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Review

Corneal thickness: measurement and implications

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Abstract

The thickness of the cornea was reported in more than 100-year-old textbooks on physiological optics (Helmholtz, Gullstrand). Physiological interest was revived in the 1950s by David Maurice, and over the next 50 years, this 'simple' biological parameter has been studied extensively. Several techniques for its measurement have been described and physiological and clinical significance have been studied. In this review, the different methods and techniques of measurement are briefly presented (optical, ultrasound). While the corneal thickness of many animals are the same over a considerable part of the surface, in the human cornea anterior and posterior curvature are not concentric giving rise to a problem of definition. Based on this the precision and accuracy of determining the central corneal thickness are discussed. Changes in corneal thickness reflects changes in function of the boundary layers, in particular the endothelial barrier. The absolute value of thickness is of importance for the estimation of IOP but also in diagnosis of corneal and systemic disorders. Finally it is discussed to what extent the thickness is a biometric parameter of significance, e.g. in the progression of myopia or in the development of retinal detachment.

Keywords: corneal thickness; parameter; ultrasound

1. Introduction

According to ancient literature the thickness of the human cornea is about 1 mm. This statement originated from post mortem anatomical measurements and corresponds to the thickness of the maximally swollen human cornea.

The first direct optical measurement of the thickness of the cornea of the living human eye was performed by Blix (1880). From measurements on ten eyes he concluded that the thickness was about 0·5 mm in young men. However, it was not until the middle of the last century that the study of the corneal thickness was taken up and more simple instruments were devised. This interest arose not least from the studies of David Maurice (1957) on transparency of the corneal stroma, which implied a control of interfibrillary distance, water content and corneal thickness. David Maurice had designed a useable pachymeter already in 1951 (Maurice and Giardini). Since that time an increasing number of studies using corneal thickness as outcome parameter have been published.

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2. Basic implications of corneal thickness measurements

The cornea swells if the epithelial or endothelial layers are removed or their biological activity is reduced by cooling of the tissue. The corneal thickness increases due to a net water influx and, therefore, depends upon the hydration of the corneal stroma. Under many conditions, experimental as well as clinical, the corneal thickness is an indicator for the endothelial pump and barrier function. The endothelium mediates the flux of water and solutes across the posterior corneal surface and thereby maintains corneal thickness and transparency. The barrier is located to the apical cell junctions. These junctions increase during development, in good agreement with the greater corneal thickness in human newborns compared to adults (Ehlers et al., 1976).

The biological variability in corneal thickness between otherwise normal individuals is believed to be caused by variations in the amount of corneal stromal tissue: collagen fibrils and interfibrillary substance. In healthy individuals, corneal thickness is, therefore, a measure of tissue mass and corresponding biomechanical parameters such as bending rigidity. In diseased corneas, an increased thickness is only known to be caused by increased corneal hydration.

A decreased corneal thickness is seen in many corneal dystrophies and secondary to ulcerative inflammatory diseases of various origins. In these cases, loss or redistribution of corneal tissue mass is thought to be the cause of decreased thickness.

The corneal thickness is, therefore, an interesting dimension, not only regarding physiology and pharmacology but also the variation of the 'normal' thickness is of diagnostic, epidemiological and pathological importance. Therefore, a considerable interest is attached to its precise and accurate measurement.

3. Optical pachymetry

The optical principles that have been applied to the measurement of the thickness are: (i) focussing on anterior and posterior surface (successively or simultaneously); (ii) using specular reflexes from anterior and posterior corneal surface (obtained successively or simultaneously) (Fig. 1); (iii) using light scattered from optical section to identify anterior and posterior boundary (Fig. 2). The principles together with a review of early literature was presented by Ehlers and Hansen (1971).

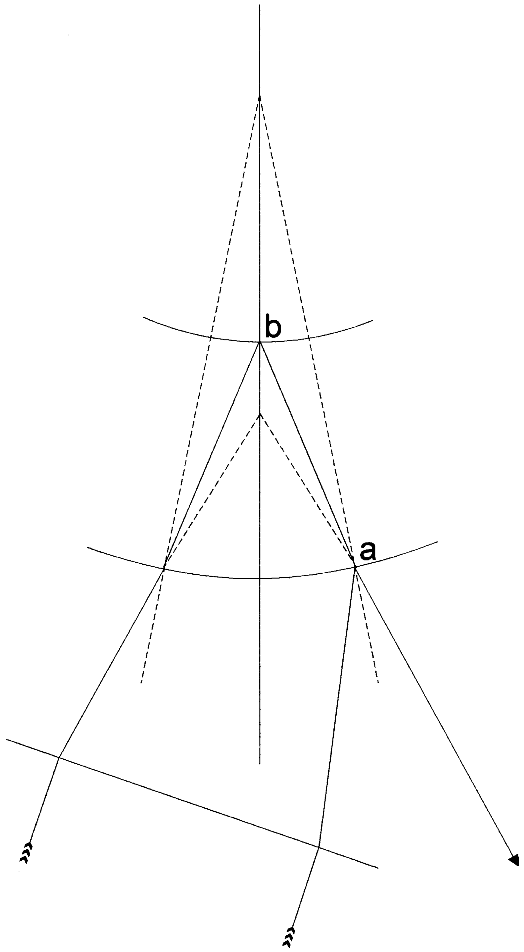

Fig. 1. Principle of specular pachymetry. (a) and (b) indicate specular reflections from anterior and posterior corneal surface (Maurice and Giardini, 1951).

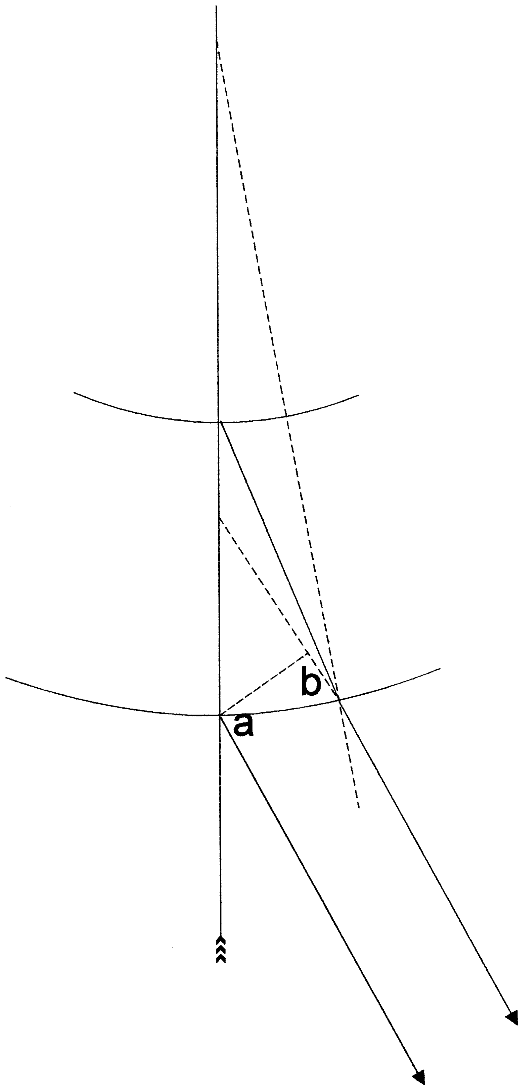

Fig. 2. Principle of optical pachymetry based on scatter. (a) and (b) indicate scatter reflections from anterior and posterior corneal surface.

The apparatus of Maurice and Giardini (1951) was based on principle ii and was an attachment to the 'old' Haag–Streit slit-lamp 360. In 44 subjects they found a mean value of 0·507 ± 0·0042 mm (S.E.M, $N = 44$). The precision of the method was estimated by taking 25 readings in one position in one eye, resulting in a standard deviation of 0·011 mm (var. coeff. 2·2%). Using a similar specular method Olsen and Ehlers (1984) found in a random sample of 115 subjects a normal distribution of the corneal thickness with an average value of 0·515 ± 0·0031 mm (S.E.M., $N = 115$). The influence of physiological variation in corneal curvature and index of refraction was shown to cause only insignificant errors in the estimate of thickness.

Over the last decades the most widely used optical pachymeter has been the attachment I to the Haag–Streit slit-lamp 900 applying the light scatter principle described by Jaeger (1952). The thickness of the optical section is estimated by an image doubling where epithelium and endothelium are aligned. The relation between the apparent thickness (optical section) and the real corneal thickness depends on the anterior curvature of the cornea and, ideally, measurements have to be corrected properly. With this instrument Hansen (1971) found a mean value of 0·520 mm ± 0·0021 (S.E.M., $N = 76$). The precision of the method calculated from five readings in each eye of 37 subjects was found to be 0·008 (S.D.). Olsen et al. (1980a,b) studied the sources of error in this method. Interobserver errors up to 0·02 mm were found, while intraobserver errors amounted only to 0·005–0·006 mm (S.D.) between consecutive readings. Changes in corneal thickness, measured by the same observer can, therefore, be determined with great accuracy.

Commercially available computerised specular microscopes are available today. The S.D. for repeated measurements have been found to be 0·008 mm (Tam and Rootman, 2003).

4. Interferometry

A potentially very precise method for estimating thickness and distances of transparent structures is optical interferometry. The accuracy of the instrument is related to the speed of light within the cornea, and the plane where a change in speed of light gives rise to a back-reflection. Green et al. (1975) already showed the applicability of the principle to measure corneal thickness. While optical coherence tomography for retinal studies was developed several years ago, the simple interferometric approach to measure central corneal thickness (CCT) has only recently been commercialised by Haag–Streit and described as optical low-coherence reflectometry (Wälti et al., 1998, Böhnke et al., 1999).

5. Ultrasonic pachymetry

Where interferometry is based on light, ultrasound distance measuring techniques are based on the speed of sound. The time lap between an ultrasound emitted pulse and the reflected echo from an acoustic interface is, through the velocity of sound of the media of interest, directly related to the thickness of the tissue. Echoes result from changes in the speed of sound within the tissue.

In the 1980s corneal refractive procedures were introduced. In radial and other types of keratotomy procedures, it was believed essential to measure the corneal thickness in order to avoid perforations of the cornea. Attempts were also made to dosage the effect of the procedure by varying the relative depth of the incisions. Due to considerable inter-observer variability in traditional optical pachymetry, ultrasound pachymetry became popular, also because measurements of peripheral corneal thickness could be obtained with apparent ease. In ultrasound pachymetry, the probe applanates the anterior corneal surface. Squeezing away of the tear film and some compression of the epithelial cells are to be expected by the manoeuvre. The exact location within the corneal borders that generates the major echo is not clear.

The literature includes numerous comparative studies of optical and ultrasound central pachymetry. Generally, smaller inter-observer variation is achieved with ultrasound pachymetry, whereas the actual correspondence between the two methods varies greatly, possibly mainly depending on the make of the ultrasound device. Today, the precision (S.D. of repeated measurements) by ultrasound pachymetry may be as low as 0·004 mm (Tam and Rootman, 2003).

6. Recent developments

From the late 1980s computerised devices for measuring corneal topography were developed. These machines are mainly based on analysis of Placido disk images, while one apparatus, the Orbscan, uses a scanning slit principle to directly measure the anterior shape of the cornea. The scanning slit also allows visualisation of the apparent corneal thickness towards the periphery. Thus, with proper correction for the local curvature of the cornea, the real thickness can, in theory, be computed. Methodological studies with the Orbscan show high reproducibility (Marsich and Bullimore, 2000). The accuracy of the technique and the dependence of the measurements on the actual anterior curvature has not been verified.

The Humphrey ultrasound biomicroscope (UBM) is a B-mode high-frequency (50 MHz) scanner which can resolve structures within the anterior segment of the eye. The probe operates in a water-bath in front of the cornea and the anterior as well as he posterior corneal borders are to be identified. The reproducibility of the device has been studied extensively (Urbak, 1998) and CCT measurements can be repeated with a coefficient of variation less than 3·8%.

Recently an instrument called arc-scanning very high-frequency digital ultrasound has become available. The principle was developed throughout the 1990s at Cornell University Medical College. Ultrasonic waves with a frequency up to several hundred Hertz are emitted and fine details within the corneal tissue can be resolved. The principle has been used to study epithelial thickness changes after corneal refractive surgery. Repeatability studies have shown that epithelial thickness can be measured with a standard deviation of 0·002 mm (Reinstein et al., 1994).

Ophthalmic optical coherence tomography was originally used for visualising intra-retinal structures (Puliafito et al., 1995). A modified apparatus is available for imaging a profile of the corneal thickness (Muscat et al., 2002). Pachymetry can be performed on the generated images, and the inter-operator reproducibility is high.

7. Experimental devices

Confocal or specular reflex scanning through the corneal tissue with simultaneous measurement of the back-scattered light level by a photo-multiplier has been used in vitro to study not only the thickness of the cornea (Klyce and Maurice, 1976), but also the hydrodynamic distribution behaviour of fluorescein (Maurice and Srinivas, 1994). Later, confocal through-focussing microscopes equipped with a image grabber have been used in vivo to quantify the thickness of layers within the cornea and the back-scatter properties of their constituents (Li et al., 1997). These devices have mainly been custom built for experimental studies.

8. Definition of central corneal thickness

As the radial distance between two concentric spheres the definition of CCT is self-evident. This may be the situation in some animals but regarding the human eye, it would rather be an exception. The anterior and posterior surfaces of the cornea are not concentric and at least the anterior is not spherical. Several possible 'definitions', therefore, exist (Fig. 3).

Measuring the thickness along the line of sight introduces a systematic right–left difference. Which reading will be the thicker depends upon whether the light comes from left or right side. The difference relates to the angle Kappa between the optical axis and the line of sight. The difference 'disappears' by securing a perpendicular incident light (Mishima and Hedbys, 1968, Ehlers and Sperling, 1977).

9. Accuracy and precision in CCT measurements

Gaussian statistics assume the existence of an objective distance in describing the accuracy. Regarding the cornea the tearfilm is known to drain between two blinks causing a constant decrease in thickness. With a film thickness of less than 10 μm this change is hardly more than a few microns and thus of little practical importance. Another source of error arises from identifying the exact location of the posterior boundary. In specular reflection methods this could be the anterior or the posterior endothelial aspect, introducing an 'error' of around 5 μm.

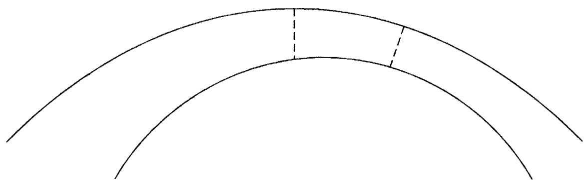

Fig. 3. Exaggerated sketch of non-aligned, decentered, and aspheric surfaces of the cornea. Dashed lines indicate possible locations for measurement of central corneal thickness.

Theoretically, thus, it makes no sense to give values for corneal thickness more precise that ±1–2 μm (0·001–0·002 mm). Nissen et al. (1991) compared optical and ultrasonic pachymetry in normal and oedematous corneas. For normal corneas there was no statistically significant difference, whereas the oedematous cornea was estimated significantly thinner by ultrasound (0·602 versus 0·618 mm).

10. IOP–CCT correlations

The principle of the Goldmann applanting tonometer is highly dependant on a constant relationship between the bending rigidity of the cornea and the surface tension between the cornea and the tonometer head. Goldmann found that, on average, these forces were balanced at an applanation diameter of 3·06 mm which also nicely corresponded to an applanation force of 0·1 g per mmHg of intraocular pressure (Goldmann and Schmidt, 1957). Goldmann's design eliminated the importance of individual variations in ocular rigidity which were critical in the Schiøtz indentation tonometry method (Gloster, 1966). For two decades applanation tonometry was believed to be independent of corneal factors, at least from a clinical viewpoint. In 1975 it was demonstrated experimentally that the reading in applanation tonometry did depend on the CCT, to such an extent that it could have clinical implications in glaucoma diagnosis. The pressure is measured too high in non-edematous thick corneas, and too low in thin corneas and in edematous corneas (Ehlers et al., 1975).

With improved diagnostic and therapeutic possibilities in glaucoma, the impact of CCT variations on tonometry measurements has been revived (Whitacre and Stein, 1993). A recent meta-analysis of possible association between CCT and IOP measures of 133 data sets, regardless of the type of eyes assessed, revealed a statistically significant correlation; a 10% difference in CCT would result in a 3·4 ± 0·9 mmHg difference in IOP. The association was most pronounced in eyes with acute onset disease, but negligibly in healthy eyes (Doughty and Zaman, 2000).

In the normal cornea, thickness is possibly a good estimator for the bending rigidity of the tissue. For corneal surgeons, however, it is clinically evident that the bending rigidity is also dependent on the age of the subject. As corneal thickness does not change much with age (Olsen and Ehlers, 1984), additional studies are needed to elucidate how age–in addition to corneal thickness–affects the reading of applanation tonometers.

Corneal hydration also influences readings in applanation tonometry. In acute changes in corneal hydration, the tissue mass is not changed and some influence of corneal hydration on tonometry readings has been observed (Whitacre and Stein, 1993). The relation has not been clearly described and preliminary studies suggest that the relation may be highly non-linear (Maurice, 1999).

In recent years non-invasive pneumotonographic measurements of intraocular pressure has become popular. Preliminary studies suggest an even larger effect of corneal thickness (bending rigidity and corneal hydration) on the readings of pneumo-tonometers (Graf, 1991).

11. Biomechanics and corneal thickness

This issue is very interesting in relation to understanding the pathogenesis of corneal diseases, especially keratoconus, and at least in a quantitative matter, when it comes to surgical and refractive procedures on the corneal tissue. There is some empirical evidence that older patients respond more to incisional refractive procedures than younger patients (Lynn et al., 1987) and that the variability of laser refractive procedures are age depending (Huang et al., 1999). Experimental studies have revealed that Descemet's membrane is much more elastic than the corneal stroma (Jue and Maurice, 1986) and that corneal hydration greatly affect the outcome of incisional refractive procedures (Hjortdal, 1998).

Advanced, physiologically based individual finite-element mathematical analysis of the response of the cornea to well defined force applications may, at some future point, be able to accurately describe the behaviour of the individual cornea to refractive surgical procedures (Chang et al., 1993).

12. Corneal and systemic disorders

Measurement of the corneal thickness is of importance in the diagnosis of macular dystrophy (Groenouw II). The reduced thickness (0·380–0·435 mm, Ehlers and Bramsen, 1978) can probably be related to the pathological composition of the stromal polysaccharides. The swelling pressure at the observed thickness seems to be normal (unpublished observation). Also systemic disorders (e.g. Osteogenesis imperfecta) may be reflected in the corneal thickness which is reduced to around 0·40 mm.

Corneal pachymetry has a particular position in the postoperative control of a graft. The thickness in the first postoperative days reflects the inflammatory condition of the eye, as well as the surgical trauma. During the following month thickness decreases steadily to reach a minimum after about 6 months. Normal thickness is approached over the next 1–2 years. Changes in endothelial permeability, notably rejection episodes can be clearly seen (Ehlers, 1974).

13. Corneal refractive surgery

Corneal excimer laser procedures for myopia–photorefractive keratectomy, LASIK, and LASEK–all reduce the CCT. Less corneal tissue is available for bearing the intraocular pressure, and the stress level on the corneal fibrils increase. In acute pressure loading studies of enucleated human eyes and in the eyes of living patients, the elastic properties of the corneal tissue is only altered negligibly by excimer laser treatment (Hjortdal, 1998). It is, however, evident that corneal ectasia can develop in the months or years after a LASIK procedure, especially if the amount of tension bearing collagen fibrils become small (Seiler et al., 1998). Although the mechanism of this keratoconus-like complication is poorly understood, corneal thickness measurement before excimer laser surgery has become mandatory in clinical practice.

14. CCT as biometric parameter

The corneal thickness seems to be a relatively stable value for the single person. The normal adult value is reached during the first year or two and the age decrease is small. The growth of the eye during myopinisation has not been studied in detail.

The growth of the eye might suggest a growth in thickness, an expansion of the eye would favour a thickness decrease with degree of myopia. Even if mean values are not different, a larger scatter in myopia could suggest a bipartition of the population and thickness might be a prognostic factor. The new objective pachymeters seem to by accurate and precise enough the answer these questions.

Similarly, early studies suggest that the cornea is thin in retinal detachment. Again objective data are needed to give an answer (Hansen et al., 1971).

15. Final remarks

Since David Maurice introduced corneal thickness as an interesting parameter in experimental corneal physiology the number of publications relating to this little dimension of around 0·5 mm has been overwhelming. This is, however, well understood. Changes in this dimension is an important indicator for acute ocular diseases. The absolute value of the thickness may tell something about chronic conditions in the eye and in the body. Many of the older studies were done with subjective methods. One can hope that the new instruments, whether optic or ultrasonic will provide quantitative data which will increase and document our knowledge still further.

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