Clinical Applications of Corneal Optical Coherence Tomography

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Financial Interests:
Dr. D. Huang has a significant financial interest in Optovue, a company that may have a commercial interest in the results of this research and technology. This potential individual conflict of interest has been reviewed and managed by OHSU.
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Carl Zeiss Meditec, Inc.: patent royalty

New OCT Technology Lead to An Explosion of New Products for Anterior Segment Imaging

Zeiss Visante
Zeiss Cirrus
Optovue RTVue
Optovue iVue
Bioptigen Envisu
Heidelberg SL-OCT
Heidelberg Spectralis
Tomey CASIA
Optopol Copernicus

David Huang, MD, PhD www.COOLLab.net
Anterior Segment OCT Systems

Dedicated systems scan wider (12-16 mm) and deeper (6-7 mm)
- Zeiss Visante
- Heidelberg SL-OCT
- Tomey CASIA

Systems converted from retinal scanners have limited scan ranges (~6mm width & 2mm depth)
- Optovue RTVue
- Optovue iVue
- Zeiss Cirrus
- Heidelberg Spectralis
- Bioptigen Envisu
- Optopol Copernicus

Wavelength Matters

- 1310 nm gives deeper penetration.
  (Axial resolution: 17-18 µm)
  - Zeiss Visante
  - Heidelberg SL-OCT
  - Tomey CASIA

- 830 nm systems have higher axial resolution.
  (Axial resolution: 3-5 µm)
  - Optovue RTVue
  - Optovue iVue
  - Zeiss Cirrus
  - Heidelberg Spectralis
  - Bioptigen Envisu
  - Optopol Copernicus

David Huang, MD, PhD  www.COOLab.net
Better penetration at 1310 nm
Greater resolution achieved w/ 830 nm systems

![1310 nm](image1) ![830 nm](image2)

- Scleral spur
- Angle recess
- Schwalbe's line
- Endothelium

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**Fourier vs. Time Domain**

- **Time domain systems** are slower
  - Zeiss Visante (2 kHz)
  - Heidelberg SL-OCT (200 Hz)
- **Fourier domain systems** are much faster
  - Optovue RTVue (26 kHz)
  - Optovue iVue (26 kHz)
  - Zeiss Cirrus (27 kHz)
  - Heidelberg Spectralis (40 kHz)
  - Bioptigen Envisu (17 kHz)
  - Optopol Copernicus (20 kHz)
  - Tomey CASIA (30 kHz)
Clinical Applications of Corneal OCT

LASIK planning  Keratoconus Detection  FS Laser AK

Guiding PTK  IOL Power Calculation  Intacs

Keratoconus Diagnosis with OCT

Yan Li, PhD  Bing Qin, MD, PhD
Forme fruste keratoconus is the most important risk factor for post-LASIK corneal ectasia

Topography does not screen out all eyes at risk

<table>
<thead>
<tr>
<th>Topography</th>
<th>Normal</th>
<th>Suspicious</th>
<th>Abnormal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td># Ectasia Cases</td>
<td>25</td>
<td>27</td>
<td>33</td>
<td>93</td>
</tr>
<tr>
<td>Percent</td>
<td>27%</td>
<td>29%</td>
<td>41%</td>
<td>100%</td>
</tr>
</tbody>
</table>


OCT could provide more accurately map corneal thickness, epithelial thickness, and corneal cuvatures

RTVue (Optovue, Inc.)

David Huang, MD, PhD www.COOLlab.net
Corneal Mapping over 8 Meridians (8 x 1019 A-scans) in 0.31 Second

- RTVue FD-OCT (Optovue, Inc.)

Detecting Keratoconic Thinning with OCT Pachymetric Indices

- General thinning
  - Min
- Focal thinning
  - Minimum - median
- Asymmetric thinning
  - I-S
  - IT-SN
  - Y location of the Min

Minimum = 404 μm
Y = -710 μm

Visante Prototype (Carl Zeiss Meditec, Inc.)

OCT Keratoconus Pachymetric Variables

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Explanation</th>
<th>Keratoconus Cutoff (1 percentile)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IT-SN</td>
<td>Average thickness of the IT octant minus that of the SN octant</td>
<td>&lt; -51 μm</td>
</tr>
<tr>
<td>I-S</td>
<td>Average thickness of the inferior (I) octant minus that of the superior (S) octant</td>
<td>&lt; -49 μm</td>
</tr>
<tr>
<td>Min</td>
<td>Minimum corneal thickness</td>
<td>&lt; 455 μm</td>
</tr>
<tr>
<td>Min - Med</td>
<td>Minimum corneal thickness-median corneal thickness</td>
<td>&lt; -29 μm</td>
</tr>
<tr>
<td>Y Min</td>
<td>Y coordinate of minimum corneal thickness</td>
<td>Y &lt; -1.35 mm</td>
</tr>
</tbody>
</table>

Based on 66 normal and 52 keratoconus subjects from the following:
- David Huang, MD, PhD, Doheny Eye Institute, Los Angeles
- Qinmei Wang, MD, Wenzhou Medical College, Wenzhou
- Robert Brass, MD, Brass Eye Center, New York
- RTVue FD-OCT (Optovue, Inc.)

Yan Li, PhD; David Huang, MD, PhD  www.COOLLab.net

OCT pachymetry map-based keratoconus score table

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum</td>
<td>&gt;499</td>
<td>499~476</td>
<td>475~455</td>
<td>&lt;455</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum-Median</td>
<td>&gt;-21</td>
<td>-22~25</td>
<td>-26~29</td>
<td>&lt;29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-S</td>
<td>&gt;-30</td>
<td>-30~40</td>
<td>-41~49</td>
<td>&lt;50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IT-SN</td>
<td>&gt;-33</td>
<td>-33~42</td>
<td>-43~51</td>
<td>&lt;51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y location of the min</td>
<td>&gt;-734</td>
<td>-734~1069</td>
<td>-1070~1353</td>
<td>&lt;1353</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Keratoconus Risk Score

Each variable will be assigned a score of 1, 2, 3 if it exceeds 20, 5, 1 percentile thresholds. The keratoconus risk score of the eye is the summation of all scores.

Keratoconus risk score = \(0\sim1: \text{low risk;}\)
\[2\sim3: \text{moderate risk;}\]
\[\geq4: \text{high risk.}\]

Yan Li, PhD; David Huang, MD, PhD  www.COOLLab.net
Histogram of the Keratoconus Score

Diagnostic criterion:
Keratoconus score ≥ 4

Sensitivity = 86%
Specificity = 94%
AROC = 0.951

Epithelial Thinning Over Cone

Epithelial Thickness  Pachymetry  Axial Power

Epithelial mapping software pending FDA Approval
Epithelial Thickness Map by FD-OCT

- 2 group of subjects: normal and keratoconus
- Exclusion criteria: eyes with late keratoconic changes such as scar or hydrops

Epithelial Map Repeatability

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Central</th>
<th>Superior</th>
<th>Inferior</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>103</td>
<td>0.7 µm</td>
<td>0.8 µm</td>
<td>0.7 µm</td>
</tr>
<tr>
<td>Keratoconus</td>
<td>35</td>
<td>1.0 µm</td>
<td>1.0 µm</td>
<td>1.0 µm</td>
</tr>
</tbody>
</table>

pooled standard deviation (SD)

Average epithelial thickness maps show inferotemporal thinning

**Epithelial Map Variables**

- Minimum epithelial thickness in µm
- Minimum – maximum (MIN-MAX) focal thinning in µm
- Map standard deviation (MSD) in µm
- Pattern standard deviation (PSD)

<table>
<thead>
<tr>
<th></th>
<th>Minimum</th>
<th>MIN-MAX</th>
<th>MSD</th>
<th>PSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>45.9 ± 4.7</td>
<td>-8.9 ± 3.4</td>
<td>2.1 ± 0.7</td>
<td>0.031 ± 0.008</td>
</tr>
<tr>
<td>Keratoconus</td>
<td>40.0 ± 6.0*</td>
<td>-18.7 ± 8.0*</td>
<td>4.7 ± 2.0*</td>
<td>0.105 ± 0.030*</td>
</tr>
<tr>
<td>AROC</td>
<td>0.84</td>
<td>0.88</td>
<td>0.89</td>
<td>1.0</td>
</tr>
</tbody>
</table>

* Statistically significant difference was detected between normal and keratoconic eyes. AROC = area under the receiver operating characteristic curve.

Yan Li, PhD; David Huang, MD, PhD  www.COOLLab.net
Pattern Standard Deviation (PSD) of epithelial map was highly accurate in *forme fruste* keratoconus (FFK) detection

- Pilot study
  - 17 FFK eyes
  - 17 normal eyes

- AROC = 1.0 for FFK detection
  - 100% sensitivity
  - 100% specificity

Conclusions

- OCT measures many variables that provide accurate keratoconus diagnosis
  - Pachymetry map variables
  - Epithelial thickness map variables
  - Anterior curvature
  - Posterior curvature
OCT for the LASIK surgeon

Flap thickness varies from setting

IntraLase 120 µm setting

138-165 µm

RS035KA, OD

117-131 µm

RSAA, OS

David Huang, MD, PhD www.COOLLab.net
OCT Flap & Bed Thickness Measurements are Precise

1 week post-iLASIK

<table>
<thead>
<tr>
<th>Position</th>
<th>-2,5mm</th>
<th>-1,5mm</th>
<th>-0,5mm</th>
<th>+0,5mm</th>
<th>+1,5mm</th>
<th>+2,5mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>POOLED SD (μm)</td>
<td>2.3</td>
<td>1.3</td>
<td>3.1</td>
<td>3.0</td>
<td>2.0</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Consecutive series of 17 eyes of 10 patients, Intralase 110 μm setting

David Huang, MD, PhD  www.COOLLab.net

Routinely use OCT to check flap thickness one week after LASIK and calculate statistical upper bound

- Intralase 110 μm setting (my surgeries)
- OCT measurements in 21 eyes
  - Mean = 124 μm
  - standard deviation (SD) = 7 μm
- Upper bound = mean + 2 SD = 138 μm
  - < 5% of flaps will exceed this thickness

David Huang, MD, PhD  www.COOLLab.net
Before enhancement, use OCT to predict residual stromal bed thickness

Residual bed thickness = 451 – 143 – 37 = 271 µm

Ablation depth

OCT map minimum

Central flap thickness

>250

Post-LASIK interface fluid & epithelial ingrowth

Epithelial ingrowth

Fluid

Fibrosis

Planning Phototherapeutic Keratectomy

Not A Candidate for PTK

Full thickness scar -> PK needed
Nodular degeneration is peeled

Nodular scar above Bowman’s layer

Peel and then polish using laser with masking agent

Example: Granular Corneal Dystrophy

Before PTK

UCVA: 20/80-1
MR: -2.00+2.00x100°

BSCVA: 20/50-2
Sim-K: 42.2/44.8@98°
**PTK Simulation**

- Transepithelial PTK
  - 6.0 mm AZ circle, 64µm
- Refractive correction
  - -3D + 2.2D x 100°
  - 6mm x 4.5mm

Simulation software is experimental and not commercially available

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**Comparison of Simulated and Actual PTK Outcome**

*en face*

- **Before PTK**
- **Post-PTK Slitlamp photo**
- **Simulated Outcome**
- **Actual Outcome**

Yan Li, PhD; David Huang, MD, PhD  [www.COOLLab.net](http://www.COOLLab.net)
Comparison of simulated and actual PTK outcome in cross-section

Before PTK

Simulated Outcome

Actual Outcome

OCT ablation efficiency analysis

- VISX S4 excimer laser
- Laser ablation efficiency
  \[
  \text{Laser ablation efficiency} = \frac{\text{actual ablation depth}}{\text{nominal ablation setting}}
  \]
- **Central** (average within 1 mm diameter): 120%
- **Periphery** (5 mm diameter ring): 126%

David Huang, MD, PhD [www.COOLab.net](http://www.COOLab.net)
Epithelial thickness profile predicts spherical equivalent refractive change

\[
\text{Refractive change} = -0.29 + 0.141 \times (\text{PTK depth} - \text{CET}) - 0.159 \times (\text{CET-PET}) - \text{refractive ablation setting}
\]

CET = central epithelial thickness
PET = peripheral epithelial thickness

OCT is Useful in PTK Planning

- Is PTK the best option?
  - Deep opacity \(\rightarrow\) keratoplasty is needed
  - Opacity above Bowman’s layer \(\rightarrow\) peel

- Plan transepithelial ablation
  - Measure opacity depth
  - Measure actual laser ablation depth
  - Calculate ablation needed to remove opacity
  - Measure epithelial thickness distribution
  - Predict refractive outcome
Intraocular Lens Power Calculation

The problem with keratometry after laser vision correction

The extrapolation no longer works!
OCT-based IOL Power Formula

Position | Vergence (D)
--- | ---
Back of IOL | \( V_1 = \frac{1000}{(AL-ELP-CCT-0.15)/n_2} \)
Front of IOL | \( V_1' = V_1 - \text{IOL power} \)
Back of cornea | \( V_2 = \frac{1000}{[1/V_1'] + (ELP+CCT)/n_2} \)
Front of cornea | \( V_2' = V_2 - \text{ECP} \)

\( n_2 \) = refractive index of vitreous and aqueous (1.336)

AL = axial eye length (mm)
ELP = effective lens position (mm)
CCT = central corneal thickness (mm)
ECP, effective corneal power (D)

\[ ELP = 0.711 \times (ACD-CCT) - 0.25 \times Pp + 0.623 \times AL_{adj} + pACD - 8.11 \]

ACD = Anterior chamber depth (mm)
CCT = Central corneal thickness (mm)
Pp = posterior corneal power (D)
\( AL_{adj} = \sqrt{AL + 0.8(24.4-AL)} \), if AL < 24.4mm
\( pACD = ACD_{-constant} \)
\[ pACD = \frac{[(A-constant\times0.5663)-65.6+3.595]}{0.9704} \]


Input Variables

1) ACD – anterior chamber depth
2) AL – axial eye length
3) Net corneal power
4) Anterior corneal power
5) Posterior corneal power
6) Central corneal thickness

Partial coherence biometer (e.g. IOL-Master, Carl Zeiss Meditec) or ultrasound A-scan

Fourier-domain OCT (RTVue, Optovue, Inc.)
Prospective clinical study on post-laser vision correction cataract surgery

<table>
<thead>
<tr>
<th>Clinical Site</th>
<th>Myopic LVC (eyes)</th>
<th>Hyperopic LVC (eyes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cullen Eye Institute</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Doheny Eye Institute</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>22</strong></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>

LVC = laser vision correction

Postoperative manifest refraction spherical equivalent was evaluated at 1 month


Accuracy of OCT-based IOL power calculation compared with Haigis-L after myopic LVC

<table>
<thead>
<tr>
<th>Keratometry Method</th>
<th>IOL Formula</th>
<th>Prediction Error (D)</th>
<th>Range (D)</th>
<th>MAE (D)</th>
<th>Within 1D</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOL-Master</td>
<td>Haigis-L</td>
<td>-0.35 ± 0.94</td>
<td>(-2.32, 1.30)</td>
<td>0.73</td>
<td>73%</td>
</tr>
<tr>
<td>OCT</td>
<td>OCT</td>
<td>0.07 ± 0.80</td>
<td>(-1.24, 2.15)</td>
<td>0.57</td>
<td>82%</td>
</tr>
</tbody>
</table>

p = 0.19. n = 22 eyes of 16 subjects.
Accuracy of OCT-based IOL power calculation compared with other methods after myopic LVC at the Doheny Eye Institute

<table>
<thead>
<tr>
<th>Keratometry Method</th>
<th>IOL Formula</th>
<th>Prediction Error (D)</th>
<th>Range (D)</th>
<th>MAE (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical History</td>
<td>Hoffer-Q</td>
<td>0.31 ± 2.52</td>
<td>-1.47 to 2.09</td>
<td>1.78*</td>
</tr>
<tr>
<td>CL Overrefraction</td>
<td>Holladay II</td>
<td>0.01 ± 2.08</td>
<td>-3.09 to 3.19</td>
<td>1.46*</td>
</tr>
<tr>
<td>IOL-Master</td>
<td>Haigis-L</td>
<td>-0.28 ± 1.19</td>
<td>-2.32 to 0.98</td>
<td>0.88</td>
</tr>
<tr>
<td>Orbscan II</td>
<td>Holladay II</td>
<td>0.17 ± 1.61</td>
<td>-2.72 to 1.51</td>
<td>1.28</td>
</tr>
<tr>
<td>OCT</td>
<td>OCT-based</td>
<td>0.49 ± 0.64</td>
<td>-0.33 to 1.58</td>
<td>0.60</td>
</tr>
</tbody>
</table>

*p<0.05 compared to OCT.
N = 10 eyes.
The standard IOL formula that provided the smallest MAE was used for all keratometry methods except OCT.

OCT-based IOL calculation was significantly better than clinical history and contact lens over-refraction methods.

Maolong Tang, PhD, David Huang, MD, PhD www.COOLLab.net

Conclusion

- The predictive accuracy of OCT-based IOL power calculation is equal to or better than current standards for post-LVC eyes.
- More improvement are possible
  - Aberration measurement or ray tracing
  - Better prediction of IOL position
  - Prediction of astigmatism outcome

Maolong Tang, PhD, David Huang, MD, PhD www.COOLLab.net
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Jason Tokayer, MS
Kathleen S. Torok, MA
New Technologies from The Laboratory

HIGHER SPEED
GREATER DEPTH RANGE

Anterior Segment Imaging and Extraction of Biometric Parameters

- James G. Fujimoto, Massachusetts Institute of Technology

Volumetric OCT data → OCT registration → 3D refraction correction → 3D OCT biometry
I. Grulkowski et al., *Volumetric anterior segment biometry using OCT registration and refraction correction techniques*, manuscript in preparation

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I. Grulkowski et al., *Volumetric anterior segment biometry using OCT registration and refraction correction techniques*, manuscript in preparation
360° Anterior Chamber Angle Survey

I. Grulkowski et al., *Volumetric anterior segment biometry using OCT registration and refraction correction techniques*, manuscript in preparation

Anterior Segment Imaging Using VCSEL

- VCSEL technology
- Long coherence length

Full Eye Imaging for Non-Contact Ocular Biometry

**Intraocular Distances**

- Central Corneal Thickness: 0.527±0.003mm
- Aqueous Depth: 3.305±0.030mm
- Anterior Chamber Depth: 3.831±0.029mm
- Lens Thickness: 3.880±0.030mm
- Vitreous Depth: 18.674±0.018mm
- Axial Eye Length: 26.384±0.016mm

Speckle free imaging – cornea in-vivo

- **a.** Epithelium & Bowman’s Layer
- **b.** Endothelium
- **c.** Epithelium & Bowman’s Layer
- **d.** Endothelium


Courtesy of Maciej Wojtkowski, Nicolaus Copernicus University, Torun, Poland
Speckle free imaging – eye lens in-vivo

Segmented tomogram
Segments: 1000
Averaging: 16
Tomo. lines: 1000
Acq. time: 250 ms

Capsule
Epithelium

Corneal Penetrating Keratoplasty

<table>
<thead>
<tr>
<th>Corneal Topography</th>
<th>Placido Tomography</th>
<th>Scheimpflug camera</th>
<th>SS-OCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keratoplasty</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior surface</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K1 (ax)</td>
<td>38.38 D (165°)</td>
<td>9.64 mm 43.8 D (56.8°)</td>
<td></td>
</tr>
<tr>
<td>K2 (ax)</td>
<td>43.88 D (80°)</td>
<td>7.98 mm 42.3 D (56.9°)</td>
<td></td>
</tr>
<tr>
<td>Posterior surface</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K1 (ax)</td>
<td>9.64 mm 45.8 D (146°)</td>
<td>6.82 mm 49.5 D (56°)</td>
<td></td>
</tr>
<tr>
<td>K2 (ax)</td>
<td>8.39 mm -5.8 D (146.8°)</td>
<td>5.75 mm -7.8 (56.5°)</td>
<td></td>
</tr>
<tr>
<td>Pachymetry min. Thickness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>519 µm</td>
<td>572 µm</td>
<td></td>
</tr>
</tbody>
</table>


Courtesy of Maciej Wojtkowski, Nicolaus Copernicus University, Torun, Poland
Conclusions

- Future commercial OCT systems will be faster
- Accurate topography of optical surfaces
  - Optical modeling and ray tracing
- High quality 3D imaging
  - Contact lens fitting
  - Implant fitting
  - 3D angle evaluation
  - Surgery simulation