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Abstract. Optical properties of cornea and sclera of the eye and their alterations under the effect of 1.56-µm laser radiation are studied. The laser settings corresponded to the laser treatment regimens used (1) to correct the shape of the cornea and change the refraction of the eye and (2) to improve the hydraulic permeability of the sclera in glaucoma cases. A fiber-optical system to investigate the dynamics of the reflected and transmitted scattered laser radiation and a setup with a double integrating sphere to determine the optical properties of the ocular tissues on the basis of the Monte-Carlo simulation of the propagation of light was used. When the radiation characteristics corresponded to the treatment regimens for correcting the shape of the cornea, no noticeable changes were detected in its optical properties. When irradiating the sclera in conditions corresponding to the treatment regimens for improving its hydraulic permeability, the optical characteristics of the tissue showed definite changes. The results obtained as to the dynamics of the optical signals during the course of laser irradiation of the cornea and sclera create prerequisites for designing test systems to be used with novel medical laser techniques for correcting visual abnormalities. © 2013 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: 10.1117/1.JBO.18.5.058003]

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1 Introduction

To optimize laser treatment regimens and provide for the safety of medical laser techniques, especially where the strict control of the temperature field produced in the laser-exposed tissue¹ is a must, a rather exact knowledge of the optical parameters of the tissue and their alterations during laser treatment is required. Investigations into the optical properties of ocular tissues have been conducted for a long time (see, e.g., Refs. 2-8 and references cited therein), but there is scarce information concerning the response of the tissues to near-infrared (IR) radiation. Of special interest is the $1.56 \mu m$ radiation that is being predominantly absorbed in an interstitial fluid layer around 1 mm in thickness, which is close to the characteristic thicknesses of the ocular tissues. At the same time, there is but little information in the literature on the changes that the optical parameters of the tissues undergo during laser treatment. This is especially true of the alterations in their light scattering characteristics. The scattering of light affects its depth of penetration into tissues and strongly depends on their structure. For this reason, the magnitudes of optical parameters can substantially differ between the cornea and the sclera of the eye that are closely similar to each other in chemical composition, but are unlike in structure. The importance of the research into the dynamics of alteration of the optical characteristics of biological tissues during the course of their laser treatment is also due to the fact that this method can prove very effective in the nondestructive testing of the structural changes suffered by the tissues,⁹ as well as

in the further development of laser therapy feedback control systems.¹⁰ Medical systems including 1.56- μ m fiber lasers are now being widely used for the thermoplasty of the nasal septum¹¹ and ear conch,¹² regeneration of articular cartilages and intervertebral disks,¹³ and cutaneous remodeling by the fractional photothermolysis technique.^{14,15} Also actively pursued are investigations into the use of erbium-doped glass fiber lasers in other branches of medicine, for example, in ophthalmology to correct eye refraction through the laser thermoplasty of the sclera and to lower the intraocular tension in glaucoma cases by improving the hydraulic permeability of the trabecular region and sclera of the eye.^{16–19}

Since ablative laser technologies (PRK and LASIK) are widely used for changing refraction characteristics of the eye, the problem of safe and stable correction of cornea shape and refraction is not fully solved. A new approach of cornea reshaping is based on the essential property of the cornea-temporal thermoplasticity.¹⁶ A new, desirable shape of the cornea is created with a lens with proper shape and then stabilized with laser irradiation, increasing cornea plasticity and, hence, changing its radius of curvature. After cooling, the mechanical properties of the cornea return to its initial values, however, the newly obtained shape is stable.¹⁷ The nondestructive character of a new technique provides its advantage compared to known methods of laser refractive surgery using ablative ultraviolet lasers and thermal keratoplasty using a continuous wave laser for shrinkage of cornea stromal collagen.¹⁸ Glaucoma is one of the most common diseases of the eye. Although a number of pharmacological and surgical therapies to decrease intraocular pressure

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are employed, none resolve the disease completely and permanently.^{18,19} The issue of the day, a new approach for normalization of the intraocular pressure in glaucoma eyes, is based on enhancing the role of uveoscleral outflow by creating permeable pathways for water transport through sclera.

To optimize laser treatment regimens in these medical procedures and develop safe test methods, it is important to know the optical parameters of the cornea and sclera at the radiation wavelength of the laser used and the changes these parameters undergo during the course of laser heating. The objective of the present work is to measure the optical parameters of the cornea and sclera at a wavelength of 1560 nm and investigate the possibility to optically test the condition of these tissues. The 0.53 micron exposure is used in existing medical setups for better aiming. One of our goals is to investigate whether it can be used in a monitoring system.

The specifics of measuring the optical characteristics of ocular tissues (cornea, lens, and retina) in the visible region of the spectrum and the various approaches to this problem were considered by Sardar et al.⁸ These authors used a double integrating sphere to measure the diffuse reflection and diffuse transmission of the probe light beam and compared between the calculation results obtained for the absorption and scattering coefficients by three different methods, namely, the Kubelka-Munk, inverse adding-doubling, and inverse Monte-Carlo ones. The results for the scattering coefficients obtained by these methods agreed well, whereas those for the absorption coefficient differed substantially between them. The first two methods assume diffuse scattering of some incident light in the sample, which is not strictly the case with thin or weakly scattering biological tissues, such as, in particular, the cornea, lens, and retina. The inverse Monte-Carlo method is not tied to such models and allows, in principle, calculating light fields for any media of given optical characteristics, and so it seems to be most suitable for measuring the optical characteristics of ocular tissues. The work by Yust et al.⁶ is essentially a sequel to that by Sardar et al.⁸ for the near-IR wavelength range of 750 to 900 nm. Note also the work by Sardar et al.,⁷ who used a double integrating sphere to measure the optical parameters of the interstitial fluid in the IR region of the spectrum, specifically at 1560 nm. The optical properties of the sclera in the visible and near-IR regions of the spectrum were also measured by means of a double integrating sphere in an earlier work by Hammer et al.²⁰ There is apparently no information available in the literature on the measurements of the optical parameters of the cornea and sclera in the region of 1560 nm. In the most closely related work by Sviridov and Kondyurin,²¹ a double integrating sphere and the Monte-Carlo method were used to determine the optical parameters of septonasal cartilages at a wavelength of 1.56 μ m and study the dynamics of their changes during the course of laser heating. These authors demonstrated that as the tissue was heated up to 70°C, its absorption coefficient decreased monotonically by approximately 20%, which was explained to be due to the deformation of the $\nu_1 + \nu_3$ absorption band of water as a result of the temperature variation.²²

The propagation of light through an inhomogeneous medium can uniquely be described, provided its absorption coefficient (μ_a), scattering coefficient (μ_s), scattering anisotropy factor (g), refractive index, and scattering phase function are known. It is accepted in medical optics that the scattering phase function, or the probability density of the scattering angle, is defined by the Henyey–Greenstein phase function.²

When calculating μ_a , μ_s , and g by the Monte-Carlo method on the basis of measurement results for diffuse reflection, diffuse transmission, and their angular distributions, a substantial error can occur in distinguishing between μ_s and g. This can happen because of the fact that with the reduced scattering coefficient $\mu'_s = \mu_s(1-g)$ being the same, the diffuse reflection, diffuse transmission, and their angular distributions depend only weekly on whether μ_s or g is being considered. Fortunately, the thermal effect of laser radiation can, in many practical cases, be evaluated accurately enough in terms of the effective absorption coefficient $\mu_{\text{eff}} = \sqrt{3\mu_a(\mu_a + \mu'_s)}$ (Ref. 1). For this reason, attention in this work was focused on measuring μ_a and μ_a' of the cornea and sclera at a wavelength of 1560 nm and their variations during the course of laser medical procedures. Also, to develop test systems, we investigated the behavior of the diffuse reflection, diffuse transmission, and paraxial transmission signals from samples of the above ocular tissues exposed to an erbium-doped glass fiber laser.

2 Materials and Methods

2.1 Ocular Tissue Samples

We experimented ex vivo on sclera and cornea samples taken from the eyes of minipigs (Svetlogorsk strain). The excised eyes were immediately frozen and stored at -4 °C for 10 to 15 days. Preparatory to the experiment, the eyes were defrosted in a saline solution for 30 min at room temperature and then prepared with a scalpel and scissors. With the eyeball dissected, its posterior pole was excised, as well as its extrinsic and intrinsic components (lens, extrinsic muscles, ciliary processes). Thereafter, 4×4 mm samples (Fig. 1) were cut out and placed in a saline solution for 5 min to prevent drying of both their internal and near-surface layers, which are responsible for the reflection and scattering of light. Before testing, the tissue samples were removed from the saline and slightly dried in air to avoid errors due to absorption of radiation by the excess water on the tissue surface and then fixed in a special holder. Exposed to radiation were (a) a central region of the cornea (near the axis of the eye, irradiated spot diameter 3 mm), (b) a peripheral region of the cornea (3.5 mm distant from the axis of the eye, irradiated spot diameter 3 mm), and (c) a part of the sclera (2.5 to 3 mm distant from the edge of the sclera,



Fig. 1 Schematic illustration of the partition of the front of the eye and laser irradiation direction: 1, sclera; 2, cornea; *a*, central region of the cornea; *b*, peripheral region of the cornea; *c*, scleral region; *X*, laser irradiation direction.

irradiated spot diameter 600 μ m). The irradiation zones are shown in Fig. 1. The hydration level in the samples was established as the same for each one and it was close to the physiological one. The number of samples for each experiment carried out was at least four. One laser spot was applied for each tissue sample.

2.2 Laser Treatment Equipment and Regimens

We experimented with erbium fiber IR laser generating 1.56- μ m radiation up to 5 W in power, along with 0.53- μ m probe radiation, of variable pulse duration (τ) and pulse repetition frequency (f). The laser radiation characteristics corresponded to the laser treatment regimens used (1) to correct the shape of the cornea (intensity 6 ± 1 W/cm², $\tau = 500$ ms, f = 1.4 Hz, exposure time $T_{exp} = 6$ s^{18,23} and (2) to improve the hydraulic permeability of the sclera (intensity 170 ± 20 W/cm², $\tau = 200$ ms, f = 2.5 Hz, $T_{exp} = 5$ s).^{18,19} To acquire the experimental data necessary to calculate the optical parameters of the ocular tissues prior to and after laser treatment, we used single short diagnostic pulses 50 ms in duration and 20 W/cm² in intensity. To reveal possible alterations of the optical characteristics of the tissues during laser treatment, we also measured the transmission of 1.56- μ m radiation at an intensity of around 20 W/cm² for 30 to 36 s, which substantially exceeded the optimal therapeutic laser exposure times for the cornea and sclera of the eye.^{18,19} The intensities reported are average intensities.

2.3 Experimental Setups

The experiments on the dynamics of scattering and transmission of the 1.56- and 0.53- μ m laser radiation were performed using a special fiber-optical system (Fig. 2), allowing the sample under test to be concurrently irradiated with radiation of the above two wavelengths. Radiation was delivered to the sample via a 600- μ m-diameter optical fiber (quartz-quartz, beam divergence angle 0.22 rad) normal to the sample surface.

The various optical signals of interest (reflected and transmitted IR and visible radiation signals) were simultaneously recorded and digitized with a multichannel optical analyzer. The digitized measurement results obtained were displayed on a computer monitor screen. Measurements taken with the aid of the above fiber-optical system were prone to error because



Fig. 2 Schematic diagram of the fiber-optical experimental setup for investigating the optical properties of ocular tissues exposed to laser radiation: 1, optical fiber; 2, tissue sample; 3, multichannel optical analyzer; $\lambda_1 = 1.56 \ \mu m$, $\lambda_2 = 0.53 \ \mu m$.

of its failure to take account that part of radiation that was not collected by the optical fiber. To obtain more accurate information allowing for the scattering of radiation in different directions, we conducted experiments on the central parts of the cornea and sclera with another setup using a double integrating sphere (Fig. 3).

This setup consists of two spheres with their internal surfaces coated with fine-dispersed barium sulfate, ensuring practically a 100% reflection of IR radiation. As a result, a uniform light field is produced within the spheres irrespective of the radiation direction, and the signal of interest can be recorded at any point therein.

The 1.56- μ m laser radiation was delivered to the sample via a 600- μ m-diameter optical fiber (quartz-quartz, beam divergence angle 0.22 rad) normal to the sample surface. Subject to measurement in real time were the total diffuse reflection R_d , total diffuse transmission T_d , and total collimated (paraxial) transmission T_c of radiation, necessary for calculating the optical parameters of the sample tissues by the Monte-Carlo method.

2.4 Calculation Method

The solution of the direct optical problem by the Monte-Carlo method consists of multiplying the repeated generation of random photon trajectories in the medium under study, with due consideration given for absorption and scattering. The photon trajectory calculation is based on several rules by which the photon enters the medium, propagates therein, and escapes from it. These rules are established by (1) the probability of a scattering or absorption event, which determines the free path of the photon between scattering or absorption events, (2) the probability that the photon trajectory would be deflected through some angle upon scattering, and (3) the probability that the photon would be reflected from the interface of two media differing in refractive index, should the photon reach it.

The diffuse reflection R_d , diffuse transmission T_d , and collimated transmission T_c were calculated with the aid of the modernized Monte-Carlo algorithm.^{24,25} As distinct from the traditional Monte-Carlo approach^{26–28} wherein subject to simulation is the propagation of single photons, the method suggested in the above-cited work²⁴ considers an arbitrary packet of photons propagating in the same direction. This approach materially improves the efficiency of simulation and cuts down the run-time in computing R_d , T_d , and T_c at a given accuracy level.



Fig. 3 Schematic diagram of the double-integrating-sphere experimental setup for measuring the optical parameters of biomaterials.

 Table 1
 Optical properties of ocular tissues prior to and after laser treatment.

	Prior to treatment		After treatment	
Tissue type	μ_a , cm ⁻¹	μ_s^\prime , cm ⁻¹	μ_a , cm ⁻¹	μ_s^\prime , cm ⁻¹
Cornea	6.1 ± 0.4	9.0 ± 0.6	$\textbf{6.1}\pm\textbf{0.4}$	9.0 ± 0.6
Sclera	$\textbf{9.7}\pm\textbf{0.9}$	$\textbf{33.2}\pm\textbf{1.2}$	11.5 ± 1.1	$\textbf{26.8} \pm \textbf{2.5}$

3 Results

The calculation results for the optical characteristics of the cornea and sclera, prior to and after their laser treatment, and obtained using the data acquired with the aid of two integrating spheres, are listed in Table 1.

The results obtained show no noticeable changes in the absorption and scattering coefficients of the cornea exposed to laser radiation in conditions corresponding to the treatment regimens used to correct its shape. At the same time, when irradiating the sclera in conditions corresponding to the treatment regimens for improving its hydraulic permeability, the optical characteristics of the tissue showed definite changes (16% to 18% increase in the absorption coefficient and 18% to 20% decrease in the scattering coefficient).

The results of our experimental investigations into the dynamics of the optical signals from the cornea exposed to the 1.56- and 0.53- μ m laser radiation (Figs. 4 and 5) allow the following observations to be drawn:

 A qualitative agreement is observed (the presence of a maximum) between the transmitted radiation signal curves obtained with the double integrating sphere and the fiber-optical system, the agreement being more pronounced for the paraxial radiation signals. The initial sections of the curves obtained by the above two methods are closely similar, as are the positions of their maxima (curves 1 and 4 in Fig. 4). The



Fig. 4 Dynamics of IR signals for the central region of the cornea (normalized to the initial value): *I*, paraxial transmitted radiation signal obtained with the double-integrating-sphere setup; 2, transmitted radiation signal obtained with the double-integrating-sphere setup; 3, reflected radiation signal obtained with the double-integrating-sphere setup; 4, transmitted radiation signal obtained with the fiber-optical experimental setup.



Fig. 5 Dynamics of the transmitted radiation signals from the cornea: 1, 0.53- μ m radiation, peripheral region; 2, 0.53- μ m radiation, central region.

intensity of the reflected radiation signal varies, but little.

2. The time it takes for the transmitted light intensity to reach its maximum differs between the central and peripheral parts of the cornea (13 and 16 s, respectively), which points to a resistance of the central parts of the cornea to the IR laser heating.

For the sclera, the dynamics of the optical signals recorded with the fiber-optical system and with the setup using two integrating spheres are presented in Fig. 6. The curves obtained by these two methods are similar: the positions of their characteristic extremums coincide.

At the same time, the time dependences of the transmitted radiation signals for the cornea and sclera presented in Figs. 5 and 6 differ qualitatively (the curves have maxima for the cornea and minima for the sclera). The time dependence of the signal for the radiation reflected from the surface of the sclera shows a distinct maximum (curve 2 in Fig. 6).

Each presented trace was independently normalized by its starting value. A sample-to-sample variability does not exceed 15%.



Fig. 6 Dynamics of the optical signals from the sclera exposed to 1.56- μ m laser radiation: 1, transmitted radiation signal obtained with the fiber-optical setup; 2, reflected radiation signal obtained with the double-integrating-sphere setup; 3, transmitted radiation signal obtained with the double-integrating-sphere setup.

4 Discussion of the Results

The effective absorption coefficients of the cornea and sclera $(16.4 \pm 0.5 \text{ and } 35.4 \pm 1.1 \text{ cm}^{-1}$, respectively) found by measuring three radiation signals in two integrating spheres allow rendering more precise results than those obtained earlier in terms of the Bouguer law using measurement results for the intensity of radiation incident on and passing through the sample $(10.5 \pm .0 \text{ cm}^{-1} \text{ for the cornea and } 27.6 \pm 1.4 \text{ cm}^{-1} \text{ for the sclera}).^{29}$ The discrepancy between results is due to different techniques used. The results obtained in Ref. 29 are the evaluation of the effective absorption coefficient based on attenuation only. Our technique appears to be more precise since it considers not only transmittance but also reflection.

The absence of any changes in absorption and scattering coefficients occurring in the cornea points to the absence of perceptible structural changes. It is one of the most important criteria that testifies to the safety of the novel eye refraction correction technique based on the nondestructive thermomechanical effect of laser radiation.¹⁸ The high-intensity laser irradiation of the sclera in conditions corresponding to the therapeutic laser effect in normalizing the intraocular tension gives rise to small changes in the optical characteristics of the tissue (16% to 18% increase in absorption coefficient and 18% to 20% decrease in scattering coefficient). These changes can be due to the laser-stimulated formation of a porous structure¹⁸ that improves the hydraulic permeability of the sclera and accordingly raises (locally) the concentration of the interstitial fluid, which increases somewhat the effective absorption coefficient. The slight decrease in the scattering coefficient of the sclera can be due to the redistribution of water in the newly formed pores that are relatively small in comparison with the laser wavelength.

The results of our investigations into the dynamics of the intensity of radiation passing through the ocular tissues during the course of their IR laser irradiation (Figs. 4 through 6) agree well with the above-described picture. The dynamics of the transmitted light signals obtained by different methods (with the fiber-optical system and with the system using two integrating spheres) are similar in character. The initial sections and positions of the maxima in the time-dependence curves of the signals (curves 1 and 4 in Fig. 4) obtained by the above two methods are close to each other, which bespeaks sufficient reliability of the measurements taken with the fiber-optical system that collects the major part of the paraxial signal recoded with the integrating spheres. At the initial stage of laser treatment, the transparency of the cornea is observed to increase a little, which can be due to the outflow of water from the irradiation region or the shift of the absorption band of water on heating.²² Sobol et al.⁴ demonstrated that the 3- μ m absorption peak of the cornea shifted on laser heating. These authors showed that increasing the intensity of 3.22-µm laser pulses from 0.07 to 0.1 J/cm² caused the effective absorption coefficient k of the cornea to increase by 40% (from 2295 to 3154 cm⁻¹), while raising the intensity of 2.81- μ m laser pulses from 0.045 to 0.063 J/cm² resulted in a sharp (almost threefold) decrease of k.

The presence of a transmission maximum for the cornea and its subsequent decline (Figs. 4 and 5) point to the onset of structural changes therein, giving rise to an increase in the size and number of its scattering centers.⁹ The strong reduction of the paraxial transmission and not so significant change of the diffuse transmission of the cornea also indicate the occurrence of additional scattering centers and the associated redistribution of light fluxes.⁹ The time dependences obtained for the intensity of radiation passing through different parts of the cornea (curves 1 and 2 in Fig. 5) show that the peripheral part of the cornea starts changing its structure earlier than the central part, which means that the periphery of the cornea is less resistant to laser heating than its center. This is apparently associated with the structure of the cornea whose central zone is most densely packed and stronger.³⁰ The nonuniformity of the structure and thermal resistance of the cornea may be the cause of the considerable difference between the experimental data, which is reported by different authors to range from 50°C to 85°C (Refs. 31–34), on the resistance of the cornea to laser heating.

The dynamics of the optical signals from the sclera obtained by means of the fiber-optical system and the system with a double integrating sphere are also similar in character (Fig. 6). Coincident here are the positions of the characteristic extremums indicating structural changes. It should be noted, however, that there is a qualitative difference in behavior between the signals from the cornea and those from the sclera (cf. Figs. 4 and 6), which is due to the differences in structure and laser treatment regimens between these tissues.³⁵ The diameter of collagen fibrils in the sclera is several times that in the cornea that, in addition, has a more ordered and denser structure, which prevents the development of the structural changes giving rise to additional scattering centers at the early stages of laser heating. This also explains the substantial difference in laser exposure time necessary for the onset of substantial changes in optical characteristics between these tissues: the cornea is much more resistant to laser-induced structural changes than the sclera.

For the sclera, the initial decline in light transmission (Table 1 and Fig. 6) can be due to formation of pores¹⁸ that become filled with the interstitial water, increasing the effective absorption coefficient. Further behavior of the signals (transmission rise following the extremum in Fig. 6) can be explained by the growth of the scattering anisotropy factor as a result of enlargement of the scattering centers, or by the growth of the regions of local coagulation of the sclera, leading to the collapse of pores and reduction of the water concentration therein, and the corresponding decrease in absorption. Such a collapse of pores resulting in worsening of hydraulic permeability was noted to take place on excessive heating of the sclera,19 and this corresponds to nonoptimal laser treatment regimens. The variation of the behavior of the reflected radiation signal (curve 2 in Fig. 6) also correlates with the changes occurring in the structure of the tissue exposed to laser radiation. The formation of a large number of pores at the initial stages of laser treatment causes the laser-exposed region of the tissue to grow thicker to form a convex lens, which augments the reflected radiation signal. The collapse of pores and coagulation of the tissue in the case of excessively long laser exposure time results in the inverse effect because of local thinning of the sample.

The results obtained for the behavior of the optical signals during the course of laser irradiation of the cornea and sclera of the eye and the correlation between the characteristic extremums in the dynamics curves and the concurrent changes in the scattering centers and structures of the ocular tissues create prerequisites for designing test systems improving the efficiency and safety of medical laser techniques for correcting the eye refraction and treating glaucoma, as was the case with the laser regeneration of intervertebral cartilages.^{10,13}

5 Conclusions

The results obtained show the absorption and scattering coefficients of the cornea to undergo no changes when exposed to laser radiation in conditions corresponding to the therapeutic laser effect in correcting its shape and refraction. At the same time, when irradiating the sclera in conditions corresponding to the therapeutic laser effect in increasing its porosity and normalizing the intraocular tension, the optical characteristics of the tissue are observed to change a little (decrease in scattering and increase in absorption).

The changes induced in the optical characteristics of the cornea by the 1.56- μ m laser radiation as a result of modification of its structure occur later in its central region than in the peripheral regions, which is evidence of the higher thermal stability of the central zone of the cornea.

The dynamics of variation of the transparency of the cornea and sclera during the course of laser treatment can form the basis for designing test systems for recording desirable and undesirable structural alterations in the ocular tissues to ensure the efficiency and safety of ophthalmologic laser techniques.

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