Optical Coherence Tomography

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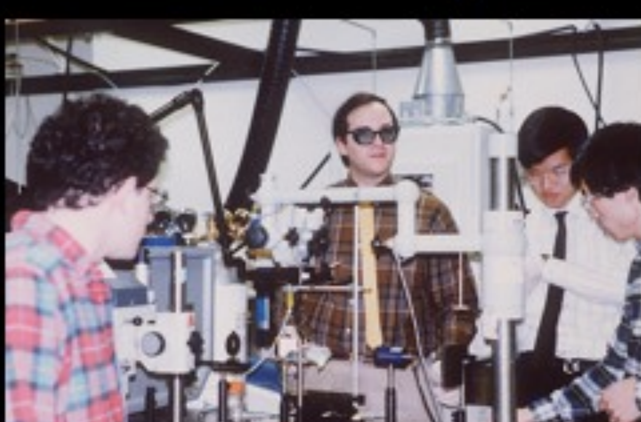
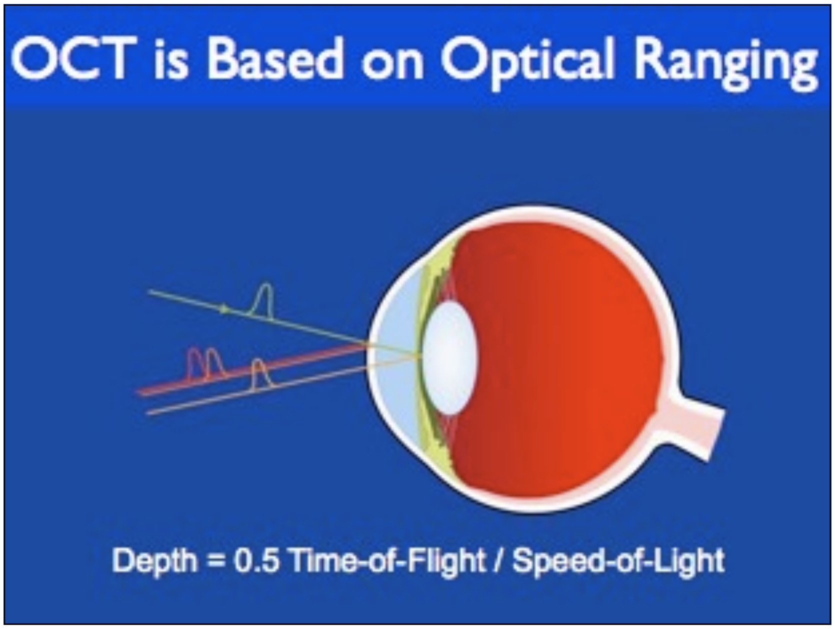
PITTSBURGH, PA USA

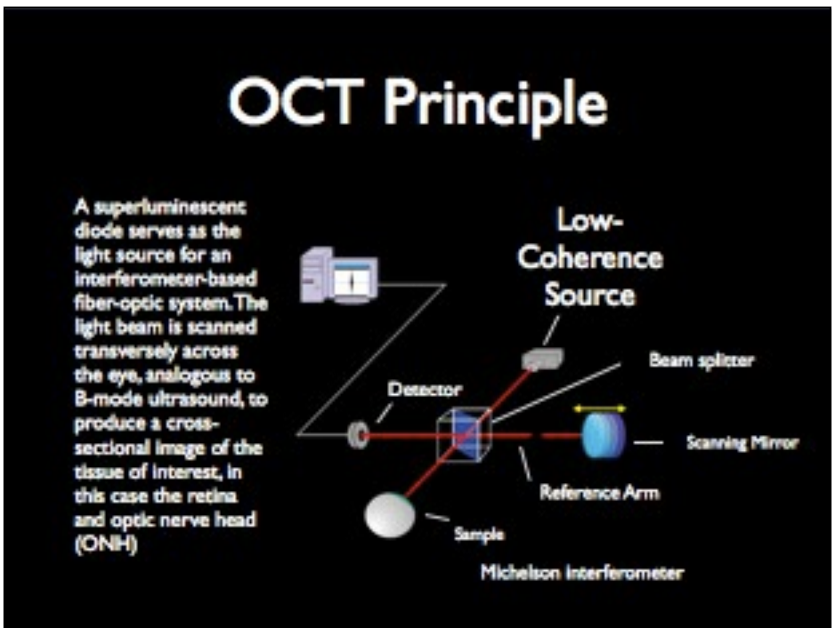
Disclosures

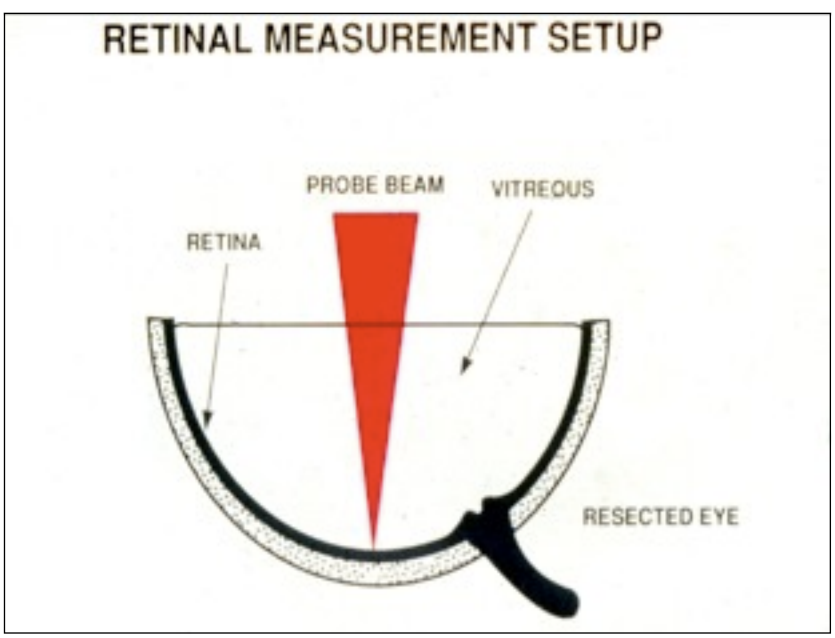
As an inventor of Optical Coherence Tomography (OCT), Dr. Schuman receives royalties for intellectual property owned by MIT and licensed to Carl Zeiss Meditec, Inc.

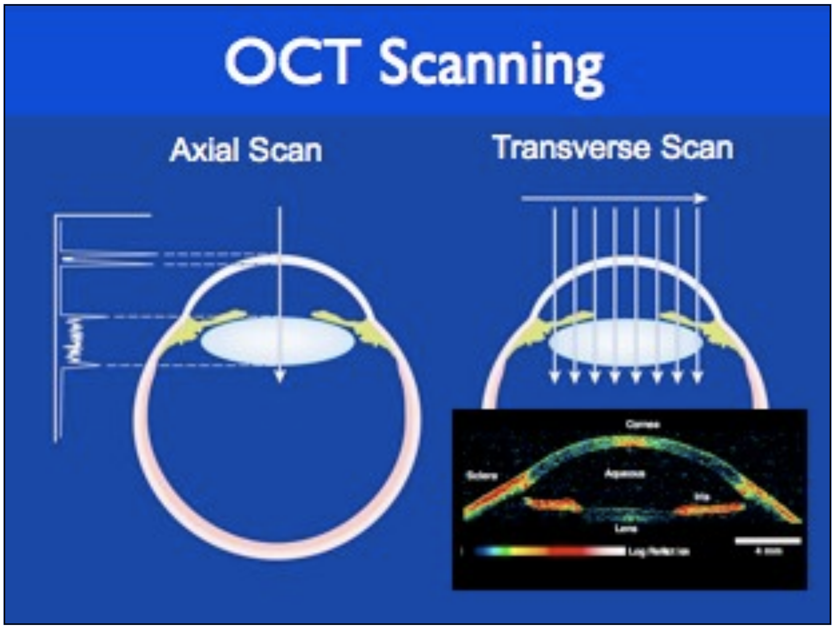
OCT Development

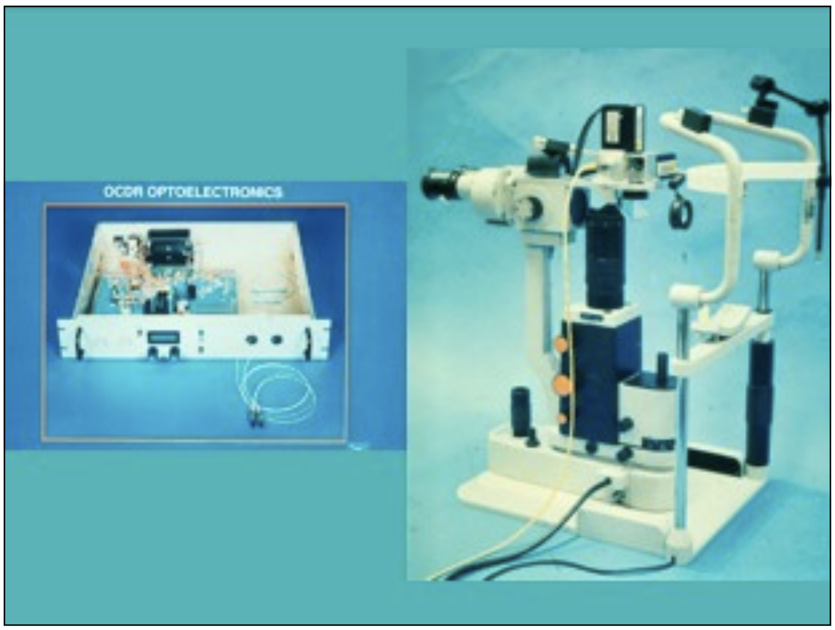


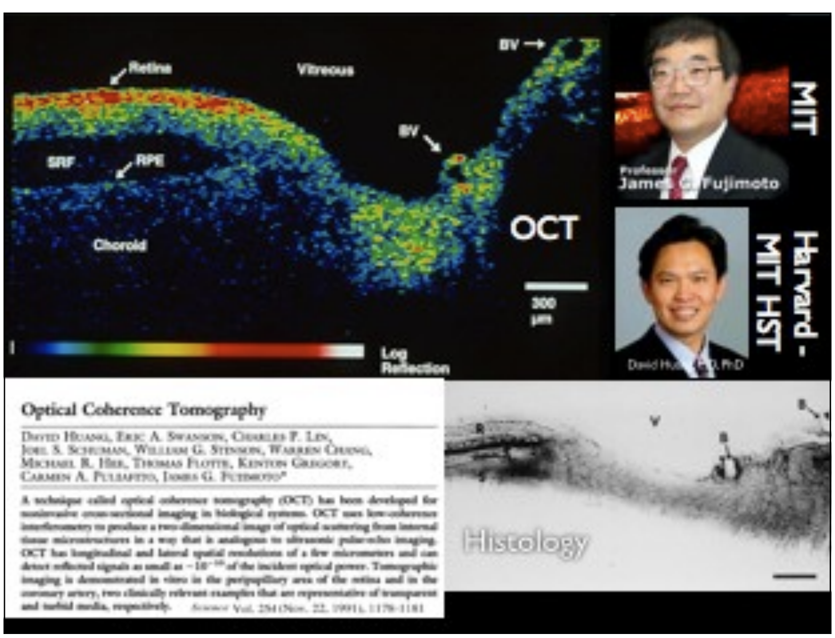

OCT is Based on Optical Ranging
Depth = 0.5 Time-of-Flight / Speed-of-Light


OCT Principle
A superluminescent diode serves as the light source for an interferometer-based fiber-optic system. The light beam is scanned transversely across the eye, analogous to B-mode ultrasound, to produce a cross-sectional image of the tissue of interest, in this case the retina and optic nerve head (ONH)
Low-Coherence Source
Beam splitter
Detector
Scanning Mirror
Reference Arm
Sample
Michelson interferometer

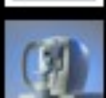

RETINAL MEASUREMENT SETUP
PROBE BEAM
VITREOUS
RETINA
RESECTED EYE

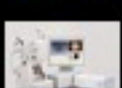

OCT Scanning
Axial Scan
Transverse Scan
Cornea
Sclera
Aqueous
Iris
Lens
Log Reflection


OCDR OPTOELECTRONICS


Retina
Vitreous
BV
SRF
RPE
Choroid
OCT
300 µm
Log Reflection
MIT
Professor James G. Fujimoto
Harvard - MIT HST
Histology
Optical Coherence Tomography
David Huang, Eric A. Swanson, Charles P. Lin, Joel S. Schuman, William G. Stinson, Warren Chang, Michael R. Hee, Thomas Flotte, Kenton Gregory, Carmen A. Puliafito, James G. Fujimoto*
A technique called optical coherence tomography (OCT) has been developed for noninvasive cross-sectional imaging in biological systems. OCT uses low-coherence interferometry to produce a two-dimensional image of optical scattering from internal tissue microstructures in a way that is analogous to ultrasonic pulse-echo imaging. OCT has longitudinal and lateral spatial resolutions of a few micrometers and can detect reflected signals as small as ~10^{-10} of the incident optical power. Tomographic imaging is demonstrated in vitro in the peripapillary area of the retina and in the coronary artery, two clinically relevant examples that are representative of transparent and turbid media, respectively.
Science Vol. 254 (Nov. 22, 1991), 1178-1181

OCT Today





Spectral-Domain Optical Coherence Tomography: A Comparison of Modern High-Resolution Retinal Imaging Systems

DANIEL F. KIERNAN, WILLIAM F. MIELER, AND SEENU M. HARIPRASAD

Am J Ophthalmol 2010;149: 18–31

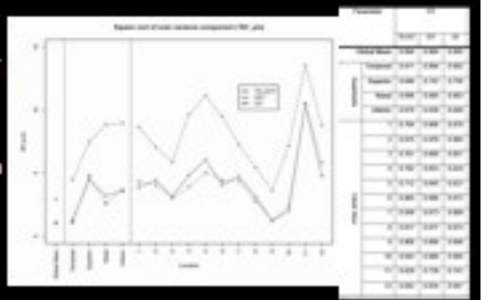
TABLE. Commercially Available Spectral-Domain Optical Coherence Tomography Systems

System (Company)	Axial Resolution (μm)	A-Scans per Second	Advanced Features[a]
Cirrus HD-OCT (Carl Zeiss Meditec)	5	27 000	Fixation-independent scan adjustment; multilayer en face C-scan visualization; high-resolution anterior segment imaging
Spectralis (Heidelberg Engineering)	7	40 000	Point-to-point registration with eye tracking; Up to 6 diagnostic methods in 1 platform; digital resolution to 3.5 μm; improved choroidal visualization
RTVue 100 (Optovue)	5	26 000	12 mm long macular scans can be overlapped; Point to point registration with eye tracking; drusen analysis and Doppler blood flow characterization; high-resolution anterior segment imaging
3D-OCT 1000	6	18 000	Nonmydriatic camera provides color fundus photographs
3D-OCT 2000[b] (Topcon)			Capable of exportation to common multimedia devices; able to import time-domain Stratus OCT images
Spectral OCT/SLO (OPKO/OTI)	5	27 000	Point-to-point registration with eye tracking; microperimetric macular analysis; high-resolution anterior segment imaging
SOCT Copernicus (Optopol)	6	25 000	Point-to-point registration with eye tracking; high-resolution anterior segment imaging; can separate and view all retinal layers; software allows intraretinal cyst volumetric analysis
SOCT Copernicus HR[b] (Canon/Optopol, Inc)	3	50 000	Highest resolution and fastest speed of available devices; multilingual interface; Doppler retinal blood flow analysis
SDOCT (Bioptigen)	4	20 000	Handheld head for pediatric patients or animal research; portability facilitates use in an operating room; Doppler retinal blood flow analysis
Retinascan RS-3000[b] (Nidek)	7	53 000	Segmentation analysis of 6 distinct retinal layers

OCT = optical coherence tomography.
[a]Based on a review of available data at the time this manuscript was prepared.
[b]Not yet approved by the Food and Drug Administration.

Reproducibility

- SD-OCT showed statistically significantly better RNFL thickness measurement reproducibility than TD-OCT
- Re-sampling circle location variation on the SD-OCT was relatively small from scan to scan
- No statistically significant difference was detected between Center Each Time and Center Once methods



Kim JS, Ishikawa H, Sung KR, Xu J, Wollstein G, Bilonick RA, Gabriele ML, Kagemann L, Duker JS, Fujimoto JG, Schuman JS. Retinal nerve fibre layer thickness measurement reproducibility improved with spectral domain optical coherence tomography. Br J Ophthalmol. 2009 Aug;93(8):1057-63. Epub 2009 May 7.

Reproducibility of RTVue Retinal Nerve Fiber Layer Thickness and Optic Disc Measurements and Agreement with Stratus Optical Coherence Tomography Measurements

ALBERTO O. GONZÁLEZ-GARCÍA, GIANMARCO VIZZERI, CHRISTOPHER BOWD, FELIPE A. MEDEIROS, LINDA M. ZANGWILL, AND ROBERT N. WEINREB

Am J Ophthalmol 2009;147:1067–1074

TABLE 2. Reproducibility of RTVue Retinal Nerve Fiber Layer Thickness Measurements in Healthy Participants and Glaucoma Patients

RNFL Parameters	Healthy Participants				Glaucoma Patients			
	Mean (95% CI)	Sw ± 1.96 sw	CV %	ICC (95% CI)	Mean (95% CI)	Sw ± 1.96 sw	CV %	ICC (95% CI)
TEMP (μm)	80.6 (77.4 to 83.8)	2.82 ± 0.52	3.54	0.92 (0.88 to 0.95)	71.2 (68.7 to 73.8)	3.36 ± 0.7	4.72	0.96 (0.91 to 0.97)
SUP (μm)	120.6 (117 to 124.3)	3.8 ± 0.57	3.16	0.91 (0.86 to 0.94)	103.2 (99.6 to 106.8)	3.67 ± 0.59	3.53	0.93 (0.89 to 0.95)
NAS (μm)	75.8 (72.8 to 78.7)	2.94 ± 0.44	3.88	0.91 (0.86 to 0.94)	68.6 (66.2 to 71.1)	3.22 ± 0.52	4.8	0.89 (0.83 to 0.92)
INF (μm)	134.3 (129.7 to 138.8)	3.53 ± 0.55	2.65	0.95 (0.92 to 0.97)	113.2 (108.9 to 117.4)	3.21 ± 0.48	2.87	0.96 (0.94 to 0.97)
AVG (μm)	102.6 (100.1 to 105.6)	1.57 ± 0.27	1.54	0.97 (0.95 to 0.98)	89.1 (86.5 to 91.7)	1.69 ± 0.23	1.9	0.97 (0.96 to 0.98)

AVG = average quadrant; CI = confidence interval; CV = coefficient of variation; ICC = intraclass correlation coefficient; INF = inferior quadrant; NAS = nasal quadrant; SUP = superior quadrant; Sw = within-subjects standard deviation; RNFL = retinal nerve fiber layer; TEMP = temporal quadrant.

Reproducibility is expressed as the Sw, the ICC, and the CV. Sw is defined as the square root of the within-subject variance (defined as the within-subjects sum of squares divided by its degrees of freedom). CV is calculated as the square root of the residual mean squared values of 3 measures, divided by mean.

Reproducibility of RTVue Retinal Nerve Fiber Layer Thickness and Optic Disc Measurements and Agreement with Stratus Optical Coherence Tomography Measurements

ALBERTO O. GONZÁLEZ-GARCÍA, GIANMARCO VIZZERI, CHRISTOPHER BOWD, FELIPE A. MEDEIROS, LINDA M. ZANGWILL, AND ROBERT N. WEINREB

Am J Ophthalmol 2009;147:1067–1074

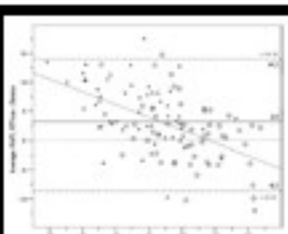


FIGURE 1. Bland-Altman plot showing the average retinal nerve fiber layer thickness (RNFL) agreement between RTVue spectral-domain optical coherence tomography (SD-OCT) and Stratus time-domain optical coherence tomography (TD-OCT) in healthy persons (circle) and glaucoma patients (triangle).

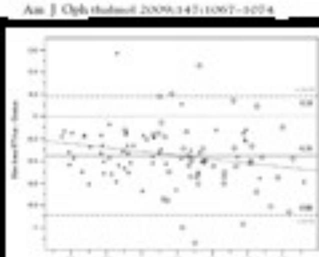
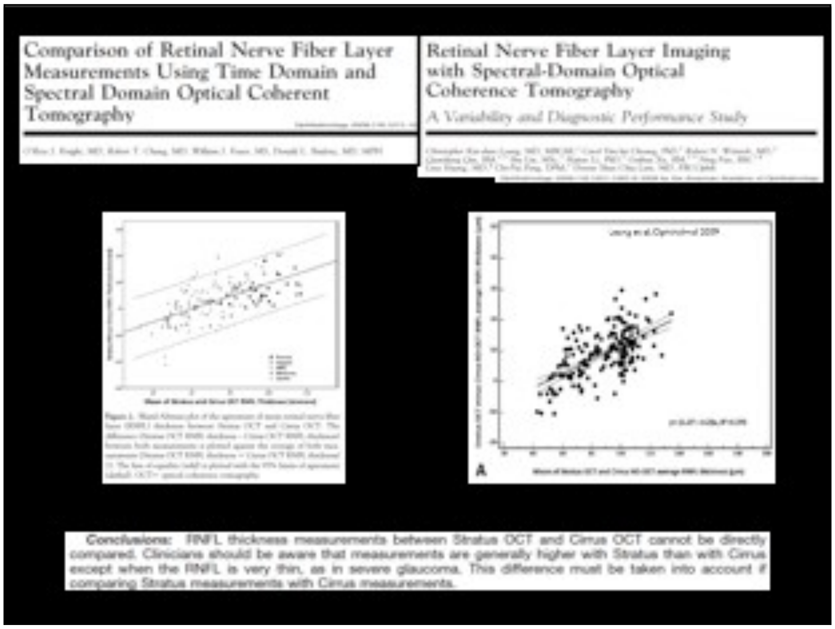
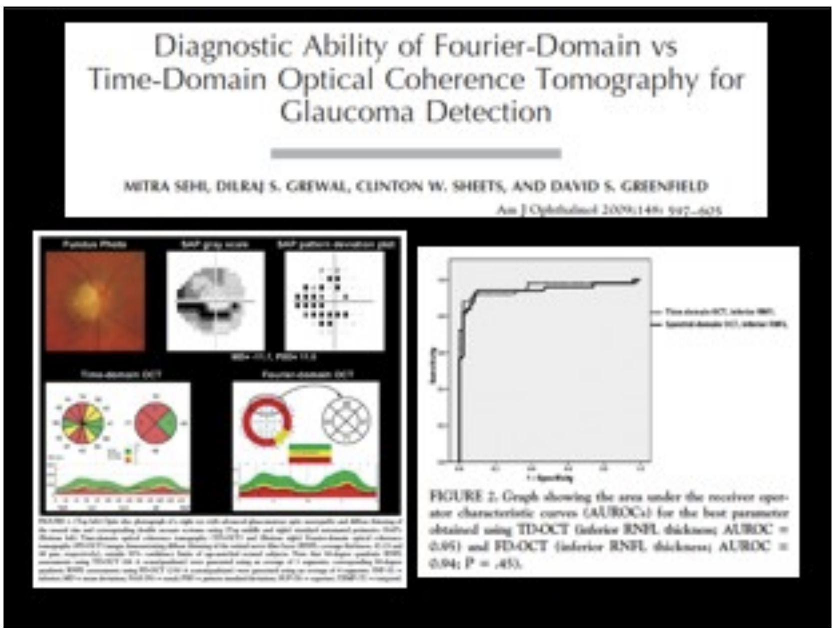
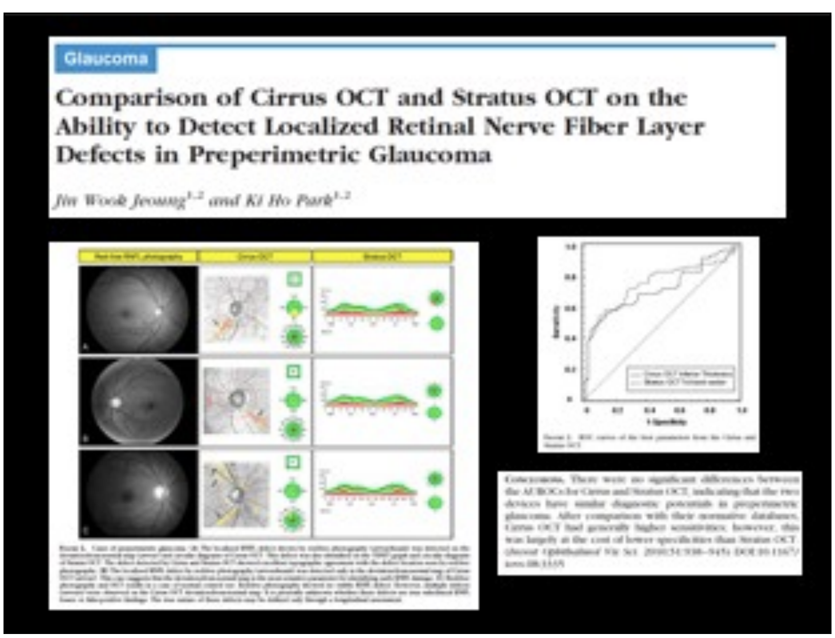


FIGURE 2. Bland-Altman plot showing the rim area agreement between RTVue SD-OCT and Stratus TD-OCT in healthy persons (circle) and glaucoma patients (triangle).


Comparison of Retinal Nerve Fiber Layer Measurements Using Time Domain and Spectral Domain Optical Coherent Tomography
Retinal Nerve Fiber Layer Imaging with Spectral-Domain Optical Coherence Tomography
A Variability and Diagnostic Performance Study
Conclusions: RNFL thickness measurements between Stratus OCT and Cirrus OCT cannot be directly compared. Clinicians should be aware that measurements are generally higher with Stratus than with Cirrus except when the RNFL is very thin, as in severe glaucoma. This difference must be taken into account if comparing Stratus measurements with Cirrus measurements.


Diagnostic Ability of Fourier-Domain vs Time-Domain Optical Coherence Tomography for Glaucoma Detection
MITRA SEHI, DILRAJ S. GREWAL, CLINTON W. SHEETS, AND DAVID S. GREENFIELD
Am J Ophthalmol 2009;148: 597–605
Fundus Photo
SAP gray scale
SAP pattern deviation plot
Time-domain OCT
Fourier-domain OCT
FIGURE 2. Graph showing the area under the receiver operator characteristic curves (AUROCs) for the best parameter obtained using TD-OCT (inferior RNFL thickness; AUROC = 0.95) and FD-OCT (inferior RNFL thickness; AUROC = 0.94; P = .45).


Glaucoma
Comparison of Cirrus OCT and Stratus OCT on the Ability to Detect Localized Retinal Nerve Fiber Layer Defects in Preperimetric Glaucoma
Jin Wook Jeoung[1,2] and Ki Ho Park[1,2]

Comparison of Retinal Nerve Fiber Layer Thickness Measured by Cirrus HD and Stratus Optical Coherence Tomography

Kyung Rim Sung, MD, Dong Yoon Kim, MD, Sung Bae Park, MD, Michael S. Kook, MD

Ophthalmology 2009;116:1264–1270

Table 1. Clinical Characteristics of the Study Population

	Glaucoma	GS	Healthy	P Value (ANOVA)
Age (yrs) ± SD	[illegible]	[illegible]	[illegible]	[illegible]
MD (dB) ± SD	[illegible]	[illegible]	[illegible]	[illegible]
PSD (dB) ± SD	[illegible]	[illegible]	[illegible]	[illegible]
Average RNFL Thickness by Stratus OCT (μm) ± SD	[illegible]	[illegible]	[illegible]	[illegible]
Average RNFL thickness by Cirrus HD-OCT (μm) ± SD	[illegible]	[illegible]	[illegible]	[illegible]

ANOVA = analysis of variance; GS = glaucoma suspect; MD = mean deviation; OCT = optical coherence tomography; PSD = pattern standard deviation; RNFL = retinal nerve fiber layer; SD = standard deviation.

Table 4. Sensitivity and Specificity (%) of Stratus Optical Coherence Tomography (OCT) and Cirrus HD-OCT

Parameter	OCT	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Average RNFL	Stratus OCT	[illegible]	[illegible]
	Cirrus HD-OCT	[illegible]	[illegible]
[illegible]	Stratus OCT	[illegible]	[illegible]
	Cirrus HD-OCT	[illegible]	[illegible]
#1 clock hours	Stratus OCT	[illegible]	[illegible]
	Cirrus HD-OCT	[illegible]	[illegible]

RNFL = retinal nerve fiber layer.

Conclusions: There were significant differences in RNFL thickness and normative classification as determined by Stratus OCT and Cirrus HD-OCT despite an excellent correlation of RNFL thickness measurement. Overall sensitivity and specificity were higher with Cirrus OCT. These findings are particularly relevant when an individual undergoes longitudinal follow-up with different OCTs.

- Assessment of glaucoma risk
  - OHTS HRT ancillary study showed positive predictive value of CSLO ONH examination at baseline
  - Similar findings with SLP and OCT in different datasets

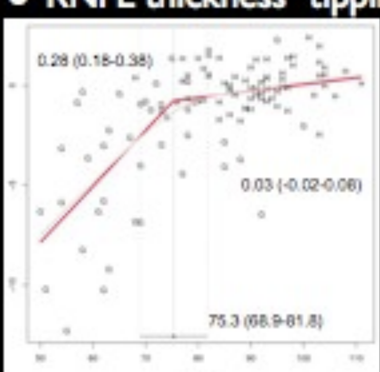
Zangwill LM, Weinreb RN, Beiser JA, et al. Baseline topographic optic disc measurements are associated with the development of primary open-angle glaucoma: the Confocal Scanning Laser Ophthalmoscopy Ancillary Study to the Ocular Hypertension Treatment Study. Arch Ophthalmol 2005;123:1188-1197.

Mohammadi K, Bowd C, Weinreb RN, et al. Retinal nerve fiber layer thickness measurements with scanning laser polarimetry predict glaucomatous visual field loss. Am J Ophthalmol 2004;138:592-601.

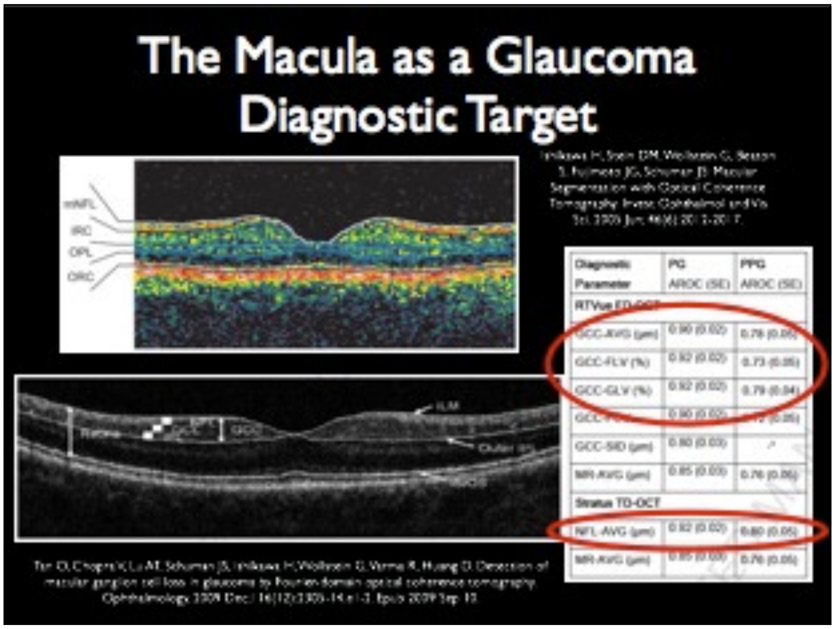
Lalezary, Medeiros FA, Weinreb RN, et al. Baseline Optical Coherence Tomography Predicts the Development of Glaucomatous Change in Glaucoma Suspects. Am J Ophthalmol 2006; 142:576-582.

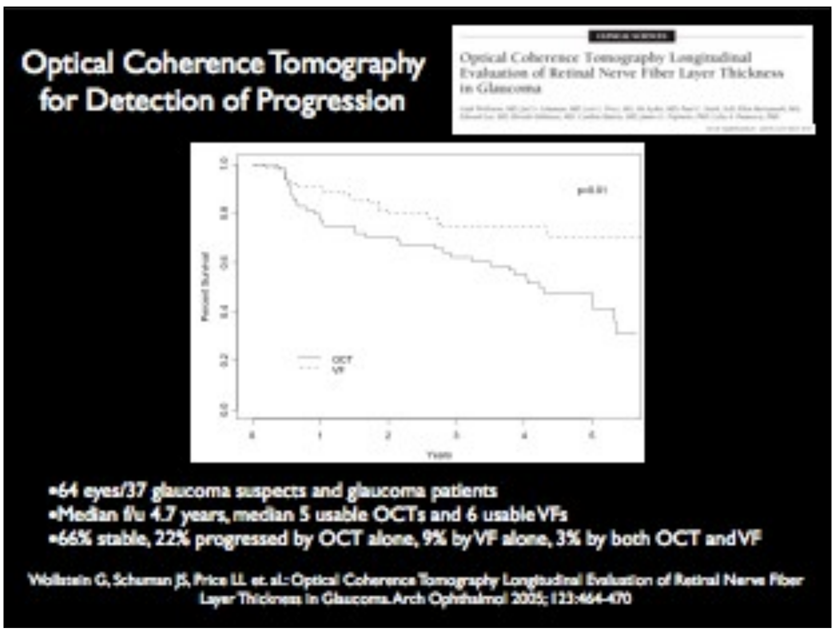
Clinical Application of SD-OCT in Glaucoma

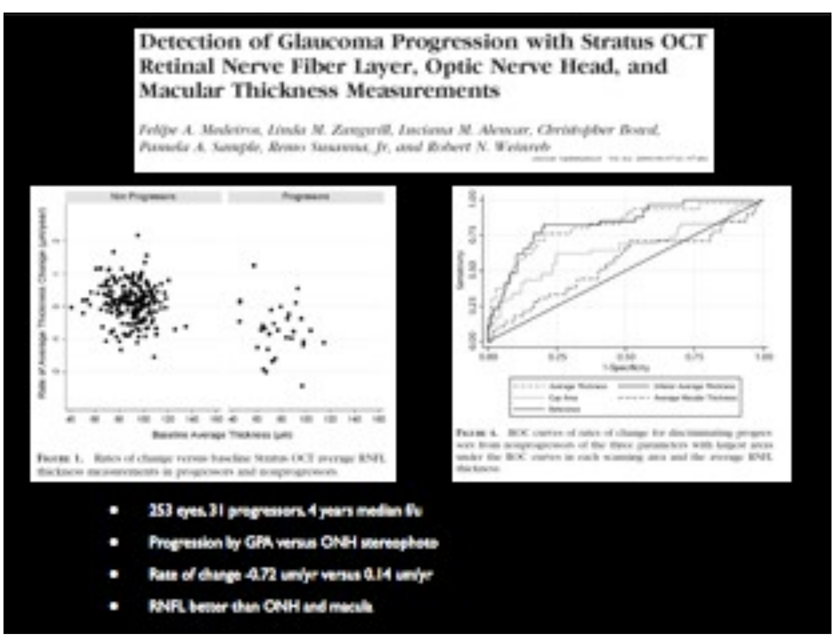
- Structure before function?
  - RNFL thickness "tipping point"



RNFL	Tipping Point (μm)	95% CI (μm)
Mean	75.3	68.9 - 81.8
Temporal	51.1	46.6 - 55.6
Superior	83.0	76.3 - 89.7
Nasal	70.2*	52.7 - 87.7
Inferior	87.5	73.6 - 101.4


The Macula as a Glaucoma Diagnostic Target
mNFL
IRC
OPL
ORC
ILM
Retina
GCC
Diagnostic Parameter
PG AROC (SE)
PPG AROC (SE)
RTVue FD-OCT
GCC-AVG (μm) 0.90 (0.02) 0.78 (0.05)
GCC-FLV (%) 0.92 (0.02) 0.73 (0.05)
GCC-GLV (%) 0.92 (0.02) 0.79 (0.04)
GCC-SID (μm) 0.80 (0.03)
MR-AVG (μm) 0.85 (0.03) 0.76 (0.06)
Stratus TD-OCT
NFL-AVG (μm) 0.92 (0.02) 0.80 (0.05)
MR-AVG (μm) 0.85 (0.03) 0.76 (0.05)

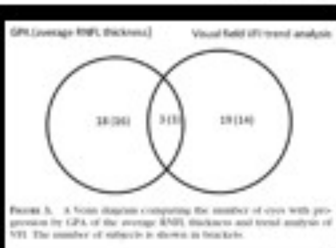

Optical Coherence Tomography for Detection of Progression
Optical Coherence Tomography Longitudinal Evaluation of Retinal Nerve Fiber Layer Thickness in Glaucoma
p<0.01
Percent Survival
Years
OCT
VF
•64 eyes/37 glaucoma suspects and glaucoma patients
•Median f/u 4.7 years, median 5 usable OCTs and 6 usable VFs
•66% stable, 22% progressed by OCT alone, 9% by VF alone, 3% by both OCT and VF
Wollstein G, Schuman JS, Price LL et. al.: Optical Coherence Tomography Longitudinal Evaluation of Retinal Nerve Fiber Layer Thickness in Glaucoma. Arch Ophthalmol 2005; 123:464-470


Detection of Glaucoma Progression with Stratus OCT Retinal Nerve Fiber Layer, Optic Nerve Head, and Macular Thickness Measurements
Felipe A. Medeiros, Linda M. Zangwill, Luciana M. Alencar, Christopher Bowd, Pamela A. Sample, Remo Susanna, Jr, and Robert N. Weinreb
Non Progressors
Progressors
Baseline Average Thickness (μm)
Sensitivity
1-Specificity
• 253 eyes, 31 progressors, 4 years median f/u
• Progression by GPA versus ONH stereophoto
• Rate of change -0.72 um/yr versus 0.14 um/yr
• RNFL better than ONH and macula

Glaucoma

Evaluation of Retinal Nerve Fiber Layer Progression in Glaucoma: A Study on Optical Coherence Tomography Guided Progression Analysis

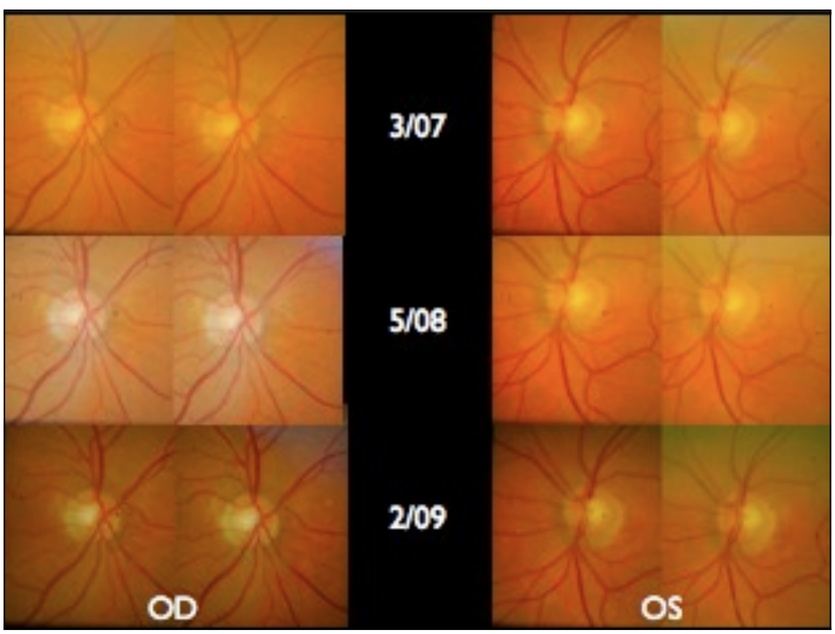
Christopher Kai-shun Leung,[1,2] Carol Yim Lui Cheung,[1] Robert N. Weinreb,[2] Kunliang Qiu,[1,3] Shu Liu,[1] Haitao Li,[1] Guihua Xu,[1,3] Ning Fan,[1] Chi Pui Pang,[1] Kwok Kay Tse,[1] and Dennis Shun Chiu Lam[1]



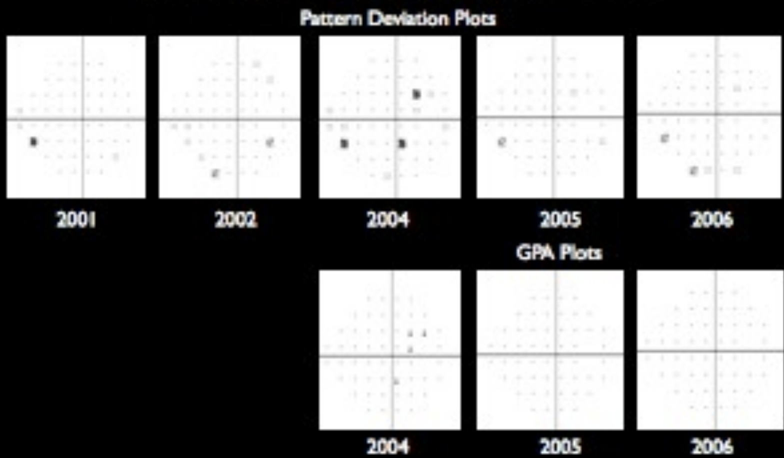
- 116 eyes of 64 patients, first and last measurements at least 3 years apart
- Progression by OCT GPA versus SAPVFI
- Median rate of change -3.3 um/yr versus 3.0%/yr
- Little overlap between VF progressors and OCT progressors

Case

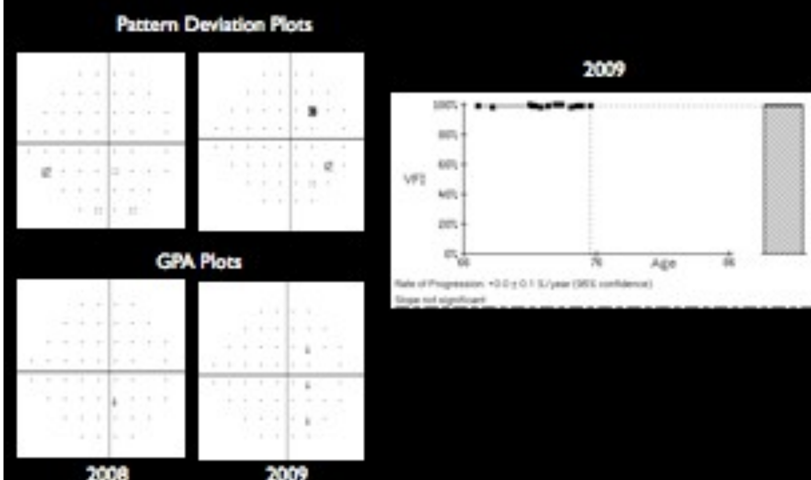
- 75 year old man
  - H/O round retinal hole
- POAG OU
- Nuclear Sclerotic Cataract OS
- Pseudophakia OD
- VA: 20/25, 20/32
- IOP: 14/18
- CCT: 585/577
- CDR: 0.8/0.8



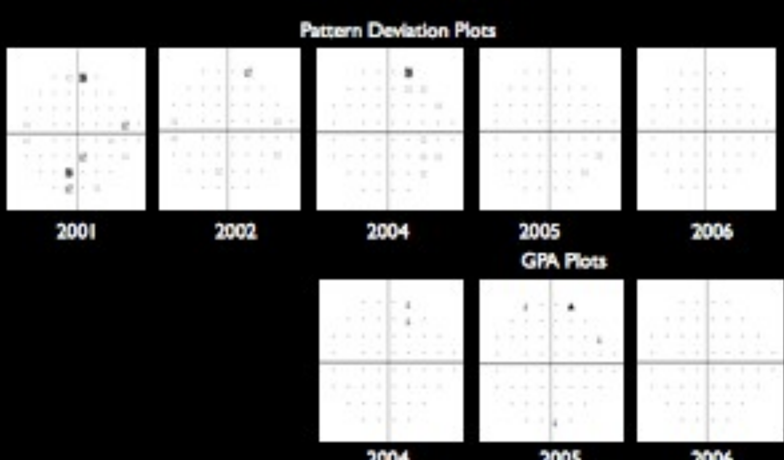
Case: Visual Field OD



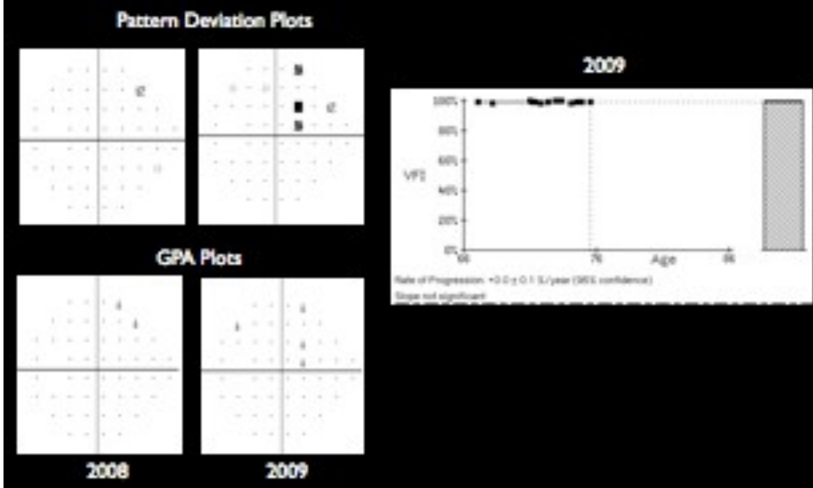
Case: Visual Field OD



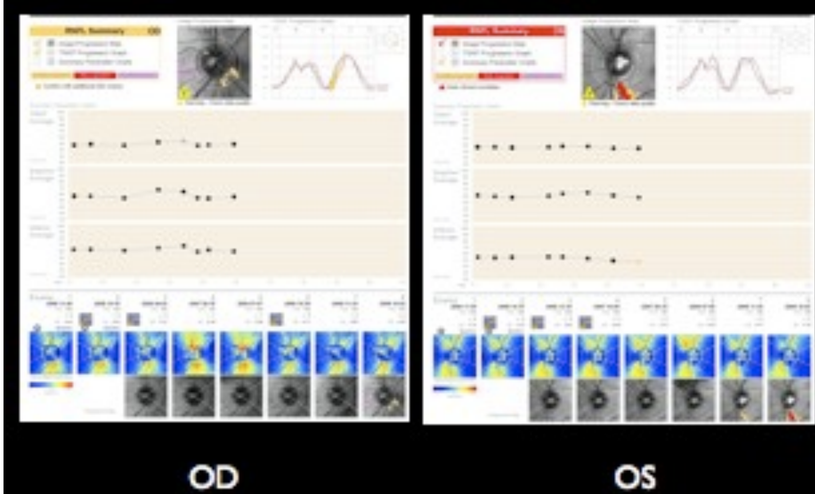
Case: Visual Field OS



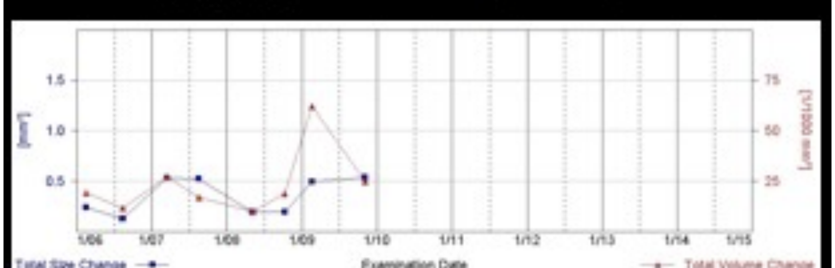
Case:Visual Field OS

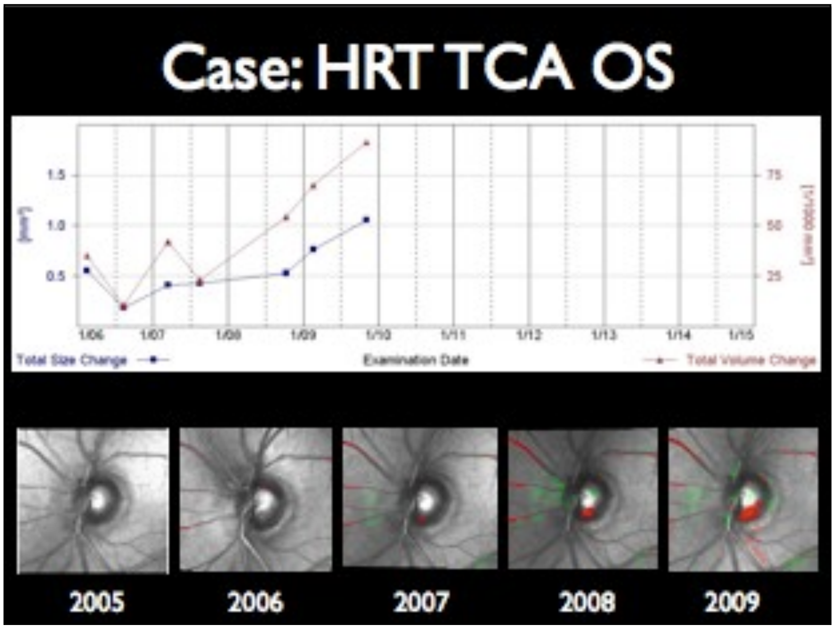


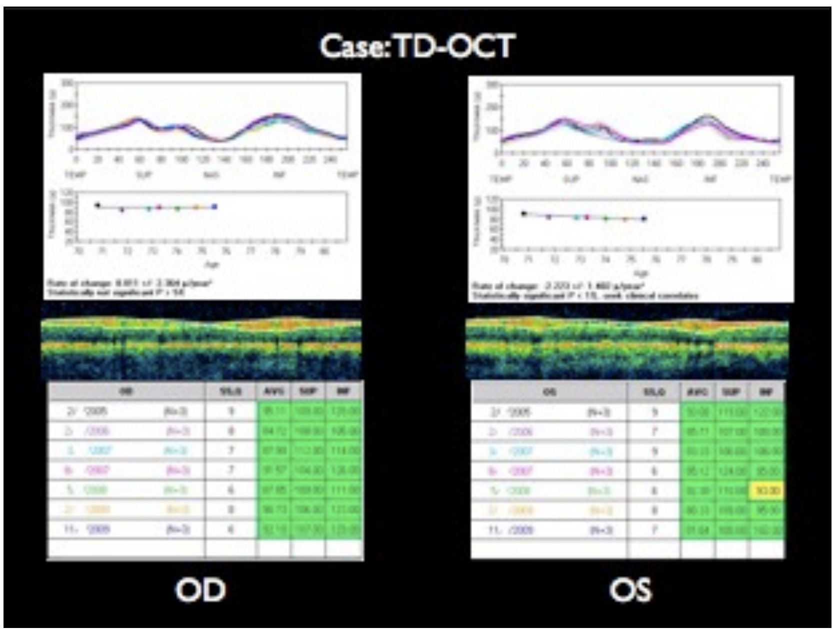
Case: GDx

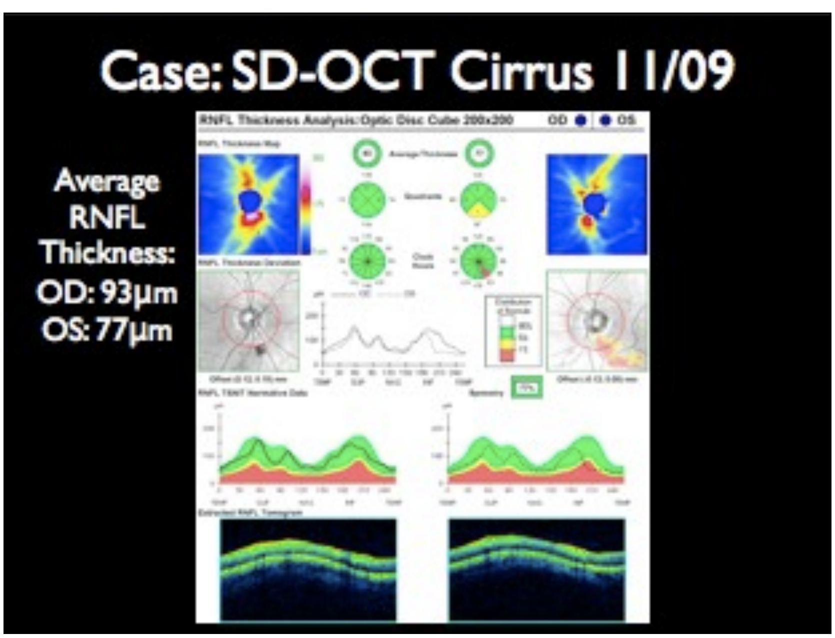


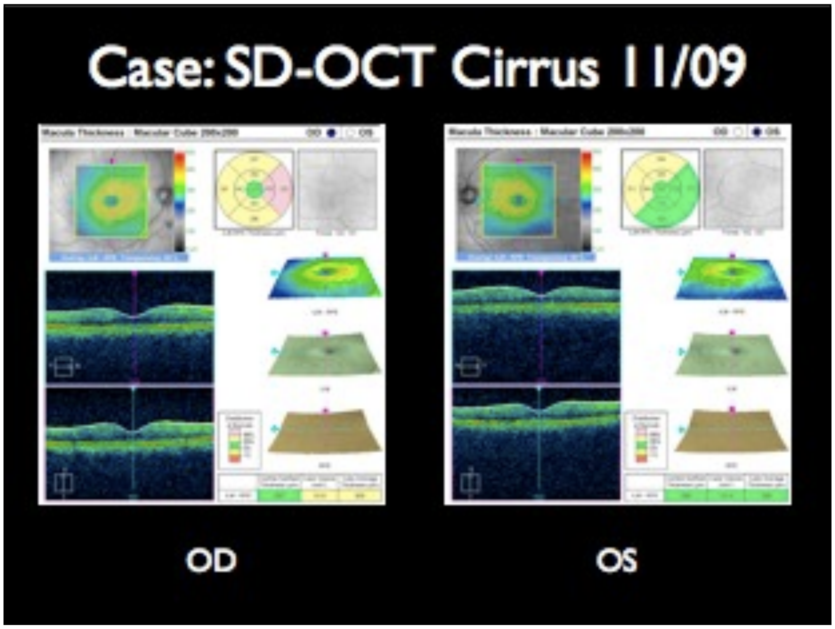
Case: HRT TCA OD

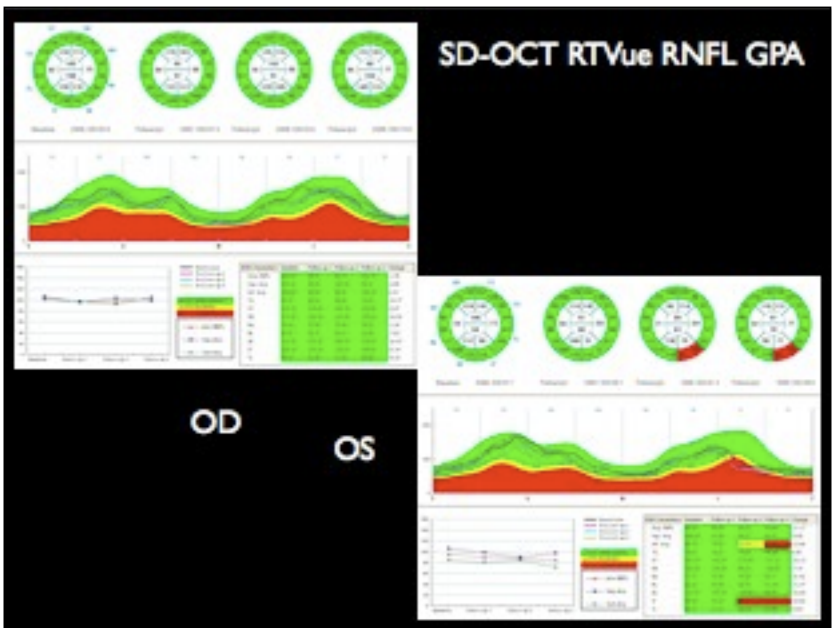


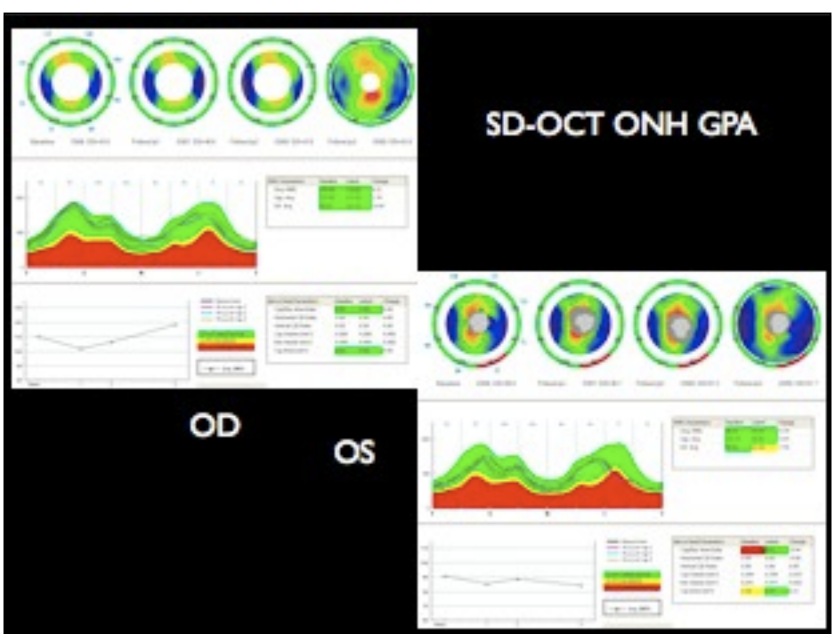

Case: HRT TCA OS
Total Size Change
Examination Date
Total Volume Change
1/06
1/07
1/08
1/09
1/10
1/11
1/12
1/13
1/14
1/15
2005
2006
2007
2008
2009

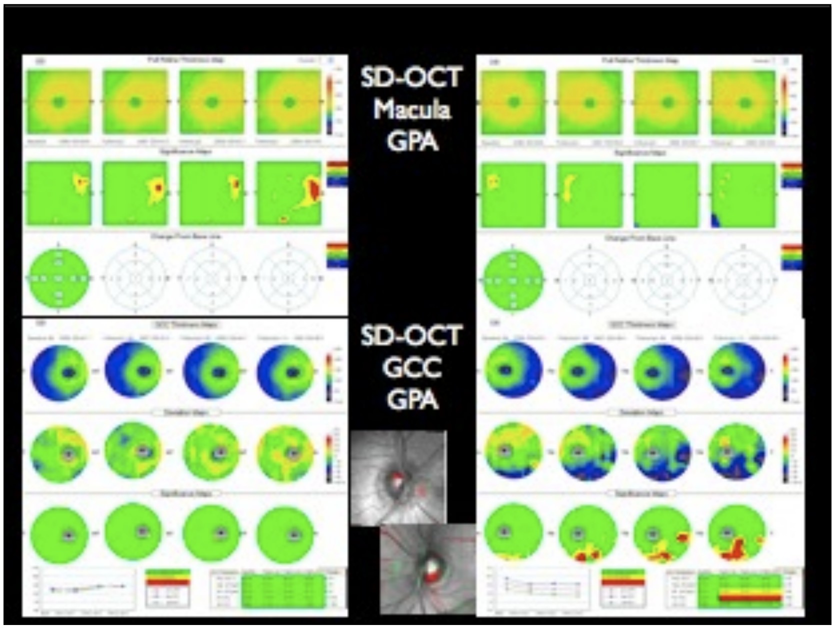

Case: TD-OCT
OD
OS


Case: SD-OCT Cirrus 11/09
Average RNFL Thickness:
OD: 93μm
OS: 77μm
RNFL Thickness Analysis: Optic Disc Cube 200x200
OD
OS


Case: SD-OCT Cirrus 11/09
OD
OS

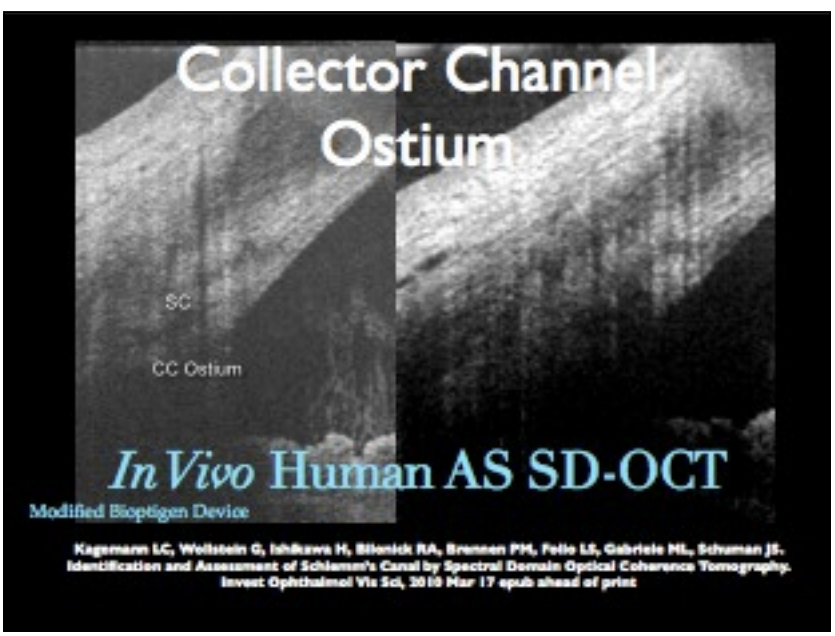

SD-OCT RTVue RNFL GPA
OD
OS

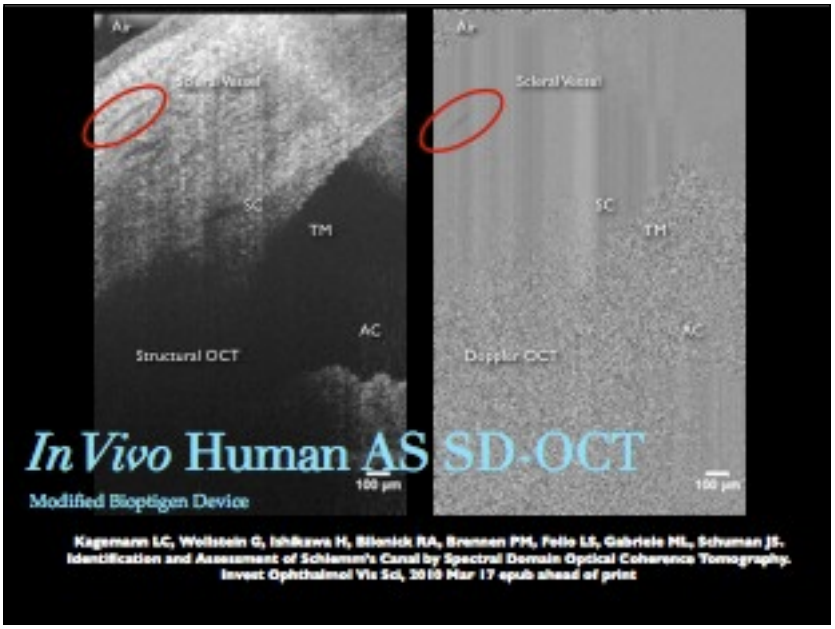

SD-OCT ONH GPA
OD
OS

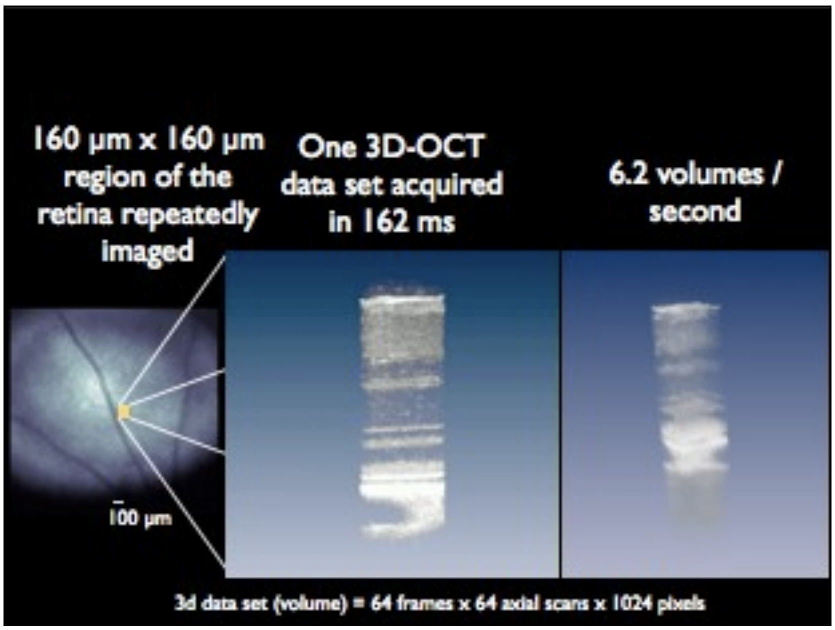


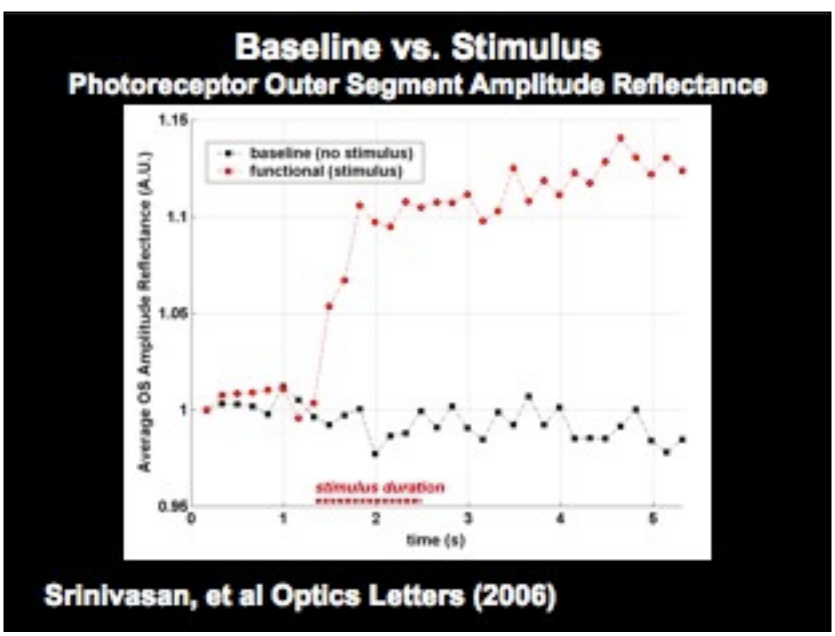
OCT in the Lab

What's New?

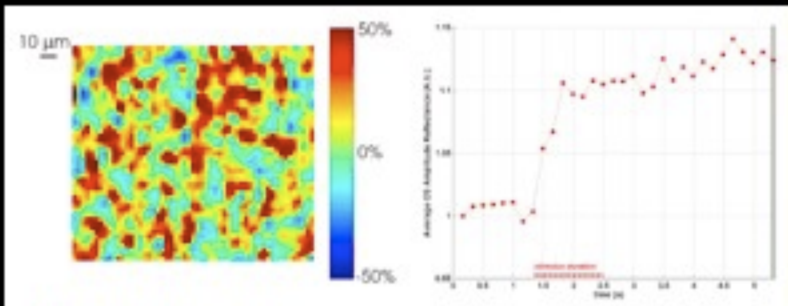



Air
Scleral Vessel
SC
TM
AC
Structural OCT
Doppler OCT
100 μm
100 μm
In Vivo Human AS SD-OCT
Modified Bioptigen Device
Kagemann LC, Wollstein G, Ishikawa H, Bilonick RA, Brennen PM, Folio LS, Gabriele ML, Schuman JS.
Identification and Assessment of Schlemm's Canal by Spectral Domain Optical Coherence Tomography.
Invest Ophthalmol Vis Sci, 2010 Mar 17 epub ahead of print


160 μm x 160 μm region of the retina repeatedly imaged
One 3D-OCT data set acquired in 162 ms
6.2 volumes / second
100 μm
3d data set (volume) = 64 frames x 64 axial scans x 1024 pixels


Baseline vs. Stimulus
Photoreceptor Outer Segment Amplitude Reflectance
baseline (no stimulus)
functional (stimulus)
Average OS Amplitude Reflectance (A.U.)
1.15
1.1
1.05
1
0.95
stimulus duration
0
1
2
3
4
5
time (s)
Srinivasan, et al Optics Letters (2006)

En Face View of Functional Response
Photoreceptor Outer Segments

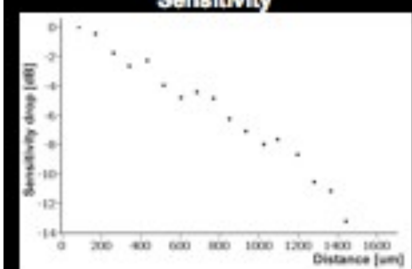


- 160 µm x 160 µm region
- Differential response in color scale (above left)
- Average normalized response shown in scatter plot (above right)

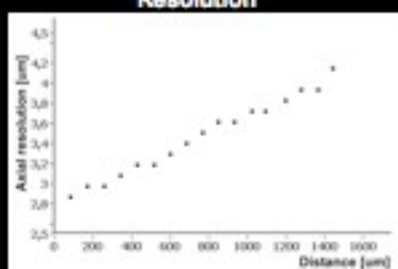
Srinivasan, et al Optics Letters (2006)

Limitations of Spectral / Fourier Domain OCT

Sensitivity



Resolution



- Sensitivity varies with depth
- Resolution varies with depth
- Speed is limited by CCD camera speeds
- Resolution / depth trade off - limited by number of CCD pixels

High Speed OCT using Frequency Swept Lasers

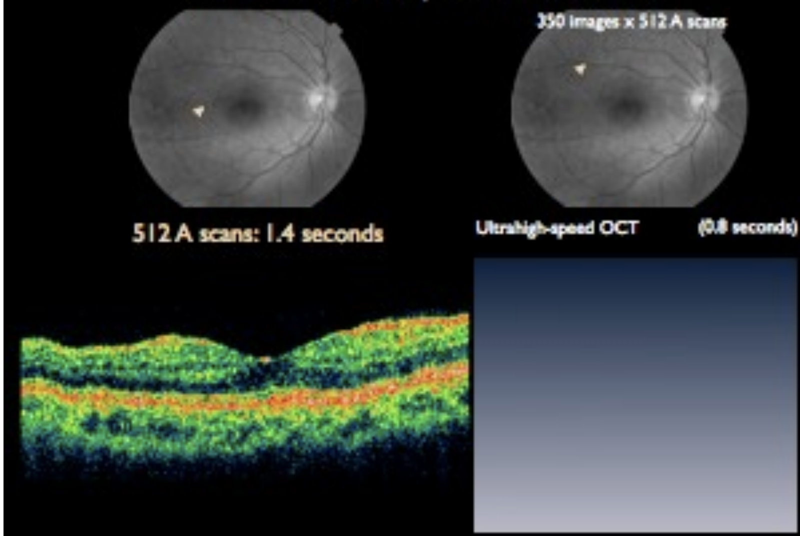
- "Swept Source / Fourier domain" detection enables dramatic improvements in speed and sensitivity
- ~500x higher speed than standard OCT
- No spectrometer or CCD required
- Uses high speed single or dual channel A/D
- Can operate at 1 and 1.3 um wavelengths
- Requires narrow linewidth, high speed, frequency swept lasers

TD-OCT v. Swept Source OCT

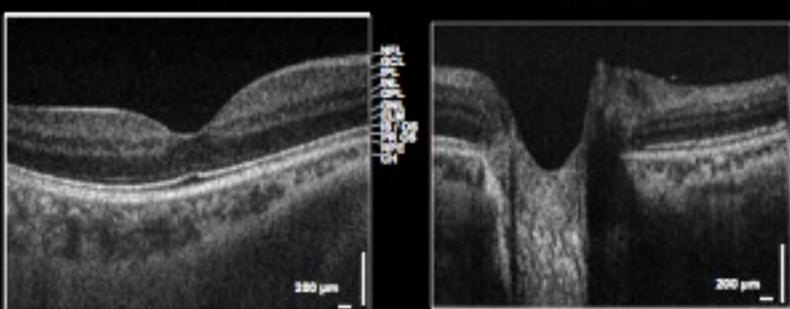
350 images x 512 A scans

512 A scans: 1.4 seconds

Ultrahigh-speed OCT (0.8 seconds)



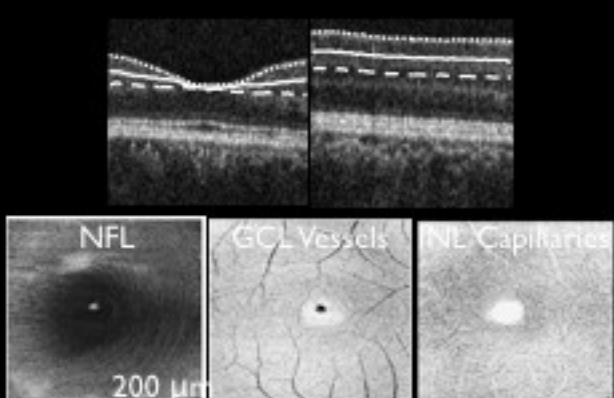
High Definition Imaging



~16,000 axial scans per image
~8 micron resolution in retina
Improved choroidal penetration at 1050 nm

Srinivasan V, Adler D, Chen Y, Gorczynska I, Huber R, Duker J, Schuman JS, Fujimoto J. Ultrahigh-speed Optical Coherence Tomography for Three-Dimensional and En Face Imaging of the Retina and Optic Nerve Head. IOVS. November 2008 Vol.49, No. 11. 5103-5118.

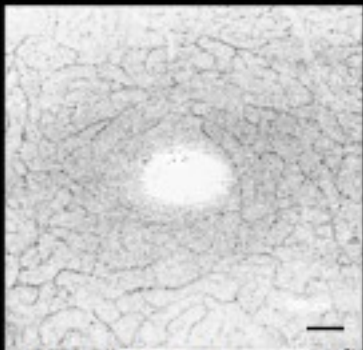
En Face Imaging of Inner Retina



512 x 850 axial scans, 2 s

Srinivasan V, Adler D, Chen Y, Gorczynska I, Huber R, Duker J, Schuman JS, Fujimoto J. Ultrahigh-speed Optical Coherence Tomography for Three-Dimensional and En Face Imaging of the Retina and Optic Nerve Head. IOVS. November 2008 Vol.49, No. 11. 5103-5118.

Imaging of capillaries near the foveal avascular zone

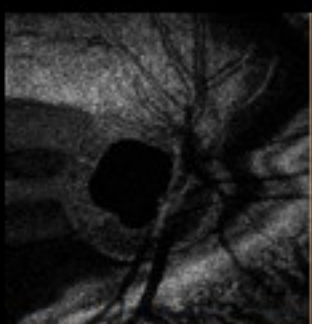


512 x 850 axial scans, 2 s

Confocal micrographs of the foveal avascular zone (FAZ) in a retinal wholemount from a young adult macaque monkey (modified from Provis et al. 2000).
The endothelial cells are immunocytochemically labeled with antibodies to CD31 and Von Wildebrand's factor.

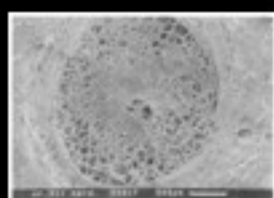
Srinivasan V, Adler D, Chen Y, Gorczynska I, Huber R, Duker J, Schuman JS, Fujimoto J. Ultrahigh-speed Optical Coherence Tomography for Three-Dimensional and En Face Imaging of the Retina and Optic Nerve Head. IOVS. November 2008 Vol.49. No. 11. 5103-5118.

En Face Imaging of the Lamina Cribrosa



En Face depth sectioning using ultrahigh speed OCT

512 x 450 axial scans, 1 sec

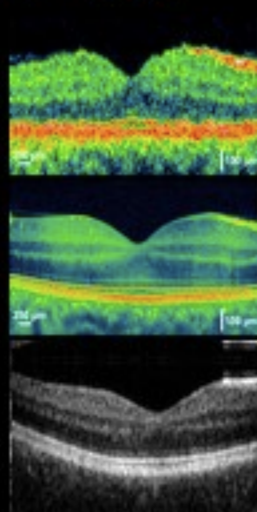


Scanning Electron Microscope Image of the Lamina Cribrosa. From Jonas et. al, IOVS, 1991

Srinivasan V, Adler D, Chen Y, Gorczynska I, Huber R, Duker J, Schuman JS, Fujimoto J. Ultrahigh-speed Optical Coherence Tomography for Three-Dimensional and En Face Imaging of the Retina and Optic Nerve Head. IOVS. November 2008 Vol.49. No. 11. 5103-5118.

OCT technologies for retinal imaging

- Time-domain OCT
  - 400 axial scans per second
  - 1 (500 pixel) image per second
  - Zeiss StratusOCT
- Spectral / Fourier domain OCT
  - ~25,000 - 55,000 axial scans per second
  - ~100 - 200 images per second
  - >7 companies marketing instruments
- Swept source / Fourier domain OCT
  - ~250,000 axial scans per second
  - ~500 images per second
  - Resolution lower than spectral OCT
  - Currently in the research stage



SD-OCT

- Limitations
  - The technology is young, still in evolution.
  - OCT imaging may be difficult in the presence of media opacities such as dense central corneal scarring, severe posterior subcapsular cataract, dense vitreous hemorrhage
  - SD-OCT still requires development of robust alignment and registration algorithms to approach its clinical potential

OCT in Glaucoma

- Optical Coherence Tomography (OCT) is a useful tool for the assessment of the presence or absence of glaucoma and its progression
  - Structure – function correlates
  - Identify areas of abnormality or change
  - Reduce uncertainty in Glaucoma Suspects
- 3D OCT imaging increases reproducibility, and may enhance sensitivity and specificity
- OCT statistical software for the measurement of glaucoma progression is now commercially available

The Future of OCT - Where Are We Going?

- Novel diagnostics are at hand for assessment of disease and its progression
- Current commercially available technology may be used in new ways to assess disease and progression

Collaboration

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Clark Glymour, PhD
Gary Miller, PhD
George Stetten, PhD
David Tolliver, PhD

Intel Labs
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Cynthia Mattox, MD
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Copernicus U.
Maciej Wojtkowski, PhD

Christian Doppler Institute, Vienna
Wolfgang Drexler, PhD

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