A Journey through the Biomechanics of the Cornea

Cynthia Roberts, Ph.D.
Professor of Ophthalmology and Biomedical Engineering
Martha G. and Milton Staub Chair for Research in Ophthalmology
The Ohio State University

ESOIRS
May 31, 2012

Disclosure

• Travel funds provided by Carl Zeiss Meditec
• Past Travel funds provided by Sooft Italia
• Consultant to Oculus Optikgerate GmbH
• Consultant to Ziemer Ophthalmic Systems AG
• Equipment provided by Ziemer
• Interest in the Galilei
BC: Before Customization

- Input was subjective refraction: measured in spheres and cylinders.
- Outcome was also measured in spheres and cylinders under high light conditions.
- The post-op shape only had to be "correct" in the center of the cornea!

Beyond Spheres and Cylinders

- Spheres and Cylinders measure the performance of the **CENTRAL CORNEA**
- Higher-order aberrations come from a larger region of the cornea
- Aberration-reducing algorithms **MUST** target a very specific shape over a much larger region of the cornea!
Shape/Power of the Post LASIK Cornea

Can we remove spherical aberration?

How can the final shape be improved?

Why should a refractive and/or corneal surgeon care about biomechanics?

Because corneal biomechanics play a significant role in the visual outcomes of Conventional, Wavefront-Guided, and new refractive and corneal procedures.
What is the Impact of Corneal Biomechanics?

- Biomechanics in Uncomplicated Surgical Procedures
  
  STABLE

- Biomechanical Decompensation:
  
  ECTASIA

What is the Target in Refractive Surgical Procedures?

- CORNEAL SHAPE?

- VISION?
How is the Laser Programmed?

DEPTH PROFILE FOR TISSUE REMOVAL
Conventional, Wavefront, Femtosecond…

SHAPE IS THE TARGET!!!!

What is The Ideal Corneal Shape?

That which produces the ideal wavefront!
Can we achieve the ideal corneal shape with
the ideal wavefront structure?

BIOMECHANICS!

The Normal Cornea

• Crosslinks (x):
  – antero-peripheral distribution
  – interlamellar cohesion
  – couple PST & central curvature

• Stroma = fibers vs matrix
A Mechanical Model of Keratectomy-Induced Flattening

- **Crosslinks (x):**
  - antero-peripheral distribution
  - interlamellar cohesion
  - couple PST & central curvature

- **Stroma** = fibers vs matrix

- **Ablation** ⇒ relaxation
  and peripheral stromal thickening

---

**Biomechanical Central Flattening and Peripheral Steepening**

- **Enhances** a Myopic Procedure
- **Reduces** the effect of a Hyperopic Procedure
- **Flattening** (hyperopic shift) in a “non-refractive” PTK
  - Including the PTK profile in one axis of an astigmatic procedure
- **Induces** unintended para-central and peripheral shape changes that result in aberrations!!

HÖWEVER,

With greater depth of incision, the cornea will decompensate and bulge

Wavefront vs Topography

Wavefront tells you the origin and destination

Shape (topography) tells you the mechanism
Wavefront cannot provide the location of an aberration-producing feature

Example:
COMA

Is the origin of 3rd order coma a central or peripheral feature?

Coma is nonspecific
Understanding Corneal Shape Changes induced by Refractive Surgery

• Increasing our understanding of post-operative shape over the entire cornea, rather than just the central region, will lead to increased success rates in either Conventional or Wavefront-guided procedures.

• 100% of induced aberrations are due to corneal shape changes!

Retrospective Study of Post-Op Shape

• 2,380 myopic LASIK patients with pre-op and 6 months post-op Orbscan topography

• Technolas 217 excimer laser
  – “Optical Zone” sizes ranged from 5.0 to 6.5mm diameter
  – Transition zones extended to 9mm diameter

• Hansatome or Automated Corneal Shaper Microkeratome

• Patients treated at the Hong Kong Sanatorium and Hospital

• Collaborators: Dr. John Chang and the refractive surgery team
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.

Data acquired at the Hong Kong Sanatorium and Hospital

Composite Anterior Difference Maps
Myopic Correction < 2 D

- n = 25
- All regions except outer elevation zone show statistically significant differences from pre-operative state.

Data acquired at the Hong Kong Sanatorium and Hospital
Composite Anterior Difference Maps
Myopic Correction from 2 to 4 D

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

Data acquired at the Hong Kong Sanatorium and Hospital

Composite Anterior Difference Maps
Myopic Correction from 4 to 6 D

- n = 635
- All regions show statistically significant differences from pre-operative state.

Data acquired at the Hong Kong Sanatorium and Hospital
Composite Anterior Difference Maps Myopic Correction from 6 to 8 D

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

Data acquired at the Hong Kong Sanatorium and Hospital

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.

Data acquired at the Hong Kong Sanatorium and Hospital
Composite Anterior Difference Maps
Myopic Correction for > 10 D

Data acquired at the Hong Kong Sanatorium and Hospital

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

Conclusions

- **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
Can the Biomechanical Response be Manipulated?

From John Marshall, Ph.D.
Contra lateral Eyes at 6 months post-op


The Transition Zone is NOT Neutral!!

WHEREVER ablation occurs, corneal structure is altered and the shape is modified
What refractive procedure?

RK? PRK? LASIK? Intrastromal Rings?

Does the Flap Change the Corneal Structure?

- Nearly circumferential severing of lamellae to a depth of approximately 160 microns
  - YES, it changes the structure!

- What about healing?
  - The flap can be lifted years later

- What is the magnitude of the flap response?
A Mechanical Model of LASIK Flap-Induced Central Flattening

- **Crosslinks** (x):
  - antero-peripheral distribution
  - interlamellar cohesion
  - couple PST & central curvature

- **Stroma** = fibers vs matrix

- Cutting the Flap \( \Rightarrow \) relaxation and peripheral stromal thickening (PST)

The Corneal Response to Keratome Incisions
Prospective Studies of Flap Response:

- Pallikaris, et. al.¹
- Porter, et. al.²
- Knorz, et. al. (unpublished)
- Potgeiter, et. al.*
- Krueger, et. al.
- Tran, et. al.*
- Durrie, et al.*

*Special Issue on Corneal Biomechanics JCRS, January 2005


Results to Date:

- Creation of a flap induces aberrations
  - Response in terms of higher order aberrations is inconsistent both across and within studies
    - Microkeratome-created flaps induce different higher order aberrations depending on device manufacturer
    - Femtosecond laser- created flaps have minimal higher order aberration induction
  - Induction of a hyperopic shift is consistent across all, including microkeratomes and femtosecond lasers
What is the Explanation??

• Hyperopic shift due central flattening is consistent with biomechanical model
  – (Note: 2 subjects in the Porter study had enough hyperopic shift from the flap that they elected NOT to have the delayed ablation and dropped out of the study.)

• Flaps created by a microkeratome are not consistent in terms of flap thickness \textit{profile} due to the mechanical nature of the cut – leading to higher order aberrations

• Flaps created by a femtosecond laser are more uniform in thickness – minimizing higher order aberration induction

Flap Response

• A mechanical device does not produce “identical” cuts to the precision required to account for induced wavefront error

• Figure provided by Dan Reinstein, M.D.
Flap Response

- Individual vs Mean Population Response!
- Figure provided by Dan Reinstein, M.D.

What have we Learned?

- Flap thickness is NOT a predictor of flap response
- Bed thickness IS a predictor of flap response
- The shape of the flap is driven by the shape of the underlying bed response!\(^3\)
- The flap profile is important ONLY in how it alters the underlying bed

\(^3\)Potgeiter, et. al., “Predicting Flap Response.” JCRS, January 2005
How is a SMILE cap different from a LASIK flap?

Finite Element Modeling

- To Compare Biomechanical Response, first look at similar flap/cap dimensions; 9mm flap/cap and 100micron thickness

LASIK

ReLEx SMILE
Stress distribution Pre-op vs post Flap/Cap in LASIK/SMILE

• Collaborator:
  – Harald Studer, Ph.D.
  – ISS Integrated Scientific Services AG
    Scientific Consulting and Research
    Senior Software and Biomedical Engineer

Stress distribution Pre-op vs post Flap/Cap in LASIK/SMILE at the level of the Residual Stromal Bed
THE JOURNEY CONTINUES…

• Previous decade devoted to development of new technology to measure ocular wavefront and corresponding wavefront customized procedures

• The Future will be devoted to development of new technology to measure corneal biomechanical properties and Biomechanically Customized procedures!

Clinical Corneal Biomechanics in Crosslinking

Cynthia Roberts, Ph.D.
Professor of Ophthalmology and Biomedical Engineering
Martha G. and Milton Staub Chair for Research in Ophthalmology
The Ohio State University

ESOIRS
May 30, 2012
Disclosure

- Travel funds provided by Carl Zeiss Meditec
- Past Travel funds provided by Sooft Italia
- Consultant to Oculus Optikgerate GmbH
- Consultant to Ziemer Ophthalmic Systems AG
- Equipment provided by Ziemer
- Interest in the Galilei

Oculus CorVis ST

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

8mm horizontal coverage

Constant metered collimated air pulse

Currently undergoing FDA approval process – NOT available in the U.S.
Normal Thick Cornea

Data provided by Renato Ambrosio, MD, PhD

Measurement Parameters

- Uncorrected IOP (IOPu)
- Pachymetry (Pach)
- Deformation Amplitude (Da)
- Radius of Curvature at Highest Concavity (rad-curve-HC)
- Width of Deformation at Highest Concavity (W_dist)
- Inward (V_in) and Outward (V_out) velocities
- First and Second Applanation Lengths (app-length1 and app-length2)
- First and Second Applanation Times (app-time1 and app-time2)
Parameter Definitions

First Applanation

Highest Concavity

Rad-curve-HC, Wdist

Second Applanation

What Influences Deformation?

• Intraocular Pressure!

• Corneal Biomechanical Properties

  • Corneal Thickness
  • Corneal Curvature

Roberts, et al. ARVO 2011
Normal Thin Cornea

IOPcc = 13.3 mmHg

Data provided by Renato Ambrosio, MD, PhD

Keratoconus

IOPcc = 13.7 mmHg

Data provided by Renato Ambrosio, MD, PhD
# Comparison of KCN to Normal Thin – Similar IOPcc and CCT

Data provided by Renato Ambrósio, MD, PhD

Video processing done by Ashraf Mahmoud, BS

Cynthia J. Roberts, Ph.D.

## KCN to NL comparison

Matched IOPcc; n=66 in each group

(Roberts, et al. ARVO 2011)

<table>
<thead>
<tr>
<th></th>
<th>Keratoconus</th>
<th>Normal</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOPcc</td>
<td>14.4 ± 2.2 mmHg</td>
<td>14.4 ± 2.5 mmHg</td>
<td>.927</td>
</tr>
<tr>
<td>Da</td>
<td>1.13 ± .12 mm</td>
<td>1.04 ± .10 mm</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>&quot;Stiffness&quot;</td>
<td>40.6 ± 4.0 mmHg/mm</td>
<td>44.4 ± 4.3 mmHg/mm</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Pachymetry*</td>
<td>475 ± 38 µ</td>
<td>520 ± 25 µ</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>rad-curve-hc*</td>
<td>8.66 ± 1.82 mm</td>
<td>11.47 ± 2.60 mm</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Wdist*</td>
<td>4.82 ± .24 mm</td>
<td>4.82 ± .26 mm</td>
<td>.9572</td>
</tr>
<tr>
<td>Vin*</td>
<td>.23 ± .04 mm/ms</td>
<td>.21 ± .03 mm/ms</td>
<td>.135</td>
</tr>
<tr>
<td>Vout*</td>
<td>-.36 ± .07 mm/ms</td>
<td>-.32 ± .05 mm/ms</td>
<td>.034</td>
</tr>
<tr>
<td>app-length1*</td>
<td>1.73 ± .45 mm</td>
<td>1.99 ± .38 mm</td>
<td>.0008</td>
</tr>
<tr>
<td>app-length2*</td>
<td>1.84 ± .43 mm</td>
<td>2.31 ± .38 mm</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>app-time1*</td>
<td>7.9 ± .4 ms</td>
<td>8.4 ± .5 ms</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>app-time2*</td>
<td>24.1 ± .6 ms</td>
<td>23.8 ± .6 ms</td>
<td>.0024</td>
</tr>
</tbody>
</table>

*significant relationship with "stiffness"
**Rad-curve-hc vs “Stiffness”**

- **KCN**
  - P < .0001
  - $R^2 = .2559$

- **Normal**
  - P < .0001
  - $R^2 = .3886$

- **Together**
  - P < .0001
  - $R^2 = .4403$

---

**W_dist vs Stiffness**

- **KCN**
  - P < .0001
  - $R^2 = .2285$

- **Normal**
  - P < .0001
  - $R^2 = .4775$

- **Together**
  - P < .0001
  - $R^2 = .2918$
Summary

• Increasing pachymetry correlates with increasing “stiffness”
• “Stiffer” corneas have lower velocities
  – initiate deformation later, but recover quicker due to lower depths
• “Stiffer” corneas have greater applanation lengths (2)
• “Stiffer” corneas have flatter curvatures at highest concavity
• “Stiffer” corneas have narrower displacement at depth
  – threshold phenomenon due to spatially distributed source with lower pressure near the edges of the air puff – not enough to displace a stiffer cornea near the edges of the air puff, but enough to displace a softer one

• WITH MATCHED IOPcc:
  – KCN corneas have lower “stiffness” and are thinner than normal
  – KCN corneas have faster recovery velocities
  – KCN corneas have shorter applanation lengths
  – KCN corneas have greater deformation depths (stiffness and thickness)
  – KCN corneas have greater curvature at depth

What Have We Learned About the Biomechanical Behavior of the Cornea in Keratoconus?
Purpose

• It has been reported\(^1\) that surface area is conserved between normal (NL) and keratoconic (KCN) corneas, indicating redistribution of surface area rather than bulging in keratoconus, except in cases of advanced disease where surface area increases.

• The purpose of the current study was to evaluate corneal arclength prior to and during deformation in KCN and NL corneas.


Methods

• Subjects
  – 16 eyes of 10 NL subjects
  – 15 eyes of 14 subjects with moderate KCN
    • Pre-op subjects recruited for corneal crosslinking study

• Groups were statistically compared with t-tests for all parameters.
Devices
(Minimum of 3 repeat exams per device)

• Intraocular Pressure (IOP) measured by:
  – PASCAL Dynamic Contour Tonometry (DCT)
    • Ziemer, Port, Switzerland
    • Quality 3 or better accepted
  – Ocular Response Analyzer (ORA)
    • Reichert, Buffalo, NY
    • IOPcc (corneal compensated IOP)

• CorVis ST
  – Oculus, Wetzlar, Germany
  – Corneal Arc Length

Corneal Arc Length

• Central 6mm of the horizontal meridian
• Maximum and minimum arc lengths were extracted from a series of images during a single exam
• Initial and final arc lengths were extracted
• Δarc length was calculated as the difference between maximum and minimum values.
Arclength Measurement

Central 6mm arclength

Maximum and Minimum Arclengths extracted within central 6mm

$\Delta$arclength calculated as maximum minus minimum
What Do We Expect?

• Arclength will shorten to applanation

• Arclength will subsequently lengthen…..

Model Orientation: In Plane

1. The model shortens to inward applanation point (black)
2. Then lengthens to concavity (green)
3. Then shortens to outward applanation point (black)
4. Then lengthens back to its normal convex State

Validation with Corneal Phantom

Corneal Phantom Deforming under an ORA Pulse

Images acquired by Dianne Henry Glass
Corneal Phantom Deforming under an ORA Pulse

Images acquired by Dianne Henry Glass
Corneal Phantom Deforming under an ORA Pulse

Images acquired by Dianne Henry Glass

Corneal Phantom Deforming under an ORA Pulse

Images acquired by Dianne Henry Glass
Corneal Phantom Deforming under an ORA Pulse

Images acquired by Dianne Henry Glass
Corneal Phantom Deforming under an ORA Pulse

Images acquired by Dianne Henry Glass
Corneal Phantom Deforming under an ORA Pulse

Images acquired by Dianne Henry Glass
In Vivo Corneal Measurements

Comparison of KCN to Normal Thin – Similar IOPcc and CCT

Data provided by Renato Ambrosio, MD, PhD

Video Processing by Ashraf M. Mahmoud
In Vivo Results....

Corneal Deformation with an Air Puff

• Corneal length as a function of time
  – Shortens as it deforms
  – Predicted by Steve Klyce, Ph.D.

• Distance between bending points (Wdist) as a function of time
  – Increases from start to maximum depth
  – Because the cornea does not stretch, it pulls more of the cornea into the deformation
In Vivo: Corneal Edges Extracted from Each of ~ 140 images in 35ms

The arclength at the initial state (up and over the top) is GREATER than the arclength at the maximum depth (down and back up).

In Vivo Results

- All eyes decreased in arclength from initial state to applanation, and then continued to decrease to maximum deformation.
- Maximum arclength corresponded to initial state and minimum arclength corresponded to maximum deformation.
- No difference was found in maximum (p=0.42) or minimum (p=0.96) arclength during deformation between NL and KCN groups.
- Δarclength was statistically greater in normal eyes (p < 0.032)
  - NL (0.124 ± 0.050mm)
  - KCN (0.093 ± 0.019mm).
- IOP was not different between groups using DCT (p=0.24) or ORA (p=0.10).
Does the Corneal Surface Experience Lateral Movement within the 6mm Window?

- Human Donor Eyes
- Sutures
- Trephine Cuts

Surface Suture Tracking
Surface Trephine Cuts
How Does the Arclength Shorten?
When the anterior surface is inverted, the posterior lamellae are put under tension and the anterior surface is forced into wrinkles → the arc length shortens.

Slide Courtesy of Steve Klyce, Ph.D.

When the cornea swells, the inner fibers relax and are thrown into waves


Slide Courtesy of Steve Klyce, Ph.D.
At normal hydration, collagen fibers are uniformly stressed.

When the cornea swells, posterior lamellae are thrown into waves.
With Swelling, Posterior Arclength becomes shorter

Posterior lamellae are thrown into waves to compensate for the shortened arclength

What Does This Mean in Keratoconus?

• Remember the Inspiration:


• Conservation of Surface Area in Keratoconus
Keratoconus

- Characterized by BOTH extremely high curvature regions AND extremely flat regions

Proposal for Biomechanical Progression in Keratoconus

**Focal** Reduction in Modulus of Elasticity (Focal Weakness)
Proposal for Biomechanical Progression in Keratoconus

*Focal* Reduction in Modulus of Elasticity
Greater deformation in weak region

**Biomechanical Cycle of Decompensation in Ectasia**

- Increased Curvature (Redistribution)
- Focally Reduced Modulus of Elasticity
- Increased Strain (Focal Thinning)
- Redistribute Stress
Redistribution

Local increase in curvature, surrounded by flattening, **WITHOUT** measureable increase in surface segment length

Microstrain in the area of the cone, rather than macroscopic bulging

---

Scheimpflug Image of Keratoconus

- Note the lack of bulging
- There appears to be a redistribution...
- Small change in elevation results in a large increase in curvature!

Slide Courtesy of Dr. Renato Ambrósio Jr
Conclusions

• A consistent decrease in arclength during deformation within the central 6mm of the cornea in both NL and KCN is consistent with conservation of arclength across the cornea.

• Results imply a redistribution of corneal mass in both normal corneas and those with keratoconus, without measurable central corneal strain under the applied load investigated.

• This is consistent with conservation of surface area and a bending vs bulging theory of shape change in keratoconus.

What happens in Crosslinking?
Topcon-Sponsored CXL Study at The Ohio State University

• Substudy
  – CorVis ST before and after CXL
  – KCN and ectasia combined to examine effect of crosslinking

• Subjects
  – 11 with one month data in treatment group
  – 8 in sham group

<table>
<thead>
<tr>
<th></th>
<th>PRE</th>
<th>POST-CXL</th>
<th>delta</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXL (n = 11)</td>
<td>-3.551mm</td>
<td>-4.036mm</td>
<td>-0.485 ± 0.369mm</td>
<td>0.0014</td>
</tr>
<tr>
<td>SHAM (n = 8)</td>
<td>-3.540mm</td>
<td>-3.595mm</td>
<td>-0.055 ± 0.384mm</td>
<td>0.6981</td>
</tr>
</tbody>
</table>
Stiffness: Resistance to Bending
3-Point Beam Bending

\[ S = \frac{M}{b \cdot k} \]

- \( M \) = bending moment (Force x length)
- \( b \) = width of beam
- \( k \) = curvature (a function of deflection)

Deformed Curvature vs Time

- **CXL**
  - The post-CXL stiffer cornea (red) is less curved during deformation than pre-CXL (blue)
- **Control**
  - No difference in curvature during deformation
Pre and Post topography-guided PRK plus CXL in Keratoconus

- Pre:

- Post:
  10 months

Data provided by Renato Ambrosio, MD, PhD

Pre vs Post topography-guided PRK plus CXL in Keratoconus: Direct Comparison

Note:
greater stability in post-op “blue” image than in pre-op “red” image

Data provided by Renato Ambrosio, MD, PhD
Summary

- Corneal Collagen Crosslinking modifies biomechanical response of the cornea, as measured by the CorVis ST

- Topographic Response requires more time to manifest

Quest for In Vivo Corneal Stiffness Continues……..

THANK YOU!
Posterior Surface

Composite Posterior Difference Maps for Entire Population

- n = 2,380
- All regions show statistically significant differences from pre-operative state.

Data acquired at the Hong Kong Sanatorium and Hospital
Composite Posterior Difference Maps Myopic Correction from < 2 D

- $n = 25$
- For elevation and tangential curvature, only the intermediate regions were significantly different from pre-op.

Data acquired at the Hong Kong Sanatorium and Hospital

Composite Posterior Difference Maps Myopic Correction from 2 to 4 D

- $n = 321$
- All regions except inner elevation and intermediate axial zones show statistically significant differences from pre-operative state.

Data acquired at the Hong Kong Sanatorium and Hospital
Composite Posterior Difference Maps
Myopic Correction from 4 to 6 D

- n = 635
- All regions show statistically significant differences from pre-operative state.

Data acquired at the Hong Kong Sanatorium and Hospital

Composite Posterior Difference Maps
Myopic Correction from 6 to 8 D

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

Data acquired at the Hong Kong Sanatorium and Hospital
Composite Posterior Difference Maps
Myopic Correction from 8 to 10 D

- n = 465
- All regions show statistically significant differences from pre-operative state.

Data acquired at the Hong Kong Sanatorium and Hospital

Composite Posterior Difference Maps Myopic Correction for > 10 D

- n = 311
- All regions except outer pachymetry zone show statistically significant differences from pre-operative state.

Data acquired at the Hong Kong Sanatorium and Hospital
Central Decompensation?

- Gryzbowski, et. al., JCRS, January 2005

Forward Vault?

- Gryzbowski, et. al., JCRS, January 2005
Inward Peripheral Movement?

Pre-op Posterior Surface
Post-op Posterior Surface

- Gryzbowski, et. al., JCRS, January 2005

Peripheral Fit of Pre and Post-Op Surfaces

- Average difference map of 2380 LASIK patients
- Consistent with *backward movement model*.
- STABLE Remodeling!

Gryzbowski, et. al., JCRS, January 2005
Posterior Surface

Patient Data is consistent with *Peripheral Inward* Movement, **NOT** outward central movement!!

Stable Remodeling!!!!!!!!!!!!!!!!

• Gryzbowski, et. al., JCRS, January 2005

---

**Nishimura, et al.: Methods**

• 161 eyes of 83 subjects had Pentacam topography
  – Pre-op, 1 week and 1 month post-op

• Subset of 84 eyes of 42 subjects also had Orbscan
  – Pre-op, 1 month post-op

• LASIK for myopia or myopic astigmatism
- No change in ACD

The ACD Significantly DECREASES at 1 week

Mean:
-0.045mm
p < 0.0001
The ACD Remains Significantly DECREASED at 1 month, but LESS

Mean:
-0.026mm
p < 0.0035

Posterior Surface

• There is a stable change in the posterior surface after LASIK that resolves over time.

• It is important to recognize NORMAL post-operative shape in order to be able to recognize ABNORMAL which does NOT resolve over time.
  – Potential to recognize EARLY on posterior surface….

• Shown with Orbscan, Pentacam, and GALILEI*

Imaging with Artemis

- Induced change in stromal thickness after refractive surgery, demonstrating increased thickness in the peripheral region


Why are Corneal Biomechanics Important?

- Scientific Curiosity?
- Improve Prediction of Refractive Outcomes?
- Identify patients at risk for iatrogenic ectasia?
- Accurate measurement of IOP?
- Biomechanics in glaucoma?
- Other new ideas?

Measurement of IOP
GAT Assumptions

• The contribution of the cornea is negligible????????????

  – CORNEAL CURVATURE
  – CENTRAL CORNEAL THICKNESS (CCT)
  – CORNEAL BIOMECHANICAL PROPERTIES

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
WHY has the influence of corneal thickness been recognized?

- Because it can be measured!!

Correcting IOP for Corneal Thickness

- 5 mmHg/70 µm  
  - Ehlers (1975)

- 2.5 mmHg/50 µm  
  - Doughty & Zaman

- 2.0 mmHg/100 µm  
  - Whitacre (1993)

- And OTHERS!

Why are they all different??

Ehlers N, Bramsen T & Sperling S.  
Applanation tonometry and central corneal thickness.  

Doughty MJ. Zaman ML  
Human corneal thickness and its impact on intraocular pressure measures: a review and meta-analysis approach.  

Whitacre MM, Stein R.  
The effect of corneal thickness on applanation tonometry.  
Measured IOP after Refractive Surgery

- Average Drop in IOP:
  - 0.46 mmHg per 10 μm (NCT)
    - Chatterjee et al. Ophthalmology 1997;104:355-9
  - 0.71 mmHg per 10 μm (GAT)
    - Cennamo et al. Ophthalmologica 1997;211:341-3

Why are they all different??

Clinical Implications of Correcting IOP for Corneal Thickness

Which one (if any) is the “correct” one??

Something is affecting accuracy of pressure measurement, IN ADDITION to 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

What is the magnitude of the measurement error in GAT if the curvature, thickness, and corneal properties (modulus of elasticity) vary from the basic assumptions of Goldmann?

Theoretical Model
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

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.

\[ \text{Difference} = 8.68 \text{mmHg} \]
\[ \text{Difference} = 2.84 \text{mmHg} \]
Modulus of Elasticity **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!!
LASIK for Myopia and Myopic Astigmatism Pre-Op and 3 Month post-op IOP

- $N = 8,113$
- mean diff IOP
  - $\sim -2\text{mmHg}$
- mean diff sph equiv
  - $\sim -5\text{diopters}$
- $R^2 = 0.009$
- $P < 0.001$
- Slope = $-0.12\text{mmHg/diopeter}$

Chang and Stulting, Ophthalmology, 2005.

Is There a Better Technique to Measure IOP?

Is There a Method to Determine Biomechanical Properties?
Pascal Dynamic Contour Tonometer (DCT)

- Manufactured by Ziemer Ophthalmic Systems AG
  - Reduces the impact of biomechanical properties and central corneal thickness in the measurement of IOP\(^1\)
    - 7mm spherically-shaped contact probe
    - External corneal forces are equalized to internal corneal forces
    - External pressure sensor
  - No significant change in IOP measurement between pre and post-op LASIK\(^2,3\)


Ocular Response Analyzer (ORA)

- Manufactured by Reichert
  - Accounts for change in Properties, leading to more accurate IOP measurement\(^1,2\)
  - Also Measures Biomechanical Visco-elastic Response:
    - Corneal Hysteresis - CH
    - Corneal Resistance Factor – CRF
  - Biomechanical Corneal Response may be altered from Normal:
    - Hysteresis DECREASES after refractive surgery\(^1\)
    - Hysteresis is significantly LOWER in Keratoconic population than normal\(^1\)

\(^1\)Luce, *JCRS*, 2005; 31:156-162.
THE ABILITY TO MEASURE BIOMECHANICAL PROPERTIES IN VIVO IN AN UNDERSTANDABLE WAY
The Clinician Could not be Concerned about Image Quality before the Development of the Wavefront Sensor

How are Biomechanical Properties Measured?

• RESPONSE to an applied force:
  – Applying a force on corneal strips and measuring strain or deformation
  – Inflation tests on whole globe and measuring strain or deformation
  – Etc.

• Previously NOT possible on a living eye
Is There a Clinical Method to Determine Biomechanical Properties?

Reichert Ocular Response Analyzer (ORA)

- The ORA is similar to a non-contact tonometer in that an air-jet is used to appplanate the cornea.

- The ORA is different than a non-contact tonometer in that additional measurements are acquired.

High Speed Imaging in Humans

Images acquired by Dianne Henry Glass, MD/PhD

Cynthia J. Roberts, Ph.D.

Biomedical Engineering

IR Source
Air Puff
Detector

Images acquired by Dianne H. Glass

Illustration © Gatin
gatinel@aol.com

Foundation Rothschild
Images acquired by Dianne H. Glass
Images acquired by Dianne H. Glass
Images acquired by Dianne H. Glass
Measurements Produced by the ORA

- **IOPg**: Goldmann Correlated IOP
  - Analogous to Goldmann Tonometry
  - Average of P1 and P2
- **IOPcc**: Corneal Compensated IOP
  - Less affected by corneal thickness and properties
  - Empirically Determined Linear combination of P1 and P2
- **CH**: Corneal Hysteresis
  - Viscoelastic Response
  - Difference of P1 and P2
- **CRF**: Corneal Resistance Factor
  - Viscoelastic Response weighted for Elasticity
  - Empirically Determined Linear combination of P1 and P2
In Vivo: Ocular Response Analyzer

- Corneal Hysteresis (CH)
  - NOT Elastic Modulus!
  - VISCOelastic parameter
    - Same CH can be measured with multiple combinations of both elasticity and viscosity

- Low Hysteresis is associated with:
  - Soft cornea (ex. keratoconus, post-LASIK)
  - Stiff cornea (ex. older cornea, high IOP)
What is on the Horizon?

Device #1: Oculus CorVis ST

Ultra High-Speed (UHS) Scheimpflug camera
- 4,330 frames per second

8mm horizontal coverage

Constant metered collimated air pulse

Currently undergoing FDA approval process – NOT available in the U.S.
Normal Thick Cornea

Data provided by Renato Ambrosio, MD, PhD