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The effect of laser/ultrasound synchronization on photo-mediated ultrasound therapy

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Background, Motivation and Objective

Photo-mediated ultrasound therapy (PUT) is a non-invasive, agent-free technique to shut down microvessels with high precision by promoting cavitation activity precisely in the targeted microvessels. PUT is based on the photoacoustic (PA) cavitation generated through synergistically applied nanosecond laser pulses and ultrasound bursts. It is imperative to properly synchronize laser pulses and ultrasound bursts in order to achieve desired cavitation activity. Here, we investigated the effect of synchronization between laser and ultrasound on cavitation in *in vitro* and *in vivo* studies.

Statement of Contribution/Methods

An integrated ultrasound transducer (0.5 MHz, H107 Sonic Concepts, Bothell, WA), laser, and CCD camera system was devised. A 10-Hz, Nd:YAG laser (Continuum Powerlite DLS 8010, Santa Clara, CA) produced 5-ns pulses at 532 nm. A 20 MHz ultrasound transducer (V317, Olympus NDT, Waltham, MA) was used as a passive cavitation detector (PCD) to detect cavitation activity. A pulse delay generator (Model DG355, Stanford Research Systems) provided all triggers to the system to achieve a precise synchronization between laser pulses and ultrasound bursts. *In vitro* study with human blood in a tubing was performed to demonstrate the relation between cavitation activity and synchronization of laser/ultrasound. Then, in the *in vivo* study, neovascularization was induced in the corneal of 10 New Zealand white rabbits by surgically placing a 7-0 nylon suture in the cornea. Two weeks after the suture placement, neovascularization in five rabbits were treated with in-phase PUT settings, where a laser pulse was synchronized to negative phase of ultrasound, and another five rabbits were treated with out of phase PUT settings, where a laser pulse was synchronized to positive phase of ultrasound.

Results/Discussion

Both numerical simulation and *in vitro* results showed that PUT could only induce cavitation when laser and ultrasound were in-phase. The *in vivo* results showed that removal of microvessels could only be achieved when rabbits were treated with in-phase PUT settings. When laser and ultrasound were not properly synchronized, no treatment effect could be observed. These results demonstrated the importance of laser/ultrasound synchronization for PUT.

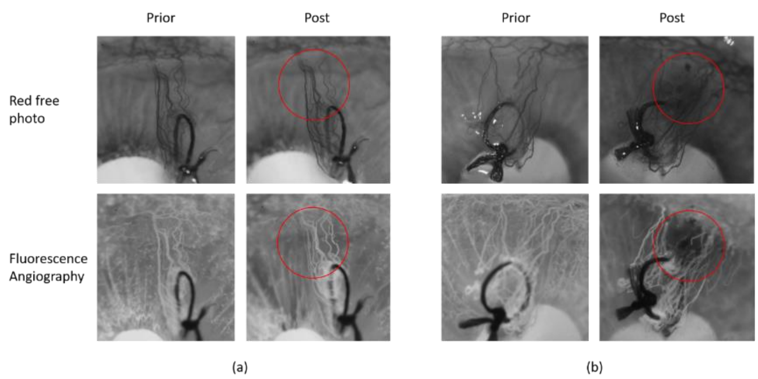

Figure 1 Phase control in vivo: (a) Out of phase. (b) In phase. The applied ultrasound pressure was 0.425 MPa at 0.5 MHz. The applied laser fluence was 3.14 mJ/cm2. The laser spot size is 5 mm diameter and the duration time is 10 min.