Clinical Standards for Assessment of Novel Anterior Segment Measurements

Yasmin Bradfield, MD
John W. Doolittle Professor
Department of Ophthalmology and Visual Sciences
University of Wisconsin-Madison

I have no financial interest in this presentation

What is the best way to validate AS OCT measurements?

- Clinically accepted way that could translate into "scientifically accepted"
- Agreement, accuracy, reproducibility of AS OCT measurements
- Large population studies of normal and ocular disease
  - Normal variance
  - Age, gender, racial differences
Where are we in 2019?

• Current state of technology?
• Which human anterior segment structures have been imaged by AS OCT?
• What has been used as comparison to validate new data?
• Large population study data available?

Current AS OCT devices

• Time Domain
  • Spectral Domain (also known as Fourier domain)
    • Faster image acquisition, higher axial resolution, Ultrahigh 1-2 μm
    • Potential disadvantage – shorter scan depth
  • Swept source
    • Frequency swept light source and high speed detector detects interference signal as a function of time, instead of a spectrometer and camera in spectral domain technology
    • Deeper tissue penetration without shadowing artifacts (vessels)
  • Microscope-integrated OCT

Handheld Anterior Segment OCT
Facilitates use in the operating room
Video capture of scanned images
Allows selection of best image

### Ocular conditions imaged with AS OCT

<table>
<thead>
<tr>
<th>Eye Condition/Disease</th>
<th>Qualitative Parameters</th>
<th>Quantitative Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corneal dysphoria, ectasia</td>
<td>Extent of deposits or bullae,</td>
<td>Thickness of cornea (μm)</td>
</tr>
<tr>
<td></td>
<td>corneal thickness</td>
<td>Depth of crosslinking treatment</td>
</tr>
<tr>
<td>Dry eye</td>
<td>Position of graft to host cornea</td>
<td></td>
</tr>
<tr>
<td>Ocular surface neoplasia</td>
<td>Neoplastic features of lesion</td>
<td>Tear film thickness</td>
</tr>
<tr>
<td>Angle closure/narrow angle</td>
<td>Angle opening distance (AOD)</td>
<td>AOD measurement (mm)</td>
</tr>
<tr>
<td></td>
<td>Trabecular iris space area (TISA)</td>
<td>TISA measurement (mm²)</td>
</tr>
<tr>
<td></td>
<td>Anterior chamber depth (AOD)</td>
<td>AOD measurement (mm)</td>
</tr>
<tr>
<td></td>
<td>Lens vault (LV)</td>
<td>LV measurement (mm)</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>Presence of Schlemm's canal</td>
<td>Area of Schlemm's canal (μm²)</td>
</tr>
<tr>
<td>Pediatric glaucoma</td>
<td>Presence of Schlemm's canal,</td>
<td>Area of Schlemm's canal (μm²)</td>
</tr>
<tr>
<td></td>
<td>Abnormal angle features</td>
<td></td>
</tr>
<tr>
<td>Intraocular mass</td>
<td>Cyst or malignant features</td>
<td>Size of mass (mm)</td>
</tr>
<tr>
<td>Pseudophakia</td>
<td>IOL position</td>
<td></td>
</tr>
<tr>
<td>Strabismus</td>
<td>Extraocular muscle insertion</td>
<td>Insertion (mm) from corneal limbus</td>
</tr>
<tr>
<td>(reoperations, trauma)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Few established parameters

• Primary or secondary outcomes in clinical trials
• Angle parameters for predictor of angle closure
• Corneal graft positioning
• Exploratory outcomes
  • % change in SC area after introducing IOP lowering drug or surgery
  • Changes of extraocular muscle insertion over time
• Cornea ectasia changes after cross linking or contact lens treatment

Comparison of imaging devices to validate AS OCT data

<table>
<thead>
<tr>
<th></th>
<th>AS OCT</th>
<th>UBM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technology</td>
<td>Optical</td>
<td>Ultrasound</td>
</tr>
<tr>
<td>Resolution</td>
<td>15 μm</td>
<td>50 μm</td>
</tr>
<tr>
<td>Largest scan dimensions</td>
<td>16 x 4 mm</td>
<td>5 x 5 mm</td>
</tr>
<tr>
<td>Contact with eye</td>
<td>No</td>
<td>Ultrasound probe does not contact the eye directly but requires immersion bath</td>
</tr>
<tr>
<td>Real-time imaging</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Imaging posterior to HM</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Quantitative measure</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Schlemm’s canal
AS OCT vs Ultrasound Biomicroscopy (UBM)
Schlemm’s canal
AS OCT vs Ultrasound Biomicroscopy (UBM)


AS OCT vs B scan ultrasound

Standardization of Obtaining AS OCT Images

- Learning curve
- Environmental factors- Lighting? Diurnal variances? Changes with accommodation (SC)?
- Currently no standardized scanning protocol
- Reproducibility of current AS OCT measurements?
Reproducibility of AS OCT

- Compared the Tomey CASIA and Heidelberg Spectralis AS OCT devices
- Adult healthy patients, 20 eyes
- Lens vault, pupil diameter, AC width, angle opening distance, Trabecular iris space area, scleral spur angle
- High intra-device reproducibility of measurements for both devices
- High inter-device correlation of values


Reproducibility of AS OCT

- Compared the swept source Fourier-Domain Tomey CASIA AS OCT and Time-Domain Visante AS OCT
- Adult patients with and without glaucoma, 53 eyes
- Moderate inter-device agreement but bias in several angle parameters, CASIA larger measurements consistently
- Cannot interchange devices when evaluating individual patient


Reproducibility of AS OCT

Need larger studies for accuracy

- Need at least 4 AS OCT measurements to determine an average measurement on an anterior segment parameter
- Need at least 8 AS OCT measurements when determining range of measurements in high variability parameters
- Range and mean values deviated 44% and 13% if used only 1 AS OCT measurement


Comparison of imaging devices to validate newer AS OCT data

- What if there is no prior imaging device to use for comparison?
- Abnormal tissue or new angle findings in glaucoma patients
- Aqueous humor outflow pathways - Collector channels contiguous to Schlemm’s canal

Globe mass
Deposits within tube shunt


Schlemm’s canal with collector channels


Intrascleral lumen- contribute to outflow?

Software to enhance raw OCT images: Doppler to assess flow within an imaged structure.

Abnormal angle tissue in pediatric glaucoma


Histopathology confirmation of new findings


Anatomy correlate with function?

- Children 4-16 yo AS OCT after cataract surgery
- Smaller SC compared to normal children
- No increase in SC size with accommodative effort, seen in normal eyes
- SC changes after lensectomy may play a role in outflow reduction, thus contributing to glaucoma development

Anatomy correlate with function?

- SC in eyes with higher IOP may be compressed or collapsed
- IOP elevation reduces SC cross-sectional area imaged with AS OCT in normal human adults


Assumption that larger SC is better

- In normal population, SC cross sectional area wide variability 1664-6007 μm²

- How do we know that a larger SC doesn’t mean there’s fluid stasis in the imaged structure?

Anatomy doesn’t necessarily equal function

Aqueous angiography

Role for animal models to validate newer AS OCT data?

- Several species studied
- Mice and rats most commonly studied due to anatomic similarities to humans, rodent-adapted OCT technology
- Corneal and anterior chamber features
  - Ocular inflammation, infection - quantify AC cells
  - Corneal transplant and wound healing
- Drug delivery/cell therapy

Keratic precipitates adhering to corneal endothelium on AS OCT correlates to histopathology in mouse model

Fluid gel containing polarized macrophages in mouse model
Potential use in drug delivery system
Imaging the Distal Outflow Pathways in LTBP2 mutant cats

- 82 total studies
- 37 case series
- 21 comparative observational studies
- 11 cohort
- 10 case studies
- No randomized trials, scarce high level evidence

Clinical Standards for Assessment of Novel Anterior Segment Measurements
- Need large population studies to determine “normal” from disease, standard scanning protocol
- Role for image processing software technology for enhanced AS OCT resolution
- Imaged AS OCT anatomy doesn’t necessarily translate to function
- Potential future use can be impactful in determining spectrum of ocular disease, individualized patient treatment planning