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PERSPECTIVES

The Combined Utilization of Epithelial Thickness Mapping and Tomography in Keratorefractive Surgery Screening: One Imaging Modality is Not Sufficient

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Abstract: Increasing popularity and utility of epithelial thickness mapping (ETM) in keratorefractive surgery screening may begin to inappropriately devalue the use of tomography. An increasing body of research suggests that the interpretation of ETM based solely on the corneal resurfacing function may be insufficient to screen and select patients for refractive surgery. ETM and tomography are complementary and, when used together, may provide the safest and most optimal tools for keratorefractive surgery screening.

Keywords: corneal tomography, corneal topography, corneal epithelial map, SMILE, LASIK, PRK

Background

The corneal epithelial thickness map (ETM) is an increasingly popular diagnostic image among refractive surgeons due to current knowledge regarding epithelial remodeling processes in response to various corneal pathologies. ETM has demonstrated impressive reproducibility, inter-device agreement and repeatability.[1–5] Research has demonstrated the value of these epithelial measurements and the significant role they can play in the preoperative screening of keratorefractive surgery candidates.[4–10] However, recent research has introduced nuances to our former understanding of the corneal epithelial resurfacing function upon which ETM interpretations are based.[11–15] These nuances include conditions, such as chalazia, dry eye disease, and less common keratoconic presentations, and settings, such as contact lens wear, in which inaccurate interpretations of ETM results may be generated.[11–16] Furthermore, various tomographic indices have been especially valuable in keratorefractive surgery screening.[17–19] Therefore, despite the increasing popularity and impressive clinical value of ETM, ETM and tomographic imaging modalities should be appraised equally in the literature. This opinion article aims to explain why ETM and tomography should be used in combination to optimize the refractive surgery screening process. Future research will continue to guide clinicians in the co-utilization of these two imaging modalities as well as novel devices.

Perspective

Poor visual outcomes after keratorefractive surgery are related to postoperative morphologic changes that often occur in undetected preoperative ectasia and biomechanical abnormalities, predisposing patients to iatrogenic corneal ectasia and surgically induced corneal weakening.[20,21] The most widely known corneal risk factor of postoperative ectasia is keratoconus (KC).[21–24] It has been shown that KC follows biomechanical decompensation of the cornea resulting in

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morphological changes (curvature, elevation, and pachymetry) in the posterior and anterior corneal surfaces, which lead to a bulging forward of the cornea.[20] Anterior corneal protrusions classically cause inferior steepening of the cornea which can be measured via keratometry. The corneal epithelium adapts to these protrusions to maintain a smooth and regular corneal surface by thickening over areas of flattening and thinning over areas of steepening.[8,20,25] This masking process is also known as the corneal epithelial resurfacing function and provides the foundation for interpreting ETMs. For example, ETMs have detected earlier forms of KC by identifying regions of epithelial thinning, even when normal corneal tomography systems have not detected significant anterior or posterior curvature changes characteristic of KC. Therefore, ETM commonly screens out patients who may have undergone keratorefractive surgery and subsequently developed visually impairing corneal ectasia due to undetected KC.

ETM also allows refractive surgeons to confidently select suitable candidates for surgery.[6,8] Due to these impressive clinical impacts, ETM has become increasingly popular. Consequently, many surgeons may be persuaded to solely utilize AS-OCT devices to obtain ETM based on its accuracy in diagnosing KC.[8,26–28] However, as discussed further, less common keratoconic and corneal presentations have been recently reported in the literature that may cause confusion due to seemingly contradictory ETM and tomographic findings based on the corneal epithelial resurfacing function.[11–14,17,25] In these cases, an ophthalmologist may wonder whether to rely on ETM or tomography. Therefore, we seek to raise

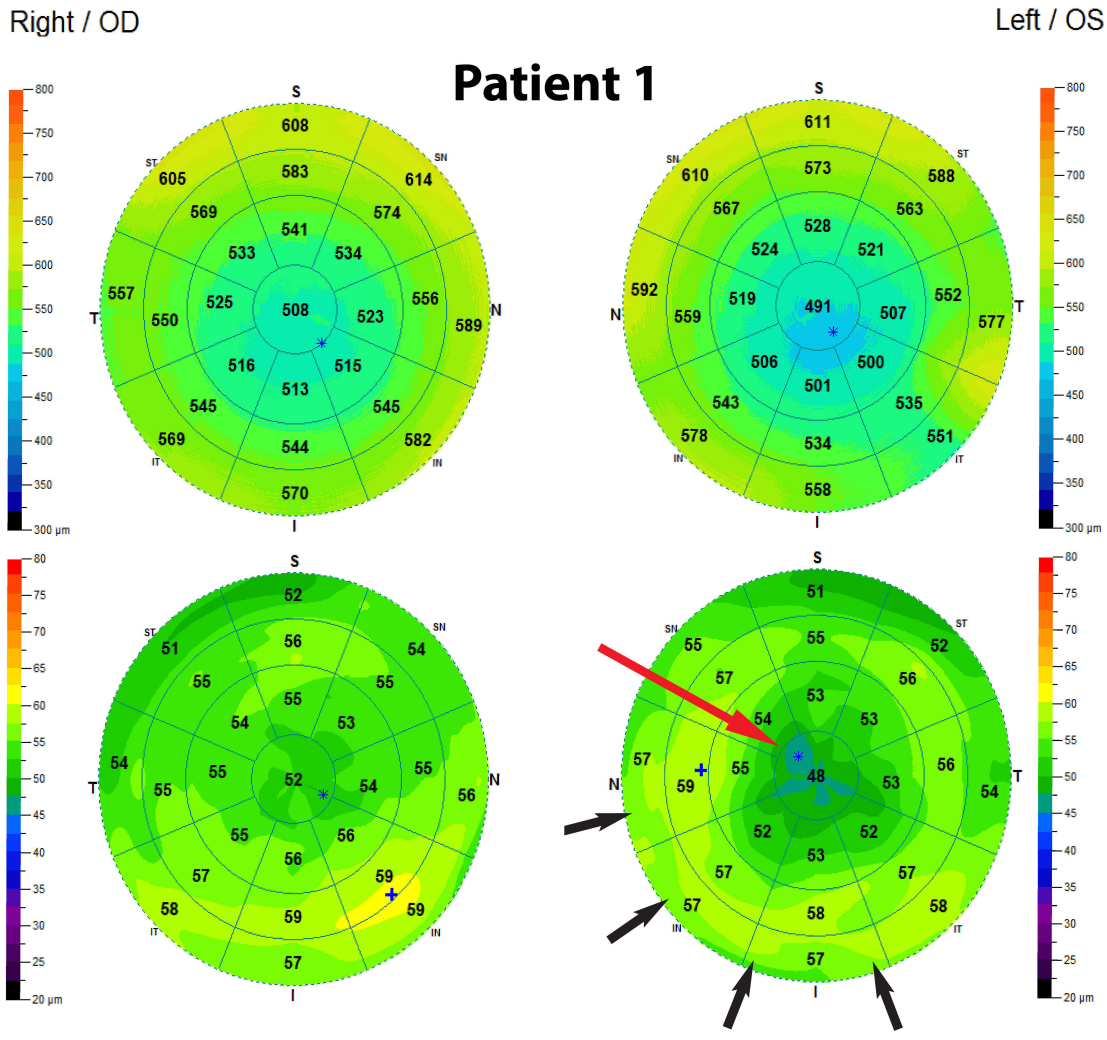

Figure 1 OCT pachymetry and ETM demonstrating normal epithelial thickness OD but marked thinning centrally (red arrow) and thickening peripherally (black arrows) OS in a "doughnut" pattern consistent with KC.

Notes: Figures 1 and 2 present a keratorefractive surgery candidate with frank KC as observed by concordant abnormal findings on both ETM and Tomography.

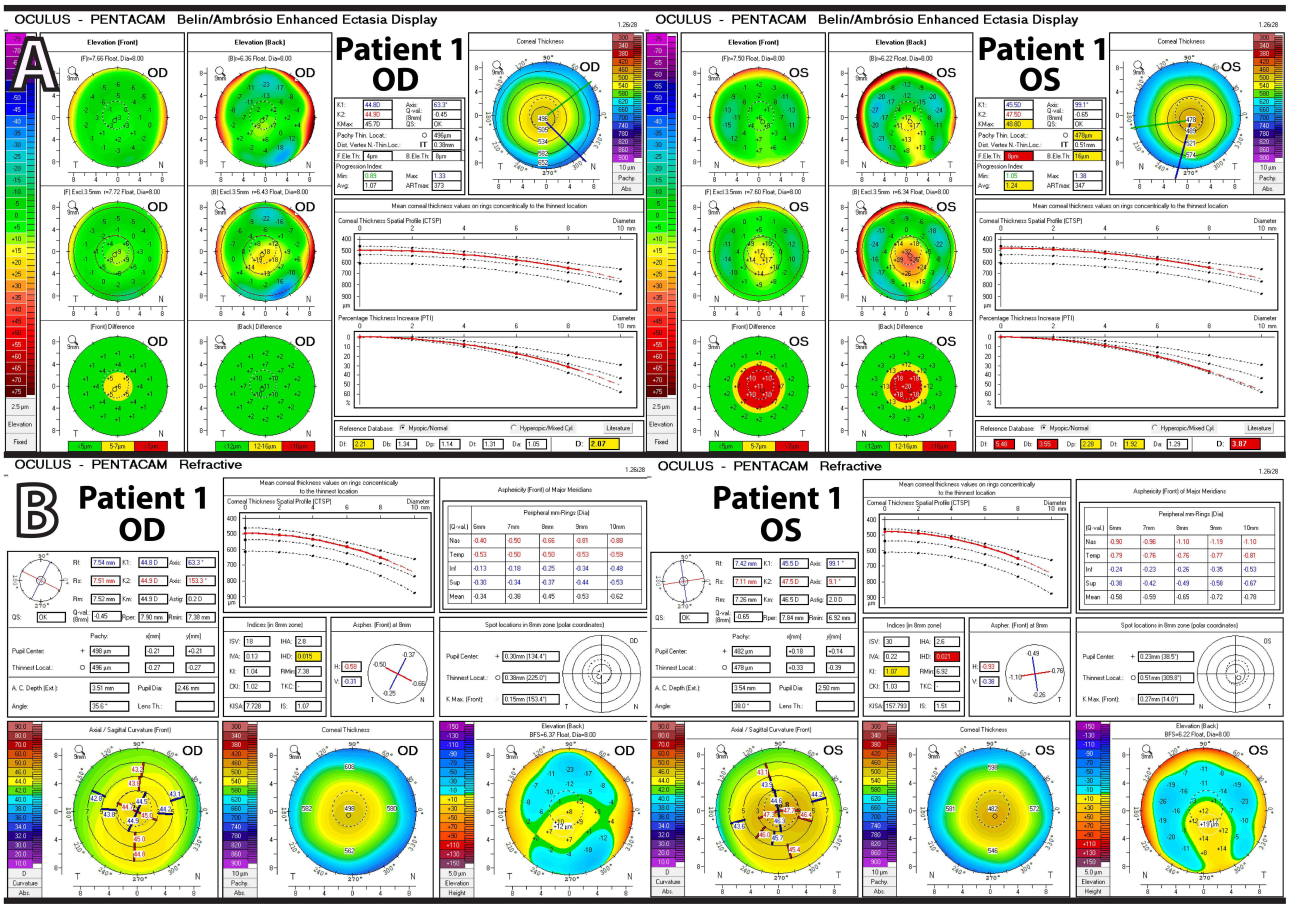

Figure 2 (**A**) Pentacam enhanced ectasia display maps demonstrating significant central thinning OU. (**B**) Pentacam refractive maps.
Notes: Figures 1 and 2 present a keratorefractive surgery candidate with frank KC as observed by concordant abnormal findings on both ETM and Tomography.

awareness among clinicians about the advantages and limitations of ETM and corneal tomography imaging modalities to help them make optimal decisions during preoperative evaluation.

Many less common abnormal corneal presentations suggest the combined use of corneal ETM and tomography imaging modalities. For example, central corneal flattening, which correlates with areas of reversible central focal epithelial thinning in patients with periocular masses such as chalazia, demonstrates the need to utilize both ETM and tomography since the classic interpretation of an ETM in patients with central corneal flattening would incorrectly suggest that these patients are experiencing central focal thickening per the corneal resurfacing function.[11] Recent research regarding another abnormal, but common corneal pathology, dry eye disease, has shown that the reproducibility and repeatability of epithelial thickness measurements in the presence of mask-associated dry eye (MADE) may lead to false-positive results, suggesting an increased value of tomographic indices.[4] Furthermore, Wardani et al reported variations from the traditional keratoconic corneal resurfacing function as they identified epithelial thickening in 12 eyes corresponding to areas of corneal steepening measured via Oculyzer tomography. These authors termed this presentation pseudo-KC and attributed its etiology to several factors, including corneal warpage, dry eyes, chronic exposure, tear film abnormalities, and subclinical anterior basement membrane dystrophy.[25] However, only half of these patients wore contact lenses, decreasing the likelihood of corneal warpage.[25] Therefore, asking patients to remove contact lenses for a specific amount of time prior to refractive surgery screening may not resolve the apparent discrepancy in the diagnosis of KC and pseudo-KC using ETM solely. Furthermore, the female-to-male participant ratio in the Wardani et al study was curiously 2:1, indicating a need to better understand the etiology, pathophysiology, and genetic and environmental factors underlying this pseudo-KC presentation.[25]

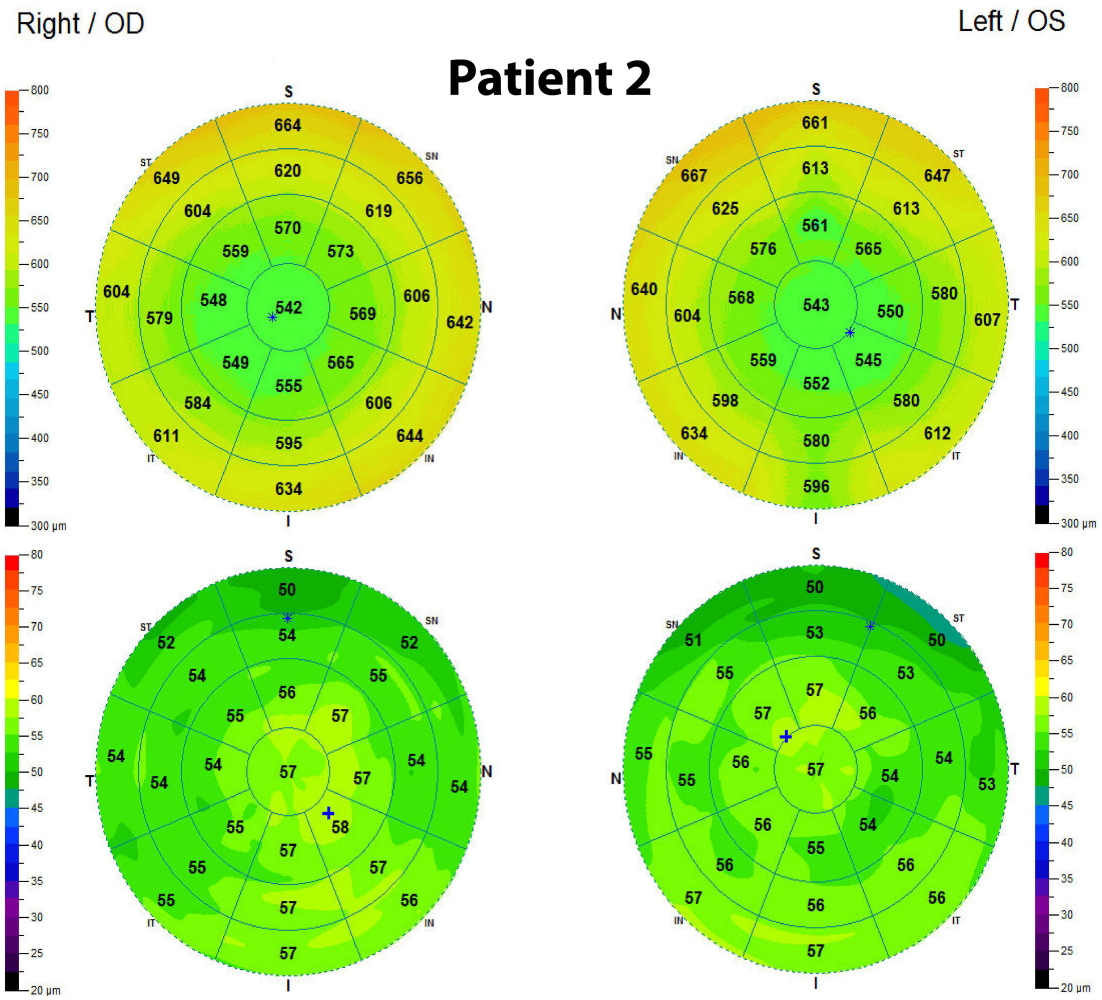

Figure 3 OCT pachymetry and ETM demonstrating normal epithelial thickness OU.
Notes: Figures 3 and 4 present a keratorefractive surgery candidate with suspected KC as observed by discordant findings on ETM and Tomography.

Mohammadi et al provided another example of research that suggests a need to understand the pathogenesis of KC. They identified several keratoconic presentations among 215 patients via computer-based videokeratography using the Scheimpflug camera imaging system on Pentacam, and then classified them into six categories: KC, atypical normal KC, FFKC, posterior KC, anterior KC, and pseudo-KC.[12] To differentiate between these various KC subtypes, they utilized criteria that included epithelial thickness measurements, many topographic parameters, keratometry reading values, and a progression index, suggesting a need for parameters other than epithelial thickness when evaluating patients with these less common KC subtypes.[12] Other studies have also suggested that tomographic measurements, such as Belin-Ambrósio enhanced ectasia total deviation index (BAD-D) and index of height decentration (IHD) parameters, play valuable roles in detecting corneal abnormalities.[22,29–31] Additionally, since KC is primarily defined as an anterior bulging of the anterior and posterior corneal surfaces, often beginning with subtle changes limited only to the posterior surface, parameters which detect these subtle elevation changes, especially in the posterior corneal surface, may be more valuable in early and accurate detection of KC and KC subtypes.[32] A recent study showed that corneal thickness maps measured on the Pentacam HR were more highly correlated with front and back corneal elevation maps than RTVue epithelial thickness maps.[33] This further suggests that tomographic imaging systems rather than epithelial thickness maps may have an enhanced ability to determine the location of KC cones and therefore allow for safer and more effective therapeutic interventions. These findings demonstrate the immense value of tomography, the limitations of ETM, as well as the various KC derivations about which we currently lack full understanding. The safer decision to "do no harm" may be to

opt patients out of keratorefractive surgery when confronted with contradictory tomographic findings and ETM interpretation based on the corneal resurfacing function.[11,12,25]

To illustrate this discussion, we present ETM and tomographic imaging for two patients who both underwent evaluation for keratorefractive surgery. Patient 1 shows a classic "doughnut" pattern on ETM with obvious epithelial thinning centrally (48um) and peripheral thickening (around 57um) in the left eye (Figure 1). This is consistent with the tomographic changes seen in the Pentacam enhanced ectasia display and refractive maps for patient 1 (Figure 2), indicating frank KC, and thus this patient was denied keratorefractive surgery. In contrast, patient 2 demonstrates normal ETM in both eyes (Figure 3) but with changes on Pentacam concerning for KC suspect (Figure 4), a finding that would be missed if ETM was the only imaging modality used. Patient 2 was also denied keratorefractive surgery.

In summary, ETM is an impressive and clinically valuable imaging tool that has been increasingly used in preoperative keratorefractive surgery screening due to its accuracy and precision in measuring epithelial thickness.[1–3,7,9,11,34] However, due to the limited information that epithelial thickness maps can provide, especially in the context of increasing awareness of keratoconic and corneal derivations from the traditional corneal resurfacing model, valuable tomographic parameters provided by other systems must be utilized in combination with ETM for optimal clinical decision making.[10–13,25] One imaging technology, the REVO NX (Optopol Technology, Zawiercie, Poland), is already moving in this direction and found to be effective in utilizing OCT scans to generate ETMs and other tomographic parameters from the same data points.[35] However, more research on this device is needed to evaluate its performance with a larger number of study subjects and a greater variety of abnormal corneal presentations. Future research studies, similar to those by Silverman et al and Yücekul et al, may also strengthen the argument for the combined use of ETM and tomography, as well as provide imaging protocols that may be utilized to optimize the clinical efficacy of both modalities.[5,10] Therefore, future research direction includes seeking an

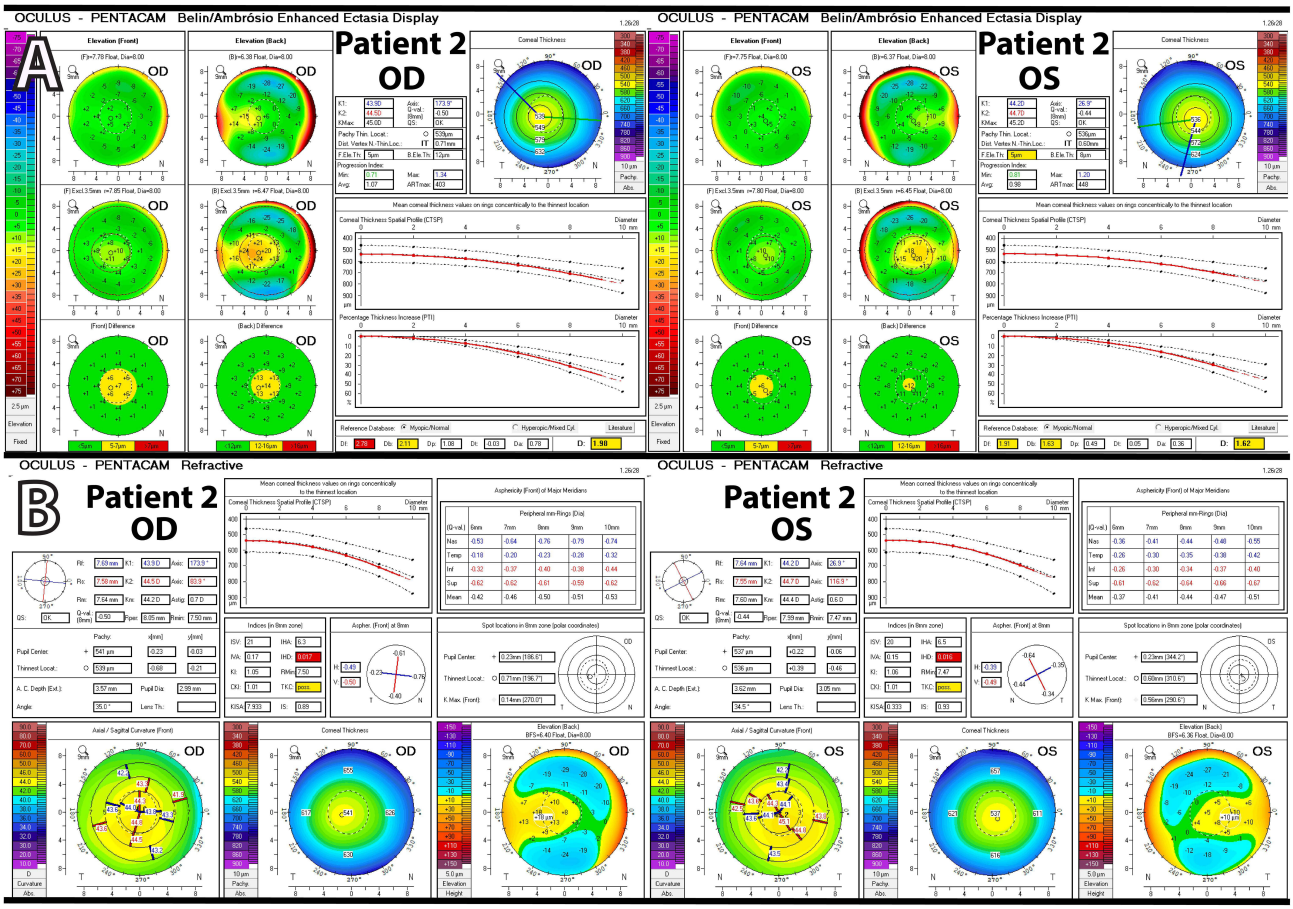

Figure 4 (**A**) Pentacam enhanced ectasia display maps suggestive of central thinning. (**B**) Pentacam refractive maps.
Notes: Figures 3 and 4 present a keratorefractive surgery candidate with suspected KC as observed by discordant findings on ETM and Tomography.

enhanced understanding of how to optimize the use of ETM and tomography when considering keratorefractive surgery in patients presenting with less common KC subtypes and specific ocular pathologies such as central corneal flattening associated with periocular masses or dry eye disease. These investigations may also include robust comparisons of the sensitivities and specificities of epithelial thickness measurements versus tomographic indices in the detection of KC and KC subtypes in a wide array of patients with various ocular presentations. As the presentation and pathogeneses of the various KC subtypes are studied more extensively, our knowledge of and ability to detect the signs of KC and KC subtypes, including at various stages of the disease, will be enhanced. Caution is advised in not overstating the use of ETM, lest refractive surgeons misinterpret research findings as advocating for the sole use of ETM. With these points in mind, approaching keratorefractive imaging research and surgical practice with an accurate understanding of ETM's limitations and the value of tomographic indices in detecting keratoconic changes will lead to advancements in patient safety and long-term outcomes.

Disclosure

The authors report no conflicts of interest in this work and have no financial interests to disclose.

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