In vitro study of cataract extraction by bursts of microsecond 1.54-µm laser pulses

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Abstract. Laser extraction of a model porcine eye cataract has been performed for the first time in an in vitro experiment using a 1.54-µm Yb, Er: glass laser generating bursts of microsecond pulses. We used effective pulse repetition rates from 36 to 75 Hz and average laser output powers from 3.9 to 5.25 W. The results demonstrate for the first time that, at an effective pulse repetition rate of 45 Hz, burst repetition rate of 15 Hz, three microsecond pulses per burst, and a burst energy from 260 to 265 mJ, the laser step duration in cataract extraction is 130 ± 10 s, which is comparable to the ultrasonic phacoemulsification and laser extraction time in the case of a Nd: YAG laser emitting at 1.44 µm. Acoustometry and high speed video recording of hydroacoustic processes accompanying interaction of water with 1.54-µm radiation from the Yb, Er: glass laser generating bursts of microsecond pulses have made it possible for the first time to detect overlap of hydroacoustic processes at the pulse spacing in bursts reduced to under 700 µs. In the case of overlap of hydroacoustic processes, despite the increase in average power and effective pulse repetition rate, acoustic wave generation is ineffective because pulses propagate through bubbles formed in the water. Laser cataract extraction is shown to be most effective at a lower average power, lower effective pulse repetition rate, and burst pulse spacing of $850 \pm 10 \, \mu s$.

Keywords: laser, cataract, microsecond pulse, pulse train, hydroacoustic signal, extraction, pulse energy, aspiration, high speed video recording.

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1. Introduction

Cataracts are the most widespread cause of blindness and low vision of millions of people all over the world [1, 2]. The main cataract treatment method is cataract surgery, which has recently been making rapid progress. Advanced cataract surgery procedures rely predominantly on ultrasonic or laser energy and allow for microinvasive and sutureless operations through microincisions 1.8-2.2 mm in size. The risk of postsurgical astigmatism or other complications is then very low because the wound requires no sutural adaptation.

In cataract surgery, laser energy has been used since the 1980s [3]. An important contribution to advances in laserassisted cataract surgery was made by Dodick [4], who proposed phacolysis technology. A serious drawback to this method, which used 1.064-µm Nd: YAG laser radiation, was the ability of the laser beam to penetrate deep into surrounding tissue, which presented a potential hazard to eyeball tissue, in particular to the retina and choroid. One step in the development of laser cataract surgery was the advent of the erbium laser, emitting at 2.94 µm [5]. One drawback to light with this wavelength was its small penetration depth, which allowed only 'soft' cataracts to be destroyed. Denser cataracts required a long time for destroying the lens nucleus and, in addition, ultrasonic energy to complete the operation. After some time, such lasers were not used in clinical practice, and lasers emitting in the range 1.064–2.94 µm began to be studied for intraocular surgery [6].

Starting in 1997, laser cataract extraction (LCE) was used in clinical practice, with a Nd: YAG laser emitting at 1.44 µm and having a pulse duration of the order of 250 µs, pulse energy of up to 300 mJ, and pulse repetition rate of up to 30 Hz [7-11]. As early as 1999, there were reports on results of a thousand LCE operations [12]. To date, a considerably larger number of such operations have been performed in Russia and abroad [13]. At the St. Petersburg branch of S. Fyodorov Eye Microsurgery Federal State Institution, this cataract surgery method has been used since 1999 [14]. Laser technology was implemented using a Rakot laser cataract extraction system (Nela Ltd., Russia) based on a lamp-pumped free-running Nd: YAG laser. This system has serious drawbacks: large dimensions and weight (of the order of 100 kg) and relatively short operational life of the pump lamp, which limits the mobility and functional capabilities of the laser.

Despite the significant advances in ultrasonic and laserassisted cataract surgery, there is currently an intensive search for new light sources for effective lens destruction (especially in the case of ultradense cataracts) and ways of improving cataract surgery procedures. Wide use is made of ultrasonic

phacoemulsification, accompanied by exposure to femtosecond laser pulses [15, 16]. Small laser sources are under development, including those based on an ytterbium-erbium glass laser emitting at 1.54 µm, which operates in useful-loss modulation mode in a cavity formed by three highly reflective mirrors, with light outcoupling through a frustrated total internal reflection shutter [17]. Interaction of human lens tissue with single microsecond pulses from a diode-pumped Yb, Er: glass laser was analysed in detail in Refs [18-21] and it was shown that the lens then disintegrated as a result of the combined effect of the laser light and laser-induced acoustic waves emerging in the collapse-rebound phase of vapour bubbles forming in the aqueous medium surrounding the lens. Processes leading to laser-induced hydroacoustic effects in water have been studied in sufficient detail [22-26]. If laser light is delivered through silica fibre, vapour bubbles in water can be produced both by a specially treated fibre tip exposed to laser light and directly by laser light. In the former case, a laser-absorbing coating is produced on the end face of quartz fibre immersed in water (e.g., the fibre is blackened). In the latter, there is no absorbing coating, and the laser light is free to travel from the fibre to the liquid.

The effect of bursts of diode-pumped microsecond Yb, Er: glass laser pulses on the human lens with various cataract densities and the resultant hydroacoustic signal in the aqueous medium have recently been studied *in vitro* [27]. A diode-pumped laser generating bursts of microsecond pulses at 1.54 µm was shown not merely to be a viable alternative to a lamp-pumped free-running laser emitting at 1.44 µm but to have the advantages of substantially smaller laser system weight and dimensions. At the same time, the effect of pulse spacing in a train of microsecond Yb, Er: glass laser pulses ($\lambda = 1.54 \mu$ m) on the laser step duration in LCE and hydroacoustic processes in the aqueous medium surrounding the eye lens has not yet been analysed, which makes it a topical issue.

Further progress in LCE with an Yb, Er: glass laser ($\lambda = 1.54 \ \mu$ m) generating bursts of microsecond pulses is highly dependent on preclinical evaluation of its performance using not only a removed lens but also eye models, which allows one to model the LCE process under conditions as similar to clinical ones as possible. In addition, it is necessary to carry out a number of physical model studies supplementing existing knowledge and providing more detailed insight into phenomena accompanying laser cataract extraction. In connection with this, investigation of the dynamics of vapour bubbles and hydroacoustic signals resulting from interaction of laser pulse bursts differing in pulse spacing with the liquid (water) surrounding the lens will make it possible to optimise the laser operation mode for clinical use.

In this paper, we report *in vitro* laser extraction of a model porcine eye cataract along with acoustometry and high speed video recording of the hydroacoustic processes accompanying interaction of laser light with an aqueous medium in order to gain detailed physical insight into the processes behind cataract extraction with the use of an Yb, Er: glass laser ($\lambda = 1.54 \mu m$) generating bursts of microsecond pulses differing in spacing.

2. Operation modes of an Yb, Er: glass laser generating bursts of microsecond pulses

In this study, we tested four laser operation modes differing in the number of pulses, pulse energy and spacing in a burst, and the burst repetition rate (Fig. 1). Previously, Belikov et al. [21] studied mode 1 and demonstrated that a diode-pumped Yb, Er: glass laser ($\lambda = 1.54 \mu m$) generating bursts of microsecond pulses was able to effectively destroy cataracts. In this mode, each burst consists of three pulses, the pulse spacing in the bursts is $850 \pm 10 \mu s$, and the burst repetition rate is 15 Hz. The energy of the first, second, and third pulses in each burst is 90, 100, and 70 mJ, respectively.

In mode 2, the average power exceeds that in mode 1 because the number of pulses per burst is increased to five and the burst repetition rate is reduced to 12 Hz. The energy is more evenly distributed over the pulses: 90, 89, 89, 90, and 77 mJ. The pulse spacing in the bursts was chosen for each pulse in order to obtain pulse energies differing as little as possible: $550 \pm 10 \ \mu$ s between the first and second pulses, $500 \pm 10 \ \mu$ s between the second and third, $500 \pm 10 \ \mu$ s between the fourth, and $700 \pm 10 \ \mu$ s between the fourth and fifth.

Mode 3 ensured the highest effective pulse repetition rate (product of the burst repetition rate and the number of pulses per burst), 75 Hz, as a result of the generation of bursts consisting each of five pulses and having a repetition rate of 15 Hz. The average power was then comparable to that in mode 2, whereas the pulse energy was considerably lower (70, 74, 75, 78, and 59 mJ). It is worth noting that, in this mode, the energy of the last pulse was below the cataractous lens destruction threshold [18]. The spacing between the first to fourth pulses was $400 \pm 10 \,\mu$ s, and that between the fourth and fifth pulses was $500 \pm 10 \,\mu$ s.

In mode 4, the highest energy of individual pulses in each burst was 112, 115, and 108 mJ. The burst repetition rate was 12 Hz, and the pulse spacing in the bursts was $800 \pm 10 \ \mu s$. The average power in this mode was comparable to that in mode 1.

In each mode, the pulse energy and pulse spacing in the bursts were chosen so as to maximise the average optical power at a constant effective pulse repetition rate, which was 36 Hz in mode 4, 45 Hz in mode 1, 60 Hz in mode 2, and 75 Hz in mode 3. The average power and pulse energy in each mode were limited by the average pump power, which was related to the maximum permissible thermal load of the active element of the laser and stacked pump diode arrays.

3. *In vitro* laser extraction of a model porcine eye cataract using an Yb, Er: glass laser generating bursts of microsecond pulses

Before *in vitro* experiments on porcine eyes enucleated within 24 h, a cataract was modelled by exposing the eyes to microwave radiation (800 W power, 1 min). The surgical steps were identical to those in conventional phacoemulsification human eye cataract surgery and included making two corneal incisions, manual capsulorhexis, hydrodissection of the lens, and subsequent laser treatment and aspiration in order to remove the nucleus and cortex of the cataractous lens. To hold (fix) the lens during laser treatment and aspirate the destroyed lens material, we used a Skat irrigation–aspiration system incorporated into a Rakot apparatus (Nela Ltd.). The lowest pressure during aspiration was 120 mm Hg and the highest irrigation pressure was 150 mm Hg. The operation was performed by an experienced eye surgeon and was begun with the destruction of the



Figure 1. (Colour online) Typical oscilloscope traces of pulses of the Yb, Er: glass laser generating bursts of microsecond pulses in modes 1-4.

centre of the cortex – the densest part of the lens – which led to the formation of a 'cup' in the centre of the lens nucleus. After that, the thinned walls of the 'cup' and the cortex were completely destroyed and aspirated.

On the whole, four laser treatment modes (see above) were studied *in vitro*. Surgery was performed on five eyes in modes 1 and 2, three eyes in mode 3, and one eye in mode 4. Table 1 summarises information about the LCE conditions and duration in each mode.

Figure 2 shows photographs illustrating the LCE steps with a laser ($\lambda = 1.54 \ \mu m$) generating bursts of microsecond pulses.

12(3)

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Mode 1 turned out to be the most surgeon-friendly. In this mode, laser destruction was reproducible and predictable. In mode 2, the laser beam effectively destroyed the nucleus, but produced a lot of splinters and suspended material in the periphery. As a result, the destruction and aspiration of the splinters terminated. Repositioning the tools in order to continue the destruction and aspiration of the splinters increased the duration of the laser step of LCE in this mode in comparison with mode 1. In mode 3, the lens destruction process was extremely ineffective, and the surgical procedure could be stopped because its duration was too long. In mode 4 (a single experiment), the aspiration tube was destroyed almost instan-

Failure of the aspiration

tube

Mode	Carrier frequency/Hz (number of pulses)	Effective frequency/Hz	Burst energy <i>E/</i> mJ Pulse energy <i>E</i> _p /mJ Average power <i>P/</i> W	Laser step duration in LCE/s
1	15 (3)	45	E = 260 - 265 $E_p = 90, 100, 70$ P = 3.9 - 3.975	130 ± 10
2	12 (5)	60	E = 435-440 $E_{p} = 90, 89, 89, 90, 77$ P = 5.22-5.28	160 ± 10
3	15 (5)	75	E = 345 - 350 $E_p = 70, 74, 75, 78, 59$ P = 5, 175, 5, 55	Longer than 300 (no complete extraction)

P = 5.175 - 5.25E = 330 - 335

 $E_{\rm p} = 112, 115, 107$

P = 3.96 - 4.02

Table 1. Operating parameters of the Yb, Er: glass laser generating bursts of microsecond pulses and LCE duration in each mode.

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Figure 2. (Colour online) Photographs of the operation area in different steps of *in vitro* investigation of laser cataract extraction with a laser ($\lambda = 1.54 \,\mu$ m) generating bursts of microsecond pulses: (a) corneal incision; (b) hydrodissection; (c) manual capsulorhexis; (d) laser treatment and aspiration of the lens nucleus; (e) laser treatment and aspiration of the periphery of the lens; (1) working part of the laser tip; (2) working part of the tip of the irrigation – aspiration system.

taneously by the laser beam, so the surgical procedure was stopped and no further attempts to perform LCR were made. In modes 1, 2, and 4, the energy of all the laser pulses in each burst exceeded the cataract destruction threshold (70 ± 5 mJ), whereas in mode 3 the energy of the last laser pulse in each burst was below the cataract destruction threshold. It is worth noting that, in mode 3, the laser system had the highest effective pulse repetition rate, and the additional heating of the aqueous medium and lens by the preceding pulses in each burst could reduce the lens destruction threshold by the arrival of the fifth pulse, but this probably had no effect on the LCR duration.

It is seen that effective laser cataract extraction is possible in the case of laser operation in modes 1 and 2. It follows from Table 1 that in mode 1 the laser step duration in LCE is shorter than that in mode 2, even though the average power and effective frequency of laser pulses in mode 2 considerably exceed those in mode 1. The likely causes of this effect are considered below.

4. Acoustometry and high speed video recording of the hydroacoustic processes accompanying interaction of water with radiation from an Yb, Er: glass laser ($\lambda = 1.54 \mu m$) generating bursts of microsecond pulses

In our experiments, we examined the hydroacoustic processes accompanying laser-water interaction. We studied modes 1 and 2 because *in vitro* laser extraction of a model porcine eye cataract using the laser in question demonstrated the possibility of effective LCE in these modes (see above). Figure 3 shows schematics of the experimental setups used to study parameters (Fig. 3a) and perform high speed video recording (Fig. 3b) of the hydrodynamic processes accompanying interaction of water with radiation from the Yb, Er:glass laser ($\lambda = 1.54 \mu m$) generating bursts of microsecond pulses.

Laser pulses were delivered to distilled water through quartz-quartz optical fibre with a core diameter of $470 \pm 10 \,\mu\text{m}$ and numerical aperture of 0.18. In studying signals in the free space of the liquid, the end face of the optical fibre was situated 10 mm from the solid interface (the surface of a quartz cube placed in the water-containing cuvette) and 45 mm from the cuvette wall.



Figure 3. (Colour online) Schematics of the experimental setups used to study laser-induced hydrodynamic processes in water using (a) acoustometry and (b) high speed video recording: (1) laser system ($\lambda = 1.54$ µm, diode pumping); (2) computer for controlling the laser system and high speed camera; (3) optical fibre in an SMA holder; (4) HGL-0200 hydrophone with a preamplifier on a rotation stage; (5) cuvette containing distilled water; (6) photodetector; (7) TDS 2022B oscilloscope; (8) DCR III light source; (9) fibre bundle of the light source; (10) FASTCAM SA4RV high speed camera.

The acoustic signal resulting from interaction of laser pulses with the liquid (distilled water) was detected by an HGL-0200 hydrophone (ONDA Corp., USA) with a preamplifier. The hydrophone was connected to a TDS 2022B oscilloscope (Tektronix Inc., USA). The active area (face) of the hydrophone was located 2.6 \pm 0.2 mm from the end face of the optical fibre, and the angle between the normal to the active area and the optic axis of the fibre was 45 \pm 1°.

Figure 4 shows typical oscilloscope traces illustrating the temporal order of pressure changes in the liquid and the laser pulses responsible for them in mode 1. It is seen that the pulse spacing in the burst exceeds the characteristic decay time of hydroacoustic processes.

Figure 5 shows histograms of acoustic signals induced in the free space of water by laser pulses of a burst in mode 1 of the laser system. The amplitude of the first hydroacoustic signal component (A1), which coincides in time with the laser pulse and results from the thermal expansion and explosive boiling of the water, was smaller than that of the subsequent components in all the pulses of the burst. The subsequent components were due to bubble collapse-rebound processes. On the whole, we detected four such events per pulse in the burst. The first and second events were accompanied by the generation of the second



Figure 4. (Colour online) Typical oscilloscope traces of (a) a burst of laser pulses and (b) the hydroacoustic signal in mode 1.

and third acoustic signal components, whose amplitudes (A2 and A3) could be measured using the hydrophone. No acoustic signals were detected in the case of the third and fourth collapse-rebound events.

Figure 6 presents photographs of vapour bubbles produced in water by the laser beam in mode 1 at the instant when they had the maximum size (indicated below each photograph is the time between the laser pulse and this instant). The photographs were obtained using high speed video recording at a picture rate of 100000 frames per second (i.e. the frame spacing was 10 μ s, and the optical exposure was then equal to the frame spacing).

Attention should be paid to the fact that, in this operation mode of the laser, the pulse spacing in the bursts is $850 \pm 10 \,\mu$ s, exceeding the characteristic time during which the bubble collapse-rebound events occur. For this reason, the hydrodynamic process induced by a given laser pulse does not have any effect on bubble formation during the next laser pulse, except for a thermal effect. Thus, in mode 1 there are no bubbles in the path of a laser pulse at the instant when it arrives, and laser pulse propagation through a distance exceeding that determined by the absorption coefficient for the laser light is impossible.

The distribution of pressure changes related to the dynamics of vapour bubbles in water correlates with the energy distribution over the burst pulses, i.e. the higher the pulse energy, the larger pressure changes in the bubble collapse-rebound phase. The largest bubble size was observed in the case of the second burst pulse, having the highest energy: \sim 3.3 mm (along the vertical axis). The smallest bubble size in the collapse stage was observed in the vertical direction: \sim 90 µm (Fig. 7). The highest speed of the bubble wall in the vertical direction was about 50 m s⁻¹ in the collapse phase and 40 m s⁻¹ in the rebound (growth) phase.

Figure 8 illustrates the temporal order of pressure changes in the liquid and laser pulses in mode 2. It is seen that the time intervals between the second and third pulses and between the third and fourth pulses in the burst are shorter than the characteristic decay time of hydroacoustic processes. Therefore, there is overlap of hydrodynamic processes, which influences the amplitude of pressure changes in the liquid and, in a number of cases, makes them difficult to measure adequately.

Figure 9 shows histograms of hydroacoustic signals induced by separate laser pulses of a burst in mode 2.

Figure 10 presents photographs of vapour bubbles produced in water by the laser beam in mode 2 at the instant when they had the maximum size (indicated below each photograph is the time between the laser pulse and this instant). The photographs were obtained using high speed video recording at a rate of 100 000 frames per second. It is seen that in mode 2 there is overlap of the hydrodynamic processes induced by neighbouring laser pulses, namely, by the second and third pulses in the burst.

Attention should be paid to the fact that, in the case of laser operation in mode 2, the time intervals between pulses 1 and 2, 2 and 3, and 3 and 4 lie in the range $500-550 \mu$ s, i.e. they are shorter than the characteristic time of bubble collapse-rebound events. In the histograms presented in Fig. 9, there is no signal amplitude for the A1 component induced by the fourth burst pulse (the A1 component was not detected because it was disguised by the A3 component from the third pulse), which is due to the overlap of the hydrodynamic processes as a consequence of the small pulse spacing in the burst. In the case of such overlap, acoustic waves are generated ineffectively because the bubble formation process is hindered by the fact that a fraction of the light passes through the bubble left from the preceding pulse (the third pulse in this case) and, for this reason, is absorbed in the bubble and not in the water.

It is important for effective LCE that, during the laser pulse burst, lens fragments do not leave the region around the input end of the aspiration tube. In such a case, the aspiration



Figure 5. Amplitudes of the components of acoustic signals induced in the free space of water by laser pulses in a burst (mode 1): (a) first pulse; (b) second pulse; (c) third pulse.



Figure 6. (Colour online) Photographs of vapour bubbles at the instant of time (indicated below each photograph) when they reach the maximum size under the effect of the first to third laser pulses in a burst in mode 1 (the outer fibre diameter is $500 \,\mu$ m).



Figure 7. (Colour online) Typical dynamics of a vapour bubble forming under the effect of laser burst pulses in mode 1 (the order of the frames is from the top to bottom); video recording at a rate of 500 000 frames per second and frame spacing of $2 \mu s$, so that the frame duration is equal to the frame spacing.

system has time to remove them before the next burst arrives. Otherwise, one has to spend additional time to reposition the laser and aspiration–irrigation tools.

Increasing the number of pulses per burst can cause lens fragments to leave the region around the input end of the aspiration tube, so that some of them will not be aspirated because each pulse will shift the fragments father from the input end of the aspiration tube. Reducing the pulse spacing in a burst can reduce the laserto-acoustic energy conversion efficiency because, as a result of the overlap of bubbles, the laser pulse will propagate not in water but in the bubble produced by the preceding laser pulse. Besides, reducing the pulse spacing in a burst can cause the laser light to leave the region determined by the absorption coefficient for the light and, as a consequence, can cause laser damage to the back wall of the lens capsule or other struc-



Figure 8. (Colour online) Typical oscilloscope traces of (a) a burst of laser pulses and (b) the hydroacoustic signal in mode 2.

tures. Under such conditions, bubbles are formed in different ways (the bubble size and acoustic signal amplitude are irreproducible from pulse to pulse) because of the instability of the temporal structure and energy of laser pulses.

5. Conclusions

The present results demonstrate that laser-induced hydrodynamic processes have a significant effect on cataractous lens removal. Not all the operation modes studied for an Yb,Er:glass laser generating bursts of microsecond pulses are suitable for use in laser cataract surgery. On the one hand, low-energy modes (see mode 3) fail to ensure LCE because the energy of some burst pulses is insufficient for lens destruction. On the other, the mode with the highest burst pulse energy (see mode 4) leads to failure of the aspiration tube during surgery, making further LCE impossible. Mode 1 ensures the best LCE results, with the shortest extraction time and reproducible lens destruction and aspiration. In this case, the pulse spacing in bursts exceeds the characteristic oscillation time of the vapour bubble produced in the liquid by a laser pulse. Mode 2, in which the pulse spacing in bursts is shorter than the characteristic oscillation time of the vapour bubble produced in the liquid by a laser pulse, is less effective than mode 1 (the LCE time in mode 2 exceeds that in mode 1) because the overlap of the hydrodynamic processes accompanying vapour bubble formation reduces the laser-to-acoustic energy conversion efficiency and makes the surgery dangerous for the surrounding tissue.

Therefore, for further detailed studies of how 1.54- μ m radiation from an Yb, Er:glass laser generating bursts of microsecond pulses influences the eye tissue surrounding the operation area (eye lens) it is reasonable to use mode 1, suitable for performing the entire laser step of LCE in 130 \pm 10 s, a time comparable to the ultrasonic phacoemulsification and LCE time in the case of a Nd:YAG laser emitting at 1.44 μ m and having a free-running pulse energy of up to 300 mJ [12, 22]. For this mode, in subsequent *in vivo* experiments one should assess the effect of LCE on the corneal endothelium, posterior lens capsule, vitreous humour, and retina.

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Figure 9. Amplitudes of the components of acoustic signals induced in the free space of water by laser pulses in a burst (mode 2): (a) first pulse; (b) second pulse; (c) third pulse; (d) fourth pulse; (e) fifth pulse.



Figure 10. (Colour online) Photographs of vapour bubbles at the instant of time (indicated below each photograph) when they reach the maximum size under the effect of the first to fifth laser pulses in a burst in mode 2 (the outer fibre diameter is $500 \,\mu\text{m}$).

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