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LASER ANGIOPLASTY: MORPHOLOGIC STUDIES

Laser Ablation of Human Atherosclerotic Plaque Without Adjacent Tissue Injury

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Seventy samples of human cadaver atherosclerotic aorta were irradiated in vitro using a 308 nm xenon chloride excimer laser. Energy per pulse, pulse duration and frequency were varied. For comparison, 60 segments were also irradiated with an argon ion and an Nd:YAG (neodymium:yttrium aluminum garnet) laser operated in the continuous mode. Tissue was fixed in formalin, sectioned and examined microscopically. The Nd:YAG and argon ion-irradiated tissue exhibited a central crater with irregular edges and concentric zones of thermal and blast injury. In contrast, the excimer laser-irradiated tissue had narrow deep incisions with minimal or no thermal injury. These preliminary experiments indicate that the excimer laser vaporizes tissue in a manner different from that of the continuous wave Nd:YAG or argon ion laser. The sharp incision margins and minimal damage to adjacent normal tissue suggest that the excimer laser is more desirable for general surgical and intravascular uses than are the conventionally used medical lasers.

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Excision of pathologic tissue by laser energy is limited by the operator's inability to precisely control the depth of ablation and limit thermal injury to the target tissue. This may result in perforation of hollow structures or damage to adjacent normal tissue, or both (1–3). There are, however, two mechanisms by which thermal injury induced by the absorption of laser energy might be reduced or eliminated. One method, utilized in fabricating metals, involves the delivery of very short duration, high energy pulses to vaporize materials so rapidly that heat transfer to the nonirradiated adjacent substrata is minimal (4,5). The other potential method utilizes ultraviolet photons which are efficiently absorbed by organic matter. Absorbed ultraviolet photons can disrupt molecular bonds, removing tissue by photochemical rather than thermal mechanisms (6). In theory, ultraviolet laser energy delivered in nanosecond pulses might excise tissue by either or both processes. The purpose of this study is to provide the first report on the effect of near-ultraviolet, pulsed, 308 nm xenon chloride excimer laser energy on human vascular tissue.

Methods

Study cases. The aorta from eight individuals who underwent postmortem examination within 24 hours of death was removed intact from the arch to the iliac bifurcation. The aorta was rinsed in normal saline solution to remove blood. One hundred thirty aorto-iliac segments were selected for laser experiments, representing a full spectrum of gross appearances from normal through soft raised lesions to ulcerated atheroma and severe calcific atherosclerotic lesions.

Laser technique. Two excimer lasers were used to irradiate tissue: a commercial xenon chloride excimer laser that delivered 35 mJ pulses at 10 nm width, and a magnetically switched, 85 nm pulse width 70 to 145 mJ/pulse laser specially designed by Jet Propulsion Laboratories (7,8). Repetition rates from these lasers were varied from 10 to 50 Hz, and the total number of pulses was typically varied

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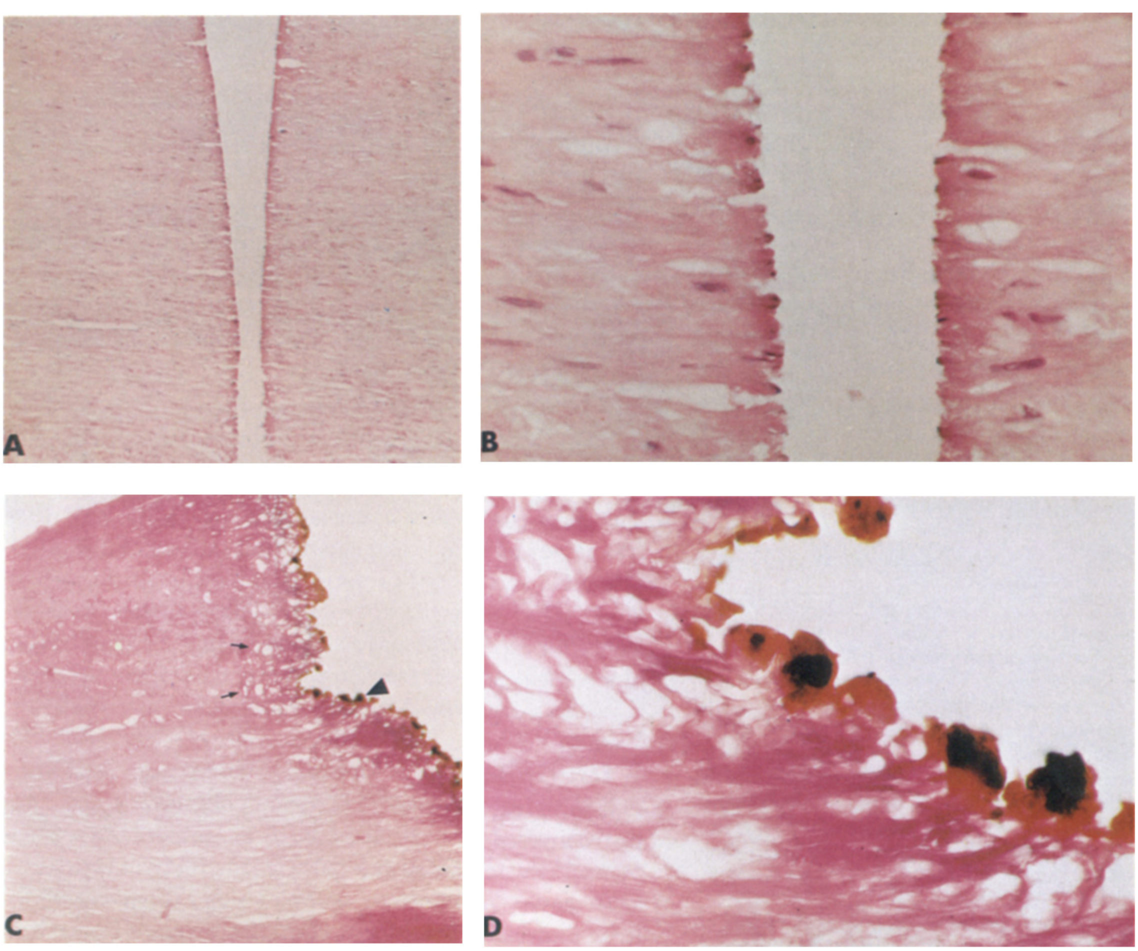
from 5 to 300. Aortic segments were irradiated in both air and saline solution. No irradiations were performed in blood.

The excimer study employed two delivery systems. Initially, the tissue was placed at the focus of a 600 mm focal length quartz lens and the samples irradiated either in air or saline solution. Sufficient excimer energy to cause tissue ablation was also delivered through a specially designed fiberoptic waveguide, which resulted in an ultraviolet beam diameter of 1.0 mm at the fiberoptic tip. In each study, the incident beam was perpendicular to the intimal surface. Energies were measured directly from the laser output and the fiber tip.

Figure 1. Color photomicrographs of cadaver atherosclerotic aorta. **A**, Effect of 102 pulses of 35 mJ each and 10 ns duration of excimer radiation directed perpendicularly to the intimal surface (100×). The incision margins are smooth and without evidence of thermal injury. **B**, High power view (400×) of the incision wall seen in **A**. Note the lack of thermal injury and the undisturbed cellular architecture adjacent to the incision. **C**, Effect of 40 watt, 2 second irradiation with an Nd:YAG laser on the intimal surface of cadavaric atherosclerotic aorta (100×). Marked thermal injury in the form of carbonization, coagulation injury (**arrowhead**) and vacuolization (**arrows**) are evident. **D**, High power view (400×) of the crater wall shown in **C**. Note the carbonization, coagulation injury, vacuolization and loss of cellular architecture; all are evidence of thermal injury. (All photomicrographs reduced by 30%.)

For comparison of the pulsed xenon chloride excimer laser irradiation of aortic tissue with those using conventional medical lasers, samples were also irradiated with a Molectron 8000 neodymium:yttrium-aluminum-garnet (Nd: YAG) continuous laser and a Laser Ionics argon ion laser. The argon ion laser emitted two lines in the visible spectrum at 488 and 514 nm and the Nd:YAG lased at 1,060 nm. Exposure times for irradiation of tissue by the Nd:YAG laser were varied between 0.2 to 10 seconds and the energy levels from 10 to 50 watts. The argon ion laser exposure times were varied between 1 to 5 seconds and the energy levels from 5 to 8 watts. These ranges of exposure times and energy levels were chosen to vary the degree of tissue damage from minimal to severe. Aortic samples were irradiated both in air and in saline solution.

Morphologic study. Tissue segments were photographed before and after laser irradiation. The visible effects of laser irradiation were recorded by the operator at the time of the experiment, and the tissue was then placed in a solution of 10% formalin. The tissue was stained with he-



matoxylin-eosin and sectioned parallel to the axis of the laser beam. The magnitude of thermal and blast injury, as well as the width and depth of ablation, were quantified by ocular micrometry.

Results

Gross observations. The excimer-irradiated specimens revealed smooth-walled incisions that corresponded to the shape of the incident beam: those irradiated through the lens system had rectangularly shaped incisions, those irradiated through the fiberoptic waveguide had circular incisions. No discoloration or carbonization was visible on the cut surface of the aortic tissue. Even at levels of energy sufficient to cut through the full thickness of the vessel wall, there was no visible evidence of carbonization on the cut surface. The excimer laser was also able to cut through heavily calcified lesions, which could not be cut with a scalpel, without gross evidence of thermal damage. At pulse energy levels of 145 mJ and at pulse durations of 85 ns, irradiation through a lens in air produced a jet of plasma approximately 1.0 mm in diameter that rose vertically from the surface of the tissue for 3 to 4 mm. The plasma jet was not seen when irradiation was conducted in saline solution.

In comparison, the tissue irradiated with Nd:YAG and argon ion laser energy demonstrated gross evidence of thermal injury. The crater margins appeared irregular and carbonization was apparent.

Histologic results. Figure 1A shows an atherosclerotic aortic segment irradiated with a xenon chloride excimer laser at 308 nm with 102 pulses at 35 mJ/pulse and 10 ns pulse width. An incision of 0.9 by 0.4 mm was formed. Cellular architecture adjacent to the incision is intact. A very thin rim of eosinophilia possibly representing thermal coagulation injury, 1.0 to 2.0 μ wide, is seen at the edge of the incision. The rim was consistently observed on those air-irradiated specimens in which a plasma jet was formed during lasing. The discoloration noted on these segments was not present on all sections. No carbon particles were observed.

Figure 1B shows a high power magnification of the incision illustrated in Figure 1A. The edges are straight with orientation of nuclei to the edge of the incision; otherwise the fiber architecture is undisturbed. Blast damage is minimal and neither carbon particles nor coagulation injury are present. These smooth-walled clean incisions were consistently obtained with the excimer laser under all operating conditions.

Figure 1C is a photomicrograph of an aortic segment irradiated with a Nd:YAG laser operated at 40 watts for 2 seconds in air. This produced an oblate spheroid crater

Figure 2. Graph demonstrating the effects of increasing the number of pulses on the width and depth of incisions induced by excimer irradiation of cadavar atherosclerotic aorta. The y axis represents a millimeter scale in 0.2 mm increments, and the x axis displays the number of pulses at 35 mJ/pulse. Depth of penetration increases in a linear fashion with increasing number of pulses, while width remains constant. For depth, standard deviations were all less than 0.07 mm and for width less than 0.06 mm.

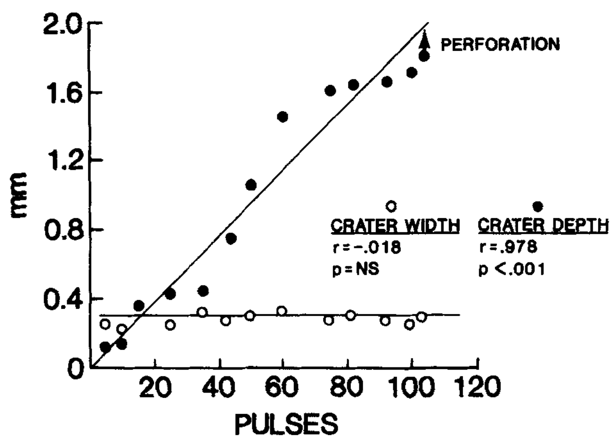
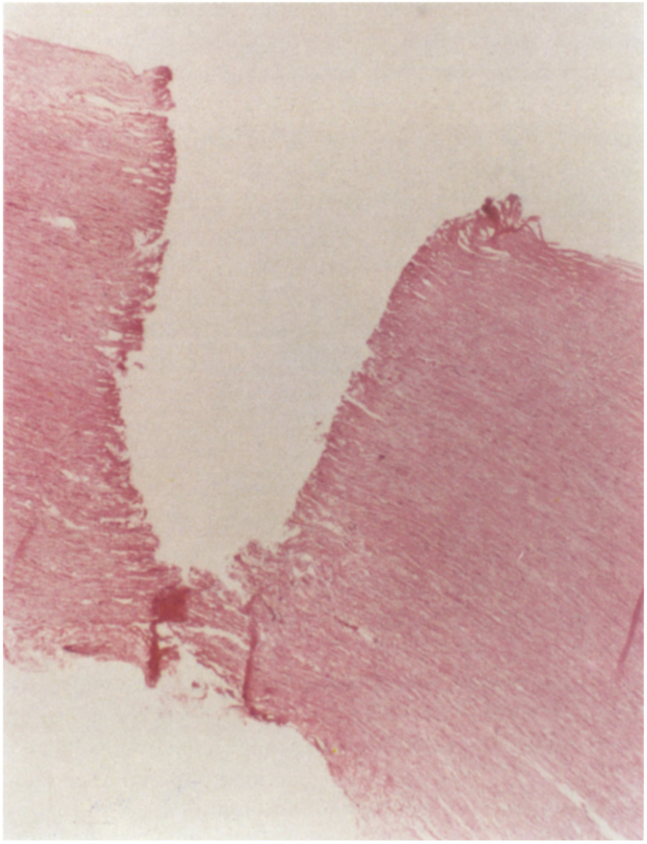


Figure 3. Color photomicrograph displays the incision produced by 60 pulses of 70 mJ/pulse, each 85 nm duration, of 308 nm excimer radiation. The incision is clean without evidence of thermal damage although the edges are slightly irregular. The slightly irregular margins may be the result of nonuniform beam characteristics. (Reduced by 30%.)



measuring 1.7 by 2.0 mm wide and 2.0 mm deep. This lesion is typical of the craters produced by the Nd:YAG laser in aortic tissue. Adjacent to the crater, there is extensive eosinophilic coagulation and carbonization with disruption of local architecture. The crater edges are irregular and vacuolated. These histologic findings are evidence of thermal injury and blast damage. The argon ion laser produced similar oblate spheroid craters with slightly less coagulation injury; however, extensive carbonization was present.

Figure 1D shows a high power magnification of a section of the crater wall illustrated in Figure 1B. Large black carbon particles and coagulation of the underlying cells are prominent. This injury is seen to extend for 1.0 to 2.0 mm around the crater in all directions.

Figure 2 plots the width and depth of the excimer laser incision as a function of the number of pulses delivered using 35 mJ pulses of 10 ns duration. Each point on the graph represents the mean measurement obtained from two to five specimens. The beam diameter at the focal point was 1.1 × 0.3 mm. The graph illustrates that the depth of penetration is directly proportional to the number of pulses. However, the width of the incision did not change, even at energies sufficient to cause perforation of the vessel wall. This is in contrast to the effect seen with the conventional lasers, whereby the width increases with incident energy (3). There was no histologic evidence of thermal or blast damage in these sections beyond that previously described. Use of high energies (for example, 70 and 145 mJ/pulse) at longer pulse widths of 85 ns produced greater depth of penetration for any given number of pulses.

Figure 3 shows an aortic segment irradiated in air using longer pulse durations from the xenon chloride excimer laser. The incision is clean with little evidence of thermal damage, although microscopic examination of the incision edges show them to be slightly more irregular. Heavily calcified lesions required more energy to attain a similar depth of ablation, but incisional width remained constant and greater thermal injury was not encountered. Uniform beam quality was essential to produce consistent depth of penetration and smooth-walled incisions.

Discussion

Our study demonstrates that nanosecond-pulsed ultraviolet laser radiation causes ablation of biologic tissue in a manner substantially different from that which occurs with conventional medical lasers. Continuous wave lasers in current medical use destroy tissue by vaporization and pyrolysis, generating a central crater surrounded by concentric zones of thermal and blast damage. For this reason, lasers presently employed for tissue ablation, including Nd:YAG, carbon dioxide and argon ion, are inherently imprecise and the depth of ablation is difficult to control (9,10).

Mechanisms of tissue ablation. In contrast to the standard medical lasers, our gross and histologic observations imply that the xenon chloride excimer laser removes biologic tissue by a different mechanism. The absence of evidence for thermal injury may be the result of either of two possible mechanisms. The first is photochemical desorption, whereby ultraviolet photons are efficiently absorbed by organic molecules and cause localized electronic excitation of molecular bonds (11). Given sufficient photon flux and efficiency of absorption, possibly through nonlinear absorption mechanisms, localized photochemical dissociation of molecular bonds can occur. This process would allow generation of energetic molecular fragments with their subsequent ejection from the tissue. Thus, much of the injected energy would be removed from the system before transfer of energy as heat could occur. An alternative mechanism derives from the extremely short nature of the excimer pulses (from 10 to 80 ns) (12). Even at 500 pulses/s, the relaxation periods between pulses are relatively long. Energy is efficiently absorbed and leads directly to conversion of the tissue to vaporized fragments. The vaporized fragments remove the energy from the system before significant heat transfer to adjacent tissue can occur. Our data do not prove which of these two mechanisms is operative during excimer ablation of atheroma. Multiple comparison studies with sophisticated physicochemical analysis of products are required for precise delineation of mechanisms. For either mechanism, the key component is the efficient localized absorption of the incident energy.

Implications. The unique precision of excimer laser tissue ablation and the lack of thermal damage to adjacent tissue suggest that pulsed ultraviolet lasers that can be transmitted through fiberoptics are well suited for a variety of medical applications. Specific applications beyond the potential vascular use implied by this study include ablation of bone or cartilage fragments during athroscopy, destruction of either stones or tumors of the biliary or urologic tracts and precise excision of neural tumors with minimal damage to adjacent tissue. The long-term effects on tissue of excimer versus argon or Nd:YAG laser energy remain to be determined.

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