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Measuring the elastic wave velocity in the lens of the eye as a function of intraocular pressure using optical coherent elastography

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Abstract. **The dependence of the elastic properties of the eye lens on the intraocular pressure is investigated in porcine eyes *ex vivo*. To measure the stiffness of the lens, the method of dynamic optical coherent elastography is used, in which the propagation velocity of surface elastic waves in the lens is measured using phase-sensitive optical coherent tomography. Measurement data show an increase in Young's modulus of the lens by ~30% with an increase in intraocular pressure from 10 to 40 mm Hg. This result allows us to conclude that the effect of intraocular pressure on the rigidity of the lens is less significant than on the rigidity of other eye tissues, such as the cornea and sclera. The method of optical coherent elastography makes it possible to measure the elastic properties of the lens without removing it from the eyeball and has considerable potential for clinical use.**

Keywords: *optical coherence tomography, elastography, shear waves, crystalline lens, intraocular pressure, Young's modulus.*

1. Introduction

The interest in the mechanical properties of the eye lens is primarily due to its role in the accommodation of the eye and the influence of the elasticity of the lens on the development of presbyopia, i.e., the loss of accommodative capabilities of the eye with age. Presbyopia develops in most people after forty years and is characterised by an increase in the rigidity of the lens, which leads to its inability to change the shape and, therefore, the focal length of the eye [1, 2]. In this regard, information about the elastic properties of the lens is necessary for better understanding of the processes of accommodation of the eye, as well as for the development of new approaches to the treatment of presbyopia by restoring the elastic properties of the lens. Several such approaches are currently under development [3, 4].

When assessing the elastic properties of the lens, it is important to take into account the effect of intraocular pressure (IOP) on the change in the mechanical properties of eye tissue. As known, an increase in IOP leads to deformation of the tissues and the manifestation of their elastic nonlinear properties, which significantly increases the rigidity of the cornea and sclera of the eye [5–11], and is also possibly one of the causes of the development of glaucoma [12]. In addition, it is well known that the internal pressure affects the elastic properties of various tissues, such as the walls of blood vessels, the liver, etc. [13–15]. However, the effect of IOP on the elastic properties of the lens in the literature is usually not considered. Since the lens is located deep inside the eyeball, the use of mechanical methods for measuring its rigidity without damaging the eyeball is difficult. As a result, information on the mechanical properties of the lens is available only after its extraction from the eyeball [2, 16–20]. To measure the rigidity of the lens inside the eyeball, we propose to use a newly developed method of dynamic optical coherent elastography, in which the propagation velocity of surface elastic waves in the lens is measured using phase-sensitive optical coherent tomography [21, 22].

The term 'elastography' was first proposed by Jonathon Ophir in 1991 and means a non-damaging measurement of the elastic properties of soft biological tissues for the purpose of their medical diagnosis [23]. This method is based on the deformation of a tissue using an external load and on measurement of the mechanical response of the tissue to this load using modern imaging methods. Depending on the applied load, elastographic methods are usually divided into static [23] and dynamic [24]. In Russia, elastography methods were actively developed by a group of scientists under the leadership of A.P. Sarvazyan and A.R. Skovoroda [25–28]. The approach proposed by A.P. Sarvazyan, based on the use of acoustic pressure for tissue deformation followed by measuring the velocity of propagation of shear waves, formed the basis of the elastography method, which is currently being actively developed in the world as a new method of medical diagnostics [25, 29]. Ultrasonic methods and methods of nuclear magnetic resonance (NMR) are now most frequently used to measure the propagation velocity of shear waves [29–31]. Optical coherence tomography (OCT) as a method for measuring tissue deformation was proposed by Joseph Schmitt in 1998 [32]. OCT has a number of significant advantages compared with ultrasound and NMR, allowing measurements to be performed with better resolution, higher sensitivity and speed [21, 33–35]. Recently, both static and dynamic methods of optical coherent elastography have been developing rapidly in Russia and abroad [21, 33–45]. These methods are especially actively developed for applications in ophthalmology, where the advantages of OCT can be fully utilised [34, 35, 41, 44, 46–48].

In our previous studies, several approaches were developed for dynamic optical coherent elastography [9, 11, 40, 49], including the measurement of the elastic properties of the lens [46, 47]. As a source of deformation and elastic waves in the

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lens, we used a short pulse of acoustic pressure created by a focusing ultrasonic transducer [19, 47, 50–52]. The use of phase-sensitive OCT makes it possible to measure small (on the order of hundreds and tens of nanometres) amplitudes of oscillations of the surface of the lens and, thereby, significantly reduce the intensity of the acoustic field required for deformation.

In this paper, we examined the IOP dependence of the velocity of propagation of elastic waves over the lens surface. The pressure inside the eyeballs was monitored with a syringe pump and a pressure sensor. To excite the elastic wave, a focusing ultrasonic transducer was used, and the surface displacements were measured using phase-sensitive OCT. The proposed approach to measuring the elastic properties of the lens has a significant potential for clinical use.

2. Materials and methods

The general scheme of the experimental setup for optical coherent elastography is shown in Fig. 1. Eyeballs (three pairs), obtained from pigs between the ages of four and six months (Sioux-Preme Packing Co., USA), were delivered by express mail, so that all experiments were performed within 24 hours after the eye enucleation. Before the experiments, the eyeballs were cleared of fat, muscles and connective tissue and placed in a special holder (Fig. 1). After the experiments, the diameter and thickness of the lenses were measured to be approximately 9.7 and 8 mm, respectively.

The pressure inside the eye was monitored using a specially developed system consisting of a pressure sensor (Keller AG, Switzerland), a syringe pump (New Era Pump System Inc., USA) and a computer with appropriate software for monitoring the syringe pump and displaying the results of pressure measurements by the sensor. Through the holes in the holder and the sclera, two needles were inserted into the vitreous body to inject a sodium phosphate buffer solution into the eyeball and to implement pressure control inside it. One needle was connected to a syringe pump, and the other to a pressure sensor (Fig. 1). With the help of software developed in MATLAB (Mathworks Inc., USA), the pressure inside the eye was stepwise increased from 10 to 40 mm Hg in increments of 5 mm Hg. Before measurements, the pressure in the eyeball was twice cyclically increased to 40 mm Hg and reduced to 10 mm Hg.

To deform the lens and excite elastic surface waves in it, we used an acoustic radiation pressure pulse created with a single-element focusing ultrasound transducer (CTS Valpey Corporation, USA) with a centre frequency of 3.5 MHz, a focal length of 19 mm and a diameter of 12.8 mm. The acoustic field was focused on the surface of the central part of the lens, so that the angle between the acoustic and optical beams was 45°. The harmonic signal from the functional generator (RIGOL Technologies, China) was amplified by a radio frequency power amplifier (Electronics & Innovation Ltd., USA) and directed to an ultrasonic transducer (Fig. 1). In the experiments, an acoustic pressure pulse with a duration of 1.06 ms was used.

To measure the speed of propagation of elastic waves over the lens surface, we used a phase-sensitive OCT system presented in Fig. 1. The radiation source was a 18 mW superluminescent diode with a centre wavelength of 840 nm and a spectral bandwidth of 49 nm. The phase stability of the system was measured experimentally and corresponded to a shift of 7 nm in air. The trigger OCT system was synchronised with the functional generator. After an acoustic pulse, a scan (a series of two-dimensional in-depth scans at a constant spatial position) was conducted in both directions at a distance of 6 mm from the focus of the ultrasonic emitter along the direction of wave propagation. The phase shift signal of the scattered radiation was recorded at 200 points for 500 ms with a sampling frequency of 25 kHz. For each pressure value, the experiment was repeated three times, followed by averaging the results in both directions.

For points on the lens surface, the phase shift of the OCT signal corresponds to the spatial displacement of each point along the optical beam during the propagation of the elastic wave. The phase shift $\varphi(t)$ is related with the displacement of the point $d(t)$ by the equation

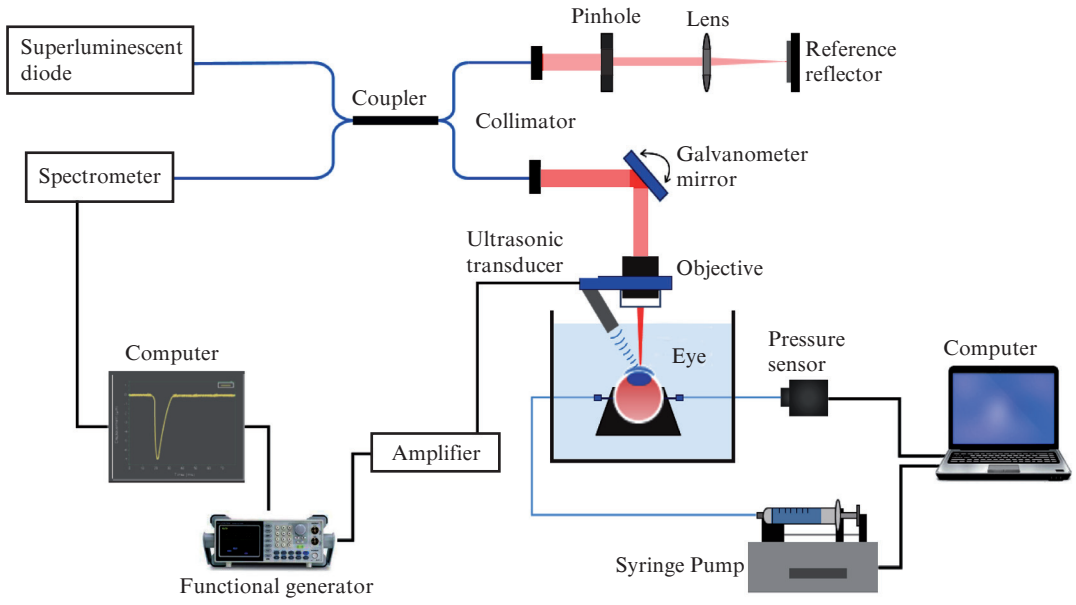

Figure 1. General schematic of the experimental setup.

$$d(t) = \frac{\lambda_0}{4\pi}\varphi(t), \quad (1)$$

where λ_0 is the centre wavelength of the radiation source; in our case, it was equal to 840 nm. An example of the displacements of the lens surface for IOP of 10 mm Hg obtained using Eqn (1) at various distances from the source is presented in Fig. 2.

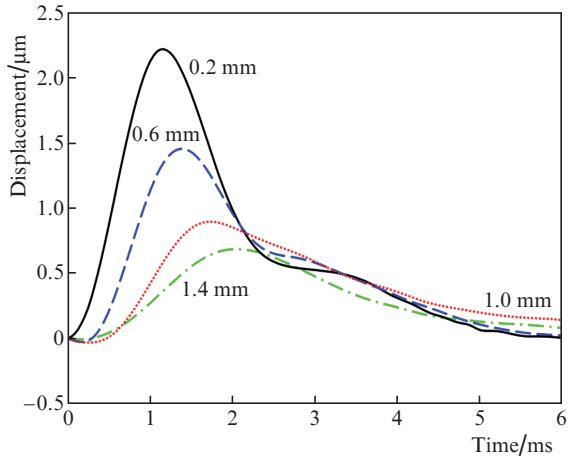

Figure 2. Time dependence of the displacement of the lens surface for IOP of 10 mm Hg, measured at different distances from the source of the perturbation.

After measuring the time dependences of the displacements at each point, the time delay of the elastic wave was calculated using the procedure of maximising the cross-correlation function of displacements between the initial point and the measurement point [49]. Then, on a segment of wave propagation, the time delay versus the distance to the source was approximated by a linear function, and the group wave velocity was calculated as the reciprocal of the slope of the appropriate straight line. This approach is described in more detail in Refs [40, 46, 49]. Allowing for the fact that the thickness of the lens is considerable as compared to the wavelength, the elastic wave in the lens can be considered as a Rayleigh surface wave. The obtained group velocity values were converted to Young's modulus values using the well-known relation for the Rayleigh wave velocity c in an incompressible medium [53]:

$$c \approx 0.955 c_t, \quad (2)$$

where $c_t = \sqrt{\mu/\rho}$ is the shear wave velocity in an infinite medium; ρ is the density of the medium, which we assumed to be 1100 kg m^{-3} for the lens [54]; and μ is the shear elastic modulus related to Young's modulus E of an incompressible medium as $\mu = 3E$ [53].

3. Results and discussion

Figure 2 shows the characteristic displacement of the lens surface with IOP of 10 mm Hg during the propagation of the surface wave. In this particular case, the wave propagation velocity was estimated as 1.7 m s^{-1}.

The results of measuring the velocity of the elastic wave on the surface of the lens for different IOP are shown in Fig. 3. It is seen that the wave velocity increases with increasing pressure, which corresponds to an increase in the rigidity of the lens under the action of growing pressure. In this case, an increase in pressure most strongly affects the wave velocity at low pressures. In the physiologically significant pressure range of 15–30 mm Hg, the velocity variation is small. Figure 4 shows the results of calculating Young's modulus of the lens based on Eqn (2). These values of Young's modulus agree with our previous results [19, 47] obtained using other methods.

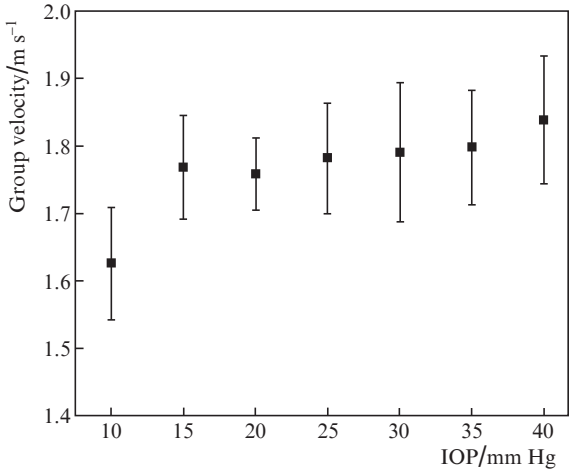

Figure 3. Elastic wave velocity on the eye lens surface versus IOP averaged over three samples. The error corresponds to one standard deviation.

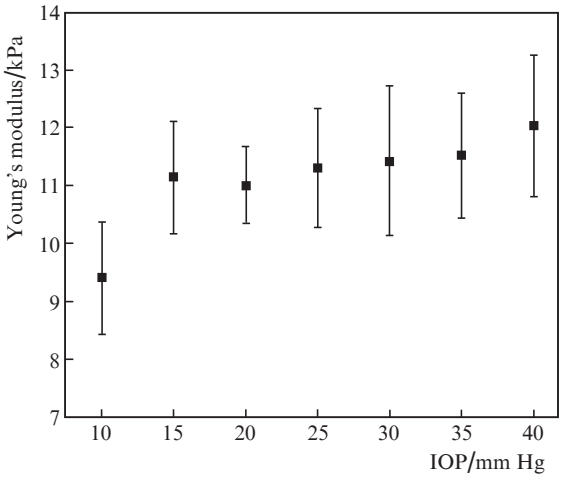

Figure 4. Dependence of Young's modulus of the lens on IOP, averaged over three samples. Young's modulus was calculated from the velocity of surface waves using Eqn (2). The error corresponds to one standard deviation.

It is important to note that, compared with other soft tissues of the eye, the modulus of elasticity of the lens weakly depends on IOP, increasing in the measured range by no more than 30%. At the same time, it is known that, e.g., the propagation velocity of an elastic wave in the cornea and in the sclera increases in this range by three to four times

[7, 9, 11, 50]. This is due to significant deformations of the cornea and sclera with increasing pressure and the manifestation of their nonlinear elastic properties. We assume that the weak dependence of the wave velocity on pressure is due to the small degree of deformation of the lens inside the eyeball during an increase in the IOP compared with the deformation of the cornea or sclera. The location of the lens inside the eyeball means that it is mainly affected by hydrostatic pressure, i.e., volume compression, so that shear deformations inside the lens are minimal and do not lead to a noticeable manifestation of its nonlinear elastic properties. In the future, we plan to conduct measurements of the elasticity of the lens depending on the duration of pressure action, in order to investigate the possible influence of fluid exchange between the lens and intraocular fluid on the mechanical properties of the lens.

The data obtained are consistent with our previous results on the measurement of the velocity of elastic waves in the cornea and in the lens of an *ex vivo* bovine eye using an ultrasonic sensor [50]. We have demonstrated that in the IOP range of 5–50 mm Hg, the velocity of propagation of an elastic wave in the cornea increases from 1 to 7 m s^{-1}, whereas in the lens it varies in the range of 1.5–2 m s^{-1} [50]. Due to the use of a low-frequency ultrasonic sensor, the data obtained had a low signal-to-noise ratio, so that their high noise levels did not allow an unequivocal conclusion about the trend in the wave velocity in the lens. In this work, the use of OCT instead of ultrasound made it possible to track the growth rate of the elastic wave in the lens and at the same time confirm the main conclusion about the weak dependence of the velocity on the IOP.

4. Conclusions

This paper demonstrates the high potential of using optical coherence elastography to measure the elastic properties of the eye lens. The results of measurements on the lens of the porcine eye *ex vivo* show an increase in the rigidity of the lens with an increase in IOP of ∼30%, but this growth is not as pronounced as the increase in rigidity in other eye tissues, such as the cornea and sclera. The developed method of optical coherent elastography can be applied in the clinical practice to monitor changes in the rigidity of the lens during corrective procedures.

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