# Corneal biomechanics for corneal ectasia: Update

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## Abstract:

Knowledge of biomechanical principles has been applied in several clinical conditions, including correcting intraocular pressure measurements, planning and following corneal treatments, and even allowing an enhanced ectasia risk evaluation in refractive procedures. The investigation of corneal biomechanics in keratoconus (KC) and other ectatic diseases takes place in several steps, including screening ectasia susceptibility, the diagnostic confirmation and staging of the disease, and also clinical characterization. More recently, investigators have found that the integration of biomechanical and tomographic data through artificial intelligence algorithms helps to elucidate the etiology of KC and ectatic corneal diseases, which may open the door for individualized or personalized medical treatments in the near future. The aim of this article is to provide an update on corneal biomechanics in the screening, diagnosis, staging, prognosis, and treatment of KC.

**Keywords:**

Corneal biomechanics, corneal ectasia, corneal imaging

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## Introduction

Knowledge about corneal biomechanical principles has been applied in several clinical conditions,[1,2] including glaucoma (correcting intraocular pressure measurements), ectatic corneal diseases (ECD), and enhanced ectasia risk evaluation in elective refractive surgery.[3] This goes beyond but not overdiagnoses of mild keratoconus (KC) into the characterization of the inherent ectasia susceptibility of each individualized cornea.

The latest concept of the pathophysiology of KC and ECD is related to the two-hit hypothesis. Biomechanical failure is associated with the biomechanical properties of the cornea and the impact on the environment.[4,5] Thus, even with the developments in corneal shape analysis, biomechanical assessment is promising to enhance the ability to characterize ectasia susceptibility.[6] Furthermore, KC and other ECD may represent a new subspecialty in ophthalmology because of the relatively high number of patients with the disease and the advances in technologies related to the diagnosis and treatment.[7]

Placido disc-based corneal topography represented a major advance in corneal imaging and increased our capacity to identify ECD in earlier stages.[8,9] The evaluation of the anterior corneal surface evolved to three-dimensional (3D) corneal tomography, with the reconstruction of front and back corneal surfaces including a full-thickness map.[10] Subsequently, the characterization of each individualized corneal layer also became possible with segmental corneal tomography, and studies have found the high accuracy of this technology to identify ectatic diseases. Beyond shape analysis, clinical biomechanical assessment has been promising as an ultimate tool for enhancing the overall accuracy for identifying mild forms of ECDs.[6,11]

## Prospective Historical Review

### Corneal biomechanical assessment

Studies have demonstrated the ability of the corneal biomechanical assessment to detect mild, forme fruste (FFKC) of subclinical KC in eyes with "innocent" and relatively normal anterior topographic map from patients with contralateral clinical KC.[12,13] For example, we reported two identical 48-year-old female twins, in which one



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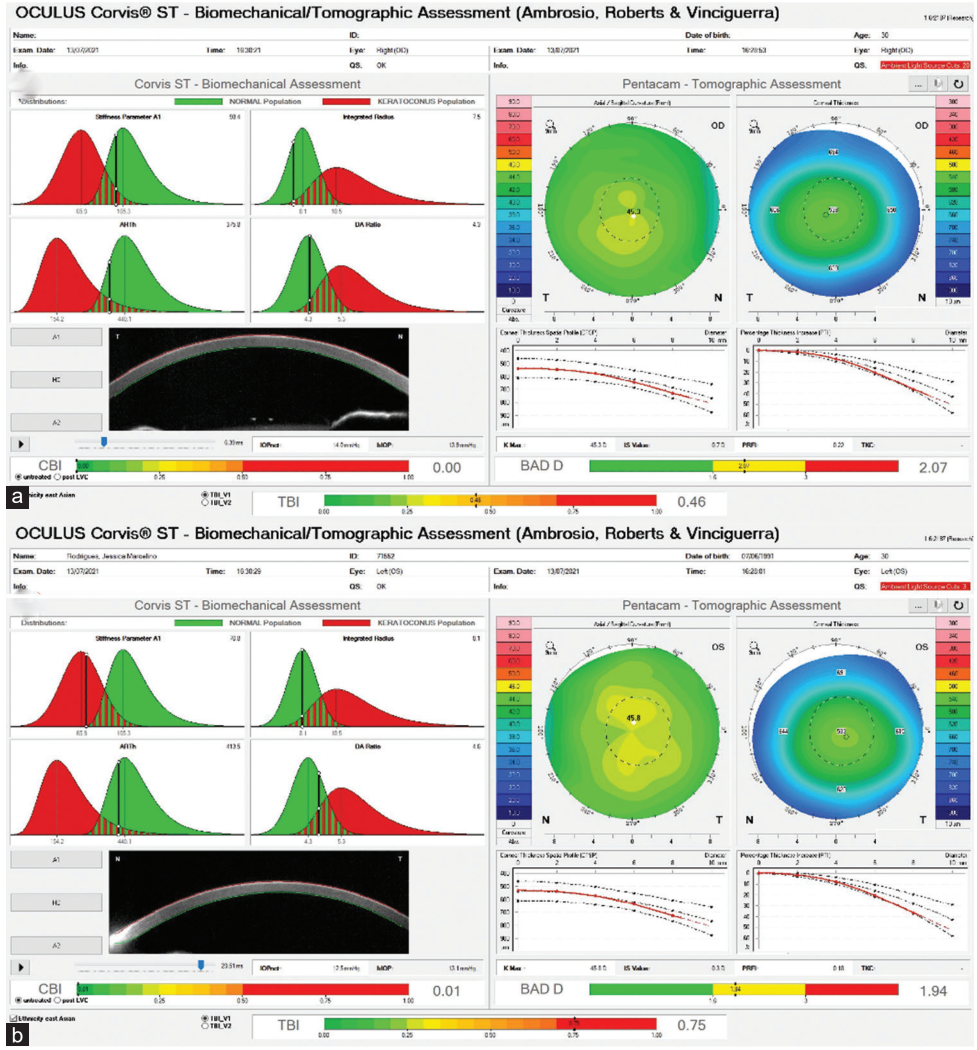


**Figure 1:** (a and b) Corvis ST tomographic biomechanical display (Ambrósio, Roberts, and Vinciguerra) from both eyes. Note that despite a relatively normal anterior tomographic assessment (top right), we can observe abnormal tomographic and biomechanical index values of 0.46 and 0.75 in OD and OS, respectively

of them, who have rubbed the eye during early adulthood, has very asymmetric ectasia with normal anterior curvature and topography in one eye, and the other twin, who denied eye rubbing, had normal topography in both eyes. Ethics approval and consent to participate: Universidade Federal de São Paulo/ UNIFESP/SP 2018 (# 2.568.770).[14]

## Ocular response analyzer

The first *in vivo* measurements of corneal biomechanical response became available with the introduction of the Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Buffalo, NY, USA) in 2005.[1,15] The ORA is a noncontact tonometer (NCT), and with a collimated air puff that indents a central 3–6 mm apical corneal area can monitor the bidirectional movement of the cornea by an advanced electro-optical system.[15-17]

The ORA generates two main pressure-derived parameters: corneal hysteresis (CH) and corneal resistance factor (CRF). Despite having a significantly different distribution among healthy and ectatic eyes, CH and CRF revealed a limited role in KC diagnosis due to a considerable overlap.[18] Studies have found better performance with the development of new parameters derived from the waveform signal. Later, investigators have found that the combination of tomographic and biomechanical parameters using logistic regression analysis was able to correctly differentiate normal eyes and fellow normal topographic eyes from patients with very asymmetric KC.[19]

## Corvis ST dynamic Scheimpflug analyzer

The Corvis ST (Oculus, Wetzlar, Germany) is an NCT system that uses an ultra-high-speed Scheimpflug camera to monitor the corneal deformation response over a 5–6 mm area during a consistent air pulse application. Once the measurement is complete, the device provides a set of deformation parameters based on the dynamic inspection of the corneal response.[20,21]

The deformation data allow more precise intraocular pressure measurements, which influence the deformation response

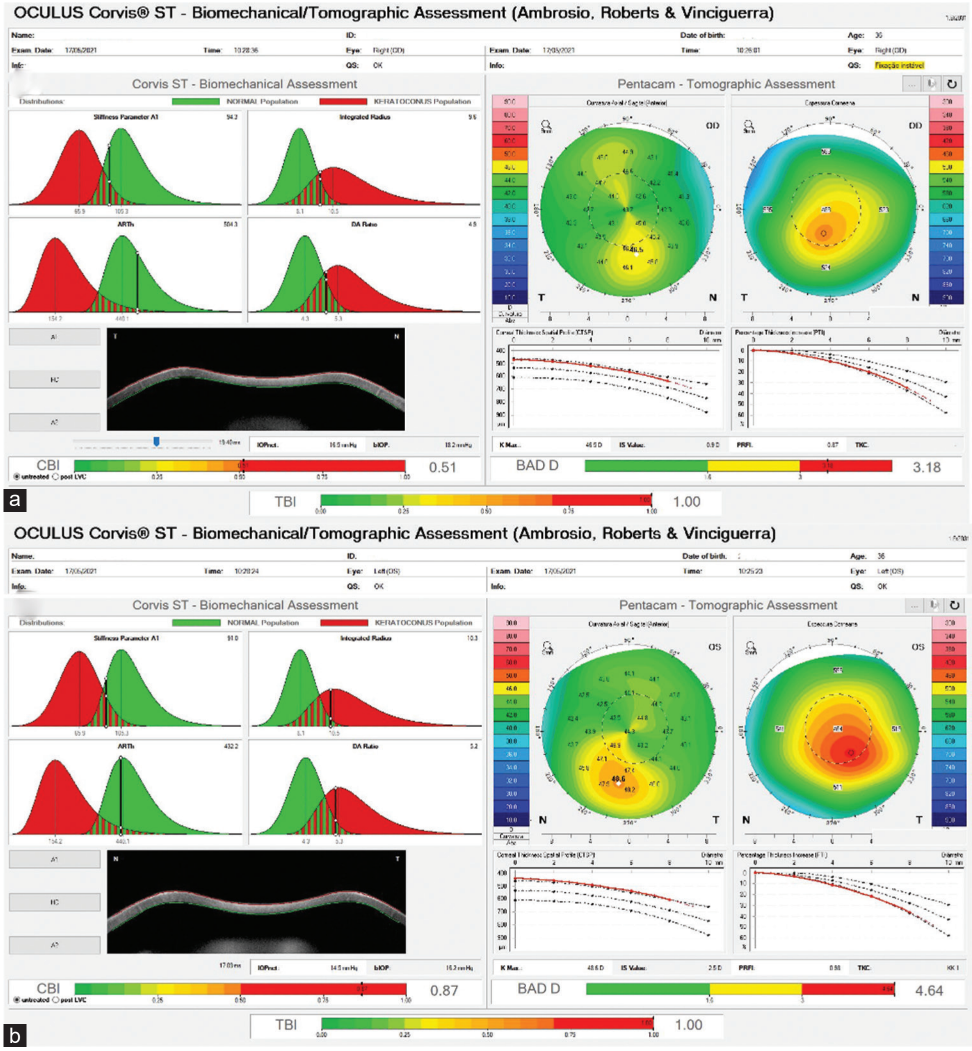


**Figure 2:** Corvis ST tomographic biomechanical display (Ambrósio, Roberts, and Vinciguerra) from OD (a) and OS (b). (a) Despite a relatively normal anterior tomographic assessment on the Pentacam (top right), corneal deformation response revealed an abnormal tomographic and biomechanical index value of 1.0. (b) Note on the Pentacam tomographic assessment (top right) that the front surface curvature demonstrates a moderate keratoconus condition on this eye

as well. Several parameters derived from this instrument have been introduced, including deformation amplitude, the radius of curvature at highest concavity, the applanation lengths, and the corneal velocities. Once again, AI algorithms demonstrated that the combination of deformation parameters was able to enhance the overall accuracy to distinguish healthy and KC eyes, even in mild stages.[21] In addition, waveform analysis of the deformation amplitude and deflection amplitude signals from the Corvis ST presented an excellent performance in differentiating normal, suspect, and KC eyes.[22]

### Brillouin optical microscopy

Brillouin optical microscopy (Harvard Medical School, Boston, MA)[23] was lately introduced to measure corneal biomechanics *in vivo* through the study of light scatter and mapping the biomechanical state of the cornea with 3D capability. *In vivo* and *in vitro* studies using this technology revealed significant differences between normal and KC eyes.[23,24] Brillouin technology has also demonstrated a focal biomechanical disturbance within the protrusion area in KC eyes, which endorses the concept that biomechanical failure initiates with a focal decompensation.[2]

Although the accuracy of the first reported findings is relatively weak, studies have found statistically significant differences when comparing normal and keratoconic corneas and demonstrated the impact of age on corneal stiffness.[25]

## Integration of Corneal Shape and Biomechanics

The combination of tomographic and biomechanical parameters from ORA and Pentacam HR (Oculus Optikgeräte GmbH, Wetzlar, Germany) using logistic regression analysis was able to correctly differentiate normal eyes and fellow normal topographic eyes from patients with very asymmetric KC.[19]

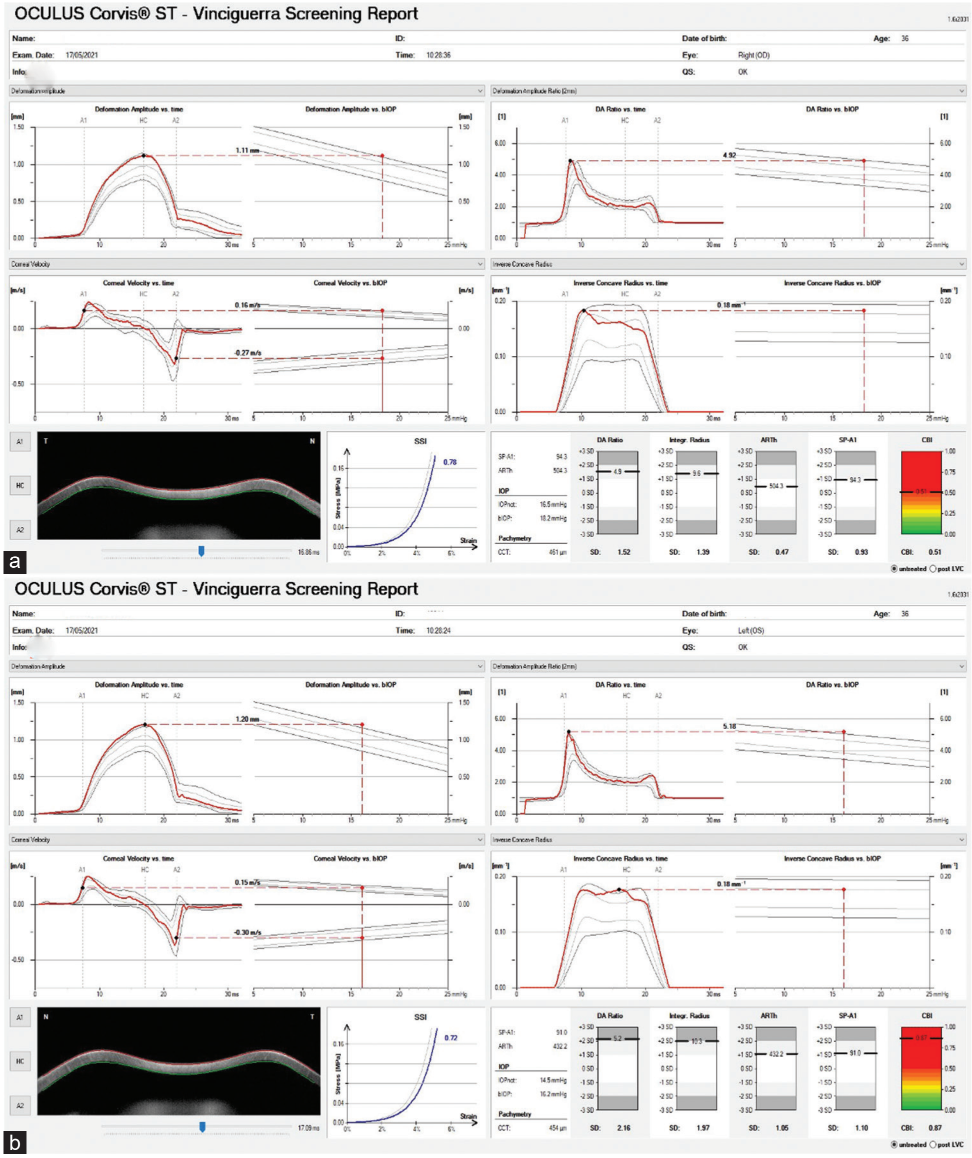


**Figure 3:** The Vinciguerra Screening Report from Corvis ST evidencing abnormal biomechanical parameters in OD (a) and OS (b), with more change values in OS (b)

In 2014, Vinciguerra *et al.* introduced a new Corvis ST biomechanical parameter, the corneal biomechanical index. (CBI). The authors introduced the Corvis biomechanical index (CBI) using linear regression analysis to combine Ambrósio Relational Thickness over the horizontal meridian with corneal deformation parameters.[26,27] This parameter was able to correctly identify 98.2% of KC cases among normal eyes with 100% specificity with a cutoff value of 0.5.[27]

Subsequently, the international investigators continued a multicenter study to enhance ectasia detection and used artificial intelligence (random forest with leave-one-out cross-validation method) to develop a new index combining tomographic and biomechanical data: the Ambrósio, Roberts, and Vinciguerra/Tomographic and Biomechanical Index (ARV/TBI) which is available on the integrated Pentacam and Corvis ST software.[28,29]

The original ARV/TBI study involved one eye randomly selected from 480 normal eyes and 204 keratoconic corneas, 94 VAE-NT eyes, and the respective 72 unoperated ectatic (VAE-E) from these patients. A cutoff of 0.79 was used, and TBI provided 100% sensitivity and specificity to detect clinical ectasia (KC + VAE-E cases). Further analysis led to an optimized cutoff value of 0.29, which provided 90.4% sensitivity and 96% specificity, with an area under the receiver operating characteristic curve of 0.985.[28] Posterior external validation studies were conducted and proved the capacity of this new index to mark ectatic disease, even in milder forms of ectasia.[3,30-34] Although some of these studies have found a moderately lower sensitivity for the VAE-NT eyes (some with normal topography and tomography – NTT), it is important to a reminder that some cases may be truly unilateral ectasia due to mechanical trauma.[35,36]

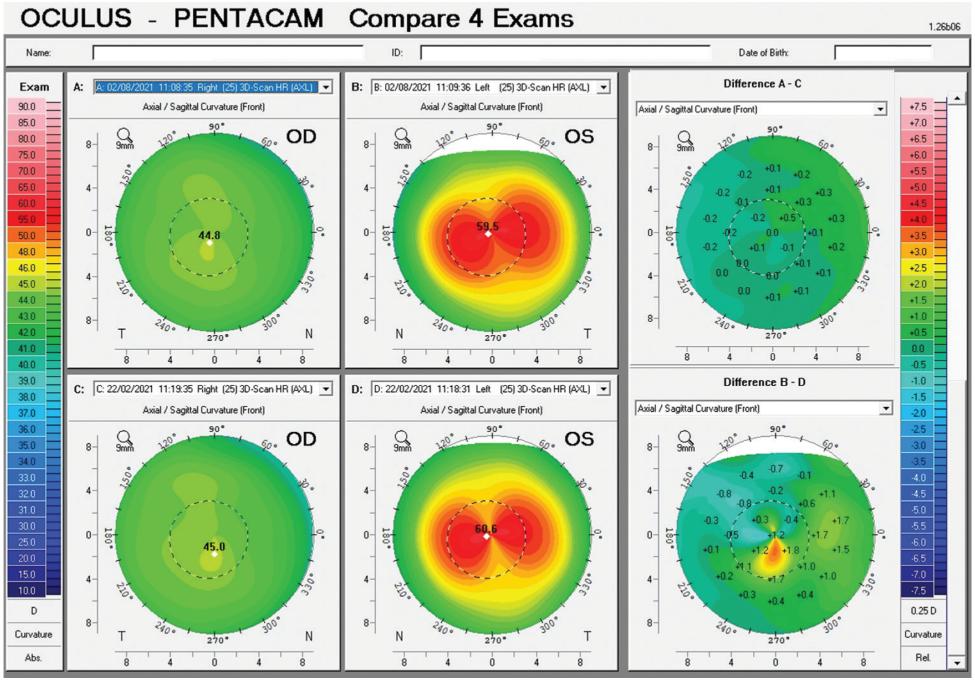


**Figure 4:** Pentacam differential map showing in A stability in OD (A-C) and in B progression in OS (B-D). Observing only K max, we tend to believe that the keratoconus has improved from 60.6 in 02.2021 to 59.5 in 08.2021

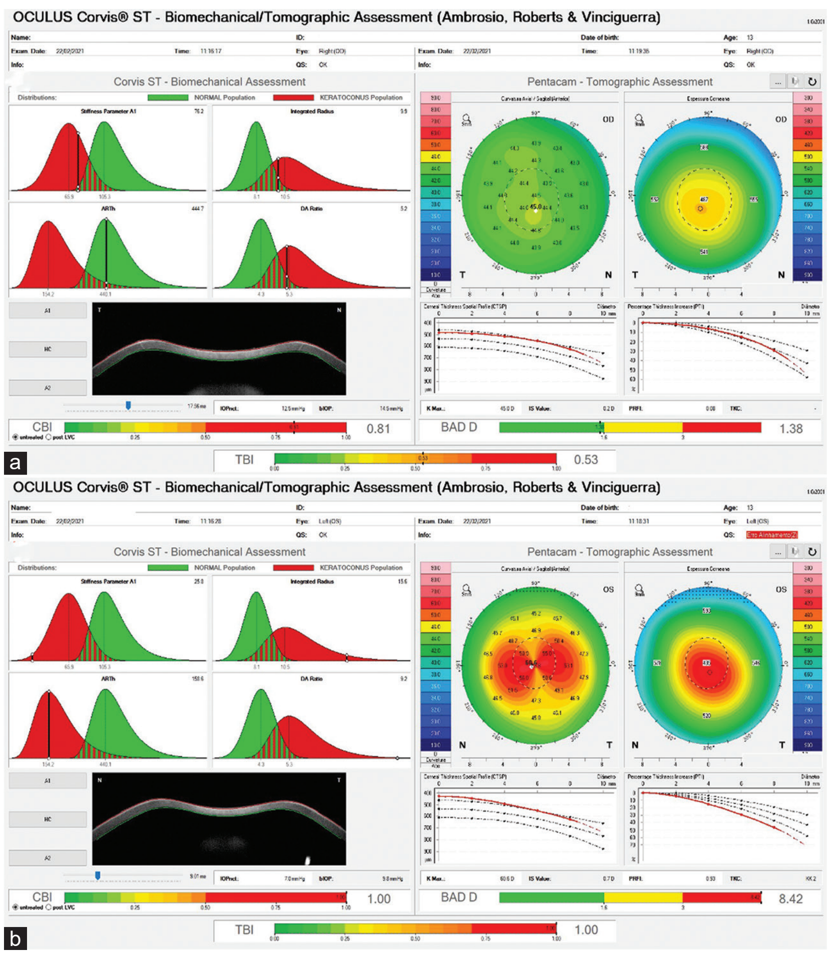


**Figure 5:** Corvis ST tomographic biomechanical display (Ambrósio, Roberts, and Vinciguerra) from OD (a) and OS (b). The diagnosis of forme fruste keratoconus was confirmed by the tomographic and biomechanical index of 0.53 in OD (a)

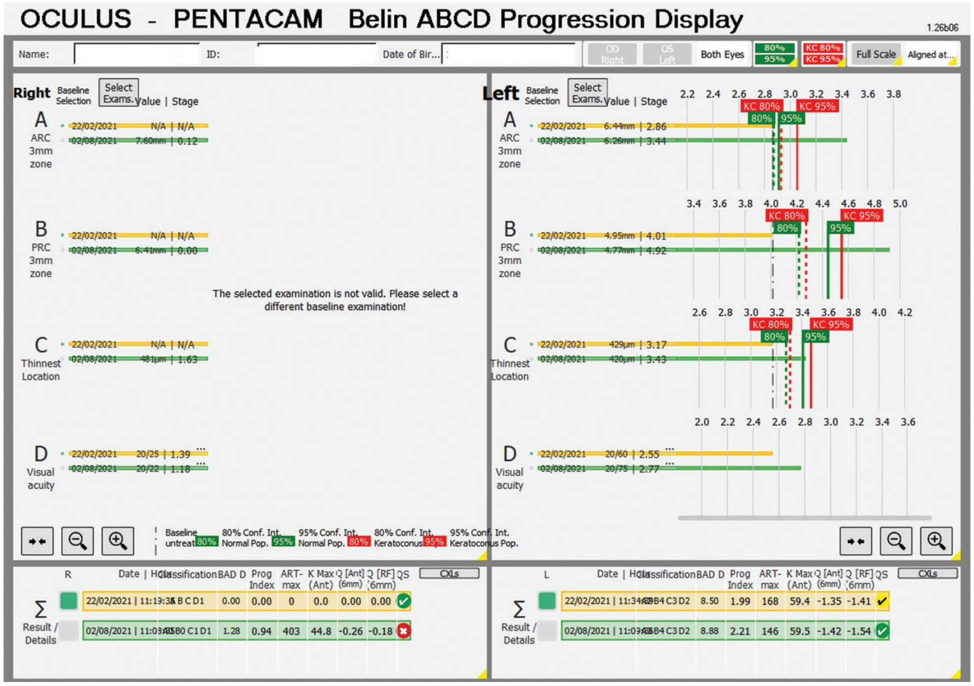


**Figure 6:** The Belin ABCD display shows stability between 6 months in the OD and progression in OS

## Clinical Examples

### Case 1 – The case of bilateral forme fruste keratoconus

A 30-year-old female patient presented in 2021 seeking a second opinion related to being a candidate for laser vision correction. Manifest refraction was −3.75/−0.5 × 35° (20/20) in the right eye (OD) and −4.00/−0.5 × 140° (20/20) in the left eye (OS), and central corneal thickness was 538 and 533 micron OD and OS.

Despite having a relatively normal topographic map, and normal central pachymetric values, both eyes demonstrated relatively high BAD-D (v3) scores. In addition, we can observe abnormal TBI values of 0.46 in OD and 0.75 in OS [Figure 1a and b]. The diagnosis of a bilateral FFKC was confirmed by the integration of the tomographic and biomechanical approaches. This example demonstrates the role of tomography and corneal biomechanics to better characterize ectasia susceptibility or subclinical/milder forms of ectatic disease.

### Case 2 – Very asymmetric ectasia with keratoconus and forme fruste keratoconus

This 36-year-old male patient came for his first consultation in 2014 with 10 years of KC diagnostic. Manifest refraction was −5.00/−5.00 × 20° (20/20) in the right eye (OD) and −8.25/−4.75 × 150° (20/25) in the left eye (OS), and central corneal thickness was 461 and 460 micron OD and OS. The integrated biomechanical and tomographic display in OD revealed CBI of 0.51, TBI of 1.0, and BAD-D of 3.18, and in OS, CBI of 0.87, TBI of 1.0, and BAD-D of 4.64 [Figure 2a and b].

Despite a relatively normal topographic map, due to the tomographic and biomechanical approach, we could diagnose FFKC in OD and KC in OS. The Vinciguerra Screening Report from Corvis ST was evidencing abnormal biomechanical parameters in both eyes [Figure 3a and b].

### Case 3 progressive ectasia OS and forme fruste keratoconus OD

A 13-year-old male patient with a very asymmetric ectasia case presented for evaluation. We noticed a moderate KC pattern diagnostic in OS and normal topography in OD at the first visit [Figure 4]. The diagnosis of FFKC was confirmed by the TBI [Figure 5]. The DCVA was 20/20 in OD and 20/60 in OS. After 6 months of follow-up, the Pentacam differential maps revealed stability in OD and progression in OS [Figure 4]. We can note the improvement of sensitivity in diagnosing progression in OS based on the axial subtraction map and Pentacam Belin ABCD display [Figure 6], despite the mild decrease in K max values from 60.6 to 59.5D.

Interestingly, we had the chance to examine his 34-year-old father (Case 4), with unremarkable clinical examination with abnormal TBI values in both eyes [Figure 7]. This patient is also considered bilateral fruste disease or with high susceptibility.

## Conclusion

*In vivo* characterization of corneal biomechanics is an important tool for clinical assessment. Understanding corneal biomechanical behavior is very useful in refractive surgery because it allows for more accurate identification of patients at higher risk of developing progressive ectasia after LVC.

The integration of tomographic and biomechanical data has demonstrated the potential to improve the accuracy to

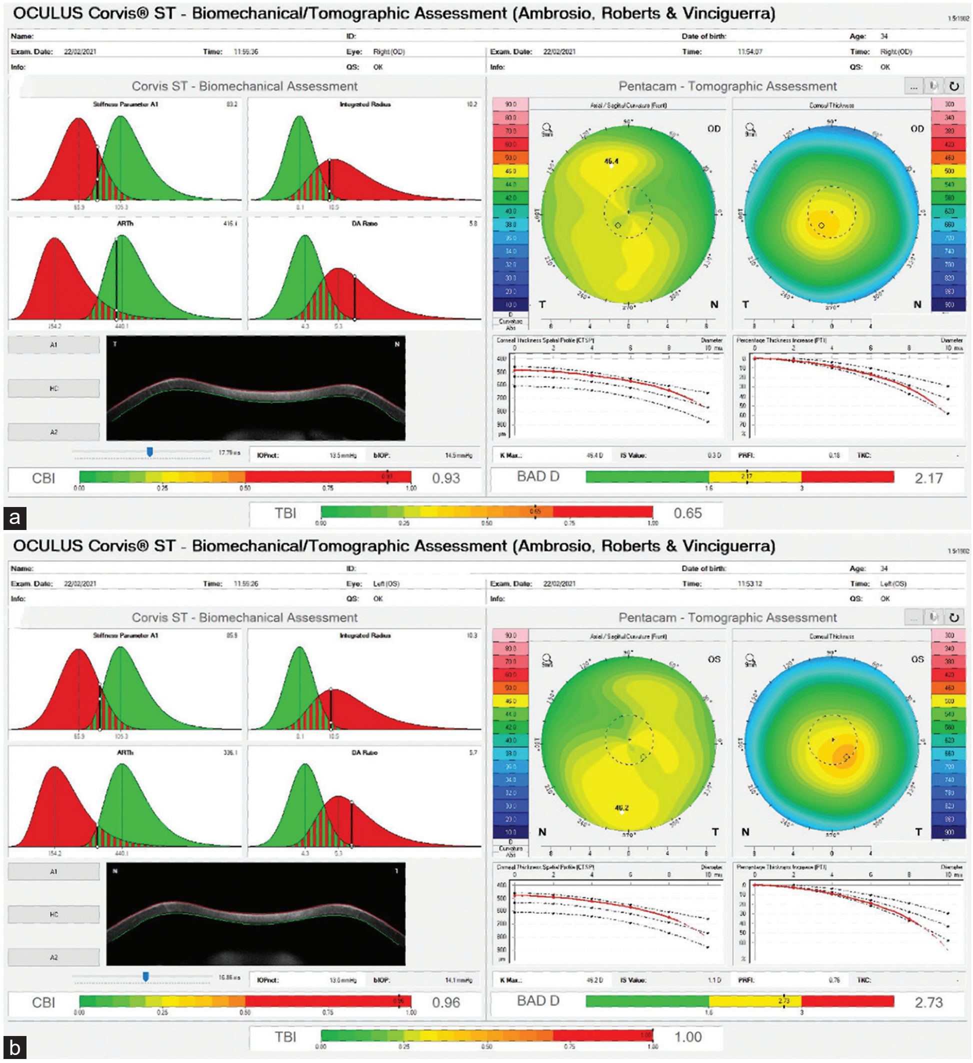


**Figure 7:** (a and b) Corvis ST tomographic biomechanical display (Ambrósio, Roberts, and Vinciguerra) from both eyes from a 13-year-old father's patient. Despite having a relatively normal anterior tomographic map, we can observe abnormal tomographic and biomechanical index values of 0.65 and 1.0 in OD and OS, respectively

detect ectatic disease and its susceptibility to develop this complication after LVC.[28,32,37,38]

In the future, further integration with other tests from multimodal imaging, such as ocular wave front, axial length, and segmental layered tomography (epithelial and stromal thickness distribution), is promising. Genetics and molecular biology could also picture the possibility of identifying inflammatory changes in KC patients and even changing the disease's definition. The continuous and accelerated development of integrating multimodal corneal imaging, biomechanics, genetics, and molecular biology will help elucidate the etiology of KC and ECD, which may increase the efficacy of patient care with individualized or personalized medical treatments.


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## Conflicts of interest

There are no conflicts of interest.


## References


1. Luz A, Faria-Correia F, Salomao MQ, Lopes BT, Ambrosio R Jr. Corneal biomechanics: Where are we? J Curr Ophthalmol 2016;28:97-8.
2. Roberts CJ, Dupps WJ Jr. Biomechanics of corneal ectasia and biomechanical treatments. J Cataract Refract Surg 2014;40:991-8.
3. Esporcatte LPG, Salomao MQ, Lopes BT, Vinciguerra P, Vinciguerra R, Roberts C, *et al*. Biomechanical diagnostics of the cornea. Eye Vis (Lond) 2020;7:9.
4. Ambrosio R Jr., Randleman JB. Screening for ectasia risk: What are we screening for, and how should we screen for it? J Refract Surg 2013;29:230-2.
5. Gomes JA, Tan D, Rapuano CJ, Belin MW, Ambrósio R Jr., Guell JL, *et al*. Global consensus on keratoconus and ectatic diseases. Cornea 2015;34:359-69.
6. Ambrósio R Jr., Nogueira LP, Caldas DL, Fontes BM, Luz A, Cazal JO, *et al*. Evaluation of corneal shape and biomechanics before LASIK. Int Ophthalmol Clin 2011;51:11-38.
7. Ambrosio R Jr. Keratoconus and ectatic diseases: Are we facing a new subspeciality? Int J Kerat Ect Cor Dis 2012;1:0-0.
8. Wilson SE, Ambrosio R. Computerized corneal topography and its importance to wavefront technology. Cornea 2001;20:441-54.
9. Maeda N, Klyce SD, Tano Y. Detection and classification of mild

irregular astigmatism in patients with good visual acuity. Surv Ophthalmol 1998;43:53-8.
10. Ambrosio R Jr., Belin MW. Imaging of the cornea: Topography vs tomography. J Refract Surg 2010;26:847-9.
11. Ambrósio R, Dawson DG, Salomão 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;26:906-11.
12. Ambrosio R Jr., Valbon BF, Faria-Correia F, Ramos I, Luz A. Scheimpflug imaging for laser refractive surgery. Curr Opin Ophthalmol 2013;24:310-20.
13. Smadja D, Touboul D, Cohen A, Doveh E, Santhiago MR, Mello GR, *et al*. Detection of subclinical keratoconus using an automated decision tree classification. Am J Ophthalmol 2013;156:237-46.e1.
14. Guerra G, de Oliveira V, Ferreira I, Ramos I, Belin M, Ambrósio R Jr. Subclinical keratoconus detection in identical twins. Int J Keratoconus Ectatic Corneal Dis 2016;5:35-9.
15. Luce DA. Determining *in vivo* biomechanical properties of the cornea with an ocular response analyzer. J Cataract Refract Surg 2005;31:156-62.
16. Pinero DP, Alcon N. *In vivo* characterization of corneal biomechanics. J Cataract Refract Surg 2014;40:870-87.
17. Roberts CJ. Concepts and misconceptions in corneal biomechanics. J Cataract Refract Surg 2014;40:862-9.
18. Fontes BM, Ambrosio Junior R, Jardim D, Velarde GC, Nose W. Ability of corneal biomechanical metrics and anterior segment data in the differentiation of keratoconus and healthy corneas. Arq Bras Oftalmol 2010;73:333-7.
19. Luz A, Lopes B, Hallahan KM, Valbon B, Ramos I, Faria-Correia F, *et al*. Enhanced combined tomography and biomechanics data for distinguishing forme fruste keratoconus. J Refract Surg 2016;32:479-94.
20. Ambrósio R Jr., Ramos I, Luz A, Faria-Correa F, Steinmueller A, Krug M, *et al*. Dynamic ultra high speed Scheimpflug imaging for assessing corneal biomechanical properties. Rev Bras Oftalmol 2013;72:99-102.
21. Salomao MQ, Hofling-Lima AL, Faria-Correia F, Lopes BT, Rodrigues-Barros S, Roberts CJ, *et al*. Dynamic corneal deformation response and integrated corneal tomography. Indian J Ophthalmol 2018;66:373-82.
22. Francis M, Pahuja N, Shroff R, Gowda R, Matalia H, Shetty R, *et al*. Waveform analysis of deformation amplitude and deflection amplitude in normal, suspect, and keratoconic eyes. J Cataract Refract Surg 2017;43:1271-80.
23. Scarcelli G, Pineda R, Yun SH. Brillouin optical microscopy for corneal biomechanics. Invest Ophthalmol Vis Sci 2012;53:185-90.
24. Scarcelli G, Besner S, Pineda R, Yun SH. Biomechanical characterization of keratoconus corneas *ex vivo* with Brillouin microscopy. Invest Ophthalmol Vis Sci 2014;55:4490-5.
25. Seiler TG, Shao P, Eltony A, Seiler T, Yun SH. Brillouin spectroscopy of normal and keratoconus corneas. Am J Ophthalmol 2019;202:118-25.
26. Lopes BT, Ramos IC, Salomão MQ, Canedo AL, Ambrósio R Jr. Perfil paquimétrico horizontal para a detecção do ceratocone. Rev Bras Oftalmol 2015;74:382-5.
27. Vinciguerra R, Ambrosio R Jr., Elsheikh A, Roberts CJ, Lopes B, Morenghi E, *et al*. Detection of keratoconus with a new biomechanical index. J Refract Surg 2016;32:803-10.
28. Ambrosio R Jr., Lopes BT, Faria-Correia F, Salomão MQ, Bühren J, Roberts CJ, *et al*. Integration of scheimpflug-based corneal tomography and biomechanical assessments for enhancing ectasia detection. J Refract Surg 2017;33:434-43.
29. Ambrosio R Jr., Correia FF, Lopes B, Salomão MQ, Luz A, Dawson DG, *et al*. Corneal biomechanics in ectatic diseases: Refractive surgery implications. Open Ophthalmol J 2017;11:176-93.
30. Kataria P, Padmanabhan P, Gopalakrishnan A, Padmanaban V, Mahadik S, Ambrósio R Jr. Accuracy of Scheimpflug-derived corneal biomechanical and tomographic indices for detecting subclinical and mild keratectasia in a South Asian population. J Cataract Refract Surg 2019;45:328-36.
31. Sedaghat MR, Momeni-Moghaddam H, Ambrósio R Jr., *et al*. Diagnostic ability of corneal shape and biomechanical parameters for detecting frank keratoconus. Cornea 2018;37:1025-34.
32. Ferreira-Mendes J, Lopes BT, Faria-Correia F, Salomão MQ, Rodrigues-Barros S, Ambrósio R Jr. Enhanced ectasia detection using corneal tomography and biomechanics. Am J Ophthalmol 2019;197:7-16.
33. Steinberg J, Siebert M, Katz T, Frings A, Mehlan J, Druchkiv V, *et al*. Tomographic and biomechanical scheimpflug imaging for keratoconus characterization: A validation of current indices. J Refract Surg 2018;34:840-7.
34. Sedaghat MR, Momeni-Moghaddam H, Ambrosio R Jr., *et al*. Long-term evaluation of corneal biomechanical properties after corneal cross-linking for keratoconus: A 4-year longitudinal study. J Refract Surg 2018;34:849-56.
35. Valbon BF, Ambrosio R Jr., Glicéria J, Santos R, Luz A, Alves MR. Unilateral corneal ectasia after Bilateral LASIK: The thick flap counts. Int J Keratoconus Ectatic Corneal Dis 2013;2:79.
36. Ambrósio R Jr., Lopes B, Amaral J, Faria-Correa F, Canedo ALC, Salomão M, *et al*. Ceratocone: Quebra de paradigmas e contradições de uma nova subespecialidade. Rev Bras Oftalmol 2019;78:81-5.
37. Vinciguerra R, Rehman S, Vallabh NA, Batterbury M., Czanner G, Choudhary A, *et al*. Corneal biomechanics and biomechanically corrected intraocular pressure in primary open-angle glaucoma, ocular hypertension, and controls. Br J Ophthalmol 2020;104:121-6.
38. Bao F, Geraghty B, Wang Q, Elsheikh A. Consideration of corneal biomechanics in the diagnosis and management of keratoconus: Is it important? Eye Vis (Lond) 2016;3:18.