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The Effects Of Spot Size, Pulse Energy, and Repetition Rate on Microsecond Ablation of Gelatin Under Water

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ABSTRACT

The efficiency of laser ablation of thrombus depends on spot size, pulse energy and repetition rate. A 1 μs pulsed dye laser (504 nm) was used to ablate a gelatin-based thrombus model containing an absorbing dye under water. The gelatin was confined in 3 mm inner diameter tubes and pulse energies of 25-100 mJ were delivered via 300, 600, and 1000 μm core diameter fibers. The experiments were conducted at pulse repetition rates of 3 Hz and 10 Hz. The amount of gelatin removed was measured using a spectrophotometric method and ablation efficiency was defined as mass removed per pulse per unit energy. Flash photography was used to visualize the ablation process in 1 cm cuvettes. Results: More material was removed using bigger fibers in the 3 mm tubes at similar pulse energies. The amount of gelatin removed per pulse increased linearly with pulse energy. There was no significant change in the amount removed at pulse repetition rates of 3 Hz and 10 Hz. In the 1 cm cuvettes, the ablation mass was roughly the same with both the 300 μm and 1000 μm fibers. Flash photography of the ablation process in 1 cm cuvettes showed that less than 1% of the laser energy went into formation of a vapor bubble. The mass removed increased roughly linearly with bubble energy. Conclusions: Ablation mass increases linearly with pulse energy, but does not have a direct relationship with radiant exposure. It is independent of the repetition rate under 10 Hz.

1. INTRODUCTION

Microsecond lasers have emerged as an effective tool to clear arteries of obstructions such as thrombus and plaque.[1–3] The absorption of the laser pulse by the thrombus leads to vaporization of part of the tissue and the formation of a vapor bubble. The bubble expands and collapses rapidly resulting in further disruption of the thrombus.

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Laser thrombolysis is potentially safer than other recanalization techniques since thrombus can be selectively removed without injuring the adjacent arterial tissue. This can be achieved by selecting a wavelength well absorbed by the thrombus, but poorly absorbed by the vessel wall. The waveband between 400-600 nm offers a high degree of selectivity in absorption between thrombus and artery.[4,5]

The high degree of selectivity makes it possible for the radiant exposure to be set such that it is above the ablation threshold of thrombus but below that of artery. To determine the optimal radiant exposure for efficient ablation it is necessary to understand the effects of spot size and pulse energy on the mass removed per pulse. The spot size also plays an important role in determining the size of the catheter delivering the laser energy to the thrombus. The pulse repetition rate is another important parameter that may potentially influence the efficiency of ablation.

In this paper, we studied the effects of spot size, pulse energy, and repetition rate on the ablation efficiency using a gelatin-based thrombus model. The use of a model eliminated the biological variability of thrombus. A 3 mm diameter plastic tube was used to simulate the artery. Since laser thrombolysis is done in a saline/contrast environment, the gelatin was ablated under water. A spectrophotometric method was used to measure the mass ablated. Flash photography was used to visualize the ablation process in 1 cm cuvettes and bubble dynamics were studied.

The results of our study show that the mass ablated increases linearly with pulse energy for a *single* spot size. Larger spot sizes were more efficient at removing material in the 3 mm tubes than smaller spot sizes. In the 1 cm cuvettes, the spot size had no significant effect on the ablation mass. This suggests that the ablation efficiency depends mainly on the pulse energy rather than the radiant exposure. The ablation efficiency was independent of repetition rate under 10 Hz. Flash photography showed that less than 1% of the pulse energy went into the formation of a vapor bubble. The bubble energy increased roughly linearly with the pulse energy.

2. MATERIALS AND METHODS

2.1. Gelatin model

The thrombus was modeled by 3.5% by weight gelatin in water. A dye (Direct Red 81, Sigma) was added to the gelatin to control the absorption at the laser wavelength (504 nm). At 504 nm, 0.1 g of the dye in 100 ml gelatin solution resulted in an absorption coefficient of 100 cm^{-1}. The absorption of the dye increased linearly with concentration. Our experiments were conducted at absorptions of 100 cm^{-1} and 300 cm^{-1} to match thrombus absorption at 490 nm 577 nm respectively, which are the currently used wavelengths in clinical trials. Liquid gel samples were drawn into 3 mm tubes (Tygon) and allowed to cure.

2.2. Laser system

A 1 μs pulsed dye laser (Palomar Medical Technologies) operating at a wavelength 504 nm was used for ablation. The maximum output energy of the laser was 200 mJ. The repetition rate was variable between 1–10 Hz. Quartz fibers of 300, 600, and 1000 μm core diameter were used to deliver the laser pulses. Spot sizes produced with these fibers 1 mm from the tip were 520, 650, and 1070 μm respectively.

2.3. Ablation in tubes

Light was delivered through a quartz fiber with its tip about 1 mm from the gel surface. A steady flow of water at 0.3 ml/s was established by a fluid injector (Medrad Mark V) and directed around the fiber to target site. Pulse energies of 25-100 mJ were delivered via 300, 600, and 1000 μm fibers at repetition rates of 3 Hz and 10 Hz. Ten pulses were fired on each sample and the ablated gel was collected by the flowing water in 1 cm cuvettes. The steady flow was continued after the last pulse until 4 ml of liquid was collected. The above procedure was repeated on control samples without light delivery to account for the gel removed by the flow of water alone. The ablated gel was dissolved completely in the water, and its mass was determined by the spectrophotometric method described below. Ten samples and five controls were used for each data point. Pulse energies were measured with a joulemeter (Molectron).

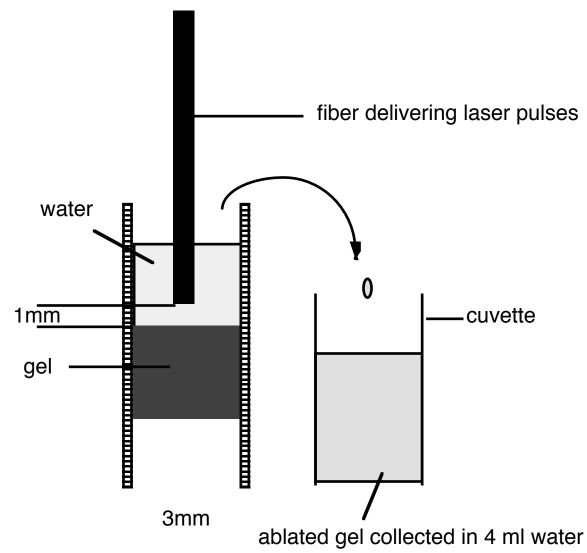

Figure 1. Gelatin containing an absorbing dye is confined in a 3 mm diameter tube. Laser energy is delivered in 1 μs pulses via a quartz fiber at a distance of 1 mm to the gelatin. The ablated material is collected in 4 ml water and the absorbance is measured in a spectrophotometer.

2.4. Measurement of ablation mass

Ablation mass was determined by measuring the amount of dye in the ablated gel. The trace amounts of dye were measured by determining the absorbance of the ablated gel in solution. A calibration curve was used to convert the measured absorbance to a mass. The calibration curve was established by measuring the absorbances of known masses of dye in 4 ml water. The curve proved to be linear, and the slope of the line provided the necessary conversion factor. The absorbances were measured at two wavelengths (510 nm and 800 nm) to minimize the noise in measurement.

2.5. Ablation in cuvettes

Gelatin was ablated in 1 cm cuvettes using the 300 μm and 1000 μm fibers, and the ablation process was captured using a CCD camera and a 1 μs strobe. The moment of image capture was controlled by a delay generator and was varied to visualize the formation and collapse of the laser-induced bubble. Bubble sizes and lifetimes were measured and bubble energies were calculated using Rayleigh's formulae given by[6–10]:

$$T_c = 0.915 R_{max} \sqrt{\frac{\rho}{p_{stat} - p_v}}$$

where R_{max} and $2T_c$ are the maximum radius and lifetime of the bubble. ρ is the density of water, p_{stat} is the vapor pressure inside the bubble, and p_v is the static pressure of the surrounding liquid. The energy of a hemispherical bubble is then given by:

$$E_B = \frac{2}{3}\pi(p_{stat} - p_v)R_{max}^3$$

The mass of gelatin ablated was measured using the spectrophotometric method.

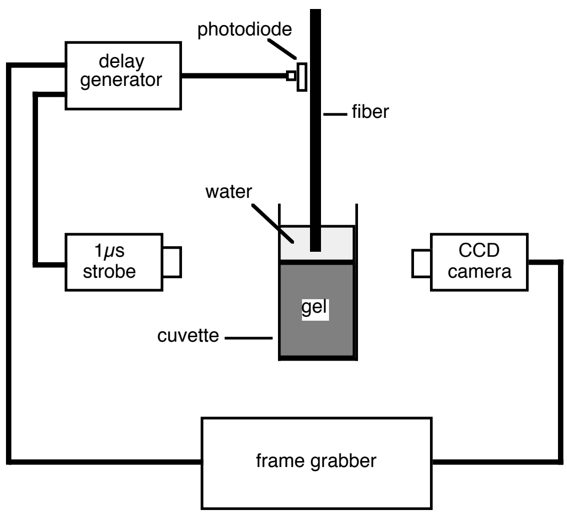

Figure 2. Flash photography: 300 μm and 1000 μm fibers were used to deliver pulse energies of 25-100 mJ. Fiber tip was maintained 1 mm from the gel surface. Absorption of the gel was 100 cm^{-1}

3. RESULTS

3.1. Ablation in tubes

More gelatin was removed with larger fibers at the same energy. The 1000 μm fibers ablated about twice as efficiently as 300 μm fibers (figure 3). The mass removal increased linearly with pulse energy for a *single* spot size. Radiant exposures were calculated by dividing the pulse energy by the spot size made by the fiber. There were no significant differences in ablation masses at pulse repetition rates 3 Hz and 10 Hz.

3.2. Ablation in cuvettes

There were no significant differences between the ablation masses in the tubes and the cuvettes using the 1000 μm fiber. Ablation with the 300 μm fiber was more efficient in the cuvettes than in the tubes. The amount of gel removed with the 300 μm fiber was roughly the same as the ablation mass with the 1000 μm fiber at similar energies.

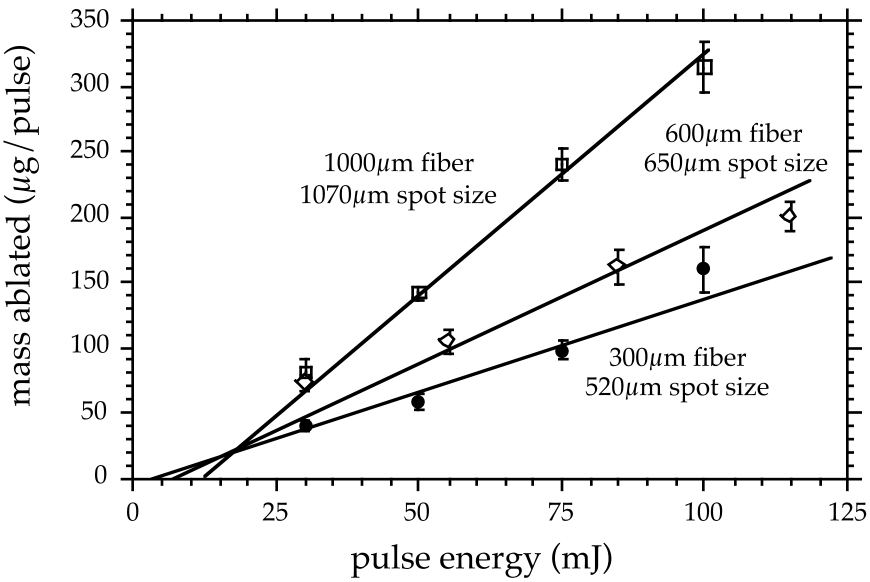

Figure 3. Ablation mass in tubes: The intersections of the linear fits with the x-axis give the threshold energy for ablation for each spot size. Error bars denote standard deviation of 10 samples.

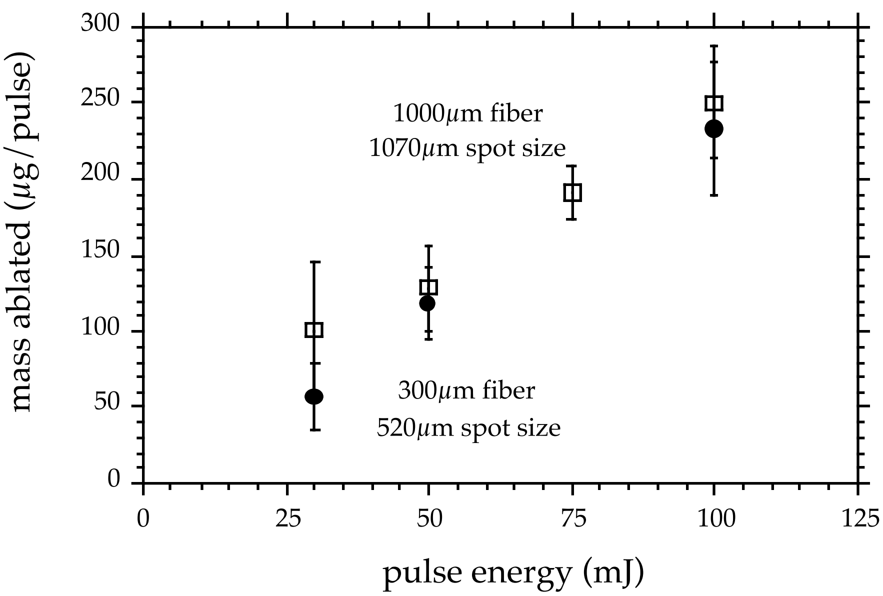

Figure 4. Ablation mass in cuvettes: Error bars denote standard deviation of 10 samples.

3.2.1. Bubble dynamics

Each bubble was a separate event and was quite reproducible. Bubbles of maximum diameter of 1–3 mm were formed and collapsed 200–400 μs after the laser pulse. The were no significant differences in bubble sizes and lifetimes produced with the 300 μm and 1000 μm fibers at 100 mJ. This is well above threshold for both fibers, 4 mJ and 14 mJ respectively. Larger bubbles were produced with the 300 μm fiber than with the 1000 μm fiber at 30 mJ. This is just above the ablation threshold energy for the 1000 μm fiber. Bubble energies were calculated based on the maximum radius and collapse time and showed that less than 1% of the pulse energy went into the formation of the bubble.

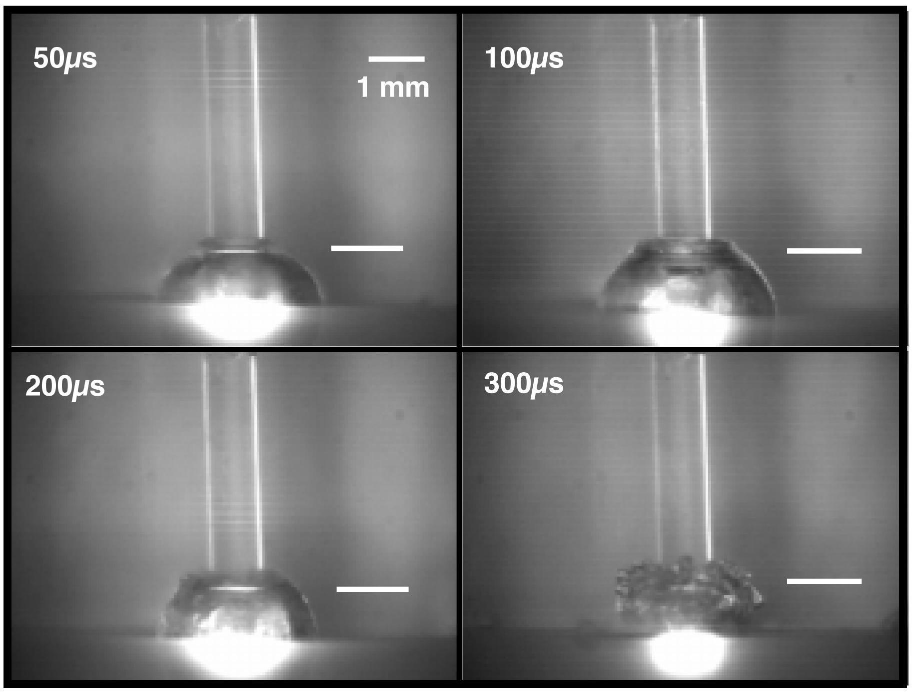

Figure 5. Bubbles formation and collapse with a 1000 μm fiber at 100 mJ. Time indicated is the interval between laser pulse and image capture. The white bars indicate the level of the fiber tip.

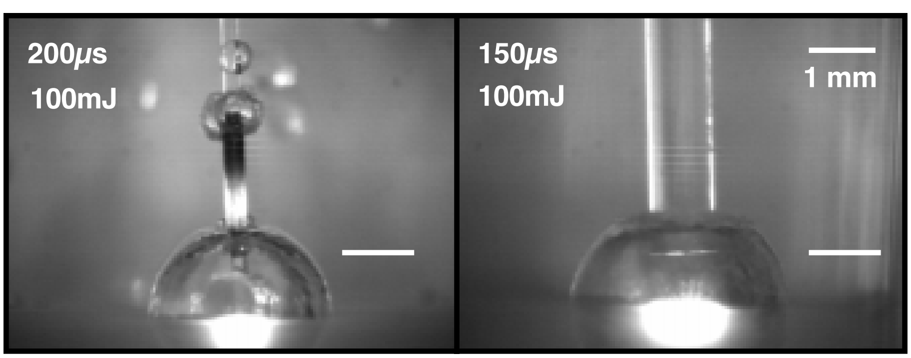

Figure 6. Biggest bubbles formed with 300 μm and 1000 μm fibers at 100 mJ. Time indicated is the interval between laser pulse and image capture. The white bars indicate the level of the fiber tip.

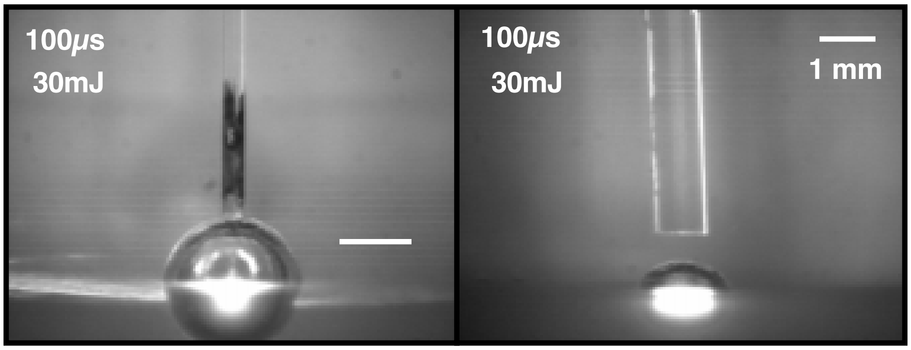

Figure 7. Biggest bubbles formed with 300 μm and 1000 μm fibers at 30 mJ. Time indicated is the interval between laser pulse and image capture. The white bar indicates the level of the fiber tip.

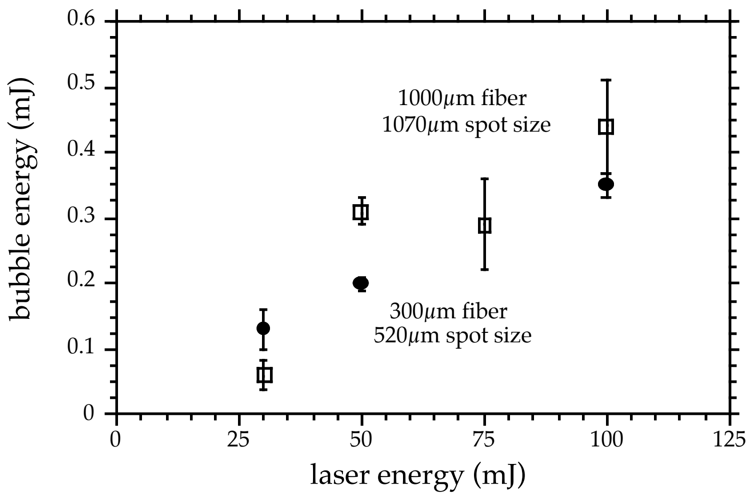

Figure 8. Bubble energies calculated using the maximum radius and lifetime of the bubbles.

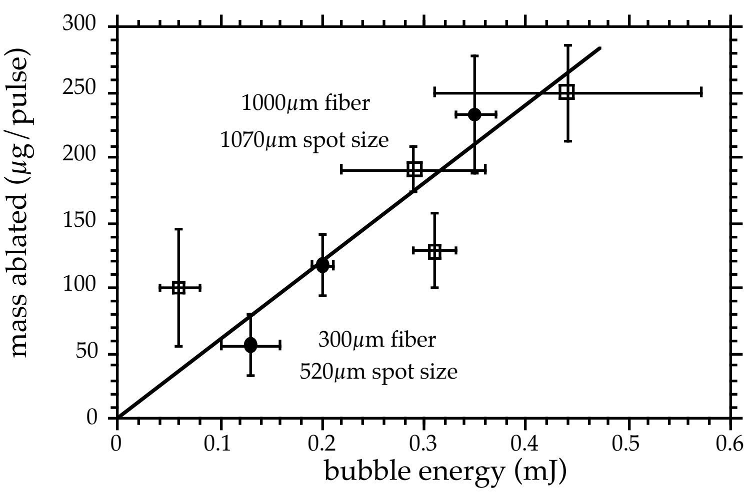

Figure 9. Bubble energies and corresponding ablation masses.

4. DISCUSSION

This study was carried out to find a suitable spot size, pulse energy and repetition rate for microsecond laser ablation of thrombus. The thrombus was modeled with gelatin in plastic tubes, and the laser energy was delivered at two repetition rates via quartz fibers of various core diameters. The amount of gelatin removed was measured using a spectrophotometric method. We used flash photography to visualize the ablation process at various radiant exposures in 1 cm cuvettes. The energies of the laser induced vapor bubbles were calculated based on their maximum size and lifetime.

It is evident from figure (3) that small spot sizes do not result in larger mass removal than large spot sizes at similar energies although the radiant exposure is higher in the first case. Previous studies have reported a linear increase in mass removal with radiant exposures.[11–13] However, in those studies the radiant exposure was varied by changing the pulse energy while maintaining a constant irradiated spot size. Therefore those results actually indicate a linear dependence of the ablation mass on the *energy*. We also observed a linear relationship between ablated mass and energy for each spot size.

A possible explanation for the higher efficiency at larger spot sizes could be that more energetic bubbles are formed. To either confirm or disregard this hypothesis, we ablated gelatin in 1 cm cuvettes to easily visualize the ablation process and chart the bubble dynamics. Laser energy was delivered via 300 μm and 1000 μm fibers. Ablation masses were measured and correlated to the bubble energies. The surprising result of this experiment was that there was no significant difference in ablation mass at the two spot sizes at energies above threshold (figure 4). Again, a linear increase in ablation mass with pulse energy was observed. Bubbles of roughly the same energies were formed with the two fibers, and a linear relationship between bubble energy and ablation mass was observed (figure 9). These results suggest that the mass removal depends on the energy of the vapor bubble formed. Similar conclusions were reached by Vogel *et al.* who studied mechanisms of damage during intraocular surgery.[7–9]

The higher ablation efficiency at larger spot sizes in the tubes is probably due to a confinement effect of the larger fibers. This suggests that larger diameter catheters would be better for laser thrombolysis. However, the size of the catheter would be limited by flexibility requirements and the size of the vessel. Higher pulse energies result in greater ablation masses. The maximum energy that can be used with a particular spot size during laser thrombolysis would be limited by the ablation threshold for the vessel wall. Ablation efficiency was roughly the same at pulse repetition rates of 3 Hz and 10 Hz. This is evidently due to the short lifetimes of the bubbles which ranged from 200–400 μs. Laser thrombolysis procedure could be therefore be done in a shorter time at higher repetition rates.

The ablation masses reported in this paper are an order of magnitude higher than those reported for ablation of tissue in air.[11,14] This again suggests that the dominant mechanism in the ablation process under a liquid is some mechanical action due to the vapor bubble. The energy balance shows that less than 1% of the laser energy goes into the formation of the vapor bubble (figure 8). Vogel *et al.* calculated their bubble energies to range between 3–25% of the pulse energy. The lower coupling efficiency reported here could be due to the longer pulse durations used and the fact that only hemispherical bubbles are formed. However, both in this study and in those by Vogel *et al.*, a large portion of the laser energy is not accounted for. This energy is most likely dissipated into heat and may or may not participate in the ablation process.

The main conclusions of this paper are: (*i*) larger spot sizes are more efficient in tubes. (*ii*) ablation efficiency is independent of spot size in an unconfined medium. (*iii*) mass removal depends primarily on pulse energy. (*iv*) less than 1% of the laser energy goes into the formation of a vapor bubble. (*v*) mass removal varies linearly with bubble energy.

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