Clinical Medicine

Lasers in Cardiovascular Surgery—Current Status

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The argon, carbon dioxide and neodymium-YAG lasers have been proposed as effective instruments for surgical procedures of the intact cardiovascular system. While argon and CO_2 lasers cause superficial (0 to 1 mm) thermal injury, the Nd:YAG laser is better suited for effecting deep thermal necrosis (3 to 4 mm). Microsurgical vessel anastomoses can be done by "tissue welding" with any of the three clinical lasers. Myocardial revascularization may be accomplished by drilling "neocapillaries" in ischemic myocardium. Endocardial resection for destroying arrhythmic pathways and removing hypertrophied septal muscle has also been successfully accomplished with laser phototherapy. Last, laser-mediated vaporization of atherosclerotic plaque in the coronary arteries and peripheral circulation may offer a percutaneous approach to the treatment of arterial occlusive disease. Cardiovascular uses of lasers are purely investigational at the current time. Much more needs to be known before widespread clinical use of lasers in the cardiovascular system can occur.

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Laser-mediated vaporization of atherosclerotic plaque has been proposed as a method to open occluded or stenotic vessels. Media attention has created a climate of expectation surrounding this procedure, but scientific articles are becoming more tempered in their handling of laser-mediated atheroablation. In this report we will introduce readers to the biomedical laser and attempt to provide an update of what is known and what needs to be studied before lasers become standard tools of cardiologists and cardiovascular surgeons. Specifically, we will address proposed methods of intravascular laser delivery and present the experience of investigators working with lasers in the cardiovascular system.

The word laser is an acronym for *l*ight *a*mplification by *s*timulated *e*mission of *r*adiation. The first observed stimulated emission of radiation in the visible spectrum came from a ruby rod, stimulated by energy from a flash lamp.[1] Within four years the argon, carbon dioxide and neodymium-YAG lasers were developed. The ruby laser was first used by ophthalmologists in 1964 for photocoagulating the retina.[2] Goldman reported his use of the ruby and CO_2 lasers on skin in 1963.[3] Ablation of a melanoma metastasis with the ruby laser was first reported by McGuff and Bushnell in 1964.[4] At the same time, they reported an ability to vaporize atherosclerotic plaque in cadaver vessels with the ruby laser. It took 15 years of technologic evolution in lasers and fiberoptics, however, before interest was rekindled in laser therapy for cardiovascular disease.

The Biomedical Laser

From a stimulated laser medium, solid or gas, photons are emitted in the form of a laser beam (Figure 1). This beam differs from an ordinary beam of light in that all photons are of the same wavelength and are in phase with one another spatially and temporally. This is termed *coherent* light. A laser beam is characterized by its wavelength—a function of the laser medium—its focal length and its power—a function of the number of photons emitted. The beam may be directed to its target by a series of mirrors or it may be directed through a small flexible quartz fiber. Quartz-wave guides range in diameter from 100 microns to 600 microns and are readily passed through the operating channel of conventional endoscopes. The three lasers currently used in clinical medicine have as their active medium carbon dioxide, argon and neodymium-yttrium-aluminum-garnet (Nd:YAG), a crystal. Laser fibers are only available for the argon and Nd:YAG lasers at this time; however, a fiber for the CO_2 laser is currently in development.

For the most part, lasers work by heating tissue. When tissue is heated to 60°C, protein and nucleotide denaturation occur. Initially, the cell is structurally intact, though the intra-

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ABBREVIATIONS USED IN TEXT

LAD = left anterior descending [artery]
Nd:YAG = neodymium-yttrium-aluminum-garnet

cellular machinery is irreparably destroyed. At 100°C, vaporization occurs. Tissue contracts as the water is evaporated. At higher temperatures all other tissue components are sublimated, leaving only a black carbon eschar (Figure 2).

Because each laser produces monochromatic light at a different wavelength, pigmented tissue components may absorb energy from different lasers differentially. For example, hemoglobin absorbs 95% of argon laser energy in 1 mm of tissue whereas water transmits 95% of the same energy. Conversely, water absorbs more than 95% of CO_2 laser energy in 1 mm of tissue and hemoglobin transmits 90% of incident energy at this wavelength (Figure 3). Because of high absorption by hemoglobin, the argon laser is currently the best laser for treating port-wine stains and telangiectasis of the gastrointestinal tract. Similarly, darkly pigmented lesions, such as melanoma metastasis, would best be approached with Nd:YAG laser. If one can selectively stain abnormal tissue with a light-activated toxic substance (such as hematoporphyrin derivative), it may be possible to selectively destroy such tissue at energy low enough to preserve adjacent normal structures.[5]

Largely because of differences in superficial tissue absorption, each laser has a characteristic depth of injury ranging from 0.1 mm for the CO_2 laser to 4 mm for the Nd:YAG laser. Thus, in choosing a laser for a particular task, the operator must consider pigmentation of the target lesion, energy requirements and desired depth of tissue injury.

Access and Delivery of Laser Energy

Endovascular access and delivery of laser energy may be accomplished through conventional surgical exposure, fluoroscopy or endoscopy. Conventional surgical exposure ultimately provides the best control of laser energy. The major shortcoming of this approach is that many conventional surgical instruments are as good or better than lasers in an open operative field. The enduring contribution of lasers in cardiovascular surgical procedures may be the ability to operate from afar.

Percutaneous transluminal surgical procedures, such as balloon angioplasty, embolectomy and thrombus dissolution, have traditionally been guided fluoroscopically. Various investigators are in the process of developing special catheters for fluoroscopically guided intravascular laser application.[6] The common design includes a balloon for occluding a vessel and centering the catheter within the vessel lumen, a channel for saline flushing and a central channel for the laser fiber. The major problem with fluoroscopic guidance is that the operator cannot see tissue effects created by the laser. Ultimately, visual inspection of the tissue effect is the best way to guide laser energy dose. Prescribed energy doses coupled with fluoroscopic imaging are less precise ways of safely achieving desired effects.

Vascular endoscopy, or angioscopy, may provide direct vision of intravascular pathologic areas when the field is cleared of blood with proximal occlusion and the infusion of transparent flush solutions. In the peripheral circulation, a saline flush system provides good visualization and will not compromise tissue viability for the duration of most procedures.[7] In the coronary or cerebral beds, it may be possible to use a transparent emulsion of fluorinated hydrocarbons to

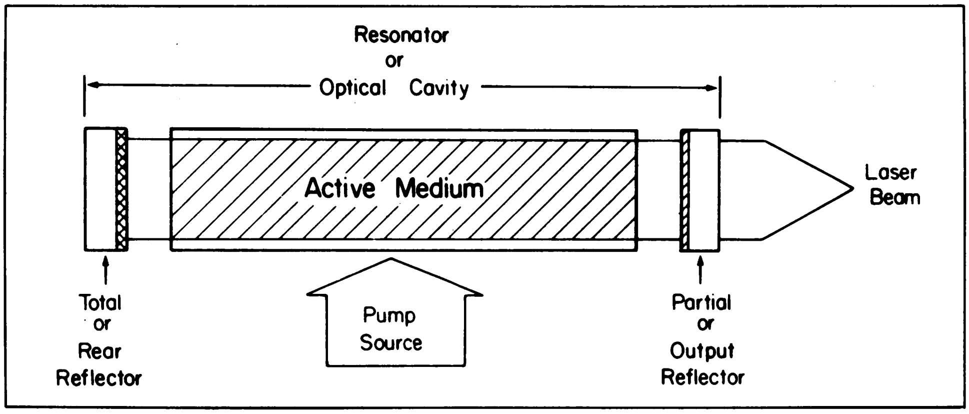

Figure 1.—Basic components of a laser. The active medium may be a gas or a crystal.

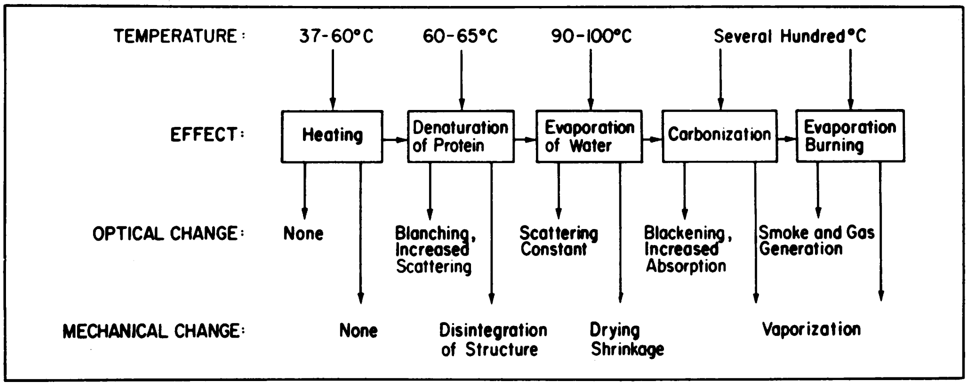

Figure 2.—Tissue effects of laser energy. Coagulation and vaporization are mediated by heating tissue to 60°C and above 100°C, respectively.

visualize vascular anatomy without compromising oxygen delivery.[8] Whether laser energy can be transmitted through fluorinated hydrocarbons is not yet known, nor has the safety of these compounds been adequately established.

There are two types of operating vascular endoscopes currently in experimental use, those with articulation and those without articulation. Lee has developed a nonarticulated operating endoscope 1.8 mm in diameter that gives access to the coronary circulation.[9] Without articulation, however, this instrument is less able to precisely deliver laser energy than articulated endoscopes. While technology currently requires articulated operating endoscopes to be at least 3.0 mm in external diameter, such an instrument is small enough to visualize the trifurcation of the popliteal artery and proximal coronary arteries. Although small vessels may be more accessible with a nonarticulated endoscope, the added precision in application given by an articulated instrument may allow more rapid and safe delivery of laser energy within the intact circulation.

Locating the target endoscopically, fluoroscopically or under direct vision is only half the battle. An instrument capable of cutting or coagulating must next be applied in a most controlled fashion to avoid untoward events. Lasers may provide the necessary control for many intravascular procedures.

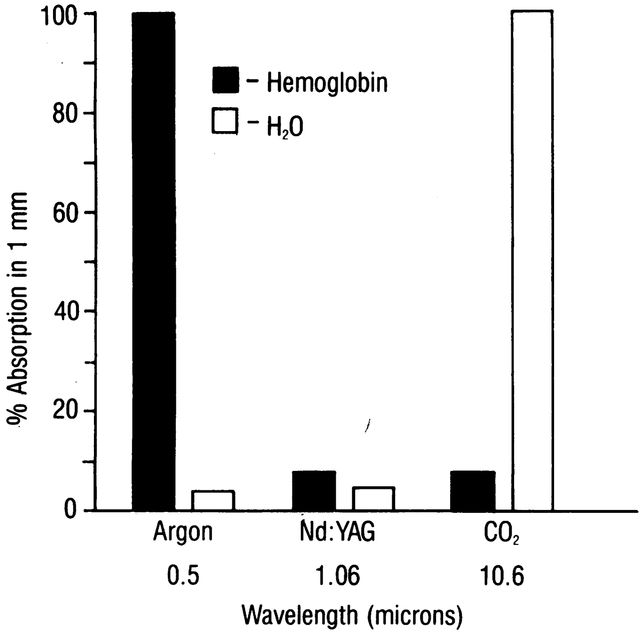

Figure 3.—Selective absorption. Argon laser is highly absorbed superficially by hemoglobin and CO_2 laser is highly absorbed by water. Nd:YAG laser penetrates deeply in tissue as superficial absorption is low.

Microvascular Welding

3-Suture & Laser	8-Suture Technique
Time: 5-10 Minutes/vessel	15-30 Minutes/vessel
Patency: 95%-100%	95%-100%
Tensile strength: Adequate	Slightly better
Scarring/stenosis: Minimal	More frequent
Pseudoaneurysms: 0%-5%	0%-5%

Figure 4.—Microvascular laser welding. Laser-mediated microvascular anastomosis is done more rapidly and with less scarring than with conventional techniques.

Applications

Laser-Assisted Microvascular Anastomosis

The first successful laser-assisted small vessel repair was reported by Jain of Munich in 1979. Jain closed 50 arteriotomies and venotomies in rat vessels less than 1 mm in diameter with the Nd:YAG laser. There was no disruption and 95% short-term patency.[10] In 1965 Yahr and co-workers first carried out laser anastomosis by glueing vessels together side to side with methyl methacrylate, then perforating the glued segment with the Nd:YAG laser to open a channel between the vessels.[11] The experimental technique frequently used today for laser-assisted small vessel anastomosis requires two steps. Three microsutures are placed evenly around the circumference of the vessels to appose the vessel edges and provide tensile strength.[12,13] The laser—either CO_2 or argon—is applied to the apposed edges at milliwatt powers for milliseconds to produce a watertight seal. The advantage of this type of anastomosis is that it is fast (a standard repair of a 1-mm vessel requires eight sutures) and that it minimizes foreign body in the wound. Patency is reported at 95% to 97%, similar to that for conventional suturing techniques. There is a low incidence of pseudoaneurysms, perhaps lower than that found with suture repair.[14] The tensile strength is slightly below that of a conventional repair but sufficient to prevent disruption at systemic blood pressures (Figure 4). It is believed that the tissue glue results from collagen denaturation in the media and adventitia as well as fibrin polymerization.[12] Healing occurs with significantly less scarring.

Laser-Assisted Myocardial Revascularization

There are at least three cardiac procedures that may be done with laser techniques: myocardial revascularization, endocardial resection and transluminal laser angioplasty. Transventricular revascularization is being studied by Mirhoseini and associates. They use the CO_2 laser at very high power to drill miniature holes in ischemic left ventricular myocardium (20 to 30 holes per cm^2)[15] to reestablish perfusion to the compromised muscle. In an experimental model, the left anterior descending artery (LAD) was ligated in 24 dogs. Of those dogs, 100% treated with the CO_2 laser in the distribution of ischemia survived without electrocardiographic or histologic evidence of myocardial necrosis. Fibrillation developed in 100% of the control animals with LAD ligation alone. All died within the first 20 minutes of ischemia.

While one might think that such small "neocapillaries" would thrombose immediately, photomicrographs taken five months postoperatively showed patent laser channels and endothelialization of the channel walls. The adjacent muscle was healthy at the time the animals were killed. Mirhoseini and associates have done this procedure in one patient at the time of coronary artery bypass grafting. Postoperatively, improved contraction of the left ventricle was found.[16]

Laser-Assisted Endocardial Operations

Intracardiac surgery done from a percutaneous transluminal approach is another new area of investigation. Precise resection of valvular calcium, hypertrophic myocardium or an aberrant conduction pathway is an extreme technical challenge when done percutaneously in a full beating heart. Transluminal valvular surgical procedures may be the most demanding of intravascular procedures. Lee and colleagues have reported one case of transluminal incision of a normal canine aortic valve with the argon laser.[17] More work in this area has been done in Brazil where Bozinis and co-workers have produced a canine model of pulmonic stenosis, then introduced an argon laser fiber into the right ventricle percutaneously. Using fluoroscopic guidance and a saline jet to clear the field, they were able to incise the valve and alleviate the pressure gradient without rendering the valve incompetent.[18] Isner and colleagues have reported success at excising calcium from stenotic aortic valves in vitro with the CO_2 laser.[19] Similarly, they have used the argon laser intraoperatively to resect myocardium in one patient with hypertrophic cardiomyopathy.[20]

Several investigators have reported tissue effects of lasers on myocardium[21,22] and are now developing techniques of percutaneous transluminal antiarrhythmia surgical procedures. Cardiac electrophysiologic studies done percutaneously delineate normal and pathologic conduction pathways on the endocardium.[23] Currently, pathologic circuits, such as Kent bundles or reentrant arrhythmia circuits, are addressed at the operating table if medical therapy fails. The pathway is either resected or cryoablated.[24] This treatment is effective in controlling ventricular tachycardia in a select group of patients, but the operation carries a 10% mortality and the same morbidity as a ventriculotomy. If the arrhythmia pathway can be located percutaneously and successfully treated with a freezer probe, it may be possible to interrupt the circuit with a laser or heater probe without an operation.

In preparing for ablating ventricular tachycardia circuits, Vincent and associates showed that the Nd:YAG laser introduced percutaneously could selectively destroy small portions of canine left ventricular myocardium without causing dyskinesis of the ventricle or measurable hemodynamic changes.[21] Narula and co-workers have been able to produce complete heart block in dogs by locating and dividing the His bundle with electrophysiologic study and an argon laser fiber introduced percutaneously.[25]

Percutaneous Transluminal Laser Angioplasty

A topic receiving a great deal of attention is percutaneous transluminal laser angioplasty. While most of the media attention is centered on recanalizing coronary arteries, this procedure is equally applicable to peripheral disease. It might appear that laser treatment of atherosclerosis started in the 1980s; however, McGuff and Bushnell first showed in 1964 that laser energy could destroy atherosclerotic plaque.[4] Little research was done in this field over the next 15 years, but there are now many investigators studying the effects of laser on atherosclerotic plaque and normal intima in animal models.[6,9,26-36] Only Ginsburg and colleagues have attempted to vaporize plaque in patients with peripheral vascular disease.[37] Investigational materials include atherosclerotic cadaver vessels in vitro, cadaver vessels transplanted into animals and animals prepared with atherogenic diets.

All three biomedical lasers appear to be effective in destroying plaque. McGuff and Bushnell reported their success in vaporizing fibrous and fatty plaque in 1964. They found it difficult to vaporize calcific plaque without injuring the native vessel.[4] Choy, Lee and Abela and their co-workers have reported success at vaporizing plaque and thrombus in cadaver coronary arteries.[6,9,26] Although the CO_2, argon and Nd:YAG lasers have all been used for intravascular studies, the argon laser is currently preferred because of its shallow penetration and fiberoptic delivery system. Several new laser wavelengths may be preferable to argon laser for destroying calcific plaque.

Absorption of laser energy may be enhanced by staining techniques. Abela and colleagues have used sudan black to increase absorption of Nd:Yag radiation by plaque.[27] Spears and associates reported selective uptake of hematoporphyrin derivative by atherosclerotic lesions in rabbit and monkey aortas, thus sensitizing these lesions to irradiation at 630 nm.[38] Such photosensitization of atheromata may allow complete vaporization at much reduced energy, thus sparing the vessel wall subjacent to treated plaque. Much experimental work remains to be done in this area.

The greatest concern about percutaneous laser angioplasty is its possible danger. Vessel perforation is the most lethal pitfall. Initial studies have addressed the effects of laser energy on normal vessel wall. All who have experimented with laser endarterectomy have found it easy to perforate the vessel wall with a misguided application. The energy required for vessel perforation is no greater than the energy required to penetrate fibrous plaque.[28] In most cases, perforation energy is significantly less than that required to ablate calcific lesions. In addition, the complex nature of most human atherosclerotic plaque may cause unpredictable and excessive thermal injury to vessel wall subjacent to an area of laser application.[29,30] Attempts have been made to quantify this injury. There are two major zones of injury recognized in laser applications, a zone of vaporization—the plaque, in this case—and a zone of thermal necrosis that may extend to the vessel wall. A third, less destructive zone of acoustic injury has been identified by Abela and colleagues.[27] Several experiments have shown delayed necrosis of the elastic lamina subjacent to vaporized plaque or thrombus. Van Stiegmann noted aneurysm formation in 100% of porcine atherosclerotic carotid arteries when they were subjected to enough Nd:YAG laser injury to cause full-thickness coagulation necrosis. When reimplanted in the aortic position, 75% of them ruptured. When the media was spared, there was no early perforation or aneurysm formation.[31] For percutaneous angioplasty to be successful, it will be necessary to ensure that no significant vessel wall injury occurs. For this to happen, the laser fiber will need to be close to the plaque, parallel to the vessel wall and well centered in the vessel lumen (Figure 5). The minimum energy for dissolving plaque must be used.

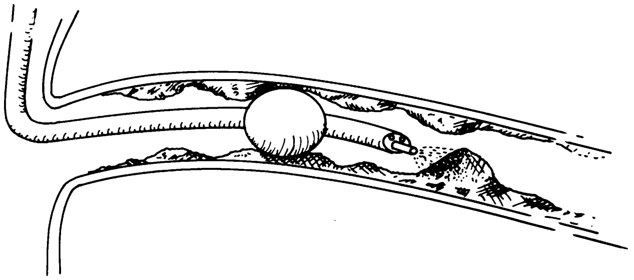

Figure 5.—Endoscopic vaporization of an atheroma. Proximal balloon occlusion clears the field of blood and centers the laser fiber in vessel lumen.

Thrombosis following laser treatment is another worry. Many investigators have shown that traumatic exposure of arterial media to the bloodstream may cause thrombosis. Will laser-denuded arterial media act similarly? Abela and co-workers found no vessel thrombosis in laser-treated canine carotid and femoral arteries despite media exposure.[32] In each case the crater made by the laser contained a fibrin/platelet thrombus, which did not project into the vessel lumen. Reendothelialization occurred within nine days. Abela and associates found the coronary arteriotomy closure to be more thrombogenic than the laser lesions. Gerrity and colleagues reported similar experience with atherosclerotic porcine aorta.[33]

While it has been well established that arterial wall trauma may accelerate atherogenesis, Gerrity and co-workers reported that porcine aortic laser burns showed no signs of increased lipid accumulation eight weeks postoperatively despite an atherogenic diet.[33] Over the same time period, atherosclerotic plaques developed in the same animals at an accelerated rate in portions of the femoral artery subjected to balloon stripping of the endothelium. No long-term studies of laser injury and atherogenesis exist.

The fear of cerebral embolism following laser treatment of carotid artery plaque has inhibited interest in this area. While no one has addressed the problem of atheroembolism scientifically, several investigators have mentioned that there was no limb-threatening ischemia or "blue toes" after laser treatment of iliofemoral atherosclerotic plaque. In the coronary bed, Choy and associates have shown that a proximally placed radiolabeled thrombus does not shower debris distally when vaporized with the argon laser. Spectrophotometric analysis showed that the products of vaporized thrombus are water vapor, CO_2 and small-chain hydrocarbons, all of which are dissolved in the serum.[6]

Conclusion

Fiberoptic technology is now available in sizes compatible with human blood vessels, and lasers are now available in many medical centers. The combination of technologies makes possible percutaneous endovascular surgical procedures. While many of the applications discussed in this review will become historical curiosities in ten years, other applications may become the standard of practice. Before the laser becomes clinically available for intravascular use, more needs to be known about the long-term effects of lasers on the heart, great vessels and peripheral circulation.

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