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## List of Abbreviations

Abbreviation	Meaning
(ACD) .....	Anterior chamber depth
(AQP) .....	Aquaporins
(BSS) .....	Balanced salt solution
(CCIs) .....	Clear corneal incisions
(CCT) .....	Central corneal thickness
(CDE) .....	Cumulative dissipated energy
(CDVA) .....	Corrected distance visual acuity
(CoV) .....	Coefficient of variation
(CP) .....	Conventional phacoemulsification
(EC) .....	Endothelial cell
(ECC) .....	Endothelial cell count
(ECCE) .....	Extracapsular cataract extraction
(ECD) .....	Endothelial cell density
(EPT) .....	Effective phacoemulsification time
(FLACS) .....	Femtosecond laser assisted cataract surgery
(FSL) .....	Femtosecond laser
(ICCE) .....	Intacapsular cataract extraction
(ICCE) .....	Intacapsular cataract extraction
(LASIK) .....	Laser assisted in situ keratomileusis
(LCS) .....	Laser cataract surgery
(LRIs) .....	Limbal relaxing incisions

Abbreviation	Meaning
(Nd: YAG) .....	Neodymium-doped yttrium aluminum garnet
(NSAIDs) .....	Non-steroidal anti-inflammatory drugs
(OCT) .....	Optical coherence tomography
(OVD) .....	Ocular viscoelastic device
(PMMA) .....	Polymethyl methacrylate
(RCTs) .....	Randomized controlled trials
(SIA) .....	Surgically induced astigmatism
(TCCI) .....	Temporal clear corneal incision
(UST) .....	Ultrasound time

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# Effect of Femtosecond Laser Assisted Cataract Surgery on Corneal Endothelium: A Comparative Study

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## **Thesis**

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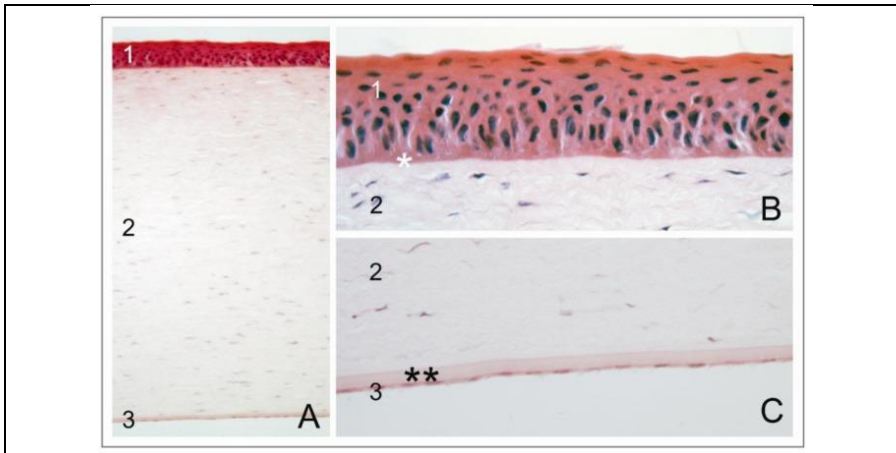
# **FUNCTIONAL ANATOMY OF**

## **CORNEAL ENDOTHELIUM**

### **The Cornea:**

The cornea is a transparent tissue with a refractive capacity of about 43 diopters that allows light to enter the eye and evoke a visual sensation in the retina. It is a bradytrophic tissue, meaning that it is avascular and not nourished via the blood system, but subsists on tear film and aqueous humor (*Brubaker, 1982*).

The cornea has a dome-shaped structure with a strictly layered architecture (**Figure 1**) (*Nishida and Saika, 2011, DelMonte and Kim, 2011*).



**Figure 1 :** Structure of the human cornea

(A) The cornea is composed of three cellular layers: (1) epithelium; (2) stroma; and (3) endothelium; (B) The epithelial layer resides on Bowman's membrane (\*); and (C) the endothelial layer resides on Descemet's membrane (\*\*).

Its average central thickness ranges from 530  $\mu\text{m}$  to 550  $\mu\text{m}$  (*Doughty and Zaman, 2000*) and increases to an average peripheral thickness of up to 670  $\mu\text{m}$  (*Funderburgh, 2010*). The anterior cornea is covered by a stratified squamous epithelium, which produces mucins to retain the tear film. Epithelial progenitor cells reside in niches at the anterior corneal limbus and ensure a continuous regeneration of the epithelium. These limbal stem cells proliferate and migrate centripetally, thereby stratifying and differentiating (*Sun and Lavker, 2004*).

The basal epithelial cells reside on Bowman's membrane, a condensed layer comprised of mainly collagen type I that cannot regenerate once it is destroyed. This membrane is penetrated by sensitive nerve fibers that form a subepithelial plexus in the central cornea (*Patel and McGhee, 2009*). The corneal stroma makes up to about 90% of the corneal thickness and is predominantly composed of collagen type I layers. These layers are interspersed with keratocytes that produce mainly proteoglycans and collagen. The collagen fibers are arranged in parallel in lamellae, and the direction of fibers in neighboring lamellae is mostly perpendicular (*Von der Mark and Park, 2013*).

Corneal avascularity and the lattice structure of stromal collagen fibers contribute to corneal transparency. Hydration of the corneal stroma plays a major role in maintaining this transparency, as glycosaminoglycan side chains of the proteoglycans, such as keratan sulfate, dermatan sulfate and chondroitin sulfate, exert a high swell pressure due to their water binding capacity. Excessive fluid imbibition by the stroma, usually due to a dysfunction in the corneal hydration regulatory system, can lead to corneal edema with haze or opacification and can eventually result in blindness. The posterior side of the corneal stroma is lined by Descemet's membrane,

the basal membrane of the posterior epithelium of the cornea, the corneal endothelium. Descemet's membrane can grow up to 10–12  $\mu\text{m}$  in thickness and is mainly comprised of collagens type IV and VIII (*Von der Mark and Park, 2013*), but does also contain fibronectin, vitronectin and various laminins (*Kabosova et al., 2007*).

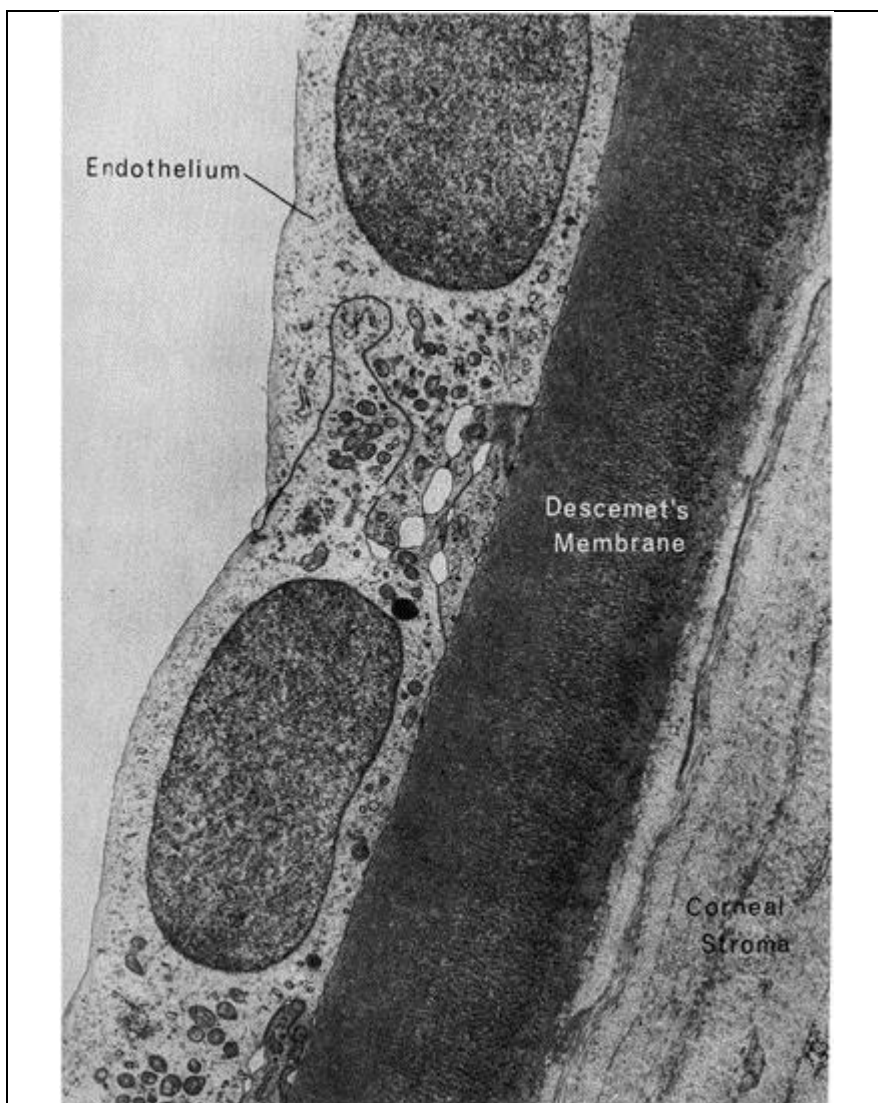
This membrane adheres only weakly to the stroma and can be detached (*McGowan et al., 2007*).

## Corneal Endothelium:

The corneal endothelium is a monolayer of hexagonal, squamous cells lining the posterior cornea. Contrasting to the anterior epithelium, the posterior corneal endothelium cannot be regenerated, although limited regeneration has been observed in some cases after graft failure in younger patients, and a report suggests that a minor regenerative capacity may exist in the utmost periphery in close proximity to the trabecular meshwork (*McGowan et al., 2007*).

The endothelium is covering the posterior surface of Descemet's membrane and is in contact with the aqueous humor (*DelMonte and Kim, 2011*) (**Figure 1**). The main function is to regulate the hydration state

through an active ATP and biocarbonate-dependent pump; thereby providing transparency to the cornea, which allows the eye to perform its visual functions (*Krachmer et al., 2005*). It is also an important system for the passage of nutrients and waste removal through simple diffusion, facilitated diffusion, and active transport mechanisms (*Bonanno, 2003*).



**Figure 2 :** Electron micrograph of corneal endothelium underlying Descemet's membrane of the human cornea. (*Zavala et al, 2013*)

The corneal endothelium is the cell layer with the lowest mitotic activity (*Joyce et al., 2002*). Given the importance of its function, damage to the

endothelium is potentially more serious than that to the other corneal layers and can result in cell loss and irreversible damage to the endothelial cytoskeleton, which ultimately affects the visual function (*Mehta and Malik, 2006*).

## Physiology:

The corneal endothelium consists of a 4- $\mu\text{m}$  thick monolayer of polygonal, mostly hexagonal cells. In the adult, the average cell density is  $\sim 3000 \text{ cells/mm}^2$  and the percentage of hexagonal cells is about 75% (*Wörner et al., 2011*). The density of corneal endothelial cells and their surface change throughout life. From the second to the eighth decade, the cell density declines to about  $2600 \text{ cells/mm}^2$  and the percentage of hexagonal cells decreases to  $\sim 60\%$ . The central endothelial cell density decreases at an average rate of 0.6% per year (*Bourne et al., 1997*).

To preserve ocular transparency, endothelial cell density must remain above a critical level, usually between 400 and  $500 \text{ cells/mm}^2$  (*Joyce, 2012*). Adjacent cells communicate through gap junctions and tight junctions, whereas the basal surface is adhered to Descemet's membrane by hemidesmosomes (*Fischbarg and Maurice, 2004*). Tight junctions (ZO-1) are