Tomographic Screening for Ectasia Susceptibility

Analysis must go beyond corneal curvature and central thickness.

BY RENATO AMBRÓSIO JR, MD, PhD; ISAAC RAMOS, MD; FERNANDO FARIA CORREIA, MD; AND MICHAEL BELIN, MD, FACS

Refractive surgeons routinely face the challenge of identifying cases at higher risk for progressive keratectasia, a rare but severe complication of keratorefractive procedures such as laser vision correction.[1] The lamellar cut and/or excimer laser ablation may cause or aggravate biomechanical failure of the corneal stroma, which, in the case of ectasia, is unable to support the continuous stresses of intraocular pressure, extraocular muscles, blinking, eye rubbing, and other forces.[2] Ectasia can occur after surface ablation procedures, but the biomechanical impact of this surgery is much less pronounced than the impact caused by LASIK. For example, a thick flap may cause biomechanical failure and ectasia progression.[3]

Prevention is the best approach for such severe complications. Thus, careful preoperative screening is crucial.[4,5] In the past, Placido disc-based corneal topography—the evaluation of corneal front surface curvature—and central corneal thickness (CCT) measurements were used as the standard methods for screening refractive surgery candidates for their risk of developing ectasia.[5-7]

The ectasia risk scoring system (ERSS) was developed by Randleman and colleagues[8] based on a retrospective case control study that evaluated anterior corneal topography, CCT, the degree of refractive correction, the depth of the residual stromal bed, and patient age. A second study by Randleman and coworkers[9] confirmed abnormal preoperative topography as the most significant predictive variable. However, the ERSS had a false negative rate of 4% to 8% and a false positive rate of 6%.[8,9] Other studies have reported false positive rates as high as 35%.[10] Additionally, a separate retrospective study of 36 cases with ectasia after LASIK identified nine eyes (25%) classified as low risk and seven eyes (19%) as moderate risk.[11] The relatively high incidence of false negatives of the ERSS along with other reported cases of ectasia after LASIK in the absence of apparent risk factors[12-15] supports the need for novel screening methods that enhance the ability to detect ectasia susceptibility or risk among refractive surgery candidates.[16]

TAKE-HOME MESSAGE

- Screening for refractive surgery should go beyond simple corneal curvature and central thickness analysis.
- Several technologies for tomography, including horizontal slit scanning, rotational Scheimpflug imaging, arc scanning with high-frequency ultrasound, and anterior segment optical coherence tomography, are available in various commercial instruments.
- Refractive surgeons should be aware that the goal of screening patients for their risk of ectasia should include detection of ectatic diseases as well as the assessment of a relatively normal cornea's susceptibility to biomechanical failure.

TOPOGRAPHY AND TOMOGRAPHY

Corneal topography, or computerized videokeratography, has had an unquestionable role in the development of refractive surgery.[17] The term *topography* is derived from the Greek words *topos* (place) and *graphein* (to write). Although topography has been classically related to the study of geographical elements, such as the Earth's surface shape and features, corneal topography is a method of front or anterior corneal surface imaging. The term *tomography* is derived from the Greek words *tomos* (a cut or section) and *graphein* (to write). Tomography is a method for mathematically calculating a 3-D structure of a solid organ. Thus, the term corneal tomography should be used for the diagnostic characterization of the front and back surfaces of the cornea, along with thickness mapping. Several technologies for tomography, including horizontal slit scanning, rotational Scheimpflug imaging, arc scanning with high-frequency ultrasound, and anterior segment optical coherence tomography, are available in various commercial instruments.[18,19]

To improve the sensitivity and specificity of screening protocols for refractive surgery candidates, corneal characterization should go beyond front surface curvature and single-point central thickness. A tomographic approach is essential.[4] Tomography combines anterior and posterior corneal elevation with complete pachymetric data to reconstruct corneal architecture in three dimensions. Interpreting such an enormous amount of data is a complex task. Refractive surgeons should be aware that the goal of screening refractive surgery candidates for their risk of ectasia should not be limited to the detection of mild or subclinical forms of ectatic diseases (keratoconus and pellucid marginal degeneration); it should also include the assessment of a relatively normal cornea's susceptibility to biomechanical failure.

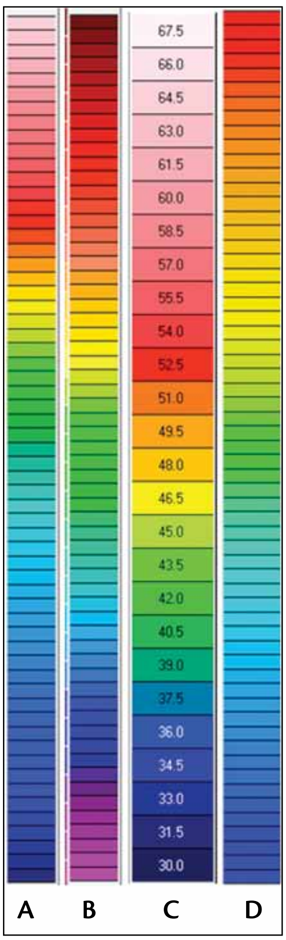

Figure 1. Color palettes of preferred use: (A) Ambrósio 2, (B) Belin Intuitive, (C) Smolek-Klyce (1.50 D absolute), and (D) Holladay Primary. The A, B, and D scales can be adjusted for being displayed with 15, 31, or 61 color steps.

PENTACAM CORNEAL AND ANTERIOR SEGMENT TOMOGRAPHY

The Pentacam (Oculus Optikgeräte GmbH) is a family of instruments that perform corneal tomography using a 360º rotating Scheimpflug camera. The WaveLight Oculyzer and Oculyzer II (Alcon Laboratories, Inc.) are built on the same platform as the Pentacam, with software capability for planning customized ablations based on corneal data. The Pentacam provides corneal and anterior segment reconstruction from limbus to limbus, up to the front surface of the iris and the crystalline lens.

TABLE 1. RECOMMENDED COLOR SCALES	
Elevation maps	Belin Intuitive Scale (relative 0.25 µm, 61 colors)
Pachymetric maps	Ambrósio 2 (absolute normal, 61 colors) Belin Intuitive Scale (absolute normal, 61 colors)
Sagittal curvature	Ambrósio 2 (absolute normal, 61 colors) Smolek-Klyce US (classic absolute scale) Belin Intuitive Scale (absolute normal, 61 colors) Holladay Primary (relative 0.50 D or 0.25 D; 15 colors)
Relative thickness	Ambrósio 2 (absolute normal, 61 colors)

A wide range of maps and displays can be generated from the Pentacam exam using many color scales.

A standardized approach to the objective evaluation of tomographic data should be implemented to facilitate diagnosis of potential corneal ectasia. We recommend that the data be evaluated in an organized, stepwise fashion. The first crucial element is to assess the quality of the exam to determine the reliability of the data. The Oculus quality score comprises an objective set of indices that asses the analyzed area, eye movements, and any loss of segments due to eyelid blinking or other factors that may influence the data.

Scheimpflug images are of interest, as they allow the evaluation of stromal transparency and scattering caused by Descemet membrane, which is consistent with the presence of cornea guttata.[20] The most commonly used displays are the Quad (4 Maps) Refractive, the Belin-Ambrósio Enhanced Ectasia Display (BAD), the topometric display, and the Fourier display. All displays have several color-coded maps. The number of colors, the step values between each color, the hottest and coolest colors, and the values and grade changes between colors can significantly influence the presentation of the display. Table 1 summarizes the best scales according to our personal preferences. The Ambrósio 2 palette (Figure 1A) of colors was inspired based on the benefits and limitations of the Belin Intuitive Scale (Figure 1B), the Smolek-Klyce (Figure 1C), and the Wilson-Klyce classic scales.[21]

There has been long debate about the advantages of absolute fixed color bars and values versus a normative or relative scale with colors and powers adjustable according to the cornea being studied. The most commonly used scales have been the absolute Smolek-Klyce scale and the EyeSys normative scale, which is similar to the Holladay Primary palette on the Pentacam (relative

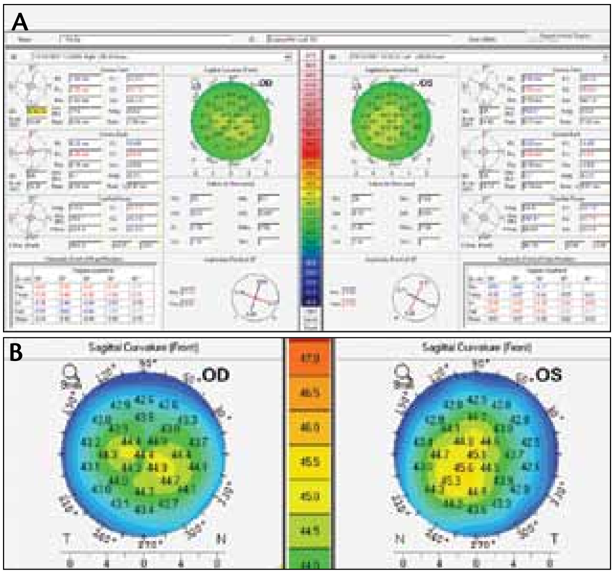

Figure 2. (A) Topometric display of a case example using the Smolek-Klyce absolute scale and (B) Holladay Normative with 0.50 D.

0.50 D or 0.25 D; 15 colors: blue to red scale [Figure 1D]). Although each scale has its advantages, we prefer to rely on absolute color scales, because this better facilitates comparison of different maps.

There is significant variability in the subjective interpretation of color-coded maps, which can lead to inaccuracy. Ramos et al[22] conducted a study among 11 corneal topography specialists, showing significant subjective variation in their interpretation of topographic maps. Using the topographic classification of the ERSS, 17 of 25 cases had classification variation of 0 to 4 across examiners using an absolute scale (Smolek-Klyce) and 11 cases had a classification variation of 0 to 4 across examiners using a normative 0.50 D scale (Holladay Primary or classic EyeSys scale). The study also showed that color scale influences the interpretation of color-coded maps, with statistically significant differences for eight of the 10 examiners.

For accurate interpretation, it is helpful to understand the analysis involved in the construction of each map and display, along with the normative values for the most accurate parameters, including the best cut-off values for distinguishing normal from ectatic corneas. The best strategy, in our experience, is to rely on objective parameters.

Topometric indices derived from the curvature of the front surface of the cornea are available on the Pentacam (Figure 2). Although these indices may be used as objective parameters to detect ectasia, it is important for the clinician to understand that they may lead to relatively later identification of ectasia with lower sensitivity than tomographic indices based on posterior elevation and pachymetric distribution.[23] Additionally, previous studies found about 10% false positive and 10% false negatives for these front-surface–derived indices (Guerra, unpublished data 2010).

THE BELIN-AMBRÓSIO ENHANCED ECTASIA DISPLAY

The BAD is a comprehensive ectasia screening display designed to present, in a consistent and simplified way, anterior and posterior elevation data along with pachymetric distribution (Figures 3 and 4). Elevation maps of the front and back surfaces of the cornea are presented with their respective best-fit sphere for a fixed 8-mm zone. The Enhanced Ectasia Display, developed by Michael W. Belin, MD, calculates a new reference best-fit sphere for the 8-mm zone, excluding an area of 3.5 mm in diameter centered on the thinnest point. The differences between the standard and enhanced best-fit spheres of the front and back surfaces are calculated. Such analysis facilitates the identification of protruding areas on the front and back surfaces of the cornea. Normal, borderline, and abnormal values are presented in a green/yellow/red color-coded bar.

A pachymetric map enables the identification of the value and location of the true thinnest corneal point. Additionally, thickness progression indices are calculated based on the relative normal increment of thickness toward the periphery.[18,24] The thickness profile is based on the physiologic concept that the cornea is a meniscus

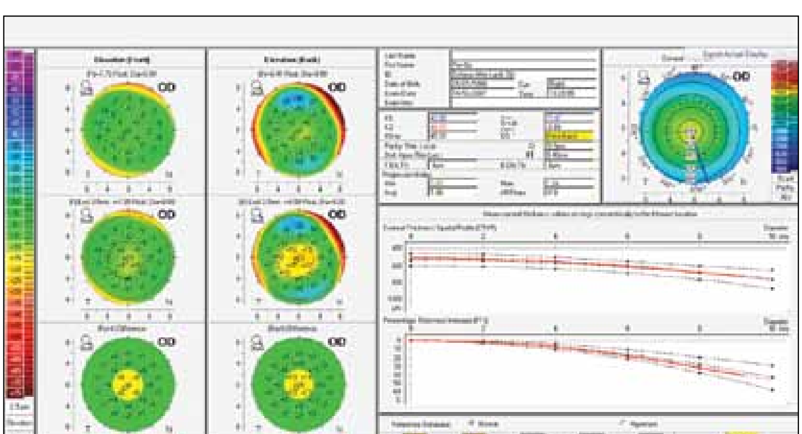

Figure 3. BAD of the right eye, showing elevation data and pachymetric distribution.

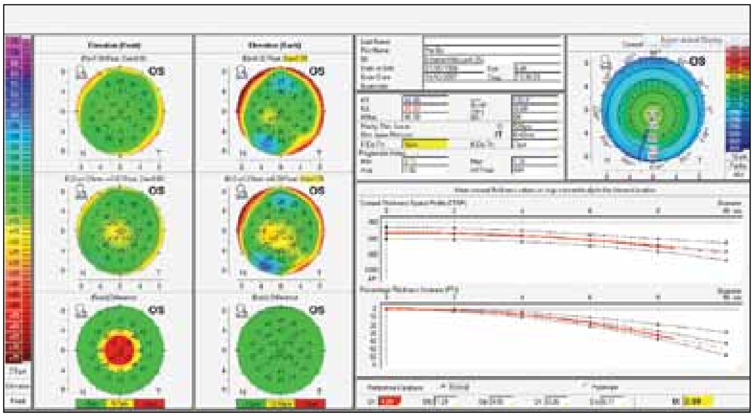

Figure 4. BAD of the left eye.

(ie, a structure that is thinner in the center and thicker in the periphery). The corneal thickness spatial profile and percentage thickness increase are displayed in graphs that also show the mean and 95% confidence interval of a normal population. The software can detect the thinnest point and calculate the rate of increase in thickness from this point outward to the periphery. This approach enables the clinician to distinguish a normal thin cornea from one with mild ectatic changes, including predisposition or susceptibility to ectasia, even in corneas with relatively normal thickness.

Indices are generated from these maps, and the deviation from normal toward ectatic disease (ie, deviation value) is calculated. A final deviation value that combines the indices is calculated based on linear regression analysis to optimize the sensitivity and specificity to detect ectasia. It is important to note that this parameter was designed to detect mild abnormalities related to ectasia, such as in contralateral eyes, with apparently normal front surface topography, of a patient with keratoconus in one eye.

CASE EXAMPLE

A 24-year-old woman presented for LASIK. Her manifest refraction was -3.25 -1.00 X 17° OD, yielding 20/15 BCVA, and -4.00 D of sphere OS, yielding 20/20 BCVA. CCT was 521 µm OD and 533 µm OS; corneal front surface curvature maps (Figure 2) were relatively normal in both eyes. The patient underwent uneventful LASIK with IntraLase-created (Abbott Medical Optics Inc.) planar flaps 120 µm thick in both eyes. The early postoperative period was uneventful, and the patient achieved 20/20 UCVA. At 6 months postoperative, however, the patient returned, complaining of reduced vision in both eyes. Regression of myopic astigmatism was observed in each eye. Further progression was observed, along with inferior steepening with mild reduction of BCVA. The patient was considered for corneal collagen crosslinking treatment.

The preoperative Pentacam data were retrieved, and a BAD display was generated (Figures 3 and 4). The Ambrósio Relational Thickness (ART) was calculated for the average and maximal progression indices (ART-Ave and ART-Max, respectively). ART-Ave was 496 µm OD and 517 µm OS, and ART-Max was 404 µm OD and 419 µm OS. The ART concept combines the thinnest corneal point with the average pachymetric progression of all meridians and in the maximal meridian. For detecting keratoconus, ART-Ave and ART-Max have areas under the receiver operating characteristic curves of 0.98 and 0.99, with cut-offs of approximately 430 µm and 340 µm, respectively.[18] However, for the identification of ectasia susceptibility, we have elected not to perform LASIK if ART-Max is lower than 405 µm or ART-Ave is lower than 500 µm. The final deviation values were 1.93 OD and 2.09 OS. Interestingly, a deviation value of more than 1.45 represents the most accurate risk factor parameter for detecting mild cases of ectasia or susceptibility.

CONCLUSION

Enhanced screening should go beyond simple corneal curvature and central thickness analysis. There has been a tremendous evolution from manual keratometry to corneal topography to corneal tomography. Studies by the Rio de Janeiro Corneal Tomography and Biomechanics Study Group have focused on identifying criteria for ectasia susceptibility, including corneal tomography and biomechanical assessment.[4,25] The Pentacam BAD provides a comprehensive refractive surgical screening tool to assist the refractive surgeon in identifying patients at risk for postoperative ectasia. Further improvements are expected with the integration of biomechanical assessment. ■

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1. Seiler T, Quurke AW. Iatrogenic keratectasia after LASIK in a case of forme fruste keratoconus. *J Cataract Refract Surg*. 1998;24(7):1007-1009.
2. Dawson DG, Randleman JB, Grossniklaus HE, et al. Corneal ectasia after excimer laser keratorefractive surgery: histopathology, ultrastructure, and pathophysiology. *Ophthalmology*. 2008;115(12):2181-2191.e1
3. Giledi O, Daya SM. Unexpected flap thickness in laser in situ keratomileusis. *J Cataract Refract Surg*. 2003;29(9):1825-1826.
4. Ambrosio R Jr, Nogueira LP, Caldas DL, et al. Evaluation of corneal shape and biomechanics before LASIK. *Int Ophthalmol Clin*. 2011;51(2):11-38.
5. Ambrosio R Jr, Klyce SD, Wilson SE. Corneal topographic and pachymetric screening of keratorefractive patients. *J Refract Surg*. 2003;19(1):24-29.
6. Oshika T, Klyce SD. Corneal topography in LASIK. *Semin Ophthalmol*. 1998;13(2):64-70.
7. Ambrosio R Jr, Wilson SE. Complications of laser in situ keratomileusis: etiology, prevention, and treatment. *J Refract Surg*. 2001;17(3):350-379.
8. Randleman JB, Woodward M, Lynn MJ, Stulting RD. Risk assessment for ectasia after corneal refractive surgery. *Ophthalmology*. 2008;115(1):37-50.
9. Randleman JB, Trattler WB, Stulting RD. Validation of the Ectasia Risk Score System for preoperative laser in situ keratomileusis screening. *Am J Ophthalmol*. 2008;145(5):813-818.
10. Duffey RJ, Hardten DR, Lindstrom RL, et al. Ectasia after refractive surgery. *Ophthalmology*. 2008;115(10):1849; author reply 49-50.
11. Chan CC, Hodge C, Sutton G. External analysis of the Randleman Ectasia Risk Factor Score System: a review of 36 cases of post LASIK ectasia. *Clin Experiment Ophthalmol*. 2010;38(4):335-340.
12. Klein SR, Epstein RJ, Randleman JB, Stulting RD. Corneal ectasia after laser in situ keratomileusis in patients without apparent preoperative risk factors. *Cornea*. 2006;25(4):388-403.
13. Amoils SP, Deist MB, Gous P, Amoils PM. Iatrogenic keratectasia after laser in situ keratomileusis for less than -4.0 to -7.0 diopters of myopia. *J Cataract Refract Surg*. 2000;26(7):967-977.
14. Ambrosio R Jr, Dawson DG, Salomao M, Guerra FP, Caiado AL, Belin MW. Corneal ectasia after LASIK despite low preoperative risk: tomographic and biomechanical findings in the unoperated, stable, fellow eye. *J Refract Surg*. 2010:1-6.
15. Tabbara KF, Kotb AA. Risk factors for corneal ectasia after LASIK. Ophthalmology. 2006;113(9):1618-1622.
16. Belin MW, Ambrosio R Jr. Corneal ectasia risk score: statistical validity and clinical relevance. *J Refract Surg*. 2010;26(4):238-240.
17. Wilson SE, Ambrosio R. Computerized corneal topography and its importance to wavefront technology. *Cornea*. 2001;20(5):441-454.
18. Ambrosio R Jr, Caiado AL, Guerra FP, et al. Novel pachymetric parameters based on corneal tomography for diagnosing keratoconus. *J Refract Surg*. 2011;27(10):753-738.
19. Ambrosio R Jr, Belin MW. Imaging of the cornea: topography vs tomography. *J Refract Surg*. 2010;26(11):847-849.
20. Kwon RO, Price MO, Price FW, Jr., Ambrosio R Jr, Belin MW. Pentacam characterization of corneas with Fuchs dystrophy treated with Descemet membrane endothelial keratoplasty. *J Refract Surg*. 2010;26(12):972-979.
21. Wilson SE, Klyce SD, Husseini ZM. Standardized color-coded maps for corneal topography. *Ophthalmology*. 1993;100(11):1723-1727.
22. Ramos I, Ambrosio R Jr, Guerra FP, Belin MW, Trattler WB. Impact of the subjective variability of corneal topography classification on the ectasia risk score system. Paper presented at: the American Academy of Ophthalmology Annual Meeting; October 24, 2011; Orlando, FL.
23. Saad A, Gatinel D. Topographic and tomographic properties of forme fruste keratoconus corneas. *Invest Ophthalmol Vis Sci*. 2010;51(11):5546-5555.
24. Ambrosio R Jr, Alonso RS, Luz A, Coca Velarde LG. Corneal-thickness spatial profile and corneal-volume distribution: tomographic indices to detect keratoconus. *J Cataract Refract Surg*. 2006;32(11):1851-1859.
25. Ambrosio R Jr, Dawson DG, Salomao M, Guerra FP, Caiado AL, Belin MW. Corneal ectasia after LASIK despite low preoperative risk: tomographic and biomechanical findings in the unoperated, stable, fellow eye. *J Refract Surg*. 2010;26(11):906-911.

3-D Corneal Tomography

This technology facilitates the diagnosis of ectatic diseases.

BY CALLAN NAVITSKY, ASSOCIATE EDITOR

For decades, ophthalmologists used 2-D, Placido-based topography systems for surface evaluation of the cornea. Tomography, however, which uses optical cross-sectioning to generate 3-D reconstructions of the anterior segment, has greater potential for the diagnosis, prognosis, and treatment planning of ectatic diseases, said Michael W. Belin, MD, at the 2011 annual meeting of the American Academy of Ophthalmology (AAO).

In a nutshell, 3-D Scheimpflug tomography provides information on both the anterior and posterior surfaces, unlike Placido-based systems, which describe the anterior surface only. With information on both anterior and posterior elevation, tomography can also generate a full pachymetric map.

Scheimpflug tomography provides greater coverage of the cornea compared with Placido-based imaging, which is limited to about 60% of the cornea for two reasons. One limitation of Placido systems is strictly anatomic: It is impossible to design a cone that will cover the entire cornea because of facial features such as the nose and the brow. The second limitation is geometric and optical: Light cannot bounce off the peripheral cornea and come back to a central camera. Scheimpflug imaging is not reflective and therefore capable of much greater corneal coverage, at times extending out to the limbus, Dr. Belin said.

Compared with a Placido-based system, the advantages of 3-D tomography include information about the posterior cornea, the ability to generate full pachymetric maps, and access to greater coverage of both anterior and posterior surfaces. As Dr. Belin explained, these capabilities aid in the diagnosis of keratoconus, pellucid marginal degeneration (PMD), and post-LASIK ectasia.

"Effective screening requires that you look not only at the anterior surface, but that you look at both pachymetric distribution and the posterior surface," Dr. Belin said. Specifically, to diagnose early keratoconus, the practitioner must look for abnormalities on the posterior surface, which are positive islands of elevation; therefore, one of the best screening indices is the absolute elevation value at the thinnest point on the cornea, he explained.

To demonstrate the effectiveness of 3-D tomography in the diagnosis of keratoconus, Dr. Belin presented a case example of a patient with unilateral keratoconus. The patient was examined using topography with automatic detection. Anterior surface mapping showed one of the patient's eyes to be highly abnormal. However, the patient's fellow eye appeared normal in terms of anterior curvature, elevation, and curvature indices.

The patient was then evaluated using 3-D tomography. On the Belin/Ambrosio display, nearly every parameter for the abnormal eye was outside the normal limits, which was approximately 12 standard deviations from the norm, Dr. Belin said. Changes on the anterior surface, the posterior surface, and pachymetric distribution were present. However, this was unsurprising, as the eye was already known to be abnormal. Full tomographic evaluation of the patient's so-called normal eye, however, revealed a positive island off the best-fit sphere on the posterior surface.

"If you only looked at anterior curvature, you would view this eye as normal," Dr. Belin said. "Most of you would say, 'That's interesting, but I would not have touched that patient because the other eye was so abnormal.' That may be true, but what would happen if both eyes looked like the [so-called] normal eye, and all you had was curvature?"

Furthermore, some patients with keratoconus retain good visual acuity. Historically, keratconus was diagnosed when the patient came to the ophthalmologist's office complaining of decreased vision. By the time these patients were examined, they already had changes on the anterior surface. With refractive surgery, so-called normal patients are being examined with advanced technology that previously was reserved for patients with known disease, revealing a number of individuals with subclinical or asymptomatic keratoconus. Subclinical keratoconus is not suspect, Dr. Belin said; it is a true disease. These corneas are abnormal based on posterior elevation and pachymetric progression; however, they have normal anterior curvature, so the patients retain good vision. Structurally, the posterior surface may be a more important indicator of pathology than the anterior surface. As a refracting surface, however, the posterior surface contributes little to the overall refractive power because it is a cornea-aqueous interface, with little change in index of refraction, in comparison with the air-cornea interface at the anterior surface.

Scheimpflug-based elevation data provides greater coverage of the cornea, which is advantageous in the diagnosis of PMD, Dr. Belin said. The classic description of PMD is a band of inferior thinning 1 to 2 mm from the limbus. This area is where the pathology of PMD is; however, it is not analyzed by Placido-based systems, which are limited to covering 60% of the cornea. The best way to truly diagnose PMD is to look at a complete limbal-to-limbal corneal thickness map, he said.

The ability of 3-D tomography to image the posterior corneal surface also accounts for its advantage over Placido-based analysis for diagnosing post-LASIK ectasia. Early diagnosis is now even more crucial with the ability to perform corneal collagen crosslinking (CXL) to prevent disease progression, Dr. Belin said. Ideally, post-LASIK ectasia would be detected before the patient has major changes on the anterior surface. To look for subtle changes associated with post-LASIK ectasia, one cannot look at the anterior surface because it has been altered. Pachymetric map indices cannot be used either, as they rely on algorithms based on a normal population, and post-LASIK patients have abnormal pachymetric progression. The normal postoperative posterior surface, however, should remain unaltered.

The best way to evaluate a patient for post-LASIK ectasia is with a subtraction map of the posterior corneal surface, which is created by taking the post-LASIK posterior elevation and subtracting the preoperative posterior elevation. If the difference represents a significant change, it is an indication of post-LASIK ectasia, Dr. Belin said. He suggested that Pentacam (Oculus Optikgeräte GmbH) users generate a follow-up map to evaluate the posterior surface of all post-LASIK patients. If the patient's changes are significant, he or she may be a good candidate for CXL, as the surgeon would want to stabilize the patient before he or she becomes symptomatic.

Overall, 3-D tomography enables a more detailed characterization of the cornea, making it an essential tool in evaluating patients with keratoconus, PMD, and post-LASIK ectasia, Dr. Belin concluded. ■