Laser Effect on a Pathologically Altered Capsule of the Lens of the Eye

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Abstract. One of the current areas of application of lasers in ophthalmology is cataract surgery and reducing the number of negative reactions to surgical intervention. In the postoperative period, clouding of the lens capsular bag and the risk of contraction capsular syndrome associated with changes in the biomechanical properties of the lens and capsular bag system are often observed. In the work, the biomechanics of such system were studied. Lenses that were placed in a 10% formalin solution to create cataract-simulating opacity for various amounts of time were studied by optical-coherent tomography, speckle-interferometry method and with fiber-optics setup for scattering dynamics registration. It was shown that speckle interferometry technique is sensitive to structural changes of lenses due to formalin exposure, which makes tissue more elastic and less transparent. OCT shows the same result and is more sensitive to the changes of laser wavelength. In addition, theoretical studies were carried out and have shown that changing laser wavelength can be dangerous for the integrity of the capsule film during medical intervention due to increase of maximum thermal stress. © 2022 Journal of Biomedical Photonics & Engineering.

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1 Introduction

One of the current areas of application of lasers in ophthalmology is cataract surgery. Despite the obvious progress in the technique of cataract surgery and a decrease in the number of negative consequences, clouding of the lens capsule in the postoperative period is not a rare complication and is detected in a significant percentage of cases [1–4].

The most common complication of laser intervention is transient hypertension of the eye associated with the inflammatory process against the release of prostaglandins in the acute period [5]. To date, there are no clear criteria for selecting laser radiation parameters that guarantee the absence of these complications during laser ablation of a clouded lens capsule, even though that attempts are being made to create algorithms that help to reduce the number of complications associated with laser intervention [6, 7]. As before, to achieve the result, the tactics of stepwise increase in energy to threshold values that allow for cutting the target tissue are more often used.

The variety of clinical and morphological forms of secondary cataracts, which have different optical and mechanical (strength) characteristics, often causes difficulties with the correct calculation of the optimal energy for laser ablation for removing the opacities; it is also the possibility of significant fluctuations in the selected radiation parameters. Errors in the calculation, in this case, also lead to damage to nearby intraocular structures. To a certain extent, the above may be due to gaps in the study of the mechanisms of laser ablation of secondary cataract films when exposed by modulated laser radiation. This indicates the need to continue research in the direction of studying the mechanisms and kinetics of thermomechanical processes during the interaction of laser radiation with multicomponent biological tissues.

The problem of the photodestructive action of lasers on the anatomical structures (Intraocular lens – IOL) of the eye and artificial intraocular elements is the subject of numerous works [8–11], which, in particular, provide data indicating the possibility of developing complications during laser dissection of secondary cataract. In most cases the posterior wall of the lens capsule (PCO) becomes coldly rather than the anterior one. The frequency of opacities in the posterior capsule can vary from 4% to 60% of cases [1, 12], the anterior capsule – 3–16% [13]. Many factors can influence the frequency and severity of "filmy" opacities, among them: age, the presence of concomitant eye, and general diseases, the state of the immunological status and the blood-ocular barrier, the biocompatibility of the IOL and its design features, as well as insufficiently complete removal of the lens masses during the operation, discrepancy between the formed hole in the anterior capsule and the diameter of the IOL [14]. These "filmy" opacities can significantly reduce visual acuity and affect the quality of life, which determines the need for repeated interventions (surgical or laser) in some cases. Unlike surgical interventions, the non-invasive nature of laser operations and the possibility of strict dosing of the energy parameters of the radiation make it possible to achieve high functional results and to repeat the procedure if necessary. At the same time, to determine the most effective mode of laser exposure, knowledge of the properties of the lens and capsular system is necessary.

Recently, methods for non-invasive determination of the mechanical properties of eye tissues are of particular interest. In recent years, it has been shown that the elastic properties of tissues measured at different depths can serve as a kind of marker of pathology, which is not inferior to traditional histological techniques in terms of selectivity [15–18]. In this direction, the method of optical coherent elastography (OCE) has been widely developed, the resolution of which is significantly superior to the method of ultrasound diagnostics and most other methods of medical imaging [17–19]. The high resolution of the OCE method in terms of the analysis time makes it possible to visualize the dynamics of deformations in the tissues of the eye during millisecond laser pulses [20].

This work is related to the development of the scientific foundations of a new laser method of exposure to "filmy" opacities in the pupil area, including both opacities of the posterior lens capsule (PCO) and anterior, accompanied by progressive contraction of the capsule (anterior capsular contraction syndrome – ACCS), leading to deformation IOL. The optical properties of the anterior and posterior lens capsules are directly related to their biomechanical properties, which affect the absorption of laser radiation in the considered range. Thus, the study of the biomechanical properties of intraocular structures and their dynamics under the influence of laser radiation can provide new information for the correction of laser modes of exposure in order to minimize side effects associated with laser ophthalmological operations. This paper presents a theoretical study of the effect of various parameters of laser exposure on thin biological films of the lens capsule, modified and intact, as well as a study of the biomechanics of the lens and capsular system, which can further help in more accurate control of the temperature and thermal stress fields during laser exposure at surgical operation.

2 Materials and Methods

2.1 Theoretical Study

The temperature field was calculated, based on the modernization of the theoretical model that describes the laser effect on the volume of biological tissue, taking into account the propagation of heat by thermal conduction, and also taking into account the attenuation of laser radiation with depth in accordance with the Bugger-Lambert-Beer law [21, 22], depending on the temporal (pulse-periodic) pattern of laser exposure and its intensity, allowing at any moment of the considered time to obtain a temperature distribution within the lens capsule volume.

The geometry of the problem took into account that the laser radiation was delivered through an optical fiber 600 μm in diameter, which was inserted into the biological sample perpendicular to its surface. The problem of heat propagation by thermal conductivity under laser irradiation at wavelengths of 1560 nm and 1450 nm was solved. The distinction between these variants of exposure consisted in different absorption of laser radiation by biotissue. So, as an absorption index for a wavelength of 1560 nm in numerical simulation, the value of 10 cm^{-1} was chosen, and for 1450 nm – the value of 33 cm^{-1}. The intensity profile at the output of the fiber was taken as a Gaussian distribution with an effective Gaussian radius of 250 μm for a fiber end diameter of 600 μm. In order for further experiments using the method of optical coherent elastography to be able to isolate the effect of only one laser pulse, without taking into account the influence of residual oscillations from previous pulses, a repetitively pulsed mode was chosen for numerical simulation with a pulse duration of 100 ms, and a 1900 ms pause between pulses, irradiation duration 20 s. The values of the laser irradiation power were chosen in such a way that tissue denaturation was not achieved and, at the same time, the amplitudes of tissue oscillations obtained experimentally by the OCE method exceeded the noise by an order of magnitude. For the selected modes, both the dynamics of the maximum temperature at each moment of time and the profiles of the temperature field for the capsule film were constructed. The calculation scheme took into account the introduction of an optical fiber into the lens capsule and irradiation of the capsule film from the inside. Laser-induced thermal stresses corresponding to the difference between the angular and radial components of the stress tensor, arising along the capsule surface, perpendicular to the radiation axis due to uneven heating in this direction, can be calculated using the formulas given in Refs. [22, 23].

2.2 Experimental Study

The study plan was approved by the local ethics committee. All procedures followed were consistent with the principles set out in the 1975 Declaration of Helsinki and its 2000 revision.

(1) Modeling Technique of Lens Capsule Opacities Using Formalin

The experiment used isolated pig eyes obtained from a slaughterhouse. The isolated eyes were stored in a refrigerator (+4 °C) in a physiological solution of 0.9% NaCl for no more than a day. After removal from the eyeballs, the lenses were immediately placed in a 10% formalin solution to create cataract-simulating opacity. The modification was carried out for 60 min with checkpoints at 15, 30, and 60 min. Obtaining a visual picture of lens changes was carried out using an Amoeba Celestron Microscope 44325 microscope.

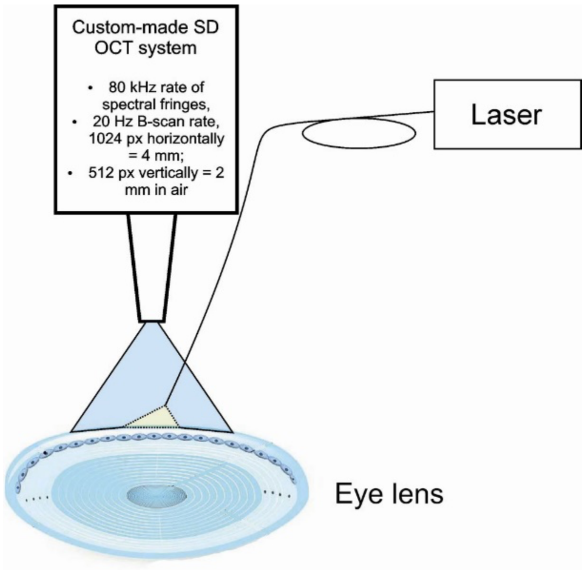


Fig. 1 Scheme of irradiation of a lens and simultaneous recording of OCE.

(2) Optical Coherent Elastography

For the subsequent study of the biomechanics of the modified and intact lens and capsular system and the influence of various laser parameters on it, experiments were carried out to determine the dynamics of thermo-elastic strains using OCE with simultaneous irradiation of the system in the selected modes. We used an OCT elastography method, previously used to study eye tissues [23–25], created at the Institute of Applied Physics, Russian Academy of Sciences, Nizhny Novgorod, by a group led by V. Yu. Zaitsev, with an imaging area of 4 mm wide and 2 mm deep, the setup made it possible to obtain the dependence of internal strains on time at a rate of 80 kHz for spectral bands and 20 Hz for B-scans.

The study of the response of the anterior and posterior capsules to a laser pulse during cataract modeling using formalin was carried out at two wavelengths of 1560 and 1450 nm. Tissue irradiation was carried out at different powers in two repetitively pulsed modes:

1. Wavelength 1.56 μm, pulse duration 100 ms, pause between pulses 1900 ms.
2. Wavelength 1.45 μm, pulse duration 100 ms, pause between pulses 1000 ms.

(3) Experiments on the Dynamics of Scattering and Transmission of Low-Intensity Scanning Laser Radiation

To carry out experiments on the dynamics of scattering and transmission of low-intensity scanning laser radiation, a scheme of a fiber-optic system was used (Fig. 2). The laser radiation was delivered through an optical "output" fiber 600 μm in diameter, inserted into the biological sample perpendicular to its surface through which the radiation passed. Beyond the sample surface, coaxially with the output optical fiber that supplied radiation to the sample, there was a "receiving" optical fiber connected to an optical multichannel analyzer in which the signal was digitized. Irradiation of the surface of each lens was carried out 4 times.

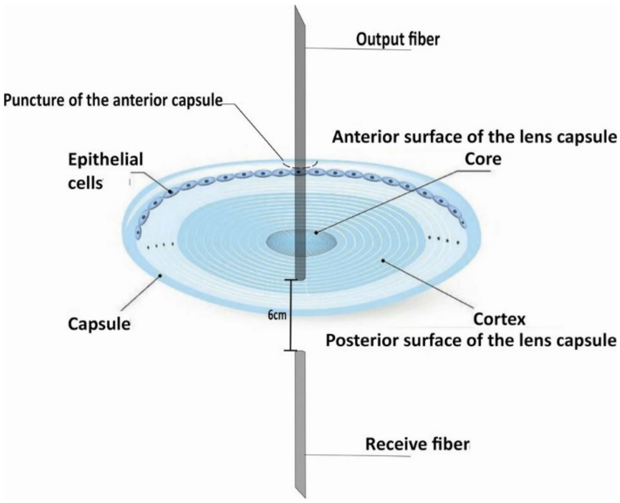


Fig. 2 Scheme of irradiation of the lens capsule and receiving optical fiber for detecting the transmitted signal.

The geometry and power of both visualizing and heating radiation were the same in all four-irradiation series. The wavelength of scanning radiation is 0.53 μm (visible range), heating 1.56 μm. Irradiation was carried out in a repetitively pulsed mode with a pulse duration of 100 ms and a pause between pulses of 1900 ms, the total duration of irradiation was 20 s (10 exposure peaks were obtained in total), the power was 0.3 W and 0.5 W.

(4) Speckle-Interferometry

Previously, we have already studied the relationship between the data obtained by the OCE method and the data of speckle interferometry [23]. In the present work, the irradiation mode corresponded to the chosen mode for experiments with the transmission of scanning radiation. The scheme of the setup for studying speckle interferometry is shown in Fig. 3. The radiation was delivered through an optical fiber with a diameter of 600 µm, directed at an angle of 15° to the normal. Simultaneously with heating, the sample was illuminated with a wide beam of a helium-neon laser with an angle of incidence of 45°. The probe beam, reflected normal to the sample, is captured by a 2D camera (Videozavr, VZ-M50S, 1296 × 972 pixels, 21 frames/s) to acquire an image and track changes in the statistical properties of speckle structures caused by heating.

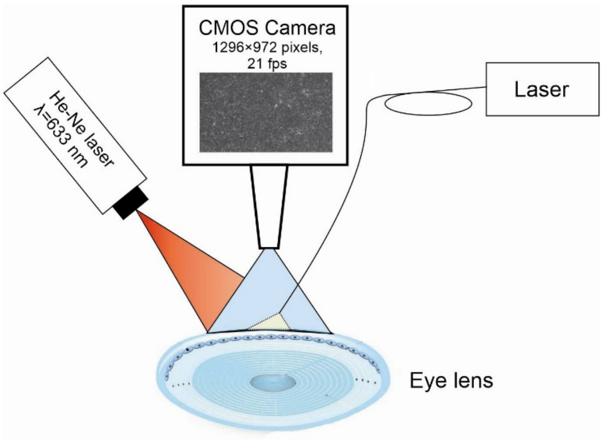


Fig. 3 Scheme of a speckle imaging setup.

The obtained images were used to calculate the statistical functions of the speckle patterns, such as the average light intensity and the Pearson cross-correlation coefficient (decorrelation function).

3 Results and Discussion

Numerical simulation for a power of 0.5 W, for a wavelength of 1560 nm made it possible to obtain at the first peak of exposure the maximum temperature change of 20.8 °C relative to the initial temperature, while at the last peak this value reached 22.2 °C.

Due to the thickness of the capsule film of a young healthy person of 11–18 µm and temperature difference of 0.20 ± 0.02 °C between boundary planes of capsule film during the pulse it can be assumed that heating is even along the radiation axis. Numerical simulation has shown that in the capsule layer at the first irradiation peak, the temperature profile can be approximated by one normal distribution, while at the last irradiation peak – by the sum of two normal distributions, one of which takes into account the propagation of heat perpendicular to the radiation axis due to thermal conductivity, and the dispersion of these two distributions differ by a factor of 20. Laser-induced thermal stresses in the lens capsule at the first and 20 peaks of laser radiation at a wavelength of 1560 nm are shown in Fig. 4.

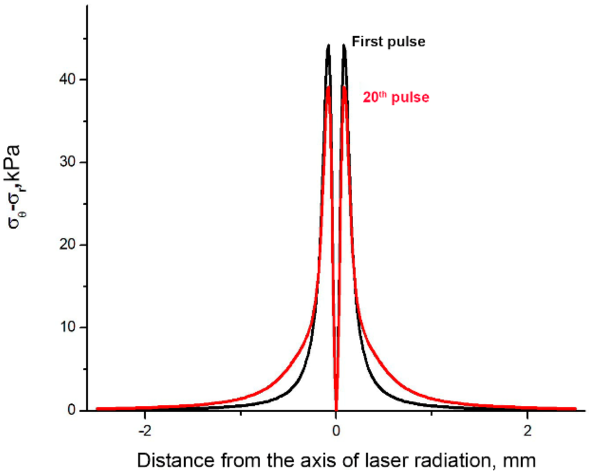


Fig. 4 Laser-induced thermal stresses in the lens capsule at the first and twentieth peaks of laser radiation at a wavelength of 1560 nm.

A similar calculation for a wavelength of 1450 nm showed that a decrease in the absorption depth by 3 times leads to the fact that at the first peak of exposure the maximum temperature change relative to the initial temperature was 55.7 °C, while at the last peak this value reached 59.7 °C. At the same time, in the capsule film, the temperature drop was 1.8 ± 0.2 °C, and the thermal stresses were 4 times greater than for a wavelength of 1560 nm, which can be dangerous for its integrity during medical intervention and can lead to additional wrinkling and the appearance of cavities and spaces in which the process of proliferation of lens epithelial cells can begin. Thus, for the subsequent experimental study with the human eye, we should choose a wavelength of 1560 nm, while in this work both wavelengths of laser radiation were used to treat pig's eyes.

3.1 Study of Visual Changes in the Structure of the Formalin-Modified Lens

As a result of a visual assessment, it was found that opacities of the lens are observed already after 15 min from placing it in formalin. Noticeable opacities with compaction of the surface layers of the lens, namely its capsule, increases with increasing exposure to soaking in a formalin solution, which is clearly seen in the presented photographs. Possibility of experimental modeling of postoperative opacification of the lens capsule of different intensity correlates with different types of opacities of the lens capsule after real cataract surgery. This makes it possible to solve applied problems of selecting the optimal parameters of laser radiation during laser dissection of secondary cataract films with different optical densities.

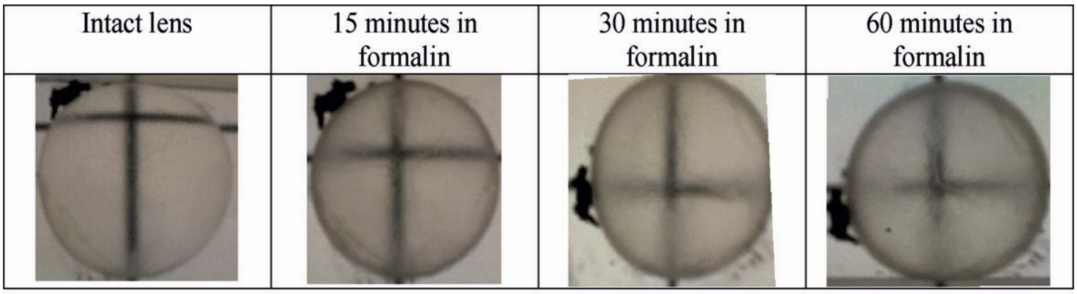
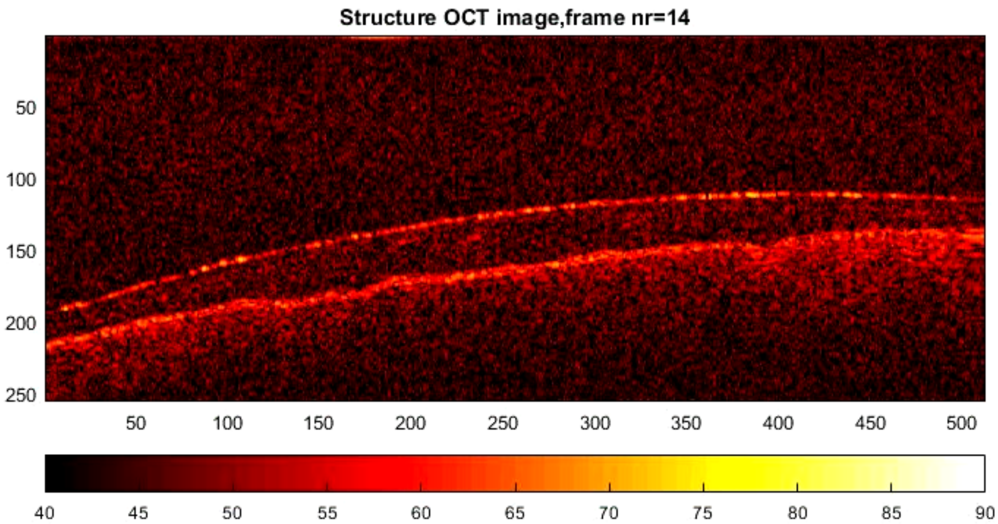
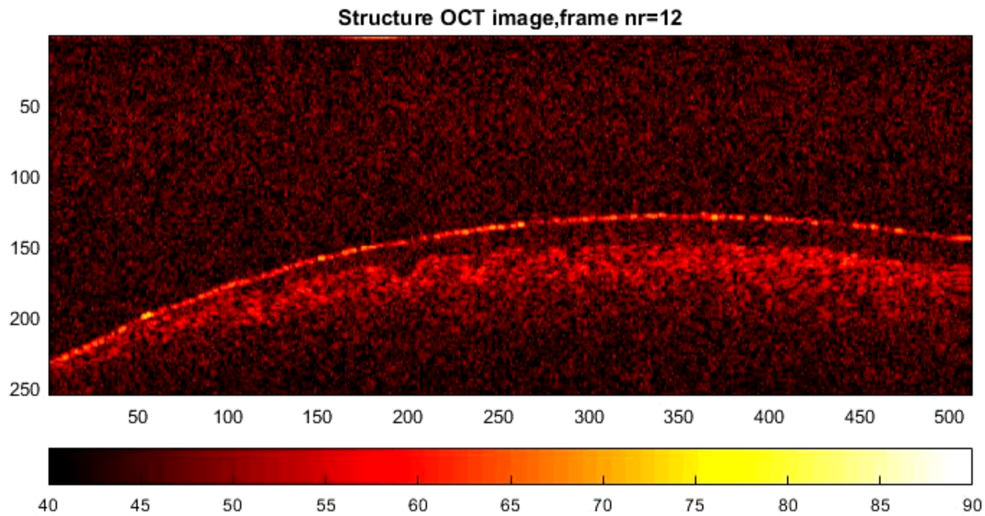


Fig. 5 Photographs of the capsule + lens system, with structure modification using formalin soak for various times for visual evaluation.



(a)



(b)

Fig. 6 OCE structural image (a) of the anterior and (b) of the posterior surface of the lens of the eye 30 min after they were exposure in formalin.

3.2 Study of Structural Changes Using OCE

The OCE setup made it possible to obtain structural images of the capsule surface area for the isolated porcine lens (Fig. 6). The evaluation was carried out on both sides of the modified porcine lens (anterior and posterior) along the center line.

When examining the intact lens tissue, it was noticed that for the anterior capsule there is a separation of the structure in the superficial layers with a very thin distance between them, for the posterior surface such separation was not observed.

Cataract modeling by placing the lens in formalin for 30 min or more led to the following changes in OCE images of the structure:

- For the anterior surface of the lens, in 60% of cases there was a significant increase in the distance between the surface (capsule) and the contents (inner layers and nucleus) of the lens. In other cases, an increase in this distance was also observed, however, not so significant.
- For the posterior surface, a discernible separation of the surface was observed in only 30% of cases.

It is important to note that this ratio appeared already after 15 min of exposure in formalin and was maintained regardless of the duration of exposure.

3.3 Evaluation of Surface Subsidence under Laser Exposure

Evaluation of the change in the height of the position of the sample surface along the central axis under laser irradiation was carried out using OCE structural images of the lens. For this, three frames were compared: the moment before the first laser pulse, the moment before the last laser pulse, and the moment 50 frames after the last laser pulse.

As a result, it was found that surface subsidence under laser irradiation does not occur for all samples. The surface of the anterior lens capsule of intact samples, and samples after being placed in formalin for 15 and 30 min experienced obvious subsidence after exposure to laser radiation with a wavelength of 1.45 µm. Moreover, the amount of sedimentation did not depend on the type of sample and the duration of its exposure in formalin. A similar laser impact on the posterior lens capsule did not cause its subsidence for both intact and formalin-modified samples.

Under laser action with a wavelength of 1.56 µm, a completely different behavior of the samples was observed. Surface settling did not occur during irradiation of the posterior or anterior lens capsule, either for intact specimens or for 15 min formalin-modified samples. However, for samples after 30 min exposure in formalin, subsidence of the surface of the posterior lens capsule was observed, while no subsidence occurred during laser exposure to the anterior capsule.

3.4 Deformation Response under Laser Action

A different pattern of deformations was observed for the formalin-modified lenses under the laser radiation with different wavelengths. Thus, for the anterior lens capsule (Fig. 7), radiation with a wavelength of 1.56 µm practically did not create any deformation patterns either on the surface or in the body of the sample.

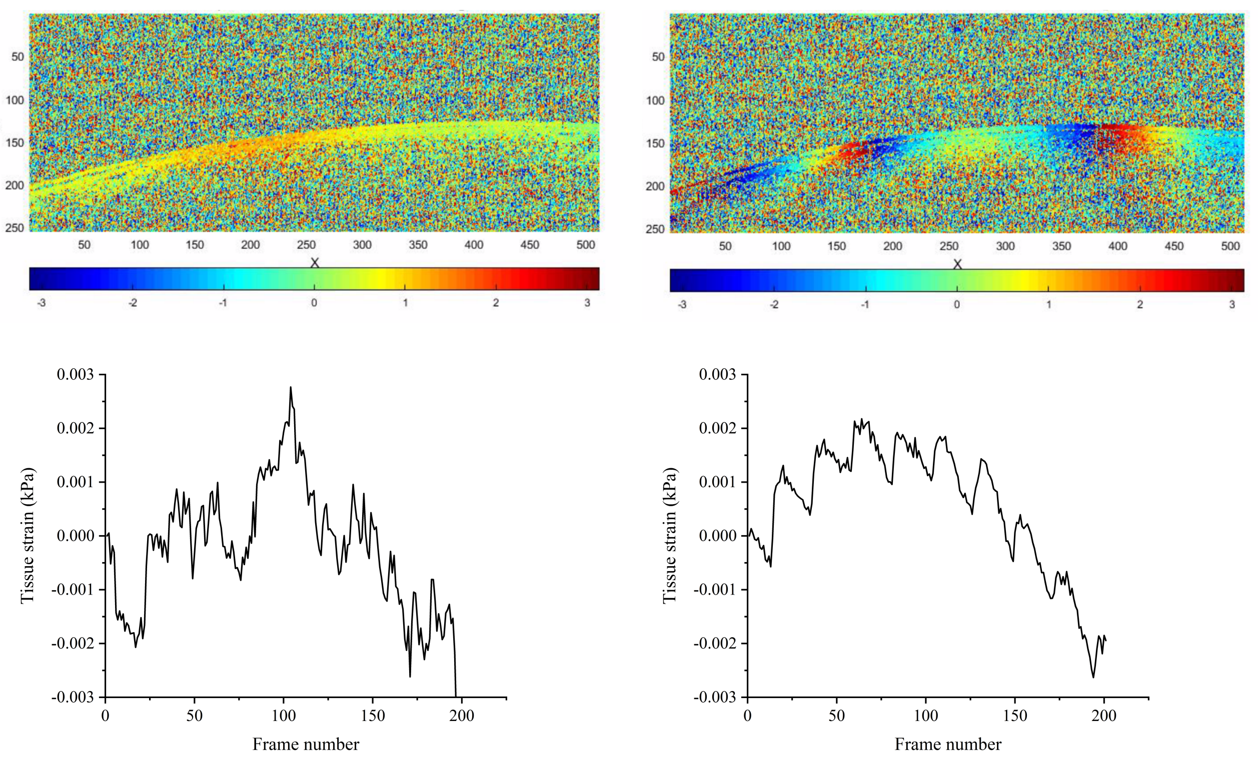
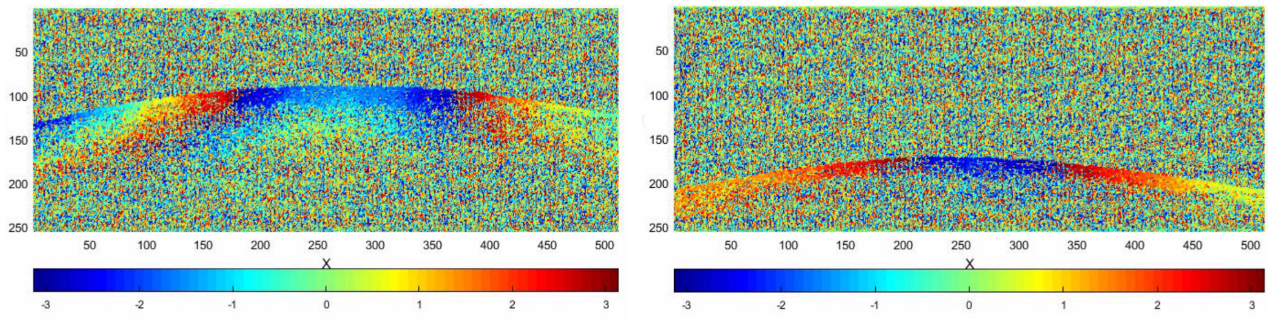
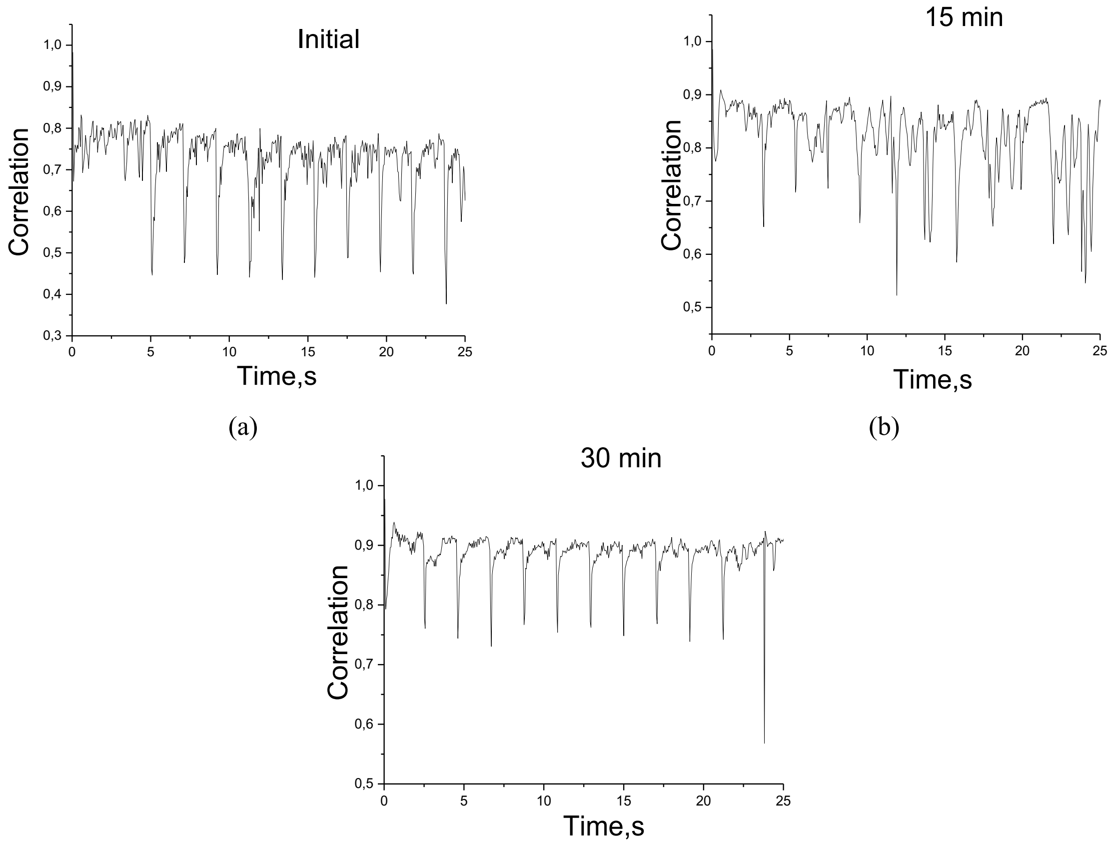


Fig. 7 Interframe phase difference and time dependence of tissue strain on the anterior capsule during laser exposure to the 15 min formalin-modified lens of the eye. Wavelength of laser radiation: (a) 1.56 µm; (b) 1.45 µm.



(a) (b)

Fig. 8 Interframe phase difference on the posterior capsule during laser exposure to the 15 min formalin-modified lens of the eye. Wavelength of laser radiation: (a) 1.56 µm; (b) 1.45 µm.



(a) (b)

(c)

Fig. 9 Decorrelation of the speckle-interferometric pattern of the porcine lens for different modification times in formalin: (a) before modification, (b) 15 min of modification, (c) 30 min of modification.

And for a wavelength of 1.45 µm, significant tissue deformations were observed throughout its depth, and the relaxation time of these deformations was much longer: 2 ± 1 frame at a wavelength of 1.56 µm for the first pulse versus 5 ± 1 frame for wavelength 1.45 µm. For the last laser pulse, the duration was 4 ± 1 and 6 ± 2 frames, respectively. Fig. 7 demonstrates interframe phase difference and time dependence of tissue strain on the anterior capsule during laser exposure to the 15 min formalin-modified lens of the eye. To determine the tissue strain value, an area along the axis of laser exposure immediately below the surface of the lens was chosen. From the graphs, the reaction of the anterior capsule to laser exposure with a wavelength of 1.45 µm is well defined, while for a wavelength of 1.56 µm, it is impossible to determine the moments of laser exposure from the graph of time dependence of tissue strain. For the posterior lens capsule, the graphs of time dependence of tissue strain also do not show an obvious response of the tissue strain amplitude to laser exposure.

From the pattern of deformation on the anterior (Fig. 7) and posterior (Fig. 8) lens capsules, the results of the assessment of surface subsidence given above become clear. Obviously, laser radiation with a wavelength of 1.45 µm has a greater effect on the structures of the anterior lens capsule.

3.5 Study of Changes in the Structure of the Lens in the Capsular Bag of the Eye when Placed in Formalin by Speckle Interferometry

Using the speckle interferometry method, videos of the surface of the porcine lens under laser exposure were obtained and processed. Fig. 9 shows the dependences of the decorrelation function on time under the influence of laser pulses for different residence times in formalin.

The relative drop in the value of the cross-correlation coefficient with laser pulses was estimated. The results are presented in Fig. 10.

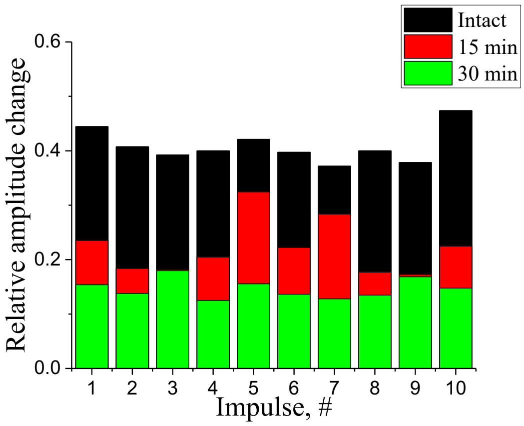


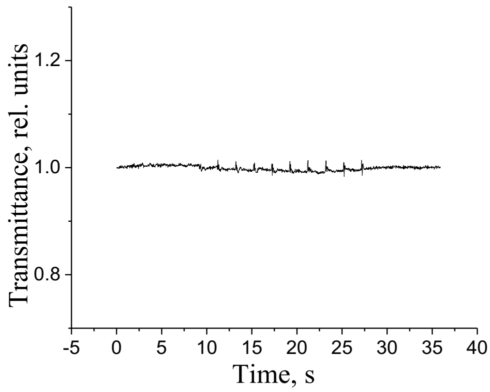
Fig. 10 Relative change in the decorrelation of the speckle interferometric pattern of the porcine lens for different modification times in formalin in response to laser pulses.

A comparison of the relative amplitudes of individual irradiation peaks for the same capsule sample showed that the relative amplitude of the peaks from the intact sample is higher than for the modified ones. At the same time, it was noted that the amplitude decreases with an increase in the time of modification of the capsule in the formalin solution, that is, with an increase in the number of crosslinks in the biological tissue, which make the sample more elastic and less transparent.

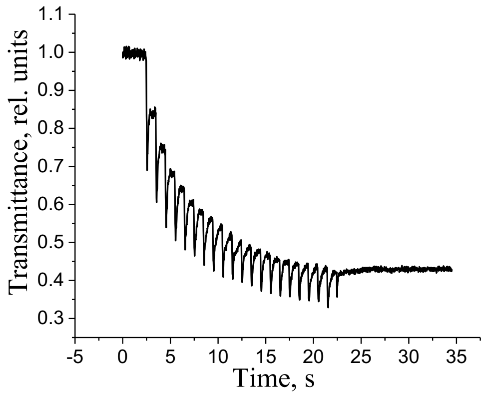
3.6 Study of the Change in the Scattering of the Lens of the Eye When Placed in a Formalin Solution

An experiment was carried out on the lenses of a pig to assess the effect of the irradiation wavelength on the response of tissue under laser irradiation. Fig. 11 shows the time dependences of the transmitted radiation for the lens of the pig's eye for wavelengths of 1.45 µm and 1.56 µm.

According to the results obtained, it can be seen that when irradiated with a wavelength of 1.56 µm, the film does not accumulate structural changes caused by laser heating, and for 1.45 µm, the transmission decreases significantly. Such an effect can be caused by the difference in absorption coefficients for these wavelengths in water, which is the main absorber in this tissue (10 cm^{-1} for 1.56 µm and 33 cm^{-1} for 1.45 µm).



(a)



(b)

Fig. 11 Transmission of laser radiation for the posterior film of the lens, exposed in formalin for 60 min, for wavelengths (a) 1.56 µm and (b) 1.45 µm.

4 Conclusions

Noticeable opacity with compaction of the surface layers of the lens, namely its capsule, increases with increasing exposure time in formalin solution, which creates the possibility of experimental modeling of postoperative opacification of the lens capsule of varying intensity, and correlates with various types of opacities of the lens capsule after real cataract surgery. This makes it possible to solve applied problems of selecting the optimal parameters of laser radiation during laser dissection of secondary cataract films with different optical densities.

At the same time, for the anterior surface of the lens, in 60% of cases there is a significant increase in the distance between the surface (capsule) and the contents (inner layers and core) of the lens. For the posterior surface, a discernible separation of the surface is observed only in 30% of cases. These changes occur during the first 15 min of exposure to formalin and then persist regardless of the exposure time.

The speckle interferometry technique is sensitive to this modification of a biological tissue, since the relative amplitude of the correlation peaks of the speckle interferometric pattern from an intact sample is higher than for modified ones, and it decreases with increasing exposure time, that is, with an increase in the number of crosslinks in a biological tissue that make the sample more elastic and less transparent.

The OCE technique can also detect the modification of biological tissue and, at the same time, this method is sensitive to changes in the wavelength of laser exposure.

For the selected exposure parameters, it was shown that a decrease in the absorption depth by a factor of 3 led to an increase in the maximum thermal stress by a factor of 4, which can be dangerous for the integrity of the capsule film during medical intervention.

Disclosures

All authors declare that there is no conflict of interests in this paper.

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