Basics of Clinical Assessment of Biomechanical Response

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17th International Conference of the Research Institute of Ophthalmology
Anterior Segment Eye Diseases: Current Status & Future Directions
Royal Maxim Palace Kempinski, Cairo Egypt
January 31, 2025

Biomedical Engineering

Medical Center

Disclosures

- Consultant to Ziemer Ophthalmic Systems AG
- Consultant to Oculus Optikgeräte GmbH

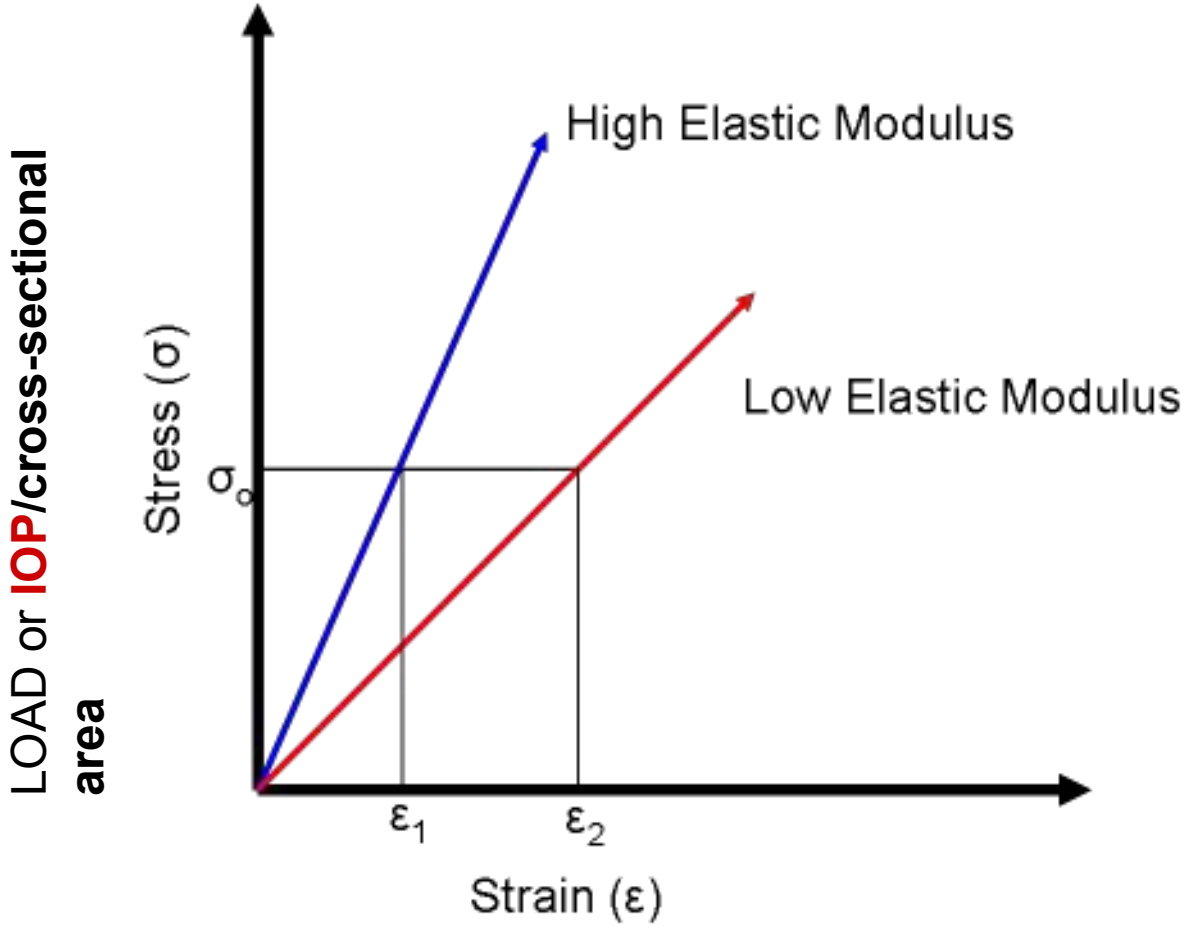
Acknowledgements

- Funded in part by Research to Prevent Blindness New Chair Challenge Grant

Basic Biomechanical Concepts

- The globe is a fluid-filled, pressurized vessel.
- The response of the ocular shell to internal pressure (IOP) depends on biomechanical properties of the shell.
- Assessment of Biomechanical Response requires an applied load or a perturbation, such as an ultrasound wave or an air puff…..

Stress and Strain: linear example



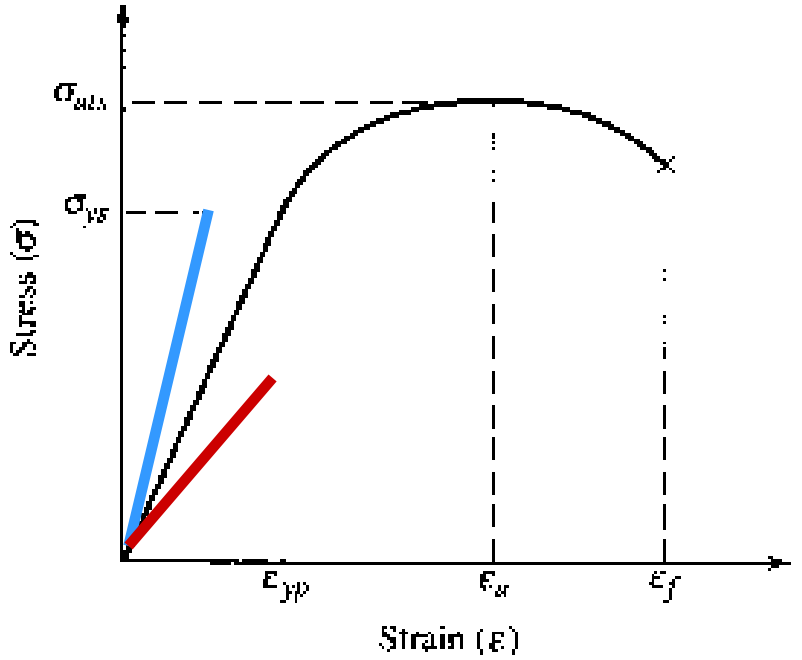
Slope of the line
= elastic modulus

(tens

Elasticity = Stress/Strain

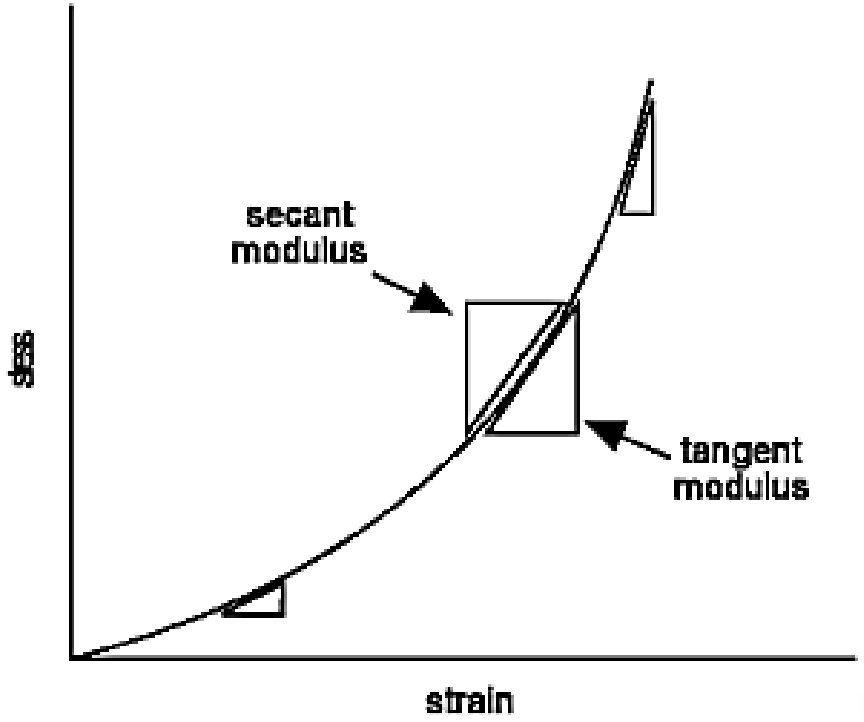
- Elasticity is the slope of the linear region.
- Loading and unloading follows the same line
- The elastic constant is called Young's Modulus (E)

High elastic modulus means the specimen stretches less.



Non-Linear Elasticity

- Biological tissues, including the cornea, exhibit nonlinear stress-strain relationships.
- This makes determining Young's modulus more complicated.
- IOP determines response!



The Cornea

- The thinner the cornea, the greater the stress for the same load
- The lower the elastic modulus (red), the greater the deformation under the same stress.

Mechanical Properties

Elasticity

"the capability of a strained body to recover its size and shape after deformation"

(Merriam-Webster Online Dictionary)

Viscosity

"the resistance of material to flow or permanent deformation"

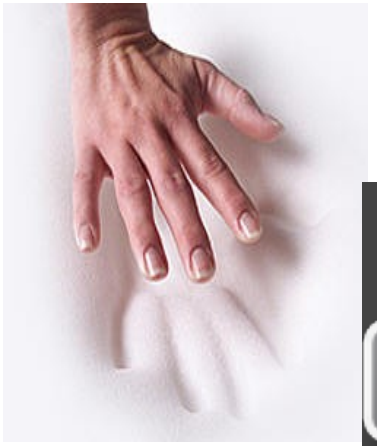
(Merriam-Webster Online Dictionary)

TIME-DEPENDENT COMPONENT!

Viscoelasticity

the presence of both viscosity and elasticity in the same material

TIME-DEPENDENT COMPONENT!



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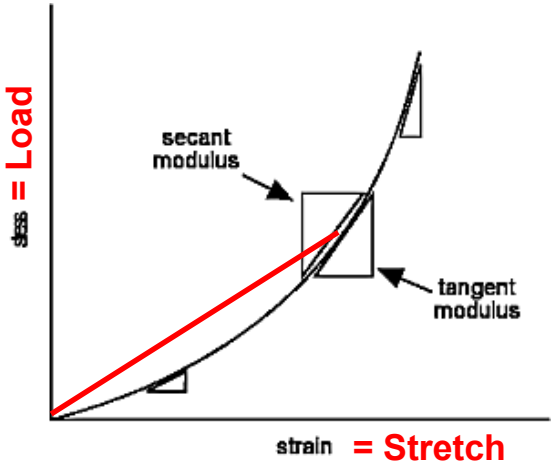
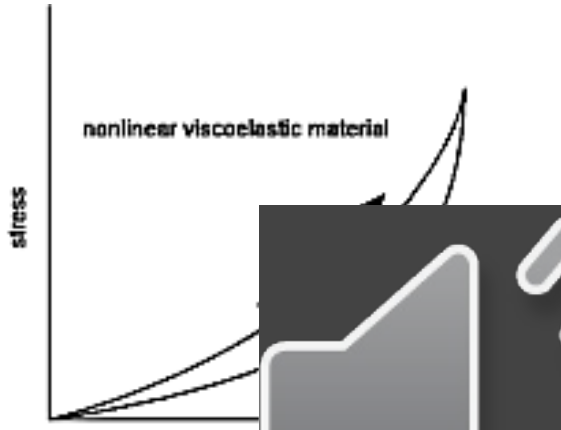
What do we know about the Cornea?

- It is NONLINEARLY elastic (hyperelastic)
  - As the IOP increases, the cornea exhibits stiffer behavior
- It is VISCOELASTIC
- Loading and Unloading have different paths, indicating energy dissipation.





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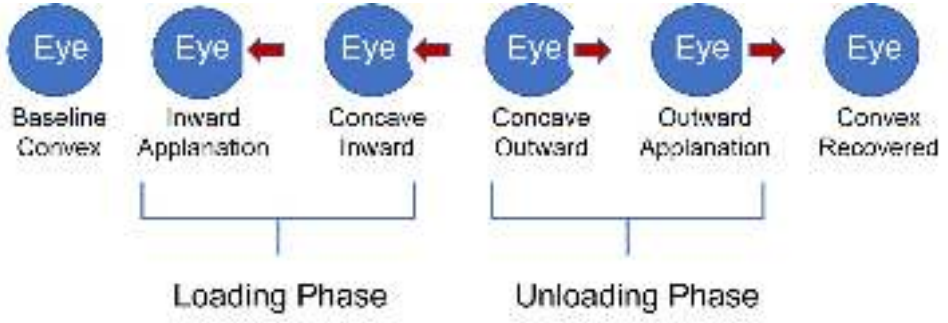
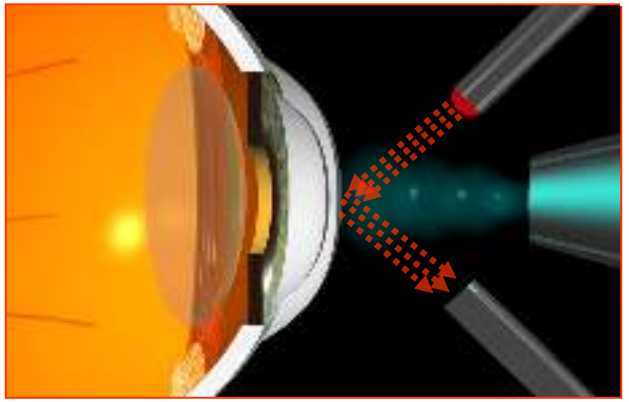
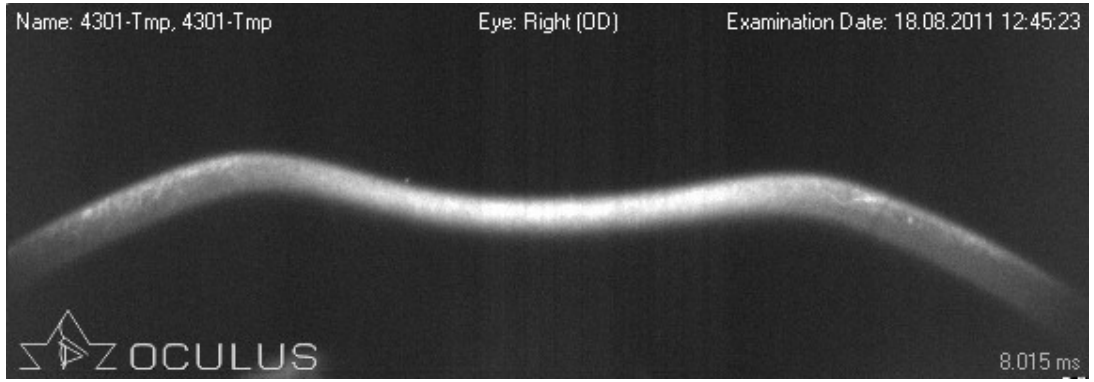
Ocular Response Analyzer



Corvis ST





Electro-optical system to detect applanation where a "mirror-like" reflection occurs
(~20 ms airpuff)
Horizontal meridian assessed
Air puffs equivalent until first applanation, then deviate based on IOP
CUSTOMIZED air puff profile for each patient
Standard parameters: **Viscoelastic**

Ultra High-Speed (UHS) Scheimpflug camera
- 4,330 frames per second
- ~140 images over a 30ms
- (~20 ms airpuff)

8mm horizontal coverage
Constant metered collimated air pu
SAME air puff profile for ALL pati
Standard Parameters: **Elastic**

Oculus CorVis ST

Oculus CorVis ST

Ultra High-Speed (UHS) Scheimpflug camera

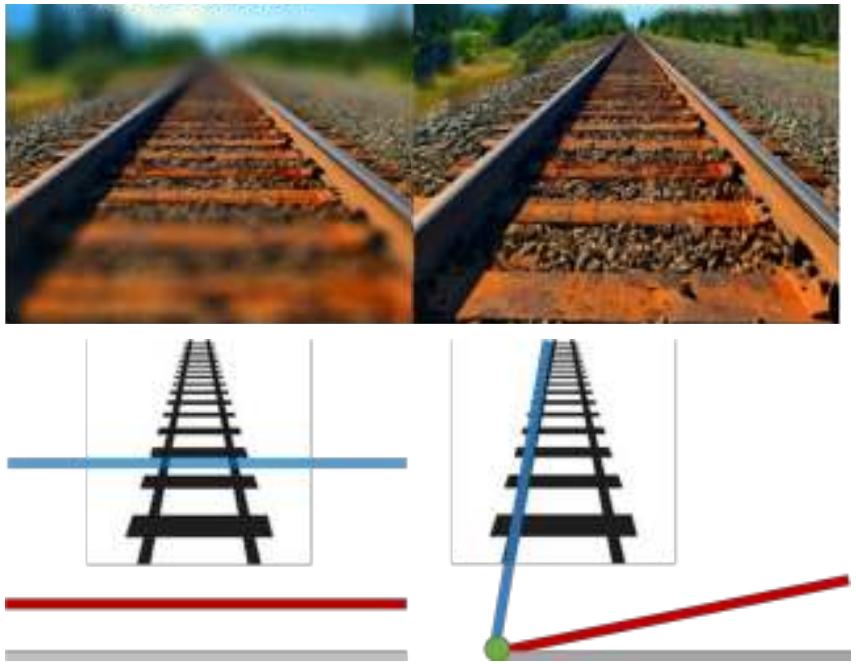
- 4,330 frames per second

8mm horizontal coverage

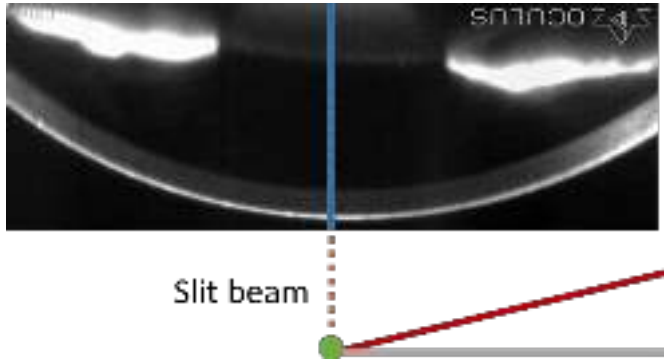
Constant metered collimated air pulse

Currently FDA approved for tonometry and pachymetry only

Scheimpflug Imaging



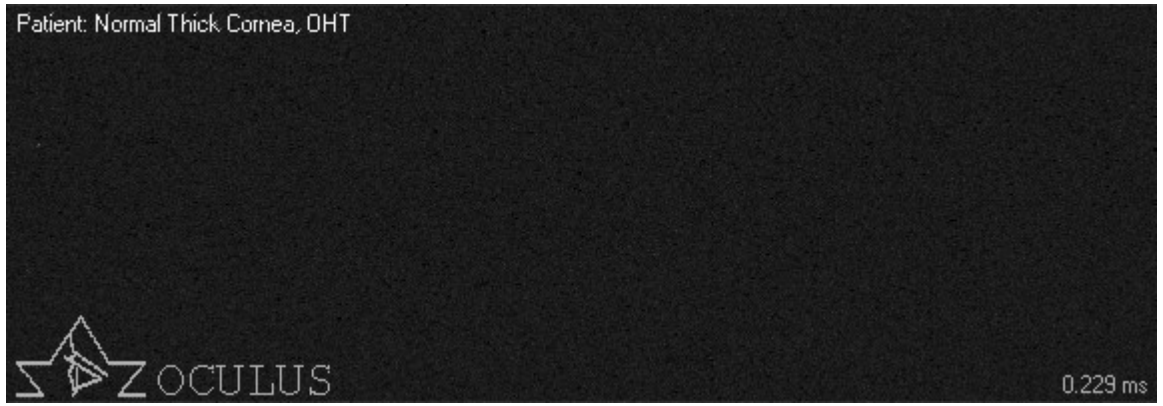
Object Plane – Blue
Lens Plane – Red
Image Plane – Gray
Scheimpflug intersection - Green



Anterior Segment of the Eye

Malmqvist E, Brydegaard M, Aldén M, Bood J. Scheimpflug lidar for combustion diagnostics. *Opt Express*. 2018;26(12):14842-14858.

Normal Thick Cornea



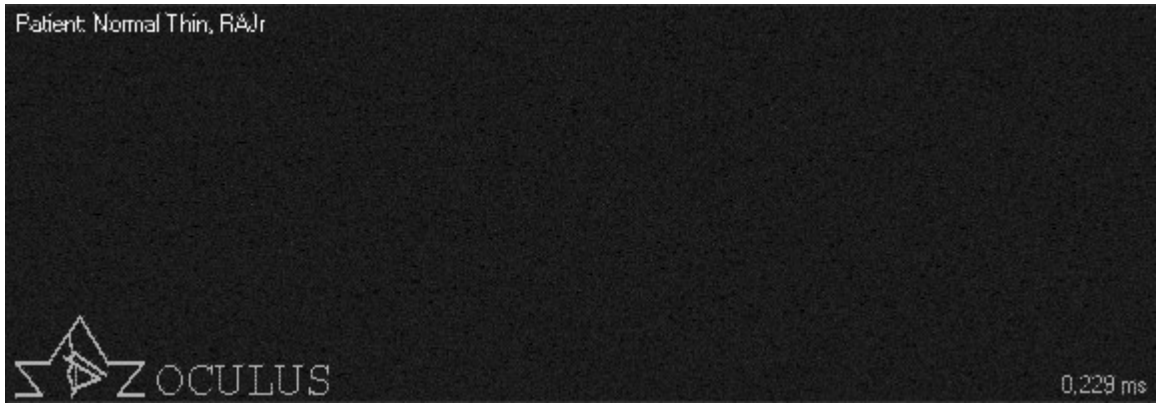
Data provided by Renato Ambrosio, MD, PhD

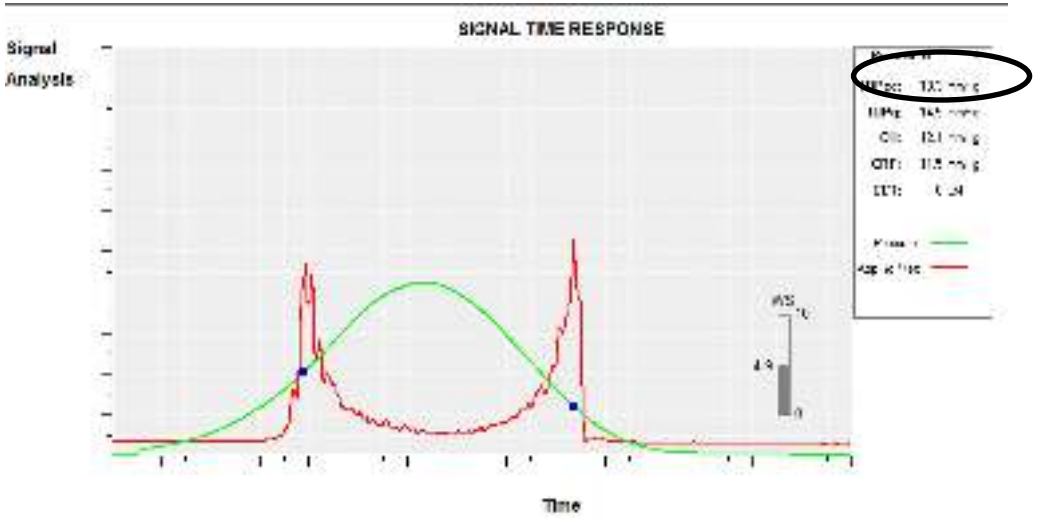
What Influences Deformation?

- **Intraocular Pressure!**
- **Corneal Biomechanical Properties**
- Corneal Thickness
- Corneal Curvature

Roberts, et al. ARVO 2011, Kling and Marcos, IOVS, 2013

Normal Thin Cornea

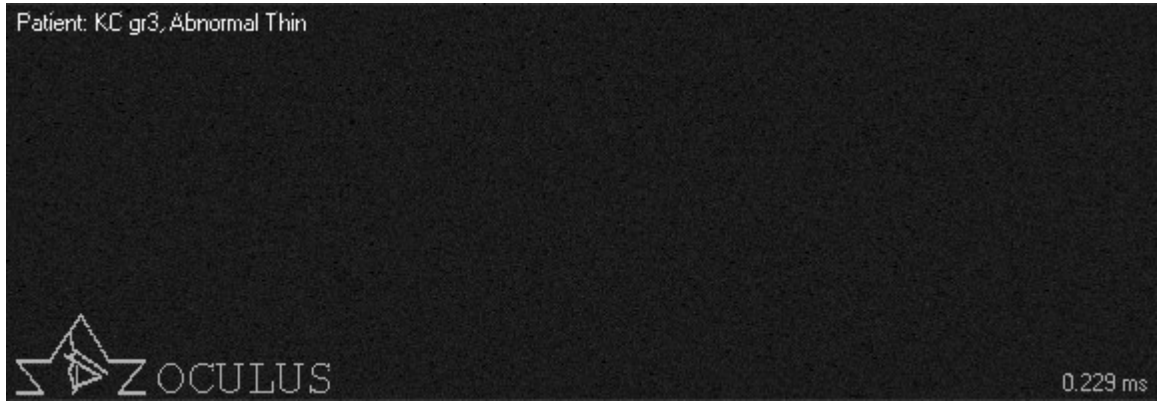


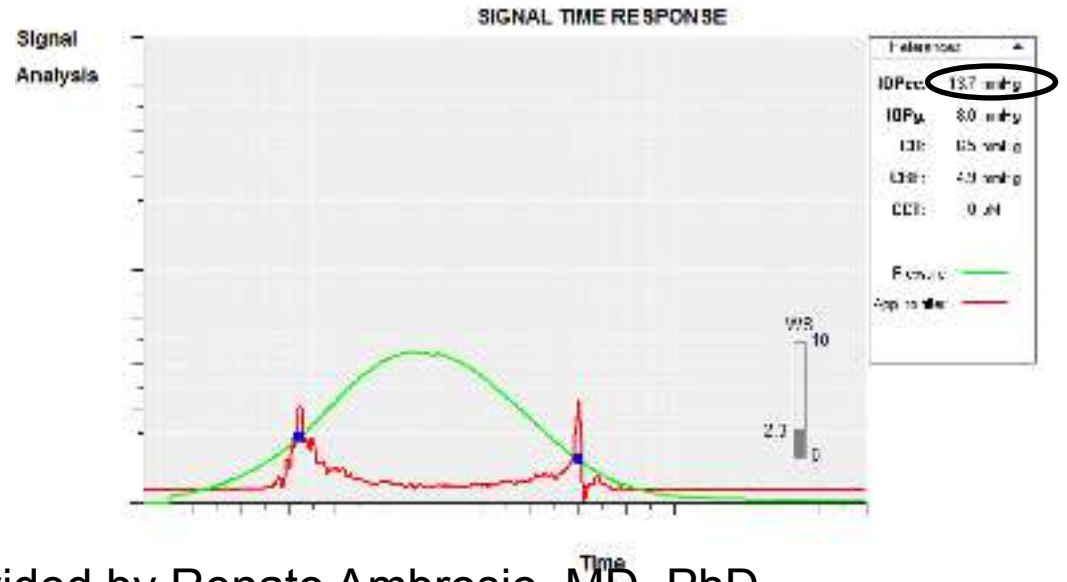


IOPcc = 13.3mmHg

Data provided by Renato Ambrosio, MD, PhD

Keratoconus





IOPcc = 13.7mmHg

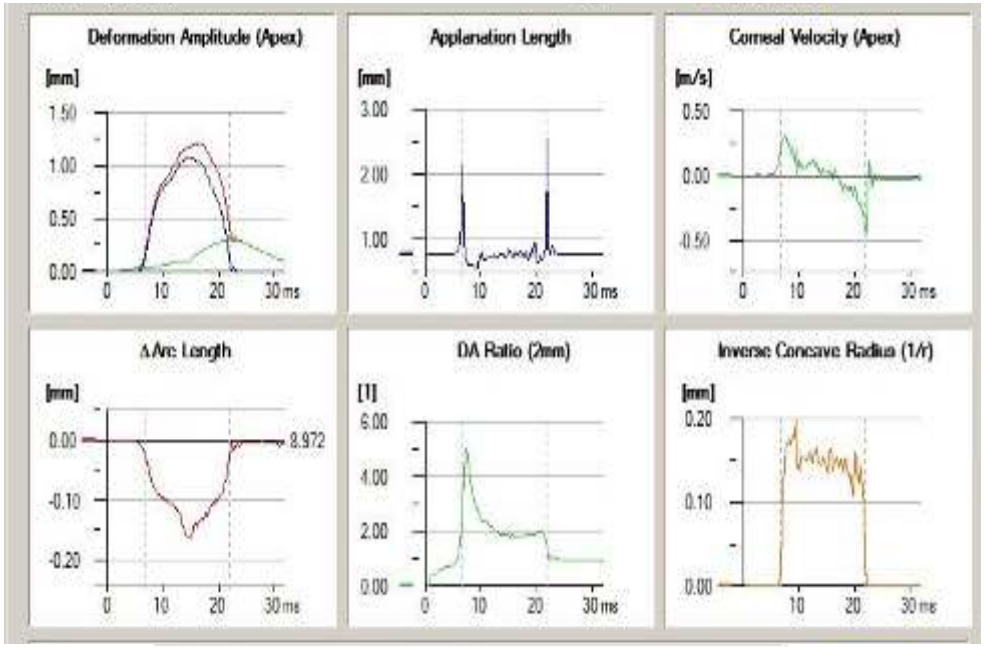
Data provided by Renato Ambrosio, MD, PhD

Comparison of KCN to Normal Thin – Similar thickness and IOP

Video Processing done by Ashraf Mahmoud

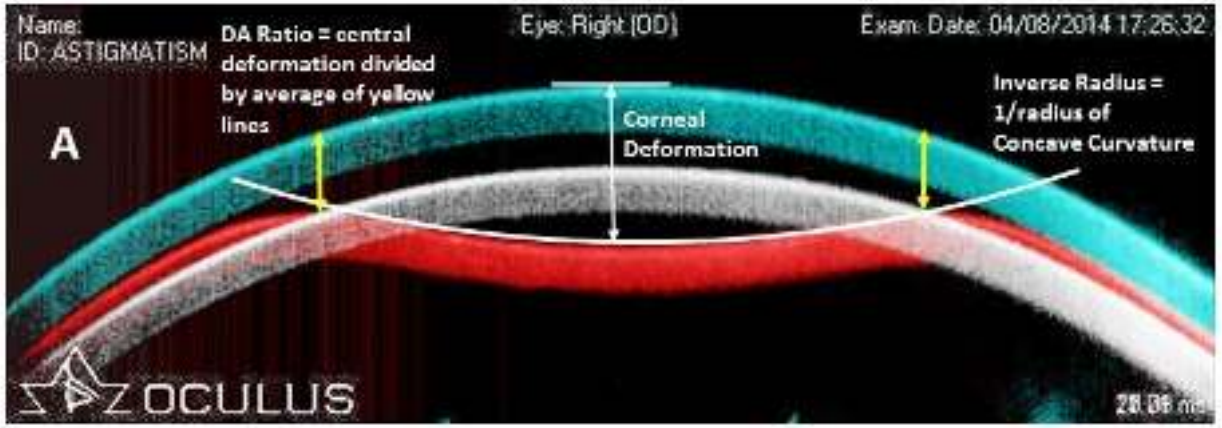
Corvis ST Deformation Parameter Classes

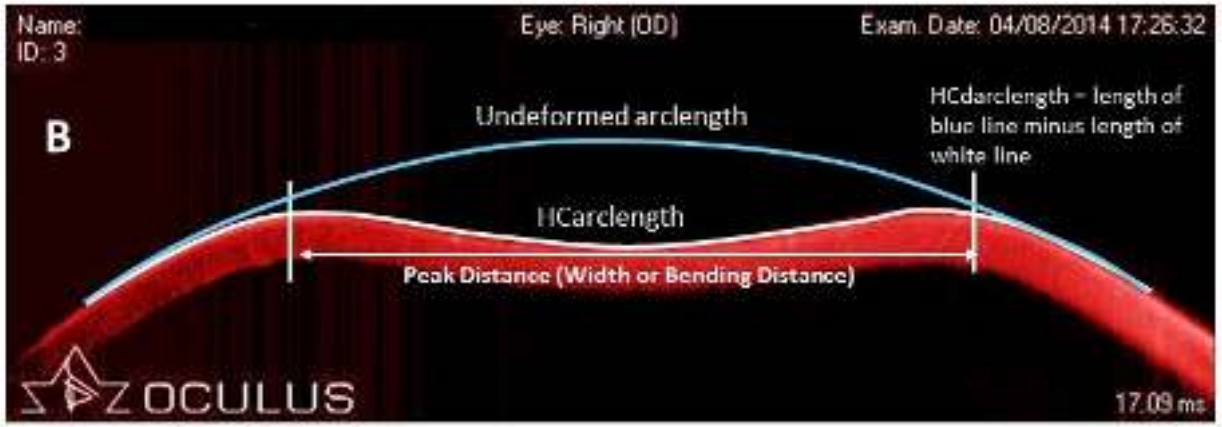
- Events: A1, Highest Concavity (HC), A2, Maximum WEM
- Amplitude of displacement
- Timing of events
- Anterior corneal velocity
- Shape of the cornea
  - HC Radius
  - DA Ratio (1mm or 2mm)
  - Integrated Inverse Radius (IIR)

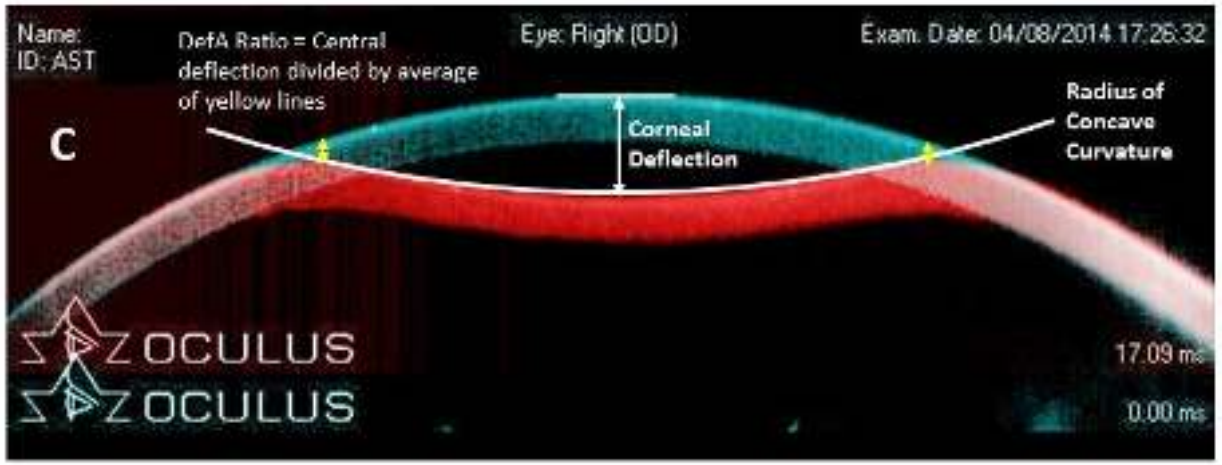


Vinciguerra R, Elsheikh A, Roberts CJ, Ambrósio Jr, Kang DS, Lopes BT, Morenghi E, Azzolini C, Vinciguerra P. The Influence of Pachymetry and Intraocular Pressure on Dynamic Corneal Response Parameters in Healthy Patients. *J Refract Surg* 2016; 32:550-561.

Distance of Apex from Nozzle







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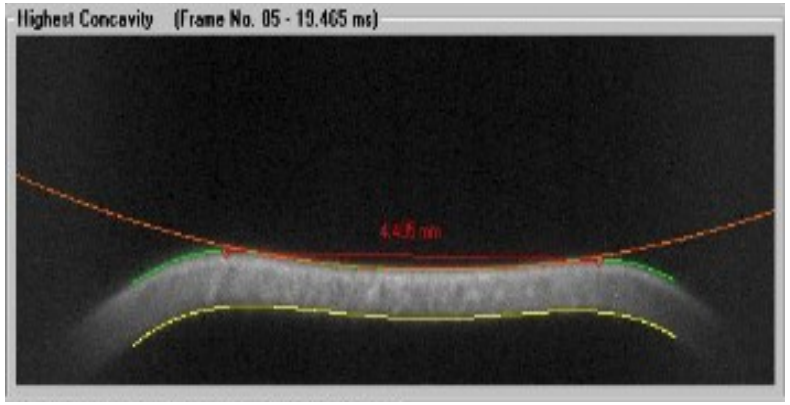
Biomechanical Deformation Parameters

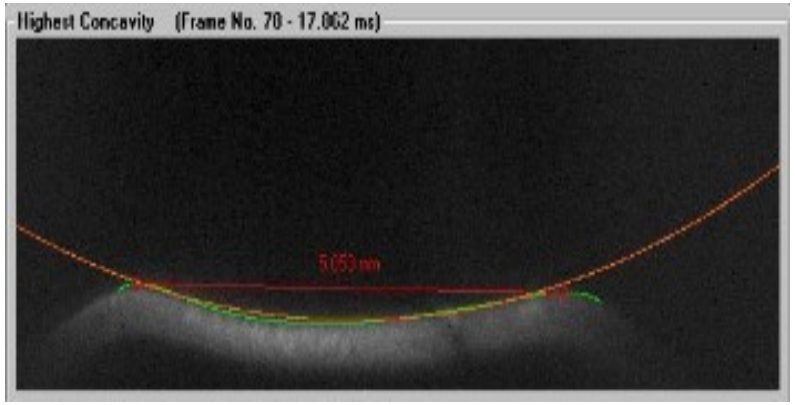
- Parameters associated with shape are relatively independent from IOP.
  - Concave radius, Inverse Radius, Ratios
- Parameters associated with depth have greater dependence on IOP.
  - Deformation amplitude, velocity, timing,

Vinciguerra R, Elsheikh A, Morenghi E, Roberts CJ, Ambrósio JR, Trazza S, Azzolini C, Vinciguerra P. The Influence of Pachymetry and Intraocular Pressure on Dynamic Corneal Response Parameters in Healthy Patients. *J Refract Surg* 2016; 32:550-561.

IOP vs Properties

- Amplitude, timing and velocity more sensitive to IOP
- Shape of corneal deformation more sensitive to properties





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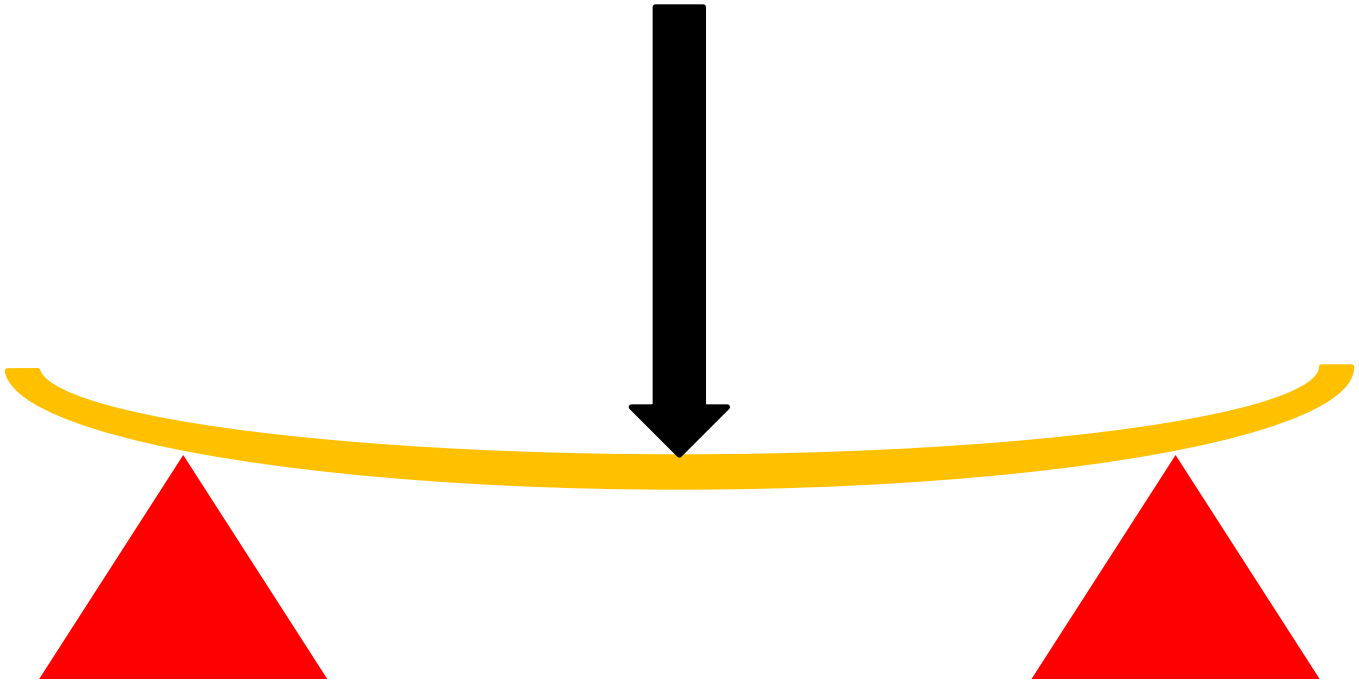
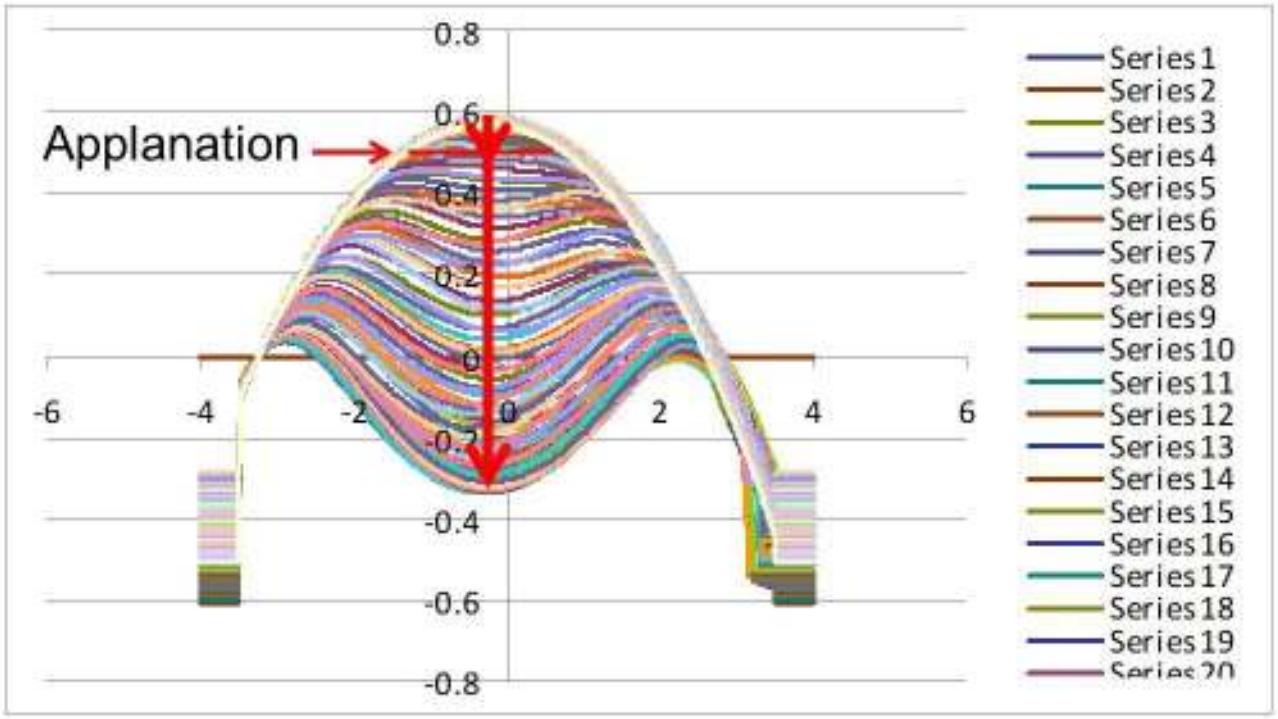
How can we determine Stiffness?

3-Point Loading

Stiffness = Load/Displacement



Stiffness Parameters: Load/Displacement



Extracted Anterior Corneal Edges

Applanation is reference since IOP is determined at this location

Displacement can be measured from:

apex to applanation (**SP-A1**)

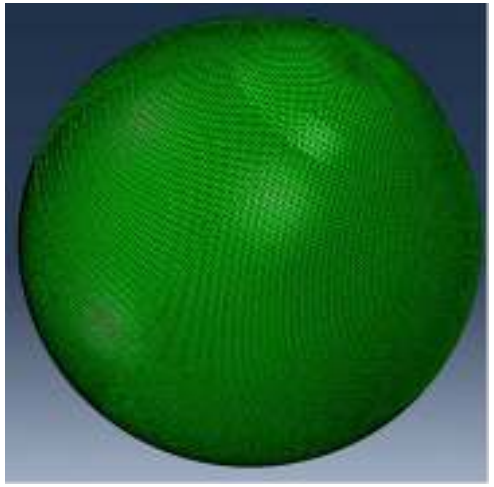
OR

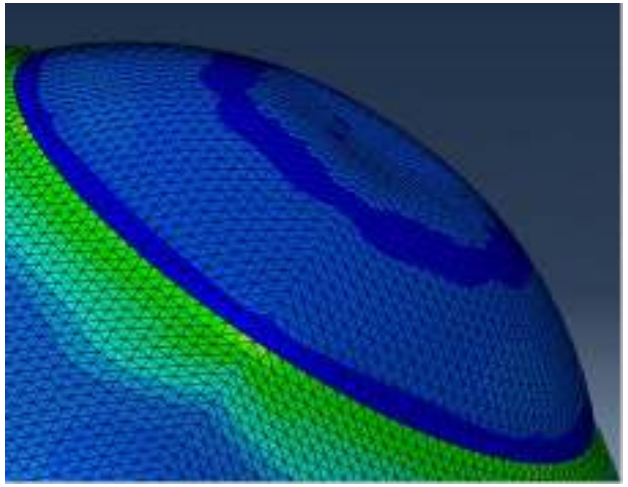
applanation to highest concavity (**SP-HC**)

Roberts CJ, Mahmoud AM, Bons JP, Hossain A, Elsheikh A, Vinciguerra R, Vinciguerra P, Ambrósio Jr R. Introduction of Two Novel Stiffness Parameters and Interpretation of Air Puff Induced Biomechanical Deformation Parameters with a Dynamic Scheimpflug Analyzer. *J Refract Surg* 2017;33(4):266-273.

Biomechanically Corrected IOP* (bIOP) on Corvis ST

- Based on Finite Element Modeling





Shown to have no significant difference before and after refractive Surgery in multiple studies.

Lee H, Roberts C, Ambrosio R, Elsheikh A, Kang DSY, Kim T-I; *J Cataract Refract Surg* 2017; 43:937-945.

- Introduced at the 2016 ESCRS

*Joda AA, Shervin MMS, Kook D, Elsheikh A. Development and validation of a correction equation for Corvis tonometry. *Computer Methods in Biomechanics and Biomedical Engineering* 2015;1-11.

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Interpretation

- SP-A1 and SP-HC
  - Higher value indicates stiffer response
  - Less displacement (denominator) for same load (numerator), so greater resistance to deformation
- DA Ratio and Integrated Inverse Radius
  - Lower value indicates stiffer response
  - Greater resistant to deformation and shape change

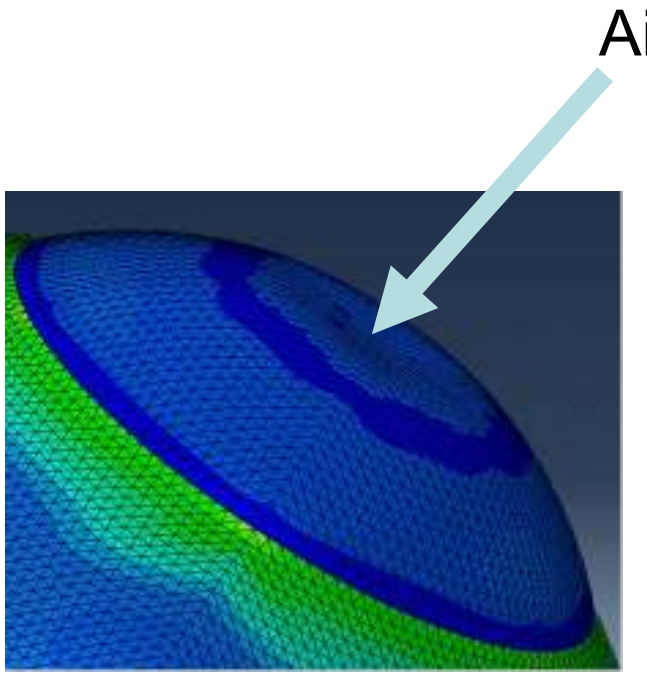
Corvis Biomechanical Index (CBI)

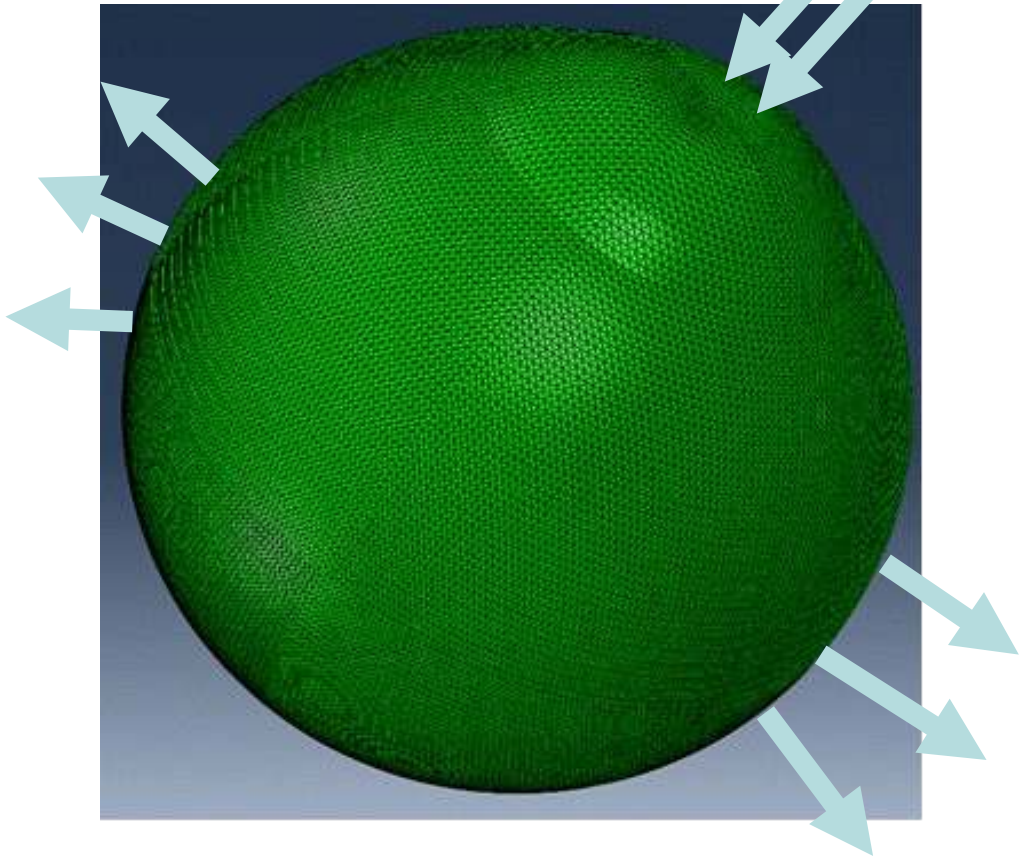
- 658 Subjects from Italy and Brazil
  - Normal
  - Keratconus
- Logistic Regression to determine optimal combination of parameters
  - One dataset for training: 98.2% classified correctly
  - One for validation: 98.8% correctly classified
- FOR DETECTION ONLY, NOT SEVERITY

Vinciguerra R; Ambrósio Jr R, Elsheikh A; Roberts CJ, Lopes B, Morenghi E, Azzolini C, Paolo Vinciguerra P. Detection of Keratoconus with a new Biomechanical Index. *J Refract Surg* 2016; 32:803-10.

Macro-Deformation with an Air Puff: Is only the Cornea Involved in Response?

Air Puff Applied to the Cornea





What about displaced aqueous when cornea is concave?

Images from: *Joda AA, Shervin MMS, Kook D, Elsheikh A. Development and validation of a correction equation for Corvis tonometry. *Computer Methods in Biomechanics and Biomedical Engineering* 2015;1-11.

IOP vs Stiffness and the Influence of Boundary Conditions (Is the Sclera Involved?)

- Paired Human Donor Corneas
  - One cornea mounted as a whole globe
  - Corneal-scleral rim excised from fellow eye and mounted in an artificial anterior chamber
- Internal Pressure varied from 10-50mmHg

Metzler, et al. JCRS, 2014

Is the Sclera Involved?

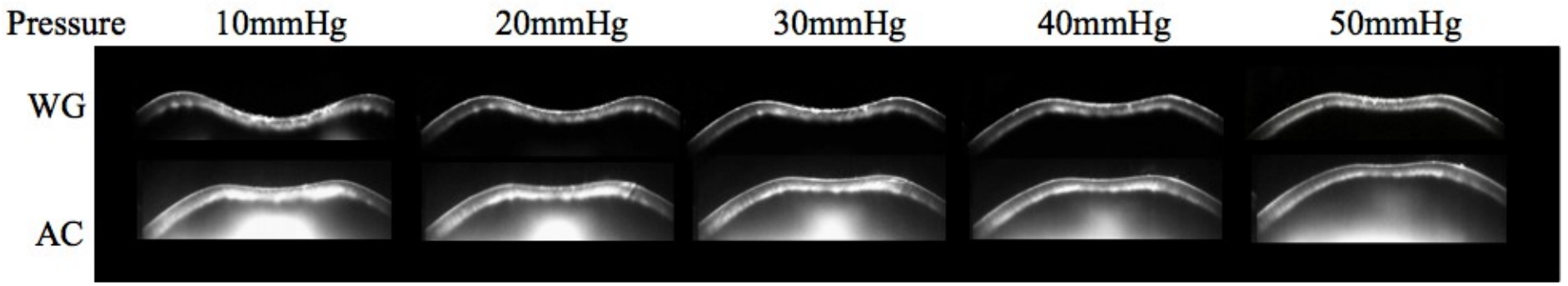
- Paired Human Donor Corneas
  - One cornea mounted as a whole globe
  - Corneal-scleral rim excised from fellow eye and mounted in an artificial anterior chamber

- Internal Pressure varied from 10-50mmHg

Metzler K, Mahmoud AM, Liu J, Roberts CJ. Deformation Response of Paired Donor Corneas to An Air Puff: Intact Whole Globe vs Mounted Corneoscleral Rim. *J Cataract Refr Surg* 2014. Jun;40(6):888-96.

10mmHg Increments of IOP

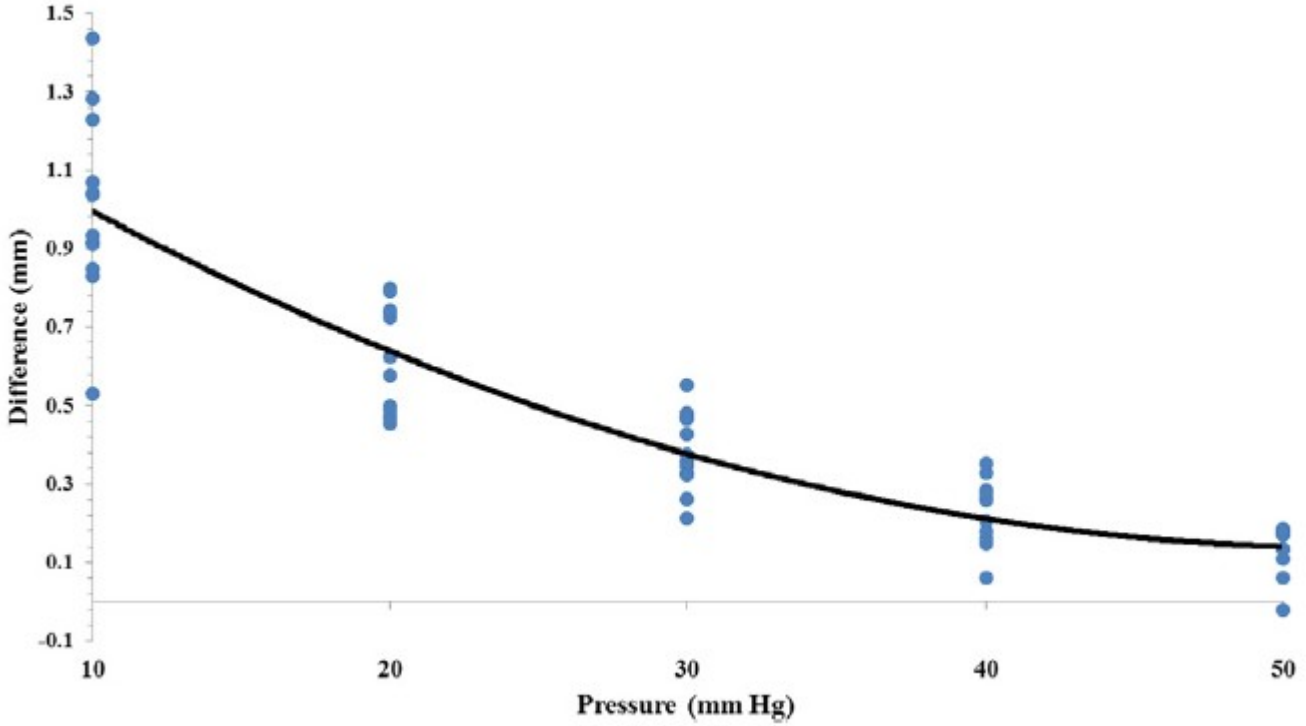
- Whole Globe (WG) vs artificial Anterior Chamber (AC)



- Applied air pressure and internal pressure interact with stiffness of the boundary/sclera which can limit response.
- The sclera behaves more like a rigid AC as IOP increases.

Metzler, et al. JCRS, 2014

Difference in Deformation vs Experimental IOP



Metzler K, Mahmoud AM, Liu J, Roberts CJ. Deformation Response of Paired Donor Corneas to An Air Puff: Intact Whole Globe vs Mounted Corneoscleral Rim. *J Cataract Refr Surg* 2014. Jun;40(6):888-96.

Conclusions:

- Greater IOP produces stiffer corneal behavior under an applied air puff
- Stiffer “globe” produces stiffer corneal behavior under an applied air puff.

Stiffer Sclera limits Corneal Deformation

frontiers in Bioengineering and Biotechnology

ORIGINAL RESEARCH
published: 10 January 2019
doi: 10.3389/fbioe.2018.00210

Biomechanical Impact of the Sclera on Corneal Deformation Response to an Air-Puff: A Finite-Element Study

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[1] Department of Biomedical Engineering, The Ohio State University, Columbus, OH, United States, [2] Department of Ophthalmology & Visual Science, The Ohio State University, Columbus, OH, United States

Experimental Eye Research

Biomechanical contribution of the sclera to dynamic corneal response in air-puff induced deformation in human donor eyes

B. Audrey Nguyen, Matthew A. Reilly, Cynthia J. Roberts

Funded by NEI/NIH R01EY027399

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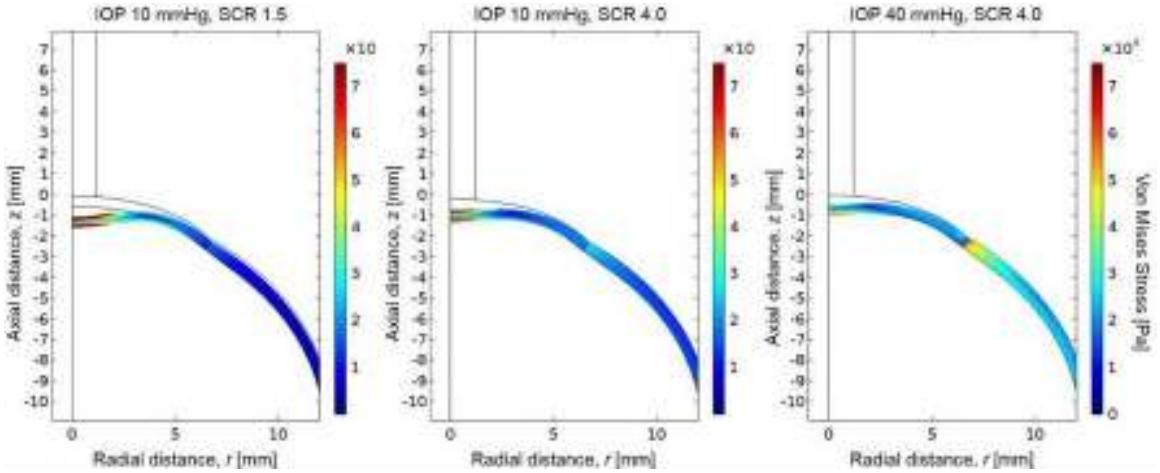
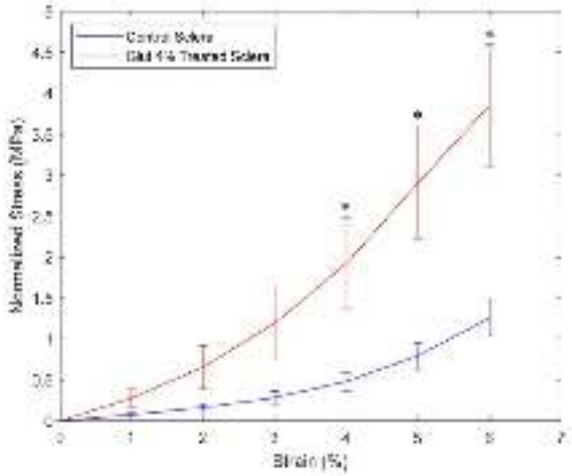
Highest Concavity Parameters Show Significant Response to Scleral Stiffening

MANCOVA: ΔDCR's between tx and control

CorVis ST DCR	log(IOP)	Scleral Modulus (E)	log(IOP)*Scl Mod (E)
Peak Dist. [mm]	0.6019	*0.0386†*	0.0949
HC Deformation Amp. [mm]	*0.2542†*	*0.0680†*	0.0335
Radius [mm]	2.7522	*0.1690†*	*0.2479†*
DA Ratio Max (2 mm)	*0.9032†*	0.0204	0.0755
Integrated Radius [mm^{-1}]	0.1979	*0.0307†*	0.0308
SP-A1-	*2.909†*	0.0019	0.112
SP-HC·	*3.7287†*	*0.0149†*	0.0368

Cohen effect sizes shown





von Mises stresses and deformation; IOP, 10, 10, 40; Scleral-Cornea Ratio of E at 1.5, 4.0, 4.0

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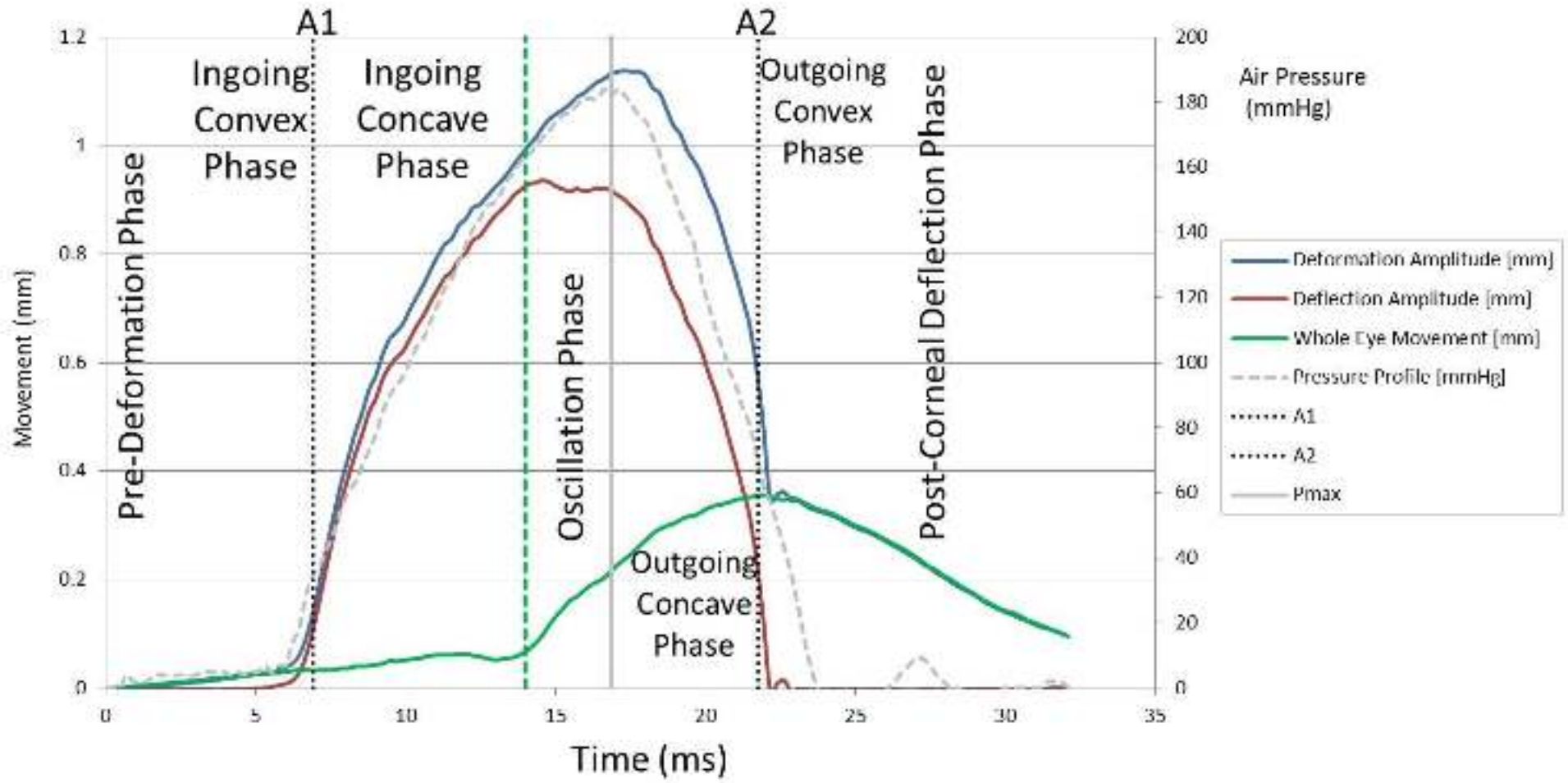
How is Scleral Response Assessed?

- SP-A1 is related to corneal response
- SP-HC is related to scleral response

Nguyen BA, Reilly MA, Roberts CJ. Biomechanical contribution of the sclera to dynamic corneal response in air-puff induced deformation in human donor eyes. Experimental Eye Research,Epub 2019.

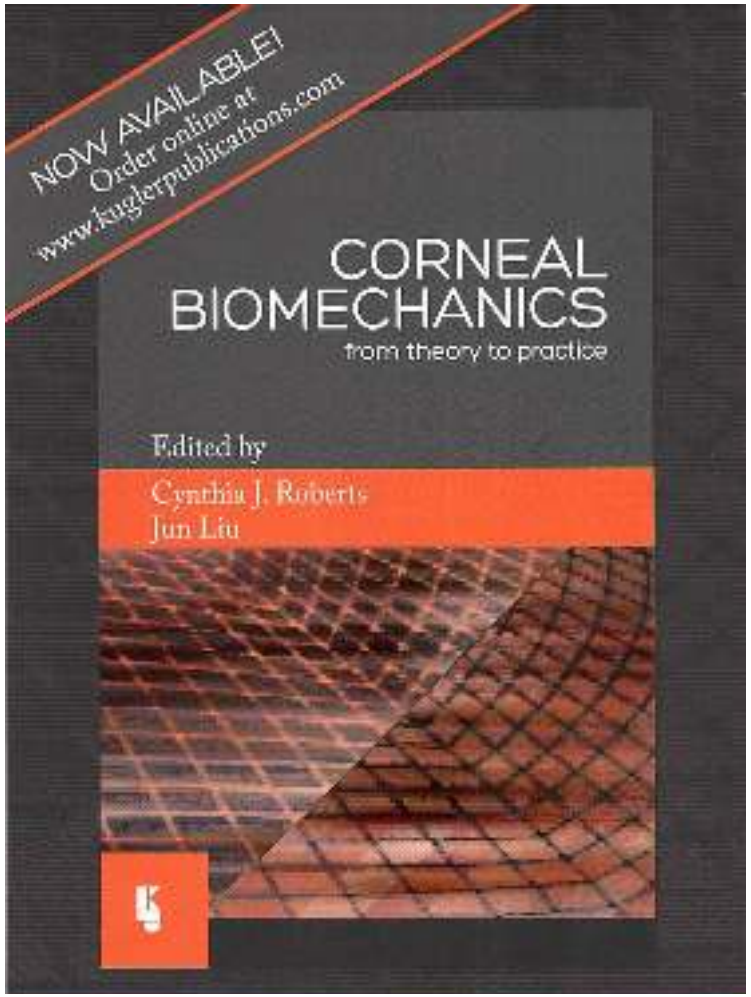
Deformation Phases



Summary

- The cornea is nonlinearly viscoelastic
  - Increased IOP leads to stiffer response
  - Response is distinct during loading and unloading
- The Corvis ST quantifies elastic response
  - Corneal Stiffness: SP-A1 and SSI
  - Scleral Stiffness: SP-HC
- Ocular Response Analyzer quantifies viscoelastic response

Thank You!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