Simplifying Ectasia Screening with Pentacam Corneal Tomography

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THE PROBLEM OF ECTASIA AFTER LVC

Since the first report of post-LASIK ectasia by Theo Seiler MD, PhD, in 1996, progressive ectasia emerged as one of the most important complications of laser vision correction (LVC) procedures. Many studies suggest that the rate of new cases of post-LASIK ectasia is declining. However, because LVC represent the most popular elective procedure performed in medicine today and the very severe devastating nature of ectasia, even a very low incidence is perturbing. Ectasia prevention is the most effective strategy. Refractive surgeons face routinely the challenge to identify cases at higher risk for ectasia. Therefore a proper understanding of this condition is critical.

Simplistically, there are two possible explanations for the development of ectasia: the presence of an ectatic disorder preoperatively and the severe impact of the surgery on the corneal biomechanical structure. In both situations, there is a process of chronic biomechanical failure of the remaining stromal tissue after the LVC procedure. In post-LASIK ectasia cases, the lamellar cut combined with the laser ablation leads to an unstable remaining residual stromal bed (RSB). Ectasia can also occur after surface ablation procedures, but the biomechanical impact of the surgery is less pronounced. The ectatic process of the corneal stroma occurs through a 2-step process of delamination and interfibril fracture because of the unsupportive corneal structure to the continuous stresses, which are caused by intraocular (IOP) pressure, extra-ocular muscles action, blinking, eye rubbing and other forces. The process is characterized clinically by thinning and bulging of the cornea, leading to a myopic shift and irregular astigmatism, reducing uncorrected and best spectacle-corrected visual acuity.

Risk factors for ectasia after LASIK surgery are well recognized in the literature. Preoperative Placido disk-based topographic abnormalities, such as keratoconus or pellucid marginal degeneration, are considered the most important risk factors. Moreover, the residual stromal bed (RSB) thickness is also important because this portion of the cornea will be responsible for maintaining the biomechanical strength of the cornea following LASIK. RSB is typically calculated by subtracting the LASIK flap thickness and laser ablation from pre-operative central corneal thickness (CCT). Therefore, thick flaps, higher corrections, re-treatments and thin corneas would be related to lower RSB. An FDA limit of 250µm has been accepted but there are cases with over 300 µm that developed ectasia and also, there are cases with RSB as low as 200 µm that remained stable with long follow up.

An ectasia risk score scale was proposed by Randleman and co-authors. The Randleman's Risk Score System (RRSS) uses pre-operative central corneal thickness (CCT) measured with the ultrasound, the axial curvature maps of the front corneal surface (Corneal Topography - CT) and the level of correction, in addition to the anticipated RSB and patient's age. The RRSS was statistically validated in a second study, where it was determined to have a sensitivity of 92% and specificity of 94%. Therefore, 6% of the cases that developed post-LASIK ectasia were not identified as high risk at the RRSS. In addition, there were 8% of the cases with good outcomes that were classified as at high risk. The incidence of such false positive cases may be as high as 35% if a younger population of LASIK cases is studied. These situations definitively illustrate the current gaps in our knowledge and the need to develop more sensitive and specific diagnostic tests for screening refractive candidates.

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Novel enhanced screening criteria based on 3D Corneal Tomography (CTm) and biomechanical analysis was proposed by our group. (Ambrósio Jr R et al. Clinical Evidence of the Enhanced Sensitivity and Specificity of Corneal Tomography and Biomechanics for Screening Ectasia in Refractive Candidates ePoster ASCRS 2009. http://ascrs2009.abstractsnet.com/acover.wcs?entryid=000161).

GOALS OF ECTASIA SCREENING

Careful preoperative screening is paramount to the success of LVC. Classically, Placido's CT and CCT have been widely considered as the classical tools that are essential for screening refractive candidates. It is well recognized that CT can detect signs of the disease before definitive symptoms or slit-lamp findings develop. These cases, typically referred as sub-clinical ectasia (or forme fruste) have demonstrated that CT is critical for the preoperative screening. However, in addition to the false negative cases at the RRSS, there are many reports of ectasia after LASIK, in which no risk factor was identified by CT, CCT and clinical parameters. It is well accepted that such cases have presented with early forms of the disease that were not detectable by CT.

In fact, the detection of the earliest of incipient ectasia or even its susceptibility should be the goal when screening refractive candidates. It is assumed that any cornea may undergo unstable, progress to biomechanical failure and ectasia if the stresses overpass its biomechanical resistance. There are also false positive cases at the RRSS, along with many reports of good outcomes after LASIK in cases with abnormalities detected at CT. Such mysteries related to ectasia would be solved if the screening process targets for characterizing ectasia susceptibility.

WHY CORNEAL TOMOGRAPHY?

Considering the importance of Corneal Topography (CT) or computerized videokeratography for the development of Refractive Surgery and the need for evolving in the diagnostic methodology, it is critical to have recognition and adherence to proper terminology. Prof. Steve Klyce, PhD has been commended for his pioneering work and many continuous contributions to this field. Topography derives from Greek words "to place" (topo) and "to write" (graphein), which

means to describe a place. This is classically related to the study of Earth's surface shape and features or those of planets, moons, and asteroids. CT should be the term used for the evaluation of the corneal anterior surface. Curvature axial or tangential maps, refractive maps, wavefront decomposition and elevation maps of the front (anterior) are possible from topographic data, which is commonly acquired from the Placido's disc. However, other technologies such as the raster photogrammetry have been also used for CT.

Tomography also derives from the Greek words "to cut or section" (tomos) and "to write" (graphein). In Medicine, tomography is a method of mathematically calculating three-dimensional structures of a solid organ. Thereby, Corneal Tomography (CTm) should be used for the diagnostic characterization of the front and back corneal shape, along with pachymetric mapping. Different technologies such as horizontal slit scanning, rotational Scheimpflug, arc scanning with very high frequency ultrasound (VHFUS) and optical coherence tomography (OCT) are available in different commercial instruments.

This article summarizes our current approach using the Pentacam Corneal Tomographer (Oculus Optikgeräte GmbH, Wetzlar, Germany).

UNDERSTANDING PENTACAM CORNEAL TOMOGRAPHY

The Pentacam is a family of instruments that perform CTm using a rotating Scheimpflug camera that runs 360º. The system can be programmed to take 25 or 50 images for the 3-D evaluation **(Figure 1)**. It has been our routine to use 25 pictures since this is a significantly faster approach and there is no difference on the

Figure 1: Recommended settings on the Pentacam.

Figure 2: Pentacam overview display. The virtual eye image provides with good interesting evaluation of the relation of the corneal apex and pupil. The Examination Quality Specification refers to a blinking error, which indicates the exam should be repeated. Some cases fail to have good quality and the clinician should evaluate the Scheimpflug images to assure the exam's trustability.

accuracy and on the repeatability of the data acquired (Ambrósio, unpublished data 2005). Once the patient is positioned on the instrument in a comfortable and aligned position, the examiner positions the camera accordingly to the patient´s eye and asks the patient to blink just and then keep the eyes wide open just before the camera is released. It is advised to use automatic release option for proper centering. This technique decreases the chances of the patient blinking during the scan. It is also preferred that no drop is applied to the patient´s eye prior to the exam since these may interfere with the tear film and affect the measurements of the cornea. However, pharmacologic dilation may be used if necessary.

When the scan is finished, the data is processed and the overview display is presented. The examiner should look at the Scheimpflug images which have indeed very relevant data for clinical interpretation. Examination quality specification should be checked so that the exam is to be repeated if necessary, accordingly to the results **(Figure 2)**. It is important to note that warning signs such as the 3-D model deviation (yellow) is not necessarily related to a poor exam. Once the data is properly acquired and this is assured to be of acceptable quality, clinical interpretation would follow**.**

TYPES OF MAPS, DISPLAYS AND COLOR SCALES

The Pentacam has developed over the past years a very wide range of possible maps and displays, as well as many different color scales. This wide variability

of options may sometimes confuse the clinician. It is relatively common to receive for a second opinion the JPEG image from the Pentacam exam with very poor presentation of the data, which definitively jeopardize clinical interpretation and limits the benefits of the technology. For practical standpoints, we focus on the evaluation of two or three displays in an organized stepwise fashion: the "Quad (4 Maps) Refractive", "Belin/Ambrósio Enhanced Ectasia Display" and the "Holladay Report". In some cases, the displays "Scheimpflug", "Topometric", "Show 2 Exams Topometric", "Show 2 Exams Pachymetry" and "Zernike Analysis" are also used.

Any color-coded map would be influenced by the color scale chosen. The number of colors, the step value between each color, the highest and lowest colors, values and the grading change between each color are the main characteristic to be considered. **Table 1** summarizes the best scales as my personal preference. In fact, it has been advocated for having a fixed set of color scales for some Displays such as the "4 Maps Refractive" Display.

Table 1 – Recommended Color Scales	
Elevation Maps	Belin Intuitive Scale (relative 0.25µm, 61 Colors)
Pachymetric Maps	Ambrósio2 (Absolute Normal, 61Colors)
	Belin Intuitive Scale (Absolute Normal, 61 Colors)
Sagittal Curvature	Ambrósio2 (Absolute Normal, 61Colors)
	Smolek-Klyce US (Classic Absolute Scale)
	Belin Intuitive Scale (Absolute Normal, 61 Colors)
	Holladay Primary (Relative 0.5D; 15 Colors)
Relative Thickness	Ambrósio2 (Absolute Normal, 61 Colors)

The Ambrósio2 palette **(Figure 3A)** of colors was developed, inspired on the benefits and limitations of the Belin Intuitive Scale **(3B)**, the Smolek-Klyce **(3C)** and the Wilson-Klyce classic scales. The concept of a wide range of colors was combined with the contrast between the highest c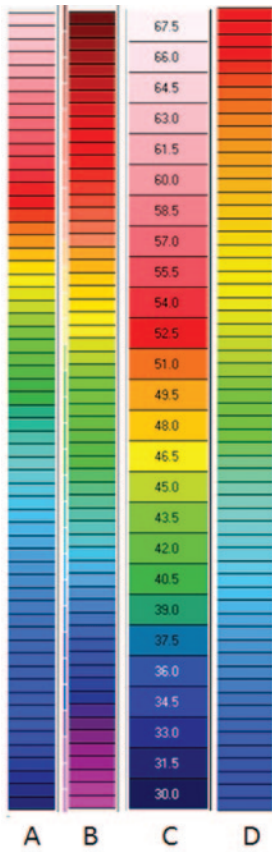olor and lower color. This color palette was originally developed for pachymetric maps, considering statistical values found in a study comprising of 226 normal corneas and 88 keratoconic corneas (Ambrósio, Caiado & Bonfadini, unpublished data 2009). In the normal population, mean thinnest point (TP) value was about 550μm and standard deviation (SD) of 30 μm. The green color was centered on the 550 and the shades of darker and lighter green were calculated to be within 1SD. The best cut off value in the Receiver operating characteristic (ROC) curve for keratoconus and normals was around 500μm, which was set for the yellow threshold. The TP had a sensitivity of 87% and specificity of 90% (p<0.001, Mann–Whitney U test). Finally, the mean TP was about 450μm for keratoconus corneas, which should be the threshold for the red color. On the thicker side, attention was given to a cohort of 34 corneas with Fuchs' Endothelial Dystrophy. Mean TP value for Fuchs' corneas and the best cut off value in the ROC curve were 625μm and 600μm, which was set for the green to blue threshold. The TP had a sensitivity of 82% and specificity of 91% (p<0.001, Mann–Whitney U test) for normals versus Fuchs'. The Ambrósio2 pachymetric scale was designed to facilitate the differentiation of normal and pathologic thin and thick corneas because it provides color information regarding the thickness profile. The distribution of the colors around the TP correlates well with pachymetric distribution graphs **(Figure 4)** and enables the identification of a normal thin cornea **(4A)** and one with similar TP value but

Figure 3: Color palettes of preferred use. A: Ambrósio 2; B: Belin Intuitive; C: Smolek-Klyce (1.5D Absolute); D: Holladay Primary
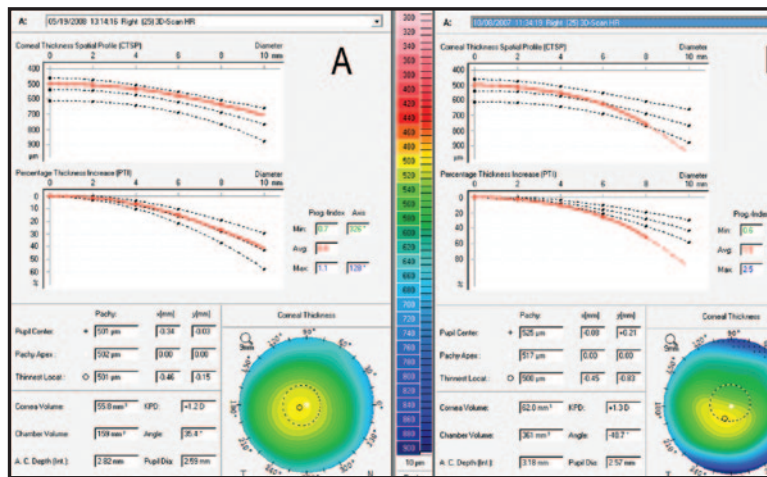

Figure 4: Composite of the Pachymetric Evaluation of two different cases. A) Normal Thin Cornea. UCVA 20/15 and this case has been stable over 5 years with no abnormality. TP is within 0.5mm of the apex, with 501μm; ART-Mid = 501/0.9 (556) and ART-Max = 501/1.1 (455). Note the CTSP parallel to the normal lines and PTI graphs just over the mean. B) Moderate Keratoconus. TP is displaced temporal-inferiorly over 0.7mm (0.95mm) with 500μm; ART-Mid = 500/1.5 (333) and ART-Max = 500/2.5 (200). Note the CTSP with a severe increase from 3mm and PTI out of the range of 95% confidence interval.
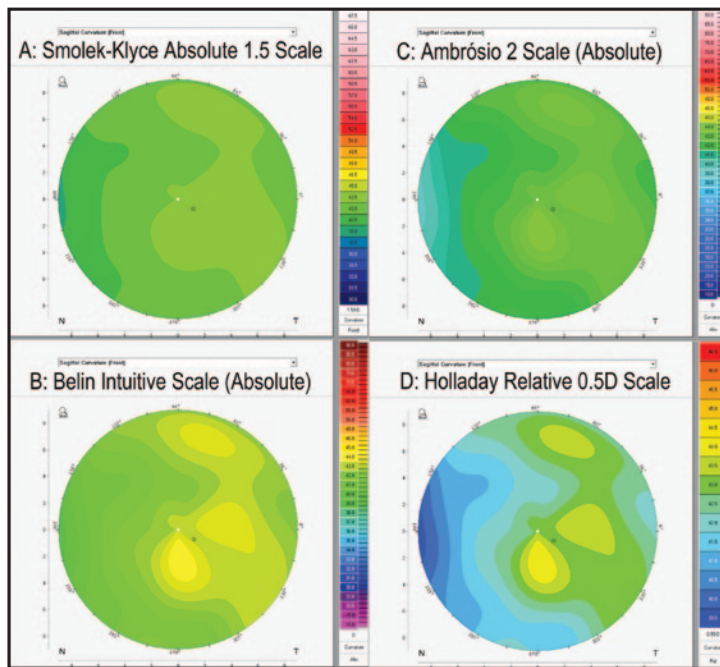
Figure 5: Sagittal (axial) curvature maps from the same normal cornea. Patient has UCVA 20/15, with normal thickness and elevation maps. Note the accentuation in detail in the adjustable Holladay Primary scale with 0.5D. This detail is not appreciated on the Smolek-Klyce scale. The Belin scale provides detailing with colors getting into the yellow to orange range (45D). The Ambrósio 2 scale provides detailing regarding corneal asphericity but the colors fall within the green range.

abnormal profile and keratoconus (**4B**). The importance of corneal thickness and pachymetric distribution evaluation were discussed in Vol. 35, issue # 4, 2007 of HIGHLIGHTS OF OPHTHALMOLOGY JOURNAL by Ambrósio, Silva and Simonato.

The color scale also impacts the representation of the curvature map. There has been a long debate on the preference for absolute fixed color bars and powers, such as the Smolek-Klyce scale, versus relative scales with adjustable colors and powers accordingly to the cornea studied, such as the ones found in the "Eye Sys" that are similar to the Holladay Primary (relative 0.5D, 15 Colors: Blue to Red Scale). There are important advantages for each direction, but generally the adjustable scales are more sensitive and the absolute scales, more specific. It has been my preference to routinely use absolute color scales because of the relative facilitation for comparison different maps.

The Ambrósio 2 scale also has some interesting features related to its use for sagittal curvature maps (**Figure 5**). Average and SD is 43.1 +/- 1.43D for central K and 44.6 +/- 3.4D for highest K (KMax) among normals (n=226). These values are well on the range of green to green-blue. The best cut off value in the ROC curve was around 48D which was set for the orange to red. The KMax had a sensitivity of 97.7% and specificity of 96.9% (p<0.001, Mann–Whitney

U test; Ambrósio, Caiado & Bonfadini, unpublished data 2009).The KMax performs by itself superiorly than the "topometric" KKS (keratoconus score) indices from the Oculus software, which are based on the 8mm front curvature data. In fact, we found the sensitivity and specificity of the KKS were 94.32% and 87.62% respectively (Guerra, Valbon & Ambrósio, unpublished data 2009).

Regarding curvature maps, it is very important for the clinician to understand the difference from sagittal (or axial) maps and tangential (or instantaneous) maps. While in the sagittal map, the curvature of the cornea is determined at each measured points at a normal (90°) angle to its surface referenced to the mid-line, tangential maps evaluate the local radius at each
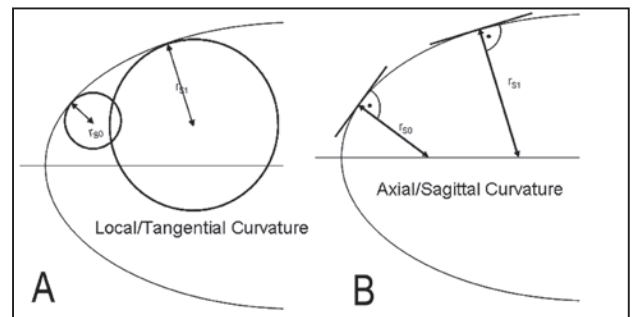

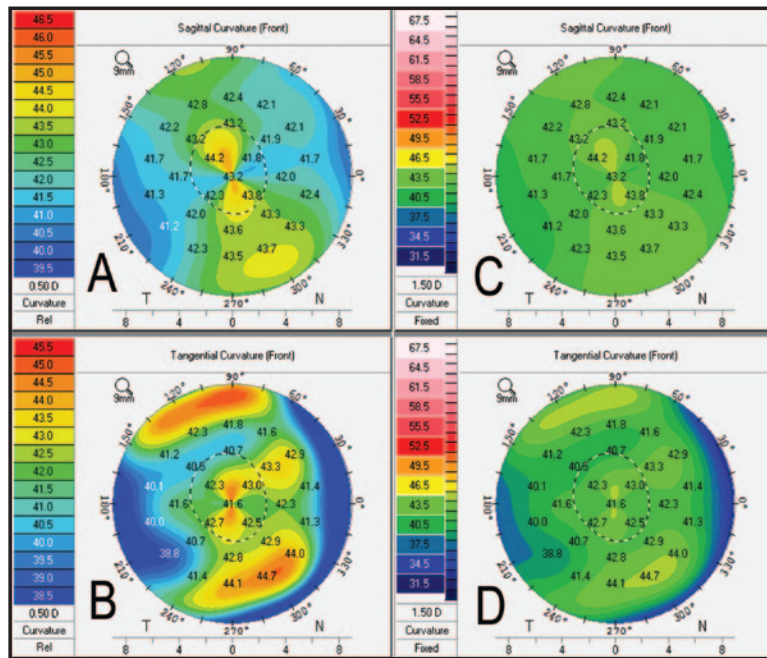Figure 6: Diagram scheme for local/tangential or instantaneous curvature and axial/sagittal curvature calculations.

Figure 7: Sagittal (A, C) and Tangential Maps (B, D) from a case with normal astigmatism using the Holladay Primary relative scale (15 colors, 0.5D – A, B) and Smolek-Klyce Absolute scale (C, D). Note the irregular pattern is more pronounced in the adjustable scale (B).

measured point of data (**Figure 6**). This highlights differences among the measured points and results in a more "noisy" color pattern for the tangential maps (**Figure 7**). It is important to note that sagittal curvature maps have been more popular for screening refractive candidates. In fact, classic screening systems such as the Rabinowitz-McDonnell were developed based on sagittal or axial maps. These indices are based on the steepness of the cornea, superior-inferior asymmetry and between eyes asymmetries.

The basics and advantages of elevation based topography were discussed by Belin and Khachikian in the Book "Elevation Based Topography-Screen-ing for Refractive Surgery" published by HIGHLIGHTS OF OPHTHALMOLOGY JOURNAL in 2008. It is important that the examiner understands that the elevation maps are in fact differential maps from the examined corneal surface and reference that was chosen. Thereby the reference would severely impact any elevation maps. For practical purposes, we have chosen to use the central 8mm of the cornea for the calculation of the reference curve, which can be the best fit sphere (BFS) or toric ellipsoid (BFTE). The elevation maps from the front and back surfaces of the cornea should be evaluated for their pattern and elevation values in corneal landmarks: apex and thinnest. In a study comprising of 100 normal corneas (50 patients) and 60 keratoconic corneas (30 patients), the ROC curves for posterior elevation values at the thinnest point considering either BFS or BFTE performed better than at the apex, but with similar performances. Best cut offs were 21 and 13 for the BFS and BFTE, with area under the ROC (AUROC) 0.98 and 0.97 respectively (Canedo, Louzada, Belin & Ambrósio, unpublished data 2009). Thereby, either BFS or BFTE perform well for diagnosing keratoconus if
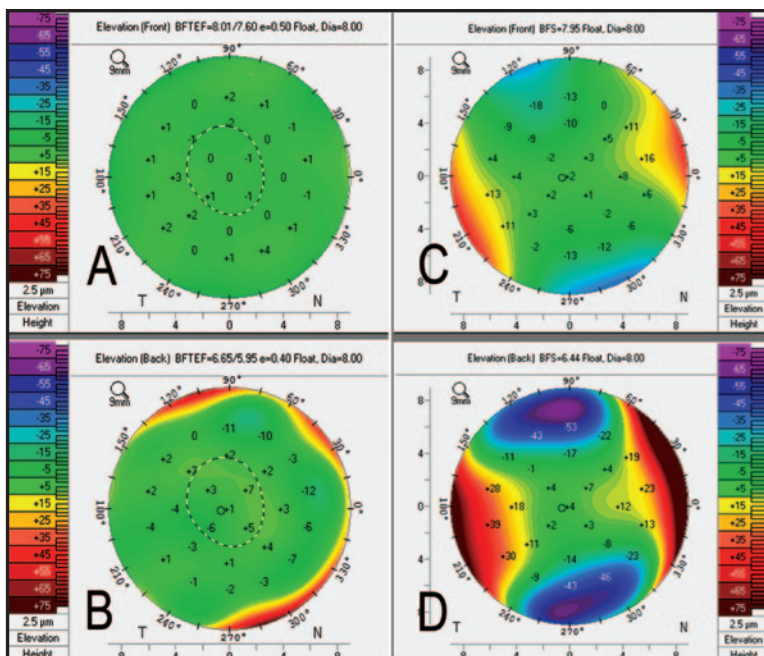

Figure 8: Elevation maps from the front (A, C) and back (B, D) surfaces of the same case as in Figure 7 or a normal astigmatism, using BFTE (A, B) and BFS (C, D). Note the low levels of irregularity on the astigmatism on the BFTE, which is related to the pattern of high order aberrations from the case. BFS has a pattern of normal astigmatism.

we consider the elevation at the thinnest point and the 8mm zone. Interestingly, these different approaches provide additional complementary information about the regularity of the astigmatism and optical quality **(Figure 8)**.

The Pentacam provides a very detailed corneal thickness distribution map with accuracy and repeatability within less than 3μm. From this data, the Corneal Thickness Spatial Profile (CTSP) and the Percentage Thickness Increase (PTI) graphs are calculated. A pachymetric progression index (PPI) is also calculated for every one degree meridian along the complete 360°, starting at the thinnest point. The average of all meridians and the one with lower and higher values are presented. In a normal population, the averages and SD of PPI of the minimal, maximal meridians and average of all meridians are 0.58 +/- 0.3, 0.85 +/- 0.18 and 0.13 +/- 0.33. The pachymetric index will be higher if the cornea gets thicker in a more accentuated pattern from the thinnest point out to the periphery (PTI and CTSP graphs falling down). Interestingly, the best parameters we have ever developed for diagnosing keratoconus are the ones related to the "Ambrósio Relational Thinnest", which is the thinnest pachymetric value divided by the pachymetric progression. The "Ambrósio Relational Thinnest" is thereby calculated for the, minimal (ART-Min) average (ART-Mid) and maximal (ART-Max). The "ART" concept combines thinnest with the pachymetric distribution, which facilitates the identification of an abnormal cornea despite its thinnest value.

The ART-Mid and ART-Max have AUROC of 0.98 and 0.99, with cut offs of 426μm and 339μm, respectively (Ambrósio, Guerra, Caiado and Belin, unpublished data 2010). For practical standpoints, we have adopted not to perform LASIK if ART-Max is lower than 400μm.

The Belin/Ambrosio Enhanced Ectasia Display (BAD) was discussed by Belin, Khachikian, Salomão and Ambrósio in Vol. 35 No. 6, 2007 HIGHLIGHTS OF OPHTHALMOLOGY JOURNAL. The goal of the BAD was to combine elevation based and pachymetric corneal evaluation in one comprehensive display to give the clinician a global view of the tomographic structure of the cornea. Deviation of normality values were implemented for the front and back enhanced elevations, pachymetric distribution and vertical displacement of the thinnest in relation to the apex. The final D was developed for having lower than 5% of false positives and false negatives. The relevance of the BAD was determined in a study of eyes with highly asymmetric keratoconus, in which it was confirmed the superior sensitivity of the display over front surface curvature and central thickness evaluation. The combination of the new elevation based approach and the pachymetric distribution has increased sensitivity to more than 90% in corneas with normal curvature maps from patients previously diagnosed with "unilateral keratoconus" (Salomão and Ambrósio, unpublished data 2007) as seen in the example **(Figures 9, 10 and 11)**.
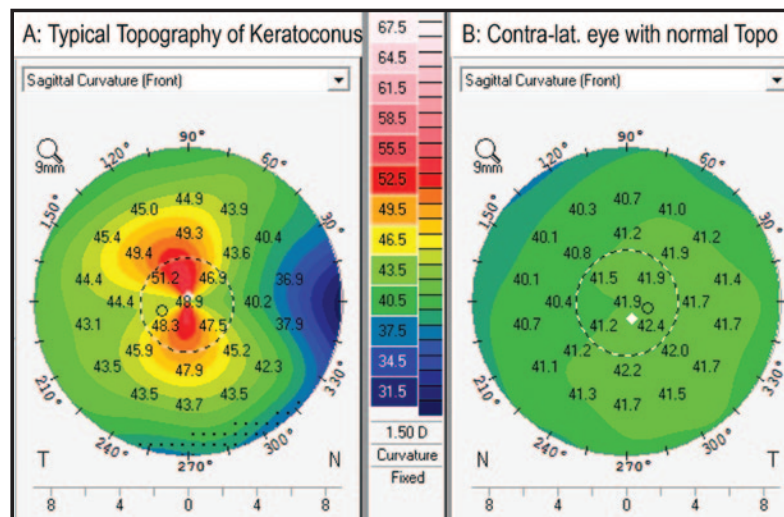
Figure 9: Sagittal curvature maps from a patient with very asymmetric keratoconus. The OS has no abnormality detected at the biomicroscopy and has BSCVA 20/20. Ultrasound CCT=493μ.
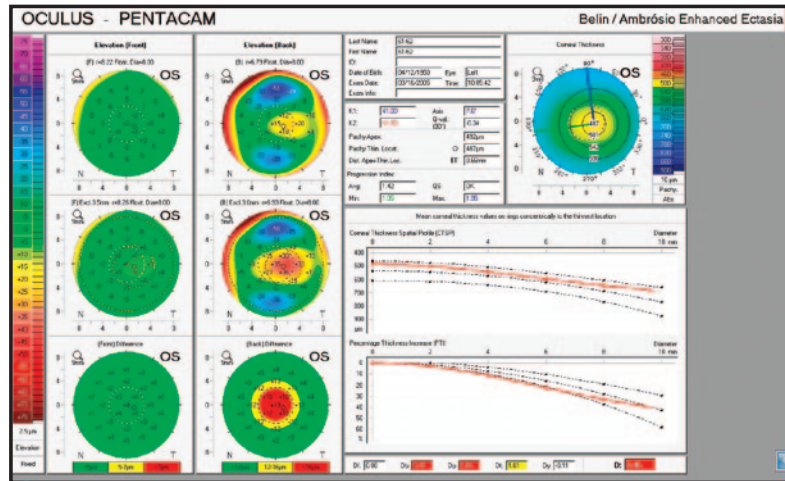
Figure 10: Pentacam "BAD" of the left eye from the same case as in Figures 9B and 11. Note the enhanced posterior elevation abnormality as abnormal thickness distribution. Deviation parameters detect abnormal values for posterior elevation and thickness distribution.
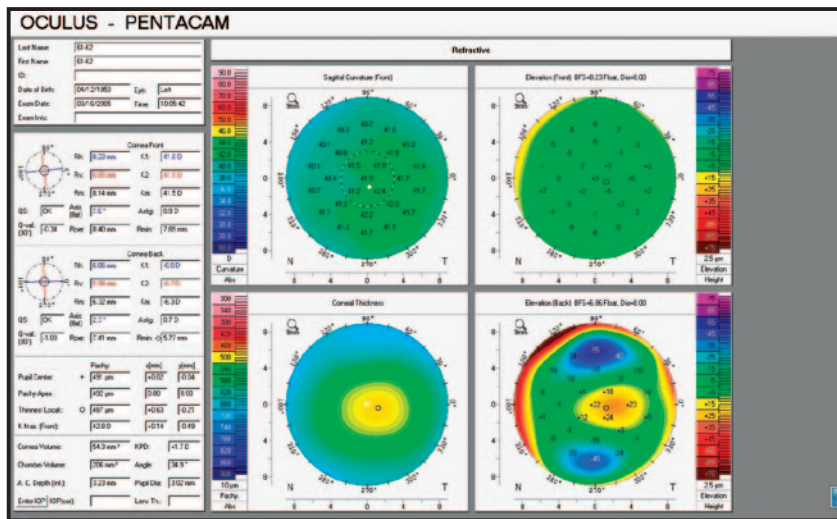

Figure 11: "4 Maps Refractive" using the Ambrósio 2 scale for the sagittal curvature map of the left eye of Figures 9B and 10. This facilitates the high asphericity of the cornea (average Q at 30° is -0.34). A posterior elevation island is detected for the BFS to the 8mm area. Elevation at the thinnest is 27µm.

CONCLUSION

Screening ectasia is a critical issue for contemporary Ophthalmology practice. The tremendous evolution from keratometry to corneal topography has continued into tomography. Careful attention for the color scale choice should be taken. Elevation maps should be referenced to the BFS or BFTE for the 8mm area. The values at the thinnest point provide the most reproducible parameter. The ART (Ambrósio Relational Thinnest) provides a novel combined parameter that combines the thickness and pachymetric distribution. New displays such as the BAD, provide a comprehensive refractive surgical screening tool to assist the refractive surgeon in identifying those patients at risk for post-operative ectasia. However, clinicians should be alert to evaluate every individual case in detail for proper identification and staging of keratoconus and related disorders. New treatments, such as collagen crosslinking and intracorneal ring

segments should be indicated and planned based on a conjunction of corneal topography, tomography and wavefront data. Biomechanical characterization is a new area for corneal propedeutics which opens a new dimension for understanding the ectasia susceptibility for each individual cornea.

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