Clinical Standards for Assessment of Novel Anterior Segment Measurements

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- I have no financial interest in this presentation

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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

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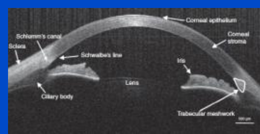
Where are we in 2019?

- Current state of technology?
- Which human anterior segment structures have been imaged by AS OCT?



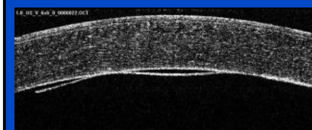
- What has been used as comparison to validate new data?
- Large population study data available?

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

Eye Condition/Disease	Qualitative Parameters	Quantitative Parameters
Corneal dystrophy, ectasia	Extent of deposits or bullae, corneal thickness Position of graft to host cornea Scleral lens positioning	Thickness of cornea (μm) Depth of crosslinking treatment
Dry eye	Tear film analysis	Tear film thickness
Ocular surface neoplasia	Neoplastic features of lesion	
Angle closure/narrow angle	Angle opening distance (AOD)	AOD measurement (mm)
	Trabecular iris space area (TISA)	TISA measurement (mm^2)
	Anterior chamber depth (ACD)	ACD measurement (mm)
	Lens vault (LV)	LV measurement (mm)

Ocular conditions imaged with AS OCT

Eye Condition/Disease	Qualitative Parameters	Quantitative Parameters
Glaucoma	Presence of Schlemm's canal	Area of Schlemm's canal (μm^2)
	Presence of bleb	
Pediatric glaucoma	Presence of Schlemm's canal, Abnormal angle features	Area of Schlemm's canal (μm^2)
Iris mass	Cyst or malignant features	Size of mass (mm)
Pseudophakia	IOL position	
Strabismus (reoperations, trauma)	Extraocular muscle insertion	Insertion (mm) from corneal limbus

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

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Comparison of imaging devices to validate AS OCT data

Table 1. ASOCT versus UBM

	ASOCT	UBM
Technology	Optical	Ultrasound
Resolution	15 μm	50μm
Longest scan dimensions	16 x 6 mm	5 x 5 mm
Contact with eye	No	Ultrasound probe does not contact the eye directly but requires immersion bath
Real-time imaging	Yes	Yes
Imaging posterior to iris	No	Yes
Quantitative measurement	Yes	Yes

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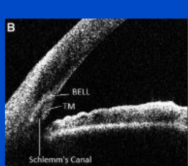
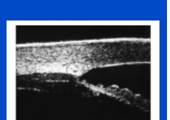
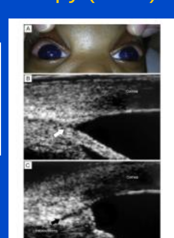
Schlemm's canal
AS OCT vs Ultrasound Biomicroscopy (UBM)

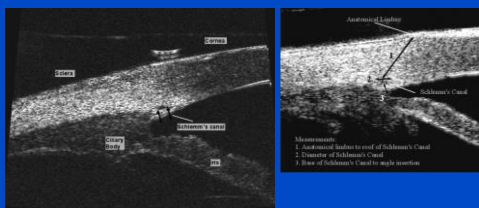






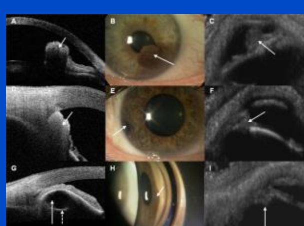
Tandon A, Watson C, Ayyala R. Ultrasound biomicroscopy measurement of Schlemm's canal in pediatric patients with and without glaucoma. J AAPOS. 2017 Jun;21(3):234-237.
Crowell EL et al. Characterizing anterior segment OCT angle landmarks of the trabecular meshwork complex. Ophthalmology 2018;125:994-1002.

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



Irshad FA, et al. Variation is Schlemm's canal diameter and location by ultrasound biomicroscopy. Ophthalmology 2010;117:916–920.

AS OCT vs B scan ultrasound

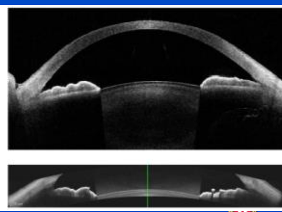


Standardization of Obtaining AS OCT Images

- 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



Xu BY et al. Reproducibility and Agreement of Anterior Segment Parameter Measurements Obtained Using CASIA2 and Spectralis OCT2 Optical Coherence Devices. J Glaucoma 2017:974-979.

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Reproducibility of AS OCT

- Compared the swept source Fourier-Domain Tomey CASIA 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*

Chansangpetch S et al. Agreement of Anterior Segment Parameters Obtained from Swept-Source Fourier-Domain and Time-Domain Anterior Segment OCT. IOVS 2018:1554-1561.

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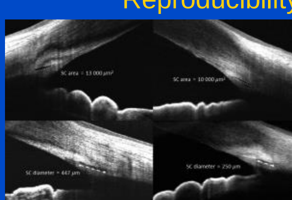
Reproducibility of AS OCT



Fernandez-Vigo J et al. Schlemm's canal measured by optical coherence tomography and correlation study in a healthy Caucasian child population. Acta Ophthalmologica. 2018;1-6.

Table 4. Reproducibility of Schlemm's canal diameter and area measurements made by Fourier-domain optical coherence tomography.

Intra-observer	Mean ± SD	ICC	95% CI
SC diameter temporal (μm)			
Session 1	299 ± 77	0.963	0.937–0.979
Session 2	295 ± 80		
SC diameter nasal (μm)			
Session 1	293 ± 75	0.987	0.970–0.995
Session 2	290 ± 74		
SC area temporal (μm²)			
Session 1	0.011 ± 0.004	0.972	0.933–0.988
Session 2	0.011 ± 0.004		
SC area nasal (μm²)			
Session 1	0.010 ± 0.003	0.955	0.910–0.978
Session 2	0.010 ± 0.003		

Inter-observer	Mean ± SD	ICC	95% CI
SC diameter temporal (μm)			
Observer 1	299 ± 77	0.962	0.856–0.987
Observer 2	308 ± 82		
SC diameter nasal (μm)			
Observer 1	293 ± 75	0.986	0.965–0.994
Observer 2	295 ± 73		
SC area temporal (μm²)			
Observer 1	0.011 ± 0.004	0.954	0.893–0.981
Observer 2	0.012 ± 0.005		
SC area nasal (μm²)			
Observer 1	0.010 ± 0.003	0.936	0.816–0.973
Observer 2	0.011 ± 0.003		

95% CI = 95% confidence interval, μm = microns, ICC = intraclass correlation coefficient, SC = Schlemm's canal, SD = standard deviation.

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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

Xu BY et al. Benefit of Measuring Anterior Segment Structures Using an Increased Number of Optical Coherence Tomography Images: The Chinese American Eye Study. IOVS 2016:6313-6319..

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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*

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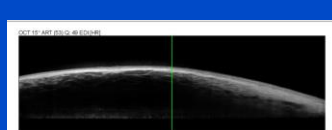
Globe mass



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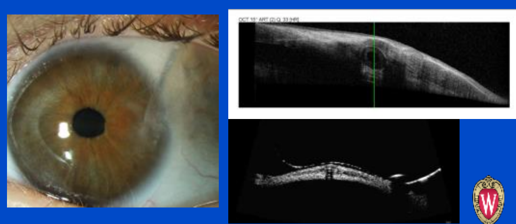
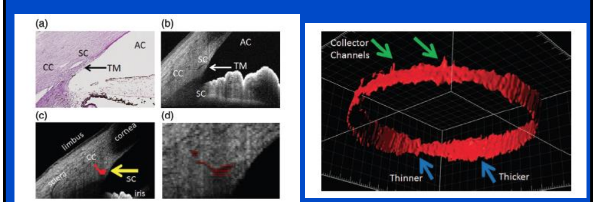
Deposits within tube shunt

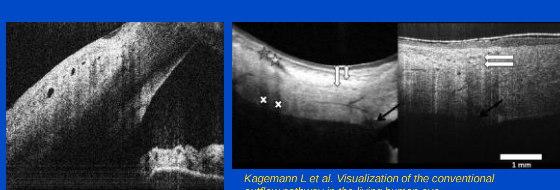




Schlemm's canal with collector channels

Huang AS, Francis BA, Weinreb RN. Structural and functional imaging of aqueous humour outfloe: a review. Clinical and Experimental Ophthalmology 2018 Mar;46:158-168.

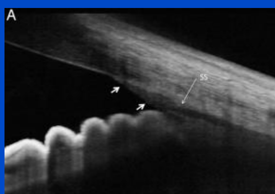
Intrascleral lumen- contribute to outflow?

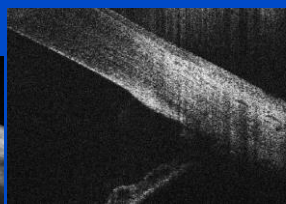


Kagemann L et al. Visualization of the conventional outflow pathway in the living human eye. Ophthalmology 2012;119:1563–1568.

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

Abnormal angle tissue in pediatric glaucoma





Gupta V, et al. In Vivo Analysis of Angle Dysgenesis in Primary Congenital, Juvenile, and Adult Onset Open Angle Glaucoma. IOVS 2017; 58:6000-6005.

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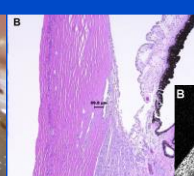
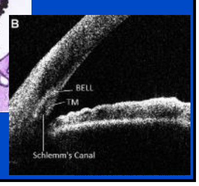
Histopathology confirmation of new findings





Crowell EL et al. Characterizing anterior segment OCT angle landmarks of the trabecular meshwork complex. Ophthalmology 2018;125:994-1002.

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

Daniel MC et al. Childhood lensectomy is associated with static and dynamic reduction in Schlemm's canal size. Ophthalmology. 2018;1-9.

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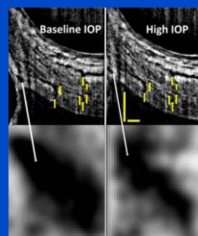
Anatomy correlate with function?

- 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



Kagemann L, Wang B, Wollstein G, Ishikawa H, Nevins JE, Nadler Z, Sigal IA, Bilonick RA, Schuman JS. IOP elevation reduces Schlemm's canal cross-sectional area. Invest Ophthalmol Vis Sci. 2014 Mar 25;55(3):1805-9.

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Anatomy doesn't necessarily equal function

- Assumption that larger SC is better
- In normal population, SC cross sectional area wide variability 1664-6007 μm^2
- How do we know that a larger SC doesn't mean there's fluid stasis in the imaged structure?

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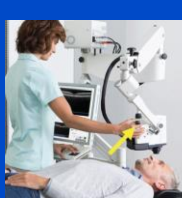
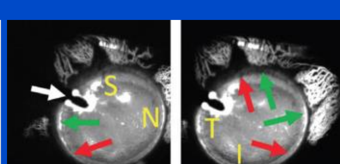
Aqueous angiography





Huang AS, Francis BA, Weinreb RN. Structural and functional imaging of aqueous humor outflow: a review. Clin Exp Ophthalmol. 2017;1-11.

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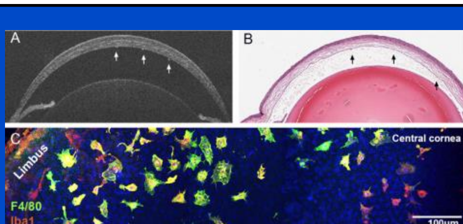
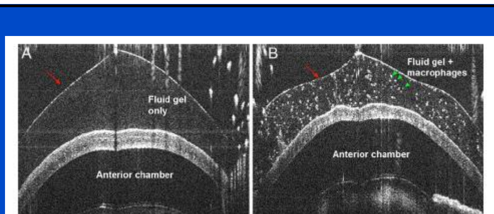
Role for animal models to validate newer AS OCT data?

- 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

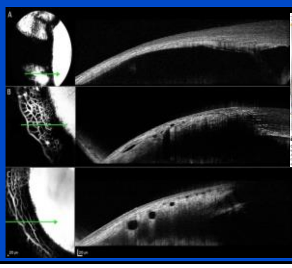


Keratic precipitates adhering to corneal endothelium on AS OCT correlates to histopathology in mouse model



Fluid gel containing polarized macrophages in mouse model
Potential use in drug delivery system

Imaging the Distal Outflow Pathways in *LTBP2* mutant cats



CLINICAL AND EXPERIMENTAL
OPTOMETRY

INVITED REVIEW

Anterior segment optical coherence tomography and its clinical applications: a review

Clin Exp Optom 2019 DOI:10.1111/cxo.12869

- 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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