Corneal Densitometry Changes after Epithelium-Off Corneal Collagen Crosslinking

Thesis

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Karim Nasr Eldin Abbas

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Abb.	Full term
ALL	Anterior limiting lamina
CACXL	Contact Lens-Assisted Collagen Cross-Linking
CL-ACXL	Continuous-light accelerated corneal collagen cross linking
CXL	Corneal collagen cross-linking
D	Diopter
DALK	Deep Anterior Lamellar Keratoplasty
ECM	Extracellular matrix
EDTA	Ethylenediaminetetraacetic acid
Epi-off	Epithelium-off
Epi-on	Epithelium-on
GSUs	Gray-scale units
HM	Highly myopic
ICRS	Intracorneal ring segments
I-CXL	Iontophoresis
KC	Keratoconus
KP	Keratoplasty
PK	Penetrating keratoplasty
PL-ACXL	Pulse-light accelerated corneal collagen cross linking
PLL	Posterior limiting lamina
PMMA	Polymethyl methacrylate
PTK	Phototherapeutic Keratectomy
SRAX	Relative skewing of the steepest radial axes
UVA	Ultra Violet A

INTRODUCTION

Keratoconus (KC) is a non-inflammatory bilateral progressive but asymmetrical disease. Described as corneal ectasia, thinning, gradual corneal protrusion and irregular astigmatism ***(Rabinowitz, 1998)***. It usually starts during puberty with 75% of cases diagnosed before the age of 25 years ***(Kennedy et al., 1986)***.

Pentacam HR has helped us to detect early topometric and posterior corneal changes in subclinical and definite Keratoconus cases hence facilitating early diagnosis ***(Khan, 2016)***.

Corneal cross-linking (CXL) has been described as the only modality in halting the disease progression over the past decade ***(Alió et al., 2015)***, by using Riboflavin eye drops and ultraviolet A UVA light this creates bonds between corneal collagen fibers in the stroma ***(Ho et al., 2009)***. Cross-linking has been shown to generate various effects in the cornea such as increased stiffness, changes in biomechanical and bioelastic behavior of corneal collagen tissue and different visual, refractive, topographic and abberometric changes ***(Meek and Hayes, 2013)***.

Variant protocols were conducted with variability in the riboflavin used and UV exposure time ***(Wollensak et al., 2003)***.

Corneal densitometry enables the objective assessment of corneal clarity. The total corneal densitometry measured with Scheimpflug corneal topography is the sum of epithelial, stromal, and endothelial light scattering. The anterior superficial corneal

epithelial cell layer and the corneal endothelium are the major sources of light scatter, while corneal stroma retains low scattering due to regular arrangement of collagen fibrils and to the precise organization of the extracellular matrix ***(Otri et al., 2012)***.

Aim of the Work

To investigate the changes in the values of corneal densitometry using the Pentacam Scheimpflug after epithelium-off CXL.

Chapter 1

ANATOMY OF CORNEA

The cornea is a transparent avascular tissue that acts as a structural barrier and protects the eye against infections ***(DelMonte and Kim, 2011)***. Along with the tear film, it provides a proper anterior refractive surface for the eye. The cornea contributes to two-third of the refractive power of the eye.

The cornea is horizontally oval, measuring 11–12 mm horizontally and 9–11 mm vertically ***(Fares et al., 2012)***. The cornea is convex and aspheric. The anterior curvature is 7.8 mm and the posterior curvature is about 6.5 mm. The cornea contributes to about 40–44 Diopter (D) of refractive power and accounts for approximately 70% of total refraction. The refractive index of cornea is 1.376. There is a gradual increase in thickness from the central cornea to the periphery ***(Feizi et al., 2014)***.

The cornea is made up of cellular and acellular components. The cellular components include the epithelial cells, keratocytes, and endothelial cells. The acellular component includes collagen and glycosaminoglycans. The epithelial cells are derived from epidermal ectoderm. The keratocyte and endothelial cells are derived from the neural crest. The corneal layers include epithelium, Bowman's layer, stroma, Descemet's membrane, and endothelium as shown in Figure (1). Recently, a layer of the

cornea that is well defined, acellular in pre-Descemet's cornea is getting attention with the development of lamellar surgeries ***(Dua et al., 2013)***.

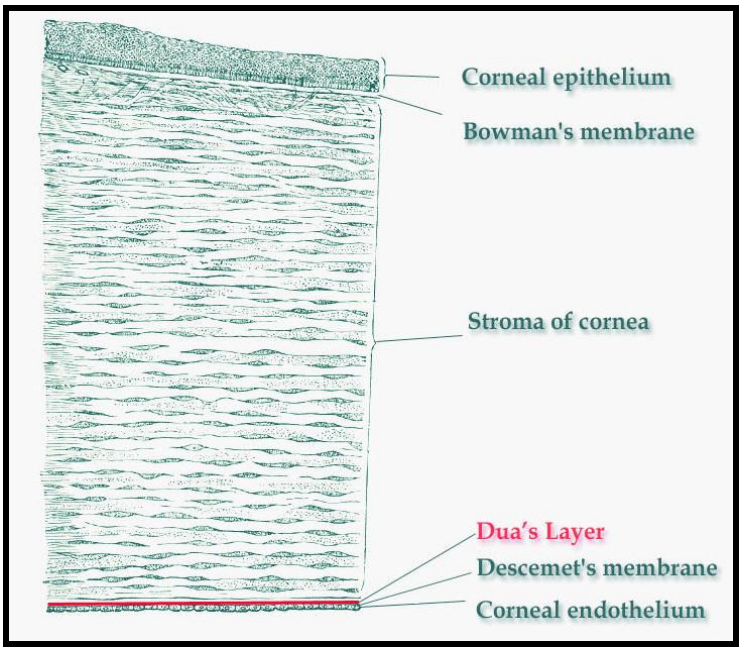

Figure (1): Layers of the cornea.

The corneal epithelium is composed fairly uniformly of 5–7 layers of cells. It is about 50 μ in thickness. The epithelium is uniform to provide a smooth regular surface and is made up of nonkeratinized stratified squamous epithelium. as shown in figure (2).

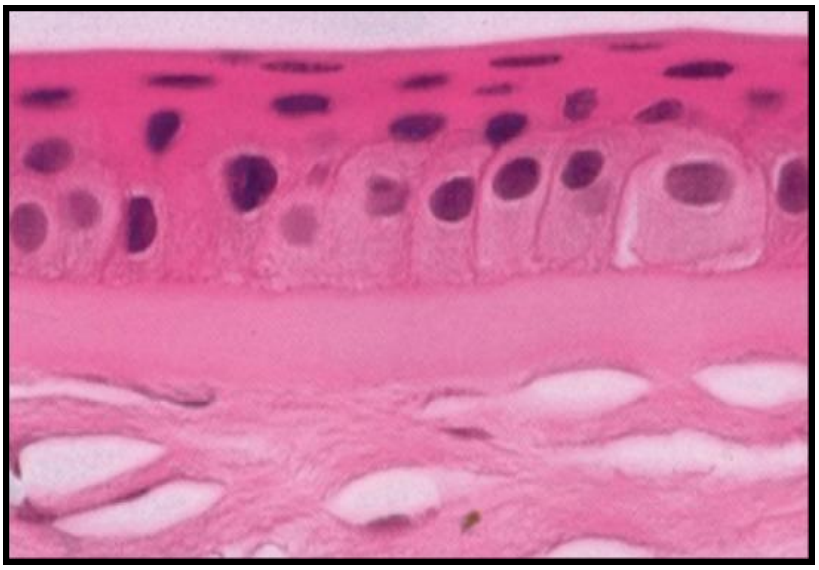

Figure (2): Histopathology of corneal epithelium and Bowman's membrane.

Corneal epithelial cells have a lifespan of 7 to 10 days undergoing involution, apoptosis, and desquamation. The epithelium is a 5–6 layers structure with three types of cells: superficial cells, wing cells, and basal cells. The superficial cells are 2–3 layers made up of flat polygonal cells. Desmosomes form the tight junction between the superficial cells. Wing cells are 2–3 layered and are named as they have wing-like shape. Basal cells are a single layer of the epithelium which is cuboidal or columnar. They have abundant organelles and they are active mitotically.

The deepest cell layer of the epithelium is the basal layer, which compromises the single-cell layer of epithelium approximately 20 μ tall. Besides the stem cells and transient amplifying cells, basal cells are the only corneal epithelial cells

capable of mitosis. They are the source of a wing and superficial cells ***(Feizi et al., 2014)***.

The basement membrane of epithelial cells is 40–60 nm in thickness and is made up of Type IV collagen and laminin secreted by basal cells.

There are differences between the epithelium of the central and peripheral cornea. In the central cornea, the epithelium has 5–7 layers. The basal cells are columnar. There are no melanocytes or Langerhans cells. There is a smooth basal cell layer with keratan sulfate, and there are no lymphatics. In the peripheral cornea, the epithelium is 7–10 layered ***(Dua et al., 2013)***.

Bowman's membrane is the condensation of collagen and proteoglycans. It is a 12 μ structure and is made up of Type I and V collagen as well as proteoglycans. Bowman's membrane lies just anterior to stroma and is not a true membrane. It is an acellular condensate of the most anterior portion of the stroma. This smooth layer helps the cornea maintains its shape. When injured, this layer does not regenerate and may result in a scar ***(Meek and Knupp, 2015)***.

The corneal stroma forms the bulk of the structural framework of the cornea and comprises approximately 80%–85% of its thickness. The stroma is characteristically transparent which is the result of a precise organization of stromal fibers and

extracellular matrix (ECM). The collagen within corneal fibrils is predominantly Type I, Type VI collagen and Type XII collagen is also found in the stroma. The collagen fibers are arranged in parallel bundles called fibrils. These fibrils are packed in layers or lamellae ***(Meek and Knupp, 2015)***.

Keratocytes are the major cell type of stroma. They are involved in maintaining the ECM environment. They can synthesize collagen molecules and glycosaminoglycans, while also creating matrix metalloproteinases (MMPs), all-important in maintaining stromal homeostasis. Most of the keratocytes reside in the anterior stroma ***(Li and Pflugfelder, 2005)***.

The Descemet's membrane is a 7 μ structure. It is made up of Type IV collagen and laminin. Descemet's membrane begins in utero at the 8-week stage. Endothelial cells continuously secrete Descemet's membrane. The anterior 3 μ secreted before birth has a distinctive banded appearance. Descemet's membrane produced after birth is unbanded and has an amorphous ultrastructural texture. Descemet's membrane can be up to 10 μ in thickness with age. The Descemet's membrane is elastic and curls on getting severed ***(Dua et al., 2013)***.

The endothelium is a single layer, 5 μ thick structure. The cells are hexagonal and are metabolically active. There is an endothelial pump that regulates water content. The endothelium is