Study of ns and fs pulse laser-induced effects in biological-tissue models and corneal tissue

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Abstract. This work presents a study of photo-induced effects in biological-tissue models made from agar gel and porcine cornea samples. We used a Nd:YAG (5 ns) and a Ti:sapphire (90fs) lasers to irradiate the samples. The main objective in this study is to understand some aspects of the interaction between pulsed lasers and biological tissue, of especially interest for us are vascular and corneal tissues. Our research includes laser heating of vascular-like tissue and laser-induced cavitation bubble formation in cornea. For the laser heating studies we used tissue models composed by a single or up to four stack layers made of agar gel (of between 200 and 500μm thickness per layer); for the laser-induced bubble formation we used corneal tissue which was obtained from regular porcine corneas. In order to emulate blood vessels, we designed an organic dyed agar gel layer made off an organic dye whose absorption coefficient is similar to that of hemoglobin. We will present results of laser heating of vascular-like tissue, and its dependence on laser fluence and pulse duration. Also, we will present results of cavitation bubble formation (100-600 μm deep) for agar gel and corneal tissues. Our results show that there exists a well determined threshold fluence for the onset of bubble formation; the laser-induced bubbles on agar gel and cornea can be permanent or transient depending on the laser irradiation parameters. The diameter of the cavitation bubbles is clearly dependent on the laser fluence. Some interesting dermatological and ophthalmic applications related to the above effects will be suggested and discussed throughout this work.

Keywords: Pulsed laser, biological tissue, corneal tissue, medical applications.
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INTRODUCTION

As any other material, biological tissue can be exposed to optical radiation in order to generate ablation of the sample [1]. The objective of this work is to study the effects produced on the interaction between short laser pulses and biological tissue.

Our work will be presented in two parts; the first one is the irradiation of vascular tissue models *"phantoms"* made of agar gel and an organic dye, being the objective to study the viability of short laser pulses as a novel tool to treat birthmarks like port wine stain; and the second part is the application of short laser pulses for corneal surgery [2]. We made irradiations with ns and fs laser pulses on both samples in order to prove that short laser pulse irradiation of bio-tissue presents features that can be applied in medicine [3].

VASCULAR TISSUE MODELS IRRADIATION

Threshold Fluence Determination

An ablation interaction can be well characterized using the parameter known as the ablation threshold fluence (F_{th}). The formation of cavitation bubbles in the bulk occurred either for ns or fs laser irradiation for both transparent and dyed (Direct Red, Fischer Scientific) agar. The bubble formation was characterized by a well defined laser fluence. In order to find such a threshold fluence, we studied two sample configurations, as shown in figure 1(b) and (c), where a blood vessel is emulated using the direct red; for both configurations we used four different dye concentrations.

The threshold fluence experiments were carried out using a frequency doubled Nd:YAG laser (λ=532nm), pulse duration of 5ns; a focusing lens (f/# =1.27) to give us a beam waist of ~ 6μm. The samples were irradiated with a single pulse focusing the beam at a depth of 100μm within the dyed layer as it is shown in figure 1.

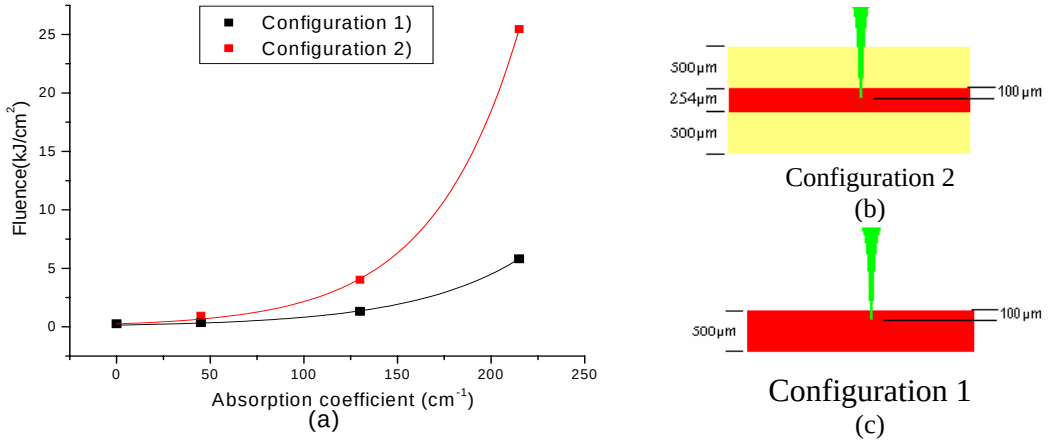


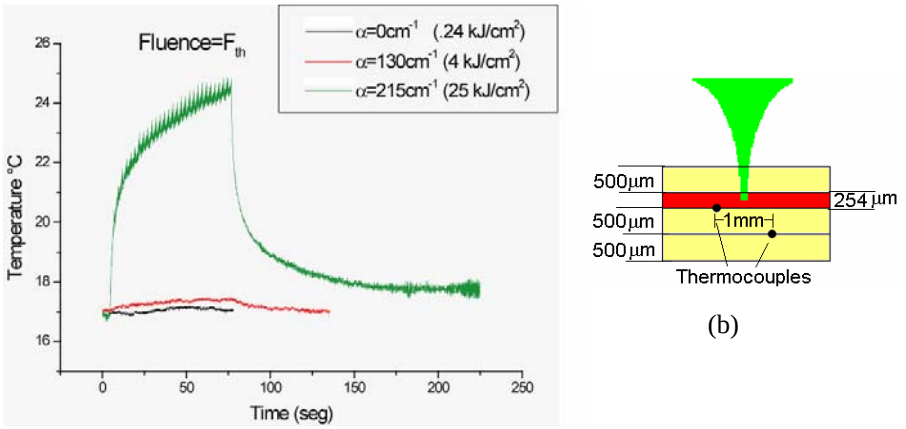
FIGURE 1. Threshold fluence for the agar phantoms (a) vs absorption coefficient. Irradiation configurations (b), (c).

Contrary to what it could be expected from a dominating thermal mechanism, it was found that as long as the absorption coefficient increases, a bigger fluence is needed in order to form the cavitation bubble. It is believed that the bubble forms from a thermal mechanism contribution which is accompanied by a dielectric breakdown process, i.e. the intensity (not only the energy) of the laser pulse is of significant relevance for the bubble formation. An interesting result is that diameter of the bubble formed at F_{th}, for all the samples, is of 70μm. In the case of bubbles formed with fs laser pulses, they were transient when the irradiation fluence is only slightly above threshold.

Temperature Change Experiments

Using the F_{th} results (figure 1a) we designed a set of experiments to measure the temperature changes associated to the bubble formation at different fluences. For this purpose we used a *phantom* made of four agar gel layers as shown in figure 2b. Monitoring of temperature changes were carried out by using thermocouples placed as

indicated in the same figure. The experiments consisted of sample irradiation with the 5ns Nd:YAG laser for 60sec at a laser pulse delivery rate of 10Hz, the beam was focus at a depth of 100μm within the dyed layer.



(a) (b)

FIGURE 2. Temperature change comparison at bubble formation F_{th} for three different absorption coefficients (a). Experimental setup for temperature change measurements (b).

As it was expected, as the absorption coefficient increases, the temperature change would increase too, as it can be clearly seen from our heat diffusion results plotted above (figure 2a). When irradiating the α=215cm^{-1} sample with 90fs laser pulses, λ=800nm at a frequency of 10Hz, we found a quite interesting and important result shown in figure 3. In this case a $3F_{th}$ made not temperature change, but it did form a cavitation bubble. This result is a preliminary confirmation of the intensity dependence of the bubble formation mechanism, without the need of a thermal contribution.

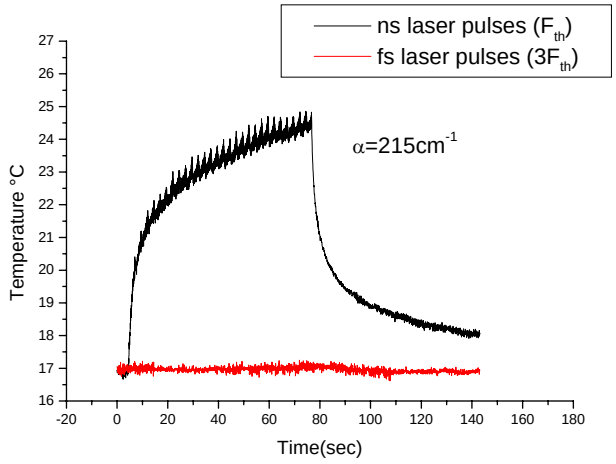


FIGURE 3. Temperature measurement comparison on the same sample using ns and fs laser irradiation.

CORNEAL TISSUE IRRADIATION

The above results on tissue *phantoms* motivated us to take another step in our research and we started doing irradiations on real tissue. The objective of this part of our work is to used the cavitation bubbles previously demonstrated to form cavitation channels inside the cornea. We used porcine cornea due to its similarity to human cornea [4]. In our experiments, we irradiated the samples with the 5ns Nd:YAG laser and using the same optics than in the agar gel *phantoms*. In this case, we made linear scans moving the samples at a velocity of 250μm/sec and irradiating at a laser pulse delivery rate of 3Hz. The results of the irradiation on porcine cornea are shown in figure 4(a) and (b).

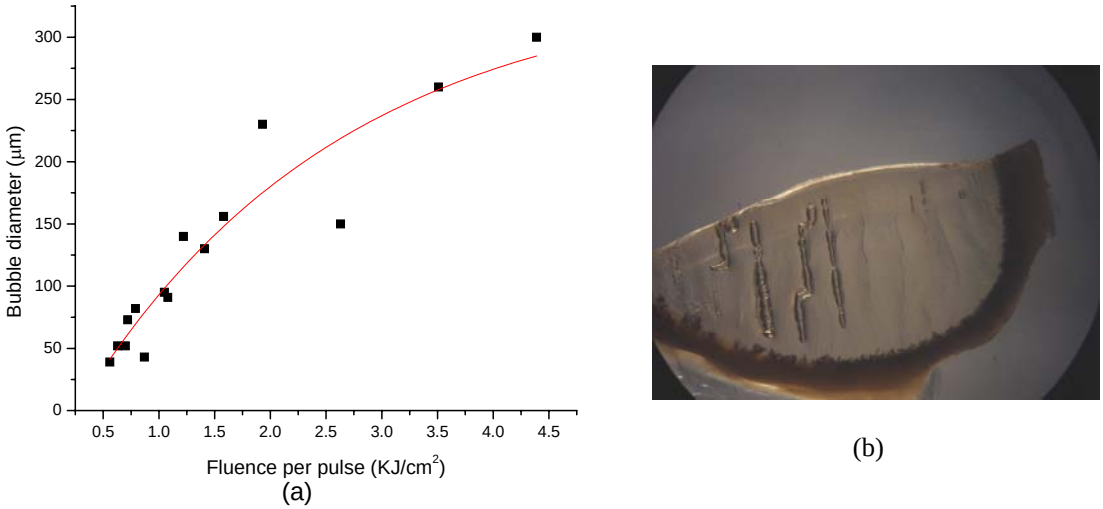


FIGURE 4. Bubble diameter in porcine corneal tissue dependence on the pulse fluence (a). Porcince cornea tissue irradiated by 5 ns laser pulses, λ=532nm at a frequency of 3Hz (b).

The laser was focus at a depth of 400μm inside the cornea. As it was expected from the previous experimental results, in the agar gel, the size of the cavitation bubbles formed in cornea also depends on the laser fluence used on the irradiation. We must note that the bubble diameter in cornea follows the same trend as a function of fluence as it occurs for bubbles formed in agar gel.

CONCLUSIONS

There exists a well determined threshold fluence for the bubble formation in agar gel and real cornea tissue, which is quite useful to study and understand the short pulse laser interaction with tissues. Although in the case of ns laser irradiation the bubble formation mechanism has an important thermal contribution, the fs laser irradiation of agar gel samples allowed us to show good evidence of the bubble formation mechanism dependence on laser pulse intensity, i. e., the bubble formation on set has a dielectric breakdown origin in addition to a thermal contribution. More interestingly, the bubble formation using fs laser pulses takes place without significant heating

effects, suggesting a laser-tissue interaction with negligible collateral thermal damage. Our results prove short pulse lasers very promising for medical applications.

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