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***Review on Corneal hysteresis and its Measurement in vivo using
Ocular Response Analyzer***

Essay

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Abstract

Corneal hysteresis is an important indication of the biomechanical properties of the cornea it is an indicator of viscous damping in the cornea during inward and outward applanation pressure events that is the ability of the tissue to absorb and dissipate energy, a property that is determined by the visco-elastic properties of the corneoscleral shell.

Abnormalities in corneal hysteresis have been detected in a variety of corneal diseases including keratoconus, fuch's dystrophy and post lasik surgeries; it is possible to predict which patients stand the greatest risk for postoperative ectasia and other corneal pathologies.

Corneal hysteresis can be measured in vivo using Ocular Response Analyzer.

Key words:

Corneal hysteresis, Ocular Response Analyzer.

List of abbreviations

CCT	central corneal thickness
CH	corneal hysteresis
CRF.....	corneal resistance factor
GAT.....	Goldmann applanation tonometer
GAG	glycosaminoglycan
IOPG.....	Goldmann-Related IOP Measurement
IOP.....	Intraocular Pressure
IOPCC.....	Corneal Compensated IOP
KC.....	Keratoconus
LASIK.....	laser in situ keratomileusis
NTG.....	Normal Tension Glaucoma
OHTS.....	Ocular Hypertension Treatment Study
ORA.....	Ocular Response Analyzer
POAG.....	Primary Open Angled Glaucoma
PRK	Photo Refractive keratotomy
TCA cycle.....	the tricarboxylic acid cycle

Chapter (1)

Anatomy of the cornea

Anatomy of the cornea

The cornea is a transparent avascular tissue with a smooth, convex surface and concave inner surface, which resembles a small watch-glass. The main function of the cornea is optical; it forms the principal refractive surface, accounting for some 70% (40-45 dioptres) of the total refractive power of the eye. Refractive requirements are met by the regular anterior curvature of the cornea and the optically smooth quality of the overlying tear film. The resistance of the cornea, which provides a protective layer and resists the ocular pressure, is due to the collagenous components of the stroma. Transparency of the corneal stroma is achieved by the regularity and fineness of its collagen fibrils and the closeness and homogeneity of their packing. Water is constantly pumped out of the cornea by its posterior layer, the endothelium. This maintains the optical homogeneity of the corneal layers and prevents swelling and clouding. The cornea is thus an evolutionary compromise, being a multicomponent, thick, tough avascular tissue with a smooth surface and uniform curvature. (*Bron et al., 1997*)

In front the cornea appears elliptical, being about 11.7 mm wide in the horizontal meridian and 10.6 mm in the vertical meridian in adults. (*Maurice, 1970*)

The posterior surface of the cornea appears circular, about 11.7 mm in diameter. This difference is due to the greater overlap of sclera and conjunctiva above and below than laterally. The axial thickness of the cornea is about 0.52 mm with a peripheral thickness of 0.67 mm. (*Bron et al., 1997*)

The cornea forms part of what is almost a sphere, but it is usually more curved in the vertical than the horizontal meridian, giving rise to astigmatism 'with

the rule'. In the optical zone, the radius of curvature of the anterior surface is about 7.8 mm and that of the posterior 6.5 mm, in adult males. The natural and normal cornea is generally prolate, with steeper curvature centrally and relatively flatter peripherally. (*Bron et al., 1997*)

The corneal structure behind the precorneal tearfilm consists of five tissue layers including the epithelium, Bowman's Layer, stroma, Descemet's membrane and endothelium. (*Bron et al., 1997*)

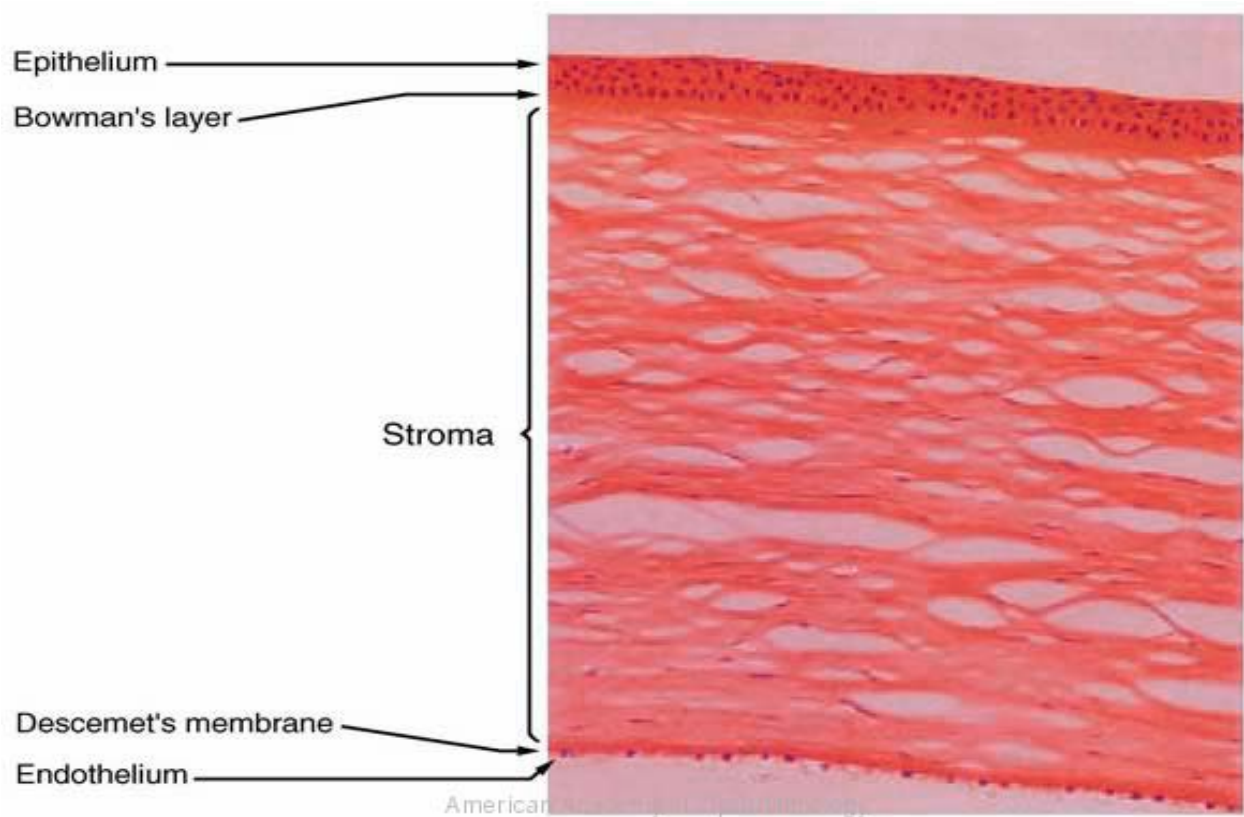


Fig (1.1). Histological view of the corneal layers
From **American academy of ophthalmology (2003)**(*Tsubota K et al ,.92*)

Corneal epithelium

The corneal epithelium is stratified, squamous and non-keratinized. It is continuous with that of the conjunctiva at the corneal limbus, but differs strikingly in possessing no goblet cells. The epithelium is 50-90 μm thick and consists of five or six layers of nucleated cells. (*Maurice. 1970*)

The deepest of these, **the basal cells**, stand in a palisade like manner in perfect alignment on a basal lamina. They form the germinative layer of the epithelium, continuous peripherally with that of the limbus. These basal cells are columnar (10 μm wide and 15 μm tall), with rounded heads and flat bases. Each nucleus is oval and oriented parallel to the cell's long axis. (*Mathers et al., 1992,*)

The second epithelial layer (the '**wing**' or '**umbrella**' cells) consists of polyhedral cells, convex anteriorly, which cap the basal cells, and send processes between them. The long axes of their oval nuclei are parallel to the corneal surface. (*Tsubota et al. ,1992*)

The next two or three layers are also polyhedral and become wider and increasingly flattened towards the surface. The surface cells have the largest surface area and being greater in the periphery (e.g. 850 μm above) compared to centrally (560 μm). The most superficial cells may be as wide as 50 μm and 4 μm in depth; they retain their nuclei, and do not show keratinization. Their flattened nuclei project backwards, leaving their surface perfectly smooth. (*Tomii et al.,1994*)

The most superficial cells of the epithelium are mostly hexagonal and firmly attached to each other at relatively straight cell boundaries. They exhibit surface microvilli or microplicae..(*Tomii et al.,1994*)

The plasma membranes of contiguous cells interdigitate with their neighbors with an intervening space of no more than 20 nm. Adhesion is achieved by numerous desmosomes, the basal cells are connected to one another also by desmosomes and to the underlying basal lamina by hemidesmosomes.(*Tomii et al.,1994*)

The entry of water and small molecules from the stroma is not restricted, which permits the occurrence of epithelial oedema, with widening of the intercellular space, for instance when the endothelial pump fails.(*Foster et al.,2004*)

Basal lamina

The basal lamina is secreted by the basal cells, which also synthesize the hemidesmosomal structures concerned in attachment of epithelium to the lamina .The basal lamina is an irregular zone (0.5-1 μm wide) of granuloamorphous and filamentary materials. A deep osmiophilic lamina densa (30-60 nm) and a superficial lamina lucida (24 nm) are distinguished ultrastructurally.(*Snip et al.,1980*)

It is traversed by electron-dense anchoring fibrils which form narrow bundles which insert into the subjacent stroma or Bowman's layer, terminating in anchoring plaques. This arrangement accounts for the tight adherence of the basal epithelium to subjacent cornea.(*Gipson et al .,1989*)

Bowman`s layer (anterior limiting layer)

Bowman's layer is a narrow, acellular homogeneous zone, 8-14 μm thick, immediately subjacent to the basal lamina of the cornea epithelium. (*Bron et al., 97*)

Ultrastructurally Bowman's layer consists of a felted meshwork of fine collagen fibrils of uniform size, lying in a ground substance. Fibril diameter (24-27 nm) is less than that of substantia propria. In the posterior region of this layer the fibrils become progressively more orderly in their orientation, blending and interweaving with the fibrils of the anterior stroma. Here and there anteriorly, bundles of the stromal lamella insert into the Bowman's layer. The compacted arrangement of the collagen confers great strength, to this zone. Bowman's layer is relatively resistant to trauma, both mechanical and infective; once destroyed it is not renewed but is replaced by coarse scar tissue. It is perforated in many places by unmyelinated nerves in transit to the corneal epithelium. (*Muller et al., 2001*)

Stroma (substantia propria)

The stroma, about 500 μm thick, consists of regularly arranged lamellae of collagen bundles. They lie in a proteoglycan ground substance together with a small population of cells, **the keratocytes**, which occupy 2.5-5% of stromal volume and are responsible for synthesis of the stromal collagen and proteoglycan during development and maintaining it thereafter. (*Bron et al., 1997*)

Transparency of the corneal stroma depends particularly on the degree of spatial order of its collagen fibrils which are narrow in diameter and closely packed in a regular array. The collagen fibrils themselves are weak scatterers, since their fibril diameter is less than the wavelength of light, and fibril refractive index is close to that

of the ground substance. There is little variation in fibril diameter and separation between the anterior and posterior cornea. (*Muller et al.,2001*)

The stromal fibrils are further organized into bundles, or lamellae, of which there are approximately 300 in the central cornea and 500 close to the limbus. The posterior lamellae course directly across the full width of the cornea without a break, having their origins in fibers which wind around the limbus at the corneoscleral junction or, have a pseudocircular organization at the limbus, forming the ligamentum circulare corneae. (*Muller et al.,2001*)

The anterior and posterior stroma differ in specific ways. In general the posterior stroma is more ordered, more hydrated, more easily swollen and has a lower refractive index than the anterior stroma. The posterior lamellae are also wider and thicker (100-200 μm wide and 1.0-2.5 μm thick) than the anterior (0.5-30 μm wide and 0.2-1.2 μm thick). There are also differences in keratocyte morphology. It has been also established that the posterior lamellae of the human corneal stroma are arranged parallel to the plane of the corneal curvature. (*Muller et al.,2001*)

In the anterior stroma there's a marked anteroposterior lamellar interwave in which lamellae can be shown to pass obliquely from one layer to another, sometimes passing across several lamellae to reach their destination. A proportion of the anterior lamellae are known to be inserted directly into Bowman's layer and it has been suggested that the latter contribute to the formation of the anterior corneal mosaic. It has also been found that the anterior stroma 100-120 μm deep to Bowman's layer, is responsible for the structural stability of this region of the cornea, a feature which is of importance to refractive surgery