Percentage Thickness Increase and Absolute Difference from Thinnest to Describe Thickness Profile

To the Editor:

In the September 2009 issue of the Journal of Refractive Surgery, Reinstein et al published a study characterizing the normal stromal thickness profile.\textsuperscript{1} The authors should be commended for the very interesting and elegant approach that enhances the pioneering work of Mandell and Polse\textsuperscript{2} using horizontal profile as a tool for diagnosing keratoconus. Stromal profile has great potential in the early identification of stromal thinning disorders, which may impact screening for refractive candidates.

Reinstein et al\textsuperscript{1} used Artemis very high-frequency digital ultrasound scanning (ArcScan, Morrison, Colo) across the central 10-mm corneal diameter on 110 normal eyes. The authors found a mean stromal thickness at the thinnest point of 461.8±37.3 µm. For calculating the absolute stromal thickness progression, the averages of the thickness at 35 annular ring bands (0.06-mm wide), centered on the thinnest point with central radii increasing in 0.1-mm increments, were calculated. Reinstein et al then calculated the absolute difference between the stromal thickness of each annular band and the thinnest stroma at each radial distance of each eye. The averages of these differences were plotted against the distance from the thinnest point and a second order polynomial (quadratic) equation was used to describe the averages of absolute stromal thickness differences from the thinnest point with an excellent fit and very high correlation ($R^2=0.999$). Interestingly, the absolute stromal thickness differences were independent of stromal thickness at the thinnest point.

This approach is similar to the one our group described previously for calculating the corneal thickness spatial profile (CTSP) using the Pentacam (Oculus Optikgeräte GmbH, Wetzlar, Germany).\textsuperscript{3} In agreement with our results on corneal thickness in normal corneas, a tight range was observed for the gradual increase of stromal thickness from the thinnest point towards the periphery. The authors considered the absolute difference between each annular band and the thinnest instead of the percentage of increase. They state that the percentage increase can be misleading because the percentage increase would be greater for a thin cornea than for a thick cornea, which would lead to false positives in normal thin corneas and false negatives in cases with keratoconus and normal central thickness. However, this is exactly the opposite of our experience using the Pentacam software. In fact, the absolute difference in thickness (ADT) was tested, as we first started performing thickness profile studies using the Orbscan (Bausch & Lomb, Rochester, NY).\textsuperscript{4} The decision for proceeding with the percentage thickness increase (PTI) was based on statistical evidence of its superiority as a test for diagnosing keratoconus (Luz and Ambrósio, unpublished data 2004).

For comparing the performance of the PTI and ADT for describing thickness increase from the thinnest point, we analyzed a database comprising both eyes of 113 normal patients (n=226) and 44 patients with keratoconus (n=88). For every radii, there was a statistically significant difference among normals and those with keratoconus for either the PTI and/or ADT parameters

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure1}
\caption{Sensitivity and specificity of the spatial annular thickness averages in relation to the thinnest for keratoconus detection in 226 normal eyes and 88 eyes with keratoconus.}
\end{figure}
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(P<.001, Mann-Whitney U test). The receiver operating characteristic curves for each radial distance were calculated to provide the best cutoff value, sensitivity, and specificity for the PTI and ADT at each radii up to 4.6 mm (9.2 mm in diameter). Figure 1 illustrates that both sensitivity and specificity of the PTI parameters were better than the ADT values. The best performances for PTI and ADT were found at the diameters from 3.6 and 6.0 mm. The best performance was for the PTI at 5.2 mm in diameter, in which a percentage increase of 17.97% from the thinnest point led to 97.3% specificity and 95.5% sensitivity. For the ADT, 4 mm in diameter provided the best parameter, resulting in 94.3% and 93.4% sensitivity and specificity, respectively, for a cutoff of 57 µm of difference.

The examples in Figure 2 demonstrate the Pentacam findings of a normal thin cornea with normal topography and normal CTSP and PTI graphs in both eyes and a case with bilateral keratoconus despite >540 µm of central corneal thickness and abnormal thickness profile graphs. Either case could have been false positive (thin cornea) and false negative (keratoconus) if considering the ADT instead of the PTI.

I applaud the authors for the interesting work but urge caution when deciding not to use the percentage increase in favor of absolute difference. In fact, differences arise from the corneal thickness and stromal thickness and also from optical blue light Scheimpflug and high frequency ultrasound. Thereby, the performance of the PTI and ADT approaches should be scientifically tested before deciding which one should be used and most importantly, criticizing one or the other may be based on false impressions.

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REFERENCES
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Reply:
We thank Dr Ambrósio for his letter referring to our paper describing the stromal thickness profile in a population of normal eyes.1 Our finding that the stromal thickness profile was independent of central stromal thickness was both surprising and interesting; it seems remarkable that the thickness profile would be the same despite the large range in minimum corneal thickness from 450 to 650 µm in the population. This result seems to show that the cornea is biologically programmed to have a specific thickness progression regardless of the minimum central corneal thickness.

If percentage thickness increase (PTI) is used, there can be no argument that the PTI of a keratoconic eye with central corneal thickness of 550 µm will be lower (and closer to normal) than if the same eye had a central corneal thickness of 450 µm. On the other hand, the absolute difference in thickness (ADT) will be the same for both eyes. This means that these two eyes might be classified differently according to PTI, whereas they would be considered identical according to ADT.

The outstanding question is whether this has an impact on screening for keratoconus.

Dr Ambrósio described a study that found PTI to be statistically superior for diagnosing keratoconus compared to ADT. However, this result is not surprising when comparing a normal population with a frank keratoconic population, given the corneal thinning associated with keratoconus. In a case of advanced keratoconus, the PTI is taking advantage of the thin cornea to accentuate the difference compared with normal eyes. However, the issue is not about identifying cases with keratoconus that can already be diagnosed by topography or tomography. Our goal now is to improve the sensitivity and specificity of keratoconus screening in equivocal cases—cases in which a confident diagnosis is not possible based on topography alone. In early or mild cases of keratoconus, it is unlikely that the cornea will have thinned significantly, which means that the PTI will not be able to rely on the extra diagnostic factor of the low corneal thickness, as in cases of more advanced keratoconus. This seems to imply that the sensitivity and specificity of the PTI might be reduced for early or mild keratoconus and there may be greater opportunity for type I and type II errors.

The question that needs to be answered is whether the sensitivity and specificity is higher when using PTI or ADT for these suspect keratoconus cases, and further study is required in this area.

It is unlikely that any single parameter is going to provide a definitive answer for keratoconus screening. The ideal solution for keratoconus screening will be an analysis that considers information from all available keratoconus screening techniques, including front and back surface topography, minimum corneal thickness, coincidence of front and back surface topography and pachymetry, pachymetric progression and profile, thinnest pachymetry location, Ocular Response Analyzer (Reichert, Depew, NY) signal analysis (or other biomechanical measurements), magnitude and axis of astigmatism, keratometry, higher order aberrations, age, fellow-eye asymmetry, ethnicity, corrected distance visual acuity, contrast sensitivity, and epithelial thickness profiles.2,3 Alternatively, we may be fortunate to find a genetic or enzymatic test to rule keratoconus “in” or “out.”4 We acknowledge that PTI is a step along this road in that it combines minimum corneal thickness and pachymetric progression into one analysis. However, it is valid to question whether the PTI method gives too much influence to minimum corneal thickness. Also, when we do get to the stage of throwing everything into a single analytical pot, using PTI would effectively mean adding minimum corneal thickness twice.

We would like to thank Dr Ambrósio for highlighting this point for debate as the robustness of ADT across the range of corneal thickness was certainly a result that surprised us and one that we believe merits further study.

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REFERENCES
4. Rabinowitz YS, Dong L, Wistow G. Gene expression profile
Artisan Phakic IOL for the Correction of Ametropia After Deep Anterior Lamellar Keratoplasty

To the Editor:

We present our experience with the Artisan phakic intraocular lens (IOL) (Ophtec BV, Groningen, The Netherlands) for the correction of ametropia following deep anterior lamellar keratoplasty in two patients. Both patients were chosen due to the presence of low regular astigmatism.

Both patients (25 and 27 years old, respectively) were keratoconic with poor vision due to corneal scarring. Both patients underwent deep anterior lamellar keratoplasty using the Melles technique.

In the first case, uncorrected distance visual acuity (UDVA) in the right eye 3 years after deep anterior lamellar keratoplasty was 20/120 and corrected distance visual acuity (CDVA) was 20/30 with a refraction of −4.50 −1.20 × 105. Uncorrected distance visual acuity in the left eye was 20/30. A 6.0/8.5-mm, −6.50-diopter (D) Artisan phakic IOL was implanted uneventfully in the right eye. Preoperative keratometry readings were 46.80/47.50 D. Anterior chamber depth was 4.67 mm. Preoperative endothelial cell count was 1991 cells/mm². One week postoperatively, UDVA had improved to 20/20. At 6 months postoperatively, the patient achieved UDVA of 20/20 and CDVA of 20/16 (from 20/30 to 20/16 in the first case and from 20/30 to 20/20+ in the second case) was most likely due to patient fatigue in the preoperative assessment. After the procedure, both patients were extremely satisfied with the result and were more motivated during final refraction test.

To our knowledge, this is the first report of the use of Artisan phakic IOLs for the correction of ametropia after deep anterior lamellar keratoplasty.

Compared to wavefront-guided photorefractive keratoplasty, Artisan IOL implantation carries no risk of postoperative haze, and it is an excellent option in settings where access to laser refractive equipment is not available. The procedure is reversible, and it does not compromise the structural integrity of the graft. It can offer an excellent visual outcome in carefully selected cases with previous deep anterior lamellar keratoplasty. Longer follow-up is needed to study the rate of endothelial cell loss in these eyes and the stability of the refractive outcome.

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REFERENCES