Taiwan Academy of Ophthalmology
Taipei, March 31, 2012

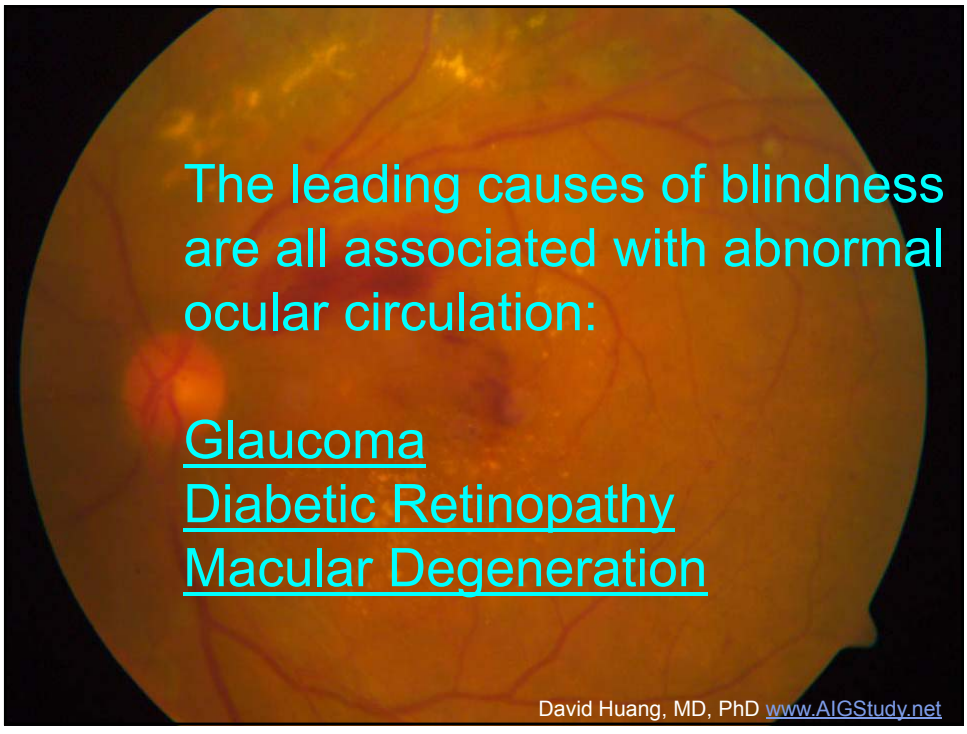
Measurement of Blood Flow in the Retina and Optic Disc with OCT

David Huang, MD, PhD
Weeks Professor of Ophthalmic Research
Professor of Ophthalmology & Biomedical Engineering
Casey Eye Institute, Oregon Health & Science University
Portland, Oregon

OREGON HEALTH & SCIENCE UNIVERSITY
OHSU

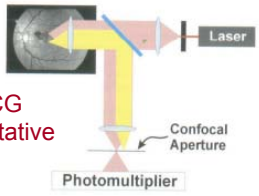
CASEY EYE INSTITUTE

Financial Interests:
Dr. D. Huang has a significiant 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.
Optovue, Inc.: stock options, patent royalty, grants, speaker honorarium & travel support
Carl Zeiss Meditec, Inc.: patent royalty

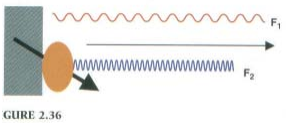


A technique for rapid & accurate quantitation of total retinal blood flow is needed

Fluorescein & ICG angiography - qualitative



Laser doppler flowmeter – time consuming



GURE 2.36

Doppler ultrasound - inaccurate

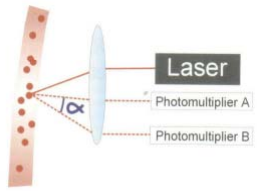


FIGURE 2.41

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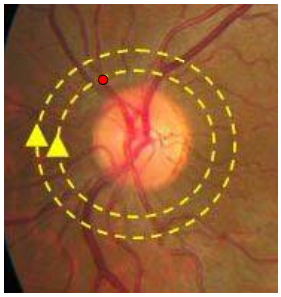
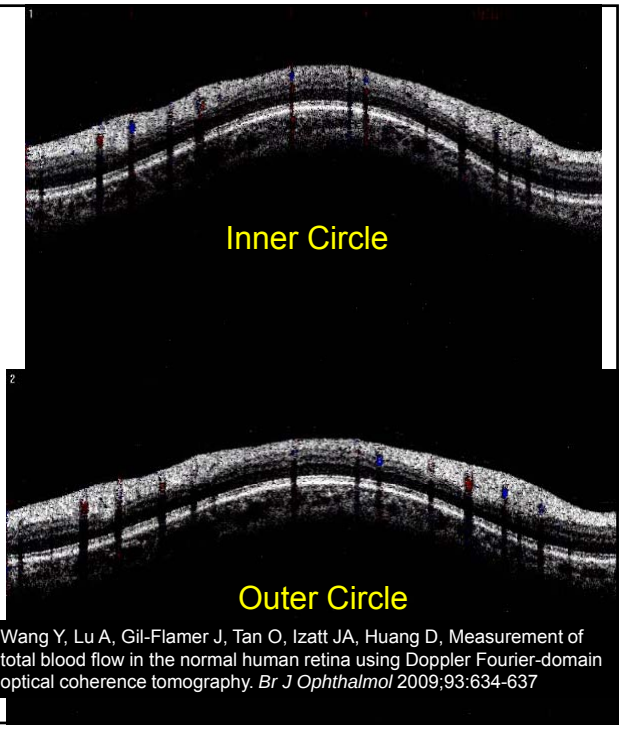
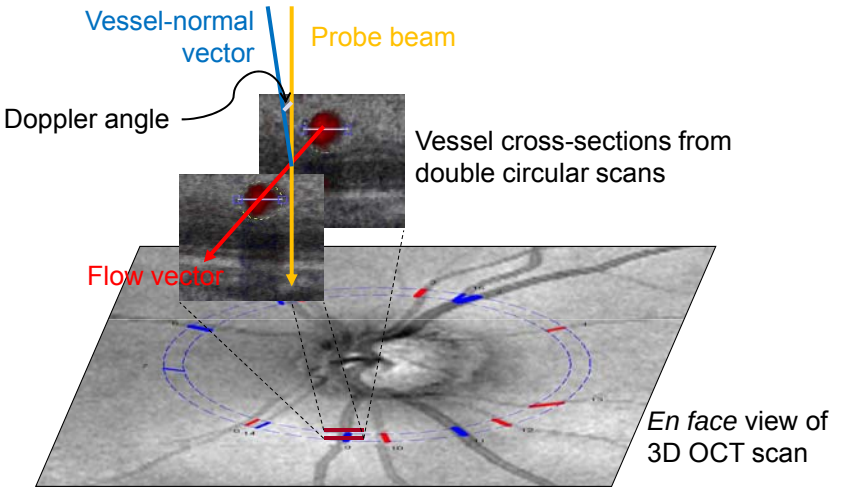
Double circular scan transects all retinal branch vessels 12 times in 2 seconds





Wang Y, Lu A, Gil-Flamer J, Tan O, Izatt JA, Huang D, Measurement of total blood flow in the normal human retina using Doppler Fourier-domain optical coherence tomography. *Br J Ophthalmol* 2009;93:634-637

Semi-automated grading software was developed for Doppler OCT reading center



Doppler OCT of Retinal Circulation (DOCTORC) software uses both double-circular and 3D volumetric scans

Ou Tan, PhD & David Huang, MD, PhD www.COOLLab.net

Glaucoma, treated proliferative diabetic retinopathy, and optic neuropathy all reduce retinal blood flow

Group (# of eyes)	*Blood Flow (µl/min)*
Normal (20)	47.6 ± 5.4
Glaucoma (16)	34.1 ± 4.9 (p<0.001) ↓
NAION (7)	28.2 ± 8.2 (p<0.001) ↓
PDR (5)	15.8 ± 10.1 (p<0.001) ↓

Wang Y, Fawzi AA, Varma R, Sadun AA, Zhang X, Tan O, Izatt JA, Huang D. Pilot Study of Optical Coherence Tomography Measurement of Retinal Blood Flow in Retinal and Optic Nerve Diseases. *IOVS* 2011; 52:840

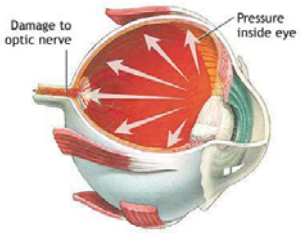
Doppler OCT detects decreased blood flow in HIV microvasculopathy

	HIV (n=22)	Controls (n=23)	P value
Total Blood Flow[a]			
Mean ± SD (µL/min)	38.2 ± 8.1	47.2 ± 7.0	**0.0007**
Median (range, [µL/min])	39.0 (22.7 to 53.5)	44.4 (38.1 to 62.4)	

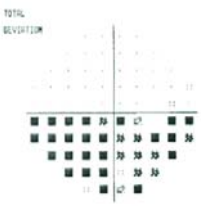
Courtesy of Drs. Partho Kalyani & Gary Holland (UCLA)

What is the role of blood flow in glaucoma?

Elevated IOP



Loss of retinal ganglion cells & nerve fibers



Loss of visual field

?

Decreased blood flow

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Visual field, total retinal blood flow, and neural tissue loss were studied

Optovue RTVue Fourier-domain OCT system
Overall average thickness of the nerve fiber layer (NFL)
Overall average thickness of the ganglion cell complex (GCC)
Total retinal blood flow (Doppler software not yet FDA-approved)

Heidelberg Retina Tomograph (HRT3) confocal scanning laser ophthalmoscopy (cSLO) system
Optic nerve head rim area

Huang JC, Konduru R, Zhang X, Tan O, Francis BA, Varma R, Sehi M, Greenfield DS, Sadda SR, Huang D. Relationship among visual field, blood flow, and neural structure measurements in glaucoma. *IOVS* 2012; in press

Perimetric glaucoma and age-matched normal subjects in the Advanced Imaging for Glaucoma study cohort were studied

Characteristic	Normal	Glaucoma	p-value
Patients, n	27	42	
Eyes, n	27	47	
Age (Years)	62.1 ± 9.0	61.4 ± 8.7	0.73
Diabetes Mellitus, n (%)	1 (4)	3 (7)	0.99
Systemic Hypertension, n (%)	10 (37)	15 (36)	0.84
Systemic Antihypertensive Medication, n (%)	4 (15)	11 (23)	0.56
Intraocular Pressure (mmHg)	14.3 ± 2.1	13.5 ± 2.4	0.13
Diastolic Blood Pressure (mmHg)	82.5 ± 8.6	80.3 ± 8.0	0.32
Systolic Blood Pressure (mmHg)	130.3 ± 17.1	124.6 ± 12.0	0.12
Diastolic Ocular Perfusion Pressure (mmHg)	68.6 ± 8.9	66.8 ± 7.5	0.41
Systolic Ocular Perfusion Pressure (mmHg)	116.4 ± 17.6	111.1 ± 11.1	0.27

Huang JC, Konduru R, Zhang X, Tan O, Francis BA, Varma R, Sehi M, Greenfield DS, Sadda SR, Huang D. Relationship among visual field, blood flow, and neural structure measurements in glaucoma. *IOVS* 2012; in press

Total retinal blood flow and vascular caliber were reduced in glaucoma subjects

Parameter	Normal	Glaucoma	p-value
Total Retinal Blood Flow (µl/min)	45.5 ± 9.5	34.9 ± 8.5	< 0.001
Arterial Area (mm^2)	0.033 ± 0.0077	0.028 ± 0.0074	0.006
Venous Area (mm^2)	0.047 ± 0.012	0.041 ± 0.0086	0.01

Huang JC, Konduru R, Zhang X, Tan O, Francis BA, Varma R, Sehi M, Greenfield DS, Sadda SR, Huang D. Relationship among visual field, blood flow, and neural structure measurements in glaucoma. *IOVS* 2012; in press

Blood flow was highly correlated with visual field, but not with structural parameters

Spearman's correlation coefficient *R*

Parameter	Visual Field MD (dB)	Blood Flow (dB)	cSLO Rim Area (dB)	OCT NFL (dB)
Blood Flow (dB)	0.48 (<0.01)			
cSLO Rim Area (dB)	0.34 (0.02)	-0.02 (.91)		
OCT RNFL Thickness (dB)	0.37 (0.01)	0.19 (0.23)	0.36 (0.02)	
OCT GCC Thickness (dB)	0.20 (0.20)	0.03 (0.84)	0.31 (0.04)	0.68 (<0.01)

- All values in dB scale normalized against 27 normal eyes.
- Age, blood pressure, intraocular pressure, and ocular perfusion pressure were not significantly correlated VF, blood flow, or structural measures

Huang JC, Konduru R, Zhang X, Tan O, Francis BA, Varma R, Sehi M, Greenfield DS, Sadda SR, Huang D. Relationship among visual field, blood flow, and neural structure measurements in glaucoma. *IOVS* 2012; in press

Visual field loss was independently correlated with both blood flow and neural tissue loss

Multivariate regression and analysis of variance for visual field mean deviation (MD)

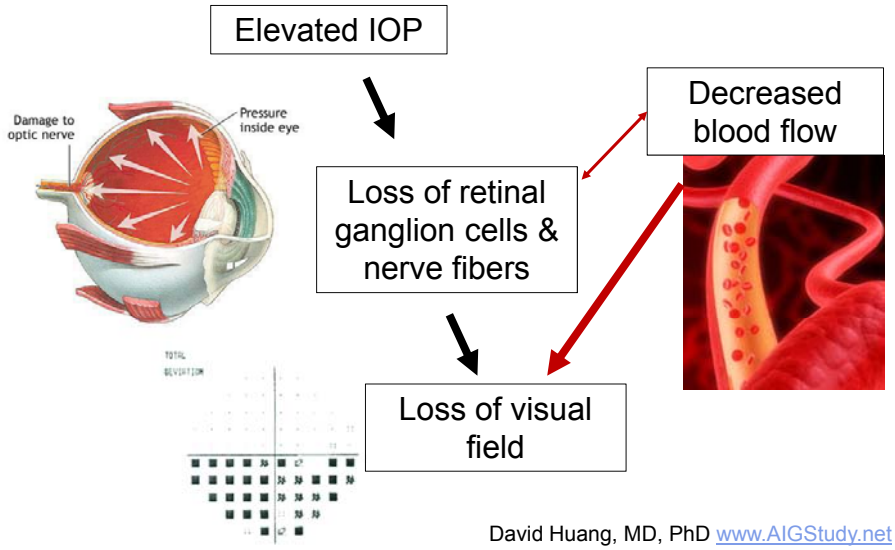
	Variable 1	Slope (p)	R^2	Variable 2	Slope (p)	R^2	Total R^2
Model 1	Blood Flow	1.91 (<0.001)	0.26	Rim Area	1.15 (0.006)	0.10	0.36
Model 2	Blood Flow	1.62 (0.001)	0.24	NFL	2.56 (0.03)	0.09	0.33

- All values in dB scale normalized against 27 normal eyes.
- Age, blood pressure, intraocular pressure, and ocular perfusion pressure were not significant factors when added to the multivariate models

Blood flow is >2 times as important as structural variables in explaining the variation in visual field deviation

Huang JC, Konduru R, Zhang X, Tan O, Francis BA, Varma R, Sehi M, Greenfield DS, Sadda SR, Huang D. Relationship among visual field, blood flow, and neural structure measurements in glaucoma. *IOVS* 2012; in press

Blood flow has a direct effect on visual function independent of neural structural loss



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OCT Split-Spectrum Amplitude-Decorrelation Angiography (SSADA)

David Huang, MD, PhD
Yali Jia, PhD

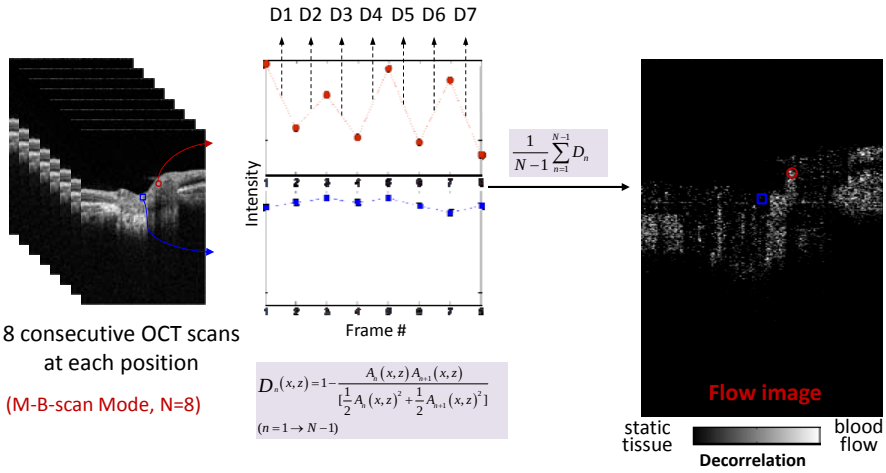
Ultrahigh-Speed Swept-Source OCT

Developed by MIT Optic & Quantum Electronic Group (Fujimoto) and OHSU Center for Ophthalmic Optics and Lasers (Huang)

Performance features:

- 100,000 axial scans/sec
- 1050 nm tunable laser (deep penetration)
- 6 µm axial resolution in tissue

OCT amplitude-decorrelation angiography uses intrinsic contrast – no dye injection!



8 consecutive OCT scans at each position

(M-B-scan Mode, N=8)

$$D_n(x,z) = 1 - \frac{A_n(x,z)A_{n+1}(x,z)}{[\frac{1}{2}A_n(x,z)^2 + \frac{1}{2}A_{n+1}(x,z)^2]}$$
$$(n = 1 \to N-1)$$

Problem: 8 frames at one position do not provide sufficient angiography quality

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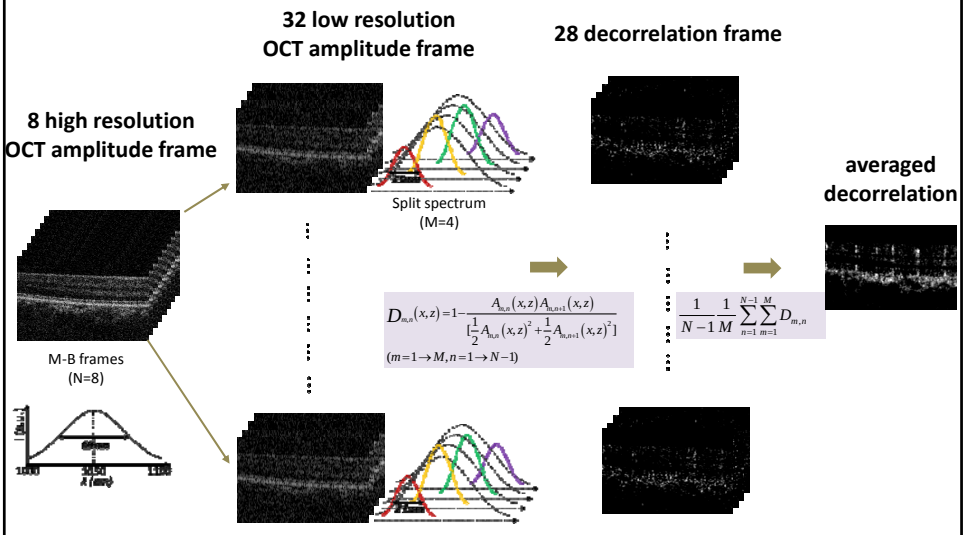
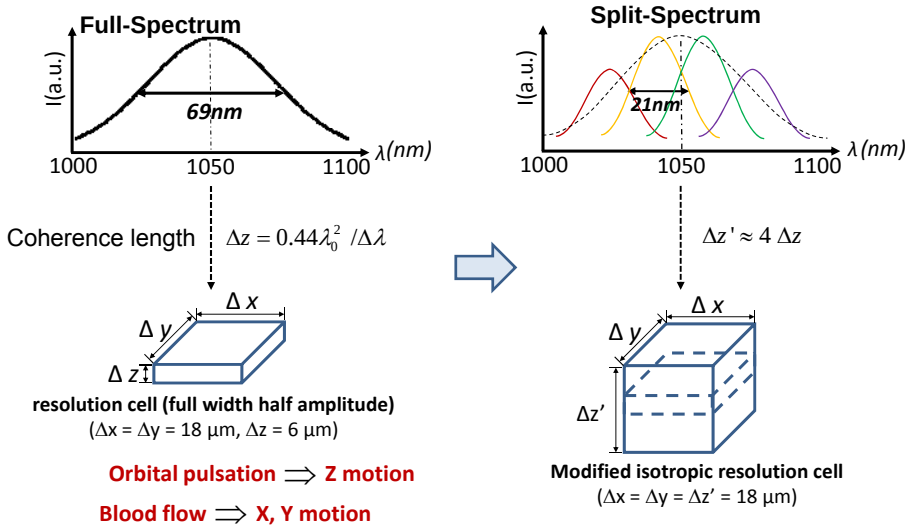
Solution: Split-Spectrum Amplitude Decorrelation (SSADA) Algorithm



8 frames at one position now provides good angiography quality

Intentional lowering of OCT resolution to optimize flow detection



resolution cell (full width half amplitude)
(Δx = Δy = 18 µm, Δz = 6 µm)

Orbital pulsation ⟹ Z motion

Blood flow ⟹ X, Y motion

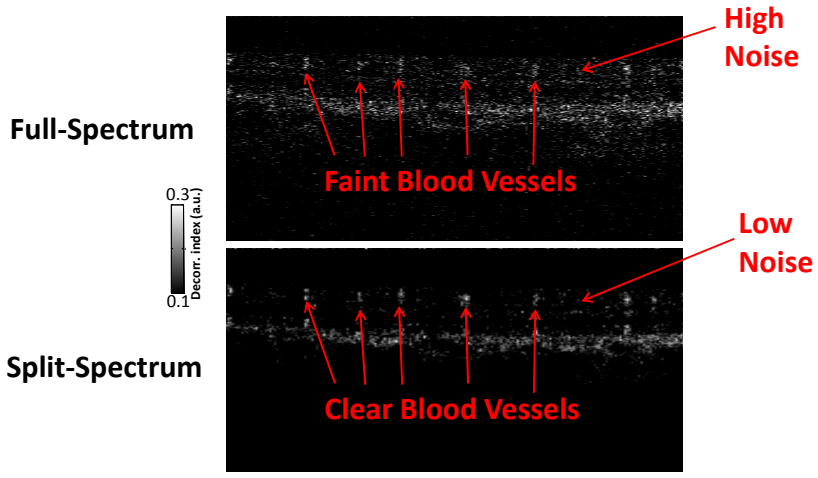
More sensitive to noise than flow

Modified isotropic resolution cell
(Δx = Δy = Δz' = 18 µm)

More channels of flow information
Less axial motion noise

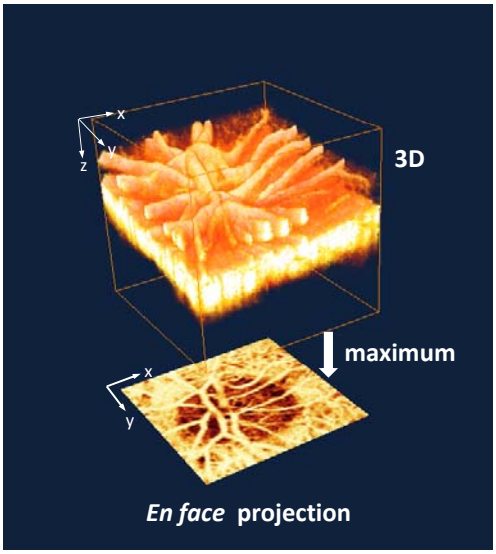
Yali Jia, PhD, David Huang, MD, PhD www.COOLLab.net

Comparison of Cross-Sectional Decorrelation Angiograms



Jia Y, Tan O, Tokayer J, Potsaid B, Wang Y, Liu JJ, Kraus MF, Subhash H, Fujimoto JG, Hornegger J, Huang D.
Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. *Optics Express* 2012; 20:4710

En face Projection Angiogram



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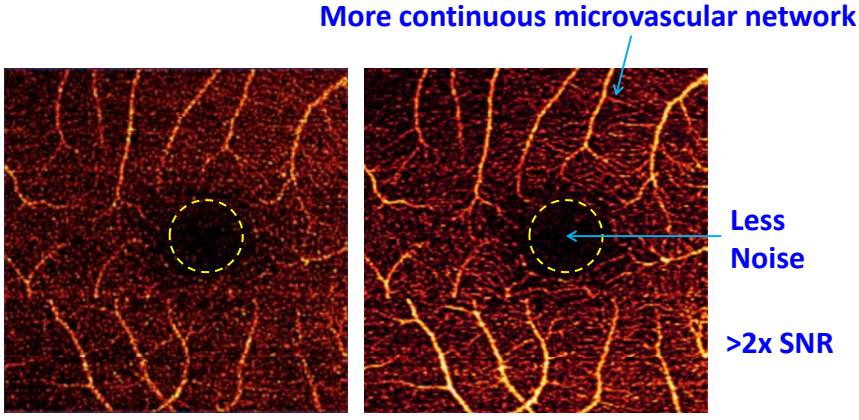
Comparison of Angiography Algorithms



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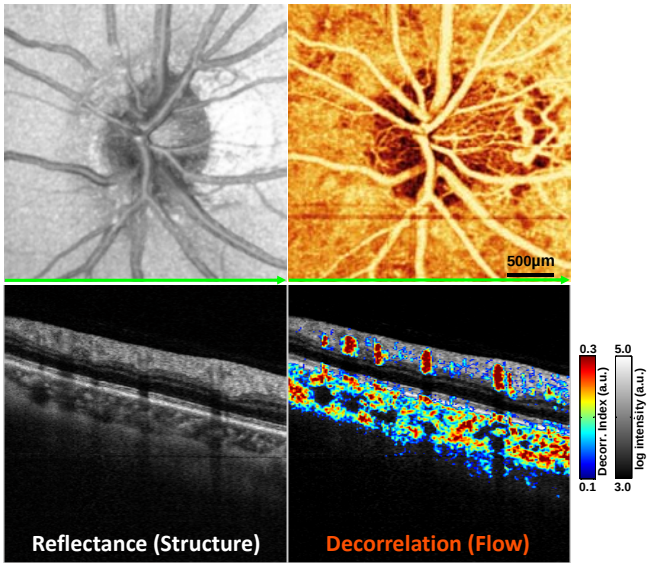
OCT angiography is 3 dimensional

SSADA algorithm used

3x3x3 mm OCT 3D angiography acquired in a 3-second scan



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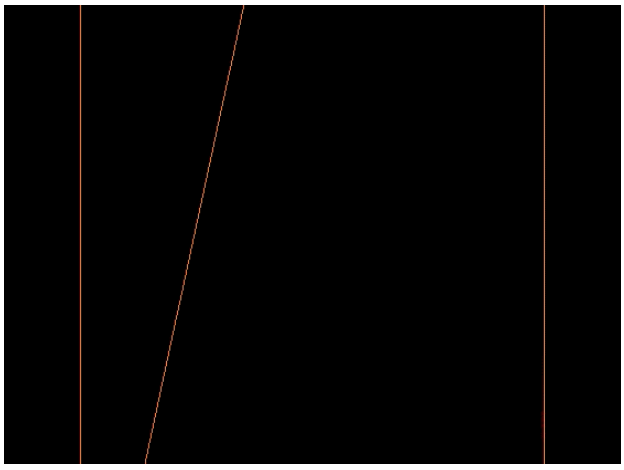
OCT Angiography of the Optic Nerve Head – Layer by Layer

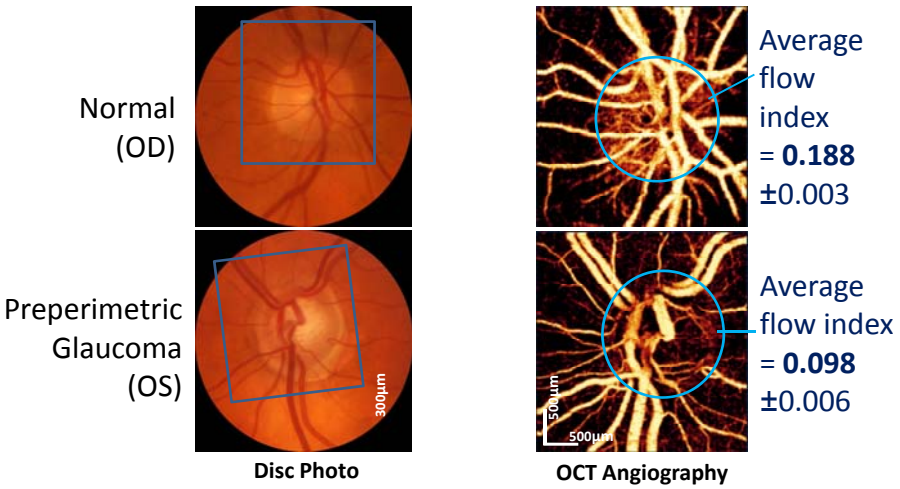
SSADA algorithm used

3x3x3 mm OCT 3D angiography acquired in a 3-second scan



Jia Y, Tan O, Tokayer J, Potsaid B, Wang Y, Liu JJ, Kraus MF, Subhash H, Fujimoto JG, Hornegger J, Huang D. Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. *Optics Express* 2012; 20:4710

OCT Angiography Showing Reduced ONH Blood Flow in Glaucoma



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OCT Angiography (SSADA) v. Fluorescein/ICG Angiography

OCT Advantages

- 3 dimensional
  - Easily separates disc, retinal, and choroidal circulations
  - Sections & projections along any plane
- Quantitative
  - Flow index
- No injection
  - No vomiting or anaphylactic reaction

OCT Disadvantages

- Small field (3 mm)
  - Field will increase with higher speed
- No visualization of leakage and stain
  - But can visualize fluid space and thickening

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Applications of OCT Angiography & Doppler OCT

- Diabetic Retinopathy:
  - Assess capillary dropout & macular ischemia
  - Visualize Neovacularization in 3D
  - Evaluate global reduction in blood flow
- Age-related macular degeneration
  - Assess choroidal ischemia
  - See flow in choroidal neovascular membrane
- Glaucoma
  - Evaluate global reduction in blood flow
  - Evaluate reduced disc perfusion
  - Evaluate reduced macular ganglion cell perfusion
- Diagnosis, prognosis, tracking, assessing treatment effectiveness

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Advanced Imaging for Glaucoma

R01 EY013516 www.AIGStudy.net


Consortium PI: David Huang MD, PhD


Ou Tan, PhD


Yimin Wang, PhD


Xinbo Zhang, PhD


Site PI: Rohit Varma, MD, MPH


Brian Francis, MD


Vikas Chopra, MD


Site PI: David Greenfield, MD


Mitra Sehi, PhD


Carolyn Quinn, MD


Krisha S. Kishor, MD


Robert DiLaura


Sharon Bi, MCIS


Site PI: Joel S. Schuman, MD


Robert Noecker, MD


Gadi Wollstein, MD


Hiroshi Ishikawa, MD


Larry Kagemann, MS


Site PI: James G. Fujimoto, PhD

Acknowledgement of other supports

Unrestricted grant from
Research to Prevent Blindness

Material support from Optovue, Inc.

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David Huang, MD, PhD


Ou Tan, PhD


Yimin Wang, PhD


Maolong Tang, PhD


Yan Li, PhD


Xinbo Zhang, PhD


Yali Jia, PhD


Michelle Montalto


Janice Van Norman, COT


Jason Tokayer, MS


Matthew Bald


Kathleen S. Torok, MA