A Viscoelastic Biomechanical Model of the Cornea Describing the Effect of Viscosity and Elasticity on Hysteresis

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PURPOSE. To develop a method for evaluating viscosity and elasticity of the cornea and to examine the effect that both properties have on hysteresis.

METHODS. A three-component spring and dashpot model was created in Simulink in Matlab to represent the purely elastic and viscoelastic behavior of the cornea during a measurement using device called an ocular response analyzer (ORA). Values for elasticity and viscosity were varied while sinusoidal stress was applied to the model. The simulated stresses were used to determine how hysteresis is affected by the individual components of elasticity, viscosity, and maximum stress. To validate the model, high-speed photography was used to measure induced strain in a corneal phantom during ORA measurement. This measured strain was compared with the strains simulated by the model.

RESULTS. When the spring in the viscoelastic portion of the model was stiffened, hysteresis decreased. When the spring in the purely elastic element was stiffened, hysteresis increased. If both springs were stiffened together, hysteresis peaked strongly as a function of the viscosity of the viscoelastic element. Below the peak value, lower elasticity was associated with higher hysteresis. Above the peak value, higher elasticity was associated with higher hysteresis. In addition, hysteresis increased as the air maximum pressure was increased. Measurements from phantom corresponded to predictions from the model.

CONCLUSIONS. A viscoelastic model is presented to illustrate how changing viscosity and elasticity may affect hysteresis. Low hysteresis can be associated with either high elasticity or low elasticity, depending on the viscosity, a finding consistent with clinical reports. (Invest Ophthalmol Vis Sci. 2008;49:3919–3926) DOI:10.1167/iovs.07-1321

The biomechanical properties of a tissue determine how it will respond and deform when placed under stress. In recent years, researchers have begun to look at the biomechanical properties of ocular tissues in diseases such as glaucoma, in which stress increases as intraocular pressure (IOP) increases, and keratoconus, which is characterized by corneal deformation. Evidence suggests that the biomechanical properties of the cornea and sclera are altered in glaucomatous eyes and that elasticity is altered in keratoconic corneas.3–6 A better understanding of the biomechanical nature of the cornea may lead to increased understanding of these disease processes.

Thus far, efforts to measure biomechanical properties have focused on testing ex vivo corneal tissue. However, the cornea has an extremely complex microstructure whose composition is tightly regulated by the body. After death, the cornea swells and loses its tear film and its optical clarity. These changes, along with temperature and tissue degradation, have been shown to change the biomechanical properties of the cornea.7 In addition, the cornea is not purely elastic but rather is viscoelastic,8 which means the rate at which a load is applied changes the measured value for the Young modulus. All these factors have contributed to the surprisingly large range of values for the Young modulus reported in the literature. Values range from 0.159 MPa9 to 57 MPa,10 with many other studies6,11–18 reporting values somewhere in between.

In addition to the difficulties regulating the ex vivo composition of the cornea, the availability of tissue specimens is a concern. Those available to researchers are unfit for transplantation, for reasons including, but not limited to, donor age, ocular disease, positive serology, or number of days in storage. All these factors could alter the biomechanics of the corneal specimen, making the determination of a range of normal biomechanical properties extremely difficult. There is a clear need for a method that measures corneal biomechanical properties in vivo but allows thorough biomechanical characterization of normal and diseased populations. In addition, the ability to measure the corneal biomechanical properties of a patient may provide new screening methods if there is a detectable difference in the viscoelastic properties of the normal and keratoconic or glaucomatous cornea.

In 2005, the ocular response analyzer (ORA; Reichert Ophthalmic Instruments, Depew, NY) was introduced as a device capable of acquiring an IOP measurement less sensitive to corneal thickness and material properties than had been acquired by other application measurement modalities. In addition, the machine offers a new metric, corneal hysteresis, that represents viscoelastic biomechanical properties.19 The ORA uses a focused air jet, with a pulse of approximately 20 ms, to perturb the surface of the cornea. The brief pulse causes the cornea to move inward, past applanation and into a concave state. As the air pressure decreases, the cornea passes back through applanation and regains its original shape. An infrared light is reflected off the surface of the cornea during perturbation. When the cornea undergoes applanation, the reflected light is maximally aligned with the detector, generating a signal peak.

This allows the ORA software to detect the two applanation events and the pressure required to achieve applanation. The two applanation pressures (loading [P1] and unloading [P2])
are different; P1 is higher than P2. This difference between P1 and P2 is called hysteresis and represents the viscoelastic nature of the cornea. Since the introduction of the ORA to clinical practice, there has been a flurry of research looking at the relationship between hysteresis and a variety of parameters such as age, central corneal thickness, intraocular pressure, progression of glaucoma, and presence of keratoconus. Low hysteresis has also been reported in patients after LASIK procedures. The relationships between hysteresis and altered corneal states demonstrate that the biomechanics of the cornea are affected by age, disease state, and surgical procedures.

Although hysteresis is a valuable measure of the viscoelastic response of the cornea, it represents the combined effect of component biomechanical properties. The primary purpose of this article is to develop a method for decomposing the hysteresis measurement into the biomechanical components of elasticity and viscosity. A mathematical model of viscoelastic behavior was developed to look at the behavior of the cornea equally as well as the model we chose, but it lacks the ability to facilitate clear separation of the purely elastic and viscoelastic components.

The chosen model relates stress (σ) to strain (ε) through equations 1 and 2. Both equations are derived by summing the forces at node 1 and node 2 (Fig. 1). When these equations are simultaneously satisfied, they predict the elongation of the model given values for stress, elasticity (E1 and E2), and viscosity (η1).

\[ E_1(\varepsilon_0 - \varepsilon_1) = E_2\varepsilon_1 + \eta_1\dot{\varepsilon}_1 \]  \hspace{1cm} (1)

\[ \sigma = E_2(\varepsilon_0 - \varepsilon_1) \]  \hspace{1cm} (2)

To maintain a level of pressure inside the eye that is higher than atmospheric pressure, the radial pressure load has to be balanced by a force in the cornea. This balancing force could be generated from the resistance of the cornea to bending or stretching. Because very low moments are required to bend the cornea, the resistance to bending in the cornea is considered to be negligible. The cornea’s resistance to stretching (elasticity) is the force that balances IOP. This force takes the form of tension in the lamellae (corneal wall stress). During ORA measurement, an air jet applies an external radial force to the cornea. This pressure balances some of the IOP, effectively reducing the amount of IOP that has to be borne by the cornea. This, in turn, reduces the tension in the lamellae, allowing the cornea to shorten.

To simulate this behavior, the viscoelastic model described here is used. The cornea is assumed to be an isotropic spherical membrane of uniform thickness. The load across the affected area of the cornea is assumed to be uniform, and deformation is assumed to be axisymmetric. Based on the ultrastructure of the cornea, the model neglects shear and bending forces and focuses on the tensile forces acting in the plane of the lamellae. The model is oriented in the plane of the corneal lamellae, as seen in Figure 2. In this orientation, the model aligns with the forces generated in the lamellae and represents the elongation and shortening of the lamellae as the wall stress in the cornea changes during ORA measurement. As air pressure from the ORA increases, a section of the cornea flattens and becomes shorter (represented by shortening of the model). After the cornea undergoes application in the inward direction, air pressure from the ORA continues to increase, subsequently indenting and elongating that section of the cornea. This orientation also has the advantage of isolating material properties from the structural properties of the cornea, such as curvature or thickness. One limitation of this model is that it is linear.

The ORA applies a focused stream of air to the external surface of the cornea. According to work done by Liu and Roberts, the deflection at application of the cornea can be calculated by subtracting the internal pressure from the external air pressure applied to the cornea and the small physiological force created by the surface tension of the tear film.

\[ P_e + s - IOP = P_r \]  \hspace{1cm} (3)

where \( P_e \) is the externally applied pressure, IOP is the intraocular pressure, and \( s \) is pressure created on the surface of the cornea by the

**Materials and Methods**

**The Model**

When loaded, the cornea demonstrates some instantaneous deformation (purely elastic behavior) followed by progressive deformation (viscoelastic behavior). These behaviors can be modeled with a fairly simple spring and dashpot system. The dashpot represents time-dependent viscous resistance to an applied force, whereas the springs represent purely elastic behavior. We selected this Kelvin-Voigt model with an additional spring (Fig. 1) not only for its simplicity but also because it allows for the clear and intuitive separation of the purely elastic and viscoelastic strain response of the cornea. This is similar to the configuration of Kobayashi et al., who used two Kelvin-Voigt models in series with a spring to compare fast and slow viscoelastic responses.

Other viscoelastic models commonly used are the Maxwell, Kelvin-Voigt, and Standard Linear Solid models. The Maxwell model was not chosen because it continues to creep indefinitely when a load is applied. In the cornea, creep approaches an asymptote. Another limitation of the Maxwell model is that it does not fully recover from a deformation caused by the purely viscous component. The pure Kelvin-Voigt model was not selected because it does not have a purely elastic component and thus does not allow for any instantaneous stretching (elasticity) is the force that balances IOP. This force takes the form of tension in the lamellae (corneal wall stress). During ORA measurement, an air jet applies an external radial force to the cornea. This pressure balances some of the IOP, effectively reducing the amount of IOP that has to be borne by the cornea. This, in turn, reduces the tension in the lamellae, allowing the cornea to shorten.

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The tear film is included in the equation because the surface tension creates a pressure that opposes intraocular pressure. The literature states that this tear film pressure is 4.15 mm Hg. Equation 3 is an appropriate representation of the tear film interaction with the cornea as long as the cornea is in a convex state. During ORA measurement, the cornea undergoes applanation and then is indented to a state of concavity. When the cornea is concave, the tear film tension acts in the opposite direction, pulling the cornea back toward applanation. The effect of the air puff on the integrity of the tear film has yet to be measured, but the reflection of the infrared light gives indirect evidence that the film remains intact (Kahook MY, et al. IOVS 2007; 48:ARVO E-Abstract 1255).

Intraocular pressure applied to the posterior surface of the cornea can be translated from radial stress to membrane stress with the Laplace law, where stress ($\sigma$) is calculated using resultant intraocular pressure ($P_o$), radius of curvature ($R_{curve}$), and thickness ($t$) of the cornea. In the current model, stress is calculated using the original radius of curvature.

$$\sigma = \frac{P_o \cdot R_{curve}}{2 \cdot t} \quad (4)$$

Exposing an area of the cornea to a high-pressure stream of air flattens the affected region. As the cornea becomes flatter, the radius of curvature increases and the length of arc AB decreases, as shown in Figure 3. In the model, it is assumed that the curvature of the cornea in the area affected by the air pressure smoothly increases to applanation, then passes through planar and into concavity. The curvature and position of the tissue outside the area of the air stream is assumed to be unaffected. Using diameter of the affected area ($2c$), original corneal radius of curvature ($R_0$), and depth of vertical depression ($b_{depressed}$), equations 5 to 10 can be used to determine the arc length of the cornea affected by the air stream ($L_{arc}$). A diagram showing $c$, $R_0$, and $b_{depressed}$ can be seen in Figure 4.

The cornea elongates as its apex moves away from applanation. As a result, it is necessary to translate $b_{depressed}$ into the vertical distance from the apex of the cornea to its position during applanation ($b_0$). This is done with equations 5 and 6, using the distance of the undisturbed apex of the cornea to its applanation position and the original corneal radius of curvature, $b_0$ and $R_0$, respectively:

$$b_0 = R_0 - \sqrt{R_0^2 - c^2} \quad (5)$$

$$b = |b_0 - b_{depressed}| \quad (6)$$

Using $b_0$ and $R_0$, the original arc length of the cornea ($L_0$) is calculated with the use of equation 7. As the air pressure applied to the cornea increases, the arc length of the cornea decreases, and the changing arc length is found using either equation 8 or 9 as applicable.

$$L_0 = 2R_0 \left[ \sin^{-1} \left( \frac{c}{R_0} \right) \right] \quad (7)$$

$$L_{arc} = \frac{c^2 + b^2}{b} \sin^{-1} \left( \frac{2cb}{c^2 + b^2} \right) \quad \text{for } b \neq 0 \quad (8)$$

$$L_{arc} = 2c \quad \text{for } b = 0 \quad (9)$$

From these values for arc length, the strain ($\varepsilon_{arc}$) induced in the cornea can be calculated with equation 10.

$$\varepsilon_{arc} = \frac{L_{arc} - L_0}{L_0} \quad (10)$$

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**Figure 2.** The orientation of the model is in the plane of the cornea. In this orientation, the model represents the increased and decreased elongation with changing tension as the wall stress changes during the ORA measurement.

**Figure 3.** As the cornea becomes flatter during an applied air puff, the radius of curvature increases and the length of arc AB decreases.

**Figure 4.** Diagram defining variables.
equal to $E_2$, and they were varied together to look at their cumulative effect on hysteresis. The maximum stress is represented by the wave amplitude ($P_{max}$).

To investigate the effect of different maximum stresses on hysteresis, the elasticity of $E_1$ and that of $E_2$ were set equal to one another and held constant while viscosity was plotted against hysteresis for three different $P_{max}$ values. This process was repeated for $E_1$ holding $E_2$ constant and $E_2$ holding $E_1$ constant. The process was also repeated by which $E_1$ was set equal to $E_2$, and they were varied together to look at their cumulative effect on hysteresis.

**Model Validation**

To evaluate the validity of the model, a phantom of the cornea was created to allow the experimental measurement of strain. A soft contact lens (Surevue: Johnson & Johnson, New Brunswick, NJ) and an artificial anterior chamber (Barron; Katena, Denville, NJ) were used to measure hysteresis and internal pressure using the ORA. The soft contact lens was selected because it has a curvature (7.2 mm) similar to that of the cornea and an optical surface. The thickness was 144 μm, as measured by calipers. For the ORA to take reliable measurements, a specular reflection of the infrared light directed at the object surface is necessary. Soft contact lenses are ideal for use with the ORA. They allow for the detection of sharp IR peaks, which in turn allows for the determination of applanation pressure.

The artificial anterior chamber was pressurized to 15 mm Hg to mimic intraocular pressure, and the pressure was monitored (TC Bedside Monitor; Spacelabs, Issaquah, WA). A high-speed camera (Motionscope PCI-500; Redlake, Tucson, AZ) was used to film the surface of the contact lens during ORA measurement. The film was taken at 500 frames per second. Each image was composed of 320 × 280 pixels, and each pixel was approximately 34 μm in length. Both the phantom and the camera were fixed to a metal plate so that the profile of the lens could be seen. The experimental setup is shown in Figure 5. The plate ensured that the artificial anterior chamber and the camera remained stationary during the measurement. Vertical displacement measurements were made from the image series. A ruler was imaged to determine the length of a pixel. With the use of commercial software (Photoshop 5.5; Adobe, San Jose, CA), a curve was fitted to the surface of the undisturbed contact lens (Fig. 6, right column, at 2 ms). This curve and the measure tool in the software were used to determine the radius of curvature and to measure the maximum vertical displacement of the contact lens. To determine the radius of curvature, the length of a cord (2c) on the circle and the maximum distance of this cord from the circle ($b_0$) were measured. These values and equation 5 were used to solve for the radius of curvature ($R_c$). For each subsequent image, white markers were manually placed on the images using a cursor to outline the deformation. To measure the vertical displacement ($b_{max}$) of the contact lens, each of the deformed images was overlaid on the original circle to allow the maximum distance between the markers and the circle to be measured (Fig. 6, right column, 10–18 ms).

The ORA uses an infrared light to measure applanation of the cornea. This light is activated for a fixed time before the ORA fires the piston that creates the air pressure stream and begins collecting pressure data, and it allows for the synchronization of the camera images and the pressure data from the ORA.

The radius of applanation was determined by using the timing of the two applanation events recorded by the ORA and the corresponding images taken immediately before and after the applanation. The timing of the applanation events is part of the data that can be downloaded from the ORA with the export data function. With vertical
displacement data from the acquired images before and after applanation and the timing of the applanation events, the vertical displacement at applanation was interpolated. The vertical displacement values \( h_0 \) for the two events were then averaged. We used equation 5 to calculate the radius of applanation area \( c \), and we used equations 6 to 10 to calculate the strain in the contact lens at each point during the ORA measurement.

Applied air pressure values and timing from the ORA were used to drive the viscoelastic model and generate a strain pattern. To simulate the model passing through applanation and into concavity, the sign of the stress and the action of the tear film were inverted at the applanation times. For validation, the values for springs \( E_1 \) and \( E_2 \) were assumed to be equal. Assuming the cornea to be axisymmetric, a single elastic constant should govern corneal behavior. The spring constant and the viscosity value were adjusted until the strain pattern achieved a best fit with the experimentally measured strain. The best fit was determined by minimizing the sum of the squared differences between the experimentally measured strain and the simulated strain at the same point in time.

**RESULTS**

**Model Results**

As seen in Figure 7, when a step function stress was input into the Simulink model, the purely elastic portion of the model strained instantaneously; the viscoelastic element demonstrated a strain that increased with time at a decreasing rate and eventually reached an asymptote. This behavior demonstrates that the model behaves viscoelastically.

When sinusoidal stress was applied to the model, it was found that hysteresis increased as \( P_{\text{max}} \) increased. This is clearly demonstrated in Figure 8. Further examination of Figure 8 reveals that hysteresis peaks as a function of viscosity. This is found to be true regardless of the values for elasticity, though the elastic constant influences the viscosity at which hysteresis peaks. Lower values for elasticity reach maximum hysteresis at a lower viscosity than do higher values of elasticity.

For a given viscosity, the relationship between elasticity and hysteresis is the opposite for springs \( E_1 \) and \( E_2 \), demonstrated in Figures 9 and 10. As the elastic constant \( E_1 \) (in parallel with the dashpot) increased, hysteresis decreased; for \( E_2 \) (purely elastic component), hysteresis increased as the elastic constant increased. When \( E_1 \) and \( E_2 \) were set equal and varied together (Fig. 11), \( E_1 \) appeared to dominate at lower viscosities (increasing the elastic constant decreases hysteresis), whereas the effects of \( E_2 \) dominate at higher viscosities (increasing the elastic constant increases hysteresis).

**Phantom Results**

Figure 12 is the signal from the ORA measurement of the soft contact lens (Surevue; Johnson & Johnson). The light gray line tracks the amount of infrared light detected by the sensor. Applanation of the corneal phantom coincides with the two sharp peaks. A good quality signal is one that is fairly symmetric and has sharp peaks. This image confirms that the ORA can measure hysteresis of a soft contact lens mounted on an artificial anterior chamber and pressurized. The value for measured hysteresis is 3.0 mm Hg. This value is lower than the value for human corneas, reported to be near 9.6 mm Hg.

Figure 6 (left column) contains a series of images from a high-speed movie of a contact lens being deformed during measurement with the ORA. In these images, the contact lens is detectably deforming and appears to be doing so in a uniform fashion. After the images were captured, they were analyzed to measure the experimental strain in the contact lens. The stress values from the ORA pressure wave were used to drive the viscoelastic model. The viscous and elastic constants were calculated from the best fit of the simulated strains to the experimentally measured strains. The fit of the simulation to the experimental data can be seen in Figure 13. Elasticity was 2.51 MPa, and viscosity was 9.02 KPa-s. This solution is convergent. In Figure 13, the points of minimum strain correspond

![Time vs. Strains and Strain rates](image1)

**Figure 7.** When a step function stress was input into the Simulink model, the purely elastic portion of the model strained instantaneously; the viscoelastic element demonstrated a strain that increased with time at a decreasing rate and eventually reached an asymptote. This behavior demonstrates that the model behaves viscoelastically.

![Hysteresis Vs. Viscosity](image2)

**Figure 8.** Elasticity is held constant while viscosity is varied for three different maximum pressure values.

![Viscosity Vs. Hysteresis](image3)

**Figure 9.** Spring \( E_2 \) is held constant while viscosity is varied for five different values of \( E_1 \).
with applanation. Experimental positional data were gathered every 2 ms because of equipment limitations. As a result, the true minimum strain was not perfectly captured.

It is important to keep in mind when interpreting Figure 13 that the strains depicted are strains in the plane of the corneal phantom. These are not to be confused with the vertical displacement measured in the images of the phantom taken during deformation. The points of minimum strain in Figure 13 correspond to the applanation events seen in the ORA signal in Figure 12.

DISCUSSION

The role of biomechanics in the development, progression, and diagnosis of ocular diseases, such as keratoconus and glaucoma, is the subject of much research. Keratoconus is characterized by a thinning and bulging of the cornea. Keratoconic corneas demonstrate a decrease in the Young modulus and an increase in distensibility. Early clinical detection of keratoconus can be difficult; the ability to measure early changes in the elastic and viscoelastic properties of the cornea may help address this problem.

According to Prevent Blindness America, more than 3 million Americans have glaucoma, but it has been diagnosed in only half. The primary risk factor is ocular hypertension, and the primary method of treatment is to lower intraocular pressure (IOP). Goldmann Applanation Tonometry is the gold standard for measuring IOP. Unfortunately, this technology is influenced by the biomechanical properties of the cornea, which may disguise ocular hypertension. Failure to promptly and accurately diagnose ocular hypertension could delay treatment; prompt diagnosis and treatment are critical to preventing irreversible vision loss. It is clear that more advanced screening tools are needed for the early detection of glaucoma. Investigating the association between biomechanical changes in the cornea and IOP is one potential avenue toward more robust screening methods.

The ORA provides hysteresis as a measurement that represents the biomechanical nature of the cornea. However, because it represents a combination of biomechanical factors, a direct comparison of raw hysteresis values from one subject to another is difficult. Our model predicts that hysteresis will increase as the maximum pressure reached by the ORA during a measurement increases. This prediction is consistent with the results of a recent clinical study in
healthy subjects that showed increasing hysteresis as a function of increasing maximum pressure until a plateau is reached (Rouse EJ, et al. IOVS 2007;48:ARVO E-Abstract 1247). The maximum pressure reached is a function of the first applanation pressure, P1, at which the first applanation event occurs.19 The ORA turns off the piston driving air pressure shortly after P1 is reached. Inertia in the piston causes the pressure to continue to increase before it reaches a peak and subsequently decreases. In addition, P1 has been reported to decrease with a decrease in IOP.20 A cornea that undergoes applanation at a lower pressure turns the piston off sooner and ultimately experiences lower maximum applied pressure. Lower IOP is a contributor to this phenomenon, but low viscosity or elasticity and thinner corneas may also contribute to applanation at lower pressures. Clinically, hysteresis has been shown to be an independent, but weak, risk factor for glaucomatous damage.4 Patients with untreated glaucoma can have intraocular pressures much higher than those receiving treatment. Viscosity, elasticity, or both may have a strong correlation with the progression of glaucoma but may not be seen in hysteresis. Viscosity and elasticity affect hysteresis in potentially offsetting ways. One or both of them may correlate more strongly with glaucomatous damage than hysteresis alone. Better understanding of the role corneal biomechanical properties play in glaucoma could also result in new treatment modalities for glaucoma.

Hysteresis is low in patients with keratoconus,19 in whom it is known that the elastic modulus is also low.5 In apparently contradictory studies, hysteresis has been shown to decrease during aging.20 when the cornea is known to stiffen, as well as decrease after the cornea has been stiffened by cross-linking techniques (Nogueira GE, et al. IOVS 2007;48:ARVO E-Abstract 1860). The output of the three-element viscoelastic model described behavior consistent with clinical data of increasing or decreasing hysteresis with stiffening of the cornea and low hysteresis associated with low elastic modulus (as in keratoconus) or high elastic modulus (as in advanced age).4,6 This model illustrates how changing viscosity and elasticity affect the hysteresis measurement in various ways. It also illustrates how measurements of viscosity and elasticity may be calculated from hysteresis with the use of clinical data (position, time, and stress) from ORA signal analysis.

The limitations of the current method for determining elasticity and viscosity include the assumptions that the cornea is spherical and of uniform thickness and that the airstream applied to the cornea is of uniform pressure. These assumptions lead to stress calculations that are higher for some regions of the cornea and lower for others. The assumption that bending forces are negligible in the cornea is another potential limitation of the model. Bending forces would act to resist the forces generated by the applied air pressure. Their neglect may cause overestimation of the tensile stress acting in the plane of the cornea induced by the air pressure. In addition, the biomechanical properties of the cornea are known to have regional differences.1,3 Our method examines the bulk corneal properties.

A linear, isotropic, viscoelastic corneal model was presented and validated using a corneal phantom. Ultimately, this model may be used to explore how changes in viscosity and elasticity affect hysteresis and to determine whether either component is a stronger predictor than hysteresis alone of glaucomatous damage or corneal behavior in pathologic conditions.


