Discussion on the Corneal Biomechanical Properties and Clinical Measurement Methods

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Abstract. This study focuses on exploring the influence of corneal biomechanical parameters on clinical treatment outcomes. While current research has simplified corneal structural modeling to enhance treatment effects, there is often a tendency to overlook the specific impact of corneal structure on treatment efficacy. The primary objective of this research is to underscore the importance of strengthening the study of corneal biomechanical parameters, particularly the intricate relationship between corneal structure and biomechanical properties, in order to provide more precise guidance for personalized treatment strategies. Beginning with an analysis of corneal biomechanical parameters and specific physical models of the cornea, this paper delves into the measurement methods of representative clinical biomechanical characteristics, such as tensile stress-strain tests, enzymatic digestion, intraocular pressure (IOP) measurements, and Optical Coherence Elastography (OCE). This study holds significant implications for enhancing corneal treatment outcomes and delivering improved eye health services. By advancing our understanding of corneal biomechanics, we can further optimize treatment approaches and contribute to the advancement of personalized ophthalmic care, ultimately benefiting patients and promoting overall eye health.

Keywords: Cornea, Biomechanical properties, Clinical treatment

1 Introduction

In the field of ophthalmology, the cornea, as the transparent structure at the front of the eye, plays a crucial role not only in visual function but also in its biomechanical properties. The biomechanical properties of the cornea, including elasticity, stiffness, and deformability, are essential for maintaining the stability, resistance to pressure, and structural integrity of the eyeball. Additionally, clinical measurements of the cornea's biomechanical properties are of significant importance. Ensuring accurate measurements of the cornea's biomechanical properties not only helps in identifying early risk factors for eye diseases but also guides the development of personalized treatment plans, thereby improving treatment outcomes and prognosis. Therefore, this study aims to explore the biomechanical properties of the cornea and its measurement methods, and to discuss how these properties can be utilized to enhance the diagnosis, treatment, and postoperative recovery processes of ocular diseases.

Corneal biomechanical properties are of great importance, as highlighted by David

Y. Yue (ed.), *Proceedings of the 2024 International Conference on Mechanics, Electronics Engineering and Automation (ICMEEA 2024)*, Advances in Engineering Research 240,
https://doi.org/10.2991/978-94-6463-518-8_35

P Piñero et al., who emphasized the significant clinical implications of these biomechanical parameters, particularly in the fields of glaucoma and corneal reshaping [1]. Most scholars mainly describe the biomechanical properties of the cornea using viscoelasticity, with Sabine Kling and other scholars providing detailed insights into corneal viscoelasticity [2]. Furthermore, numerous scholars have modeled the biomechanical properties of the cornea, with the most common and basic models being the Kelvin-Voigt model and Maxwell model, as mentioned by Mitchell A. Kirby and colleagues in their detailed modeling of the cornea [3]. These models can provide a preliminary description of the cornea's biomechanical properties, albeit in a somewhat rudimentary manner. Additionally, the measurement of corneal biomechanical properties has received widespread attention from scholars. There are numerous methods for measuring the biomechanical properties of the cornea, each with its own advantages and disadvantages. For instance, the tensile stress-strain test yields good measurement results but may potentially damage the cornea [4], while the mechanism of action of Enzymatic digestion remains unclear [5]. Optical Coherence Elastography (OCE) has shown promising potential in clinical medicine [3].

This study aims to delve into the biomechanical properties of the cornea and its measurement methods, and to explore how these properties can be utilized to enhance the diagnosis and treatment of ocular diseases. Subsequent sections will focus on the measurement methods of corneal biomechanical properties, their association with ocular diseases, and their application in clinical practice. Through an in-depth exploration in this study, we hope to provide new insights and inspirations for the application of corneal biomechanical properties in the field of ophthalmology.

2 Corneal Biomechanics Property

When discussing the biomechanical properties of the cornea, viscoelasticity is a key aspect. Elasticity describes the cornea's ability to deform and recover after being subjected to stress, determined by its collagen microstructure's stretching properties. Viscosity, on the other hand, reveals the cornea's dynamic response to sustained stress, including the diffusion of water molecules in the matrix and the electrostatic interactions between GAGs and collagen [2]. By considering both elasticity and viscosity, viscoelastic properties can succinctly and effectively describe the characteristics of the cornea, providing important clues for a better understanding and research of the cornea's biomechanical behavior.

2.1 Elastic Properties

The elasticity properties primarily describe an object's ability to deform reversibly when subjected to compressive and tensile forces during a static process and return to its original shape once the forces are removed. When an external force is applied to an object, the object will deform, but once the external force is removed, the object will return to its original state, and this ability to recover is known as elasticity. Elasticity is an inherent property of an object, and it is described by the elastic modulus to quantify the degree of deformation of the object under stress. Different materials have different elastic moduli, which determine their deformation and recovery capabilities under stress.

When describing the elastic properties of the cornea, we can consider it as an elastic body that follows a linear relationship between stress and strain. The equation for this relationship is given by:

$$E = \frac{\sigma}{\varepsilon} \tag{1}$$

where E represents the Young's modulus, a physical quantity used to describe the stiffness or rigidity of a material, σ denotes the stress applied to the elastic body, and ε represents the strain experienced by the elastic body. The Young's modulus can effectively reflect the elastic properties of the cornea, making the measurement of the corneal Young's modulus extremely important.

When describing the elastic properties of the cornea, it is crucial to consider its distribution in three-dimensional space. Introducing Lamé coefficients can more accurately describe the relationship between stress and strain in three-dimensional space, taking into account the shear effects in the model to accurately determine the distribution of stress and strain in three-dimensional space [6]. However, for soft tissues like the cornea, although they are not completely incompressible, the shear modulus is typically small and can be ignored. Additionally, compared to other factors, static hydrostatic pressure has a greater impact on the cornea. Therefore, simplifying the analysis to a one-dimensional force situation can yield a linear relationship between stress and strain, which is a very reasonable explanation [3].

2.2 Viscoelastic Properties

Viscoelastic properties primarily reflect the energy loss in materials due to the friction and adhesion between internal molecules or structures when subjected to external stress. Typically, viscoelastic deformation is completely reversible over time. In viscous properties, materials exhibit a time-dependent strain rate, characterized by sustained deformation and energy loss under stress. This energy loss manifests as dissipative energy during loading and unloading processes, often released in the form of heat.

When it comes to viscoelastic properties, we often utilize the complex dynamic modulus to describe the relationship between stress and strain in viscoelastic materials under continuous loading conditions [2]. The modulus of the complex dynamic modulus is also known as the dynamic modulus and can be expressed by the following relationship.

$$\widetilde{E} = E_1 + iE_2 \tag{2}$$

$$E_1 = \frac{\sigma}{\varepsilon} * \cos\delta \tag{3}$$

$$E_2 = \frac{\sigma}{\varepsilon} * \sin\delta \tag{4}$$

Where E1 represents the storage (elastic) modulus, E2 represents the loss (viscous) modulus, and δ defines the phase of the material response at a specific mechanical frequency.

Based on the above equations, we observe that a resonance phenomenon occurs when we apply a frequency that causes the storage and viscous components to load in-phase, and this frequency is known as the natural frequency. In the case of simple geometric constraints, there is a straightforward relationship between the resonant frequency and Young's modulus. By further deriving the natural frequency equation in such scenarios, we can obtain the damped natural frequency, which can be used to derive biomechanical properties such as Young's modulus of the cornea [3].

However, obtaining the precise natural frequency is closely related to the geometry of the material, as energy propagation will reflect multiple times on the material's geometric surface. Additionally, due to the time-dependent nature of viscoelastic properties, we need to measure the values of E1 and E2 multiple times at different strain rates, which severely limits the feasibility of using this method to measure the biomechanical properties of the cornea in clinical applications.

2.3 Simulation Models

In order to obtain more accurate biomechanical properties and gain a deeper understanding of the complex behavior of corneal tissue, we chose to utilize theoretical frameworks such as the Kelvin-Voigt and Maxwell models for computational simulation. These models are capable of effectively describing the nonlinear, viscoelastic, and anisotropic characteristics of corneal tissue, thereby assisting us in comprehensively understanding the response and behavior of the cornea under different stress conditions.

Kelvin-Voigt Model. The Kelvin-Voigt model is widely used in the study of soft tissues and polymers, typically to describe materials that exhibit both elastic deformation and a certain degree of viscous behavior when subjected to stress. The application of this model is of significant importance for investigating the viscoelastic properties of the cornea.

The classical Kelvin-Voigt model (CKVM) consists of parallel-connected spring and damper, as shown in Fig. 1. In this case, the spring and damper are connected in parallel, so their strains are the same, the strains of the spring and damper are equal. This is because they are connected in parallel, so they undergo the same strain under the same deformation. The total stress is equal to the sum of the stresses of the spring and damper [4]. The properties of the model can be described by the following equation:

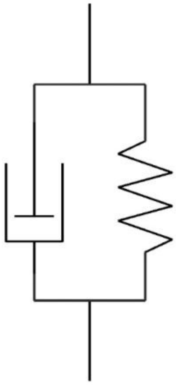

Fig. 1. Simplified diagram of Kelvin-Voigt Model [4]

$$\sigma_{total} = \sigma_{spring} + \sigma_{damper} \tag{5}$$

$$\varepsilon_{total} = \varepsilon_{spring} = \varepsilon_{damper} \tag{6}$$

This model has been found to be particularly effective in studying the behavior of certain tissues within specific frequency ranges. Its ability to accurately capture the viscoelastic response of materials under varying loading conditions makes it a valuable tool for exploring the mechanical properties of soft tissues and polymers. Additionally, the Kelvin-Voigt model has been instrumental in understanding the dynamic behavior of biological tissues, providing insights into their viscoelastic properties at different frequencies and loading rates.

Maxwell Model. The Maxwell model describes the material as a Newtonian fluid [7], The Maxwell model is a classical material mechanics model consisting of a series connection of Hooke springs and Newton dampers, as shown in Fig. 2. It is used to describe the viscoelastic behavior of materials. The strain and stress response of materials under loading. By simulating the interaction between the spring and damper, the Maxwell model can help us understand the mechanical properties and response characteristics of materials.

In the Maxwell Model, the stress applied to the spring and damper is the same, and the total strain is equal to the sum of the strains of the spring and damper, which can be described by the following equation:

$$\sigma_{total} = \sigma_{spring} = \sigma_{damper} \tag{7}$$

$$\varepsilon_{total} = \varepsilon_{spring} + \varepsilon_{damper} \tag{8}$$

Fig. 2. Simplified diagram of Maxwell model [3]

In the Maxwell model, the phase velocity and attenuation are very different from what is predicted by the Kelvin-Voigt model. Some tissues can be well described by the Maxwell model within a limited frequency range, but neither the Kelvin-Voigt nor the Maxwell model can accurately describe the viscoelasticity of tissues [3]. More complex models are required to adequately describe a wider range of tissues. In practical theoretical studies, it is challenging to provide a universal theoretical formula that can encompass the viscoelastic response of all tissues. To accurately consider viscosity, an appropriate viscoelastic model must be selected in computational simulations to cover the wave propagation range of experimental frequencies. Additionally, it is crucial to incorporate geometric and material dispersion dependencies in these simulations. Therefore, future research efforts should focus on developing more precise models to better explain the viscoelastic properties of different tissues, thereby advancing the understanding and application of tissue properties in the field of medicine.

3 Methods and Limitations of Corneal Biomechanical Measure

When measuring the biomechanical properties of the cornea, understanding its significance in clinical practice is crucial. These measurements can assist ophthalmologists in evaluating the health status of the cornea, diagnosing eye diseases, guiding surgical decisions, and monitoring treatment outcomes. By comprehending the biomechanical properties of the cornea, doctors can tailor treatment plans more effectively, enhancing the vision and quality of life for patients. Therefore, the importance of assessing the biomechanical properties of the cornea in clinical settings is self-evident.

The tensile stress-strain test is a widely used method in the engineering field to measure the macroscopic mechanical properties of tissues within standardized settings. This method involves fixing tissue samples of predefined dimensions in a frame, applying predefined loads, and measuring the corresponding displacements. It is commonly used in experimental research, such as in studies on corneal cross-linking (CXL), to effectively measure the biomechanical properties of the cornea. For in vivo measurements, Pallikaris et al. developed a protocol where the whole eye is inflated during surgery, and the corresponding rise in intraocular pressure is measured to determine ocular rigidity. This protocol allows for the method to be well-applied in in vivo measurements [4]. However, the limitation of whole-eye measurements is the inability to differentiate between corneal deformation and scleral deformation, leading to a rough estimate of the average macroscopic corneal stiffness. Despite this limitation, the tensile stress-strain test remains a valuable tool for assessing the mechanical properties of tissues in various research settings.

Enzymatic digestion is a technique used to evaluate the biomechanical properties of tissues by exposing them to specific enzymes that degrade the extracellular matrix (ECM). Different enzymes target specific chemical bonds in the ECM, leading to varying rates of degradation. While enzymatic digestion may not directly measure the stiffness of the cornea, it can provide valuable insights into the impact of cross-linking therapy on corneal biomechanics [5]. The rate at which corneal samples are digested by enzymes can indicate the level of cross-linking in the tissue and provide an estimate of corneal stiffness. For example, enzymatic digestion techniques can be utilized to assess the effects of collagen cross-linking therapy on treatment outcomes. In a study where corneas were treated with riboflavin UVA cross-linking therapy, the results demonstrated that cross-linked corneas exhibited increased resistance when exposed to gastric, pancreatic, and collagenase enzymes compared to untreated control corneas. This suggests that enzymatic digestion evaluation can effectively assess the changes in corneal biomechanical properties and treatment outcomes resulting from collagen cross-linking therapy. However, further research is needed to elucidate the specific effects of enzymatic digestion on the biomechanical properties of the cornea.

The close correlation between intraocular pressure (IOP) measurement methods and corneal biomechanical characteristics is crucial for accurate measurement of IOP. Intraocular pressure plays a significant role in eye disease research, especially in the success of cataract surgery.

Pallikaris and other researchers found a linear relationship between IOP and anterior chamber aqueous volume, which is important for cataract surgery. However, traditional invasive methods carry the risk of eye damage and cannot be used for clinical diagnosis. The Goldmann applanation tonometry is commonly accepted as the gold standard. However, the IOP measured by traditional methods is effective only under the assumption that all subjects have the same ocular rigidity. Even with the same IOP, some subjects may have different ocular rigidity. Aberrant rigidity may lead to overestimation or underestimation of IOP by traditional tonometry. The proposed method of measuring ocular rigidity can help detect eyes that are misestimated and aid in early detection of glaucoma [7].

Several scholars such as Kohlhass and Feltgen have studied the relationship between IOP and corneal thickness and curvature using different methods. They conducted experiments using tools like GAT and pneumatic tonometry and arrived at different conclusions. Generally, the measurement of IOP is influenced by central corneal thickness, with the impact of corneal curvature being relatively minor.

Kaneko and others studied the stiffness and damping of the eye through a dynamic eye model, providing important insights for further understanding of IOP measurement [8, 9]. These research results demonstrate the exploration of the relationship between IOP and corneal biomechanical characteristics using different methods, providing valuable insights for further research in the field. However, the specific biomechanical mechanisms of IOP in relation to the cornea are still in the exploratory stage and require further investigation.

Optical Coherence Elastography (OCE) is an elastography method based on Optical Coherence Tomography (OCT) technology, which infers local mechanical properties by measuring tissue displacement and strain [10]. In recent years, with advancements in OCT technology, OCE has shown significant potential in ophthalmology. Through improved light sources and scanning methods, OCE can provide high-resolution, quantitative elastography, particularly suitable for clinical applications in the anterior segment of the eye. This method can aid in identifying tissue types related to diseases and monitoring treatment outcomes. Compared to other medical imaging systems, OCE offers higher resolution in quantifying elastic modulus, enabling precise biomechanical models to predict changes in the shape of the eye's main focusing apparatus. If successfully validated in clinical settings, OCE could become a crucial guiding tool for personalized therapeutic interventions, advancing ophthalmic clinical practice.

When discussing the potential value of Optical Coherence Elastography (OCE) in clinical practice, it is crucial to emphasize its significance in screening for corneal refractive surgery. By providing high-resolution maps of corneal elasticity, OCE enables physicians to create personalized treatment plans, enhancing surgical success rates and reducing the risk of complications [3]. Additionally, OCE plays a critical role in the diagnosis and management of eye diseases such as keratoconus and glaucoma. By measuring parameters like intraocular pressure and local modulus, OCE offers more accurate diagnostic and therapeutic guidance, leading to improved treatment outcomes for patients. Furthermore, OCE can be utilized to study the elastic properties of eye tissues such as the lens and vitreous, providing comprehensive insights into the structure and function of the eye for eye care professionals. Overall, the application of OCE in clinical settings provides ophthalmologists with more accurate and comprehensive diagnostic and treatment strategies, with the potential to enhance visual health and quality of life for patients.

4 Discussion

When discussing the impact of corneal biomechanical parameters on clinical treatment outcomes, it is essential to recognize both their advantages and limitations, and to provide corresponding recommendations to guide future research and clinical practice.

Current research has simplified and streamlined the modeling of corneal structure, providing some assistance in enhancing treatment outcomes. The application of these simplified models makes clinical treatment more manageable and practical, offering healthcare providers more intuitive treatment guidance.

Despite the positive outcomes achieved through current research methods and clinical treatments, the specific influence of corneal structure on treatment is often overlooked, particularly concerning individual patient differences. The current modeling of corneal structure still has imperfections, with most theoretical models simplifying the cornea to an ideal viscoelastic material, making it difficult to consider the impact of corneal structure on treatment. Furthermore, the collection of corneal biomechanical parameters in clinical settings is costly and technically challenging, limiting in-depth research on the cornea and impeding the development of clinical applications.

To guide future research and clinical practice, researchers should intensify their study of corneal biomechanical parameters, focusing on the specific relationship between corneal structure and biomechanical properties. In-depth exploration of the structural characteristics of the cornea can lead to more accurate predictions of treatment outcomes and provide better guidance for personalized therapy. Additionally, the investigation of new technologies and methods, such as Optical Coherence Elastography (OCE), can offer comprehensive corneal biomechanical information, enhancing the accuracy of clinical diagnosis and treatment. Emphasis should also be placed on the development of individualized treatment plans, integrating corneal biomechanical properties to deliver more effective treatment strategies for patients. Lastly, fostering interdisciplinary collaboration is crucial to advancing the field of ophthalmology and providing superior eye health services to patients.

5 Conclusion

In this study, we have delved into the importance of corneal biomechanical parameters on clinical treatment outcomes. Through the analysis of existing research and clinical practice, we have found that corneal structure significantly influences treatment effects, particularly in terms of individual variations. Therefore, future clinical practices need to delve deeper into the specific relationship between corneal structure and biomechanical characteristics. This exploration can not only provide a more precise and universally applicable basis for theoretical models but also help explore new methods and technologies at the clinical technical level. By studying corneal biomechanical properties in depth, we can improve treatment outcomes, develop more personalized treatment plans, and enhance patients' quality of life.

Future research directions should focus on how to better utilize corneal biomechanical properties to guide clinical practice. By establishing more accurate models, we can better predict treatment outcomes and reduce the risk of complications. Additionally, exploring new technological means, such as Optical Coherence Elastography (OCE), to provide more comprehensive corneal biomechanical information can offer doctors more precise diagnostics and treatment guidance. Furthermore, attention should be paid to the relationship between corneal biomechanical properties and other eye diseases (such as glaucoma, keratoconus, etc.) to comprehensively understand the biomechanical characteristics of ocular tissues, providing new insights and methods for the further advancement of the ophthalmic field. Through ongoing research and practice, we aim to provide more effective treatment options for patients, achieve personalized medicine goals, and drive progress and development in the field of ophthalmology.

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