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We investigate laser-induced shock waves from melanin particles as a possible cause of retinal injury from ultrashort pulse laser exposures. Melanin granules were isolated from calf retina and suspended in gels. The melanin particles were irradiated with 100 psec laser pulses from an amplified, mode-locked Nd:YAG laser and shock waves were observed under a microscope using a time-delayed strobe pulse. Spherical shock fronts were observed at incident laser fluences] 4J/cm2 and were imaged as close as 20um from the melanin particles. Multiple shock fronts were resolved when several melanin particles were irradiated simultaneously. Shock front radii were measured as a function of photographic delay time and laser fluence. Average shock fron velocitites during the first 10 nsec ranged from 2500 to 4000 m/sec. A velocity of 3000 m/sec corresponds to a shock pressure of 11 kbars. These results indicate that shock wave emission from melanin particles in the retinal pigment epithelium is a potential cause of retinal injuryffrom ultrashort laser pulses.

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Technical Report

May 31, 1994

AFOSR Contract No. F49620-93-1-0337
Title: "Retinal Injuries from Single and Multiple Picosecond Laser Pulses"

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Abstract

We investigate laser-induced shock waves from melanin particles as a possible cause of retinal injury from ultrashort pulse laser exposures. Melanin granules were isolated from calf retina and suspended in gels. The melanin particles were irradiated with 100 psec laser pulses from an amplified, mode-locked Nd:YAG laser and shock waves were observed under a microscope using a time-delayed strobe pulse. Spherical shock fronts were observed at incident laser fluences > 4 J/cm^2 and were imaged as close as 20 μm from the melanin particles. Multiple shock fronts were resolved when several melanin particles were irradiated simultaneously. Shock front radii were measured as a function of photographic delay time and laser fluence. Average shock front velocities during the first 10 nsec ranged from 2500 to 4000 m/sec. A velocity of 3000 m/sec corresponds to a shock pressure of 22 kbars. These results indicate that shock wave emission from melanin particles in the retinal pigment epithelium is a potential cause of retinal injury from ultrashort laser pulses.

Introduction

During the past contract year, our group has engaged in two parallel studies aimed at 1) non-invasive in vivo diagnostic imaging of retinal injuries and 2) understanding injury mechanisms from ultrashort laser pulses. In the first project, performed in collaboration with Professor James G. Fujimoto's group at MIT, a new optical diagnostic technique called optical coherence tomography (OCT) is being developed for noninvasive in vivo histopathology of the retina. The high-speed, high-resolution optical sectioning capability of OCT is a potentially powerful tool for detecting threshold laser injuries and for studying injury progression. Progress related to OCT studies will be presented in Professor Fujimoto's report.

In the second project, we investigate the mechanism of retinal injury from ultrashort laser pulses, focusing on the role of acoustic and shock wave formation as a possible injury mechanism. Although acoustic injury is a well known side effect which can arise during nanosecond Nd:YAG laser surgery in the eye when optical breakdown is created, it is less well understood whether acoustic and shock wave effects are significant at threshold retinal injury levels, i.e. at levels below the onset of optical breakdown. Optical breakdown is a nonlinear phenomenon in which the laser-induced plasma provides nonlinear absorption of the incoming radiation. Below the optical breakdown threshold, the melanin granules in the retina are the primary linear absorbers of visible and near infrared radiations. Melanin absorption is believed to play a central role in laser injury of the retina.

For nanosecond and longer pulse durations, the energy absorbed by the melanin causes a temperature rise in the surrounding retina through thermal diffusion. Injury is produced if the temperature rises above a critical value. The thermal injury mechanism is the basis of the current ANSI exposure guideline for nanosecond and longer pulse durations.

For pulse durations shorter than 1 nsec, absorption of pulse energy by the melanin can create not only a rapid rise in temperature but also an (almost instantaneous) increase in pressure. The pressure transient can result in the disruption of the melanin and the RPE and can also propagate into the surrounding tissue. Such an acoustic mechanism has been proposed as a possible cause of retinal injury, although direct measurement and characterization of the pressure transient have so far not been carried out.

We have set up an experiment to investigate shock wave formation from melanin particles, using fluence levels which are relavent to retinal injury threshold. In this setup, an amplified mode-locked Nd:YAG laser pulse with a 100 psec pulse duration is used to irradiate melanin particles isolated from calf retina and suspended in gels. A delayed visible strobe pulse is used to image the shock waves emitted from the melanin at various time delays after the pump pulse. The shock front radius, measured as a function of the delay time, yields the shock velocity. The shock

pressure is calculated from the observed shock velocity, together with conservation equations and the equation of state of water.

Materials and Methods

The picosecond irradiation and flash photography setup is shown schematically in Figure 1. The laser source is a mode-locked, Q-switched Nd:YAG laser whose output at 1064 nm consists of a train of ~15 pulses, each 100 psec in duration and separated by 13 nsec. A single pulse is extracted from the pulse train using an electro-optic pulse selector and injected into a flash-lamp pumped Nd:YAG amplifier which amplifies the pulse energy from 100 μJ up to 3 mJ. The amplified pulse then goes through a second harmonic (KTP) crystal. The second harmonic (532 nm) output is separated from the IR beam using a dichroic filter and injected into an optical delay line with a continuously variable delay time from 1 to 50 nsec. The remaining near-infrared light is used as the pump pulse. After attenuation by calibrated neutral density filters, the IR pulse is focused through a microscope objective onto the melanin particles. The spot size of the pump pulse is adjusted to be 50 μm at the sample. The strobe pulse is provided by pumping a Rhodamine 6G dye cell with the delayed second harmonic pulse. Strobe images taken at various delay times are collected by the same microscope objective (0.25 N.A.) and digitized using a CCD camera. The sample consists of melanin granules extracted from calf retina and suspended in a thin layer of gelatin. With this setup, the shock waves produced from irradiated melanin particles can be observed with subnanosecond time resolution and ~1 μm spatial resolution.

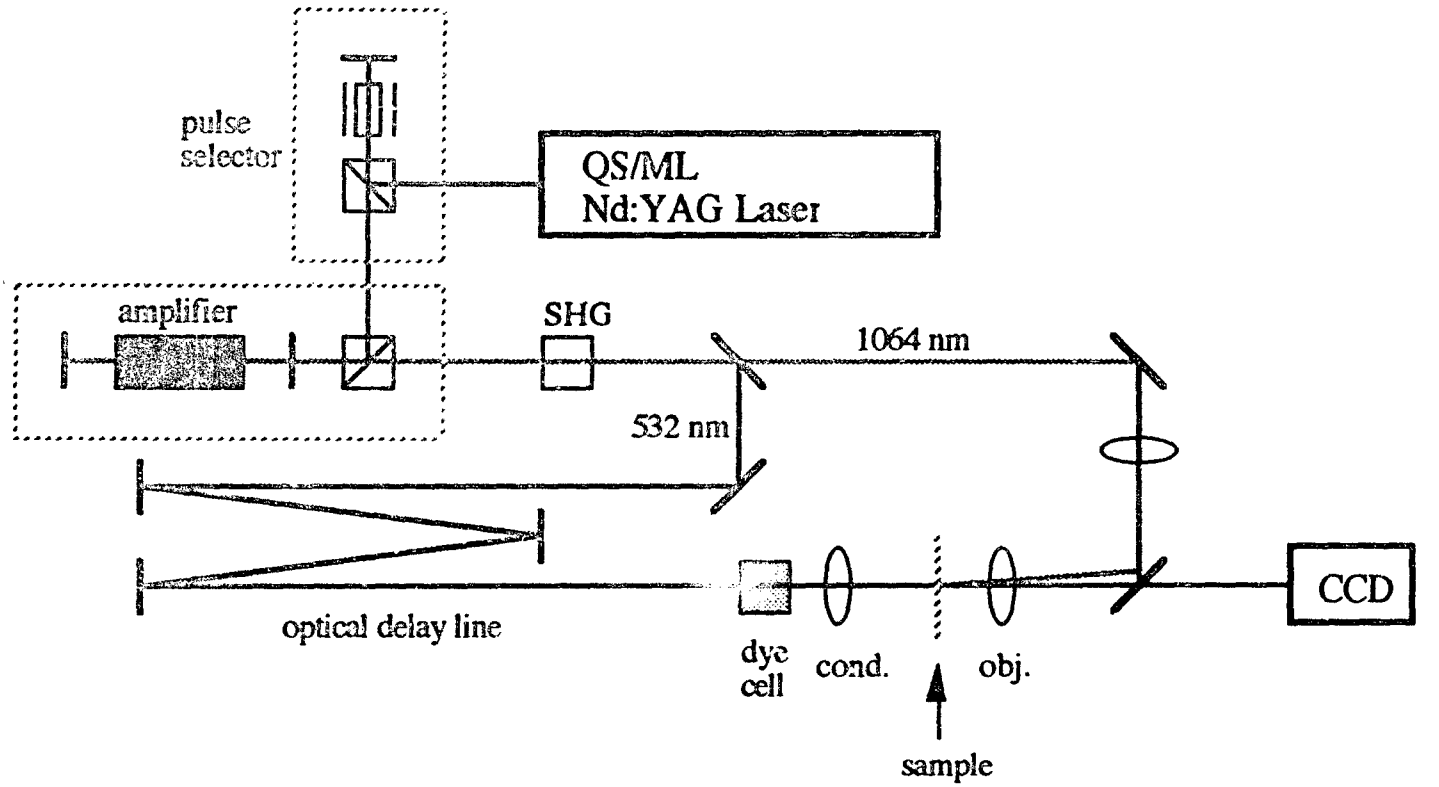

Figure 1. Experimental Setup

Results and Discussion

We have successfully imaged shock wave emission from isolated melanin particles. An example is shown in Figure 2a, an image taken at 26 nsec after the incident laser pulse (fluence 8 J/cm^2). A spherical shock front with a 66 μm radius is observed to originate from a single melanin particle. The shock front is visible because it creates a refractive index gradient which scatters the strobe light away from the collecting optics. The black sphere at the center of the shock wave has a diameter of about 10 μm and is attributed to either an expanding melanin particle (original diameter 1 μm) or a expanding cavitation bubble. An example of multiple shock fronts originating from more than one melanin particles is shown in Figure 2b. This image, taken at an earlier time (about 7 nsec after the incident laser pulse) shows a correspondingly smaller shock front radius (23 μm).

A series of images were taken at various delay times and the measured shock front radii were plotted against the delay time, as shown in Figure 3. At distances less than 30 μm from the melanin, the observed shock velocity was greater than 3000 m/sec with incident fluences of 7-12 J/cm^2. The corresponding shock pressure, calculated from the conservation equations and the equation of state of water, is found to be >22 Kbar. One can therefore conclude that the cell walls of the retinal pigment epithelium (RPE, cell diameter ~10 μm) can experience a pressure transient of >22 Kbar when the melanin granules contained within the cells are exposed to these laser fluences. How the structure and the function of the RPE cells and the surrounding retina are affected by these high pressure transients is the subject of ongoing investigation. It is known, however, that <1 Kbar of pressure can be lethal to cells.

The lowest laser fluence for which the shock wave can be observed using the present setup is 4 J/cm^2. This does not imply that no shock wave is generated below 4 J/cm^2, but rather that the pressure gradient generated is not strong enough to cause an appreciable amount of refraction of the strobe light in our experiment. A more sensitive technique to measure smaller refractive index gradients is being pursued.

The observed shock wave formation at 4 J/cm^2 can be compared to currently available threshold retinal injury data in vivo, which range from 10^{-4} to 10^{-5} J/cm^2 at the cornea (about 1 to 10 J/cm^2 at the retina) for 1 psec to 1 nsec pulses at 1064 nm. Whether the shock wave is a primary cause of the observed retinal injury, however, remains to be established.

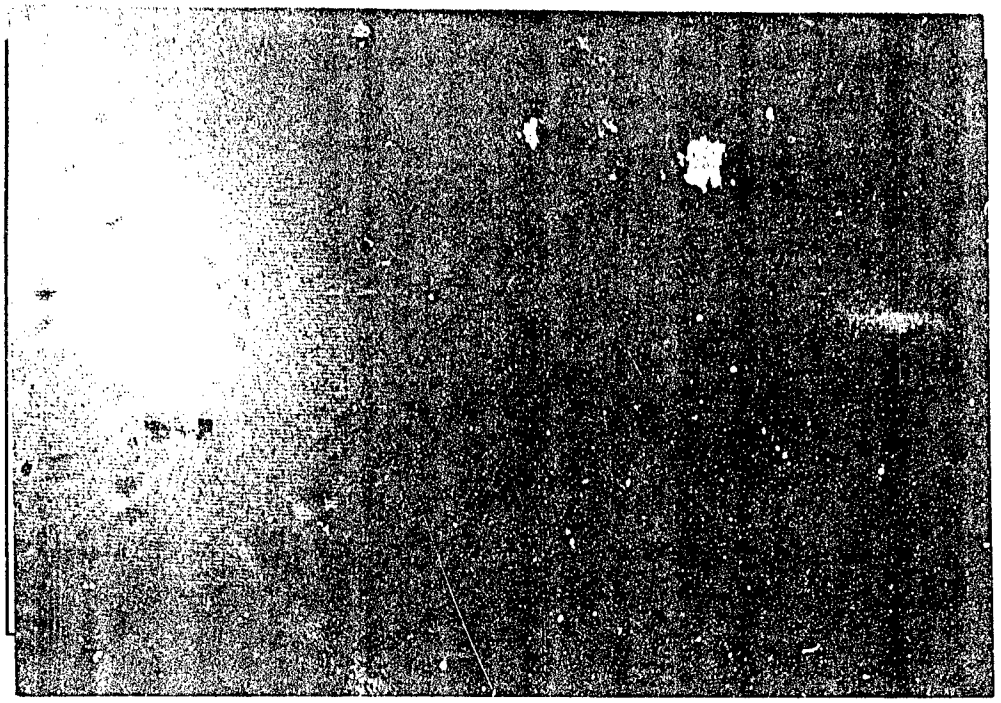

Figure 2a

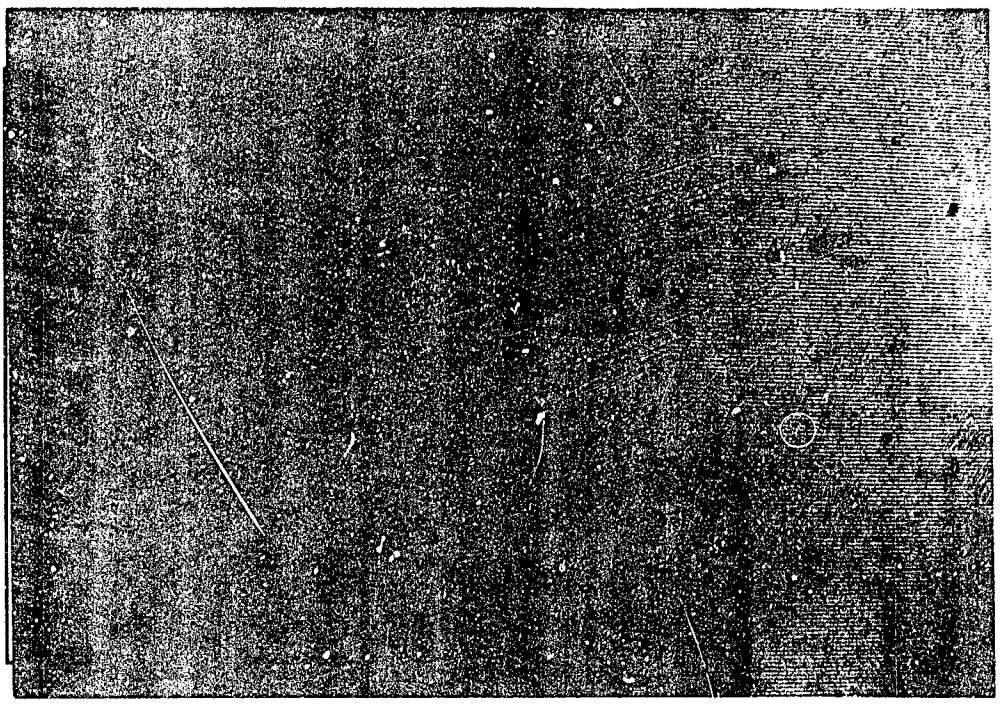

Figure 2b

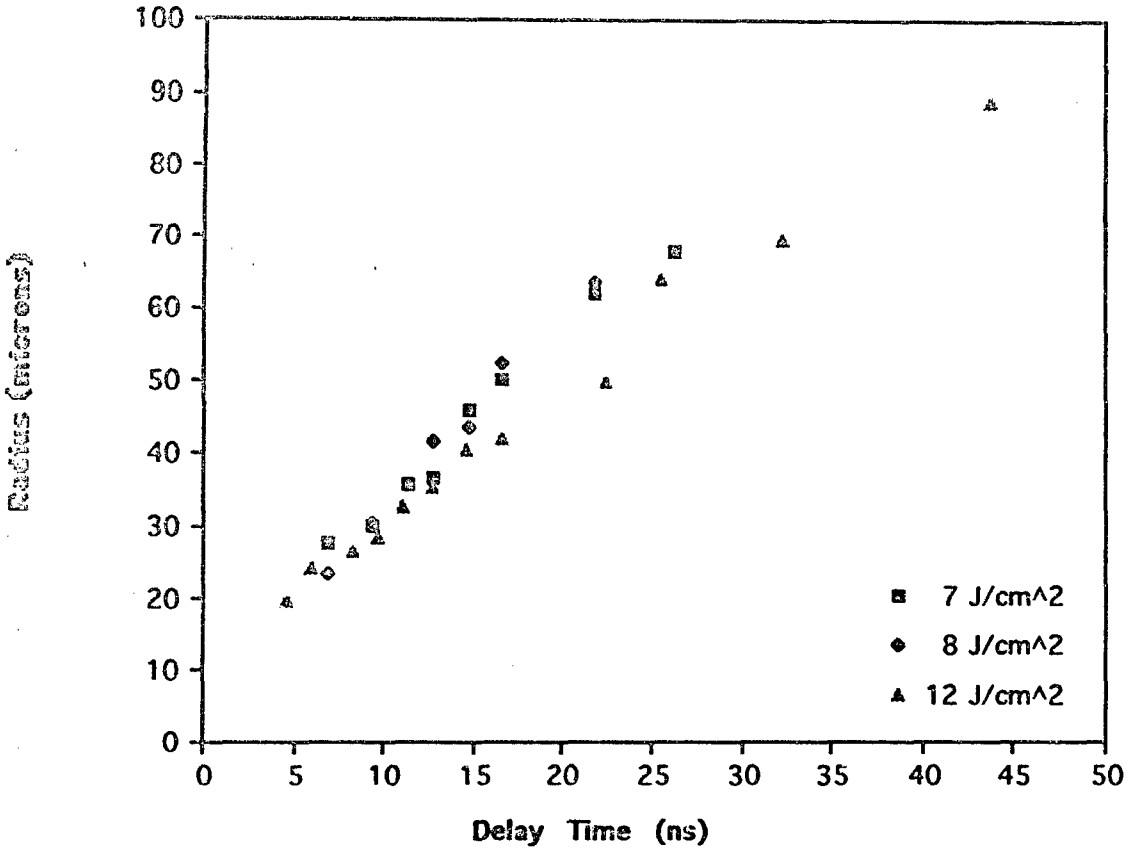

Figure 3. Shock front radius as a function of delay time.

List of Publications

1. Swanson EA, Izatt JA, Hee MR, Huang D, Lin CP, Schuman JS, Puliafito CA, Fujimoto JG. In Vivo Imaging Using Optical Coherence Tomography. Optics Letters 1993; 18:1864-1866.

2. Izatt JA, Hee MR, Huang D, Fujimoto JG, Swanson EA, Lin CP, Schuman JS, Puliafito CA: Ophthalmic Diagnostics using optical coherence tomography. Ophthalmic Technologies III, Ren Q, Pavel J-M, Eds. Proc SPIE 1877, 1993.

3. Izatt JA, Hee MR, Swanson EA, Huang D, Lin CP, Schuman JS, Puliafito CA, Fujimoto JG: Optical coherence tomography of the human anterior segment. Arch Ophthalm, in press.

4. Hee MR, Izatt JA, Swanson EA, Huang D, Schuman JS, Lin CP, Puliafito CA, Fujimoto JG: Optical coherence tomography of the human retina. Submitted for publication.

5. Puliafito CA, Hee MR, Lin CP, Reichel E, Schuman JS, Duker JS, Izatt JA, Swanson EA, Fujimoto JG: Imaging of macular diseases with optical coherence tomography (OCT). Submitted for publication.

6. Lin CP, Weaver YK, Birngruber R, Fujimoto JG, Puliafito CA. Intraocular Microsurgery with a Picosecond Nd:YAG Laser. Lasers Surg Med (in press).

Thesis

Kelly, Michael W., Master of Sciences in Electrical Engineering, Tufts University, Medford, MA. "Shock Wave Generation in Retinal Melanin using a 100 ps 1064 nm Laser Pulse".