

Oculus Corvis ST

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Measuring corneal biomechanics in vivo

- Measuring biomechanical properties clinically is currently one of the most exciting fields in modern ophthalmology.
- *Biomechanical properties* are defined as the response of a biomechanical tissue to a force.
- The cornea is **visco-elastic** which means that it exhibits both viscous and elastic biomechanical behaviour.

IOP-Measurements: closer to the physiological IOP

- The intraocular pressure measurement by applanation tonometry is highly influenced by the **biomechanical properties**.
- Therefore, taking biomechanical properties into consideration will provide a much more accurate IOP reading, closer to the **physiological IOP**.

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- In ***conventional Goldman tonometry*** ***IOP*** readings can be completely off when the biomechanical properties of the cornea are altered – as for example after LASIK.
 - This could lead to wrong decisions in the diagnosis and management of glaucoma.

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- The impact of IOP on corneal biomechanical performance was highlighted by **Ramos and collaborators** in a movie that reviewed the relevance of this technology in different clinical applications (Scheimpflug Revelations).
 - **Mazzeo and collaborators** reported a case of bilateral post-LASIK ectasia associated with pigmentary glaucoma in which the IOP was underestimated by Goldmann's applanation tonometry (18 mmHg in both eyes).

Post-LASIK Ectasia associated with Pigmentary Glaucoma: Tomographic and Biomechanical Characterization

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⁶Giovanni Colombini, ⁷Renato Ambrósio Jr

A case of bilateral post-LASIK ectasia associated with pigmentary glaucoma in which the IOP was underestimated by Goldmann's applanation tonometry (18 mmHg in both eyes).

- **ORA** detected ocular hypertension with IOPcc (ORA) being 47.8 mmHg OD and 43.8 mmHg OS.
- With the Corvis ST, the **biomechanically-corrected IOP (bIOP)**, developed to reduce the effect of stiffness on IOP estimates, was 62.9 mmHg OD and higher than 70 mmHg.

Scheimpflug-based tomography and biomechanical assessment in pressure-induced stromal keratopathy.

J Refract Surg. 2013; 29(5):356-8


Faria-Correia F; Ramos I; Valbon B; Luz A; Roberts CJ; Ambrósio R

A case of pressure-induced stromal keratopathy (PISK), which was misdiagnosed as diffuse lamellar keratitis (DLK).

- Goldmann applanation tonometry was 12 mm Hg, whereas CorVis intraocular pressure was 53.5 mm Hg with deformation amplitude of 0.42 mm.
- stressed the relevance of biomechanically-corrected IOP measurements for identifying ocular hypertension


Biomechanical properties as independent risk factors for glaucoma


- Despite leading to a more accurate measurement of IOP, the biomechanical properties of the eye ball are supposed to be independent risk factors for glaucoma.
- This allows screening for normal tension glaucoma by biomechanical parameters such as stiffness.


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- The biomechanical properties of the cornea can be measured by the evaluation of the response of the cornea when placed under stress.
 - This can be achieved by an external force such as an air pulse – as done with the **Corvis® ST**.


Corvis® ST: Measurement Principle

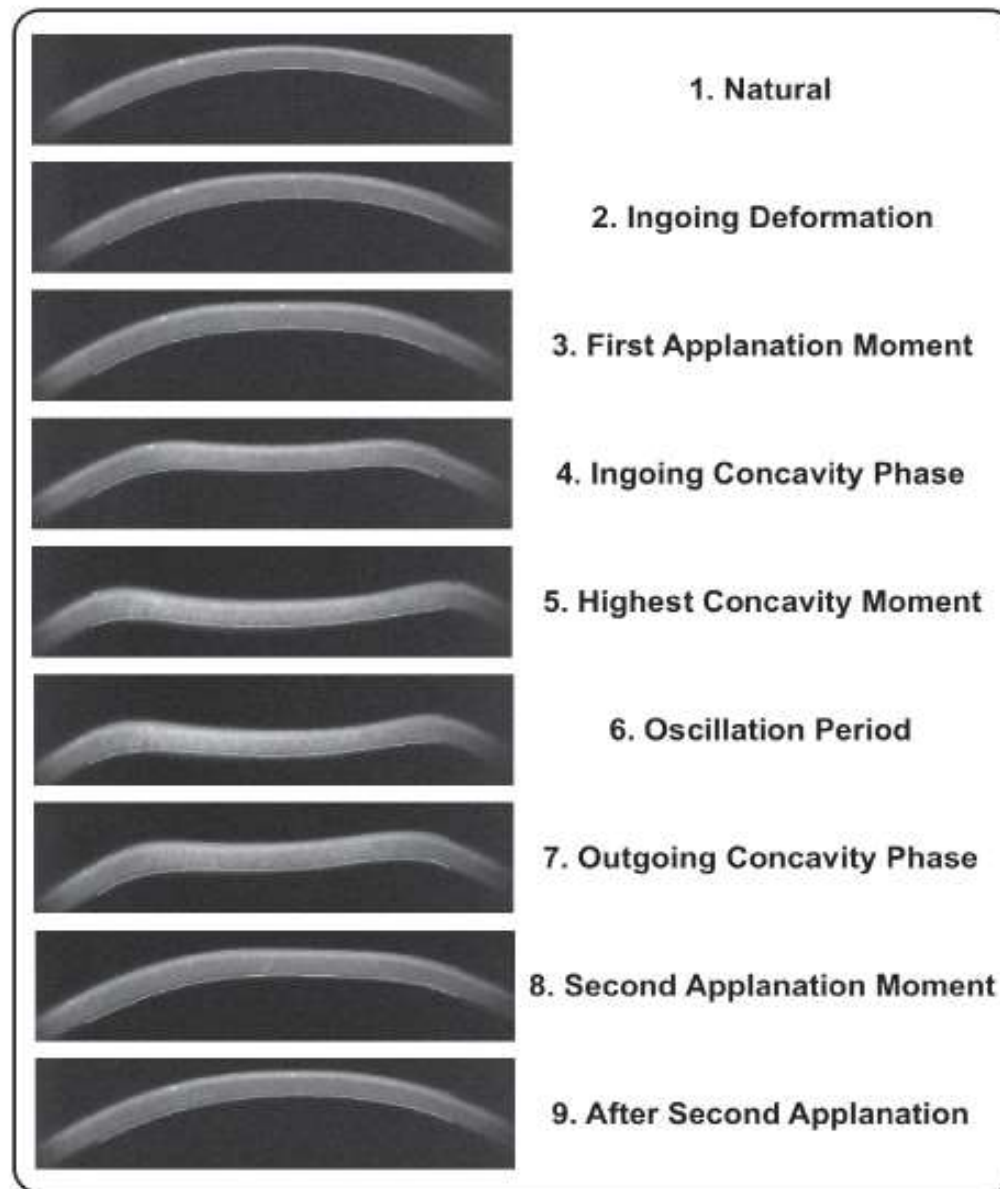
- The **Corvis® ST** is a combination of an air pulse tonometer with an ultra-high-speed Scheimpflug camera.
- Shortly before the air pulse starts the cornea is illuminated by a blue slit light.
- At this moment ***corneal thickness*** is measured as well.

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- Afterwards the **high-speed camera** tracks the biomechanical response of the cornea.
 - Within 31 ms the camera records **140 images** of the horizontal sectional plane. This is a frame rate of more than 4300 images / second
 - Deformation characteristics are extracted directly from these acquired images to characterize the corneal deformation response

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- The movement of the cornea is mainly influenced by *three factors* which can be measured by the instrument:
 - Intraocular pressure (IOP)
 - Biomechanical properties of the cornea.
 - Corneal thickness.

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- All 140 images depict a complete picture of the biomechanical response of the cornea.
 - At the beginning the cornea is in its initial **convex shape**.
 - The air pulse drives the cornea backwards until the ***first applanation*** occurs.

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- Afterwards, the cornea is further deformed until the moment of **maximal concavity**.
 - After an oscillation phase the cornea returns back to its original shape.
 - Before it reaches the initial state it passes through a **second appplanation**, where the cornea is flat again.



Graphic presentation of the air pressure (internal) and the corneal apex signal with detected applanation moments

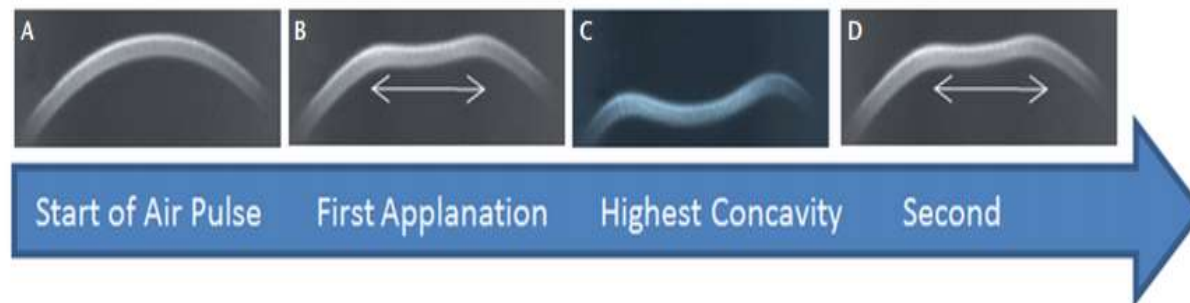
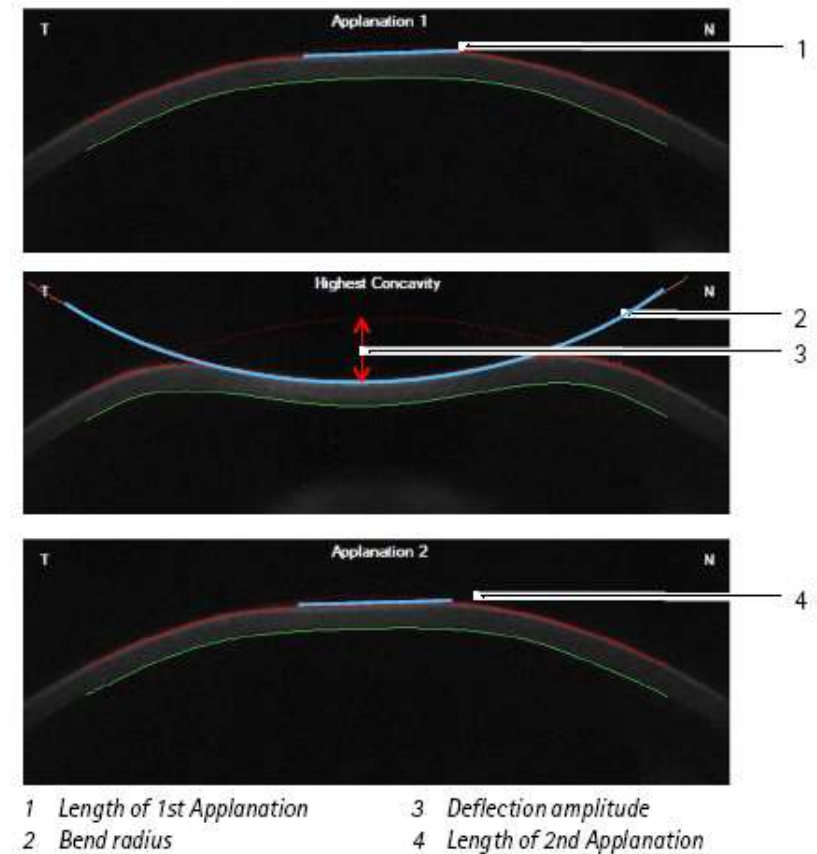



FIGURE 2. Four phases of corneal response to Corvis ST air pulse. In response to the air pulse, the undisturbed cornea (A) goes through 4 main phases of corneal deformation. When the air pulse hits the eye, the cornea goes into the first applanation phase (B), which is the point where the cornea flattens. The Corvis ST will capture the time and length of the flattened cornea. The cornea continues to deform until it reaches its highest concavity of deformation (C). The Corvis ST can measure the maximum deformation amplitude. After this moment, the cornea returns back to its undisturbed state by going through a second applanation (D). Again, the Corvis ST records the time and length of this second applanation like the first one. The double-headed arrows depict the length measurements at the time of applanation.

- During this dynamic corneal response three moments in time are of major interest:
- The ***first applanation***, when the cornea is flat.
- The moment of **highest concavity**.
- The ***second applanation***, when the cornea is flat again before it returns to its original state.



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- The Corvis® ST is able to measure important ***Dynamic Corneal Response parameters*** during the whole process.
 - The complete biomechanical response is described in detail by Cynthia Roberts.

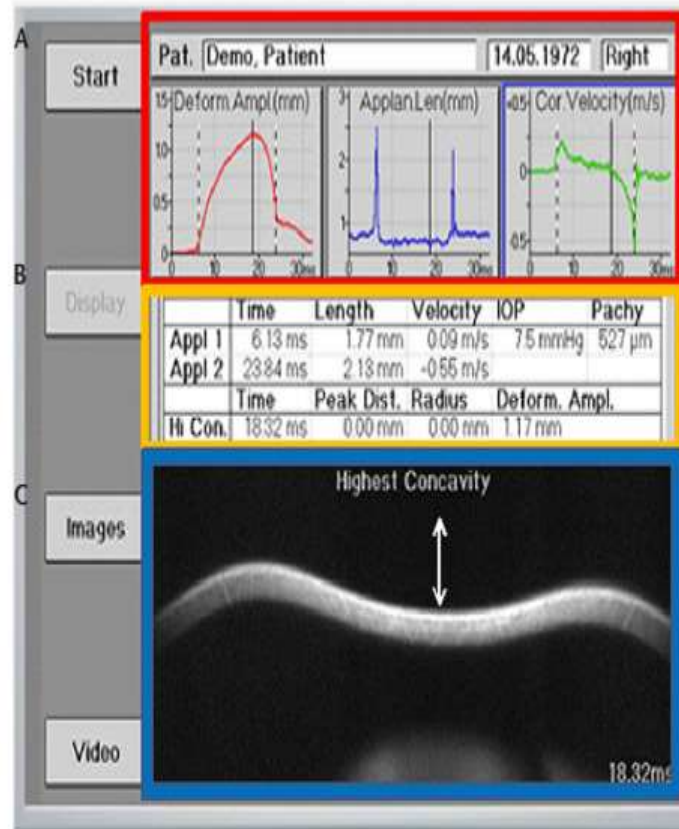


FIGURE 1. Corvis ST sample data collection and device. (A) Plots of the deformation amplitude (red), applanation length (blue), and corneal velocity (green) are shown graphically as functions of time. (B) The instrument calculates the time, length, and velocity at the first and second applanation moments, and the time, peak distance, radius, and deformation amplitude at the highest concavity. (C) Image of the cornea at the highest concavity is shown. The blue box shows where an undisturbed cornea would be expected, and the double-headed arrow depicts how the deformation amplitude is calculated.

Deformation Amplitude

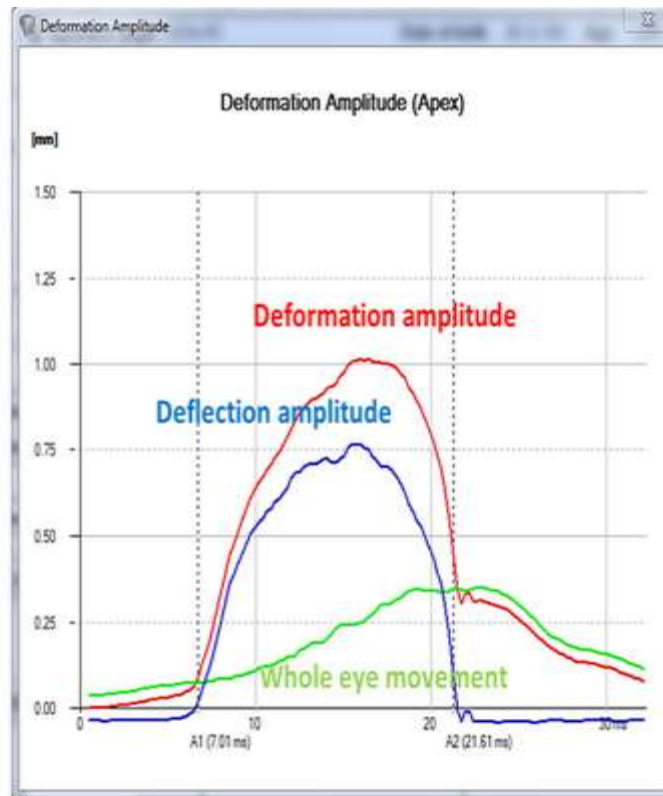
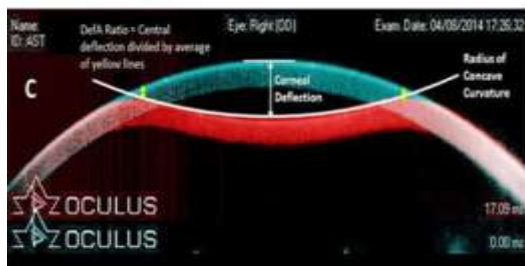
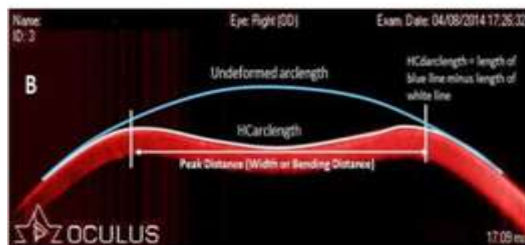
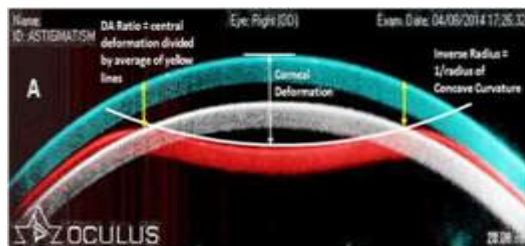
- The **Deformation Amplitude** describes the movement of the apex in vertical direction.
- This movement depends on the overall corneal stiffness and the intraocular pressure as well.
- The **higher** the corneal stiffness, the **smaller** the Deformation Amplitude.

Whole Eye Movement

- The ***Whole Eye Movement*** describes the movement of the whole eye in vertical direction.
- It depends on the biomechanical properties of the ***sclera*** and the fat tissue behind the eye.

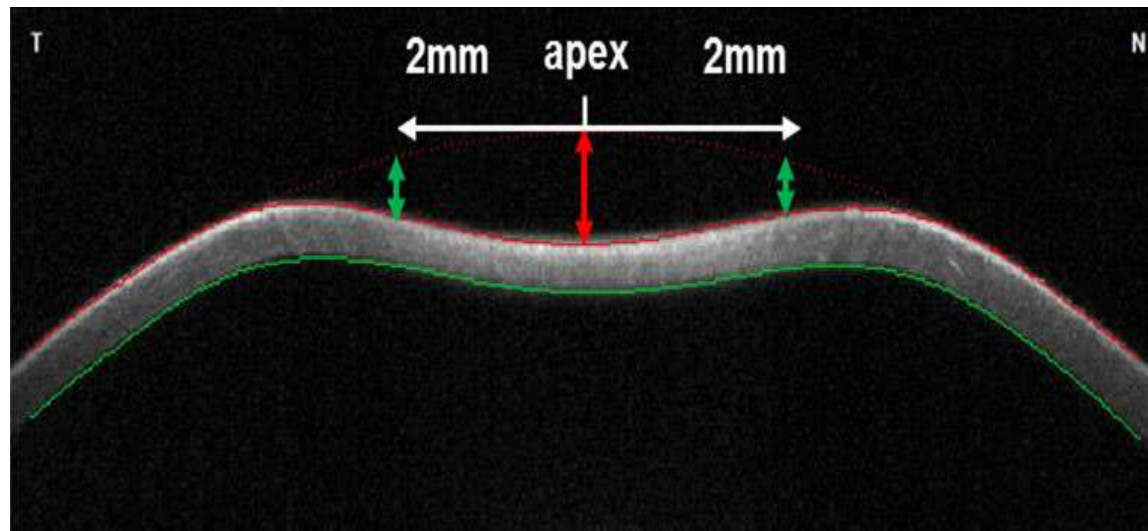
Deflection amplitude


- The ***Deflection amplitude*** describes the movement of the cornea and therefore has a stronger dependency on corneal properties.
- It is calculated as the difference between **Deformation Amplitude** and **Whole Eye Movement**.



DA/ratio 2mm

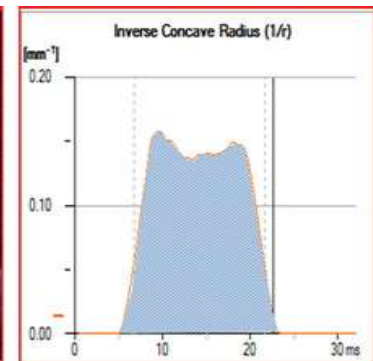
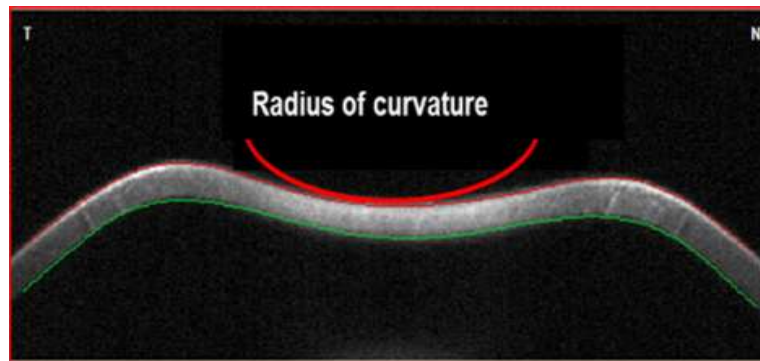
- This parameter is calculated based on the ratio between the Deformation Amplitude (vertical displacement) at the corneal apex and the ***Deformation Amplitude at 2 mm nasal and temporal*** from the apex.
- In case of a softer tissue the cornea starts to ***deform only in the center*** whereas the paracentral part of the cornea deforms much less.




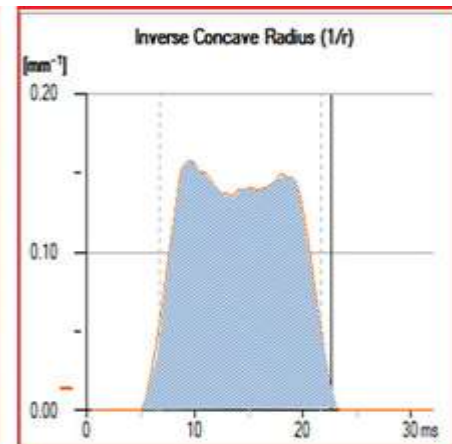
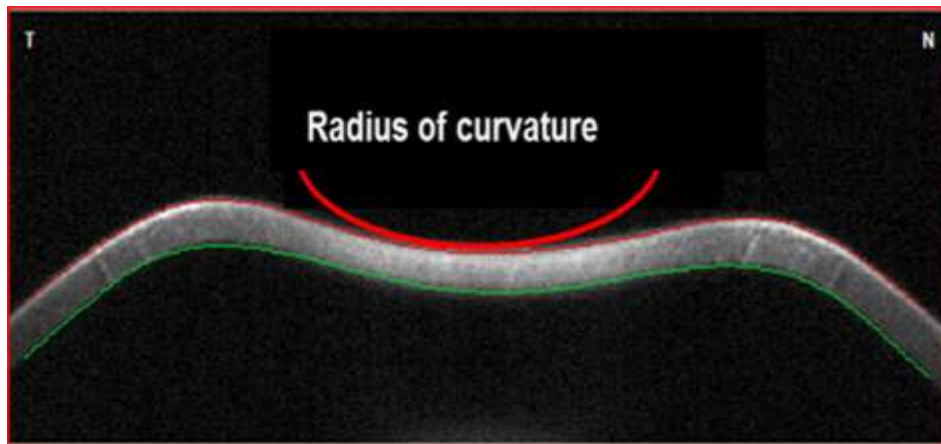
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- Therefore, the DA/ratio is ***higher*** in softer corneas than in stiffer corneas.
 - In stiffer corneas the central and paracentral parts of the cornea are deformed at the same time and the DA/ratio is **relatively small**

Integrated radius

- During the concave phase of the deformation the central Radius of curvature is calculated.
- A softer tissue exhibits a smaller radius as stiffer corneas do.
- The inverse Radius ($1 / R$) is calculated and the area under this inverse Radius vs. time curve is determined.



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- This area is called ***integrated Radius*** and is a very good parameter to quantify the effect of corneal cross-linking.
 - If this parameter gets smaller it indicates a stiffening of the cornea.



Biomechanical corrected IOP(BIOP)

- Applanation tonometry and non-contact tonometry are both based on a simple principle:
- Applying a ***mechanical force*** on the cornea and correlation of the force that is needed to flatten the cornea with the intraocular pressure (IOP).

Biomechanical corrected IOP(BIOP)

- The measured IOP values are influenced by the **corneal thickness and the corneal elasticity** – and therefore by **corneal stiffness**.
- ***Corneal stiffness*** is strongly changed for example in case of keratoconus but also after corneal refractive surgery.

Biomechanical corrected IOP(BIOP)

- Moreover, **age** is known to influence the elastic biomechanical properties.
- These changes of **biomechanical properties** can lead to a larger over- or underestimation of the IOP and therefore lead to a wrong management of glaucoma.

Biomechanical corrected IOP(BIOP)

- The equation was derived based on so-called **finite element simulations**.
- In numerical simulations the influence of **corneal stiffness, corneal thickness, curvature** and the **biomechanical properties** on **IOP measurements** was analysed systematically.

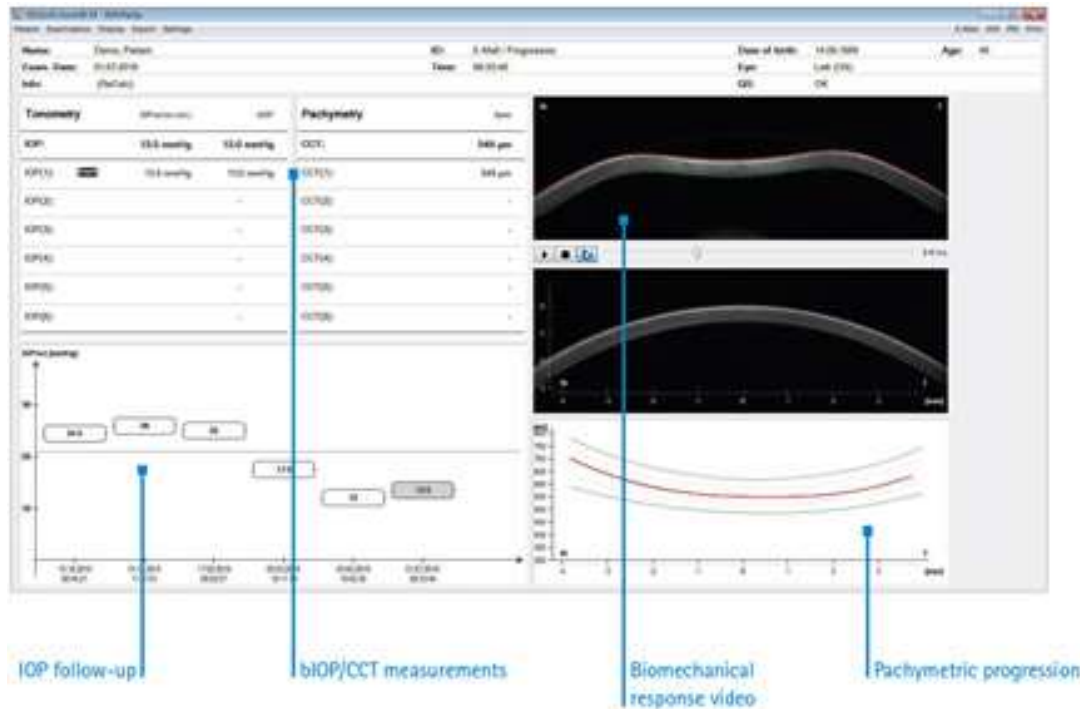
Biomechanical corrected IOP(BIOP)

- The **biomechanical corrected IOP (bIOP)** is based on **corneal thickness**, **age** and the **biomechanical response** of the cornea. Due to the measurement principle, the IOP measurements are not influenced by tear film.
- This enables an accurate IOP estimation even in case of altered biomechanical properties.


Biomechanical corrected IOP(bIOP)

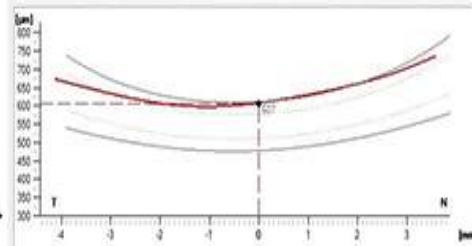
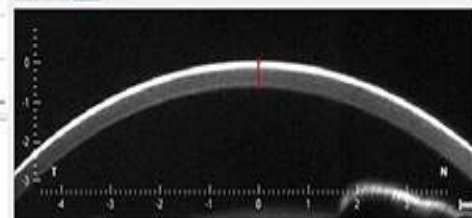
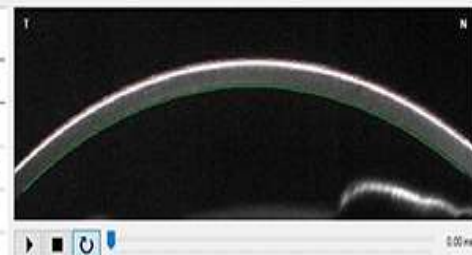
- Based on these results an equation was developed that compensates for these ***influencing factors***.
- Experimental and clinical studies have proven the accuracy of the bIOP.
- Especially after refractive surgery the ***bIOP*** is much more accurate than ***conventional*** methods for IOP measurement.

Biomechanical corrected IOP(BIOP)



1.6175

Tonometry			Pachymetry	
	IO (Pre-pro con.)	IOF		Apex
IOP:	15.0 mmHg	12.5 mmHg	CCT:	608 µm
IOP(1):	 15.0 mmHg	12.5 mmHg	CCT(1):	608 µm
IOP(2):	-	-	CCT(2):	-
IOP(3):	-	-	CCT(3):	-
IOP(4):	-	-	CCT(4):	-
IOP(5):	-	-	CCT(5):	-
IOP(6):	-	-	CCT(6):	-



“Dynamic Corneal Response” (DCR) Screen



1 Scheimpflug images

2 Scheimpflug images/video

3 Buttons for video function

4 Buttons for deformation displays

Fig. 4-7: “Dynamic Corneal Response” screen

5 Table

6 Diagrams

7 Patient and examination data

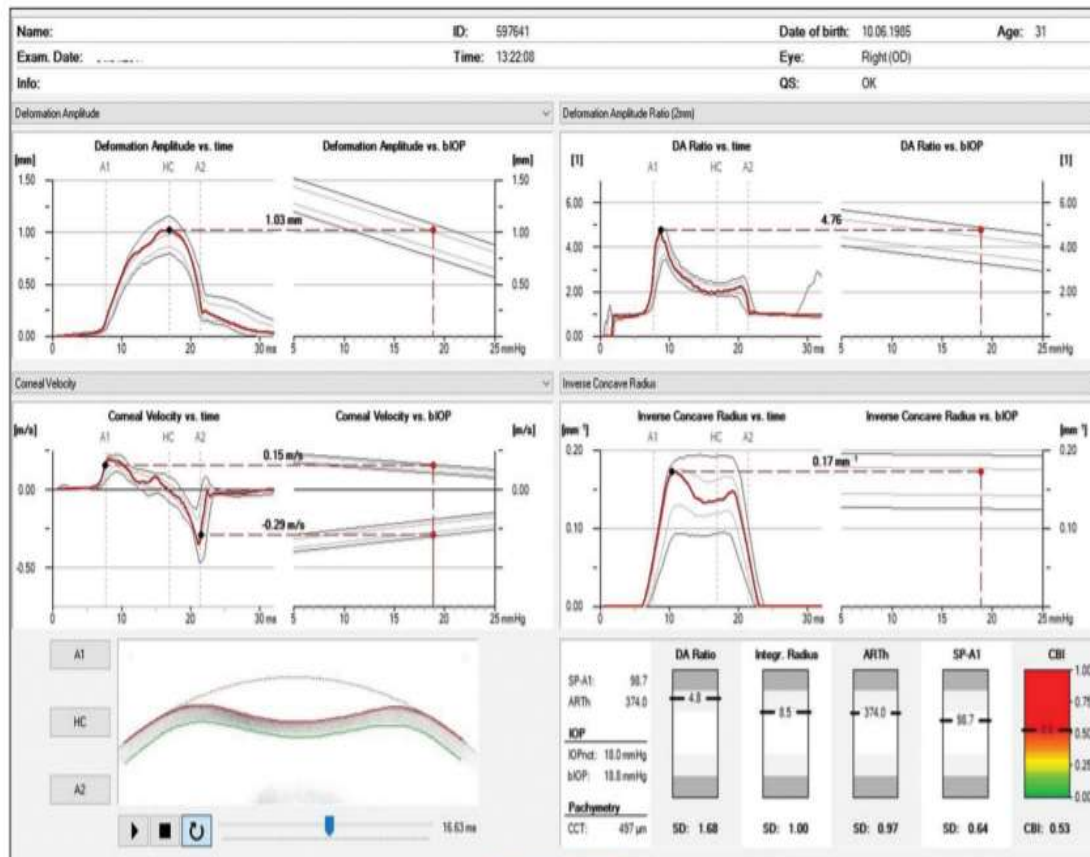



Figure 2: Corvis ST corneal biomechanical index display

Biomechanical Glaucoma Factor (BGF): Screening for normal tension glaucoma

- Given that intraocular pressure (IOP) is a well-recognized risk factor for glaucomatous disease,
- ***low-tension glaucoma or normal-tension glaucoma (NTG)*** may be more difficult to diagnose relative to circumstances when a patient has above average IOP

- The clinician must pay careful attention to ***structural and functional*** optic nerve parameters in the diagnosis of NTG, which can easily be missed if IOP measurement is used as a glaucoma screening tool.
- Previously described ***risk factors*** for NTG include older age, female sex, Japanese and Korean ancestry, migraine headache, sleep apnea, hypotension, anemia, and Raynaud's disease.
- In Europe up to 30 percent of primary open angle glaucoma patients have a normal intraocular pressure, in Asia the incidence of NTG is even higher

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- Patterns in 24-hour diurnal measurements of IOP and ocular perfusion pressure have been postulated to help exclude false diagnoses of NTG, but they are not practical alternatives for NTG screening, particularly given the relatively higher costs associated with such methods compared with serial IOP measurement.
 - Thus, there is interest in identifying other ***pressure-independent biomarkers*** to aid in early diagnosis of NTG.

- Over the past decade, advances in corneal biomechanical assessment of the eye using the ***Ocular Response Analyzer*** (ORA; Reichert, Depew, NY, US) have provided clinical insight regarding the complex relationship between IOP and NTG.
- The ORA tests corneal stiffness by calculating measurements: ***corneal hysteresis (CH)*** and ***corneal resistance factor (CRF)***.

Biomechanical Glaucoma Factor (BGF)

- The DBGF (Dresden biomechanical glaucoma factor) was calculated using **5 Corvis ST parameters**, which showed the best discrimination power:
 - Deformation amplitude ratio progression,
 - Highest concavity time,
 - Pachymetry slope,
 - **Biomechanically corrected intraocular pressure** and
 - **Pachymetry.**

- With stepwise logistic regression analysis using a GEE (generalized estimating equation), a combination of **5 Corvis ST parameters** was found to best fit in an equation to calculate the DBGF.
- The DBGF with a ***cut-off value of 0.5*** discriminated well between normal eyes and eyes with NPG and correctly classified about 76% of the cases.

A new biomechanical glaucoma factor to discriminate normal eyes from normal pressure glaucoma eyes

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ABSTRACT.

Background: To test the ability of the newly calculated Dresden biomechanical glaucoma factor (DBGF) based on dynamic corneal response (DCR) deformation and corneal thickness parameters, to discriminate between healthy and normal pressure glaucoma (NPG) eyes.

Methods: Seventy healthy and 70 NPG patients of Caucasian origin were recruited for this multicentre cross-sectional pilot study, which included both eyes for analysis. Logistic regression analysis with generalized estimating equation (GEE) models to account for correlations between eyes and a threefold cross-validation were performed to determine the optimal combination of Corvis ST parameters in order to separate normal from NPG eyes.

Results: The DBGF was calculated using 5 Corvis ST parameters, which showed the best discrimination power: deformation amplitude ratio progression, highest concavity time, pachymetry slope, the biomechanically corrected intraocular pressure and pachymetry. In a threefold cross-validation, the receiver operating characteristic (ROC) curve confirmed an area under the curve (AUC) of 0.814 with a sensitivity of 76% and a specificity of 77% using a logit cut-off value of a DBGF = 0.5.

Conclusion: The DBGF shows to be sensitive and specific to discriminate healthy from NPG eyes. Since diagnosis of NPG is often challenging, the DBGF may help with the differential diagnosis of NPG in daily clinical practice. Therefore, it might be considered as a new possible screening method for NPG.

does often not occur until late stages. However, as the disease may cause irreversible damage, it is of utmost importance to diagnose it at an early stage.

Several studies have shown glaucoma to be associated with extracellular matrix remodelling that increases the stiffness of the sclera, lamina cribrosa and cornea (Sigal et al. 2005; Lopes et al. 2017; Liu et al. 2018). This influences the biomechanical stress in the optic nerve head caused by IOP fluctuation and elevation (Sigal et al. 2014). There might be also a genetic connection between stiffness in glaucoma and the vascular system (Borras 2017).

Currently, there are two instrumen-

- **Normal eyes** had a DBGF lower than 0.5, where as **NPG** eyes had a DBGF higher than 0.5.
- This finding supports the idea that NPG eyes **behave biomechanically** different compared to controls and that the DBGF has the ability to discriminate between these two groups

Biomechanical Glaucoma Factor (BGF)

- It has been shown recently that biomechanical properties can serve as an ***independent risk factor*** for NTG as the corneas of NTG patients are more deformable than age-matched healthy controls.
- This was the basis for the development of the Biomechanical Glaucoma Factor (BGF).
- The BGF is an independent risk factor for normal tension glaucoma and can be used to screen for NTG patients.

Exam Date: 07.09.2021

Time: 09:41:33

Eye: Right (OD)

QS: OK

Info:

Tonometry IOPnd (no cor.) bIOP

IOP: 18.0 mmHg 16.3 mmHg

IOP(1): 19.0 mmHg 17.2 mmHg

IOP(2): 17.0 mmHg 15.4 mmHg

IOP(3): -

IOP(4): -

IOP(5): -

IOP(6): -

Pachymetry

Apex

CCT: 583 μ m

CCT(1): 583 μ m

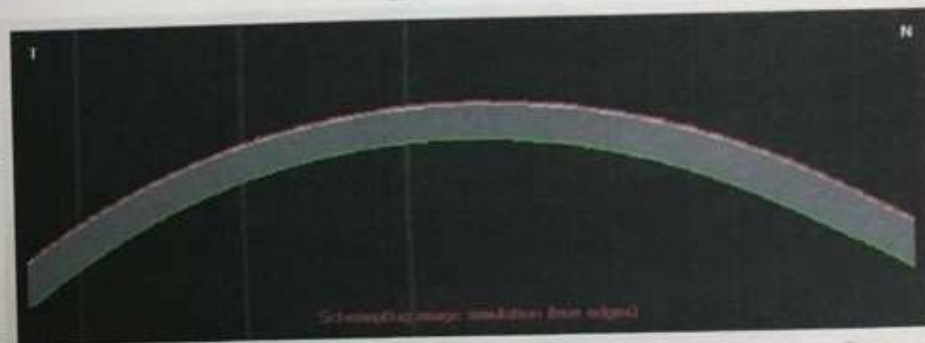
CCT(2): 582 μ m

CCT(3): -

CCT(4): -

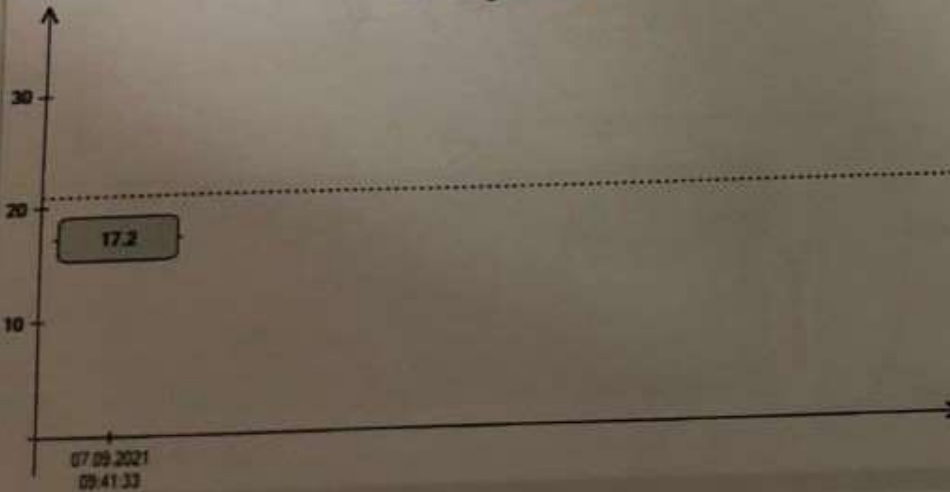
CCT(5): -

CCT(6): -

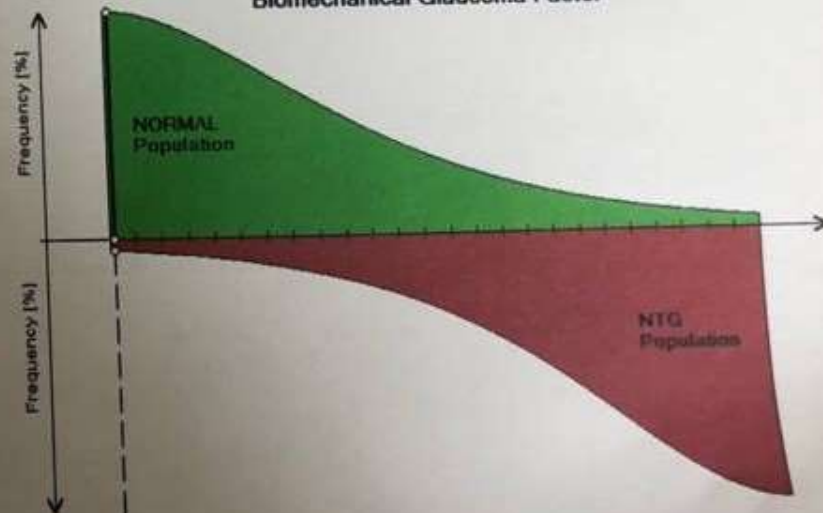


32.11 ms

bIOP (mmHg) IOP Progression



Biomechanical Glaucoma Factor



BGF

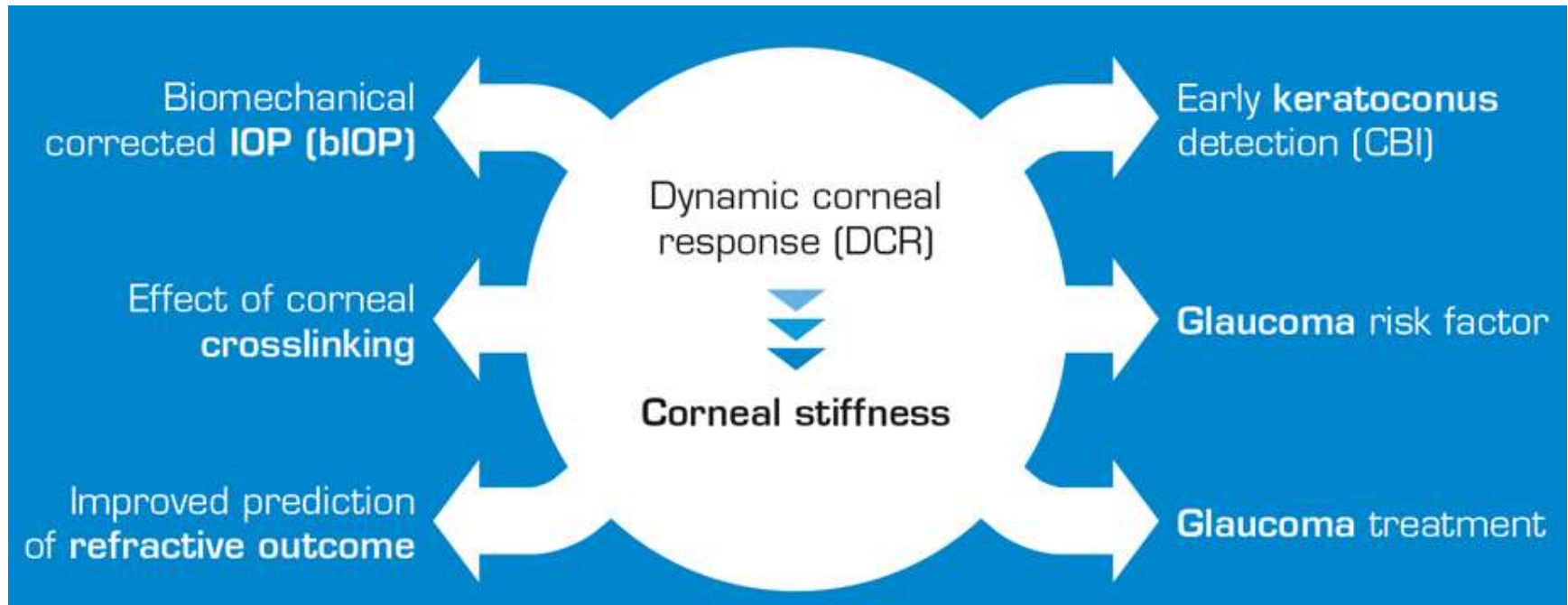
0.25


0.50

0.75

1.00

Oculus Corvis ST



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- NCT approved by the United States F.D.A. for tonometry and pachymetry, biomechanical assessment of the cornea.