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Laser Thrombolysis Using Long Pulse Frequency-Doubled Nd:YAG Lasers

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Background and Objective: **Laser thrombolysis is a means for clearing blood clots in occluded arteries. Many researchers have studied the mechanisms of clot ablation, and research clinicians have used the technique to treat myocardial infarction with a number of different laser systems. Specifically, a 1-μsec pulsed dye laser has been used clinically to remove blood clots in coronary arteries. As a comparative study, the ablation characteristics of lasers with pulse durations in the ranges of 50–150 μsec and 2–10 msec were investigated. Two frequency-doubled Nd:YAG lasers at 532 nm were used in this study. Ablation threshold and ablation efficiency of gel phantoms and thrombus using these two lasers were measured and compared with the results of the pulsed dye laser. The pulsed dye laser in this study operated at 522 nm.**
Study Design/Materials and Methods: **Gelatin samples with 150 cm^{-1} absorption coefficient at 532 nm and animal clot were confined to 3-mm silicone tubes to measure ablation parameters. Additional samples with 150 cm^{-1} absorption coefficient at 522 nm were prepared for use with the pulsed dye laser. A fluorescence technique and photographic bubble detection were used to determine ablation threshold. A spectrophotometric technique was used to determine ablation efficiency.**
Results: **The ablation threshold of the gel phantoms for all three lasers was determined to be 17 ± 2 mJ/mm^2. Ablation efficiency for the gel phantoms was 1.7 ± 0.1 μg/mJ. Clot had an ablation efficiency of 2.9 ± 1.0 μg/mJ.**
Conclusions: **Ablation threshold and efficiency are independent of laser pulse duration for 1-μsec, 50–150-μsec, and 2–10-msec pulses ($P < 0.05$). Lasers Surg. Med. 25:379–388, 1999.**

Key words: ablation; ablation efficiency; ablation threshold; clot, flash photography; fluorescence; thrombus

INTRODUCTION

Laser thrombolysis, the clearing of thrombus-obstructed arteries by means of laser energy, has been investigated extensively and demonstrated in clinical situations [1–11]. Clinical trials have demonstrated the efficacy of laser thrombolysis for coronary vessels [6,8,10,11]. An excellent review of lasers in cardiology was written by Topaz [10] and includes sections on the use of lasers for treatment of acute myocardial infarction and for peripheral laser angioplasty. The use of pulsed dye and Ho:YAG lasers have successfully ablated blood clot in coronary vessels. Whereas the Ho:YAG uses a nonselective acoustic effect on fibrin in the clot, the pulsed dye laser exploits a selective absorption of laser energy in the target clot [10]. The importance of laser thrombolysis in

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the treatment of myocardial infarction is emphasized when one notes that fewer than half of all patients qualify to receive thrombolytic agents, a competing therapy. In addition, only about 70% of such cases achieves vessel patency after treatment with thrombolytic agents [9,10]. Such drugs are associated with bleeding risk, and their effect is only on the proximal surface of the occluding clot, thus severely limiting the ability of the drug to interact with the clot.

The success of laser thrombolysis in coronary applications suggests that the method can be adapted for restoring arterial flow in cerebral vessels affected by ischemic stroke. Currently, 500,000 new cases of stroke result in 150,000 deaths each year [12]. Many stroke cases are due to ischemia, and currently there exists no effective solution for restoring blood flow in the brain. Laser thrombolysis may provide the means for the clinician to treat stroke quickly and effectively.

Previous work by Sathyam et al. [1,2] investigated microsecond ablation threshold and ablation efficiency of gel phantoms and clot. Sathyam et al. also studied the effect of the cavitation bubble resulting from target vaporization and its effect on ablation efficiency. They determined the optimal parameters for laser ablation of thrombus and thrombus phantoms with respect to laser energy, target absorption, pulse repetition rate, and spot size using a pulsed dye laser with a 1-μsec pulse [1,2].

The effects of laser ablation with 260-, 460-, and 1,100-μsec pulse durations have been studied with holmium lasers using the 30 cm^{-1} absorption of water at 2.12 μm [3]. In these studies, the absorber was in direct contact with the delivery fiber, unlike the situation encountered with laser thrombolysis, in which the fiber, housed in a catheter, may be more than 1 mm from the target thrombus. This difference may be significant in the ablation dynamics and, as a consequence, significant in the ablation parameters. Clinical trials for laser thrombolysis have been conducted with holmium lasers, but selective ablation of thrombus over the normal artery wall is not available at laser wavelengths in the infrared wavelength region [5,10].

This study investigates the use of solid-state frequency-doubled Nd:YAG lasers at 532 nm with pulse durations in the ranges of 50–150 μsec and 2–10 msec as alternatives to the 1-μsec pulsed dye laser. The present experiments explore the parameters for safe, efficient ablation of gel phantoms and clot in vitro. Thrombus phantoms and animal thrombus were confined to 3-mm silicone tubes to simulate a thrombus-occluded artery. Laser energy was then delivered through an optical fiber to determine ablation parameters.

Laser thrombolysis for stroke treatment requires the use of a flexible quartz optical fiber housed within an interventional catheter less than 300 μm in diameter. This small size is needed to achieve the flexibility required to navigate the tortuous path anticipated for treatment of ischemic stroke. A drawback of the small fiber size is the ability to launch a large amount of power into the fiber face. For instance, a 100-μm fiber face has about 10% of the surface area of a 300-μm fiber. This means that the smaller fiber will reach optical breakdown of the quartz face when one-tenth of the power required to reach optical breakdown in a 300-μm fiber is launched into the 100-μm fiber. Because laser power can be reduced by keeping the energy constant and increasing the pulse duration, longer pulses would allow launching of the laser beam into a small delivery fiber without approaching the optical breakdown of the quartz. If ablation efficiency is equal or better for the long pulse durations than the 1-μsec pulses, then the use of small flexible optical fibers in the treatment of ischemic stroke will be practical and achievable. In addition, the solid-state lasers should prove more suitable to a clinical environment after considering space and electrical constraints.

The results of present study showed that the long pulsed Nd:YAG lasers have an ablation efficiency comparable to that of the 1-μsec pulsed dye laser. Ablation efficiency remained constant while changing the repetition rate, radiant exposure above threshold, and pulse duration.

MATERIALS AND METHODS

All ablation experiments in tubes were conducted with the apparatus shown in Figures 1 and 2. The fiber was housed in a catheter so that the ablation process occurred with fluid flow of 2 ml/min. The fluid provided the means for carrying the ablation debris away for later mass measurement. For the gel targets, the fluid was deionized water. For the clot targets, the fluid was 0.9% sodium chloride solution (Baxter Healthcare Corp., Deerfield, IL). The 3-mm-diameter silicone tubes were secured in a frame while delivering pulses. The fluid containing the ablation debris

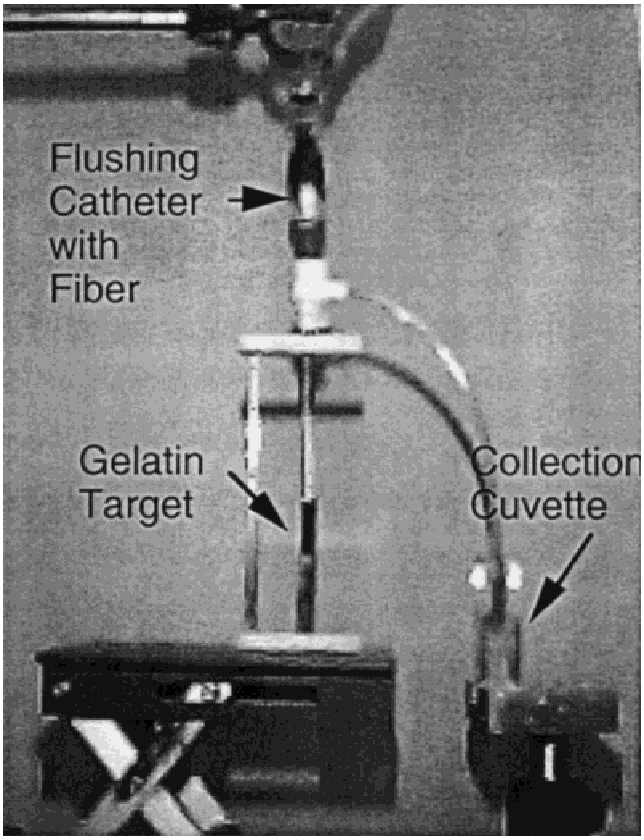

Fig. 1. The 3-mm tube containing the ablation target was housed in a frame that coupled it to the flushing catheter. The catheter contained the optical fiber delivering laser energy. The cuvette collected the ablated mass in the fluid delivered by the flushing catheter.

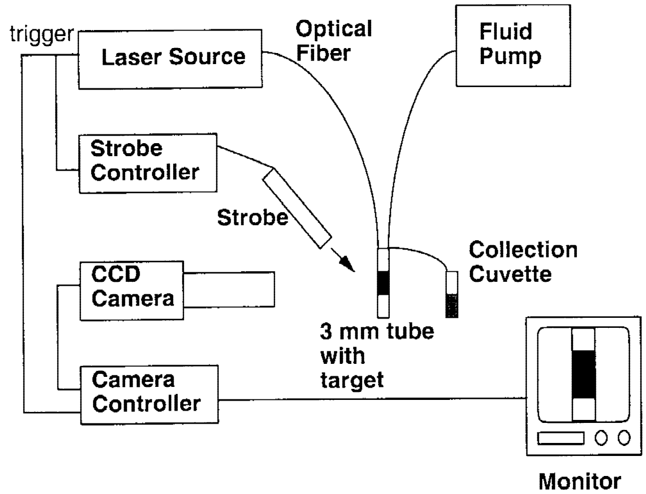

Fig. 2. Experimental setup for ablation threshold detection and ablation efficiency experiments. The laser sources were the 1-μsec, 100 μsec, and the millisecond lasers. The CCD camera was used to monitor fluorescence for detection of ablation threshold. The fluid pump flushed the target of ablated material, which was collected into the cuvette. The cuvette contents were later analyzed for ablation mass.

was collected in a 1-cm cuvette for determination of ablated mass.

Laser Parameters

Two frequency-doubled Nd:YAG lasers operating at 532 nm were used in the ablation studies. The results were compared with those of ablation studies using a 1-μsec pulsed dye laser.

One laser, hereafter referred to as the 100-μsec laser (Schwartz Electro-Optics, Concord, MA), delivered pulse durations in the range of 50–150 μsec. The beam was launched into 300-, 600-, and 1,000-μm fibers. The spot-size diameters for the fibers were 350, 675, and 1,050 μm, respectively, with a fiber-to-target distance of 500 μm. The energies used were in the range of 2–17.5 mJ. These energies should correspond to those preferred for clinical practice. The repetition rate was changed between 1 and 9 Hz for repetition rate studies.

The second laser, hereafter referred to as the millisecond laser, delivered pulse durations of 2, 5, and 10 msec (Coherent-VersaPulse, Santa Clara, CA). This laser was launched into a 300-μm fiber for a spot size of 350 μm, with a fiber-to-target separation of 500 μm. The energy output was a constant 20 mJ. The repetition rate was 3 Hz.

A 1-μsec pulsed dye laser (Palomar Medical Technologies, Lexington, MA) operating at 522 nm was also used in the ablation studies to provide a comparison of the effects of pulse duration. The beam was launched into a 300-μm quartz fiber. The fiber was positioned 500 μm above the target for a spot size of 350 μm. The energy of the dye laser was set to 5 mJ to match a dataset for the 100-μsec laser. The repetition rate was set to 1 Hz.

Target Preparation

Thrombus phantoms were prepared with 3.5% gelatin (175 Bloom, Sigma Chemical Co., St. Louis, MO) in water with 0.18% Direct Red 81 (Sigma Chemical Co.) as a chromophore to produce samples with an absorption coefficient of 150 cm^{-1} at 532 nm. The bulk absorption coefficient of thrombus at 532 nm is approximately 200 cm^{-1} [1]. Additional gel samples were prepared for use with the pulsed dye laser to have an absorption coefficient of 150 cm^{-1} at 522 nm. Liquid gel samples were drawn into 3-mm-diameter silicone tubes (Patter Products, Inc., Beaverton, MI) and allowed to cure overnight. The tubes were approximately 6 cm in length, with the middle 2 cm containing the gel.

Clot samples were also prepared for use in the ablation studies. Canine whole blood was drawn and cured overnight at 37°C. The resultant clot was cut into 1–2-cm-long sections and drawn into 3-mm-diameter silicone tubes. To keep the target stationary during the ablation process, silicone sealant was injected below the clot and the intervening air was removed with a syringe. The sealant was allowed to cure.

Flash Photography

Flash photography was used to set up the ablation and threshold experiments in the microsecond regime with a high degree of repeatability. Photographic images were used to monitor fiber to target distance. Images were also used to monitor fluorescence, thereby providing a means to detect ablation threshold, as described below.

The flash or moment of image capture was controlled by a delay generator (Stanford Research Instruments DG 535, Sunnyvale, CA). The flash lamp controller for the 100-μsec laser supplied a trigger signal for the 100-μsec laser experiments, and the millisecond laser experiments were triggered by a photodiode monitoring a reflected component of the laser beam. The trigger signals were then routed to the delay generator. The delay generator triggered the white-light microsecond photographic strobe (MVS-2601, EG&G, Wellesley, MA) and a CCD camera (CV 251, Motion Analysis, Eugene, OR). The CCD camera was attached to a zoom macro lens (VZM II, Edmund Scientific, Barrington, NJ) for magnification. A filter for the 532-nm light was attached to the macro lens to avoid blinding the camera. The video frame from the camera was recorded as an 8-bit gray-scale, 640 × 480 pixel image by using a frame grabber card (Data Translation, Inc., Marlboro, MA).

Ablation Threshold

Ablation threshold was predicted in these experiments by the partial vaporization theory proposed by van Leeuwen et al. and Jansen et al. [4,13,14]. This theory states that vaporization of water occurs when the temperature is raised to 100°C. The full energy of vaporization is not required before certain nucleation sites begin to form vapor bubbles. Thus the onset of ablation can be predicted by the following equation:

$$E_{th} = \frac{\rho c \Delta T_{100}}{\mu_a} \tag{1}$$

where E_{th} is the energy required to reach ablation threshold, ρ is the density, c is the specific heat, ΔT is the number of degrees needed to reach 100°C, and μ_a is the absorption coefficient. This theory applies when the laser pulse is thermally confined, i.e., when the laser energy is deposited in the target absorber before the resultant heat has time to diffuse. Thermal confinement is achieved when the following equation is satisfied:

$$\tau_p < \tau_{th} = \frac{\delta^2}{\kappa} \tag{2}$$

where τ_p is the laser pulse duration, τ_{th} is the time of thermal confinement, δ is the absorption depth, and κ is the thermal diffusivity of the material. For the gel used in these experiments, $\kappa = 0.0014$ cm²/sec and $\delta = 0.007$ cm. This gives a thermal confinement time of about 35 msec, which is longer than the pulses used in these experiments.

Ablation threshold for the 1-μsec laser pulses was determined by visual inspection of bubble formation in the gel within the 3-mm tubes by using the flash photography setup. A 100-μm fiber was positioned 500 μm above the gel surface to produce a spot size of 190 μm. Spot size was determined by irradiating black ablation paper under water. Four gel ablation threshold trials were conducted for the 1-μsec laser.

For the long pulse lasers, the ablation threshold was determined with fluorescence. The chromophore Direct Red in the gel fluoresces when irradiated with 532-nm light. By collecting the fluorescent light from the surface of the gel, a sensitive, visual assay for changes in the surface topography is achieved that is independent of transducer (e.g., acoustic) sensitivity. Gel fluorescence enabled a CCD camera to detect changes in the surface level, even when the surface might be obscured by bubble formation. This technique proved superior to white-light reflectance because the targets were so highly absorbing.

The optical fiber delivering the laser light was positioned 500 μm above the target to illuminate a spot of predetermined size. Successive pulses of increasing energy were delivered until a crater was formed. The process is detailed in Figure 3. Crater detection was performed by using a CCD camera that was triggered during a laser pulse to record fluorescence photographically. A subthreshold pulse of about 5 mJ/mm² was directed at the surface of the target, creating a fluorescent image of the surface of the target. This pulse energy equated to a temperature rise of

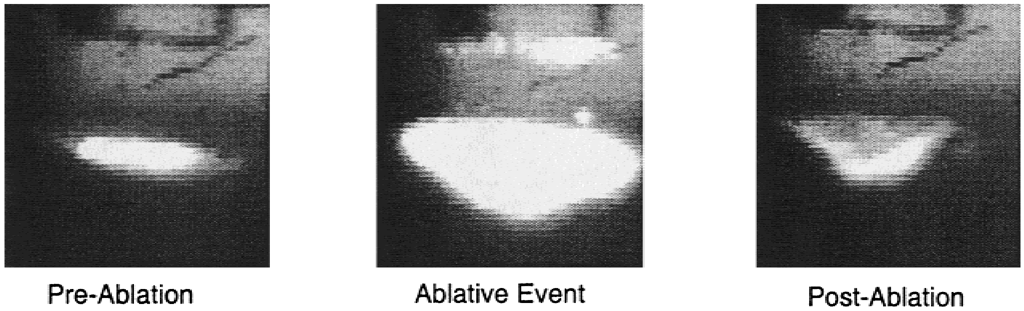

Fig. 3. The left (control) image shows the surface of the gelatin by using a low energy (subablative) pulse. The middle image was taken during the ablation attempt. The right image, measured with a low-energy pulse, shows crater formation on the surface of the gel. Pulse energies below threshold showed no changes in the surface.

about 20°C. A second higher energy pulse was then delivered to the target as an ablative attempt. A subthreshold pulse was fired again to detect any changes on the surface. This procedure was repeated with ablative pulses of increasing energy until the fluorescence of the gel indicated a change in the position of the gel surface, indicating crater formation. The lowest pulse energy resulting in crater formation was termed *threshold.* The procedure was then repeated, using previous results to gain more precise threshold information.

The 100-μsec laser had the ability to continuously change energy from 0 to 100 mJ, so threshold experiments were performed in this manner. Three experiments at 100-μsec were conducted for each of the spot sizes 350, 675, and 1,050 μm. The fluorescence technique was also used with the millisecond laser, but because it delivered a constant 20 mJ of energy, neutral density filters were used to change the energy to threshold and subthreshold levels. Three experiments were conducted for each pulse duration of 2, 5, and 10 msec with a 350-μm spot using a 300-μm fiber.

Spot size for a fiber positioned 500 μm above a target was determined by ablating thermal paper and red filter film under water. Spot sizes were determined by the average of five samples from each of the paper and film targets. The paper and film were then examined with a microscope to determine spot size.

Ablation Efficiency

Ablation efficiency experiments were conducted by directing laser energy onto gel and thrombus targets. The laser light was launched into an optical fiber that was housed in a catheter connected to a syringe pump (Syringe Infusion Pump 22, Harvard Apparatus, Dover, MA). The catheter was then positioned 500 μm above the target surface. The targets were in silicone tubes. A steady fluid flow of 2 ml/min was established by the syringe pump and directed around the fiber to the target site. The fluid flow collected the ablated mass and was sent to a cuvette for later mass measurement. Flow was continued until all of the ablated mass was collected into the cuvette. This procedure was repeated on control samples where no laser energy was delivered to account for the removal of mass by fluid flow alone.

Multiple laser pulses were delivered to the targets because a single pulse would ablate only micrograms of target. The tube containing the target sample was laterally translated with respect to the delivery fiber to maintain a constant spot size because as few as 5–10 pulses can form an ablation crater that alters the spot size. With a lateral translation distance on the order of the size of the original spot, the fiber would be directed at a fresh surface to maintain the appropriate spot size.

1-μsec pulsed dye laser. Ablation efficiency experiments with the 1-μsec pulsed dye laser were conducted with a 300-μm fiber and 5 mJ of energy at 3 Hz. The target was irradiated with 100 pulses. Three samples were taken and averaged. Pulse energies were measured with a joulemeter (JD500 and J50, Molectron).

100-μsec laser. Pulse energies of 2.5–17.5 mJ were delivered through 300-, 600-, and 1,000-μm fibers at repetition rates of 1–9 Hz with a pulse duration of 100 μsec. For the 1-Hz experiments, the fluid flow was reduce to 1 ml/min to collect all of the ablated mass. In addition, experiments were performed with a 300-μm fiber at 3 Hz at 50-μsec pulse durations. One hundred pulses were delivered onto the target. Five samples were taken at each of three energies in the range noted above. Total energy was maximized for each fiber size, and because larger fibers transmitted more energy, the three energies used were on the higher end of the range. Likewise, for the smaller fiber, the energies used were on the lower end of the range. Pulse energies were measured with a joulemeter (JD500 and J50, Molectron, Beaverton, OR).

Millisecond laser. For the millisecond laser, pulse energies of 20 mJ were used at 2, 5, and 10 msec. Laser energy was launched into a 300-μm fiber at 3 Hz. Thirty pulses were fired onto the target. Five samples were taken at each pulse duration. Pulse energies were measured with a calorimeter (AC5000, Scientech, Boulder, CO).

Spectrophotometric Mass Measurement

Ablation mass was determined by measuring the amount of dye in the ablated gel. This was accomplished with a spectrophotometer [1]. The ablated gel was dissolved in water due to the flushing action of the catheter. This solution was analyzed by the spectrophotometer. The absorbance measured was compared with a calibration curve established by measuring the difference in absorbance at 510 nm and 800 nm of dye solutions of known different concentrations. These two wavelengths were chosen because the peak absorption of the dye is at 510 nm, and 800 nm is in a low absorption range. Sathyam et al. [1,2] found the measurement errors to be less than 5%. The calibration curve was linear in the realm of interest. The slope of the curve provided the necessary conversion factor between the calibrated measurements and the measurement of absorbance of the ablated gel solution. The same procedure was used to determine ablation mass of clot by using the wavelengths 577 nm and 800 nm. The conversion scheme took into account the amount of dye in solution due to the flowing action of the flushing catheter. These data were provided by control samples in which no laser energy was delivered.

RESULTS

Ablation Threshold

Ablation thresholds for 1 μsec, 100 μsec, and 2, 5, and 10 msec are shown graphically in Figure 4. The ablation thresholds are also shown in Table 1. The temperature is calculated by adding the initial room temperature of 25°C, measured with a mercury thermometer (Fisher Scientific, Fair Lawn, NJ), to the increase in temperature predicted by equation (1).

TABLE 1. Threshold Radiant Exposure for Gel Phantom Versus Pulse Duration With Corresponding Gel Temperature

Pulse duration	Threshold (mJ/mm^2)	Gel temperature (°C)
1 μsec	21 ± 2.1	100 ± 10
100 μsec	19 ± 1	93 ± 4
2 msec	15 ± 4.5	77 ± 15
5 msec	16 ± 2	81 ± 6
10 msec	12 ± 1	68 ± 5

Ablation Efficiency

1-μsec pulsed dye laser. The ablation efficiency of the 1-μsec pulsed dye laser was determined for comparison with the ablation efficiency of the 100-μsec and millisecond lasers. The 1-μsec ablation efficiency was 1.7 ± 0.1 μg/mJ.

100-μsec laser. The effects of pulse duration, repetition rate, and spot size were determined for gel phantoms and clot with the 100-μsec laser. Ablation efficiencies with respect to laser pulse duration are shown in Figure 5. Spot size comparisons are shown in Figure 6. Repetition rate effects on canine clot are shown in Figure 7. The ablation efficiencies for 300-μm fiber at 5 mJ for 50, 100, and 150 μsec were 2.2 ± 0.2, 1.7 ± 0.1, and 2.0 ± 0.1 μg/mJ, respectively. The ablation efficiencies for a 100-μsec pulse in the 350-, 675-, and 1,050-μm spots were 1.7 ± 0.1, 1.4 ± 0.1, and 0.7 ± 0.1 μg/mJ, respectively. The ablation efficiencies for canine clot for 1, 3, 6, and 9 Hz were 2.8 ± 0.7, 1.8 ± 1.2, 1.8 ± 1.0, and 3.7 ± 1.0 μg/mJ, respectively.

Millisecond laser. The ablation efficiencies of the millisecond laser for gel phantoms were determined for pulse durations of 2, 5, and 10 msec by using a 300-μm fiber. The ablation efficiencies were 1.5 ± 0.1, 1.7 ± 0.1, and 1.9 ± 0.1 μg/mJ for the 2-, 5-, and 10-msec pulses, respectively. A comparison of the 1-μsec pulsed dye laser, the 100-μsec laser, and the millisecond laser is shown in Figure 5.

Gel Versus Clot Ablation Efficiency

The ablation efficiencies for a 5-mJ pulse from a 300-μm fiber onto gel and clot targets are 1.7 ± 0.1 and 2.9 ± 0.7 μg/mJ, respectively. The clot ablation efficiency was determined by the average of five samples from a 100-μsec pulse at 1, 3, 6, and 9 Hz. The spot sizes were 350 μm.

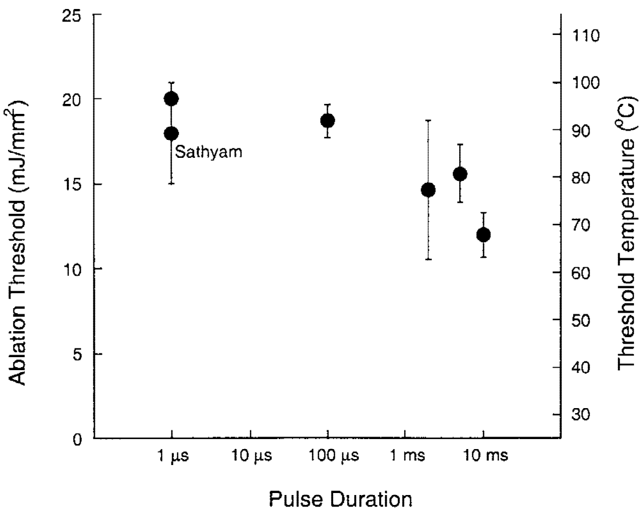

Fig. 4. Ablation thresholds for 1 µsec, 100 µsec, 2 msec, 5 msec, and 10 msec. All fiber sizes were 300 µm except for the 1-µsec pulse, which used a 100-µm fiber. The ablation thresholds all agree ($P < 0.05$).

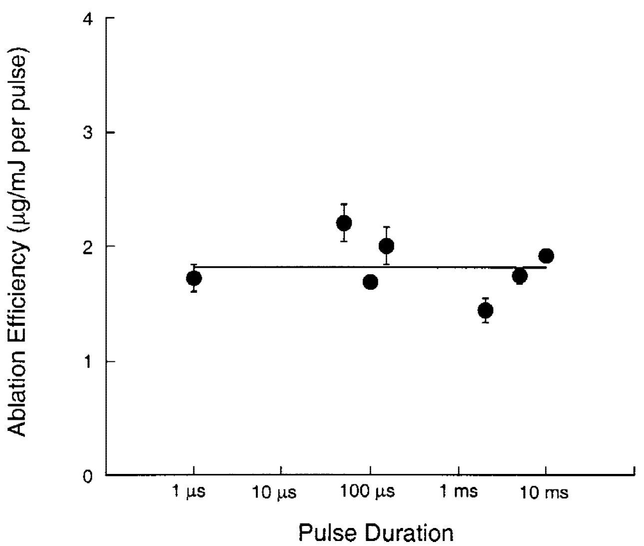

Fig. 5. The ablation efficiencies of the 1-µsec, 50-µsec, 100-µsec, 150-µsec, 2-msec, 5-msec, and 10-msec pulses. All fibers used were 300 µm. All experiments were conducted at 1 Hz. The ablation efficiencies agree ($P < 0.05$).

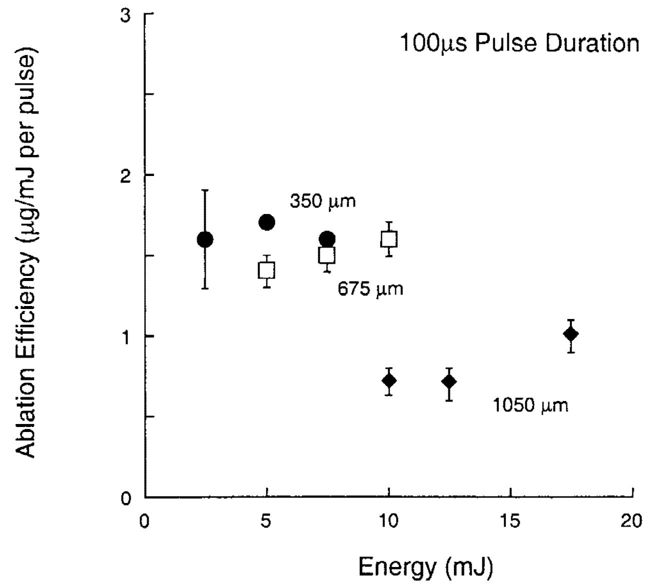

Fig. 6. The dependence of spot size on ablation efficiency. A 100-µsec pulse was used. The ablation efficiency of the 350-µm and 650-µm spot sizes agree ($P < 0.05$). The ablation efficiency of the 1,050-µm spot is lower than that of the smaller spots ($P < 0.05$).

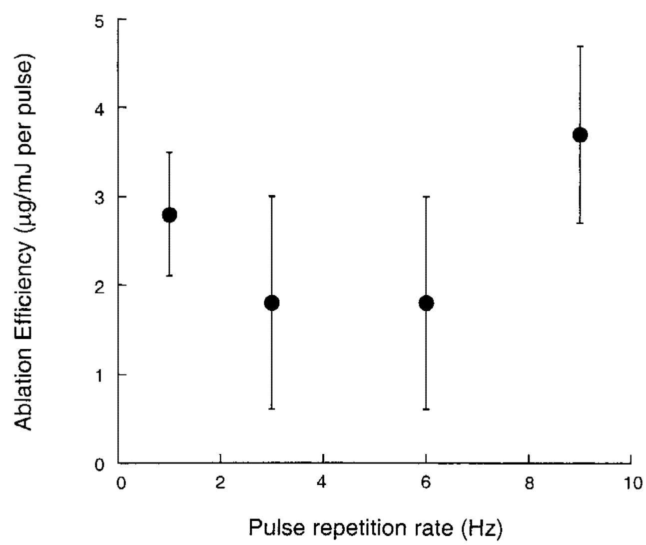

Fig. 7. The effect of pulse repetition rate on clot ablation efficiency. The fiber size was 300 µm. The pulse duration was 100 µsec. All ablation efficiencies agree ($P < 0.05$).

DISCUSSION

Previous Work

Considerable study has been conducted on bubble dynamics and tissue ablation with lasers with pulse durations on the time scales observed in the present study. Jansen et al. and van Leeuwen et al. used holmium lasers to study aspects of experimental cardiology, including laser angioplasty [3,15]. Jansen et al. used a Q-switched and a free running holmium laser to investigate the mechanical injury to tissue at the ablation site. The Q-switched laser had a pulse duration of 500 nsec and 14 mJ of energy, and the free running laser had a pulse duration of 100–1,100 µsec with 200 mJ of energy. The targets were water and polyacrylamide gels. They found significant pressure waves generated by the Q-switched pulse, although the acoustic effects could be reduced by a factor of 10 by stretching the pulse duration to 460 μsec. Concerns for increasing thermal damage were alleviated by the fact that thermal relaxation in tissue is on the order of 100 μsec.

Van Leeuwen et al. investigated mechanisms for arterial damage in pigs and rabbits in vivo by using a holmium laser at 2.12 μm and an excimer laser at 308 nm [15,16]. Damage mechanisms included direct laser irradiation and acoustic wave damage due to cavitation bubble formation. They investigated the role of the rapidly expanding vapor bubble on vasodilation and consequent damage to the artery.

LaMuraglia et al. [11] conducted ablation experiments on thrombus, emboli, vena cava, pulmonary artery, pulmonary valve, and endocardium. They used a pulsed dye laser operating at 482 nm with a 1-μsec pulse duration. They established selective ablation based on optical absorption of the thrombus and emboli over the other tissues. The selectivity principle showed that ablation of thrombus in a venous or arterial system had a great margin of safety.

Extensive research on laser thrombolysis was performed by Topaz et al. [7]. They showed fibrinolysis in vitro by using a Ho:YAG laser operating at 2.1 μm with a 250-msec pulse duration due to a photoacoustic effect [7]. They conducted several clinical studies in which effective and safe revascularization in acute myocardial infarction was demonstrated. In one study, a Ho:YAG laser was used to ablate thrombus in a human patient experiencing acute myocardial infarction, after failing treatment with thrombolytic agents [8]. In another study, a holmium–thulium:YAG laser was used in nine patients experiencing acute myocardial infarction. In all cases reduction of stenosis due to laser thrombolysis was achieved. In an even larger study, 25 patients were treated with laser thrombolysis using a Ho:YAG laser. All patients either did not successfully respond to pharmacologic therapy or pharmacologic therapy was contraindicated. Twenty-four of the 25 patients were treated with the laser successfully as indicated by decreased stenosis, elimination of chest pain, and no death [10].

Sathyam et al. [1] determined ablation parameters for gel targets by using a 1-μsec pulsed dye laser. They reported that ablation efficiency was nearly independent of absorption or radiant exposure. They also reported that ablation commenced when the temperature of the gel target reached 100°C. Using a 1-μsec pulse at 532 nm with a gel target of 300 cm^{-1}, they reported ablation efficiencies of 1–3 μg/mJ for 520-, 650-, and 1,070-μm spots for pulse energies above threshold.

Ablation Threshold

The ablation thresholds detected with the fluorescence technique agreed with the visual method of detecting bubble formation. The thresholds were also consistent, with a threshold temperature of 86°C ($P < 0.05$). Although this does not unequivocally comply with partial vaporization theory, the number of samples for five different pulse durations indicate a correlation to the partial vaporization model. The small shortfall in reaching 100°C may also be due to local hot spots in the laser beam profile, initiating vaporization at local nucleation sites.

All threshold experiments were done in 3-mm tubes using 300-μm fibers or smaller. Sathyam et al. found that 1,000-μm fibers had higher efficiencies, probably due to the confining geometry of the tubes, but found no such effect for 300-μm fibers [1].

Threshold fluences for holmium lasers showed an effect that is not evident in this study. Jansen et al. [3] and van Leeuwen et al. [4] found that a Q-switched holmium laser pulse at 1 μsec would reach threshold fluence in water before a free running holmium laser pulse at 250 μsec. Plasma formation during the Q-switched pulse was not responsible for the difference because it did not reach the requisite peak intensities required for plasma formation (10^9–10^{12} W/cm^2). Possible explanations of the difference included acoustic transients in the Q-switched pulse decreasing ablation threshold and differences in mode structure of the Q-switched and free running pulses. No difference in threshold fluence was found for the Nd:YAG laser pulse durations in this study.

Ablation Efficiency

The ablation efficiency of gel for 1-μsec, 50-μsec, 100-μsec, 150-μsec, 2-msec, 5-msec, and 10-msec pulse durations are all 1.7 ± 0.1 μg/mJ ($P = 0.05$). Ablation efficiency of clot for 1, 3, 6, and 9 Hz are 2.9 ± 1.0 μg/mJ ($P < 0.05$). Previous work with 1-μsec pulse durations [1] measured ablation efficiencies of gel phantoms to be 1–3 μg/mJ. The ablation mechanism has been suggested to be due to some mechanical action of the vapor bubble because the efficiency is about an order of magnitude higher than the efficiency results of ablation studies in air [1]. If this mechanism is water jetting as a result of bubble collapse, then the mechanism may be common to all laser pulses with durations less than the thermal relaxation time, assuming that the bubble lifetime is longer than the pulse duration. This last assumption assures that the laser energy is applied toward the bubble dynamics and, hence, toward ablation. Without some method to visualize the bubble dynamics that are obscured photographically by gel fluorescence, this contention would be hard to demonstrate.

Because the ablation efficiency of the longer pulse duration lasers falls within the range of efficiencies of the 1-μsec pulsed dye laser, the longer pulse lasers may be considered suitable alternatives for laser thrombolysis. Having longer pulse durations decreases the significance of acoustic wave generation due to cavitation bubble collapse, which has been shown to produce arterial damage in vivo [14,15]. In addition, a longer pulse duration would facilitate launch into smaller fibers.

Gel Versus Clot Ablation Efficiency

The gel phantoms had an ablation efficiency of 1.7 ± 0.1 μg/mJ, whereas the clot had an ablation efficiency of 2.9 ± 1.0 μg/mJ. Gel phantoms were used extensively in these experiments because they provide a reproducible model for clot. A gel phantom has a homogeneous nature with regard to gelatin and absorbing dye concentration; thus, its strength and optical absorption coefficient are likewise homogeneous within and between samples. This results in small variances in data due to sample-to-sample variations.

Clinical Implications

All experiments indicate that a 10-msec laser pulse is as effective at ablating thrombus as the 1-μsec pulsed dye laser. The frequency-doubled Nd:YAG lasers used in this study can replace the pulsed dye laser previously used because they maintain the ablation efficiency. They also maintain the advantage of selective ablation over the mid-infrared lasers, such as the Ho:YAG laser. The long pulse duration may also reduce mechanical damage to tissue due to acoustic events. The ablation threshold and efficiency are the same as the 1-μsec pulse, meaning that the same amount of energy could be used to clear artery occluding clot. The longer pulse is better suited for coupling into small fibers, a clear advantage, because the small, tortuous vessels in the brain require a small, flexible delivery fiber. These factors promote the use of a long pulse, solid-state laser for further study in developing laser thrombolysis for stroke applications. In particular, in contrast to the Ho:YAG laser, where significant clinical success was demonstrated, the Nd:YAG laser could be as efficacious and safer because of the selective ablation of thrombus over artery wall.

The results in this study also showed ablation efficiency to be independent of pulse repetition rate in the range of 1–9 Hz. Assuming that a clot mass is in the order of a gram, the calculated ablation efficiency indicates that 50-mJ pulses at 9 Hz would completely ablate the clot in about 10 min. Actual time for laser use would be even less because the entire clot would not necessarily be ablated to restore blood flow, especially if the clinical protocol coupled laser thrombolysis with thrombolytic agents. This method would be synergistic because the breakup of clot by the laser irradiation would increase the surface area of the clot, thereby increasing the ability of the thrombolytic agents to break down the clot.

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