

Chapter 2

Corneal Biomechanics

Fabio A. Guarnieri

1 Introduction

The cornea is the first and most powerful refractive surface of the optical system of the eye.

The production of an accurate image in the retinal receptors requires the cornea to be transparent and have a suitable refractive power [1–3].

The structural integrity of the cornea can be altered in the CR modifying its refractive properties. These procedures have been developed empirically without detailed knowledge of corneal behavior.

Measuring the change in corneal shape has been available in the past decade through computerized analysis of the reflection of photokeratoscopic ring surface of the cornea (corneal topographer).

Little is known about the behavior of the internal structure of the cornea. Although the ultrastructure was analyzed by electron microscopy, the role of each one of the layers has not been examined in detail. We shall see below attempts to define such roles, which still need further analysis.

The tools to measure and understand these processes arise from mechanical engineering and have been used in other medical specialties, such as orthopedics, which evaluates quantitatively the requirements of the prosthesis. Many of these methods are not suitable for soft tissue such as the cornea, but the general principles can be applied.

F.A. Guarnieri, Ph.D. (✉)

Department of Bioengineering, Centro de Investigación de Métodos
Computacionales (CIMEC), Predio CONICET Santa Fe, Colectora Ruta Nac 168,
Km 472, Paraje El Pozo, 3000 Santa Fe, Argentina
e-mail: aguarni@santafe-conicet.gov.ar

2 The Cornea

2.1 *Anatomical and Physical Properties*

The refractive power of the cornea depends on the curvature at its anterior and posterior surfaces, its thickness, and the refractive index difference between the air and the aqueous humor. The radius of curvature on the anterior surface of the cornea varies from the center (apex) toward the periphery. It is steeper in the central and somewhat flattened at the periphery. Average values of 7.8 and 6.7 mm from anterior to the posterior surface (Fig. 2.1).

At the apex, a wide range of variation of the radius of curvature of 7–8.5 mm is compatible with good visual function, and in pathological conditions increases even more the spectrum. Short radii result in refractive power and high myopia. Conversely, large rays give a low dioptric power and farsightedness. Furthermore, the central corneal curvature is often not equal in all meridians. The focus of the rays reflected by a point object does not form a point image on the retina. In these cases occurs astigmatism (a, without; stigma, point).

The curvature of the cornea changes somewhat with age. It is more spherical in childhood and changes to the rule astigmatism (more curved horizontal meridian) in adolescence.

Then again it becomes more spherical in adulthood to turn against the rule astigmatism (steepest vertical meridian) with senility.

The thickness also varies from the center to the periphery. This causes the difference in curvatures of the anterior and posterior surfaces. It has an average value of 0.5 mm center, increasing toward the periphery at an average of 1.2 mm at the limbus (limit of the cornea with sclera).

The corneal thickness is determined largely by corneal hydration that increases with increasing hydration and slightly with the age. The refractive index of the cornea is 1.376, and an average refractive power is 48.8 D (diopter). The concave posterior surface of the cornea is wetted by the aqueous humor, which has a lower refractive index (1.336), so that the average dioptric power in this area is -5.8 D.

To calculate the total dioptric power we rely on Gullstrand corneal thick lens equation, giving a value of 43 D, about 70 % of the overall refractive power of the eye. The lens only contributes 20 D convergence.

The cornea presents diurnal fluctuations in its topography in spite of relatively stable visual acuity. The factors involved in these variations are both physiological and anatomical, as the pressure of the eyelid, the time of day (especially during sleep), the tonicity of the tear film, and hormone levels.

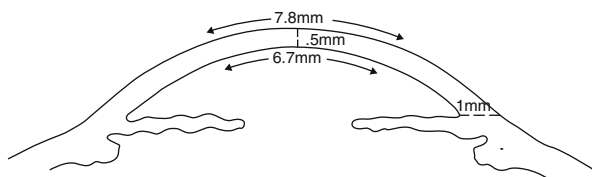


Fig. 2.1 Mean corneal radii of curvature and thicknesses

Fig. 2.2 Scanning electron microscopy of ablated cornea with a 211-nm laser (picosecond). Magnification 550x (Xin-Hua Hu, Ph.D., UC Irvine, CA, EEUU)



2.2 Histology of the Cornea

To perform a structural study of the cornea it is necessary to know not only the geometry but profoundly its internal components and functions performed to maintain corneal integrity. Furthermore, due to cuts or laser ablations performed in refractive surgery, it is vital to understand the healing process of wounds and scarring and to predict the refractive outcome of such processes. In Fig. 2.2, there is a scanning electron micrograph of an incision with laser wavelength of 211 nm, where the Bowman is observed (top) and multiple layers of collagen fibers.

The cornea is composed of five layers:

1. The epithelium consists of 5 or 6 layers of cells. The more superficial are flat and are superimposed like the skin, but are not keratinized. The following layers are arranged more stacked tightly together. Between epithelium and Bowman's membrane there is a basal membrane of 60–65 nm thick.
2. Epithelial cells form a layer of uniform thickness and great regularity. Their function is to maintain the stability of the tear film.
3. Bowman's membrane tissue is a transparent sheet of approximately 12 μm . It is acellular and is composed of densely packed collagen fibrils that are in random direction. Its absence in inferior animals is associated with a plasticity of corneal stroma.
4. The stroma is composed of film layers that run the entire length of the cornea; although the bundles are interlaced with each other, they are nearly parallel to the surface. The sheets are bonded together only loosely and are formed by bundles of collagen fibrils (bands of 64 nm) separated by a basic substance and water mucopolysaccharides. The latter are responsible for maintaining the hydration and transparency of the cornea and sclera that is not clear and does not contain mucopolysaccharides. The content of cells per unit volume is small. The cell bodies are flat, so they are also arranged parallel to the corneal surface. This arrangement of optical fibers provides uniformity to the cornea. The stroma constitutes approximately 90 % of the thickness of the cornea.

5. The Descemet membrane is approximately 10 nm thick. It is considered a secretion of endothelial cells. The membrane is comprised of type IV collagen fibers with similar characteristics to those of other basal membranes of blood vessels and lens capsule. It has a similar structure to the corneal stroma in terms of its regularity. It is highly elastic and represents a barrier against punctures.

The endothelium is a single layer of cells lining the Descemet membrane. Its inner surface is bathed by the aqueous humor. In humans the reproducibility of these cells is limited. The age causes cell loss and the remaining cells become larger and spread. Endothelial cells provide a barrier to the passage of water of the aqueous stroma. It prevents the cornea becoming hydrated with the aqueous humor. Cell losses are key factors the corneal edema and thickening of the thickness.

2.3 Corneal Wound Healing

The accidental or surgical injury of one or all of the layers of the cornea results in increased hydration and loss of transparency. Therefore, it is necessary and appropriate rapid healing of wounds to prevent scarring or opacities. The speed and the type of healing depend on several factors; among them are the anatomical location (limbal or corneal), the size of the wound, the layer of the cornea involved, bacterial, viral, or fungal infection, and drug administration therapeutic purposes. Thus, the damage of the corneal epithelium in general trauma heals in 24–48 h in a normal eye. Bacterial, viral, or fungal ulcers or those involving the deeper layers of the stroma can take weeks to heal. Therefore, deep laceration or surgical incision takes several weeks to heal completely.

The normal healing process of cuts on the central area of the cornea involves a cytological response and sleeve. Sometimes, for reasons not very clear, blood vessels can grow from the healed corneal tissue. The normal cornea is completely devoid of blood vessels. The capillaries extend just 1–2 mm beyond the limbal zone.

3 Measurements of the Mechanical Parameters

3.1 Extensibility of the Cornea

In 1937, Friedenwald [4] developed a formula which relates changes in intraocular pressure (IOP) with intraocular volume during Schiötz tonometry:

$$\log \frac{P}{P_0} = K \Delta V \quad (2.1)$$

where P_0 = initial pressure; P = pressure following the change of volume ΔV ; K = coefficient of ocular rigidity.

Friedenwald established that the value of K eyes remained constant for pressure higher than 5 mmHg (133 Pa/mmHg).

Many researchers, including Gloster and Perkins in 1957, attempted to determine experimentally the rigidity coefficient. Contradictory results were obtained concluding that K is not constant in the physiological range of IOP.

Therefore, the formula (Eq. 2.1) was invalidated. It was suggested that studies of the extensibility of the cornea and sclera in uniaxial test could help explain such changes. Already in 1864, Schelske gave way to a coefficient of elasticity for the cornea and sclera of humans and rabbits. He found that the coefficient for meridional scleral strips was 7 % more extensible than the equatorial, and the cornea was twice extensible than sclera. Weber in 1877 had found a large variation in scleral extensibility strips between different human eyes. Perkins and Gloster performed extensibility measurements with corneal and scleral strips isolated from rabbits, using weights that produce stresses as close as possible to those of a normal eye. They compared these results with the determinations made by the authors of the intact eye strain. They found that the eye became less distensible at high pressures, consistent with the fact that the scleral strips became less extensible to the increased tension to a certain point (20 N/m) where extensibility became more constant. But they also noted that the strips did not return to their original length after the weights were removed. They found the creep phenomenon (temporary slow deformation with time) in strips with an instant length change of 81.8 % and 6' to reach the stationary state. During distension of the intact eye, the cornea and sclera extend in two directions where the stresses are distributed and the thickness decreases. In the case of uniaxial test strips there is a single direction, length, and decrease in both the thickness and width. Therefore, Perkins and Gloster did not justify performing a close analogy between distension of an intact eye and scleral and corneal strips.

Woo and Kobayashi [5] came to the same conclusion as Gloster and Perkins in human eyes. They added that exposing the free ends of collagen fibers caused a minor elastic response of the material and the straightening of the curved strips into a uniaxial test caused a significant error in elasticity measurements. They argued that it is important to consider, for volume changes to changes in IOP, the geometry variations and corneal material inhomogeneity. They did not consider the viscoelasticity and large deformations. Kobayashi and Woo devised a method for determining the elastic properties of the sclera and the cornea retaining its natural geometry. They sectioned equatorially enucleated eyes (1–3 days post mortem) and placed each half shell (anterior and posterior) in a pressure chamber. They found that both the shell and the subsequent previous corneosclera bear their weight without IOP. They measured with a scanner system the deformation of the horizontal surface while the pressure was increased. A photomultiplier detects the

reflection of light at two targets located at two points of the cornea. The light was generated by a cathode ray tube driven by a triangular wave generator. They also measured lateral deformations (0° , 45° , 90°) to determine the isotropy of the material. They found that the deformation in three directions was very small. Moreover, they conducted a hysteresis test resulting in a minor viscoplastic (time dependent but not temporary deformation) effect. They considered the material as isotropic assuming that stresses across the thickness were only 10 % of the other planar strains in the corneal cap. Based on pressure–deformation curve measures, Woo and Kobayashi considered it also as nonlinear. In order to obtain stress–strain curves in the natural three-dimensional state of the cornea, they constructed a mathematical model [6] using effective stress and effective trilinear deformation.¹ The model parameters were adjusted iteratively until deformations predicted by finite element analysis agreed with those obtained experimentally (a technique called inverse method). Once the fit is reached, trilinear relations were converted to an exponential function through least squares method (best fit optimization method), obtaining

$$\begin{aligned}\sigma_e &= 18(e^{41.8\epsilon_e} - 1)\text{kPa (stroma)} \\ \sigma_e &= 5.4(e^{28.0\epsilon_e} - 1)\text{kPa (cornea)}\end{aligned}\quad (2.2)$$

To validate the equation, a pressure–volume curve of the anterior segment of the eye was compared with experiments obtaining good agreement except for high pressure. Concentrated high stresses in clamped edges and possible swelling of the cornea by humid air are potentially the causes of high pressure discrepancy.

Schlegel et al. [7] investigated the viscoelastic properties in human enucleated eyes using ultrasonic waves by measuring changes in ocular diameter while IOP was cyclical. They found that pre-pressurized eyes had a substantially less viscoelastic response. Using the same protocol of Schlegel, Kobayashi et al. [8] determined the viscoelastic response of human corneas subjected to PIO from the same procedure of Woo et al. The purpose was to isolate the effect of viscoelastic pressure decay over time by measuring pressure with a tonometer. In pre-pressurized eyes the answer was almost negligible. The viscoelastic response was characterized in pre-pressurized eyes with a five-element linear viscoelastic model. They found average values of $53.68 \pm 83.03'$ to the slow time constant and $11.1 \pm 0.71'$ for the fast time constant. The average instantaneous elastic modulus was 1.11 MPa. A nonlinear viscoelastic mode I (Fung hereditary integral) found a better characterization of the viscoelastic parameters.

¹

$$\begin{aligned}\text{Effective stresses and strain are : } \sigma_e &= \frac{1}{3}\sqrt{(\sigma_1 - \sigma_2)^2 + (\sigma_2 - \sigma_3)^2 + (\sigma_3 - \sigma_1)^2} \text{ and } \epsilon_e \\ &= \frac{2}{3}\sqrt{(\epsilon_1 - \epsilon_2)^2 + (\epsilon_2 - \epsilon_3)^2 + (\epsilon_3 - \epsilon_1)^2}\end{aligned}\quad (2.3)$$

Greene and McMahon [9] studied in enucleated intact rabbit eyes the primary, secondary, and tertiary scleral creep function of temperature (26–48) and IOP (15–100 mmHg). In physiological conditions (37 °C and 15 mmHg), there is a speed creep of 0.06 %/h corresponding to 0.5 D/day. This measure has no physiological meaning in humans.

Russell and Klyce [10] modeled with FEM the corneal hydration regulation.

Parameters as permeability and solute transport through the intervening membrane were determined. It was simulated corneal hydration dynamics, thickness variations at different boundary conditions, such as hypertonic solutions, cold environments, high IOP (glaucoma), and destruction of limiting cell membranes (epithelium and endothelium). They predicted that the removal of the epithelium (as in laser photokeratectomy) causes an increase of the stromal thickness by 25 % for 1 h, consistent with the results *in vivo*.

Greene [11] examined the stresses undergone by posterior sclera at the accommodation produced by zonular fibers, convergence, vitreous pressure, and extraocular muscles. He noted that animals can myopize experimentally. He concluded that the oblique muscles are capable of originating local stress concentrations near the entry of the optic nerve.

Arciniegas et al. [12] found a relationship between the elastic modulus and the proportional limit with the age for high loads ($\sigma \gg 14$ kPa) in 24 eyes of 24 human scleras of various ages. They found that from birth both are high and decrease with age to stabilize after 20 years approximately. This reflects that the surgery should be performed after stabilization refraction. While there may be other parameters to ensure this, it is possible that there is a dependent refractive corneal elasticity. Creep was also measured in corneal-scleral shells of 30 rabbits being of 1.4222 %/h for 20 mmHg a value higher than in rabbits (Greene and McMahon). One important measurement in the diagnosis of glaucoma was to compare the pressure measurements with the Goldmann tonometer and a sensor implanted within the vitreous chamber of the eye of a rabbit. They found an average of 2.74 times greater IOP measurement with the sensor. Deficiencies the Goldmann tonometer is allotted not consider in corneal thickness, mechanical properties, the geometric shape of the eye, and creep.

Nash et al. [13] conducted a uniaxial test strips for low loads ($\sigma < 250$ kPa), finding the nonlinear relationship, but found no association with age eyes because they took ages over 20 years. They determined that the elasticity in normal corneas and keratoconus were equal. Creep was measured in human strips with a load of 150 psi for 2–20 h, finding similar results compared in Greene and McMahon.

Kamm and Battaglioli [14] found that the compressive Young's modulus through thickness is hundred times smaller than tensile (27–41 0.2 kPa). They also calculated Poisson's ratio across the thickness (0.46–0.50) resulting in a nearly incompressible material in that direction. However, they explained that the hydration and viscoelastic effect could influence the results, being even a lower compressive modulus.

3.2 *Keratoconus Biomechanics*

Edmund [15], in 1989, conducted a study of 27 patients with keratoconus and 37 normal to determine and describe corneal topography and pachymetry of their eyes and to evaluate the hypothesis that the difference is elastic. Methods and descriptive models were developed for characterizing corneal shape based on the central curvature and radial variation coefficient, eccentricity and function of the central curvature, the corneal thickness profile, fitted with a parabola, and the corneal-limbal ring, adjusted to an ellipse. Also, methods for estimating Young's modulus [16] and mass-based corneal topographic descriptive parameters were developed. An estimation of the stiffness from measurements of corneal tonometry with various weights and calibration tables from Friedenwald were derived.

He also showed that the stationary Young's modulus and stiffness (which would be related to instantaneous Young's modulus) is lower in keratoconus but have no correlation between them. It was shown that only in an advanced stage of keratoconus (>7.5 D) the corneal mass decreases. Based on the thickness and topographical changes, stress distribution is altered also based on the membranal theory (or law of Laplace) in keratoconic corneas. Tension along the meridian in normal corneas decreases while in keratoconic corneas increases. This increased tension would cause a second growth process of keratoconus in the corneal periphery as shown in the growth found in the periphery of the corneal thickness, contrary to the hypothesis of elastic keratoconus. It seems that the instantaneous Young's modulus reflects the immediate response of the collagen fibers, to match the value calculated from the ocular rigidity in comparison with the experimental measurements cornea strips. While the Young's modulus response appears to reflect steady elastic matrix glycosaminoglycans, consisting of the matrix compression and slippage of the collagen fibers, and that the estimated values are of the same order the Young's modulus of the matrix, also indicating that the collagen fibers are rather relaxed in the physiological state. This would be consistent with the theory that the slippage increases keratoconus collagen fibers due to reduced adhesion to Bowman's membrane and a matrix synthesis altered corresponding to an increase in the elasticity of the corneal tissue. Keratoconic biochemical studies demonstrating a normal collagen and altered proteoglycan synthesis confirm this hypothesis. On the influence of genetics and environment in keratoconus, see [Edmund] p. 30.

Hjortdal et al. [17] repeated the test of Woo and Kobayashi in ten corneas maintaining human corneal hydration normal IOP for a range of 2–10, 10–25, and 25–100 mmHg, finding values of 3, 9, and 20 MPa, respectively. The authors explain that the results of Woo and Kobayashi and Jue and Maurice give greater deformations due to greater corneal hydration. They assume that the values found still underestimate the Young's modulus values in a constant corneal volume.

In 1996, Hjortdal [18] studied in vitro the elasticity of the cornea and limbus by regions. He found rigidity at the limbus preferentially in a circumferential direction and to a lesser extent in the peripheral cornea preferentially in a meridional orientation. The same study was made after four radial keratotomy incisions by

Hjortdal et al. [19]. Normohydrated corneas were found to have an important role of local bending undamaged stromal tissue underneath the incision to generate the opening of the incision. He also found that compression of circumferential tissue disappears somewhere between the endothelium and epithelium to become taut.

Purslow et al. (1996) conducted a study of the relationship of IOP vs. volume based on the intrinsic stiffness Young's modulus. They found a relationship between the incremental values of Young's modulus at a given pressure proportion to the fourth power of the radius of the sphere eyepiece. They assumed that the Poisson's ratio is 0.5 confirming experimentally pachymetric measures.

3.3 *Stromal and Descemet Membrane Extensibilities*

Jue and Maurice [20] studied the mechanical properties of the stroma and Descemet membrane separately, using the principles of measuring the geometry of the intact eye.

The system consisted of a keratometer that viewed through a reflection prism two drops of mercury placed in the corneal surface. Full enucleated eyes were taken from rabbits and humans aged 45–90 years. Hysteresis tests were performed, responses to low and high tension, of the cornea intact isolated stromal and membrane isolation. Descemet's membrane is more extensible, in a nonlinear way. The stroma is virtually non-extensible and mimics intact corneal stromal mechanical properties.

From the high pressure curve, the elasticity modulus of the stroma is calculated. The stroma is composed of 70 % of its dry weight collagen fibers. The value of the elastic modulus of the collagen fibers can be obtained from the literature. Assuming constant voltage across the thickness, Laplace's equation gives the value for the case of spherical surfaces of thickness t radius of curvature R , under an internal pressure IOP

$$\sigma = \frac{P_{IO}R}{2t}; \quad \text{Laplace's equation} \quad (2.4)$$

Dry stromal thickness is 0.07 mm; therefore, the thickness of collagen in the stroma is equal to 0.05 mm. Curve obtained high pressures relationship IOP/ ϵ which is 9.106 Pa. Then within 7 mm, the Young's modulus ($E \sigma/\epsilon$) of the stroma, without considering the extensibility of the ground substance, is in the order of 0.6 at 1 GPa. The procedure is to calculate the Young's modulus of Descemet's membrane at low tension. With a thickness of 12.5 μm , with a 150 cm H_2O /unidad deformation, Laplace equation leads to 5 MPa.

Considering the fundamental substance of stroma with a modulus of elasticity between 1 and 100 kPa (depending on stromal hydration) and as the volume ratio of collagen fibers and ground substance is 1:9 according to Maurice, we calculate the modulus of the stroma in fiber direction. This value has a range, depending on hydration of 11 MPa to 100 GPa.

Hanna et al. [21] used a mathematical technique to estimate the homogenization modulus of the stroma considering its fibrillar structure. This technique allows to describe macroscopic stress–strain relationship of materials whose microscopic structure is periodic. They conducted a model based on stromal microscopic measurements by X-ray diffraction of wet rat tendon similar (but not identical) to that of human corneal stroma and also based on transmission electron micrographs of human corneal stroma to estimate the relative contribution between the fibers and the ground substance. In the model we used the following values:

- Collagen fibers 35 % by volume
- Fiber diameter 25 nm
- Space between fibers 48 nm
- 20 % hydration fixed (both for fibers and for substance)
- E 1 GPa longitudinal fibers

Poisson's ratios calculated for the fibers and the ground substance and the Young's modulus for the basic substance, adjusting the coefficients until homogenization values, agreed with the experimental values found in the literature. The results are consistent with previous experiences, which validates the model clinically. For holographic interferometry, Kasprzak et al. [22] Elastic Modulus measured bovine corneal tangent for high pressures coincide with curves and Maurice Jue.

3.4 Bowman's Membrane Importance

There are controversies regarding the role of Bowman's membrane in corneal structure [23]. It is believed that Bowman's membrane contributes to the stability of the corneal curvature and is also protective against injury and infections. While it has not been shown experimentally, this hypothesis is taken into account in refractive surgery to preserve it.

On the contrary, in photorefractive keratectomy, made with UV excimer laser or IR, the flattening is achieved by removing tissue from the anterior surface of the cornea, sacrificing central portions of Bowman's membrane.

Clinical experiences indicate that Bowman's membrane should be incised for changes in the anterior corneal curvature in refractive procedures.

Incisions within the stroma without breaking the Bowman's membrane curvature will not change much anterior curvature, but it can change the posterior curvature. It is considered that the removal of part of the Bowman membrane Excimer laser is a potential source of instability in the cornea long term. Although such considerations have not been demonstrated clinically.

Theo Seiler et al. [24] conducted a study showing that after 6 months of an excimer laser photorefractive keratectomy, the refractive result was stable.

Hjortdal et al. [25] found no significant mechanical contribution of Bowman's membrane in the instantaneous or short-term response.

3.5 Viscoelastic Parameters

Theo Seiler et al. [24] conducted a study of the viscoelastic properties of strips of cornea without Bowman's membrane. Creep tests performed (tissue exposed to constant load, measuring the extent as a function of time) and stress relaxation (the tissue exposed to a constant elongation measuring the tension as a function of time) into strips enucleated eyes cornea. To remove the layer of Bowman, perform excimer laser keratectomy. The results showed that the strips of cornea are average stress-strain relationship with 5 % higher Bowman without it. This value could be higher because the experimental error was 10 %. Furthermore, viscoelastic properties in this experiment did not differ. They found a fast relaxation time of 10.58 and 269 s for the slow corneal stripping of Bowman's membrane.

Smolek et al. [26] obtained spectrum by applying shear compliance spectroscopy technique compliance dynamic mechanical cutting cylindrical specimens explanted human corneas, according to corneal hydration and temperature, and in the frequency range of 0.1 MHz–100 Hz found that a myopic cornea is significantly softer than emetropic corneas in both low and high frequencies. They found that thickness change varies with the shear compliance significantly (600 times of 0.2–1 mm at 1 Hz) and also corneal hydration and temperature change significantly the shear compliance. They considered that it is important to detect the frequency range interest 0.1 Hz–1 MHz

Buzard et al. [27] monitored every 1 min corneal topography after placing a Honan balloon for 5 min, increasing IOP to 30 mmHg. Normal corneas found that very little change topography after 3 min in contrast corneas after 3 months of radial keratotomies flattened almost 1 D to 0.40 D minute to 3 minute. At 9 months this group flattened 0.10 D per minute. On jobs investigating corneal hydration and its implications for the CR, we refer the reader to the references [28–30, 10].

4 Biomechanical Models

In 1972, Woo et al. [5] input the results of the characterization of corneal and scleral field into a mathematical model by EF human corneal-scleral shell. This model was used to compute the nonlinear relationship between the intraocular pressure (IOP) and the volume of the eye and analyze the structural response during applanation tonometry [31]. The model was axisymmetric, with the geometry based on an idealized eye quadrilaterals with 665528 nodes. Bowman's membrane had the same elastic properties with that of the stroma, Descemet's membrane, and the sclera. Poisson's ratio equal to 0.49 was considered. Tests were performed with Poisson's ratio of 0.5 obtained differences in voltages 0.5 % to an IOP of 17 mmHg. The limbus was modeled by varying the elastic modulus in seven increments between stromal and scleral modules. They found that the tensions were greater at the limbus and at the Ecuador than in other areas. Other studies found that the

stiffness coefficient decreased when Friedenwald increased IOP. The results were similar to data obtained *in vivo* by several researchers, but differed from results obtained in enucleated eyes because the model did not consider the additional stiffness post mortem produced in the choroid. In the simulation of applanation, modified stroma elastic properties (modulus perpendicular to the plane of the cornea = 20 kPa) to account for the collapsing of the collagen fibers under compression tonometer indenter. In this area the bending rigidity is decreased. They found that it is consistent with empirical results.

In 1988, Hanna et al. [32] used the FEM to build a mathematical model of the eye that analyzes the stress–strain relationship of corneal-scleral shell. They used an axisymmetric model, without considering the curvature aspheric anterior cornea. Simulated lamellar keratectomy and laser myopic keratomileusis. The material used was linear, elastic, isotropic, and having a modulus of elasticity $E = 5$ MPa and $\nu = 0.49$. They did not consider the initial stress state. The mesh elements 600 comprising half with four elements in thickness. The results presented were stress curves, meridional circumferential compression and shear.

Membrane behavior found in the posterior half of the eye, from limbo, to match the thickness meridional and circumferential stresses (in-plane stresses). In the cornea they found a linear variation in the thickness of meridional and circumferential stresses. The stresses in the outer layers were lower than in the internal. At the limbus, they were reversed.

Compressive stresses were small void in the outer layer (relative to atmospheric) and equal to the IOP except around the eye at the limbus, where they found no explanation of fluctuation. The shear stresses were zero except at the limbus, where bending. Decreasing the thickness keratectomy, stress increases and the remainder meridional not altered. In keratomileusis, the central zone behaves like a membrane and the rest of the eye is not altered.

In 1989, Hanna et al. [33] created a mathematical model EF to simulate radial keratotomies. Corneal asphericity was considered by using Lotmar equation for the cornea, assuming a moderately myopic cornea (5–6 D). Corneal material was elastic, nonlinear, and isotropic. They used a Mooney–Rivlin model quasi-incompressible elasticity taking values of 2.2–2 MPa for cornea and sclera. They used a 2-layer 3D mesh with 27-node isoparametric elements. The incisions were not refined in the eye and considered axisymmetric considering a quarter mesh. Gullstrand optics was used to calculate the refractive changes. The stress distribution in a cornea without cuts was similar to earlier work except in the compressive stresses where values were different. Eight radial incisions showed the pattern of changes in meridional stresses and circumferential compression along a meridian. The model predicted the central flattening and steepening in the medial periphery. They showed the effect of the number of incisions, IOP, the thickness of the incision, incision length, the central radius of curvature, and Young's modulus, consistent with clinical studies [34], except for the effect of IOP, which was greater, and incision length of small diameter optical zone with no effect. The authors suggest a nonlinear viscoelastic anisotropic full eye 3D model, including muscle forces. They made no quantitative clinical validation of the model.

Kwitko et al. [35] used a digital videokeratoscope system to evaluate changes in corneal topography after strabismus surgery practiced on extraocular muscles of 36 eyes of rabbits. They compared the results with the simulation of surgery in control eyes. They found the importance of considering the stress state of the extraocular muscles on the sclera, affecting corneal topography, corroborated by clinical studies. The material model was linear, elastic, and isotropic, in an eye with axisymmetric geometry. The mesh included two elements in the thickness of the sclera and 4 in the thickness of the cornea, with two closure elements representing the Bowman and Descemet's membrane. The limbus was modeled with triangular elements. Muscles were modeled as nodal forces and orbital tissues that stabilize the balloon radial elastic elements on the back of the ocular globe. They predicted qualitatively corneal topographic change strabismus surgery.

Rand et al. [36] introduced a model for studying human corneal refractive changes of radial keratotomy, using a thin spherical shell model that is linear and elastic. They assume axisymmetry and isotropy. The surgery is simulated by changing the Young's modulus and the thickness at the position of the incisions. The model behaves purely membranous. The results are compared with other models in FE, agreeing in some features, such as the effect of IOP, depth of incisions, and irregular topography in the optical zone.

Pinsky and Datye [37, 38] proposed a thick membrane model. The RK incisions were simulated by introducing anisotropy and inhomogeneity in the membrane stiffness. Pinsky et al. assume that the cornea does not support bending and the cut fibers lose their ability to load stress due to low shear modulus of the matrix. They use a linear elastic material with moderate rotations (nonlinear geometric), with a high Young's modulus calculated by considering the microstructure of the corneal stroma as a composite of collagen fibers with a small area and a matrix. The cornea is allowed to rotate in the limbus, whereas the collagen fibers are more oriented circumferentially and offer great resistance against expansion due to high hoop stress therein. The results are compared with surgeons nomograms known as Arrowsmith, Deitz, and Sawelson. The Young's modulus is calibrated to approximately match the nomograms.

Buzard et al. [39] used a model to simulate axisymmetrically an FE inflating a human enucleated eye and measure the lateral displacement. The mesh had two elements in thickness. The model successfully match experimental data for pressures around physiologic, being very stiff at low pressures. In another study [40] they measured with a Baribeau microscope with a resolution of 1 μm , the opening of the surgical incision in a diagram of four radial incisions in enucleated human eye with a 3-mm optical zone, increasing IOP 25–100 mmHg. Using 26 biomechanical eye model membranous theory and considering the average values of corneal thickness and curvature determined the Young's modulus of 7.58 MPa. The maximum dispersion 25 mmHg was 50 μm at a distance of 3.5 mm from the apex.

Sawusch et al. [41] conducted a study of the opening of the incision comparing the results with a geometric model called "tissue addition" and a model in EF. The tissue addition model assumes that the opening of the incision is initially filled by

epithelial and fibrous tissue. This model correlated well with human studies. The model consisted in a finite element mesh of a quarter of the eye assuming radial symmetry, two elements in the thickness of the sclera and limbus, four elements for the cornea, and shell elements representing the Bowman and Descemet's membranes. An isotropic linear elastic material assuming small displacements was considered. For four incisions with a 4-mm optic zone and a central curvature of 44 D, the EF model predicted central flattening 3.05 D and an opening in the middle area of 47 μm cut. For the same cornea, an intrastromal cut predicted no significant topographical changes. It also predicted the opening is greater at the periphery than near the corneal center, which was confirmed by histopathological studies. The tissue addition model predicted 3.10 D of flattening by using the incision gape calculated using the FE model and histopathological studies.

Vito et al. [42] examined different models of EF cornea comparing them to determine the relative importance of factors such as boundary conditions, thickness, and the number of corneal layers needed to adequately model it. They validated the model with corneal tonometry studies [6]. Shell model was dismissed due to high gradients of stresses in the thickness during an indentation, despite having a low thickness/radius of curvature ($t/R = 0.0625$) ratio. They also considered important to use models with large deformations. They modeled axisymmetric meshes with different boundary conditions with and without limbo. The material was considered isotropic linear elastic and quasi-incompressible. It was found that for the inflation of the cornea with IOP of 20 mmHg, the model with free boundary without limbo approached a membrane model. The same occurred in the central area of the model with free boundary in limbus and the horizontal direction. For the same model it was found that a higher elastic modulus of 2 MPa produced no changes in central curvature, showing a membrane behavior in the central area, and that the bending is only important in the contour. Different models with the membrane theory were compared with tonometry. Contact with the indenter using gap elements was also modeled.

It was shown to be necessary to consider geometric nonlinearity in the model. The boundary conditions did not affect the result. They introduced a model of corneal layers free to slide without friction between them. Their behavior, as the number of layers is increased, approached the membranal. The pressure distribution at the interface between the cornea and the indenter is not uniform. This indicates that the bending is important in tonometry, which would explain the discrepancies found between the tonometry and direct measurement of the IOP [43]. They also used this dependence to estimate the bending rigidity of the cornea [44].

Wray et al. [45] developed a 3D model of a fragment symmetrical to radial keratotomy eye including corneal nonlinear properties of the material obtained from in vivo data. Generally were selected as the constitutive equation proposed by Woo et al. [6]. Then they adjusted the parameters using in vivo data from a study of radial keratotomy in 290 eyes and performed a sensitivity study of different surgical parameters, obtaining comparable results with reality.

5 Toward a Computer-Aided Design of the Refractive Surgery

These papers consider the cornea as axisymmetric without cuts, i.e., the cornea is equivalent to a sphere. Thus, it is only possible to represent corneas with nearsightedness and farsightedness. It is possible to represent different cases of astigmatism (myopic, hyperopic, mixed). Neither is it possible to represent real corneas where the vertical diameter is less than the horizontal. Besides the geometrical data are obtained from the information keratometer, which only measures the average curvature of the corneal apex to 3 mm. It has been found that the error in systems based on corneal spherical mapping aspherical surfaces (such as the cornea after surgery) is significant [46].

Regarding the model of corneal material, nonlinearity has been modeled in small deformations by Woo et al. Bryant et al. attempted to adjust the experimental curves with hyperelastic models without result. No model represents the long-term effect of the cornea. There are attempts to model the effect of the corneal viscoelasticity Le Tallec [47, 48], but no clinical nor numerical data validation was found.

The author's thesis [49] developed a biomechanical model of the cornea incorporating the following guidelines:

- Precise geometric model incorporating technological advances in data acquisition such as corneal digital videokeratoscope and ultrasonic pachymetry [50, 51]
- Optical model suitable for further processing and suitable for clinical analysis ophthalmologist
- Suitable material model to mimic the behavior in the different corneal refractive surgery procedures, both in the short and long term
- Validation of elements with real patient data

This required the following characteristics of the model:

1. The 3D geometry, with change of corneal thickness, performing an interface with the data acquisition equipment
2. Optical thick lenses and topographic map to evaluate results
3. Hyperelastic nonlinearity viscoelastic material

April. Actual patient data (topography, pachymetry, clinical data, pre- and postsurgical) for radial and astigmatic keratotomy and excimer laser photokeratectomy

Figure 2.3 is a flow diagram to model the cornea.

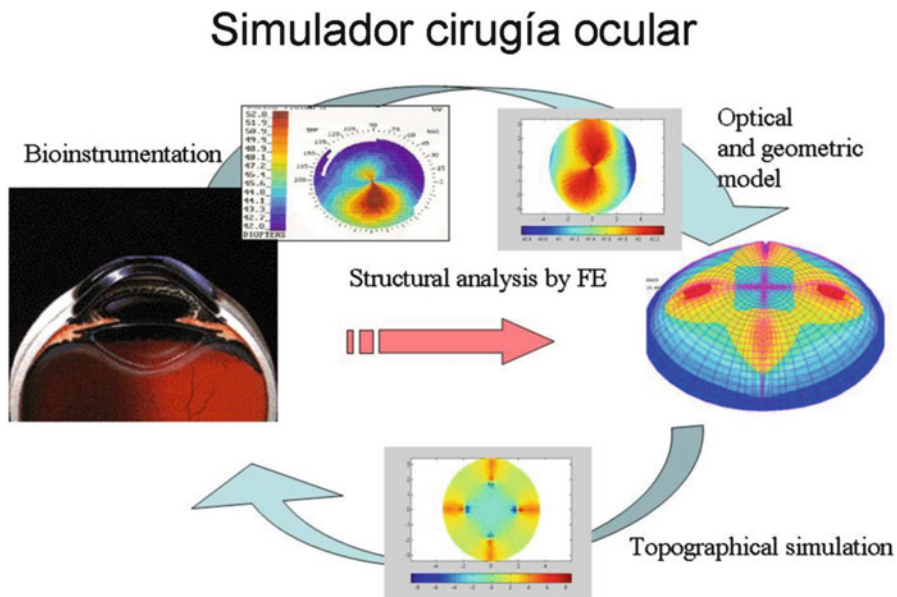


Fig. 2.3 Flow diagram to model the cornea

6 Data Acquisition

Optical and geometric data were obtained from instrumentation commonly used in the ophthalmology clinic (there is no instrumentation that obtains the spatial geometry of the cornea in a direct way). The ultrasonic pachymeter, a slit lamp, and a digital videokeratoscope were used.

6.1 Corneal Thickness

The ultrasonic pachymeter utilized point measurements performed on the cornea. It was assumed that the measurements were made normal to the anterior corneal surface. Initially two steps, one at the apex and another at the limbus (corneal periphery), were performed. Edmund [15] described a parabolic variation between the central thickness and the peripheral

$$T(x) = T(1 + T_V x^2) \quad (2.5)$$

where $T(x)$ is the corneal thickness on the chord segment x from the apex. T denotes the central corneal thickness. T_V is defined as the coefficient of variation of thickness and is constant.

6.2 Corneal-Limbal Ring

Corneal-limbal ring (CLR) denotes the boundary between the cornea and the remaining eye most highly curved.

Through a slit lamp it is possible to measure corneal diameters. Generally, the vertical to the horizontal diameter is less than 1 or about 2 mm. The CLR was adopted as an ellipse where a and b are the major and minor diameters of the ellipse:

$$y^2 = b^2 - \frac{b^2}{a^2}x^2 \quad (2.6)$$

where a and b are the diameters of the ellipse.

6.3 Anterior Surface

The corneal topographer (e.g., EyeSys) is based on equally spaced projecting concentric rings onto the cornea (Placido disk) where radius maps are obtained. They are deployed in one angular degree separated by meridians. The detailed description of the algorithm is in reference [52].

The rate of change of direction (curvature) at a point is (for flat curves)

$$\kappa = \frac{z_{,rr}}{(1 + z_{,r}^2)^{3/2}} = \frac{1}{\rho} \quad (2.7)$$

Assuming smoothness and the center of the cornea is the apex (condition alleged by the corneal topographer) is possible to calculate the elevation at each meridian. Differential equation is solved in each meridian z assuming a variation of the radius of curvature in one direction, the meridional. This hypothesis agrees with that made by the reconstruction algorithm of the corneal topographer.

The posterior surface is generated from the spatial coordinates of the anterior surface calculated and the thickness measured (typically 5,760 points).

6.4 Intraocular Pressure

The intraocular pressure (IOP) is measured with a Goldmann tonometer [31]. There are controversies on the validity of the ocular tonometry, especially for corneas that do not approach the average eye (thin corneas, very elastic, very rigid, very flat or highly curved, very aspherical) [3].

6.5 Ocular Length and Depth of the Anterior Chamber

A-scan ultrasonographer (linear 1D) measures the length of the eye, the depth of anterior chamber, and the axial crystalline lens axially from the cornea of the eye to the fovea. This length allows the full refraction of the eye and along with the corneal and lens refraction the calculus of the total refraction required to correct ametropia (Fig. 2.4).

Chamber depth is the distance between the cornea and iris. It is about a few millimeters. It can be measured with a B-mode ultrasound sensor (sweep 2D) (Fig. 2.5).

6.6 Objective and Subjective Refraction

Higher aberrations can be measured by Foucault knife-edge test, which retinoscopy is based, where a very small source is used to analyze aberrations of the eye. In order to quantify the wave aberration function, interferometry is being used in a modified Twyman–Green arrangement [53].

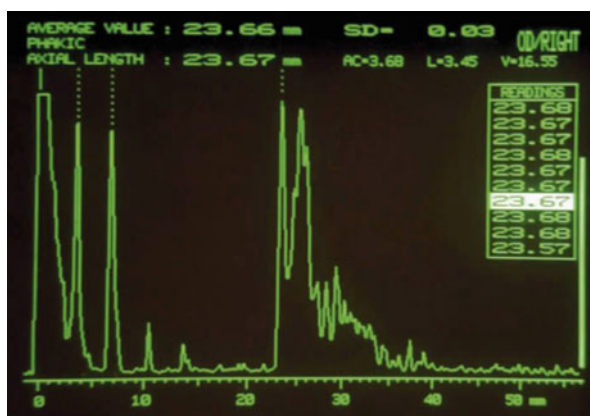


Fig. 2.4 A-scan ultrasonographer

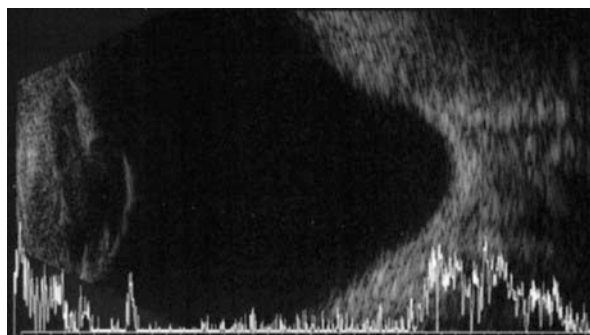


Fig. 2.5 B-mode ultrasonography

7 Optical Model

It is important to determine the optical model of the eye in a biomechanical model that includes an analysis of stresses and strains. These strains will alter eye refraction.

In the author's thesis [49] a three-dimensional optical model was developed taking into account the optics of thick lenses. The diopter power of each of the components in the complete refractive eye (cornea, aqueous humor, lens, vitreous, and retina) considering a paraxial theory assumed by the disk-based corneal topography (Placido) and keratometry was calculated [54]. This allowed increase accuracy in evaluating the results of refractive surgery simulation so as the procedure performed on the actual patient.

It is also important in the optical model considering the number of points acquired and interpolated in corneal topography and pachymetry. This will allow to generate the geometry of the biomechanical model and the precision of the structural analysis of stresses and strains, which, as previously stated, will determine the precision of the optical analysis post biomechanical changes in eye structure. In the author's thesis [49] data for mesh generation needed in structural finite element analysis are prepared by an interpolation by moving-least-squares [55] allowing the use of different types of corneal topographers (based and not based on Placido disks).

In postprocessing the point-to-point curvature is calculated on the anterior surface carrying a map of diopters, which simulate the corneal topography. An ophthalmologist would compare preoperative and postoperative topography (simulated). An estimate of the dioptric power of the refractive system of the eye is performed after the simulation, analyzing the outcome of refractive surgery with the desired results.

7.1 *Generation of Incisions*

Radial keratotomy and arcuate keratotomy were simulated. It was necessary to perform a model of the incision that affects the geometry of the corneal structure. The characteristics of the relaxing incisions are:

- Depth variation.
- Incision with the scalpel does not remove tissue.
- Not create perforations (not touch Descemet's membrane).
- The incision space is completely filled with scar tissue.
- The incision is perpendicular to the corneal surface.

8 Mechanical Models

Finite elements based on elastic, hyperelastic, and viscoelastic theories were implemented. Both small and large displacements and deformations are taken into account.

8.1 Elastic Model

A linear isoparametric solid element with geometric nonlinearity and linear elastic and isotropic material was implemented. The values of Young's modulus and Poisson's constant were taken from [41, 56]. The corneal orthotropicity was not initially considered because we assume that the stresses in the direction perpendicular to the corneal plane are negligible, compared to the stresses in that plane. These considerations were made following the work of Woo and Kobayashi [5].

8.2 Hyperelastic Model

In order to consider the nonlinearity materials described in the work of Woo and Kobayashi hyperelastic model was performed. The material models were implemented: (1) Blatz–Ko, for compressible hyperelastic; (2) Mooney–Rivlin, for quasi-incompressible; (3) Hart–Smith, for quasi-incompressible; (4) and a new exponential hyperelastic model developed in this thesis for human corneal tissue and other biological materials with high nonlinearity.

To adjust the models with experimental tests, tensile test on strips of cornea and inflation tests were used in intact eye. The new model was the only one capable of adjusting the intact cornea test in the inflated, i.e., beginning with IOP = 0, due to the highly nonlinear.

The materials in the test model of corneal inflation parameters, fitted using an axisymmetric model as a numerical optimization scheme via finite element method (inverse method). The parameters were varied in an iterative manner based on a nonlinear optimization algorithm originally implemented by R. Hooke and T.A. Jeeves [57]. The error function consisted of the mean square error between the experimental curve of corneal inflation and simulation analysis in FE.

8.3 Viscoelastic Model

To take into account the viscoelastic properties of the cornea and predict the response to medium term refractive surgery, finite element corneal model was

performed using a 3-element model (Zener type) in large deformations. The viscoelastic parameters were adjusted to experimental creep and dynamic tests with sinusoidal load on corneal strips.

9 Boundary Conditions

Given that the model of the cornea is a part of the complete structure of the eye, special considerations must be taken when defining the boundary conditions. If the spherical eye was considered, taking only the cornea in the model, it would be enough, as boundary conditions, to restrict the movement toward the sclera or to the rest of the eye.

But the cornea is aspherical, and the radius of curvature of the sclera is not equal to the radius of curvature of the cornea. The limbus is the transition zone between these radii of curvature. From the spatial reconstruction of topographic data, it is not possible to determine the geometry of limbus since the corneal topographer does not measure its curvature.

Following the work of Datye and Pinsky [37, 38], the cornea is allowed to rotate, considering that the collagen fibers are oriented circumferentially to this area.

10 Initial Conditions

Corneal deformation under the effect of relaxing incisions in the refractive surgery is caused by the intraocular pressure. Assuming that the intraocular pressure is constant before and after the operation performed, the effect is attributed to the change in thickness located in the incised area, causing a change in the stress of the affected tissue and a deformation on the initial state.

11 Summary

A number of studies have been undertaken in an attempt to characterize the mechanical properties of the cornea. The corneal biomechanics has been described by in vitro simple tension [4, 12, 13, 24, 58], inflation [5, 17, 20, 56, 59], and compression tests [14]. The biomechanical response of the cornea *in surgical procedures* has been described mostly for radial keratotomy by measuring local deformations [19, 40, 60]. Others have used finite element models with different assumptions regarding corneal geometry and material properties. Some have assumed that the cornea is a homogeneous linear elastic [42, 52, 61], nonlinear elastic [21, 45, 56, 60] solid, and nonhomogeneous membrane [38].

Attempts to verify the models have been done with inflations tests [56] in hydrated corneas and with local deformations [60] in normo-hydrated corneas. The relationship between corneal strain and intraocular pressure was found to be nonlinear, showing a typical stress-stiffening behavior. A material model by Woo et al. [5] has been used to account that nonlinearity [45, 56, 60].

The anisotropy of the cornea is evidenced by its microstructure as a reinforced composite with collagen fibers immersed in a jelly-like matrix of mucopolysaccharides. There have been attempts to account the anisotropy of the cornea, with transverse isotropy, but since the cornea is also nearly incompressible [14] violates the restrictions on the elastic constants [62]. Pinsky et al. modeled the anisotropy produced by the relaxing incisions in a thick membrane model. But local bending effects near the incision were found to be an important factor [19].

The hydration has a profound effect on the extensibility of the stroma [19], and viscoelastic properties have been measured in vivo after radial keratotomy [27]. A complete model of the cornea should take into account the poroelasticity, viscoelasticity, and anisotropicity of the cornea.

Hyperelastic models are proper for material and geometrical nonlinearities. Geometric nonlinearities appear in inflation tests as well as in refractive procedures like those involving the insertion of intrastromal rings. They are also suitable for further extension to anisotropy and inelasticity. There were attempts to use rubber-based hyperelastic models, like Mooney–Rivlin [33, 56] and Ogden [56], but they did not reproduce the high nonlinearity of the cornea.

In the next chapters it will be described a hyperelastic model that accounts for the nonlinearity of the cornea, both material and geometrical, and is suitable for viscoelasticity [63] and poroelasticity. Inflations tests [56, 17, 62] in hydrated and normo-hydrated corneas will be used to obtain the material parameters of the model and simulate and attempt to predict the behavior of relaxing incisions, ablation of the cornea and insertion of intrastromal ring segments to correct different ametropias (myopia, hypermetropia, astigmatism) and keratoconus.

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