BACK TO SURFACE ABLATION IN REFRACTIVE SURGERY

M.Sc. ESSAY PROTOCOL
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By
Laila kourani Mohammed
M.B.B.Ch
Faculty of Medicine –Cairo University

SUPERVISORS

Prof. Dr. Ali Mohammed Taha

Professor of Ophthalmology
Faculty of Medicine
Cairo University

Prof.Dr.Hisham Fath-Allah

Professor of Ophthalmology
Faculty of Medicine
Cairo University

Ass. Prof. Dr. khaled AbuEl-Einen

Assistant prof. of Ophthalmology
Faculty of medicine
Cairo University

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ABSTRACT

The best outcomes with surface ablation. Surface ablation and laser in s itu keratomileusis are comparable in terms of safety and quality of vi sion. Wavefront-guided surface ablation offers better acuity and less induction of higher order aberrations thanwavefront-guided laser in situ keratomileusis.

KEY WORDS

Paemature Growth resonance

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Introduction

Excimer laser surface ablation has been used since 1987 to treat myopia, the original procedure was termed photorefractive keratectomy (PRK) in which the epithelium is scraped prior to laser refractive surgical correction, major disadvantage is the great and persistent postoperative pain associated with de-epithelialization and the exposure of traumatized corneal nerve ending., slow visual recovery, and stromal haze, these complications drove to the appearance of LASIK.

In LASIK surgery a stromal flap is created using the microkeratome technology and remains connected by a hinge with the rest of the cornea, folded back, and after laser photoablation repositioned to its original place.

LASIK offers the advantages of minimal discomfort, rapid corneal healing, minimal stromal haze, and proved to be safe, effective in treatment of low to moderate degrees of myopia.

LASIK becomes the leading procedure for photorefractive correction of ametropia; however the rise of a number of complications as postoperative ectasia, epithelial ingrowth and flap related complications renewed the interest of surface ablation.

LASEK is another approach to PRK., which creates an epithelial flap using diluted alcohol solution, this flap is replaced after laser ablation to the Bowman's and anterior stromal layers, this results in less postoperative haze, more favorable visual outcome, and retains the biomechanical stability of the cornea.

LASEK is safe and effective in treating low and moderate degrees of myopia, and eliminates LASIK related flap complications; however there is concern about the probable toxic effects of alcohol on epithelium and underlying corneal stroma.

Epi-LASIK is an alternative surgical approach for surface ablation, the epithelium is mechanically separated by a motorized mechanical epi-separator device, laser ablation is performed, and then the epithelial sheet is repositioned again to its place.

Epi-LASIK incorporates the advantages of LASIK and LASEK and avoids the potential risk posed by the creation of the LASIK flap, therefore it is possible that the quality of vision would be better in Epi-LASIK treated patients than in LASIK treated patients, meanwhile Epi-LASIK avoids the alcohol related side effects of LASEK, which believes to be associated with less postoperative pain, faster visual recovery and less haze.

While LASIK is still by far the most frequently performed refractive surgical procedure, Epi-LASIK early clinical results showed good surgical outcome, which shows that it is an encouraging new technique and is a predictable and safe method for the treatment of myopia, however larger series with adequate follow up are needed to observe the long term outcome.

AIM OF THE WORK

To review the literature on the different ablation profiles in excimer laser corneal refractive surgery & find out the advantages & disadvantages of each to be able to choose what suits each eye.

Surgical corneal anatomy
In relation to refractive surgery

Macroscopic anatomy & measurements:

The cornea is a clear, transparent, colorless avascular structure richly supplied with sensory nerve endings that generally subserve touch and pain . It covers the anterior one-sixth of the total circumference of the globe . **(William et al 2007)**.

The thickness of the cornea varies from 0.51 to 0.56 mm centrally to 0.63 to 0.67 mm peripherally. Although a wide variety of different corneal shapes can be seen between individuals, it is frequently more curved at the temporal cornea than the nasal cornea, and in the vertical plane than in the horizontal plane. **(Eysteinsson et al 2002)**.

The optical zone of the cornea is the central one-third, approximately 4 mm in diameter. The anterior and posterior surfaces of the cornea are relatively spherical in this region **(Edelhauser 2000)**.

Microscopic anatomy:

The cornea consists of five layers as shown in figure 1: Epithelium; Bowman's layer; stroma; Descemet's membrane; and endothelium. **(Tasman et al 2007)**.

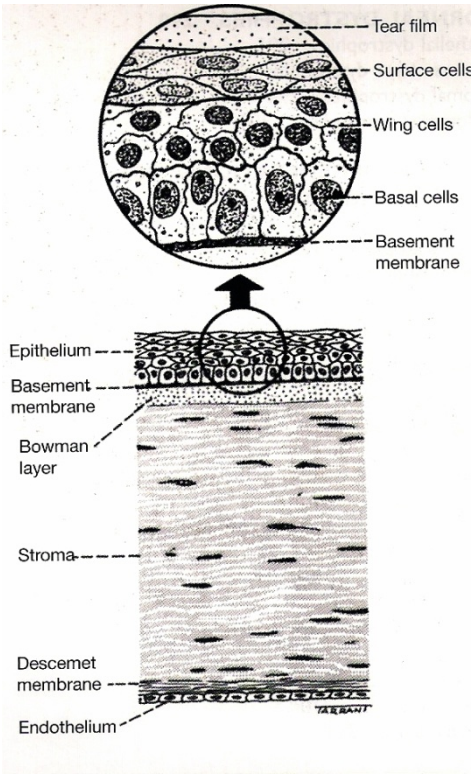

Figure8: Microscopic anatomy of the human cornea. **(Kanski 2008)**.

The Epithelium:

The anterior surface of the human cornea is covered by a transparent, non keratinized, stratified (five- to seven-cell layer) squamous epithelium uniformly around 50 µm in thickness. The epithelial cells differentiate from the basal layer to form two to three cell layers of wing cells and finally to form two to three cell layers of

squamous cells . The basal corneal cells actively secrete extracellular material (type IV collagen, laminin, heparin, and small amounts of fibronectin and fibrin) that forms an underlying75-nm thick basement membrane called the basal lamina. **(William et al 2007)**.

It assists in the attachment of the epithelium to the underlying stroma. Its presence may modify wound healing and eliminate the haze. **(Robin 2004)**.

The squamous cells form a barrier junction because they are surrounded by a continuous encircling band of zonula occludens tight junctions, which serve as a semipermeable, high-resistance membrane by closing off the intercellular space. This barrier prevents the movement of fluid from the tears into the stroma and also protects the cornea and intraocular structures from infectious pathogens. **(William et al 2007)**.

The apical surface of the corneal epithelium is specialized to maintain the tear film as microplicae and microvilli on the surface of the most superficial epithelial cells are covered with membrane-spanning mucins (MUC 1 and possibly MUC 4). **(Argueso & Gipson 2001)** .

The corneal epithelium is in a state of constant healing as squamous cell are continuously shed into the tear film. It is estimated that all the cell layers of the corneal epithelium completely turn over every 7 to 10 days. The epithelial surface is maintained by basal epithelial cells, which can undergo mitosis. In addition to basal epithelial cell mitosis, the corneal epithelium is maintained by migration of new basal epithelial cells into the cornea from the limbus. **(William et al 2007)**.

The epithelium functions as a barrier to both mechanical forcesas well as diffusion of fluids and substances. In addition, its ability to provide a smooth optical surface is imperative to good visual function. **(Robin 2004)**.

Bowman's layer:

An acellular structure which consists of interwoven collagen fibrils, is 8 to 14 µm in thickness, with the peripheral one-third being slightly thicker than the central two-thirds. Peripherally, the collagen fibrils of Bowman's layer become more loosely arranged and end abruptly at the limbus. The deep surface of Bowman's layer merges into the corneal stroma. **(Tasman et al 2007)**.

Stroma:

The corneal stromal thickness ranges from 500 µm centrally to 700 µm peripherally. It represents about 90% of the corneal thickness. It consists of approximately 200 to 250 collagen lamellae, each having a thickness of 2 µm and a width ranging from 9 to 260 µm. These lamellae, as well as the collagen fibrils composing them, are parallel, regularly arranged, and layered **(Tasman et al 2007)**.

It is predominantly composed of water (78% hydrated), which is stabilized by an organized structural network of insoluble and soluble cellular and extracellular proteins. The dry weight of the adult human corneal stroma is made up of collagen (68%), keratocyte constituents (10%), proteoglycans (9%), salts, glycoproteins and other substances: **(William et al 2007)**.

Collagen: is a water-insoluble structural protein organized into an inextensible scaffold that forms the basic structural framework of connective tissues. It is a highly-ordered lattice-like structure in the secondary cellular stroma . They are functionally important in establishing tissue transparency and in resisting tensile forces because collagen fibrils and filaments hold the cornea together (i.e. cohesive strength), ultimately defining the size of the tissue. **(William et al 2007)**

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Keratocytes: make up the second major component of the cornea's dry weight. Interspersed between collagen lamellae , they form a closed, highly-organized syncytium. They function as modified fibrocytes where they maintain the extracellular matrix of the corneal stroma, usually in an inconspicuous, or relatively transparent, fashion. **(William et al 2007)**.

Proteoglycans: which are water-soluble glycoproteins, are the third major component of the cornea's dry weight. Their primary function is to provide tissue volume, maintain spatial order of collagen fibrils, and resist compressive forces. **(William et al 2007)**.

Water, collagens, proteoglycans and keratocytes work together to maintain and establish a transparent cornea, while also creating a tough and resistant structure that keeps ocular integrity intact and maintains a stable shape. **(William et al 2007)**.

Descemet's membrane:

The composition of Descemet's membrane is primarily collagen. It 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 8 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**,(Edelhauser 2000).**

It is a temporal record of the physiologic state of the endothelium. **(William et al 2007)**

The Endothelium:

The cells lie on the posterior surface of the cornea and form an irregular polygonal mosaic. The tangential appearance of each corneal endothelial cell is uniquely irregular, usually uniform in size to one another, and typically six-sided (i.e. hexagons). **(Edelhauser 2000)**.

Because endothelium maintains its continuity by migration and expansion of surviving cells, it is not surprising that the percentage of hexagonal cells decreases (pleomorphism) and the coefficient of variation of cell area increases (polymegathism) with age. The primary function of the corneal endothelium is to maintain the health, deturgescence, and clarity of the cornea through a pump-leak mechanism first described by David Maurice. Secondarily, it is also known to secrete the anteriorly-located basement membrane (Descemet's membrane). **(Yee et a 1985)**.

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Corneal wound healing

Importance:

The physiologic process of wound healing has been described as a complex cascading sequence of events that normally contribute to wound repair and re-establishing normal function. Biologic diversity in the corneal wound healing response is a major factor in the outcome of all keratorefractive surgical procedures. It is an important determinant of overcorrection, undercorrection, regression, and other complications, such as haze and refractive instability. **(Netto et al 2005 a)**.

Role of Keratocytes:

The corneal stroma undergoes homeostatic remodeling via the functions performed by keratocytes and, possibly, other cell types including bone marrow–derived cells and myofibroblasts. Keratocytes are non contractile cells responsible for production and maintenance of the extracellular matrix of the corneal stroma. **(Netto et al 2005 a)**.

Changes in environmental conditions, such as surgical trauma, modulate keratocyte phenotype, resulting in functional changes in gene expression, contractility, matrix production, and other characteristics that contribute to the wound healing response. **(Jester & Chang 2003)**.

Components of the wound healing response:

Figure35, summarizes corneal wound healing events of particular relevance to corneal refractive surgery. **(Dupps & Wilson 2006)**

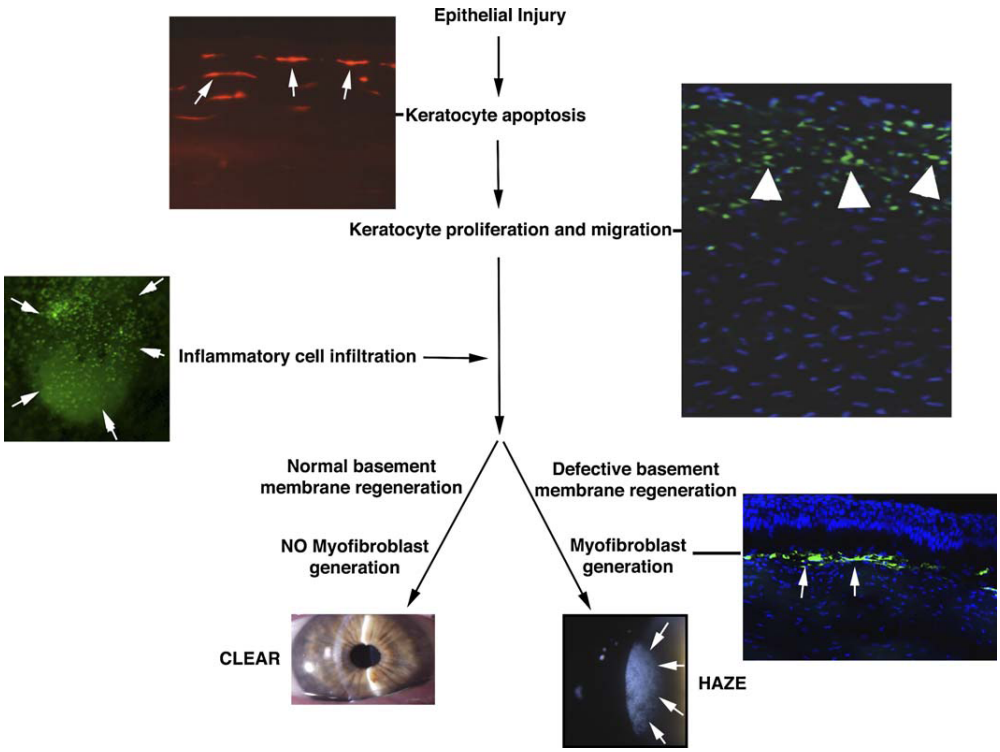

Fig.22:Corneal wound healing events. **(Dupps & Wilson 2006)**.

The process begins with an epithelial insult, which may take the form of microkeratome or femtosecond laser-mediated disruption, alcohol exposure or a mechanical scrape. This is followed by release of cytokines from the injured epithelium and epithelial basement membrane, including, interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-alpha), bone morphogenic proteins (BMP) 2 and 4, epidermal growth

factor (EGF) and platelet derived growth factor (PDGF). **(Dupps & Wilson 2006)**.

These factors and others derived from the tears, trigger a variety of responses in underlying stromal keratocytes, that induce apoptosis (a programmed form of cell death with minimal collateral damage due to a relative absence of cell lysis and lysozomal enzyme release). A compromised epithelial barrier potentiates the effects of liberated epithelial and lacrimal cytokines by providing unhindered access to the stroma. After the initial wave of keratocyte apoptosis, increasing numbers of cells undergo the more pro-inflammatory process of necrosis. **(Wilson et al 2001)** .

Proliferation and migration of remaining keratocytes begins within 12 to 24 h, giving rise to activated keratocytes, fibroblasts and possibly myofibroblasts responsible for repopulating the depleted stroma. Also, within the first 24h of injury, pro-inflammatory chemokines from the epithelium or from keratocytes responding to IL-1 and TNF-alpha trigger stromal infilteration by macrophages/monocytes, T-cells and polymorphonuclear cells. These cells, which arrive via the limbal blood supply as well as from the tear film, play a role in phagocytosis of apoptotic and necrotic debris and possibly serve other functions in the stroma. **(Dupps & Wilson 2006)**.

One to 2 weeks following injury, cells that stain with antibody against alpha smooth muscle actin (alpha-SMA), can be visualized in the anterior stroma directly below areas of epithelial basement membrane disruption, depending on the level of correction, surface irregularity and other factors. **(Netto et al 2006)** .