Past, Present, and Future of Ocular Biomechanics

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THE OHIO STATE UNIVERSITY

Biomedical Engineering

THE OHIO STATE UNIVERSITY 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

PAST……

Biomechanics

No ability to measure clinical biomechanical response

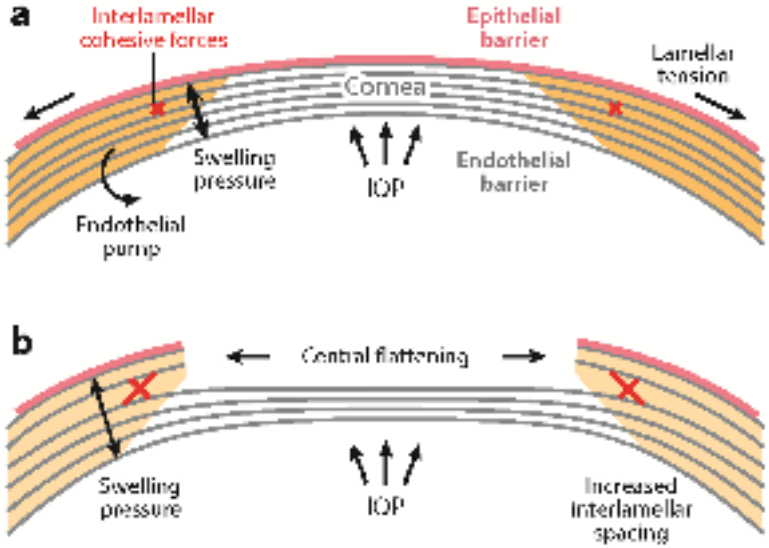
Biomechanical Response in Refractive Surgery

- Unstable decompensation (ectasia)
  - "At risk" cornea pre-operatively
  - Too much tissue altered by surgery
- Stable modification of every treatment outcome*^

^ARVO Abstract:
Dupps WJ, Roberts CJ, Schoessler JP. Geometric Bias in PTK Ablation Profiles and Associated Keratometric Changes in Human Globes *Invest Ophth Vis Sci* Suppl, 1996; 37(3):S57.

*Dupps WJ, Roberts C. Effect of acute biomechanical changes on corneal curvature after photokeratectomy. *J Refract Surg.* 2001; 17(6):658-669.

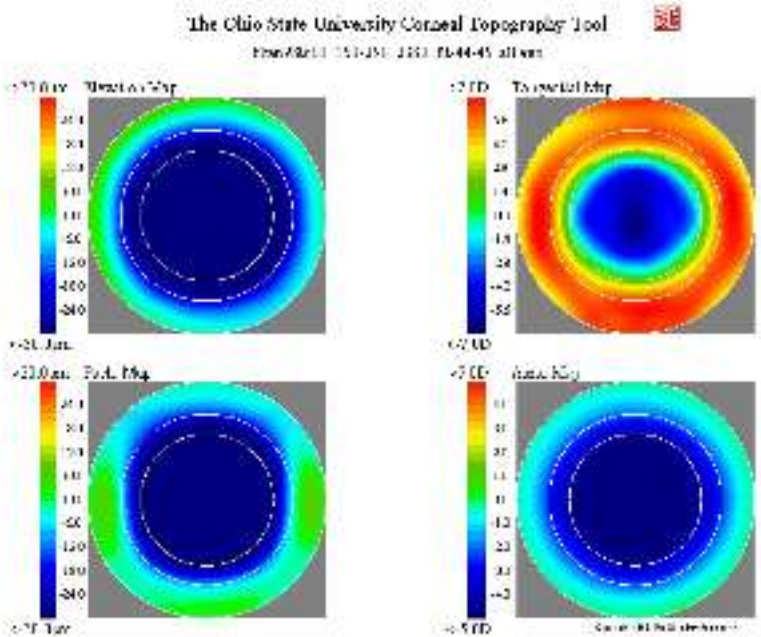
Biomechanical Response to Refractive Surgery



Ruberti JW, Sinha Roy A, Roberts CJ. Corneal Biomechanics and Biomaterials. *Annual Review of Biomedical Engineering*, 2011 Aug 15; Vol. 13, pp. 269-95.

How does the Biomechanical Response Affect Outcomes?

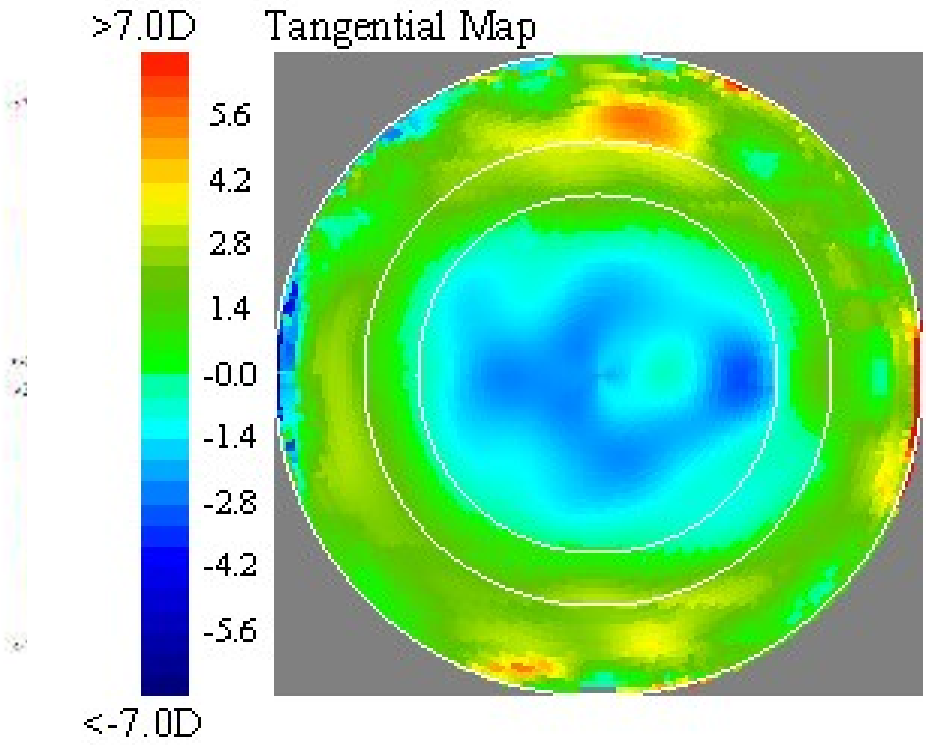
Composite difference maps for entire Population: Anterior Surface (n=2,380)



- All regions show statistically significant differences from pre-operative state.
- Although there are areas of increased height and pachymetry in the outer zone, the overall trend of the region as a whole is decreased.

Roberts CJ, Mahmoud AM. Topographic Changes after Excimer Laser Refractive Surgery, in: Kılıç A, Roberts CJ (eds). *Corneal Topography: from Theory to Practice*, Amsterdam: Kugler Publications; 2013:239-270.

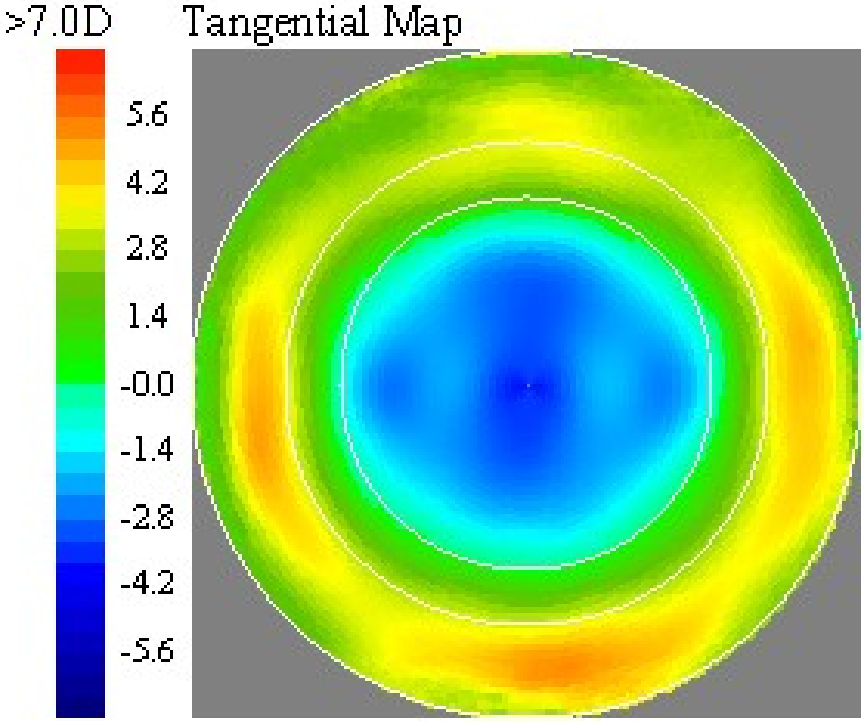
Composite Anterior Difference Maps
Myopic Correction < 2 D



n = 25

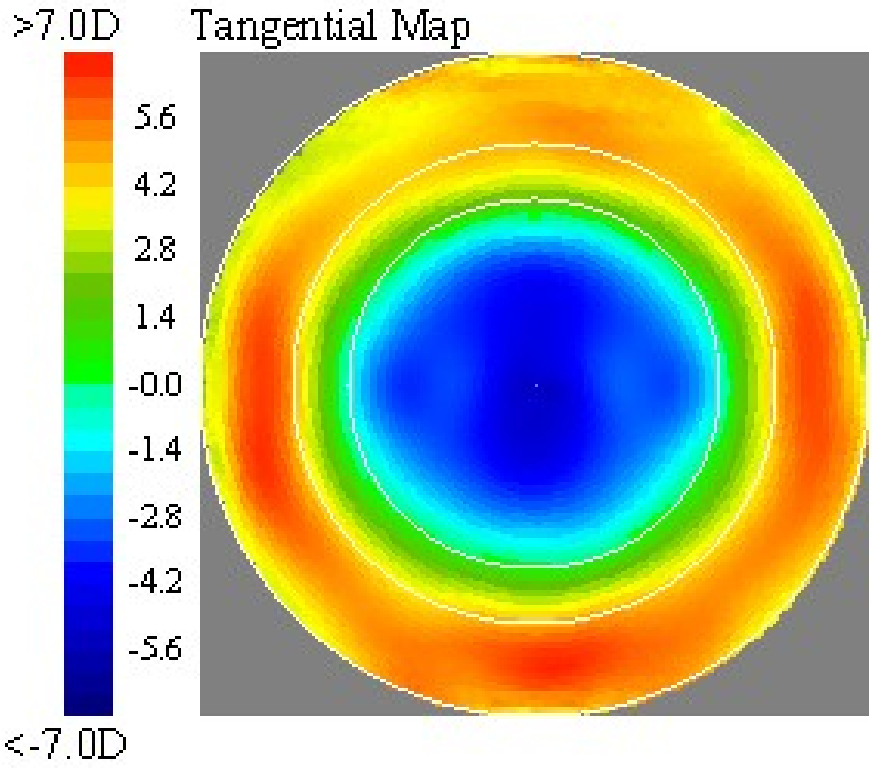
All regions except outer elevation zone show statistically significant differences from pre-operative state.

Composite Anterior Difference Maps
Myopic Correction from 2 to 4 D



- n = 321
- All regions show statistically significant differences from pre-operative state.

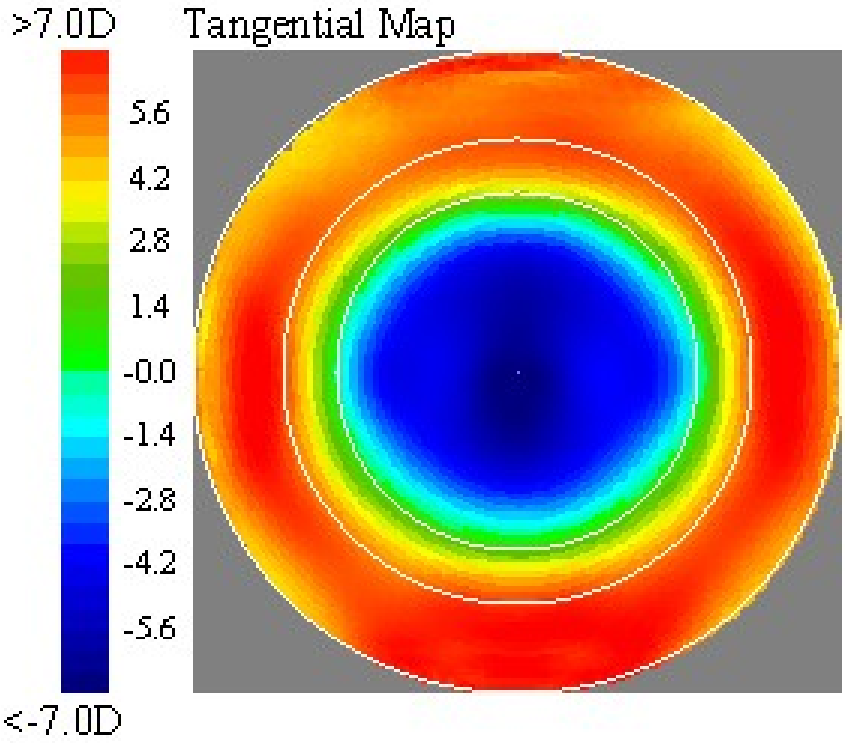
Composite Anterior Difference Maps
Myopic Correction from 4 to 6 D



n = 635

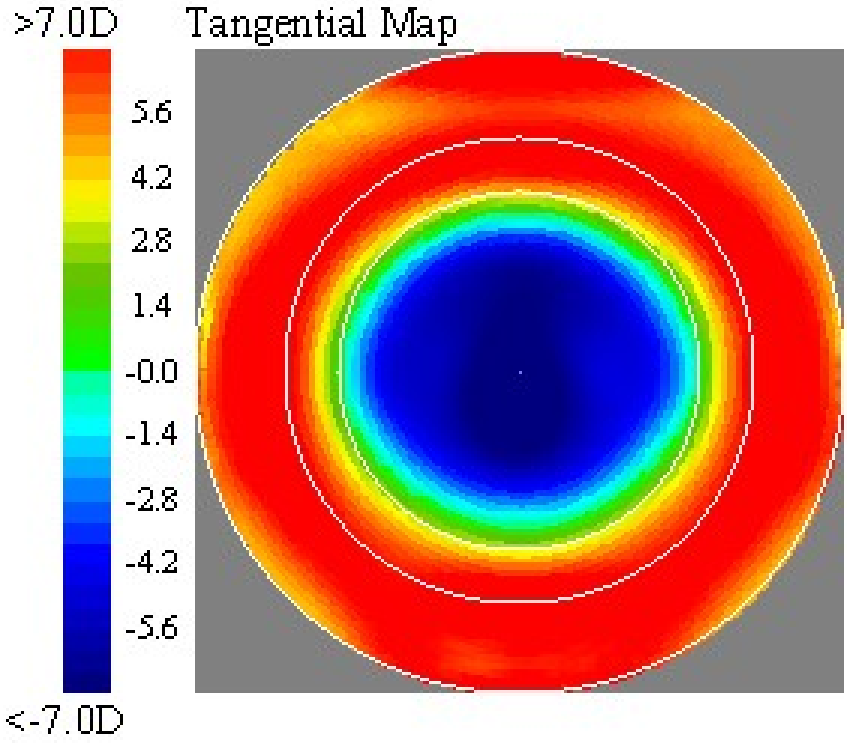
All regions show statistically significant differences from pre-operative state.

Composite Anterior Difference Maps
Myopic Correction from 6 to 8 D



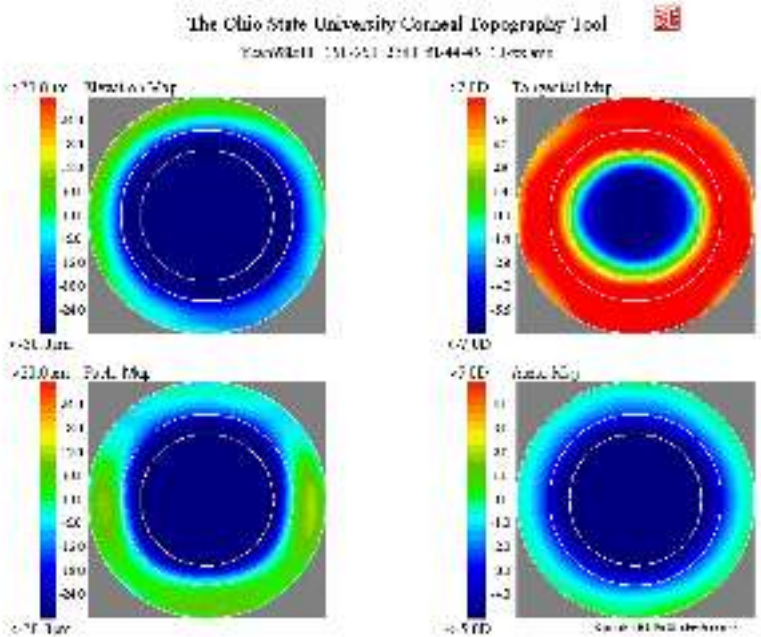
- n = 622
- All regions show statistically significant differences from pre-operative state.

Composite Anterior Difference Maps
Myopic Correction from 8 to 10 D



- n = 465
- All regions show statistically significant differences from pre-operative state.
- Note area of increased pachymetry in outer zone is larger, although trend of whole region remains decreased.

Composite Anterior Difference Maps
Myopic Correction for > 10 D



- n = 311
- All regions except outer pachymetry show statistically significant differences from pre-operative state.
- Area of central decreased curvature is diminished.

Roberts CJ, Mahmoud AM. Topographic Changes after Excimer Laser Refractive Surgery, in: Kılıç A, Roberts CJ (eds). *Corneal Topography: from Theory to Practice*, Amsterdam: Kugler Publications; 2013:239-270.

Biomechanical Response

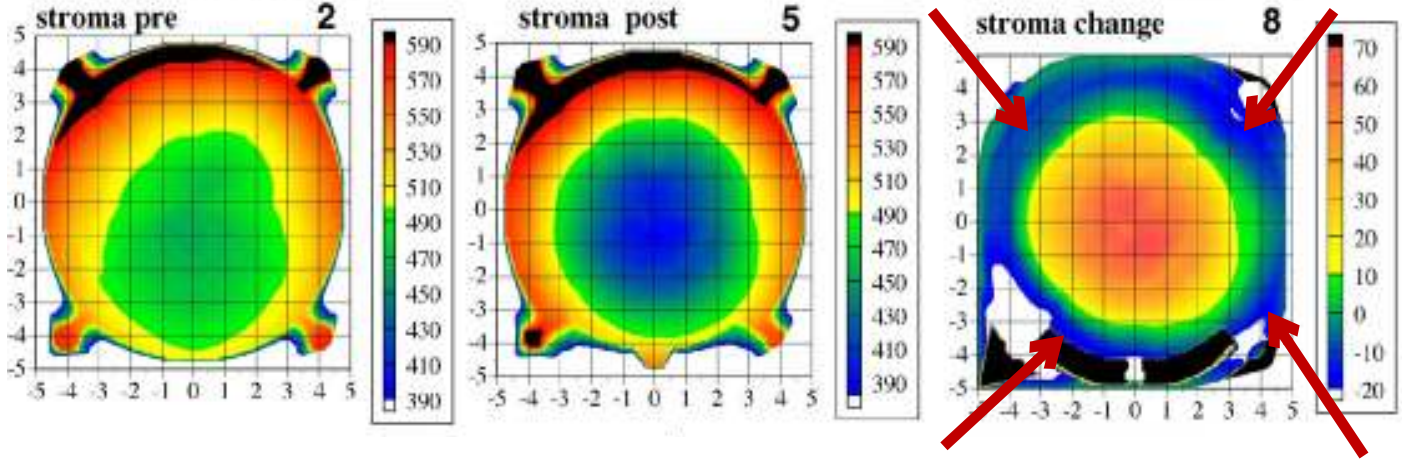
- Curvature in the outer region, which corresponds to the transition zone in the ablation pattern, increases with increasing level of correction
- Zones of increased pachymetry in outer zone DESPITE ablation in that area
- Increased curvature leads to increased spherical aberration
- Consistent with Corneal Biomechanical Model

Biomechanical *Central Flattening* and *Peripheral Steepening*

- Enhances a Myopic Procedure through central flattening

- Reduces the effect of a Hyperopic Procedure

Imaging with Artemis: Consistent with Biomechanics

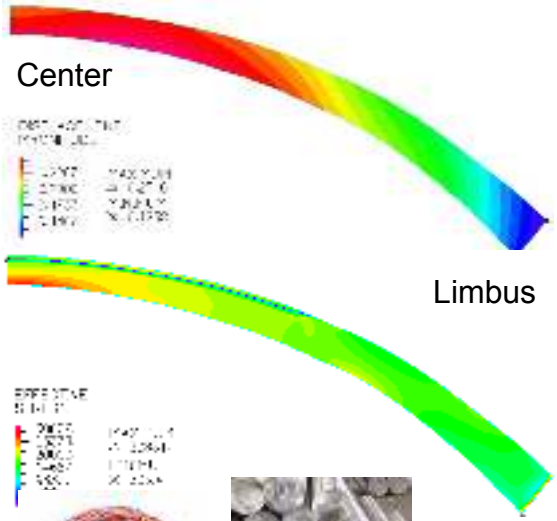


- Induced change in stromal thickness after refractive surgery, demonstrating decreased thickness in center and increased thickness in the peripheral region!

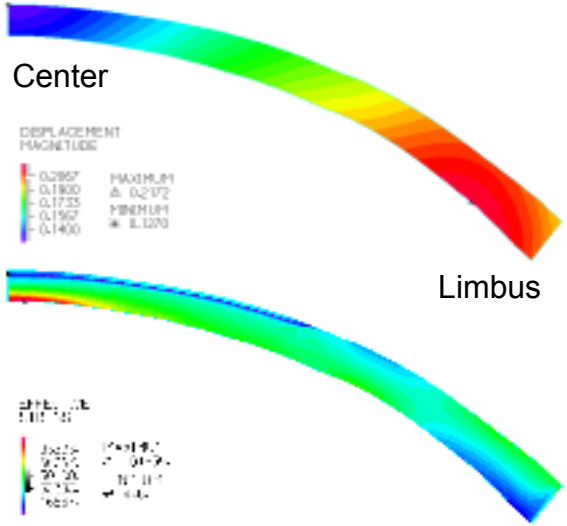
Reinstein et al. Journal of Refractive Surgery 2000 Jul-Aug;16:414-30.

Effect of a fixed myopic LASIK across a range of ex vivo corneal properties

Low stiffness=> undercorrection (± ectasia)

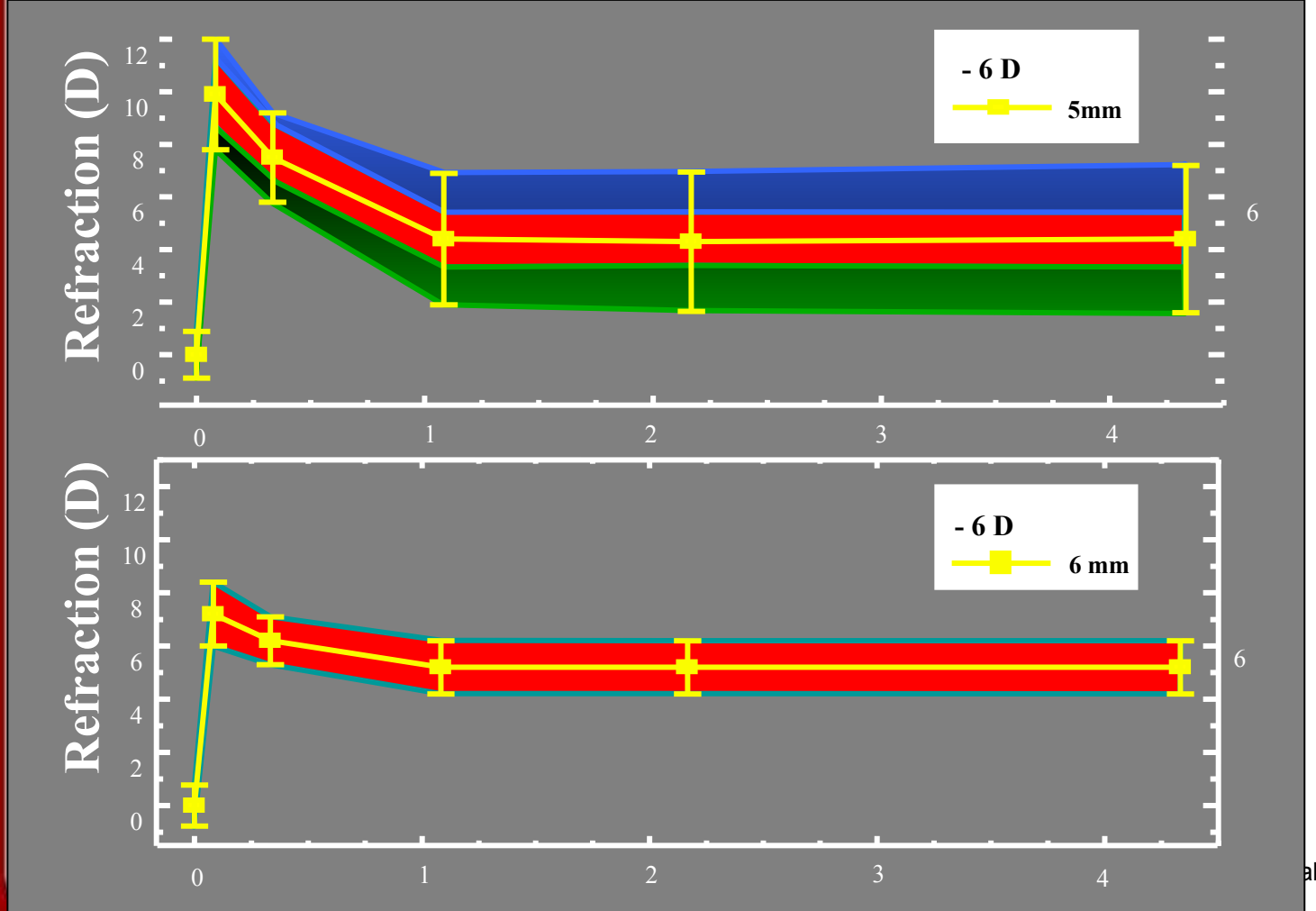


High stiffness => overcorrection



Sinha Roy and Dupps, JRS 2009

Can the Biomechanical Response be Manipulated?



From John Marshall, Ph.D.

Biomechanical variability due to larger periphery with a 5mm ablation zone

Increase to 6mm ablation zone REDUCED biomechanical variability by <u>reducing periphery</u>

al Engineering

Medical Center

Roberts, Ph.D.

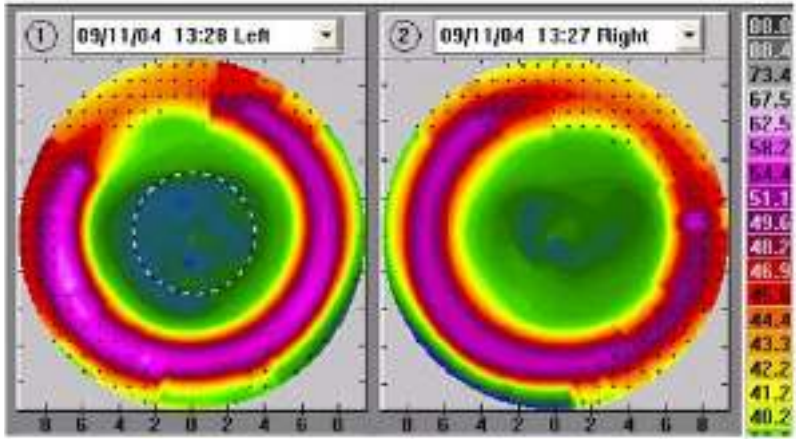
What is the Source of Spherical Aberration Induction?

- Loss of Ablation efficiency in the periphery?
  - This can be compensated by adding more pulses in the periphery (Wavelight)
  - Meta-analysis showed no difference in outcomes between wavefront-guided and conventional treatments.*
- Biomechanics?
  - Peripheral thickening and steepening

*Li S-M, Kang M-T, Wang N-L, Abariga SA. Wavefront excimer laser refractive surgery for adults with refractive errors. Cochrane Database Syst Rev. 2020; 12:CD012687.

Contralateral Eyes with Pre-Op Refraction of -8.0 diopters

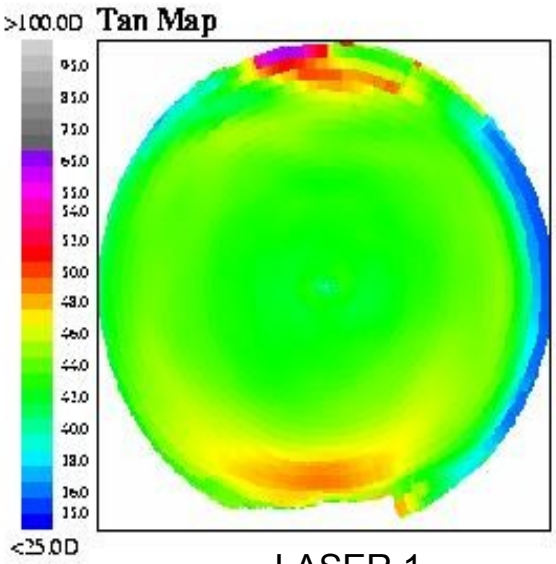
Wavefront-Optimized Profile:
Compensates for the loss of ablation efficiency in the periphery



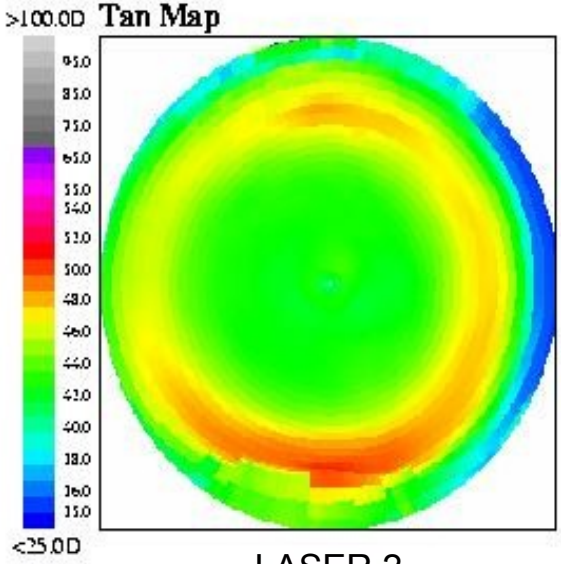
F-CAT Profile:
Includes an additional aspheric component that adds more ablation in the mid-periphery

Courtesy of Dr. Jerry Tan of Singapore
Wavelight laser

Roberts C. Biomechanical Customization: The Next Generation of Laser Refractive Surgery. *J Cataract Refract Surg.* 2005; 31(1): 2-5.



LASER 1



LASER 2

Contralateral Eyes at 6 months post-op

Average of n= 30 tangential maps
Optical Zone = 6.5mm
Ablation Zone to 9mm

Average of n = 30 tangential maps
Optical Zone = 6.5mm
Ablation Zone to 8mm

Twa MD, Lembach RG, Bullimore MA, Roberts C: "A prospective randomized clinical trial of laser in-situ keratomileusis with two different lasers." *American Journal of Ophthalmology*, 2005, 140(2):173-183

The Transition Zone is NOT Neutral!!

WHEREVER ablation occurs,
corneal structure is altered and
corneal shape is modified

PRESENT…….

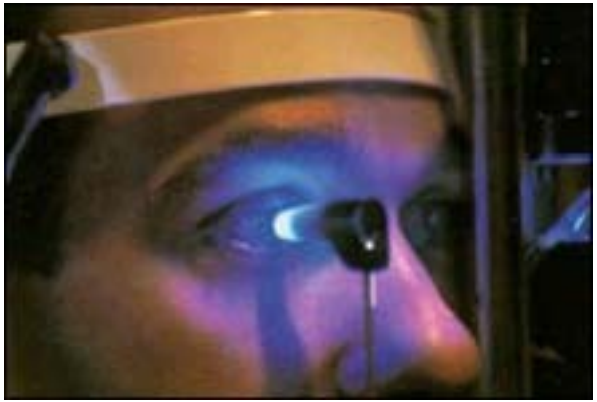
Biomechanics

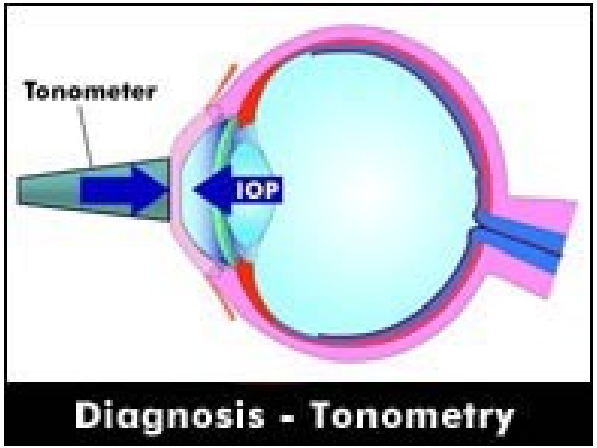
- Elastic Response
  - Corvis ST
  - Global response to applied air puff - consistent
- Viscoelastic Response
  - Ocular Response Analyzer
  - Global response to applied air puff - customized

IOP Estimation after Laser Refractive Surgery

Goldmann Applanation Tonometry (GAT)

Based on the theory that the force required to applanate the cornea is proportional to the intra-ocular pressure (IOP)





How Does CCT affect the Measured IOP?

- A “thin” cornea will require less force to applanate than a “thick” cornea, independent of the true IOP.
  - Therefore, a “high” measured IOP may simply be that the cornea is thick, leading to overestimation.

- Conversely, a “low” measured IOP may simply be that the cornea is thin, leading to underestimation.

Measured IOP after Refractive Surgery

- Average Drop in IOP:
  - −0.46 mm Hg (CCT)
    - Chatterjee et al. Ophthalmologica 1997;211:355-9
  - −0.71 mm Hg (AT)
    - Cennamo et al. Ophthalmologica 1997;211:341-3

Why are they different??

Clinical Implications of Correcting IOP for Central Corneal Thickness (CCT)

Which one (if any) is the
"correct" one??

What is affecting accuracy of pressure measurement, **IN ADDITION** to central corneal thickness?

Goldmann Applanation Tonometry (GAT)

- Based on the theory that the force required to applanate the cornea is proportional to the intra-ocular pressure (IOP)

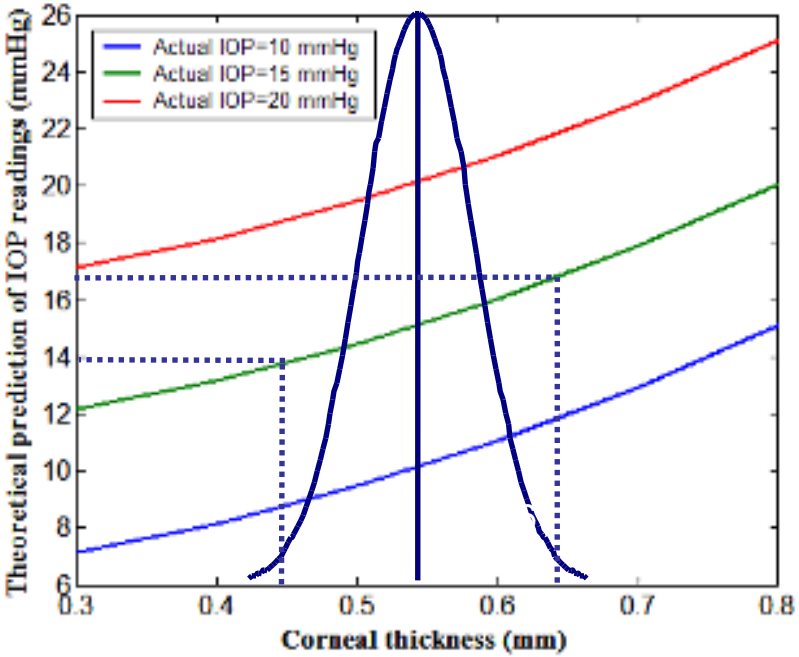
- Assumptions were made regarding:
  - CORNEAL CURVATURE
  - CORNEAL **THICKNESS**
  - CORNEAL BIOMECHANICAL PROPERTIES

Goldmann Applanation Tonometry (GAT)

- Based on the theory that the force required to applanate the cornea is proportional to the intra-ocular pressure (IOP)

- Assumptions were made regarding:
  - CORNEAL CURVATURE
  - CORNEAL **THICKNESS**
  - **CORNEAL BIOMECHANICAL PROPERTIES**

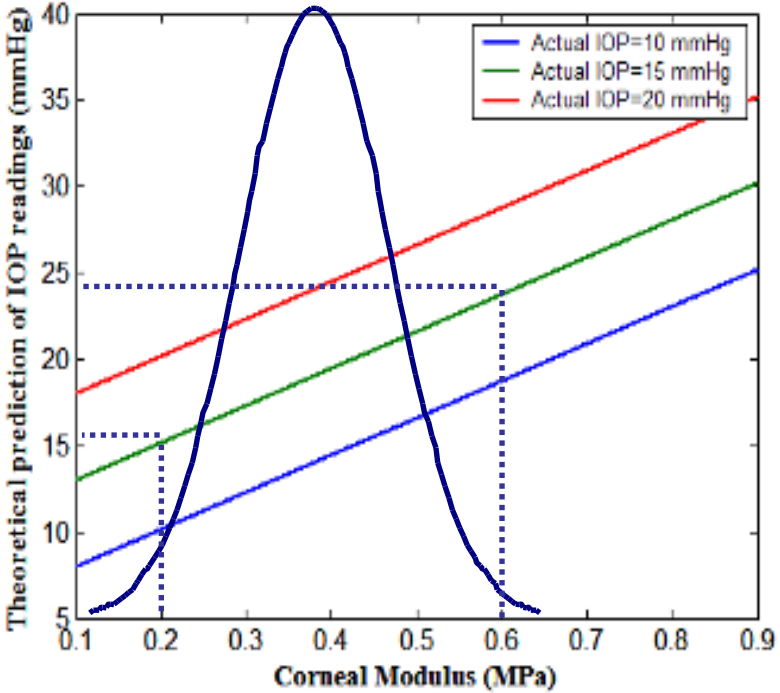
Effect of Corneal Thickness - ALONE



- The thicker the cornea, the higher the measured pressure
- The thinner the cornea, the lower the measured pressure
- Potential Error - Moderate

Liu and Roberts, JCRS, January 2005

Corneal Biomechanical Properties - ALONE



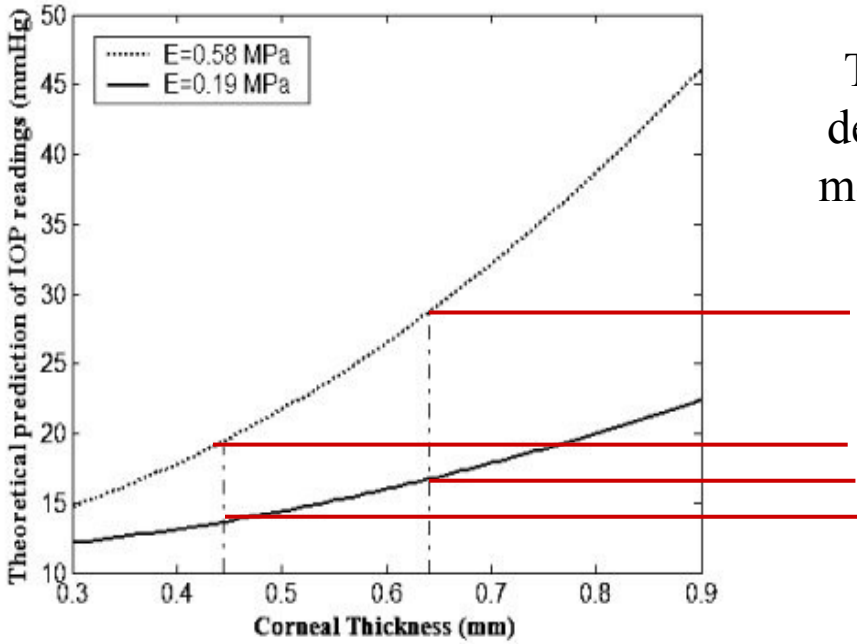
- The “stiffer” the cornea, the greater the measured pressure
- The “softer” the cornea, the lower the measured pressure
- Potential Error – **HUGE - > 10mm**

Liu and Roberts, JCRS, January 2005

We have discussed CCT and Biomechanical Properties as Independent Factors.

In Reality: Curvature, Thickness, and Properties all vary at the same time

Corneal Elasticity *and* Corneal Thickness



The effect of CCT depends on Young's modulus of elasticity

Difference = 8.68mmHg

Difference = 2.84mmHg

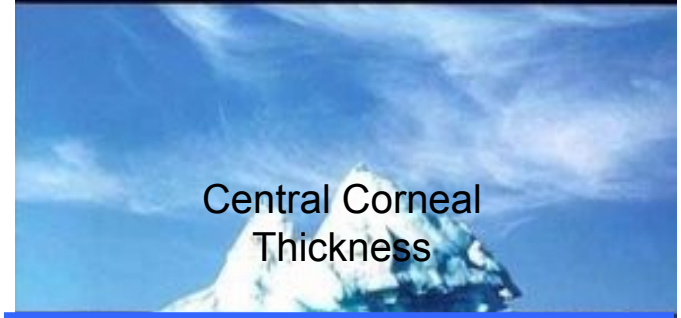
Liu and Roberts, JCRS, January 2005

Modulus of Elasticity (stiffness) *DETERMINES* the Relationship between CCT and IOP measurement error

- CCT has a strong influence on IOP measurement in a “stiff” cornea
- CCT has much less impact on IOP measurement in a “soft” cornea.

Can IOP Measurement be corrected by a simple linear conversion based on thickness?

- NOT ACCURATELY!!!
  - What about thick, soft corneas and thin, stiff corneas?
- Which parameters dominate the measurement artifact?
  - Theory predicts Biomechanical Properties dominate!!



IOP Measurement
Error

What about after Corneal Refractive Surgery?

NOT THE SAME AS A THIN CORNEA!

There is an ablation PROFILE.

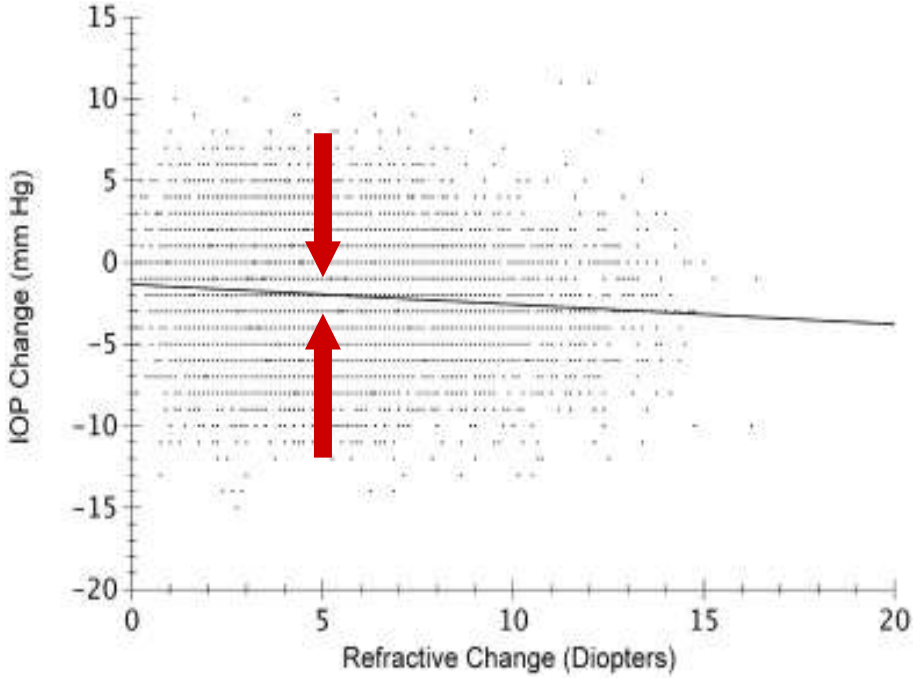
Intra-Ocular Pressure (IOP)

- What do we KNOW?
  - *Measured* IOP decreases after refractive surgery *on average* -

WHY?????

- Decrease in curvature and thickness???

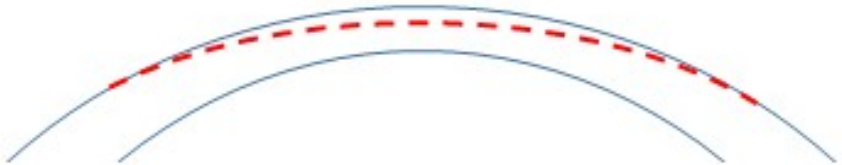
LASIK for Myopia and Myopic Astigmatism
Pre-Op and 3 Month post-op IOP



- N = 8,113
- mean diff IOP
  - ~ -2mmHg
- mean diff sph equiv
  - ~ -5diopters
- $R^2 = 0.009$
- $P < 0.001$
- Slope = -0.12mmHg/diopter

Chang and Stulting, Ophthalmology, 2005.

Changing Pachymetry Profile after Refractive Surgery



Thinning centrally for refractive effect and slight thickening peripherally due to biomechanical response

Pachymetry Profile Pre-op

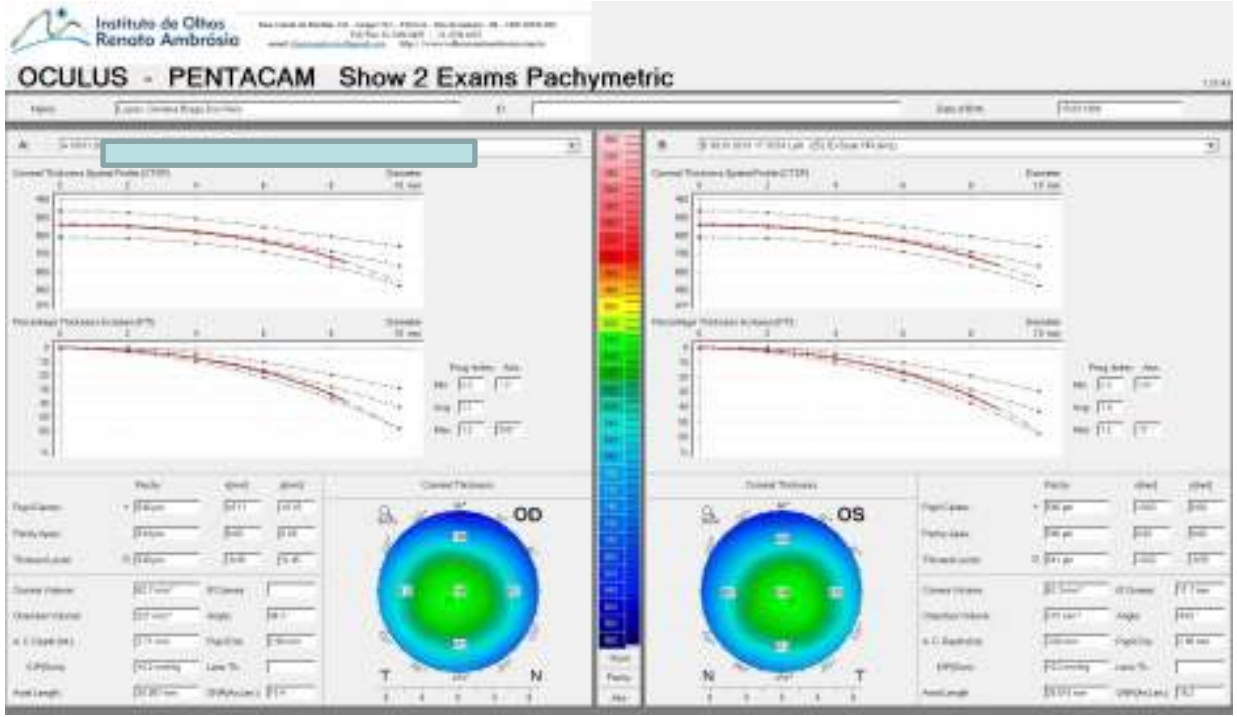


Figure courtesy of Dr. Renato Ambrósio

Pachymetry Profile Post-op

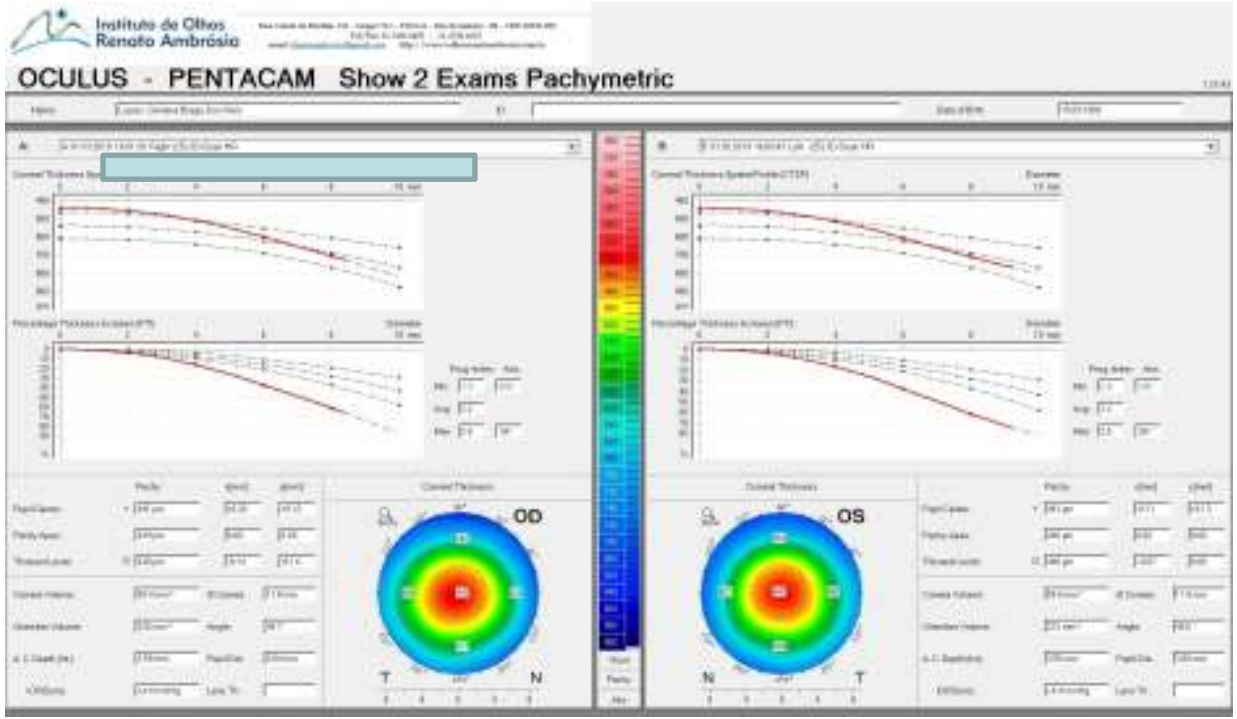
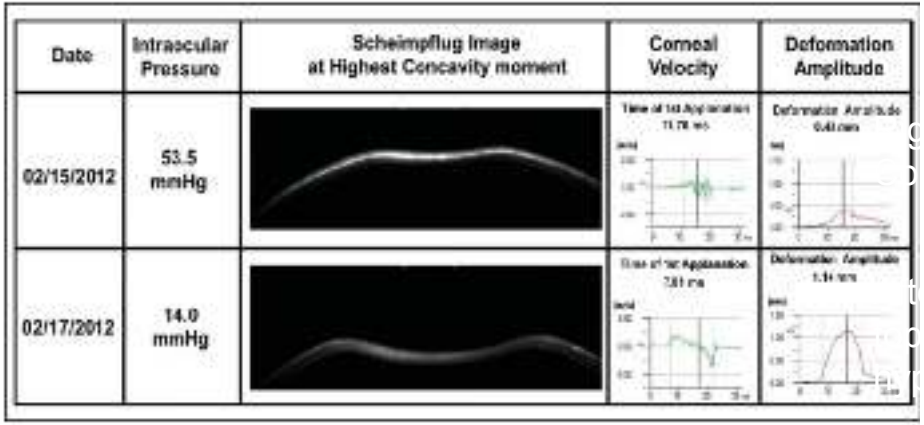


Figure courtesy of Dr. Renato Ambrósio

Pressure-Induced Stromal Keratopathy after LASIK

- GAT 12mmHg OU on 15 February 2012

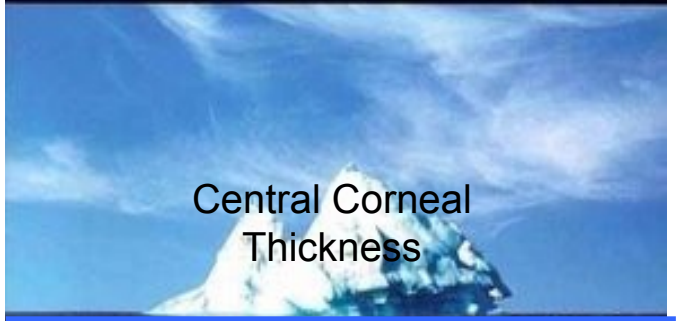


Faria-Correia F, Ramos, Valbon B, Luz A, Roberts CJ, Ambrósio, Jr R. Scheimpflug-based tomography and biomechanical assessment in Pressure-induced Stromal Keratopathy. *J Refract Surg*. 2013;29(5):356-8.

Recommendation:

DO NOT USE APPLANATION TONOMETRY AFTER REFRACTIVE SURGERY!

- The GAT probe will get lost in the flap of LASIK…
- Noncontact Tonometry (NCT) inverts the cornea so is pushing directly against the IOP.



IOP Measurement Error after Laser Refractive Surgery

Alternate Tonometers after Refractive Surgery

- Ocular Response Analyzer: IOPcc

  Reichert, Depew, NY, USA

  (Pepose, et al. *AJO* 2007; 143(1):39-47)

- Corvis ST: bIOP

  Oculus, Wetzlar, Germany

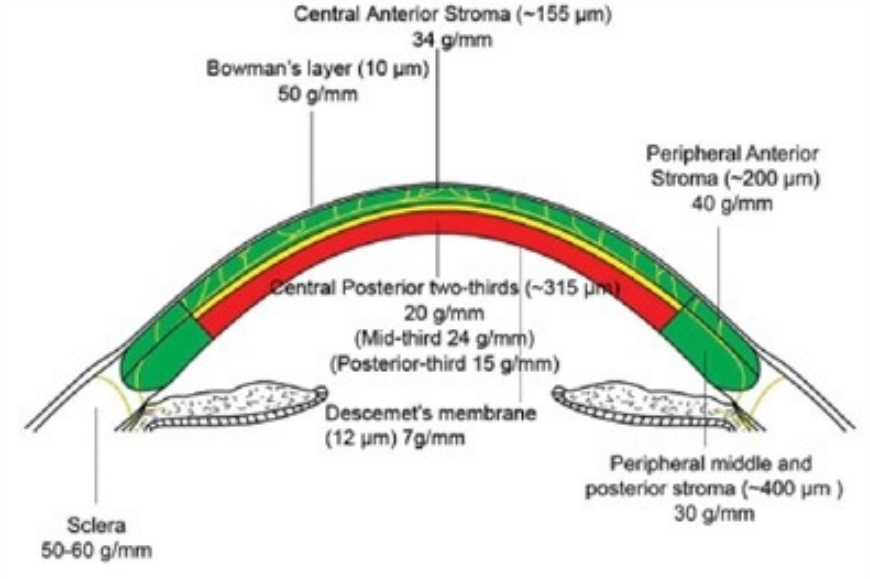
  (Lee H, et al. *JCRS* 2017; 43:1495-150)

Standard NCTs do not take into account difference in biomechanics.

Femtosecond Laser

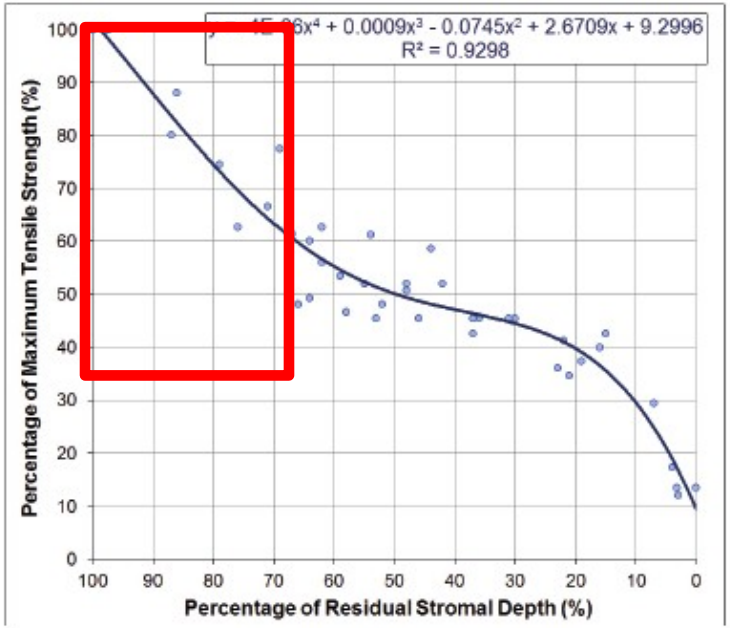
- Cutting a precise flap with a repeatable and uniform thickness
  - Widely adopted to replace microkeratome for flap cut
  - Microkeratome still in use – less reliable; less uniform thickness
- Creating a lenticule with two passes that can be extracted via a flap or a side cut
  - Femtosecond Lenticule Extraction (FLEx)
  - Small Incision Lenticule Extraction (SMILE)

Distribution of Corneal Strength



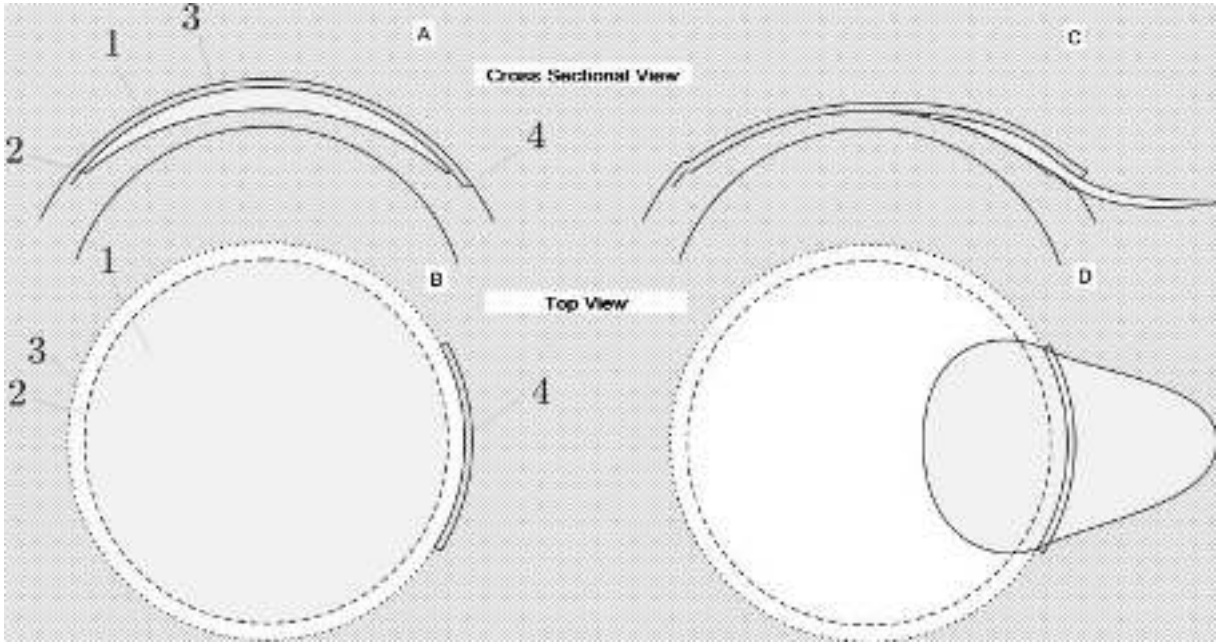
Dawson DG; Grossniklaus HE; McCarey BE; Edelhauser HF. "Biomechanical and wound healing characteristics of corneas after excimer laser keratorefractive surgery: is there a difference between advanced surface ablation and sub-Bowman's keratomileusis?." *Journal Of Refractive Surgery (Thorofare, N.J.: 1995)*, v. 24 issue 1, 2008, p. S90-6.

Depth Dependence of Corneal Tensile Strength



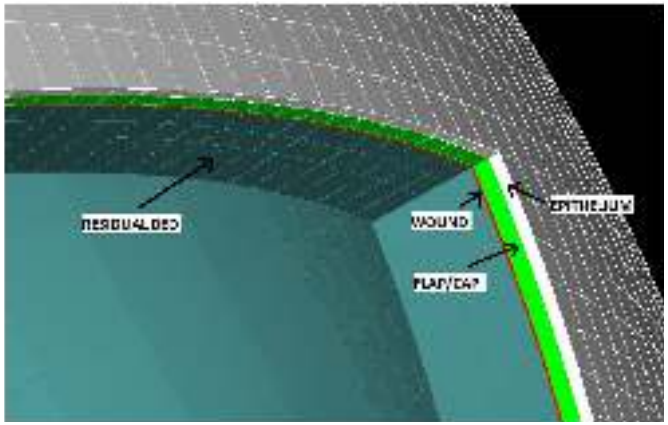
Randleman JB, Dawson DG, Grossniklaus HE, McCarey BE, Edelhauser HF. Depth-dependent cohesive tensile strength in human donor corneas: implications for refractive surgery. J Refract Surg. 2008;24:S85-89.

SMILE – lenticule creation with cap
FLEx – lenticule creation with flap



http://www.newvisionindia.com/relex-smile-the-latest-advance/
(Dr. Rupal Shah)

Flap vs Cap Contralateral Study



- Patient-specific Inverse Finite Element Analysis

- 10 eyes of 5 patients
- SMILE in one eye
- FLEx in fellow eye
- Forward analysis at elevated IOP

Seven, Vahdati, Pedersen, Vestergaard, Hjortdal, Roberts, Dupps. Contralateral-Eye Comparison of Small Incision Lenticule Extraction and Flap-Based Corneal Refractive Surgery: Computational Analysis of Biomechanical Impact. JRS 2017; 33:444-453.

Results

- FLEx produced 49% (range 2-87%) greater mean reduction in stromal collagen fiber stiffness within the flap region than contralateral cap region in SMILE

- Lower stresses and deformations within residual stromal bed in SMILE eyes with simulated IOP increase

Seven, Vahdati, Pedersen, Vestergaard, Hjortdal, Roberts, Dupps. Contralateral-Eye Comparison of Small Incision Lenticule Extraction and Flap-Based Corneal Refractive Surgery: Computational Analysis of Biomechanical Impact. JRS 2017; 33:444-453.

SMILE/LASIK Summary

SMILE offers biomechanical advantages over LASIK

However, strongest cornea is pre-op cornea!

“At Risk” Cornea

- Corneas identified as “at risk” by pre-operative screening tools may indicate an underlying biomechanical abnormality.

- This biomechanical abnormality OVERCOMES biomechanical advantages with SMILE

CAUTION

- **DO NOT PERFORM SMILE IF YOU SUSPECT AN "AT-RISK" CORNEA!**
- **If you would NOT perform LASIK, do NOT perform SMILE!**

Biomechanics of LASER Refractive Surgery

- PRIMARY EFFECT IS THE **AMOUNT OF TISSUE REMOVED** TO GENERATE REFRACTIVE EFFECT

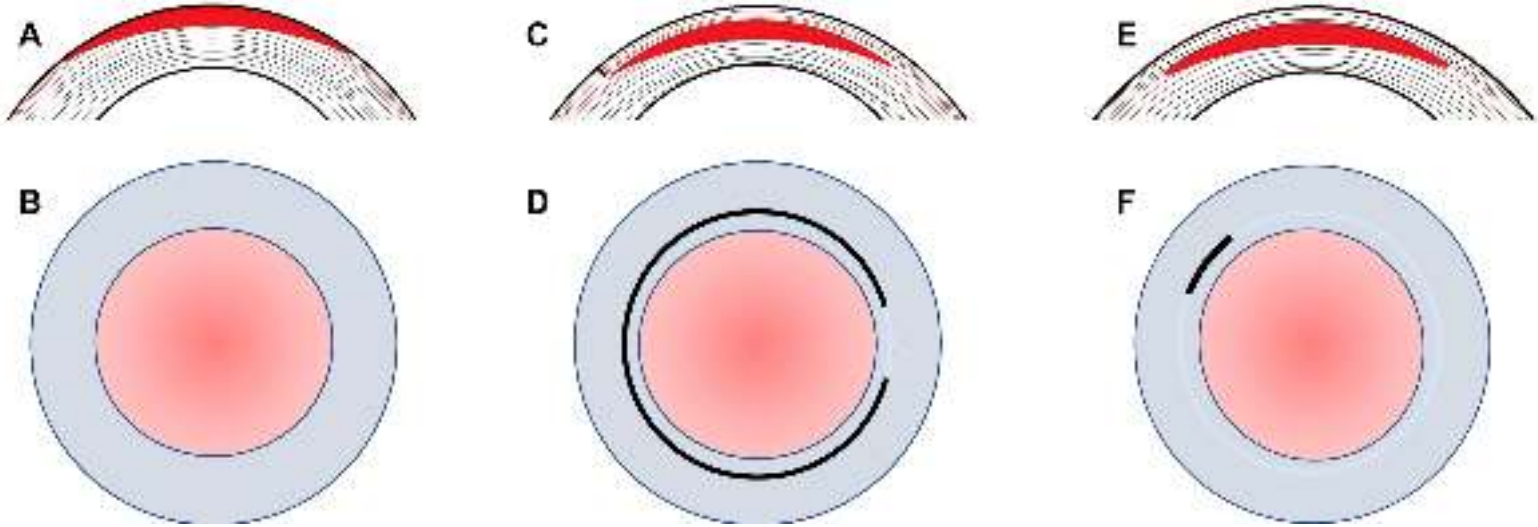
- Secondary effect is location of tissue removal, whether at the surface, under a flap or under a cap

Biomechanically Distinct Procedures

Surface Ablation

LASIK
(~Zero Tension in Flap)

KLEx (SMILE)
(Lower Tension in Cap)



Yuhas PT, Roberts CJ. Clinical Ocular Biomechanics: Where are we after 20 years of progress? Current Eye Research 2023; 48:89-104.

Reduced Tension in Cap Region

- Anterior lamellae are not engaged as they were pre-operatively, mitigating proposed advantage of maintaining intact anterior region

- Additional stress from increased IOP is carried in the residual stromal bed

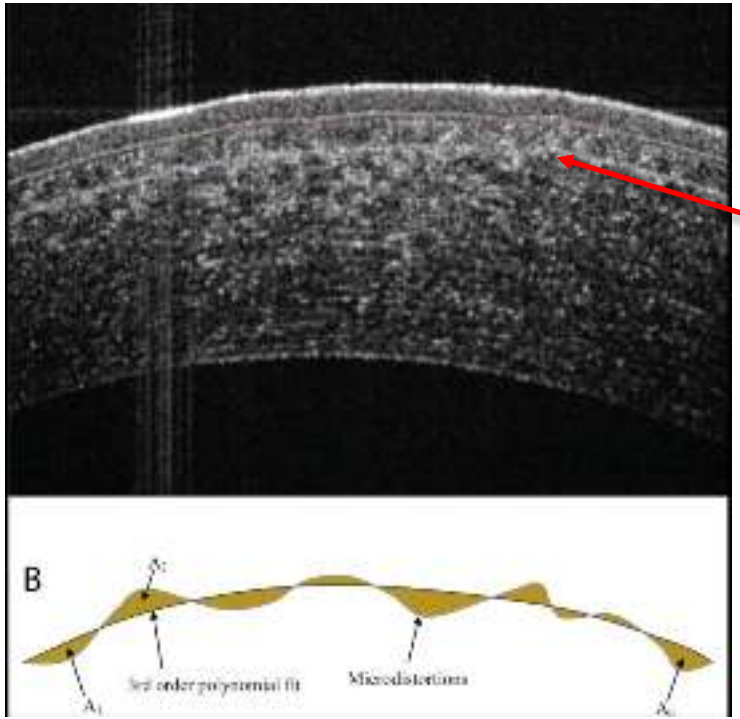
Misconception: “Preserve Anterior Stroma”

- SMILE – anterior region should be “preserved” so goal is larger cap thickness
- LASIK – smallest flap thickness possible since the procedure will produce largest “tissue affected” thickness
- PRK – anterior region removed; no cap/flap

- **Post-Operative stiffness is a function of Residual Stromal Bed!**

Hashemi H, Roberts CJ., Elsheikh A, Mehravaran S, Panahi P, Asgari S. Corneal biomechanics afer SMILE, femtosecond-assisted LASIK, and photrefractive keratectomy: a matched comparison study. Transl Vis Sci Technol 2023; 12:12. PMID: 36928130

SMILE (or other KLEx procedure)

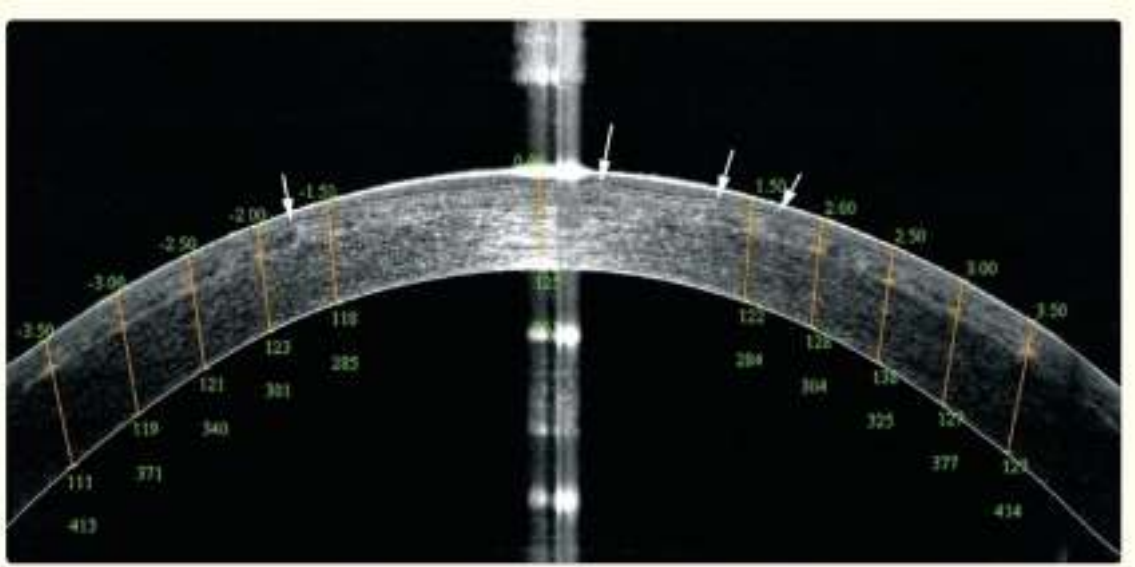


Microdistortions in Bowman's layer

They did not mark in the image, but there are also microdistortions at posterior surface of the cap!

Shroff R, Francis M, Pahuja N, Veeboy L, Shetty R, Sinha Roy A. Quantitative evaluation of microdistortions in Bowman's layer and corneal deformation after small incision lenticule extraction. Trans Vis Sci Tech. 2016;5(5):12, doi:10.1167/ tvst.5.5.12

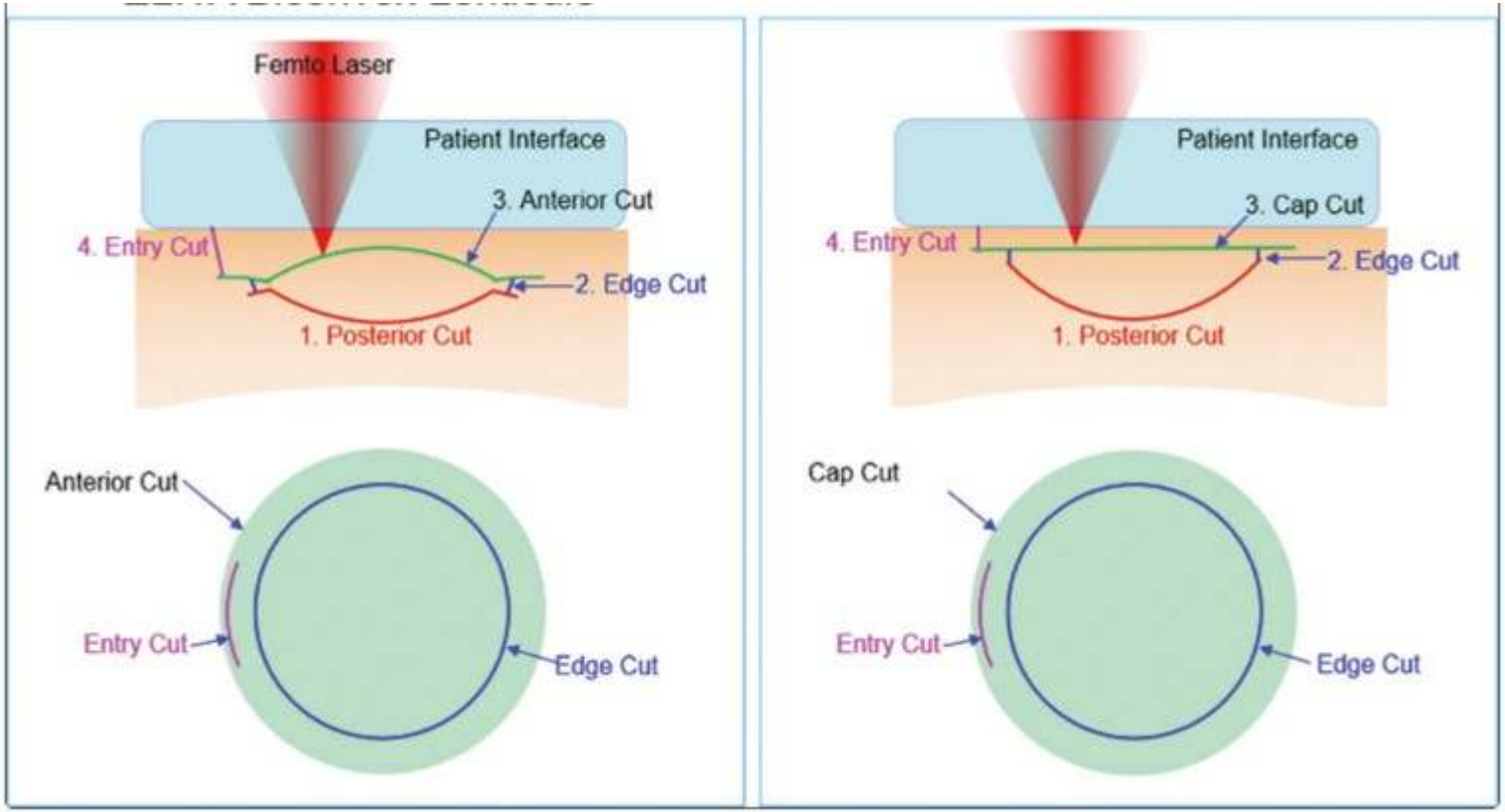
3 months after SMILE, interface shows micro-distortions indicated by white arrows



Fu D, Wang L, Zhou XT, Yu ZQ. Cap morphology after small-incision lenticule extraction and its effects on intraocular scattering. Int J Ophthalmol 2018;11(3):456-461.

FUTURE……..

Is it possible to maintain lamellar tension in the anterior region of the cap?



Sachdev MS. Smooth Incision Lenticular Keratomileusis (SILK™). Indian J Ophthalmol 2024; 72:464-467.

Tomography-Guided Customized KLEx?

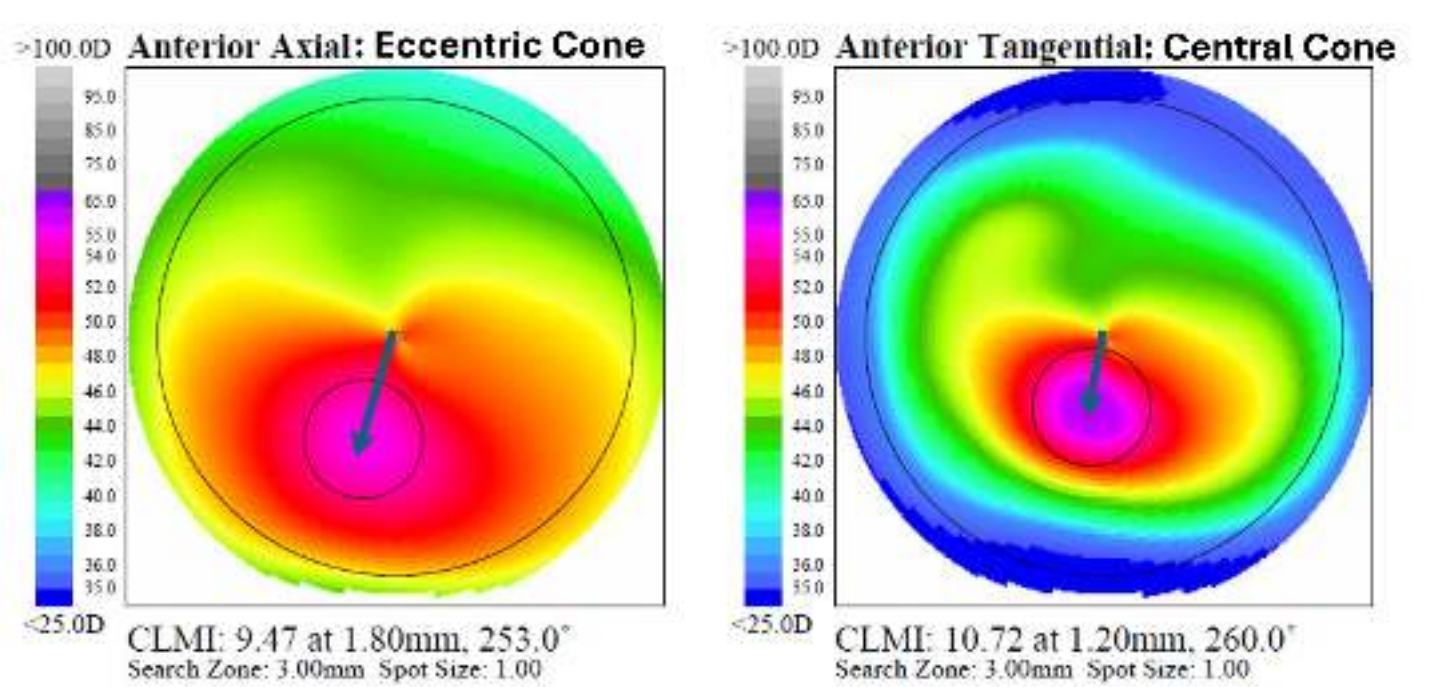
- Equal arclength on either side of lenticule allows stress to be distributed over entire corneal thickness, both above and below lenticule
- No loss of lamellar tension in anterior region
- Customized shape can be transmitted to corneal surface

Biomechanics Provides the Ultimate **KEY** to Achieving the Full Potential of **CUSTOMIZED** Refractive Surgery!

Biomechanics

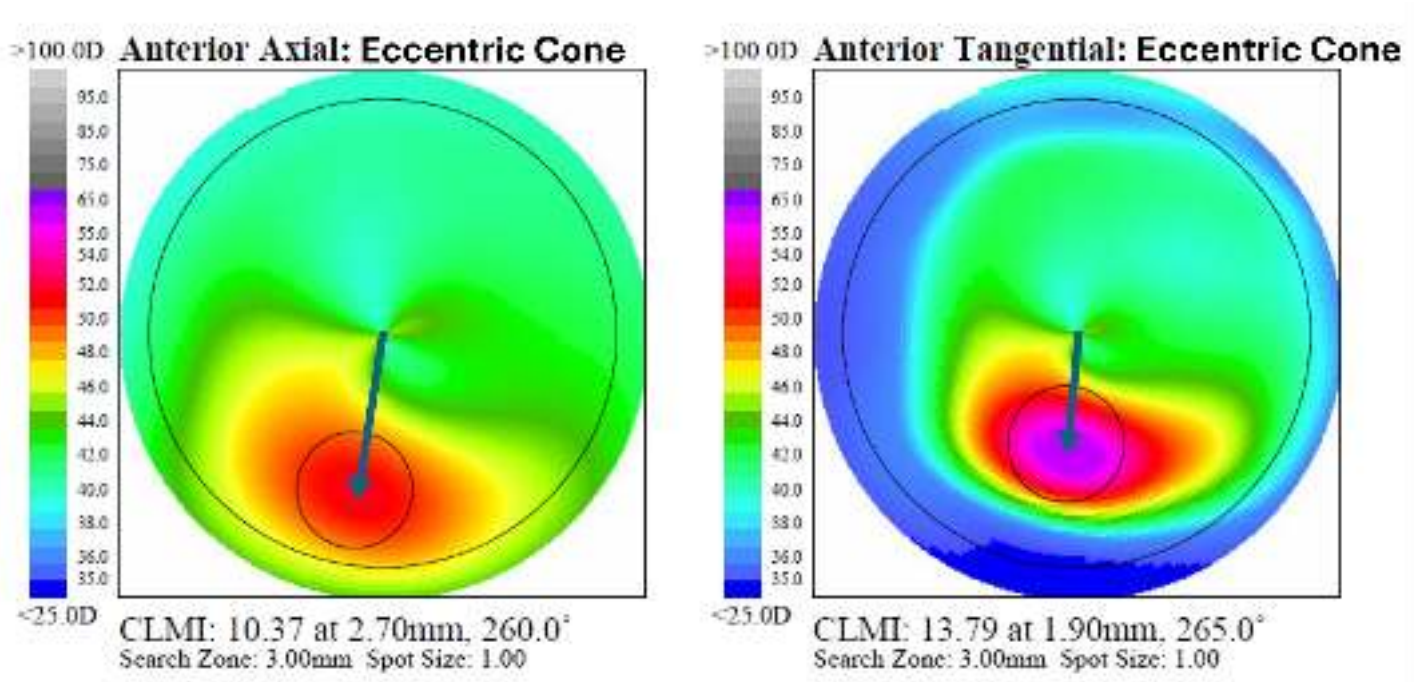
- Need to detect Asymmetry
- Spatially resolved biomechanical response
  - Brillouin Microscopy
  - Currently acquisition is a bit slow for busy clinic
  - In process of commercialization: Intelon

Eccentric cone on Axial
Central on Tangential



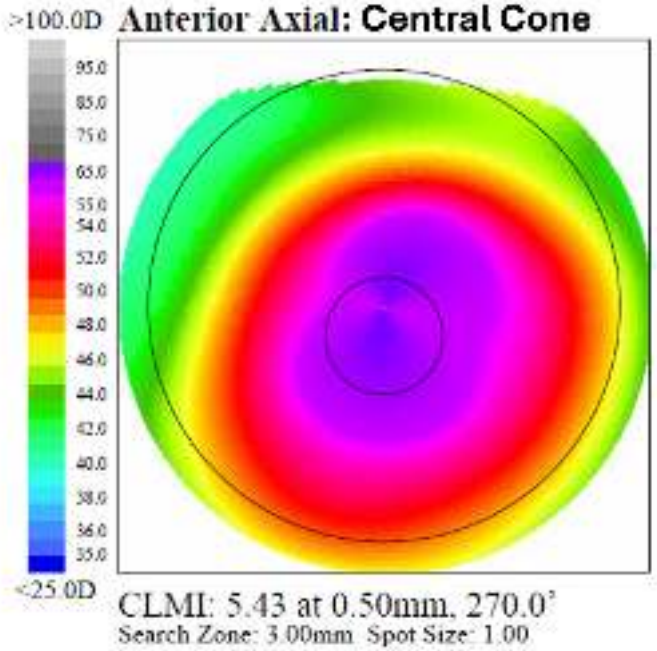
Bruner CD, Mahmoud AM, Roberts CJ. Eccentric Pathology in Keratoconus Exhibits Stiffer Biomechanical Response Than Central Pathology. Ophthalmol Science

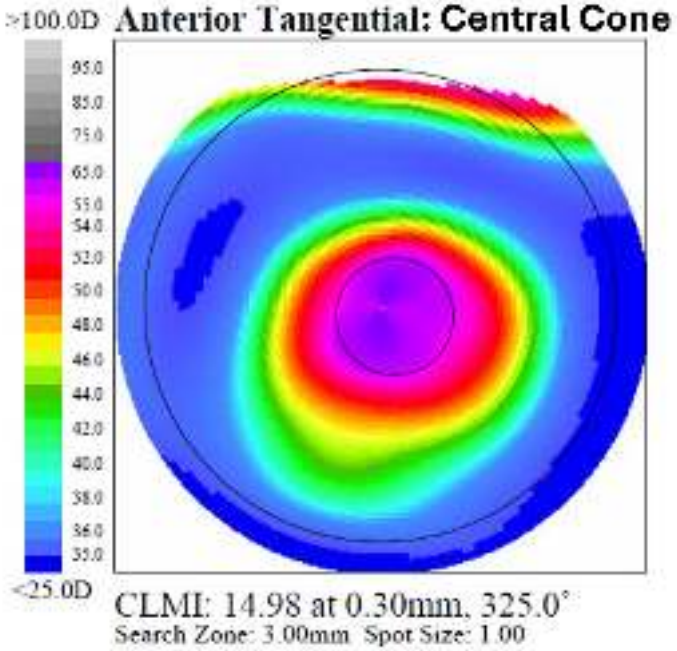
Eccentric cone on Axial
Eccentric on Tangential



Bruner CD, Mahmoud AM, Roberts CJ. Eccentric Pathology in Keratoconus Exhibits Stiffer Biomechanical Response Than Central Pathology. Ophthalmol Science

Central cone on Axial
Central on Tangential





Bruner CD, Mahmoud AM, Roberts CJ. Eccentric Pathology in Keratoconus Exhibits Stiffer Biomechanical Response Than Central Pathology. Ophthalmol Science

Keratoconus

- No one will use Kmax any longer, but rather Zonal Values
- Everyone will use Tangential maps in addition to Axial
  - Axial for screening - pattern is larger
  - Tangential (Instantaneous) when evaluating response!
- Recognize that Keratoconus is more central than eccentric

"But when the right thing can only be measured poorly, it tends to cause the wrong thing to be measured, only because it can be measured well. And it is often much worse to have a good measurement of the wrong thing – especially when, as is so often the case, the wrong thing will IN FACT be used as an indicator of the right thing – than to have a poor measurement of the right thing."

John W. Tukey

Professor of Statistics

Princeton University

Known for development of FFT algorithm and box plot

Methodology, and the Statistician's Responsibility for BOTH Acccuracy AND Relevance, *Journal of the American Statistical Association*, Vol 74. No. 368 (Dec., 1979), p 786-793.

Acknowledgements

- Mr. Ashraf Mahmoud

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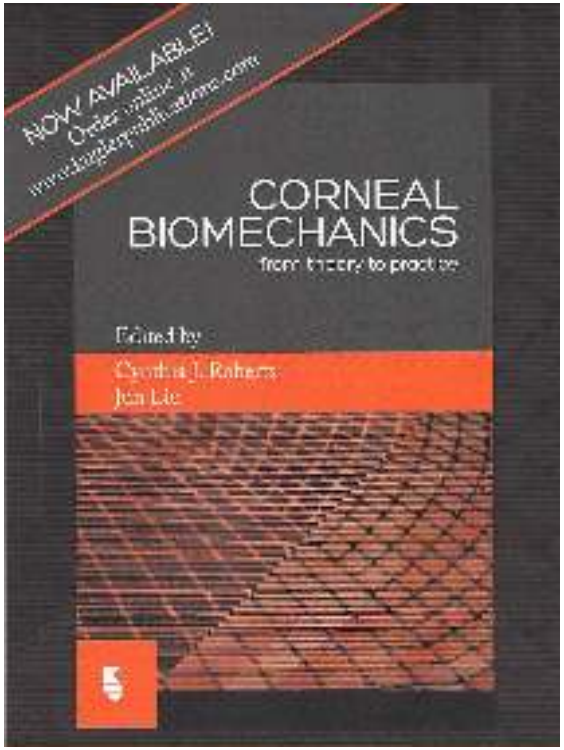
Thank You!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