of vessel perforation and small recanalization channels that complicated laser recanalization with bare fiberoptics. As listed in Table 1, these include sapphire tips, lensed tips, and a combination metal cap–sapphire tip (hybrid probe). One recent in vitro study of the Nd:YAG laser sapphire tip indicates that the mechanisms of action of this laser device may be very similar to the laser probe in that a greater volume of tissue and a wider laser crater could be created in atherosclerotic human cadaver aortic tissue compared with bare fiberoptic fibers. Preliminary reports of percutaneous peripheral laser recanalization with the Nd: YAG sapphire tip in eight patients with femoropopliteal occlusion indicate its clinical feasibility. Obviously, additional clinical studies of this and other modified fiberoptics are necessary to determine the ideal laser delivery system.

Additional approaches. Besides the above laser thermal recanalization techniques, investigation has also been directed to determine whether other factors could enhance the safety and efficacy of recanalization. Most of these approaches are still in the experimental stages of investigation; however, a few have reached early clinical trials. Briefly, these approaches include angioscopic, spectroscopic, or ultrasonic guidance rather than the current fluoroscopic control; selective plaque ablation with endogenous or exogenous chromophores; “less thermal” vaporization with shorter pulse duration lasers (excimer or Q-switched Nd:YAG); nonlaser thermal probes (electrical or chemical); and mechanical devices.

In the future, the best recanalization system may depend more on various catheter parameters such as flexibility, profile, axial strength, “trackability” over a guide wire, safety, and, ultimately, the long-term clinical outcome rather than the energy source itself.

Pathophysiological Mechanisms

Laser vaporization and thermal compression. While there is a great deal of in vitro data indicating that a variety of lasers can be used to vaporize atherosclerotic lesions, as mentioned above, in the clinical setting angiography alone is unable to determine to what extent laser recanalization is true laser vaporization. Recent elegant in vitro thermographic studies of normal and diseased human aorta do provide some insight into the mechanism of action of one laser recanalization device, the laser probe. In this study, it was found that the laser thermal probe was more effective in ablating fibrofatty plaque than nonatherosclerotic aorta. It was postulated that lower thermal conductivity and diffusivity constants of fibrofatty plaque relative to normal vessel wall were responsible for more extensive heating and evaporation of plaque. These findings confirm the in vivo experimental and clinical observations that it is easier to vaporize thrombus and atheroma and that it is actually quite difficult to perforate the structural elements of the artery, such as the external elastic lamina, which is composed of collagen and elastin. Thus, in addition to the self-centering nature of rounded tips that helps keep the device intraluminal, a natural “defense” mechanism may exist that favors vaporization of the diseased portion of the vessel wall and not the normal arterial wall.

One other interesting observation from this study was that increased pressure applied to the laser-heated probes enhanced tissue ablation. The authors postulate on the basis of their histological observations that compression of residual cellular and tissue components results in a decrease in the vacuolated cellular space. Thus, heat and pressure appear to be two important mechanisms of the “contact” laser approach to atherosclerotic lesions. Sapphire tips may have a similar mechanism of action. Additional experimental studies should help to elucidate what proportion of laser recanalization is true laser vaporization of atherosclerotic mass and how much is mechanical enlargement of the lumen.

Laser sealing. As suggested in experimental studies, there may be some benefit with laser recanalization of leaving behind a smoother surface, which is less likely to serve as a nidus for platelet and fibrin accumulation compared with balloon angioplasty. With the present fixed-size laser metal probes and sapphire tips, the diameter of the recanalized channel is limited by the size of the device. Thus, laser recanalization has to be followed by conventional balloon angioplasty and fracture, and dissection of the arterial wall by the balloon cannot be eliminated. Another intriguing laser device that may be able to leave behind a smoother luminal surface is a system in which low-level Nd:YAG laser energy is emitted from a fiberoptic with a diffusion tip positioned inside a clear balloon catheter. Experimental studies suggest that this device may be able to “seal” intimal flaps and dissection planes that probably contribute to abrupt closure and restenosis after balloon angioplasty. Experimental studies clearly indicate that intimal and medial tears after balloon angioplasty are associated with greater platelet accumulation; therefore, sealing vessel wall fracture and dissection may reduce platelet and fibrin accumulation and lead to less abrupt closure and restenosis.

Thus, laser-balloon catheters may have a clinical role after balloon angioplasty as opposed to the fixed laser recanalization devices described above, which are currently used before balloon angioplasty. Because both the laser-heated metal probes...
and sapphire tips operate by contact with the atherosclerotic tissue, the current 1.5–2.5-mm devices are unlikely to be useful in their present size for laser sealing after balloon dilation of a vessel to 5–6 mm. In the future, however, larger or expandable recanalization devices may also be effective for laser sealing after balloon dilation.

**Follow-up Results**

Clinically, it is not very worthwhile to open up peripheral artery occlusions with laser recanalization followed by balloon angioplasty if the long-term patency is poor; patency after bypass surgery would probably be superior. Therefore, as the cardiovascular applications of lasers develop, it will be important to examine their long-term results. Once again, the laser probe is the only laser catheter with adequate clinical experience to yield long-term assessment, and 1-year cumulative results were recently reported and compared with results of recently published series for conventional balloon angioplasty. When examining long-term results of peripheral angioplasty, recurrence rates varied considerably depending on the type of lesion (stenosis vs. occlusions), lesion length, and the definition of recurrence. With subgroup analysis of this initial series, a potential benefit of combined laser recanalization and balloon angioplasty was suggested. For example, 1-year recurrence rates for stenoses and short 1–3-cm occlusions were only 5% and 7%, respectively. These results were considerably better than results reported in recent balloon angioplasty series in which 1-year recurrence rates of 20–28% or more were observed for stenoses and recurrence rates of 7–33% or more were noted for short occlusions. The definition of clinical patency is important in comparing these results because a 20% redilation rate was not considered a recurrence in one of these recent balloon angioplasty series. For occlusions of greater length treated with laser-assisted balloon angioplasty, 1-year recurrence rate of 24% for 4–7-cm occlusions and 42% for occlusions more than 7 cm are also better than a recurrence rate of 50% for occlusions more than 3 cm as reported in one study.

On the one hand, these results are influenced by operator learning experience and the initial development stage of a device; clinical success and patency should improve with more experience and device modifications. On the other hand, these results could be influenced by other patient factors such as case selection, diabetes, smoking, distal vessel runoff, and medications. Obviously, these results have to be confirmed, and a multicenter randomized trial should be considered. These initial results do serve as a useful reference for future laser or mechanical devices.

Possible explanations for these lower recurrence rates after laser recanalization and balloon angioplasty are that the technique partially vaporizes or thermally compresses the atherosclerotic lesion and leaves behind a smoother less thrombogenic arterial surface. Obviously, for longer occlusions, more atherosclerotic material will have to be removed. Larger contact devices may be beneficial in removing more material or leaving behind a smoother surface with a larger lumen so that balloon angioplasty may not be required at all. Our recent study in the smaller (1–2 mm) rabbit iliac arteries suggests that laser recanalization with the laser probe device alone may cause less restenosis than conventional balloon angioplasty.

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**Figure 2.** Angiograms of a 95% middle right coronary artery stenosis. Panel A: Before treatment. Panel B: Laserprobe (1.7 mm) through the lesion after laser recanalization with two pulses of argon laser energy delivered for 5 seconds each. Panel C: Thirty percent residual stenosis after laser recanalization. Panel D: Ten percent residual stenosis after balloon angioplasty with a 3.0-mm balloon catheter. Flow to the acute marginal was initially interrupted after balloon angioplasty but subsequently was restored spontaneously.
Percutaneous Coronary Laser Feasibility

Based on this experience in peripheral vessels, clinical trials of percutaneous coronary use of lasers were recently initiated with specially designed coronary laser-heated probes.15,16 These preliminary studies indicated that a coronary laser catheter can be used percutaneously to reduce coronary stenoses as determined angiographically (Figure 2); however, laser recanalization of stenoses was limited by the inflexible, prototype nature of the device.15 Currently, catheters with improved flexibility, trackability, profile, and a central lumen design are being investigated and appear promising.

Conclusion

We are entering a new era of interventional techniques. There is already evidence that laser devices can supplement the complement of balloons and wires used in recanalizing peripheral vascular lesions that previously could not be treated. Perhaps more exciting is the suggestion that long-term results for femoropopliteal angioplasty may be improved with laser techniques.12 We have learned that bare fiberoptics are unsafe and provide inadequate recanalized channels. A second generation of modified fiberoptic tips offers significant improvements in safety and efficacy compared with bare fiberoptics. Pathophysiological studies have been key in determining the mechanisms of action of these devices, and it is possible that the improved results can be attributed to self-centering rounded tips, circumferential vaporization, thermal compression by the “contact” devices, and a residual luminal surface that has less fracture, dissection, and restenosis than balloon angioplasty. Additional laboratory research as well as randomized clinical trials are needed to determine whether laser or mechanical devices can improve on the two major limitations of balloon angioplasty—recanalization of chronic total occlusions and restenosis.

References


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