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Review Article

Optical Coherence Tomography -Derived Epithelial Mapping as an Artificial Intelligence-Based Device in Keratoconus Diagnosis

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Precise

Keratoconus patterns that are distinct include the degeneration of the epithelium layer and lower basal epithelial density, thought to come from the instability of Bowman's layer and loss of anterior stromal collagen fibrils, which can be evaluated with an epithelial thickness map of the anterior segment optical coherence tomography.

Keywords: Artificial intelligence; Contact lenses; Dry eye syndromes; Epithelium, Corneal; Keratoconus; Tomography, Optical coherence

Anterior Segment Optical Coherence Tomography and Defined Indexes

Low diagnosis accuracy in cases of haze or scarring cornea, commonly encountered in keratoconus, is a drawback of other corneal imaging techniques. By using a broad bandwidth light and spectrometer to detect the fringes, ultrahigh-resolution optical coherence tomography improves axial resolution, allowing for the more precise imaging of the cornea, conjunctiva, tear film, meniscus, and contact lens, all of which are important in distinguishing between various corneal and ocular pathologies. The computerized classification approach employing machine learning showed outstanding performance to detect subclinical keratoconus (SCKC) eyes from normal using combined techniques including ultra-high resolution optical coherence tomography (UHR-OCT) and Scheimpflug for images capturing and processing. The epithelial characteristics that were derived from the OCT images proved to be the most beneficial in the detection process. This classification approach has the ability to increase the differentiable power of SCKC as well as the effectiveness of keratoconus screening [1-5].

The main parameters in the ultra-high resolution optical coherence tomography system are epithelium, Bowman's layer, and stroma pachymetry-based measures: Include the mean thickness of the Bowman's layer, the epithelium, and the stroma in various regions (inferior, superior and total) [5]. Emin, Bmin, and Smin denote the epithelium, Bowman's layer, and stroma's thinnest thicknesses on the inferior thicknesses map, respectively. Emax, Bmax, and Smax denote the maximum thickness of the epithelium, Bowman's layer, and stroma, respectively, in the anatomically superior thickness map.

The ectasia indices (i.e., EEI, BEI, and SEI) measure the localized epithelial, Bowman's-layer, and stromal thinning along the vertical meridian. They were calculated by dividing the minimum thickness in the inferior half by the average thickness in the superior half and multiplying that by 100. Maximum ectasia index (EEI-MAX, BEI-MAX, and SEI-MAX): indicates the maximum localized thinning in the vertical meridian of the epithelium, Bowman's layer, and stroma, respectively. The minimum thickness in the inferior half was divided by the maximum thickness in the superior half, then multiplied by 100 to get the index. Profile variation (EPV, BPV, and SPV): stand for variations in the thickness profiles of the stroma, Bowman's layer, and epithelium, respectively. The root means square between the zone thickness and the profile average within a single subject was used to define it. The epithelial profile standard deviation (EPSD), Bowman's profile standard deviation (BPSD), and stromal profile standard deviation (SPSD) are the standard deviations of thickness profiles of the epithelium, Bowman's layer, and stroma, respectively, compared to individual and normal patterns. The root means square of the personal profiles' zonal thickness, and the pattern average's zonal thicknesses were how it was defined [4,6] (Figure 1).

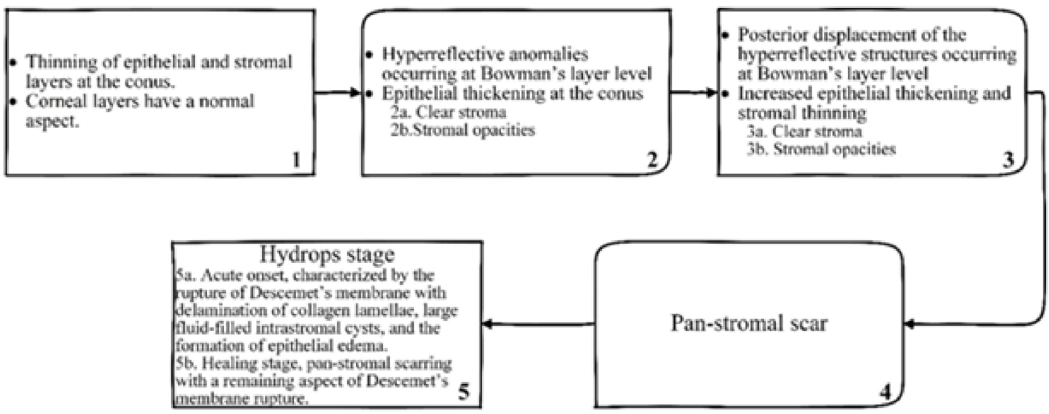

Figure 1: Keratoconus stages definition using anterior segment optical coherence tomography.

Epithelial Thickness Map

The epithelial and stromal thickness, as the essential parts of optical clarity, should be analyzed for the early identification of corneal diseases. Wang and Wu found that age was inversely correlated with Axial Length (AL) in the normal group [7], which is consistent with Tuft and Bunce finding that AL increases with decreasing age at the time of cataract surgery [8]. Compared to AL, central corneal thickness (CCT) was shown to be steady with age at the SD-optical coherence tomography resolution in high myopia and normal groups, with results comparable to those of earlier research utilizing the Scheimpflug system and optical coherence tomography [7,9]. In normal and high myope groups with high axial length, the effect of gender on central epithelial thickness and CCT may be related to the endocrine differences between men and women. Previous studies have shown that gonadal hormones can affect the development of ocular tissue through either a genomic or nongenomic mechanism [10,11].

Furthermore, concerning the significance of warpage, up to 12% of contact lens users have considerable corneal warpage; however, the frequency varies widely depending on the material and geometry of the contact lens. Although the diagnosis of corneal warpage is verified once the topographic anomalies have been corrected by quitting using contacts [12], the Epithelial Modulation Index is useful in distinguishing eyes with secondary epithelial modulation from those with primary epithelial deformation [12]. A Fourier-domain optical coherence tomography system scanned normal and warped contact lenses or keratoconus (manifest, subclinical, or forme fruste) eyes by epithelial thickness and anterior surface mean curvature maps [13]. Keratoconus eyes had a high Epithelial Modulation index due to high anterior surface mean curvature and poor epithelial thickness. Warped eyes had a normal Epithelial Modulation index [14]. Epithelial Modulation index classification accuracy was 100 ± 0% for normal and keratoconus eyes and 99.0 ± 2.0% for warped eyes during five-fold cross-validation [13,14]. Furthermore, different factors, such as age, gender, area of measurement, ocular surface health, high myopia, use of contact lenses, axial length, laser-related operations, and the presence of ectatic corneal disorders affect the thickness of the corneal epithelium. For example, it showed an inverse correlation with age, similar to the normal group's studies about axial length during cataract surgery [7].

Artificial intelligence systems improve the accuracy of diagnosis. Integration of Scheimpflug image with ultrahigh-resolution optical coherence tomography promotes the differentiation of SCKC from normal eyes. This classification approach can enhance the power of SCKC diagnosis and increase the accuracy and efficacy of keratoconus screening [5]. However, if epithelial remodeling and subsequent epithelial thickness changes as a compensatory mechanism for corneal curvature anomalies are not considered, the stromal thickness may be underestimated [15,16] (Figure 2).

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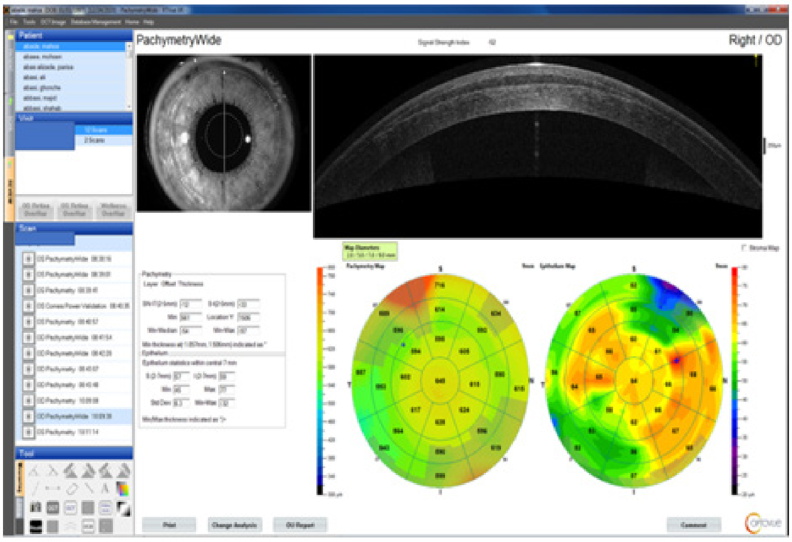

Figure 2: Comparison of Epithelial Thickness Measurements, Rtvue Sd-Optical Coherence Tomography Device (Optovue, Inc., Fremont, Ca), and Epithelial Thickness Map of a Patient After Smile's Derived Lenticule Implantation.

In an ectatic cornea, the epithelium is typically thicker than in a normal cornea, even though it is thinner above the keratoconic protrusion to a degree significantly less than what was anticipated. This difference between normal eyes, patients with untreated keratoconus eyes, and those with keratoconus eyes treated with corneal cross-linking appear clinically significant [17]. Corneal epithelial thickness (ET) measurement is possible by confocal microscopy and high-frequency scanning ultrasound biomicroscopy (HF-UBM). Furthermore, regarding optical coherence tomography, Spectral-domain/Fourier-domain optical coherence tomography such as RTVue device (Optovue, Inc., Fremont, CA) and CSO Ms39 are non-invasive imaging devices which significantly provide anterior segment images with better quality, more reliable, and faster in comparison to the time-domain. For the first time, the Food and Drug Administration (FDA) authorized the iVue Spectral Domain high-frequency scanning ultrasound biomicroscopy ETM software to measure epithelial thickness [18].

Sella and colleagues assessed not only the repeatability but also reproducibility outcomes for normal and corneal patient eyes (Dry Eye, Contact Lens, and Post Laser Refractive Surgery Sub Groups) in the peripheral and central zones, which showed similar results comparing groups, except that the reproducibility of Dry Eye group was significantly lower (Figure 3).

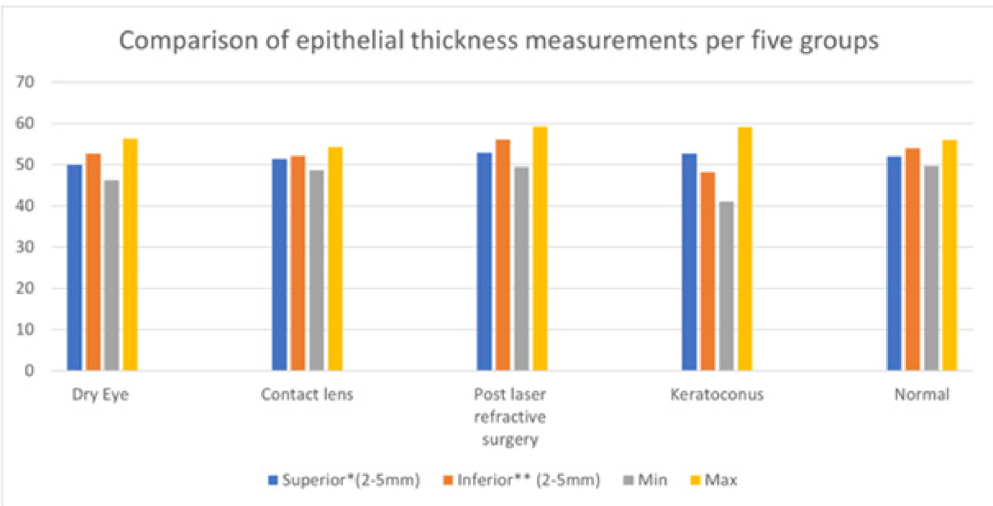

Figure 3: Comparison of epithelial thickness measurements (µm) per five groups. * S = Superior values were measured at the superior hemi circular region of the central 5mm. ** I = Inferior values were measured at the inferior hemicircular region of the central 5mm.

In the normal group, the coefficient of variance (CoV) values ranged from 0.7 to 1.4 percent for peripheral zones and 0.4 to 0.9 percent for central and paracentral zones. Whereas in the corneal patient groups, CoV values ranged from 1 to 1.7 percent for peripheral zones and from 0.7 to 1.1 percent for central and paracentral zones ($p<0.05$) [18]. In another study by De Oliveira Loureiro et al. the corneal epithelial thickness in periphery and superior quadrants was thinner but in the inferior quadrants was thicker [19]. Unlike epithelial thickness, corneal thickness is unaffected by gender. Gender-based disparities in corneal profile should be considered when assessing individuals for corneal diseases such as keratoconus. This normative database may help improve early keratoconus diagnosis in children since epithelial changes start early [19]. Moreover, another study investigated the pupil center, inferior, superior, maximum, minimum, and topographic epithelial thickness variations using AS-OCT in three individual three-dimensional epithelial thickness maps. Also, the intraindividual repeatability of measurements was analyzed. As validation, the epithelial thickness indices were compared to two AS-irregularity indices generated from Scheimpflug imaging: the index of surface variance and the index of height decentration, both of which were greatly useful in early and advanced keratoconus diagnosis. Epithelial pachymetry measurements by HF-UBM might be used as a screening tool for ectasia-prone eyes [20].

Conclusion

The connection of simple optical coherence tomography-derived epithelial mapping with known Scheimpflug-derived asymmetry topometric indices suggests that it has significant potential in early and advanced keratoconus diagnosis.

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Conflict of Interest

There is no conflict of interest.

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