دراسة مقارنة بين أثر الريبوفلافين عند استخدامه في تقوية الروابط بين ألياف الكولاجين المكونة لسدي القرنية وبين أثر زراعة الحلقات داخل القرنية في حالات القرنية المخروطية البسيطة والمتوسطة

رسالة

تمهيدا للحصول على درجة الدكتوراه

مقدمة من

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القاهرة - مصر
2011

Comparative study between the Effect of collagen cross linking and intra-corneal ring implants in cases with mild-moderate keratoconus

Thesis
Submitted for partial fulfillment of
M.D. Degree in Ophthalmology

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LIST OF ABBREVIATIONS

ALK	anterior lamellar keratoplasty
Asph	Coefficient of asphericity
BM	Bowman's layer
BFS	Best Fit Sphere
BSCVA	Best spectacle corrected visual acuity
CH	Corneal Hysteresis
C3-R / CXL	Corneal collagen cross-linking riboflavin
CCT	Central corneal thickness
CRF	Corneal resistance factor
D	Diopters
D / M	Day / Month
DK	Diffusion constant
DM	Descemet's membrane
EBM	Epithelial basement membrane
FDA	Food and drug administration
HRS	highest rate of steepening
FS	Femtosecond
I-S	Inferior-superior value
ICRS	Intra corneal ring segment
IOPCC	Corneal-Compensated Intraocular Pressure
K	Keratometry
KC	Keratoconus
KCI	keratoconus index
KG	Keratoglobus
KISA%	an algorithm that topographically quantifies the phenotypic features of keratoconus
KPI	keratoconus predictability index
Mw/cm^2	Milliwatt per square centimeter
ORA	Ocular response analyzer
PKP	Penetrating keratoplasty
PMD	Pellucid marginal degeneration
RGP-CL	Rigid gas permeable contact lens
RMS	Root mean square
SDSD	(standard deviation of the standard deviations of the radii of curvature of each ring)
SE	Spherical equivalent
UCVA	uncorrected visual acuity
µm	Micrometer
UVA	Ultraviolet A

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Anatomy of the cornea

The cornea is a unique portion of the outer fibrous tunic of the eye. It is transparent, and it serves a refractive function whilst maintaining a mechanically tough and chemically impermeable barrier between the eye and the environment. Each of these functions is provided by a highly specialized substructural organization, and in absence of vessels. [1]

The transparent cornea forms the anterior one-sixth of the outer coat of the eyeball. Although the dimensions of the cornea vary considerably from one person to another, the approximate measurements are about 10.6 mm vertically and 11.7 mm horizontally. Posteriorly, the cornea is concave and circular, measuring about 11.7 mm in diameter. The cornea is thinnest at its center, measuring about 0.5 to 0.6 mm, and thicker at the periphery, measuring about one mm. [2]

One can consider the cornea fancifully as a sandwich dipped in nutritious soup. Two surface layers, the epithelium and the endothelium, contain a central filling, the stroma. All three layers receive nourishment and oxygen from the tears, aqueous humor, and limbic vessels.[2] (Figure 1)

Epithelium:

The corneal epithelium is the anterior most cell layer of the cornea. It is typically several cell layers thick, consisting of the apical cell squamous layer; the multilayered polygonal-shaped wing cells beneath the apical layer; and the posterior most layer of basal cells. The wing cell layer is two or three cells thick in the central cornea, but tends to be four to five cells thick in the periphery. In total, the epithelium is approximately 50 μm thick in the central human cornea. [1]

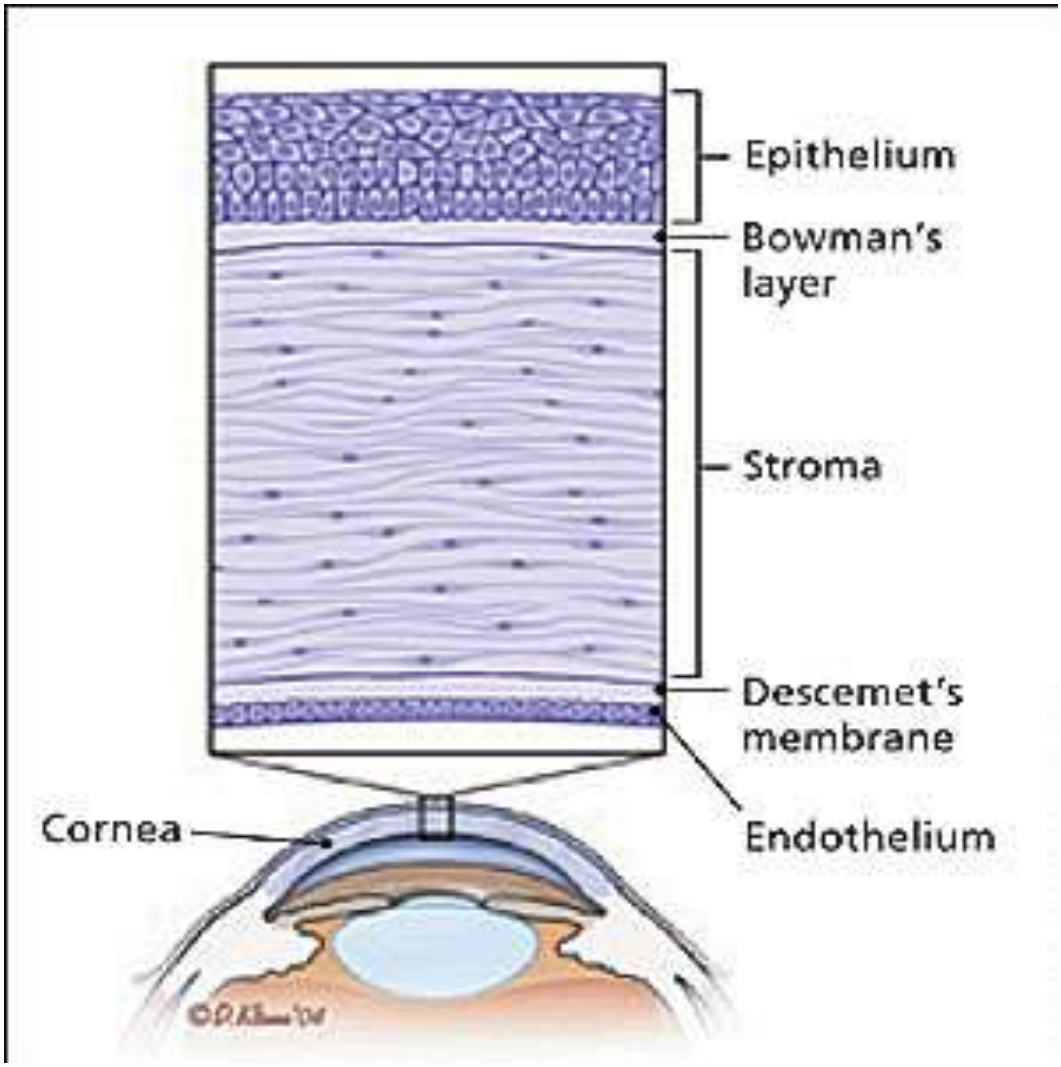

Figure 1: Anatomy of the cornea. ***Wilson et al. (2004)*** [2]

Bowman's layer:

When viewed with electron microscopy, Bowman's layer appears as a fetal-like composite of randomly oriented, striated collagen fibrils dispersed throughout an amorphous matrix. In the adult this layer is approximately 8-12 μm thick, being slightly thicker in the corneal periphery. [3]

Bowman's layer is composed of collagen type I, III, V, and VI as shown by immuno-electromicroscopy. The anterior surface is sharply defined by its interface with the lamina densa

of the overlying basal lamina. In the posterior aspect of Bowman's layer, striated collagen fibrils from the underlying stroma become contiguous with Bowman's layer. [4]

Stroma

A fibrous tissue layer approximately 450 μm thick in the central cornea. It occupies about 90% of the total corneal thickness, and is composed of collagen fibrils, keratocytes and extracellular ground substances. [4]

Collagen components constitute more than 70% of the dry weight of cornea and is composed predominantly of type I collagen with types III, V, and VI also in evidence. [4]

The structural unit of the stroma is the collagen fibril, these fibrils are combined into highly ordered sheet-like bundles called lamellae, which lie essentially parallel to the corneal surfaces. Lamellae vary in width and thickness throughout the stroma, with a tendency to have smaller dimensions anteriorly (0.5 to 30 μm wide and 0.2 to l.2 μm thick) and larger dimensions posteriorly (100 to 200 μm wide and 1 to 2.5 μm thick). [5]

Two important of characteristics of corneal collagen fibers accounts for the transparency of cornea, the first one being the highly uniform diameter of collagen fibers (25-35 nm), while the second is the highly uniform distance between corneal fibers (41.5nm) [1]

Extracellular matrix or ground substances found in cornea are mainly glycosaminoglycan. The primary glycosaminoglycans of the stroma are keratin sulfate (forms 65% of the total glycosaminoglycan content) and chondroitin sulfate.[4]

Keratocytes (corneal fibroblasts) are the major cell type of the stroma. They occupy 3-5% of the stromal volume. They are spindle shaped in cross section and found scattered in between the lamellae of collagen fibers. They synthesize collagen and extracellular matrix components and thus maintain the stroma.[3]

Descemet's Membrane:

Descemet's membrane can be thought of as the basal lamina of the endothelium, and it varies in thickness in the human from approximately 3 μm at birth to 10 μm in adulthood. The age related growth and renewal of the membrane after injury indicate that it is an extracellular secretion of the endothelium. Descemet's membrane is stratified into distinct layers according to histologic appearance and immunohistochemical labeling: a thin, unbanded zone immediately adjacent to the interfacial matrix of the stroma (approximately 0.3 μm); a banded anterior zone (2-4 μm); and an unbanded posterior zone that may be as much as two-thirds the total thickness of Descemet's membrane in adults (> 4 μm). This zone is laid down by the endothelium. [1]

Endothelium:

A single layer of 400,000 to 500,000 cells. Cells are four to 6 μm in height and 20 μm in width, and their posterior surfaces are predominantly hexagonal when viewed under specular microscopy. Cross-sectional views with electron microscopy show that cells lateral walls are extremely tortuous and interdigitate with extensive folds and fingerlike projections. Numerous gap junctions along the lateral membranes provide cell-to-cell cytoplasmic communication. [1]

Corneal shape

The average anterior and posterior corneal power is 48.6 diopter (D) and –6.8 D, respectively. To simplify it in clinical practice or in keratometry, a substitution with one refractive surface with the resulting corneal power of 42-44 keratometric D often is used. The average cornea changes little with age. It flattens about 0.5 D by age 30 years and steepens about one D by age 70 years.[6]

During adulthood, an average cornea is steeper in the vertical meridian by about 0.5 D compared to the horizontal meridian, which contributes to higher incidence of with-the-rule astigmatism in young adults. This difference between vertical and horizontal curvature diminishes with age, finally disappearing at age 70 years. Lenticular changes contribute significantly to the higher incidence of against-the-rule astigmatism with age. [6]

Normal cornea is a prolate surface, steeper in the center and flatter in the periphery. Oblate surface like surface after myopic laser photorefractive keratectomy is flatter in the center and steeper in the periphery. [6]

The visually significant area of the corneal surface is approximately the area with the same diameter as the pupil size. The pupil diameter decreases with age. A large variation exists between people in any age group. In one large study, the average pupil size in individuals aged 20 and 80 years was 4.5 mm and 3.5 mm, respectively, in bright illumination. In dim illumination, the average pupil size in individuals aged 20 and 80 years was 8 mm and 5 mm, respectively. This finding is clinically important because most refractive lasers treat an area with a 6.5-mm diameter with a surrounding blending zone. [82]

The average central corneal thickness is approximately 550 µm. In one study, the average thickness in temporal, nasal, inferior,