Chapter

Biomechanics of Eye Globe and Methods of Its Study

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Abstract

Knowledge of biomechanical properties of eye globe is necessary both for correct selection of candidates for refractive surgery and right choice of operative intervention parameters. No less important, it is for corneal ectatic disease diagnostics and monitoring. Also it gives inestimable contribution for interpretation of intraocular pressure (IOP) indices especially in cases with irregular eye shape or after past corneal surgical procedures. Moreover, it allows studying injury mechanism by glaucoma process on optic nerve head fibers. Above it, scleral biomechanical properties research is necessary for the investigation of pathophysiologic factors of myopia manifestation and progression. This chapter is devoted to review of existed to date methods of study of eye fibrous tunic biomechanical properties. It describes mathematical, experimental, and clinical models provided evaluation of unsearchable by direct measurement parameters. It also observes effective technics of impact on both sclera and cornea with the aim of correction of its biomechanical condition.

Keywords: corneal biomechanics, refractive surgery, LASIK, keratokonus, IOP

1. Introduction

The cornea and the sclera are two conjugated quasi-spherical segments with unequal curvature radii; together they form corneoscleral (fibrous) tunic—the supporting structure of the eye capsule. Their mechanical properties play a crucial role of holding together the inner ocular structures. Despite them both being composed of connective tissue, they differ in physical (particularly, optical) and biomechanical properties [1].

The cornea is the anterior part of the fibrous tunic of the eyeball, and it takes up 1/6 of its length. Despite it being relatively thin, its main function is protection—assured by its high durability. But the cornea also participates in light ray refraction, making up an important part of the visual apparatus; as such, it is characterized by high optical homogeneity and complete transparence.

The cornea is an anisotropic, inhomogeneous structure; it mainly consists of highly specific connective tissue formed by parallel collagen fibrils that extend from one limb to another and act as load supporting elements [2].

The sclera takes up the other 5/6 of the eye length and represents the posterior part of the fibrous tunic of the eyeball. Scleral tunic is the main supporting structure of the eyeball; it consists of dense collagen fibers. In contrast to cornea, the sclera has high dispersive power due to its chaotically distributed fibrils and fibers, which prevents light from entering the eye cavity from the side. In natural conditions, in the living eye, scleral elements are constantly in a strain-stress state determined by intraocular pressure and mechanical properties of the scleral tissue, as well as by anisotropy and inhomogeneity of these properties [3].

Studying the biomechanical properties of the cornea is relevant for certain clinical needs associated with the appearance of new biomechanics examination methods, as well as the need to diagnose and monitor ectatic diseases of the cornea, to adequately select the parameters for keratorefractive surgeries, to correctly interpret the intraocular pressure (IOP) values, and, consequently, to appropriately assess IOP and monitor glaucomatous process.

In addition, conducting studies on the biomechanical properties of the sclera is a necessary step in the research of pathogenic factors relevant for occurrence and progression of myopia, as well as finding effective means and methods of influencing the sclera in order to correct its biomechanical state.

However, the lack of standardized terminology and uniform classification hurts the ability to compare research results and consequently hinders their introduction into the knowledge area of ophthalmology.

2. Classification of approaches to study the biomechanics of the eye

In accordance with different approaches, eye biomechanics can be divided into the following types:

1. theoretical;
2. physical (i.e., experimental); and
3. clinical.

2.1 Theoretical biomechanics of the eye

Theoretical biomechanics is a science that employs mathematical methodology and mathematical analysis. As applied to ophthalmology, it handles with specific physical constants characterizing elasticity, strength, and other mechanical parameters of the tissues (usually measured *in vitro*).

The main theoretical approach is mathematical modeling. The research may target separate structures of the eyeball and the tunic, or the eye in its entirety. It can also include modeling of physiological or pathological processes, changes induced by specific stimuli or effects of surgical treatment.

The results obtained from modeling can be used in experimental and clinical studies. In turn, all models are based on the figures acquired in experiments or from clinical diagnostic.

Disadvantages of the theoretical approach in studying eye biomechanics are associated with structural complexity of the eyeball, inhomogeneity, and variability of morphology of the ocular structures, and dependence on the technological advancement of experimental and clinical research methods.

2.2 Physical (experimental) biomechanics of the eye

Experimental biomechanics of the eye is based on studying individual tissues and the eyeball as a whole *in vitro* or by conducting animal experiments using physical methods. It is the most developed subdiscipline of biomechanics with many years of research history. Capabilities of the approach are limited by post-mortem changes in eye tissues, and anatomical and physiological differences between humans and animals. The main purpose of experimental studies is to find potentially useful methods of studying biomechanical properties of eye tissues in clinical environment and to acquire data for mathematical modeling. The main advantages of experimental researches are the absence of restrictions for employed methods and approaches, and the choice of which is only limited by technological and scientific advancement.

Methods of experimental biomechanics allow measurement of a big number of physical parameters of the cornea:

- Young's modulus (E),
- Poisson's ratio (μ),
- Durability (σ),
- Deformation capacity (Σ), etc.

However, they do not fully reflect the properties of fibrous tunic of the eye *in vivo*.

2.3 Clinical biomechanics of the eye

Clinical biomechanics of the eye studies the influence of biomechanical properties of the fibrous tunic on the results of diagnostics, development, and treatment of various eye diseases. Clinical biomechanics operates on data obtained with specialized examination methods used in ophthalmology (*in vivo*) that characterize biomechanical properties of the fibrous tunic. Its research subject is strictly the eyeball as a whole, only allowing arbitrary delineation of the internal structures. This complicates the interpretation of data. However, in order to improve diagnostics and treatment of eye diseases, clinical methods for eye biomechanics need to have higher priority in research and development.

The following corneal parameters can be measured clinically:

- Friedenwald's rigidity coefficient;
- Corneal hysteresis;
- Corneal resistance factor;
- Coefficient of elasticity;
- Corneal deformation.

The biggest number of already existed studies are dedicated to investigation of biomechanical properties of the cornea, which is probably related to the specifics of corneal structure, or to its accessibility for examination.

3. Theoretical (mathematical) biomechanics

The originator of mathematical approach to study biomechanical properties of the cornea was F.A. Rachevsky. In 1930, in his theoretical study, he pointed "...for the first time at the paramount importance of the radius of the corneal curve and especially of its thickness for specific results of intraocular pressure tonometry." Besides that, he proved mathematically that under effect of external and internal forces, tangentially directed stress occurs in the cornea, particularly during applanation tonometry [4].

At present, the research of corneal biomechanics is conducted in two main directions. Mathematical modeling is generally used for the calculation of parameters and prediction of results of keratorefractive surgeries [5–8], as well as for the determination of possible procedural errors of applanation tonometry methods when biomechanical properties changed as the result of a surgery or a disease [9].

The main obstacle for proper mathematical modeling is anisotropy of the cornea. The majority of the proposed models does not consider it, which limits their application in practical ophthalmology [10–12].

According to Pinsky et al., the anisotropy of the cornea primarily depends on its structural features, that is, specific architectural organization of collagen fibers [13]. X-ray structural analysis revealed that collagen fibrils of the central area have orthogonal orientation predominantly in vertical and horizontal directions, while fibrils of the periphery have tangential orientation [14]. Pinsky et al. developed a mathematical model for corneal anisotropy mechanics that accounts for these findings [13]. Based on the finite element method, the model allows predicting biomechanical response of the cornea to tunnel cutting, radial keratotomy, and LASIK [15–17].

In order to determine the possible error margin of applanation tonometry methods, several mathematical models have been developed [18]. Liu et al. used mathematical modeling to study isolated effects of various biometric and biomechanical parameters of the cornea on Goldmann tonometry readings [19]. Kwon et al. developed a mathematical model demonstrating the need to take into account not only corneal thickness, but also its biomechanical properties when interpreting Goldmann tonometry readings [20].

4. Physical (experimental) biomechanics

4.1 Normal (intact) cornea

Experimental studies based on extensiometry revealed distinguishing biomechanical anisotropy and heterogeneity of the cornea. Corneal material acquired with a radial cut has the best durability and margin of deformation capacity. Those parameters decrease with distance from the radial direction. Corneal material stretched tangentially shows approximately the same elastic properties along the corneal disc. The samples stretched radially appeared to have the highest rigidity. In the course of the study, Poisson's ratio was determined for various parts of the cornea. This ratio characterizes the transverse deformation lateral to stretch direction, for radial direction, it was in the range of 0.445–0.450, and for tangential direction, it was in the range from 0.290 to 0.310 (middle periphery) and from 0.340 to 0.350 (perilimbal) [21, 22].

A variety of studies is dedicated to measuring the main elastic and strength properties of the cornea, but analysis of the data shows that isolated corneas exhibit big spread in the values—from 0.3 to 13.6 MPa. The phenomenon can be attributed to different experimental conditions and nonlinear nature of biomechanical properties of corneal material [23–26]. Andreassen et al. studied the biomechanics of corneal discs with extensiometry; the discs were taken from patients with keratoconus after they underwent penetrating keratoplasty. The study revealed significant decrease of mechanical strength properties in pathologically altered corneas [27].

Soergel et al. used dynamic mechanical spectroscopy to evaluate viscoelastic properties of the cornea in experimental environment. They found that elastic and shearing deformation depend on the hydration, time elapsed after death, and temperature of the tissue [28].

Wang et al. calculated Young's modulus by measuring the speed of ultrasound transmission through cadaver cornea and processing the data with Fourier analysis [29].

Like ultrasound spectroscopy, Brillouin microscopy can determine intrinsic viscoelastic properties decoupled from the structural information and applied pressure. In contrast, it can measure the local acoustic properties with much higher spatial resolution and sensitivity, and the measurement is performed optically without the need for acoustic transducers or physical contact with the cornea [30].

One of the techniques, holographic interferometry, is used to calculate Young's modulus. The method is to some degree similar to videokeratography, that is, holographic technologies are used to examine the changes in corneal surface. A study conducted on an intact bull's cornea showed Young's modulus being two orders lower than when measured in an experiment with corneal tissue samples. The authors summarized that localization and hydration level plays the primary roles during measurement. This method, however, is limited in terms of practical use due to requiring maximum permissible laser emission in order for the resulting images to be high quality [31].

4.2 Cornea after refractive surgery

Some studies showed significant increase of tangential elasticity of the cornea after it was incised with radial cuts (up to 46.5% with an incision depth of 0.6 mm), that is, in the direction of the lesser material rigidity [32]. In certain cases, the changes led to severe complications in the long-term postoperative period. Particularly, it manifested as a significant decrease of eyeball's resistance to trauma with potential disruption of corneal cicatrices and loss of membranes [33].

Luminescent polariscopy revealed that after radial keratotomy, the main mechanical strain fell on the middle periphery of the cornea, particularly on the bottom of keratotomic incisions. An increase of intracameral pressure (analogue to intraocular pressure) raises the strain on peripheral part of the cornea and off-loads its central part, which can cause hypermetropic shift in refraction [34].

However, with the appearance and widespread implementation of excimer laser technologies for correction of refraction errors, such risks have greatly decreased. It can be attributed to different mechanisms of corneal refraction change, that is, its thinning in the central area.

Experimental studies on biomechanical properties of the cornea after excimer laser intervention indicate that thinning of the cornea in 6.0-mm optic zone for more than 15–20% results in significant changes of its mechanical properties. In terms of clinical relevance, the most meaningful change appears to be the significant (mean 20%) decrease of breaking load for experimental samples in comparison to the control samples. Additionally, changes in deformation properties of the cornea after laser ablation should also be taken into consideration, which manifested as lowered amount of movement the punch had to do before the cornea broke in experimental eyes in comparison to the control subjects in average by 10.72% [35].

However, the mechanical properties of the data obtained using an isolated cornea cannot objectively reflect the parameters of the tissues in natural environment. Adequate information on the biomechanical state of the cornea can only be obtained from a living eye.

5. Clinical biomechanics

5.1 Normal (intact) cornea

Clinical studies on the biomechanical properties of the relatively healthy cornea have been conducted since the middle of the twentieth century, but those methods remained widely unused due to various reasons.

In 1937, Friedenwald suggested that rigidity coefficient could be calculated based on a logarithmic dependence between IOP changes and eye volume employing differential tonometry with Schiotz tonometer [36]. Friedenwald depicted the relation between pressure and volume in a coordinate system. As was shown by further clinical studies, the proposed coefficient strongly depends on the corneal curvature and thickness, as well as on the IOP level [37]. According to research results, the parameter suggested by Friedenwald—the rigidity coefficient—was inaccurate in eyes with deviations in biomechanics (thickness and curvature) from the norm. It was also strongly influenced by IOP.

In 1936, S. F. Kalfa proposed a method of elastotonometry, that is, differential tonometry with four Maklakov tonometers weighing 5, 7.5, 10, and 15 g. Connecting the dots marked on a coordinate system forms an elastotonometric curve, which appears ascending line. The difference in mm Hg between the starting and ending points of the curve, that is, between IOP value obtained using 5.0 and 15.0 g tonometers, is called elasto-ascent. Essentially, Friedenwald's rigidity coefficient and S. F. Kalfa's elasto-ascent are different expressions of the same thing. In norm, the two figures are closely related, albeit not functionally [38].

There are a number of techniques described by their authors as potential intravital methods for examination of biomechanical properties of the cornea, but they have not been adopted into clinical practice: electronic speckle interferometry [39], dynamic cornea visualization [40], corneal applanation and indentation [41], ultrasound elastometry [42], and photoelasticity method [43].

As an alternative to holographic interferometry, a noncontact, nondisruptive method of electronic speckle interferometry was suggested; it is equally sensitive because it employs close wavelength for measurement. Advantages of the method include the absence of requirement of photographic hologram recording, which simplifies the procedure and enables real-time acquisition of corneal surface shift data using a television camera. The method is recommended for evaluation of changes in corneal biomechanics after excimer laser refractive surgery [39].

Grabner et al. proposed a method of dynamic visualization of the cornea. It involves applying dosed pressure to the central area of the cornea during videokeratography by means of a special indenter and subsequent analysis of the topographic pattern. As the result, high correlation between the bending curve and depression depth was found. The form of the curve was noted to be affected by central corneal thickness, intraocular pressure, and patient age. Moreover, bending curves were different in keratoconus patients, as well as in patients who had underwent keratorefractive surgeries [40].

Chang et al. studied biomechanical properties of the cornea *in vivo* using corneal applanation and indentation on rabbit and human eyes, regarding the cornea as a transversely isotropic material. The study showed normal Young's modulus to vary from 1 to 5 MPa and transverse shift modulus from 10 to 30 KPa [41].

Some authors used photoelasticity method to evaluate mechanical stress in the cornea involving the measurement of its polarization and optical properties [43].

Scoping a large amount of clinical data, Edmund calculated Young's modulus adhering to the hypothesis that the final form of cornea is the outcome of counteraction between tissue elasticity and intraocular pressure. The modulus values were significantly lower in keratoconus eyes when compared to norm. The study also showed significant difference between healthy and ectatic patients in relative distribution of stress in the central and peripheral areas of the cornea, which can help with the understanding of keratoconus pathogenesis. However, this method generally does not find much use in clinical practice [44].

The one method most widely used in present day clinical practice involves ocular response analyzer (ORA)—a device that analyses corneal biomechanical properties based on bi-directional corneal applanation by an air pulse [45]. The method's authors proposed to evaluate biomechanical response of the cornea by quantifying the differential inward and outward corneal response to an air pulse and thus obtaining two parameters—corneal hysteresis (CH) and corneal resistance factor (CRF). Corneal hysteresis characterizes the viscoelastic properties of the cornea responsible for the partial absorption of the air pulse energy. Corneal resistance factor is a derived parameter with high correlation to central corneal thickness that reflects the elastic properties of the cornea.

Multiple studies have confirmed the usefulness of bi-directional corneal applanation for the evaluation of biomechanical properties of the cornea: they rise with the increase of the corneal thickness [46, 47]. Corneal hysteresis was in the average 10.8 ± 1.5 mm Hg and corneal resistance factor—11.0 ± 1.6 mm Hg. Statistically, a significant difference in the mean values of CH and CRF between groups of varying age was absent, with the exception of patients older than 60 years for whom the values were on lower. It is possible that the phenomenon reflects the changes in elastic properties of the cornea associated with age, but the authors also note the potential influence of other parameters (intraocular pressure and anterior-posterior axis length) that were disregarded in the study [48]. The comparison of CH and CRF in children and adults did not reveal any age-related differences [49].

Studying the diurnal variations in CH and CRF parameters revealed their hourly stability, while minor changes observed between the morning and evening measurements can be explained by diurnal IOP fluctuations [50]. CH and CRF correlated strongly with corneal thickness and to a lesser degree with an amount of astigmatism. No correlation was found with keratometry, age, gender, spherical equivalent, or IOPcc [51]. Moreover, ORA shows good repeatability of biomechanical and tonometry measurements [52].

Avetisov et al. studied the possibility of applying the dynamic pneumo-impression of the cornea approach to the existing corneal biomechanical properties analyzer (ORA). The fundamental principle was that at the curvature start point laying on the border of the impression area, the pneumatic jet is subject to the counter-force of IOP and corneal elasticity, in equal amounts. At the moment of maximum impression, the pneumatic jet is mainly countered by corneal elasticity—due to the maximum deformation of the cornea. As the result, a parameter named elasticity coefficient was calculated characterizing the elastic behavior of the cornea regardless of the IOP level [53].

The same principle was used in CorVis device (Oculus, Germany), in which corneal deformation responding to a pulse of air is monitored with high-speed Scheimpflug camera. The device can help to measure a whole range of parameters that characterize the particularities of corneal deformation during the impression process. It records the process between the initial and the second applanations involving the cornea recovering its initial form, captures the maximum indentation point, and measures IOP [54, 55].

5.2 Keratoconic cornea

Intravital measurement of biomechanical properties of the cornea in keratoconus patients performed with dynamic bi-directional pneumo-applanation showed lower CH and CRF values than in healthy eyes. Apparent negative correlation between the CH and CRF parameters and the degree of keratoconus were also evident [56].

Additionally, CH was significantly higher than CRF in the keratoconus group. The authors suggested the CH decrease of less than 8 mm Hg in conjunction with positive CH-CRF difference to be considered a stronger sign of keratoconus than isolated decrease of CH. Glaucoma patients showed reverse tendency: CRF value was higher than CH [57].

Studying the parameters obtained with dynamic Scheimpflug analysis (Covis ST) showed the possibilities of the examination method for differential diagnostics of patients suspected of keratoconus or with early keratoconus from patients with normal cornea [58].

5.3 Cornea after refractive surgery

Intravital measurements of biomechanical properties of the cornea after excimer laser surgery performed using dynamic bi-directional pneumo-applanation also confirmed the loss of corneal strength. In patients who had underwent LASIK, examination showed decrease of IOP-related parameters such as corneal compensated IOP, as well as parameters reflecting the biomechanical properties. Along with that, significant correlation was observed between the amount of myopia correction and the deterioration of the biomechanical properties [59].

Another study analyzed the results of dynamic bi-directional pneumo-applanation of the cornea and assessed the correlation between CH decrease and ablation depth in three patient groups: after photorefractive keratectomy, after LASIK with mechanical corneal flap creation, and after LASIK with femtosecond flap creation. The authors found that the strongest correlation was present in femto-LASIK group, while in the two other groups, it was significantly lower [60].

Isolated creation of corneal flap was also found to cause minor changes in corneal refraction [61]. Roberts explained the phenomenon with a theory stating that after lamellar dissection, the corneal biomechanics change in such a way so that severed fibrils contract causing traction in the direction of limbus. With that, central corneal area deflates under the action of released fibrils inducing the so-called "hypermetropic" shift [62, 63].

In parallel, a comparison of changes in biomechanical properties of the cornea after superficial and intrastromal keratectomy was done using OCULUS Corvis (Germany) tonometer. Both types of keratectomy were found to cause statistically significant decrease of biomechanical parameters [64].

Despite the existing methods of measuring biomechanical properties of the cornea and the developed biomechanical models, the detection of ectasia after excimer laser vision correction varies from 0.04 to 0.6% of cases, but according to some researchers, the numbers may be an underestimation [65, 66].

Iatrogenic keratectasia is known to develop due to two factors: an ectatic corneal disease that was undiagnosed in the preoperative stage and excessive thinning of the cornea [67]. In the first case, early detection of keratoconus poses objective challenges [68, 69].

At the same time, even when keratoconus was timely diagnosed, the selection of candidates for keratorefractive surgeries is still difficult, and the evaluation of corneal biomechanics by means of dynamic bi-directional pneumo-applanation does not yield the necessary data.

6. Correction of corneal biomechanical properties

Presently, the most common method of correcting (strengthening) biomechanical properties of the cornea is corneal cross-linking [70].

The first specialists who in the 90s of the twentieth century created corneal cross-linking method for treating keratoconus were Wollensak, Spoerl, and Seiler [71]. They developed the protocol ("Dresden protocol") for using this method of strengthening the cross-link bonds of collagen for treating progressive keratoconus involving riboflavin and ultraviolet A irradiation of the corneal stroma (UVA with a wavelength of 370 nm for peak absorption of riboflavin) [72].

Careful preclinical experimental validation showed that the combination of riboflavin and UVA leads to a significant improvement of biomechanical stability of the cornea (increase of elastic modulus approximately by 300%) and the formation of large collagen molecular aggregates, including the appearance of cross links—predominantly between the fibril surface molecules and also between proteoglycans in the interfibrillar space [73–75].

In the following decades, the corneal cross-linking technique has seen widespread clinical application with indications for its usage expanding significantly. Effectiveness of the method for strengthening biomechanical properties was confirmed for the treatment of not only progressive keratoconus, but also pellucid marginal degeneration and iatrogenic ectasia caused by excimer laser surgery [76].

An important suggestion has been made recently for reinforcing the effect of corneal cross-linking—to combine the procedure with implantation of corneal segments [77, 78]. Comparative studies of different treatments—individually and in combination—showed the most pronounced effect to be from the combination therapy starting with the implantation of corneal segments and followed by cross-linking, and not in the reverse order. Such combination therapy also helps to achieve better results (weakening of manifest refraction and keratometric indicators) in cases with keratectasia after excimer laser surgery [79].

There is another method described in the literature as directed laser ablation; it involves biomechanical approach to ablation calculations. Vaporization of the tissue thus happens on the middle periphery, which contains certain relatively flat spots, and not in the central (thin) area. The rationale is that thinning of the area leads to steepening of the cornea subsequently flattening the unablated area, which has more optical power [80]. It should be noted that in clinical practice, this method requires very careful consideration and cautiousness due to insufficient studies on its after effects.

Furthermore, a multimodal approach involving implantation of intrastromal rings, CXL, and laser ablation in different configurations may provide not only stability of corneal topography, but also positive refraction result, thanks to the combination of all the methods' advantages [81–85]. That said, the lack of established standards and clinical recommendations for combining different methods for the correction of corneal biomechanical properties may lead to various complications and unexpected aftermaths; it should be kept in mind when planning such treatment.

7. Conclusion

In summary, clinical relevance of studying biomechanics of the fibrous tunic is difficult to overestimate. The diversity of methods used for examination of biomechanical properties of the cornea means there is no single method that could fully satisfy the needs of practical ophthalmology. Further studies are necessary to develop simple, available, and sufficiently informative method for clinical assessment of ocular biomechanics. Moreover, the demand for techniques of correcting biomechanical properties keeps growing, and so this field of research has wide potential.

Conflict of interest

The author has no conflict of interest.

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