OCULUS Corvis® ST
Corneal Visualization
Scheimpflug Technology

Evaluation of corneal biomechanical response

GLAUCOMA SCREENING
Corvis® ST – all features at a glance

YOUR BENEFITS

• Evaluation of corneal biomechanical response
• Biomechanically corrected IOP (biOP)
• Optimized ectasia detection
• Biomechanical analysis after laser vision correction
• Glaucoma screening

INVESTIGATIONS

• High-speed Scheimpflug camera
• More than 4300 images per second
• Tonometry
• Pachymetry
• Biomechanical properties

SUITEABILITY

• Refractive surgeons
• Glaucoma specialists

Contact us to learn more

+49 641 2005-0
export@oculus.de
www.corneal-biomechanics.com

The innovation in corneal analysis

Thanks to the corneal biomechanics it is possible to measure what was previously not measurable. This means tomographic diagnosis and glaucoma screening to a new level. Because for the first time the perfect combination of biomechanical analysis, tonometry and pachymetry. Learn more.
OCULUS Corvis® ST
Evaluation of corneal biomechanical response, tonometry and pachymetry

The revolutionary Corvis® ST records the reaction of the cornea to a defined air pulse using a newly developed high-speed Scheimpflug camera. This camera captures over 4 300 images per second, permitting highly precise measurement of IOP and corneal thickness. Based on a video of 140 images, taken within 31 ms after onset of the air pulse, the Corvis® ST provides a detailed assessment of corneal biomechanical properties.

The information obtained on the biomechanical response of the cornea is used to calculate a biomechanically corrected IOP (bIOP). Furthermore it allows ectatic diseases such as keratoconus to be detected at a very early stage. Biomechanical properties also play an important role in the development and progression of glaucoma.
IOP/Pachy Display
Biomechanically corrected IOP (bIOP)

bIOP readings are less dependent on biomechanical properties and corneal thickness and hence more accurate than IOP readings. The data are easy to read and interpret, and the IOP follow-up chart is neatly arranged.

IOP correction is based on corneal thickness, age and the biomechanical response of the cornea. When calculated this way bIOP is less influenced by corneal properties and thickness than it is with other measurement methods. As the Corvis® ST measures both biomechanical response and corneal thickness with high precision, the device is able to correct for both factors at the same time.

Due to the measurement principle, it delivers bIOP values uninfluenced by the tear film. This and the fast auto tracking and auto release ensure highly repeatable, user-independent IOP and thickness readings.
Vinciguerra Screening Report
Corvis Biomechanical Index (CBI)

This module provides comprehensive biomechanical screening and keratoconus detection. The software displays the patient’s results against normative values in easy-to-grasp charts.

The Vinciguerra Screening Report allows fast and comprehensive screening for corneas with abnormal corneal biomechanical properties. It is the first available screening software that combines biomechanical information with pachymetric progression data. It calculates the Corvis Biomechanical Index (CBI), which enables the detection of ectatic corneas based on these findings. As keratoconus is caused by biomechanical changes and leads to progressive thinning, the software is able to detect the earliest signs of this disease.

Furthermore, the normal ranges of dynamic corneal response (DCR) parameters are shown as a function of biOP. Standardized parameters indicate whether the cornea has a normal biomechanical response.
Biomechanical Keratoconus Detection with the CBI

More information spells greater safety

The Vinciguerra Screening Display performs biomechanical screening based on the dynamic corneal response, enabling the examiner to understand the stress-strain behaviour of corneal tissue and assess ectasia risk.

**Compare with healthy patients**

The grey boxes show for each screening parameter how many standard deviations (SD) the parameter deviates from the mean of healthy patients. Positive values indicate softer/thinner tissue, negative values stiffer/thicker tissue than in the average healthy patient.

White area: within ± 1 SD
Light grey: between 1 - 2 SD
Dark grey: more than 2 SD

**Measure corneal elasticity**

Stress-strain curves describe the elastic properties of the cornea. The curves are shifted to the right if the cornea is soft and to the left if the cornea is stiff.

The stress-strain index (SSI) describes the position of the curve. A value of 1 indicates an average elasticity, a value smaller than 1 a softer and a value greater than 1 a stiffer than average behaviour.

**Detect keratoconus early**

The Corvis Biomechanical Index (CBI) is based on a logistic regression approach and was developed to detect keratoconus at an early stage. It is based on five Dynamic Corneal Response parameters and gives a score from zero (low ectasia risk) to one (high ectasia risk).
Tomographic and Biomechanical Assessment

Tomographic Biomechanical Index (TBI)

Integration of Pentacam® data for a combined tomographic and biomechanical analysis. The best of two worlds: TBI is calculated using an artificial intelligence approach to optimize ectasia detection.

By combining tomographic data from the Pentacam® with biomechanical data from the Corvis® ST one can further improve sensitivity and specificity in the detection of patients with a significant risk for developing ectasia after refractive surgery. The outcome of this analysis is supplied by the Tomographic Biomechanical Index (TBI). This index together with the comprehensive display helps you to avoid risks and to treat more patients safely.
Pentacam® and Corvis® ST Work Together

Artificial intelligence approach for enhanced ectasia detection

Gain accuracy in ectasia risk assessment by integrating tomographic data from the Pentacam® and biomechanical data from the Corvis® ST.

Combining tomography with biomechanical properties provides the highest sensitivity

Linking the Pentacam® and Corvis® ST together is very easy. Just connect both instruments to the same computer or connect them via your clinic network. The rest is done automatically: Pentacam® and Corvis® ST measurements are combined and the TBI is calculated automatically. This works with any Pentacam® model*.

* A license for the Belin Ambrósio Enhanced Ectasia Software is required.

Big data and artificial intelligence

The TBI is based on an artificial intelligence algorithm using tomographic and biomechanical data. The algorithm was trained on more than 2,000 clinical keratoconus and more than 500 forme fruste keratoconus patients. The superior accuracy of the index has been proven in several peer-reviewed studies1

The CBI-LVC measures biomechanical stability after laser vision correction. This information is key for making clinical decisions such as on retreatments after LASIK or corneal crosslinking in case of ectasia.

Various preoperatively screening methods are available for analyzing the risk for developing ectasia after laser vision correction. However, the possibilities for postoperatively evaluating ectasia risk based on objective criteria are still limited to date.

This software allows automatic assessment of postoperative biomechanical stability. The normative data for stable post-op cases are represented by the green curves, while the red curves represent post-LVC ectasia cases. Treated corneas are automatically recognized as such and analyzed against post-LVC normative data. Alternatively the user can manually select the option of analyzing a treated cornea.

As its final output the CBI-LVC estimates a patient’s risk of developing ectasia after laser surgery.
Biomechanical Comparison Display

Stress-Strain Index (SSI): quantification of early biomechanical changes

Detecting biomechanical changes over time: Early signs of improvement after corneal crosslinking can only be detected by visualization and quantification of biomechanical changes.

Visualization and quantification of biomechanical changes over time is an essential precaution in various clinical applications. Progression of keratoconus must be detected at a very early stage if a severe loss of vision is to be presented.

Even more challenging is to verify the success of treatment after corneal crosslinking. Whereas topographic changes only occur after several months biomechanical changes can be measured with the Corvis® ST already four weeks after the procedure.

This software is the ideal solution for monitoring biomechanical changes over time.
Glaucoma Screening Software
Biomechanical Glaucoma Factor (BGF)

This revolutionary software allows an easy screening for glaucoma based on the biomechanical response. It offers a new approach to detecting normal tension glaucoma (NTG) cases despite normal intraocular pressure.

Detecting normal tension glaucoma (NTG) is very challenging in clinical practice. Intraocular pressure measurement will not indicate any elevated risk for glaucoma, and the optic nerve head might also appear relatively normal.

It recently has been shown that biomechanical properties can serve as an independent risk indicator for NTG. This provided the basis for the development of the Biomechanical Glaucoma Factor (BGF).

The BGF is a very early risk indicator of NTG which will guide you to the best clinical decisions for your patient.
The World of the Corvis® ST
Discover new possibilities for you and your patients!

### Overview

**Standard software**
- Biomechanical corrected IOP (bIOP)
- Corneal thickness
- Pachymetric progression
- Biomechanical response video

**Dynamic corneal response software**
- Vinciguerra Screening Report (CBI)
- Tomographic Biomechanical Assessment (TBI)
- Post laser vision correction analysis (CBI-LVC)
- Biomechanical Comparison Display
- Stress-strain curves and SSI

**Glaucoma screening software**
- Screening for normal tension glaucoma (NTG)/Biomechanical Glaucoma Factor (BGF)

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**The brains behind the software**

"Corneal biomechanics has demonstrated to be synergic to shape analysis for providing an enhanced method to characterize ectasia susceptibility. The integration of corneal tomography and biomechanical data with artificial intelligence is currently the most accurate approach for the diagnosis of keratoconus and ectasia risk before any refractive procedure."

Renato Ambrósio Jr, Brazil

"Assessment of the biomechanical stability after refractive surgery is critical to assess ectasia risk post laser vision correction. The CBI-LVC provides an objective (the only available screening in these conditions in my knowledge) measure about the state of the cornea post-operatively. This is very important for clinical decisions such as re-treatments, regular follow-up measurements or corneal crosslinking."

Paolo Vinciguerra, Italy

"Why are corneal biomechanics important to the clinician? Clinical uses range from screening for diseases such as keratoconus and glaucoma, to overcoming the errors in measurement of IOP using the common applanation tonometer, to predicting responses to corneal procedures such corneal collagen cross-linking (CXL) and laser vision correction (LVC)."

Cynthia Roberts, USA

"The focal reduction of corneal biomechanical properties was shown from previous studies to be the “first hit” in the development of keratoconus. The Corvis Biomechanical Index (CBI) has demonstrated to be highly sensitive and specific in multiple independent studies for the diagnosis of keratoconus and early ectasia."

Riccardo Vinciguerra, Italy

"Assessment of the biomechanical stability after refractive surgery is critical to assess ectasia risk post laser vision correction. The CBI-LVC provides an objective (the only available screening in these conditions in my knowledge) measure about the state of the cornea post-operatively. This is very important for clinical decisions such as re-treatments, regular follow-up measurements or corneal crosslinking."

Paolo Vinciguerra, Italy

"The Stress Strain Index estimates the mechanical behaviour of the cornea in vivo and in real time. This parameter provides a clear indication of how soft or stiff a cornea is, points at the risk of developing keratoconus or post-refractive surgery ectasia and assesses the effectiveness of collagen cross-linking in stiffening corneal tissue."

Bernardo Lopes, UK

"The Corvis ST provides an IOP measurement that has been shown experimentally and clinically to be almost completely independent of corneal biomechanics and could therefore assist the management of glaucoma."

Ahmed Elsheikh, UK

Stay tuned at www.corneal-biomechanics.com
OCULUS Corvis® ST
Technical Data

SCHEIMPFLUG CAMERA

FRAME RATE
4 330 images per sec

MEASUREMENT RANGE
8.5 mm (0.3 in) horizontal coverage

PACHYMETER MEASUREMENT RANGE
300 - 1 200 μm

MEASURING POINTS
576 per image (80 640 per examination)

TONOMETER

Measurement range: 6 - 60 mmHg
Measurement distance: 11 mm (0.4 in)
Inner fixation light: Red LED
3D auto tracking & auto release

in accordance with Medical Device Directive 93/42/EEC
OCULUS is certified by TÜV according to DIN EN ISO 13485 MDSAP
What do the experts say about the Corvis® ST?

Do you really know what biomechanical properties are? And what they have to do with the cornea?

You have additional questions or want to receive a proposal? Contact us at: export@oculus.de, we are happy to assist you.
Further resources

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  Scheimpflug tomography with axial length, total wavefront, refraction and retroillumination

- **Smartfield**
  The modern device for standard automated perimetry

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  Vision testing device for contrast vision, mesopic vision and glare sensitivity
OCULUS has been a trusted partner for eye care professionals around the world. With the highest attention to detail, our devices are designed and manufactured at the OCULUS headquarters, located in Wetzlar, Germany. Thanks to our 11 subsidiaries in Europe, Asia and America, and more than 200 distributors in over 80 countries, OCULUS is accessible to all customers around the globe.

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Discover a New World
Gain insights into corneal biomechanical properties

Get a Complete View
Biomechanical Assessment with the Corvis® ST and Integration with Tomography

Sept 2019 Published by Jaypee Highlights Medical Publishers, Inc.

Sept 2016 Published by Jaypee Highlights Medical Publishers, Inc.

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Discover a New World
Gain insights into corneal biomechanical properties

- Introduction to Clinical Assessment of Corneal Biomechanics
- Enhanced Artificial Intelligence for the Detecting Corneal Ectasia based on the Integration of Scheimpflug Corneal Tomography and Biomechanics
- Post-operative Biomechanical Evaluation After Laser Vision Correction
- A new Biomechanical Comparison display for the Corvis ST
- Development and Validation of a Material Stiffness Parameter based on the Corvis ST
Introduction to Clinical Assessment of Corneal Biomechanics

Author: Cynthia J. Roberts, PhD (Ohio, USA)

Why are corneal biomechanics important to the clinician? They characterize the stiffness of the cornea in response to the load provided by intraocular pressure (IOP). The stiffer the cornea, the less it stretches with IOP. Therefore visual outcomes of corneal treatments or procedures may be altered by the fundamental corneal properties which influence the ultimate shape of the first refractive surface. Clinical uses range from screening for diseases such as keratoconus and glaucoma, to overcoming the well-known errors in measurement of IOP using the common applanation tonometer, to predicting responses to corneal procedures such as corneal collagen crosslinking (CXL) and laser vision correction (LVC). In addition, many new applications are under active study.

The clinical assessment of corneal biomechanics has evolved rapidly since the first instrument to provide detailed information on biomechanical deformation parameters in vivo was introduced, including the depth and shape of corneal displacement from ultra-high speed Scheimpflug imaging during air puff loading. Many of the dynamic corneal response parameters (DCRs) are heavily influenced by IOP, including deformation amplitude (DA) and other depth parameters. This makes intuitive sense since IOP opposes the deformation induced by the air puff.

However, multiple DCRs are less sensitive to IOP, and actually quite sensitive to corneal stiffness. These include: shape parameters, radius of curvature at highest concavity, inverse concave radius (which is equivalent to concave curvature), and DA Ratio, which is the ratio between the displacement in the center to the displacement in the periphery. Stiffness can be thought of as resistance to deformation, so that the lower the shape DCRs (flatter curvature, lower DA Ratio), the more resistant to deformation, and the stiffer is the cornea. On the other hand, the two stiffness parameters (SP) at first applanation (A1) and highest concavity (HC) are defined as load (air pressure minus IOP) divided by displacement, so that the greater resistance to deformation leads to lower displacement in the denominator and greater values of SP-A1 and SP-HC with a stiffer response.

The initial clinical problem to be addressed was keratoconus detection, since it was hypothesized that the first identifiable corneal modification would be biomechanical in nature, and subsequent changes in thickness profile and curvature would be secondary responses to primary biomechanical weakening. A new Corvis Biomechanical Index (CBI) was developed and implemented on the device with over 98% correct classification of healthy vs keratoconic eyes.

Subsequently, a tomographic biomechanical index (TBI) was developed based on artificial intelligence that combined biomechanical and tomographic features into a more robust tool for the detection of ectatic corneas. In addition, a biomechanically corrected IOP (bIOP) value was simultaneously developed, in order to account for the influence of both central corneal thickness and corneal stiffness on IOP measurement. It has been reported that bIOP does not change after refractive surgery, unlike applanation tonometry.

Multiple shape DCRs along with the stiffness parameters, have been shown to be sensitive to changes produced by CXL for keratoconus at 6 months (accelerated CXL), 2 years (accelerated CXL), and 4 years (Dresden CXL protocol) after CXL. The shape parameters reported to produce significant differences include inverse concave radius, integrated inverse radius, radius at highest concavity, DA Ratio, SP-A1, and SP-HC, depending on the protocol and follow-up time point. Also, the accelerated CXL used for “extra” procedures with refractive surgery has been shown to produce less change in corneal biomechanics after surface ablation than a matched group without the extra procedure. All previously mentioned shape DCRs showed significant differences in both surface ablation groups, but only inverse radius and DA Ratio were sensitive enough to differentiate the group with an extra procedure from the group without CXL.

As development continues, new algorithms are introduced which will be described in the subsequent articles, including an improvement of TBI for keratoconus detection with optimization on big data, a new post Laser Vision Correction analysis, improvement of TBI for keratoconus detection with optimization on big data, a new post Laser Vision Correction analysis, and implemented on the device with over 98% correct classification of healthy vs keratoconic eyes.

Material stiffness applies to the individual components of the cornea, independent of thickness, and SSI has also been shown to be less dependent on IOP. Structural stiffness is at the corneal tissue level, and includes thickness. For example, one chopstick could be snapped in half with only hand strength. However a large bunch of chopsticks held together cannot be snapped in half so easily. The properties of the chopsticks don’t change at the material level, but the overall stiffness changes at the bulk “tissue” level. As these new algorithms are made available, improved tools can be directly applied to patient care and exciting new research avenues will be enabled.
Enhanced Artificial Intelligence for the Detecting Corneal Ectasia Based on the Integration of Scheimpflug Corneal Tomography and Biomechanics

Author: Renato Ambrósio Jr, MD, PhD (Rio de Janeiro, Brazil)

The last three decade witnessed a genuine revolution on corneal diagnostic technologies towards multimodal imaging, which has transformed our ability to detect mild or sub-clinical forms of corneal ectasia.[14] In fact, screening for candidates at risk for "iatrogenic" progressive ectasia (keratectasia) after corneal laser vision correction (LVC) procedures has gone beyond (not over) identifying very mild keratoconus, towards characterizing the inherent ectasia susceptibility of the cornea.[15-17]

Placido-disk based corneal topography is sensitive to detect abnormalities in patients with normal visual acuity and unremarkable biomicroscopy.8 However, different studies involving eyes with regular topography from patients with clinical ectasia in the fellow eye (Very Asymmetric Ectasia, VAE-NT) have established the need and the opportunity to augment accuracy further using different technologies.[19-25]

Going beyond shape: Biomechanical characterization

Further detail of the corneal architecture is conceivable through 3-D Scheimpflug tomography (front and back elevation and thickness map),[26] and segmental tomography (epithelial and Bowman’s mapping) using spectral domain OCT and very-high-frequency ultrasound.[27,28] Nevertheless, clinical biomechanical assessments emerged as fundamental for characterizing the inherent ectasia progression susceptibility of the cornea.[29-31] The OCULUS Corvis ST has an ultra-high-speed Scheimpflug camera to monitor corneal deformation during non-contact tonometry.[32] In 2016, the Corvis Biomechanical Index (CBI) and the Tomographic Biomechanical Index (TBI) for ectasia detection were introduced for this device using machine learning algorithm.

Artificial Intelligence for ectasia risk assessment

Machine learning for generating artificial intelligence (AI) has been widely recognized in order to give clinicians aid for improving care to the patients.[23,33-38] The BAD-D, available at the Belin/Ambrósio Enhanced Ectasia Display from the Pentacam,[39] and the Corneal Biomechanical Index (CBI),[40,41] available in the Vinciguerra Screening Report from the Corvis ST, were developed using logistic regression analysis (LRA) for optimizing the detection of corneal ectasia. However, more advanced AI have been used for the Pentacam Random Forest Index (PRFI) [42] and in the Tomographic Biomechanical Index (TBI) [23,43].

The concept of integrating corneal tomography and biomechanical data for enhancing ectasia detection was established on anecdotal cases.[22,44] The TBI developed by Ambrósio, Roberts & Vinciguerra is available on the integrated Pentacam and Corvis ST software (ARV-Display).[23] Figure 1 shows the ARV-Display of a topographical normal eye whereas the fellow eye has clinical ectasia. Both CBI and TBI are clearly abnormal (0.73 and 1.00, respectively) whereas the topography and tomography show no signs of ectasia. Cases like that reflect the need of combining biomechanical data with tomographic data. Such cases with normal topography from patients with very asymmetric ectasia represent the most important model for developing and testing novel strategies for enhancing ectasia detection.

Figure 1a. Topography of the left and right eye of a case of Very Asymmetric Ectasia with normal topography OD and kc stage 2 OS.

Figure 1b. Tomographic Biomechanical Assessment OD with abnormal TBI and CBI.
Post-operative Biomechanical Evaluation After Laser Vision Correction

Authors: Paolo Vinciguerra, MD; Riccardo Vinciguerra, MD (Milan, Italy)

Laser vision correction (LVC) is widely accepted procedure to correct refractive errors such as myopia, hyperopia and astigmatism. It is known to have an excellent safety profile, however, in a small amount of cases, iatrogenic ectasia can develop, either in PRK, LASIK or SMILE.

The early detection of post-LVC ectasia is of foremost importance as it can be treated with corneal collagen cross-linking and avoid progression that can even lead to an indication for corneal transplants.

Up today, the gold standard for early post LVC ectasia detection (when diagnosis is not clear) is to perform 2 different tomographic scans that shows progression such as steepening and thinning in a localized area. Unfortunately, this approach has the drawback to accept progression to be able a clear diagnosis.

In-vivo corneal biomechanics with Corvis ST (OCULUS, Germany) has previously proved to significantly improve the diagnosis of early and subclinical keratoconus (kc), particularly when combined with tomography. Yet, CBI and TBI are always abnormal in patients after LVC because they are designed to separate normal patient from kc. In this article we present a new version of the CBI, named CBI-LVC, that aims to separate stable post LVC patients with post LVC ectasia.

This new index was created using a very large database of normal, keratoconus, stable post LVC patients (PRK, LASIK and SMILE) and diagnosed post LVC ectasia. In details we included a total of 4,422 eyes of which 1,507 normal, 1,240 keratoconus, 449 post-LVC stable patients and 21 post-LVC ectasia.

To be able to provide a semi-automatic separation also an index to separate keratoconus patients from LVC was created. As a matter of fact, both of these patients would appear abnormal with CBI.

Logistic regression was employed to determine the optimal combination of best predictors from the individual indices for the creation of a Corvis Biomechanical Index (CBI-LVC) for the accurate separation between post LVC and keratoconus and between stable post LVC and LVC induced ectasia.

With a cut-off value of more than 0.353 a mild modification of the published CBI has a Sensitivity of 87.8% and a Specificity of 95.8% to separate normal from Kc/post LVC. The second index, which was aimed to separate keratoconus from post LVC, with a cut-off of 0.7266 had a sensitivity of 94.0% and a specificity of 93.2%.

At last the CBI-LVC was able to accurately separate stable post LVC from ectasia after LVC with a sensitivity of 94.1% and a specificity of 95.5%. Figure 2 shows the step by step approach with sensitivity and specificity.

It is the first time, to our knowledge, that an index based on biomechanics is able to produce such an efficient separation between stable post LVC and LVC induced ectasia and is tested and validated in such a big database.
OUTLOOK: BIOMECHANICAL ANALYSIS POST LVC

This index will soon be implemented in the native Corvis software. When a patient is acquired with Corvis ST, three different steps are executed automatically:

1. Step 1: The CBI will automatically detect whether the cornea is normal or kc/post LVC. This is tested with the CBI logistic regression equation. If the patient is normal the biomechanical assessment is already finished after step 1.

2. Step 2: If the CBI is indicating an “abnormal” biomechanical behaviour a second logistic regression is applied that tests whether the patient has rather keratoconus or whether the soft biomechanical response is caused by laser vision correction. If the patient has more likely a keratoconus once more the biomechanical evaluation is finished after this step and the CBI provides the risk for the disease.

3. Step 3: In case the soft corneal behaviour is more likely caused by LVC the doctor will be asked to confirm whether the patient had indeed previous refractive surgery. If post LVC will be selected the software will automatically switch from CBI to the new LVC-CBI that is able to separate stable LVC from ectasia with a sensitivity of 94.1% and specificity of 95.5%.

Despite of this automatic approach the clinician will always have the possibility to choose the button “post LVC”. In this case the software will automatically present the newly developed CBI-LVC independent on the results of steps 1 and 2. In conclusion, our study introduces LVC-CBI which was shown to be highly sensitive and specific alone to separate stable from ectatic LVC eyes. We suggest the use of LVC-CBI in everyday clinical practice, together with topography and tomography, to assess the biomechanical stability after LVC and to aid the diagnosis of post LVC ectasia.

A New Biomechanical Comparison Display for the Corvis ST

Authors: Riccardo Vinciguerra, MD; Paolo Vinciguerra, MD (Milan, Italy)

The evaluation of changes in corneal biomechanics is of foremost importance for the follow up of corneal diseases in which the tissue gets softer such as keratoconus, ectasia after Laser Vision Correction and Pellucid marginal degeneration and to evaluate the outcomes of procedures that make the cornea softer (Laser vision correction for example) or stiffer (Cross-Linking).

In particular, the assessment of the effect of corneal collagen cross-linking (CXL) in the first follow-ups after the surgery is of primary importance, however, the well-known decrease of corneal thickness, the decline of visual acuity and increase of curvature in the first postoperative months make this task very challenging. The best way of judging the outcome of CXL would be to directly assess the its stiffening effect.

In previous studies we were able to show significant rise in corneal stiffness as demonstrated by a significant increase of Dynamic Corneal Response parameters (DCRs) such as Stiffness Parameter A1 (SP-A1) and Highest Concavity (SP-HC) and a significant decrease of Inverse Concave Radius (1/R), and Deformation Amplitude Ratio (DAratio) (p<0.05). The study proved that new DCRs by the Corvis ST are able to detect early changes in biomechanics following CXL and those are measurable before corneal shape modifications take place.

At last, we recently introduce the stress-strain index, that proved to be able to successfully
measure corneal material stiffness, while being less dependent on bIOP and CCT, and correlated with age in healthy population.\textsuperscript{(13)} However, until now, the comparison was still very rudimental done with the manual transcription of the parameters and subsequent evaluation.

The first step to be able to compare two exams is the knowledge of the repeatability of the instrument in normal and keratoconic patients that was done in two previous studies (keratoconus repeatability is in press in Journal of Cataract and Refractive Surgery 2019).\textsuperscript{(52)} Based on these studies it was possible to calculate the two sided confidence intervals to know whether the change in DCRs between one exam and the other is significant.

In this article we introduce a new Biomechanical Comparison display for the Corvis ST aimed to help the comparison of two different exams. (Figure 3)

The display aims to automatically provide the comparison of two exams done with the Corvis ST and indicate whether the difference between the two exams is significant (either towards the softer or stiffer side).

Below an example of the display in a patient pre and post corneal collagen cross-linking.

The biomechanical comparison display shows respectively:
- On the top the values of CCT, and pressure (bIOP and non-corrected) for both exams.
- In the middle of the display the two videos of corneal deformation pre (blue) and red (post) and the overlap of the two. In this case, as the cornea gets stiffer, we observe less deformation of the red cornea (post CXL).
- In the middle on the right the display shows the difference of SSI with the relative stress strain curves, as expected SSI gets significantly stiffer (more 95% confidence interval).
- In the bottom of the display, similarly to SSI, the values of deformation amplitude ratio, inverse concave radius, Ambrosio Thickness profile and Stiffness Parameter A1 are shown for measurements A and B. For both examinations the multiple of the standard deviation each value deviates from a healthy population is also given as "SD" value. The differences of "SD" values between measurement A and B are also shown.
- In the lowest line of the boxes it is provided whether these changes are significant or not by comparing them with the two-sided confidence interval for keratoconus eyes. It is automatically highlighted whether the changes indicate a softening, a stiffening or whether the changes are not significant.
- As expected, these parameters, except of the thickness profile show significant stiffening after CXL in the shown case. (Figure 3)

Obviously, this display could also show significant softening in cases of progressive keratoconus or ectasia.

In conclusion, we introduce a new comparison display for the evaluation of two exams of the Corvis ST of the same patients which aims to help in the evaluation of changes in corneal biomechanics.

\begin{figure}[h]
\centering
\includegraphics[width=\columnwidth]{figure3a}
\caption{Biomechanical Comparison Display with a case before and after corneal cross-linking.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\columnwidth]{figure3b}
\caption{Quantification of biomechanical changes before and after CXL.}
\end{figure}
Development and Validation of a Material Stiffness Parameter Based on the Corvis ST

Authors: Bernardo Lopes, MD, PhD; Prof. Ahmed Elsheikh, PhD (Liverpool, UK)

Measuring corneal material stiffness in vivo is of great clinical importance and it’s also a great challenge. Corneal deformation behaviour under the air puff of instruments such as the Corvis ST is highly dependent on the intraocular pressure (IOP), the shape of the eye, especially the corneal thickness (CT), and the corneal material stiffness. This makes the task of separating the effects of these three components on corneal behaviour quite difficult. While we can accurately measure the CT with Scheimpflug imaging, measuring the IOP and material stiffness is not straightforward. Furthermore, as the mechanical behaviour of the cornea is nonlinear, the tangent modulus (Et) of the tissue – a measure of material stiffness – is not constant and increases with IOP and both stress and strain.

A method to accurately measure the IOP with less dependence on the material stiffness was developed based on precise numerical simulations of the corneal deformation responses to the Corvis ST exam and extensively validated experimentally and in various clinical scenarios. (12,53-54) The biomechanically-corrected IOP (bIOP) has been shown to have no significant correlation with CCT and age, and to be unaffected by corneal stiffness changes after refractive surgery and collagen UV A crosslinking (CXL). The success in determining IOP was an important step in efforts to measure the cornea’s biomechanical behaviour, and in particular the whole stress-strain behaviour that can determine the corneal Et under any IOP.

The stress-strain index (SSI) was developed based on the results of a large numerical simulation of corneal biomechanical behaviour under the Corvis ST air pressure in eyes with a wide range of IOP, corneal shape and material stiffness. (Figure 4) (13) The expectation that SSI would be correlated with age while being independent of IOP and corneal thickness was first tested in two clinical sets from Italy and Brazil (480 healthy participants) and subsequently confirmed in a larger multicentric study involving 1664 healthy subjects and 1686 keratoconic patients. (Figure 5) In this study, it was observed that the SSI was independent of both IOP and CCT while being correlated with age in healthy (but not keratoconic) eyes. In eyes with keratoconus, the SSI further showed significant gradual deterioration in material stiffness with disease progression. (Figure 6) The SSI was then used to evaluate the short-term effect of corneal crosslinking (3 month post-CXL). A group of 41 patients submitted to the standard Dresden’s protocol was tested, and a significant increase in SSI was observed between the pre-CXL (0.78±0.19) and the post-CXL stage (0.87±0.21, p= 0.03). (Figure 7) These studies demonstrated the success of the SSI, measured in vivo, in representing the corneal material stiffness, being less dependent on bIOP and CCT, and correlated with age in healthy population. The SSI further showed deterioration with keratoconus progression and increases following corneal crosslinking. Further studies are being conducted to assess the new index as an optimisation tool for the crosslinking procedure, to assess the postoperative state of refractive surgery and the preoperative surgical screening. With this index, the Corvis ST can provide clinicians with meaningful and comprehensive corneal biomechanical evaluation in real-time.
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Biomechanical Assessment with the Corvis ST and Integration with Tomography

Two Novel Stiffness Parameters for the Corvis ST

The New Vinciguerra Screening Report and Corvis Biomechanical Index (CBI)

Ultimate Ectasia Detection 2016: Integrating Corneal Tomography and Biomechanical Assessment

Biomechanically Corrected IOP Measurement

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Two Novel Stiffness Parameters for the Corvis ST

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Corneal biomechanical characterization has generated great interest from clinicians. The Corvis ST uses a consistent air puff to deform the cornea, along with an ultra-high speed camera utilizing Scheimpflug geometry to capture images of the horizontal meridian at greater than 4,300 frames per second, resulting in 140 images during the 30ms air puff. The cornea is viscoelastic in nature, which means that biomechanical characterization depends on the magnitude of the applied load and how quickly that load is delivered, as well as on the intraocular pressure (IOP). With the Corvis ST, each cornea experiences the same load over the same time period, facilitating biomechanical comparisons between eyes. In addition, a biomechanically corrected IOP (bIOP) has been developed, the derivation of which will be explained in a later section. This is critically important, since both the cornea and sclera stiffen with increasing IOP, which influences the deformation response. A stiffer sclera will limit maximum corneal deformation since it generates greater resistance to displacing fluid.

As the air pressure reaches the cornea, it begins to deflect in the backward direction. Whole eye motion is simultaneously initiated, also in the backward direction. Dynamic corneal response (DCR) parameters which include whole eye motion are described as “deformation” parameters, and those for which whole eye motion is removed are described as “deflection” parameters. This is illustrated in Figure 1, along with some of the DCR’s. First applanation (A1) parameters include: A1 Time, A1 length, A1 velocity, A1 Deformation Amplitude, and A1 Deflection Amplitude. Parameters at highest concavity (HC) include: HC Time, Peak Distance, Radius of Concave Curvature, HC Deformation Amplitude (equivalent to Maximum Deformation Amplitude), and HC Deflection Amplitude. Parameters at second applanation (A2) include: A2 Time, A2 length, A2 velocity, A2 Deformation Amplitude, and A2 Deflection Amplitude. Additional parameters include Deformation Amplitude Maximum (which may not be at highest concavity); Deformation Amplitude Ratio (DA Ratio) which is the central deformation divided by an average of the deformation 2mm either side of center with maximum value just prior to A1; Deflection Amplitude Ratio (DeflAmp Ratio) which is similar to DA Ratio, but uses corneal “deflection” which is corrected for whole eye motion; and Maximum Whole Eye Motion which occurs near A2.

With the goal to develop a simple clinical parameter that correlates with stiffness, the spatial and temporal velocity profiles of the air puff have been experimentally measured using hot wire anemometry. The measured velocity is converted to pressure and allows the air pressure (AP) at the time and position of first applanation to be determined for each exam. This adjusted air pressure (adjAP1) minus bIOP represents the resultant pressure (Pr), or load on the cornea at A1. By dividing Pr by corneal displacement, a clinical stiffness parameter (SP) is calculated. The stiffness parameter that is most closely related to corneal properties is determined by using displacement of the apex from the undeformed state to first applanation (SP-A1). This value has already proven to be clinically useful in screening for keratoconus with the highest sensitivity and specificity of any single parameter value, which will be discussed later in this article. In addition, SP-A1 has shown a significant difference after laser vision correction in multiple datasets (unpublished data), and shows promise as being a strong indicator of corneal biomechanical properties. The stiffness parameter that is also influenced by scleral properties is determined by using displacement from first applanation to highest concavity (SP-HC). These new stiffness parameters, along with the DCR parameters can be used to biomechanically characterize eyes with specific pathologies.

Figure 1: Superimposed frames extracted from a single exam, showing A: Cornea in the Prefdeformation phase (pseudocolored blue), at maximal corneal deflection (pseudocolored red), and at maximal whole eye movement (pseudocolored white); and B: Correction for whole eye motion by aligning all corneal images in the periphery to that at predeformation. Note the crystalline lens appears to have moved toward the cornea. However, this is due to optical distortion caused by viewing through a concave surface and does not represent actual movement of the lens.
The New Vinciguerra Screening Report and Corvis Biomechanical Index (CBI)

Authors: Riccardo Vinciguerra, MD; Prof. Paolo Vinciguerra, MD (Milan, Italy)

The in-vivo evaluation and interpretation of corneal biomechanics has been a topic of great interest, as the mechanical instability of the cornea is thought to be the initiating event of keratoconus, even before notable changes in corneal morphology take place.

However, it is extremely difficult to measure the biomechanics of the cornea due to its hyperelastic and viscoelastic behavior, which makes the cornea’s behavior nonlinear and dependent on the rate of loading.

Additionally, a fundamental confounding factor is IOP: according to Laplace’s Law, the wall tension is a function of the internal pressure. This means that as IOP increases, the wall tension will increase and due to the nonlinear properties, and a soft cornea with higher IOP may exhibit stiffer behavior than a fundamentally stiffer cornea with a lower IOP. On the other hand, IOP measurements are influenced by corneal stiffness, which is not only dependent on the thickness, as widely accepted, but also the tissue’s material properties. For this reason, in order to be able to judge a possibly abnormal cornea, it is mandatory first to create normative values for each parameter as a function of age and IOP and second an index to separate normal from ectatic corneas.

The Vinciguerra Screening Report and Normative Values

The Vinciguerra Screening Report is a new display of the Corvis ST aimed to report, in a single interface, the comparison of normative values to imported exams as well as to include an index to separate normal from keratoconic patients.

The multicenter study that supported the creation of the normative values included 705 healthy patients enrolled in three continents to include variability from various ethnic groups.

The study demonstrated that IOP and pachymetry have important influences on most corneal biomechanical metrics provided by the Corvis ST and - for this reason - the creation of normative values is of crucial importance to judge the possible abnormality of a selected exam.

Figure 2 shows a clinical example of the use of normative values of the Vinciguerra Screening Report: the interface is designed with two graphs. The left one (B) shows the diagram of the selected Dynamic Corneal Response parameter (in this case Deflection Amplitude) with the normal ranges for the patient’s bIOP in the evaluated exam. The chart on the right side displays the obtained results compared to the whole normal range of bIOP. The actual profile fits inside the mean ± 2SD range of the normative values displayed.

The display also provides the absolute values and the standard deviations from the mean of the Ambrósio’s Relational Thickness to the horizontal profile, which is based on the thickness profile in the temporal-nasal direction (ARTh) and a novel stiffness parameter at first applanation (SP-A1). The standard deviations are also provided for two Dynamic Corneal Response parameters (DA Ratio and integrated Radius). In addition, the biomechanically corrected IOP value (bIOP) for the patient is provided together with the CCT of the patient.

The display may help in the evaluation of an abnormal exam where a keratoconic patient’s exam clearly extend beyond the mean ± 2SD normative value range displayed (Figure 3).

Corvis Biomechanical Index (CBI)

To further increase the capability of the Corvis ST to separate normal from keratoconic patients, a novel biomechanical index (CBI) was developed (Figure 3).

Figure 2: Normal ranges for the deflection amplitude curve for the specific bIOP of this patient and plot of maximal deflection amplitude vs bIOP with ± 2 SD range.

Figure 3: Standard Deviations from the mean for two Dynamic Corneal Response Parameters, the Ambrósio Rational Thickness (ARTh) and the Stiffness Parameter at first applanation (SP-A1) are plotted. In addition, the Corvis Biomechanical Index (CBI) was developed to identify patients with corneal ectasia.
The paper that demonstrated the capability of CBI to separate healthy from ectatic patients included 662 patients enrolled in two different continents.\[8\]

Logistic regression was employed to determine the optimal combination of best predictors from the individual indices for the creation of the CBI for the accurate separation between normal and keratoconic eyes, using one dataset for training and the other for validation to exclude over-fitting.

The results of the study showed that, with a cut off of 0.5, CBI was able to correctly classify 98.2% of the cases with 100% specificity and 94.1% sensitivity in the training dataset. In the validation dataset, the same cut-off point correctly classified 98.8% of the cases with 98.4% specificity and 100% sensitivity.\[8\]

To our knowledge, this was the first time that an index based on biomechanics has been able to produce such an efficient separation. Further to that study, we recently evaluated more than 100 forme fruste keratoconus (FFKC), defined as the normal fellow eyes (both topographically and tomographically) of unilateral keratoconus and many of those showed an abnormal CBI while the other exams were normal.

Figure 4 shows a clinical example. The Belin Ambrósio total D was 6.69 in the diseased eye while it was 1.18 in the FFKC eye indicating no abnormality. Furthermore topography revealed no abnormal pattern on the FFKC eye. Based on topographical keratoconus staging (KKS) OS was stage 2 whereas OD was not identified as keratoconus.

Figure 5 shows the Vinciguerra Screening report of the FFKC eye; CBI is above 0.5 (the cut off for abnormality) in both eyes.
Conclusion

In conclusion, the introduction of our normative value ranges inside the Vinciguerra Normative Display provides, for the first time, the possibility to interpret corneal biomechanics in the context of normative values and suspect pathology in clinical practice. Additionally CBI for keratoconus diagnosis was shown to be highly sensitive and specific alone to separate healthy from ectatic eyes.

At last, as suggested by our recent evaluation of FFKC, CBI might be an additional help to diagnose ectasia at a stage where tomography and topography are normal.

Ultimate Ectasia Detection 2016: Integrating Corneal Tomography and Biomechanical Assessment

Authors: Prof. Renato Ambrósio Jr, MD, PhD; Bernardo T. Lopes, MD (Rio de Janeiro, Brazil)

The detection of mild or sub-clinical forms of ectatic corneal diseases (ECD) has gained its momentum because these cases are at very high risk for iatrogenic progressive ectasia (keratectasia) after corneal Laser Vision Correction (LVC) procedures[9,10] In addition to elective Refractive Surgery, augmenting sensitivity for identifying very mild ectasia cases and monitoring disease progression have become of utmost importance because of the definitive paradigm shift on the management of ECD, which was related to the introduction of novel therapeutic approaches such as collagen cross-linking.[11]

Pentacam: A Revolution on Corneal Imaging

From the characterization of the front surface by Placido-disk based corneal topography, we evolved into 3D tomographic analysis, which characterizes corneal front and back elevation along with thickness mapping.[12,13] Elevation maps represent the subtraction of the corneal surface from a geometric (i.e. sphere or toric ellipsoid) reference body that is calculated to best fit the examined corneal surface.[14] Michael Belin, MD, deserves the credit for many contributions that advanced this field, including the concept of calculating a second enhanced reference with an exclusion zone that facilitates the identification of a protrusion within the area of exclusion zone,[14-16] and defining elevation metrics for monitoring ectasia progression.[17] The concept of corneal thickness profile, introduced by Ambrósio in 2004, details how the cornea gets thicker spatially towards the periphery.[18,19] The relational thickness values represent an objective method that combines the thinnest value and the pachymetric progression indices, which also improves accuracy for detecting ectasia.[20]
The Belin/Ambrósio Enhanced Ectasia Display, available on the Oculus Pentacam, combines elevation and thickness data and includes the ‘d’ indices. Considering the significant variability of subjective classification of color-coded maps,7 objective metrics are needed. The ‘d’ values were developed to represent the deviation from normality towards ectasia for different parameters. The final BAD-D, currently in its third version, combines the ‘d’ values using a logistic regression analysis to optimize ectasia detection. Different studies have found the BAD-D to be the most accurate parameter to detect ectasia.[16,21-24] For example, the analysis of a combination of the populations from two studies leading in total to one eye randomly selected from 811 normal eyes and from 422 keratoconic corneas, the area under the ROC (receiver operating characteristic) curve for BAD-D was 0.999 (95% confidence interval: 0.993 to 1.000) with 98.9% sensitivity and 99.8% specificity with a cut off value of 2.14.

Beyond shape analysis, biomechanical understanding is thereby supreme for augmenting the sensitivity for identifying mild ECD or its susceptibility. Reichert Ocular Response Analyzer (ORA) is a non-contact tonometer that monitors corneal deformation through an infrared apical reflex, providing data for biomechanical assessment.[30] While first generation pressure-dependent parameters had a relatively low accuracy for detecting keratoconus,[31] studies demonstrated that parameters derived from corneal deformation improved sensitivity to detect keratoconus and mild forms of ECD. These data were found useful to improve diagnostic accuracy when combined with Pentacam data.[13] In fact, the validity of integrating corneal tomography and biomechanical assessment for enhancing ectasia risk detection was demonstrated on anecdotal cases, such as the findings on the fellow nonoperated eye from a patient that had progressive keratectasia after LASIK with no detectable preoperative risk factors.[33]

Oculus Corvis ST & ARV (Ambrósio, Roberts & Vinciguerra) Tomographic and Biomechanical Integration

The Oculus Corvis ST is also a non-contact tonometer that uses an ultra-high speed Scheimpflug camera to monitor corneal deformation in a much higher detail than ORA.[34] The CBI was developed combining deformation parameters and the horizontal thickness profile,[35] being very effective to detect keratoconus (Vinciguerra et al., JRS 2016 in press). A new software developed by Oculus enables a robust integration with corneal tomography by Pentacam. The TBI (Tomography and Biomechanical Index) is calculated using a regression formula to optimize ectasia detection. In a study involving one eye randomly selected from 478 normal eyes and from 180 keratoconic corneas, the area under the ROC (receiver operating characteristic) curves for CBI, BAD-D and TBI were respectively 0.986, 0.999 and 1.0. Considering 94 FFKC cases, the TBI had 92.55% sensitivity with 98.74% specificity. The integration of Corvis ST and Pentacam does improve the detection of FFKC in cases with BAD-D lower than 1.6 (Figure 6).

Figure 6a: Tomographical assessment of a FFKC case (OS: stage 2, OD: topographical and tomographical normal).

Figure 6b: The biomechanical/tomographical assessment OD with Tomographical Biomechanical Index (TBI) of 0.89 indicating an ectasia in the FFKC eye.
In addition, it has been also useful to enhance specificity, as in a case with mild asymmetric bow tie on topography from a patient that had LASIK in the fellow eye with no ectasia development (Figure 7).

Future advances in corneal imaging include segmental or layered tomographic characterization with epithelial and Bowman’s layer thickness mapping. However, while genetic screening is not available, the integration of Pentacam and Corvis ST data is the ultimate approach for ectasia detection.

Biomechanically Corrected IOP Measurement

Authors: Prof. Ahmed Elsheikh, PhD; Ashkan Mohammadvali; Kai-Jung Chen; (Liverpool, UK)

Intraocular pressure (IOP) measurement, through both contact and non-contact methods, is based on a basic concept: apply a mechanical force on the eye and correlate the resistance to deformation to IOP. As such, IOP measurements are affected by ocular stiffness, which in turn increases with larger corneal thickness and age, and reduces with keratoconus and refractive surgery. This source of error can cause significant over-estimations or under-estimations in IOP measurement, leading to possible adverse effects on glaucoma management.

A method to enable the measurement of IOP in a way that is independent of ocular stiffness has been developed and validated extensively. The method relies on accurate and representative numerical simulations of ocular globes with wide ranges of tissue thickness and material behaviour, and IOP levels.

Through simulations of the Corvis procedure, and consideration of the Corvis deformation output, the new method enables the accurate estimation of an IOP that is less dependent on ocular properties, and thus biomechanically corrected IOP (biOP).

biOP has been first tested experimentally on several ex-vivo human eye globes. The eyes were subjected to known levels of IOP and to the Corvis procedure. Both the uncorrected and corrected IOP measurements were compared with the applied IOP. In all cases, biOP was significantly closer to true IOP than the Corvis measurement (the mean of the absolute differences between biOP and true IOP was 0.84±0.97 mmHg compared with 3.46±1.09 mmHg for the absolute differences between uncorrected Corvis IOP and true IOP).

biOP was then assessed clinically on a number of clinical databases involving...
thousands of Corvis measurements. In all cases, bIOP significantly reduced the association between IOP measurements and both corneal thickness and age. bIOP was also assessed for patients undergoing the LASIK refractive surgeries (Figure 10). The difference in bIOP taken before and after surgery was 1.0 mmHg (14.6±2.4 pre-surgery vs 13.6±2.1 post-surgery), compared with 3.4 mmHg for uncorrected Corvis readings (14.8±2.4 pre-surgery vs 11.4±1.9 post-surgery) and 3.1 mmHg for Goldmann Applanation Tonometry (GAT) readings (15.8±2.4 pre-surgery vs 12.7±2.3 post-surgery).

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