Future OCT Technology

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RETINAL UPDATE 2015
January 31, 2015

Disclosure

- Research Grant Recipient: Optos, Carl Zeiss Meditec, Optovue
- Consultant: Carl Zeiss Meditec, Optos

Limitations of existing SDOCT

- Retinal layers are well visualized, but not individual cells
- Speed is adequate, but still limits scanning area or amount of oversampling
- Functional data still relatively limited
- Dynamic vascular (blood flow/leakage) information is lacking
- Automatic quantitative data is limited
- Requires trained operator

Future OCT Technologies

OUTLINE

- Improved Resolution
- Improved Speed
- Improved Penetration
- Functional Information
- Vascular/Molecular Imaging
- Increased Automation

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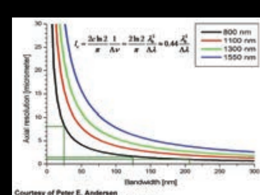
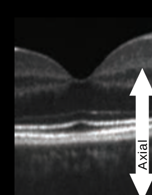
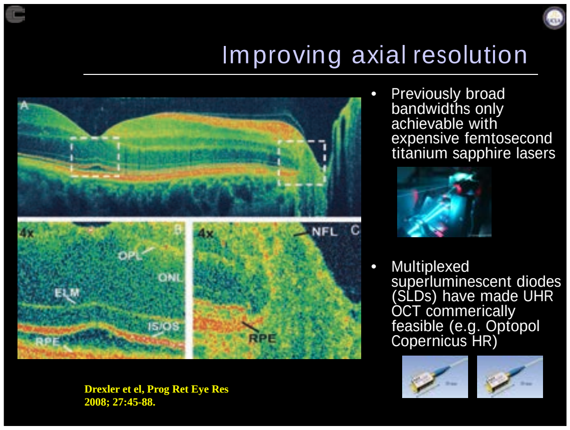
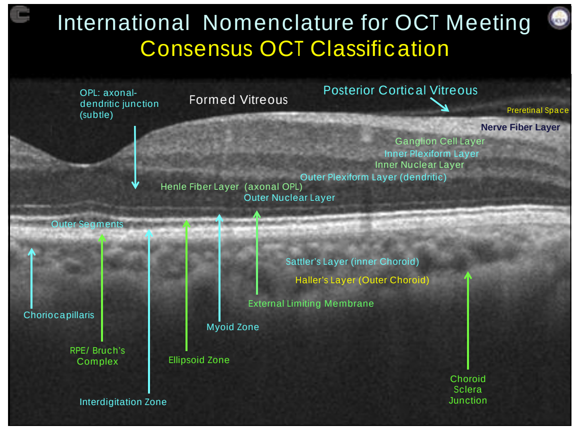
Improving axial resolution

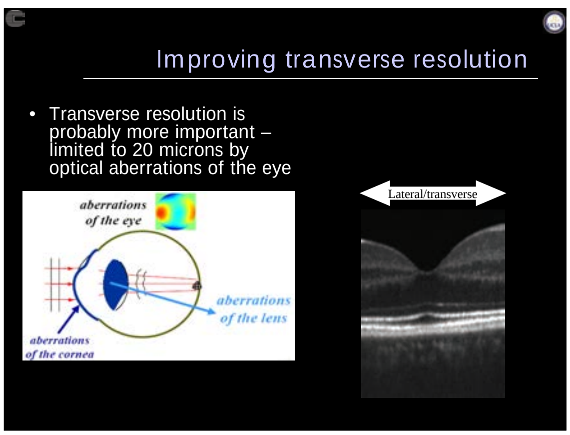
- Axial resolution depends on light source bandwidth and wavelength

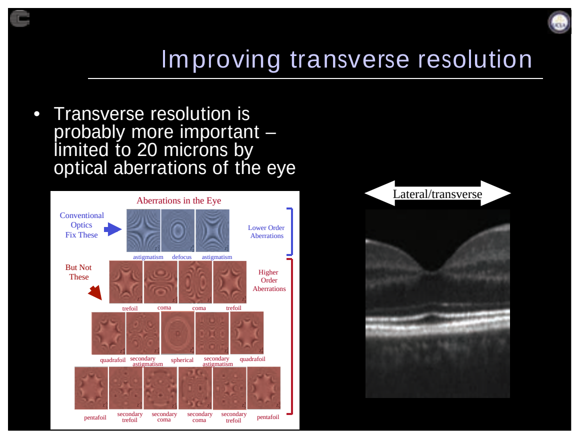


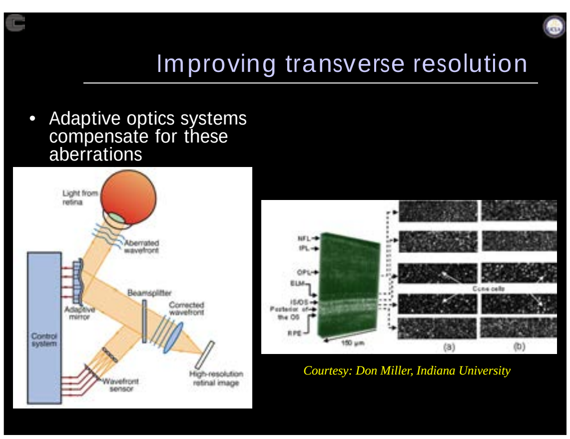


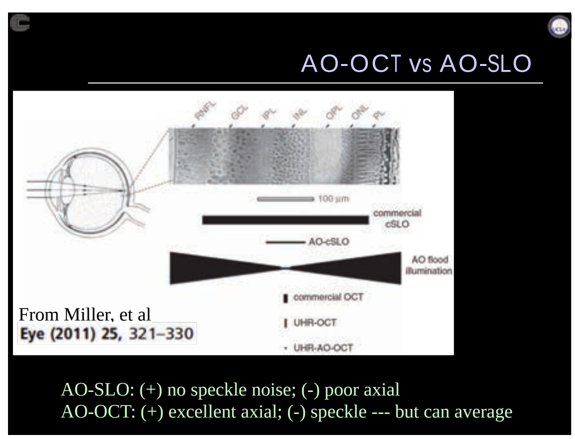

Improving axial resolution
Previously broad bandwidths only achievable with expensive femtosecond titanium sapphire lasers
Multiplexed superluminescent diodes (SLDs) have made UHR OCT commercially feasible (e.g. Optopol Copernicus HR)
NFL
OPL
ONL
ELM
IS/OS
RPE
4x
Drexler et el, Prog Ret Eye Res 2008; 27:45-88.


International Nomenclature for OCT Meeting
Consensus OCT Classification
OPL: axonal-dendritic junction (subtle)
Formed Vitreous
Posterior Cortical Vitreous
Preretinal Space
Nerve Fiber Layer
Ganglion Cell Layer
Inner Plexiform Layer
Inner Nuclear Layer
Outer Plexiform Layer (dendritic)
Henle Fiber Layer (axonal OPL)
Outer Nuclear Layer
Outer Segments
Sattler's Layer (inner Choroid)
Haller's Layer (Outer Choroid)
External Limiting Membrane
Choriocapillaris
Myoid Zone
RPE/ Bruch's Complex
Ellipsoid Zone
Choroid Sclera Junction
Interdigitation Zone


Improving transverse resolution
Transverse resolution is probably more important – limited to 20 microns by optical aberrations of the eye
aberrations of the eye
aberrations of the lens
aberrations of the cornea
Lateral/transverse


Improving transverse resolution
Transverse resolution is probably more important – limited to 20 microns by optical aberrations of the eye
Aberrations in the Eye
Conventional Optics Fix These
Lower Order Aberrations
But Not These
Higher Order Aberrations
Lateral/transverse

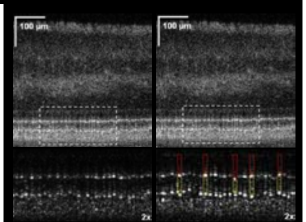

Improving transverse resolution
Adaptive optics systems compensate for these aberrations
Light from retina
Aberrated wavefront
Beamsplitter
Corrected wavefront
Adaptive mirror
Control system
Wavefront sensor
High-resolution retinal image
Courtesy: Don Miller, Indiana University


AO-OCT vs AO-SLO
100 µm
commercial cSLO
AO-cSLO
AO flood illumination
commercial OCT
UHR-OCT
UHR-AO-OCT
From Miller, et al
Eye (2011) 25, 321–330
AO-SLO: (+) no speckle noise; (-) poor axial
AO-OCT: (+) excellent axial; (-) speckle --- but can average

AO-OCT

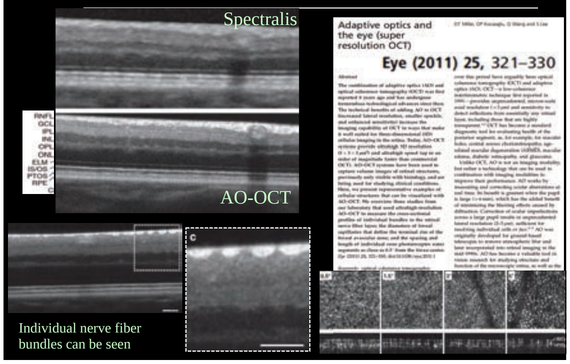
- Isotropic 3D resolution (3.5 microns x 3.5 microns x 3.5 microns)

Ultrahigh-resolution optical coherence tomography with monochromatic and chromatic aberration correction



Visualization of individual cone inner and outer segments

AO-OCT



Individual nerve fiber bundles can be seen

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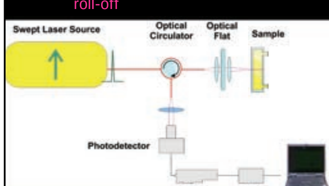
Improved Speed

- Swept Source OCT
  - Another Fourier domain OCT technology
  - 10X faster than existing SD-OCT instruments
  - Also better sensitivity with less roll-off



Ultrahigh speed 1050nm swept source / Fourier domain OCT retinal and anterior segment imaging at 100,000 to 400,000 axial scans per second

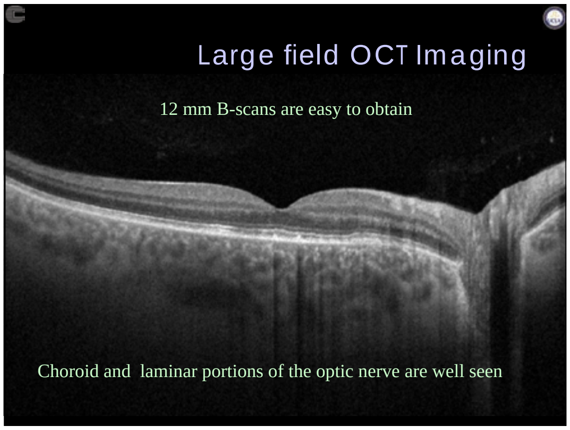
From Potsaid et al, *Optics Express 2010; 18: 20029.*

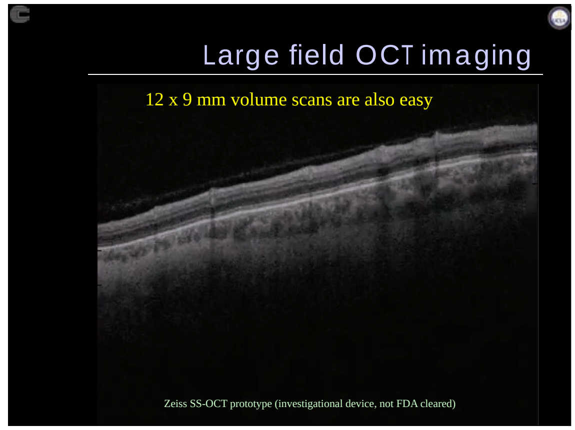
Improved Speed

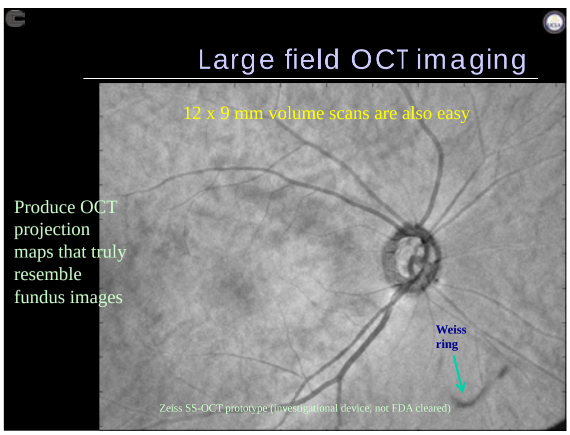
- Swept Source OCT
  - At these speeds, fixation/motion no longer an issue
  - Large areas can be scanned quickly and with extensive averaging

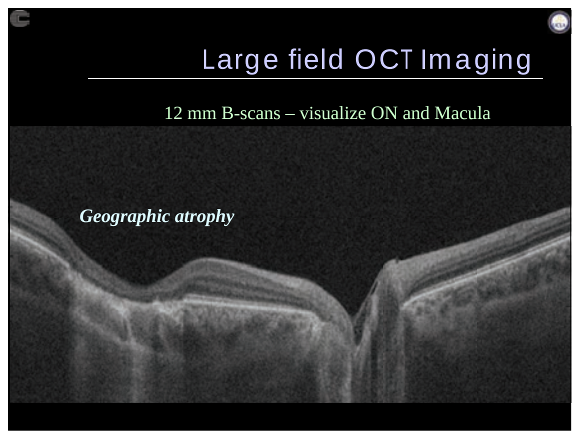
Ultrahigh speed 1050nm swept source / Fourier domain OCT retinal and anterior segment imaging at 100,000 to 400,000 axial scans per second

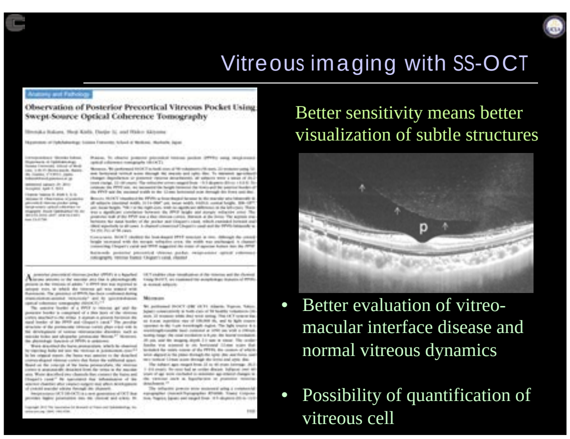
From Potsaid et al, *Optics Express 2010; 18: 20029.*

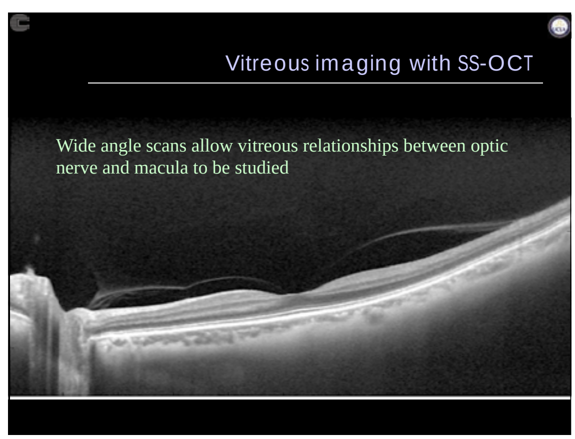

Large field OCT Imaging
12 mm B-scans are easy to obtain
Choroid and laminar portions of the optic nerve are well seen

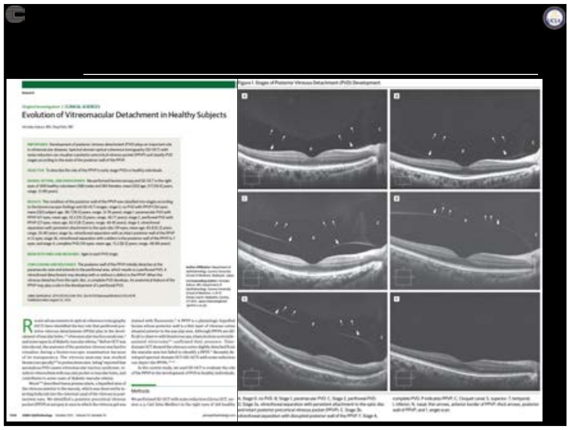

Large field OCT imaging
12 x 9 mm volume scans are also easy
Zeiss SS-OCT prototype (investigational device, not FDA cleared)

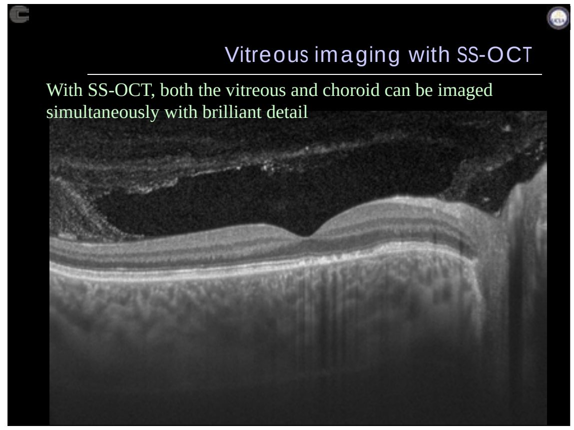

Large field OCT imaging
12 x 9 mm volume scans are also easy
Produce OCT projection maps that truly resemble fundus images
Weiss ring
Zeiss SS-OCT prototype (investigational device, not FDA cleared)

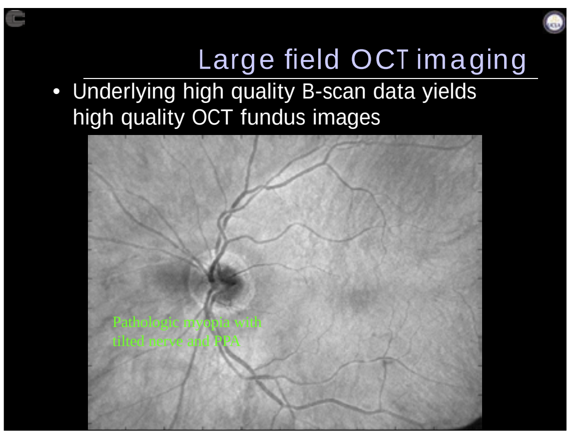

Large field OCT Imaging
12 mm B-scans – visualize ON and Macula
Geographic atrophy

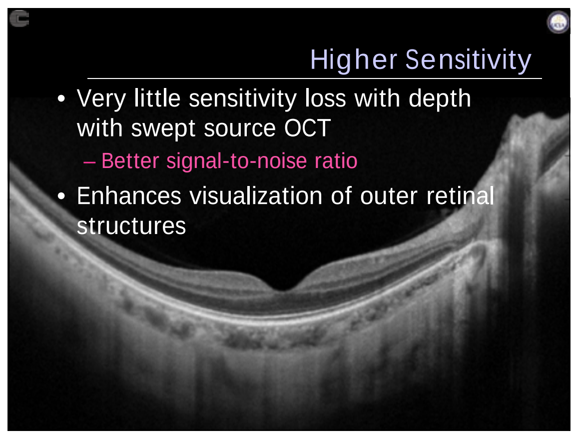

Vitreous imaging with SS-OCT
Observation of Posterior Precortical Vitreous Pocket Using Swept-Source Optical Coherence Tomography
Better sensitivity means better visualization of subtle structures
P
Better evaluation of vitreo-macular interface disease and normal vitreous dynamics
Possibility of quantification of vitreous cell

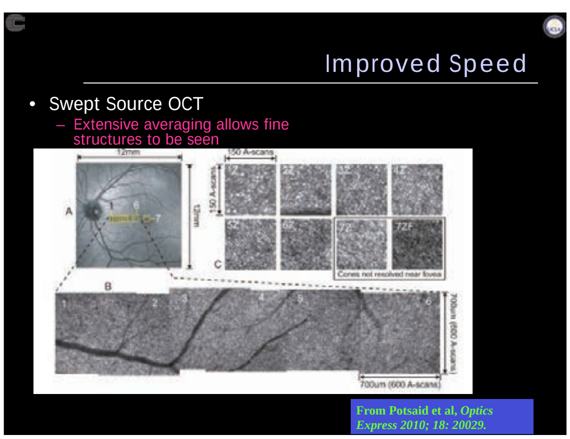

Vitreous imaging with SS-OCT
Wide angle scans allow vitreous relationships between optic nerve and macula to be studied

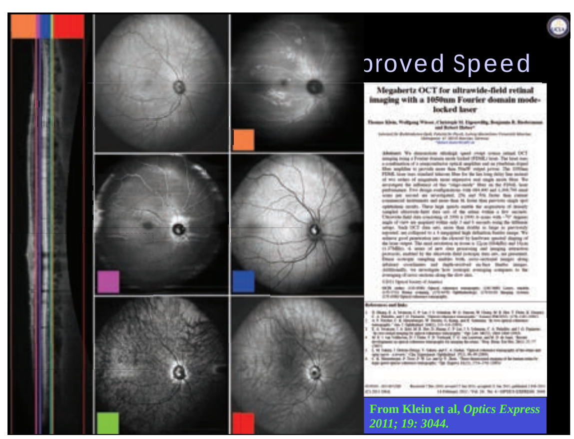

Evolution of Vitreomacular Detachment in Healthy Subjects

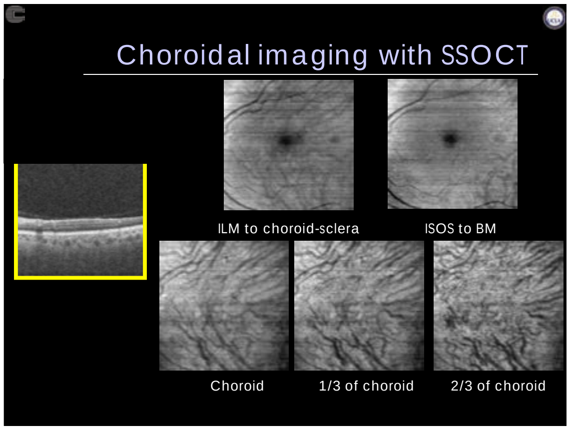

Vitreous imaging with SS-OCT
With SS-OCT, both the vitreous and choroid can be imaged simultaneously with brilliant detail

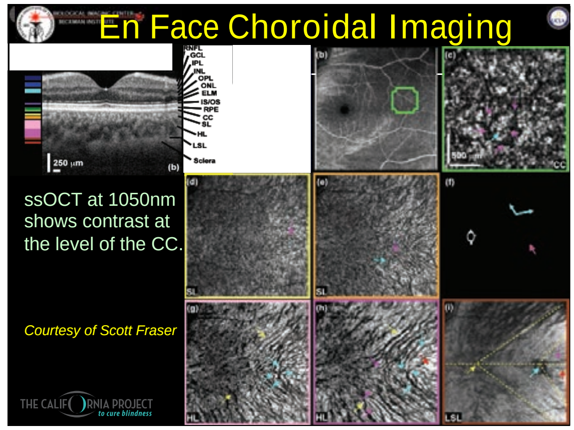

Large field OCT imaging
• Underlying high quality B-scan data yields high quality OCT fundus images
Pathologic myopia with tilted nerve and PPA

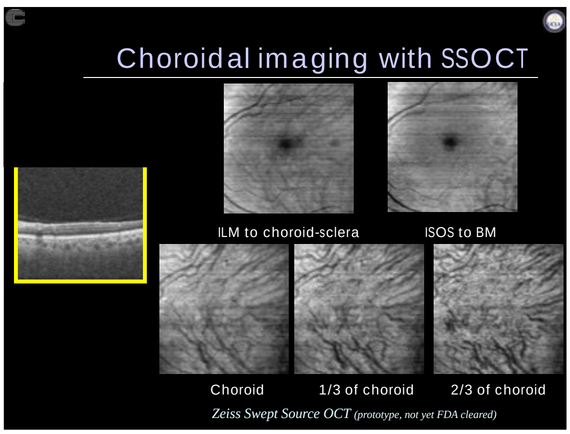

Higher Sensitivity
• Very little sensitivity loss with depth with swept source OCT
– Better signal-to-noise ratio
• Enhances visualization of outer retinal structures


Improved Speed
• Swept Source OCT
– Extensive averaging allows fine structures to be seen
12mm
150 A-scans
Cones not resolved near fovea
700um (600 A-scans)
From Potsaid et al, Optics Express 2010; 18: 20029.


proved Speed
Megahertz OCT for ultrawide-field retinal imaging with a 1050nm Fourier domain mode-locked laser
From Klein et al, Optics Express 2011; 19: 3044.

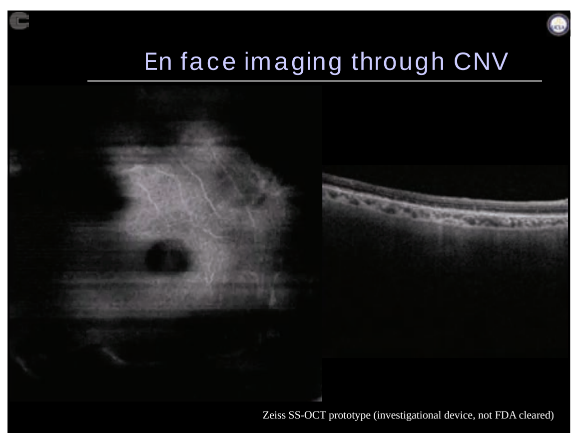

Choroidal imaging with SSOCT
ILM to choroid-sclera
ISOS to BM
Choroid
1/3 of choroid
2/3 of choroid

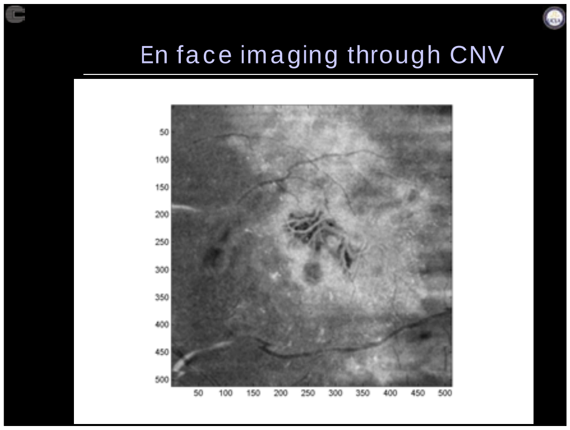

En Face Choroidal Imaging
ssOCT at 1050nm shows contrast at the level of the CC.
Courtesy of Scott Fraser
THE CALIFORNIA PROJECT to cure blindness

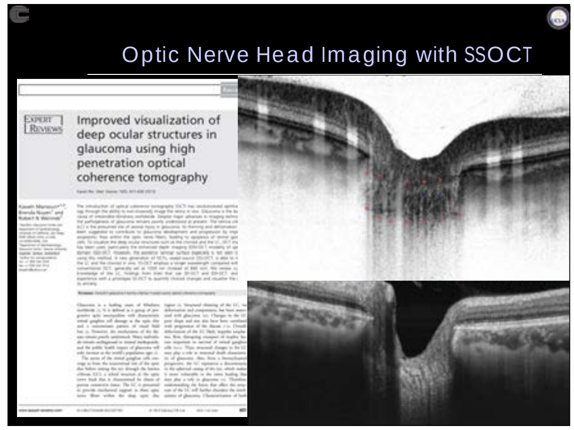

Choroidal imaging with SSOCT
ILM to choroid-sclera
ISOS to BM
Choroid
1/3 of choroid
2/3 of choroid
Zeiss Swept Source OCT (prototype, not yet FDA cleared)

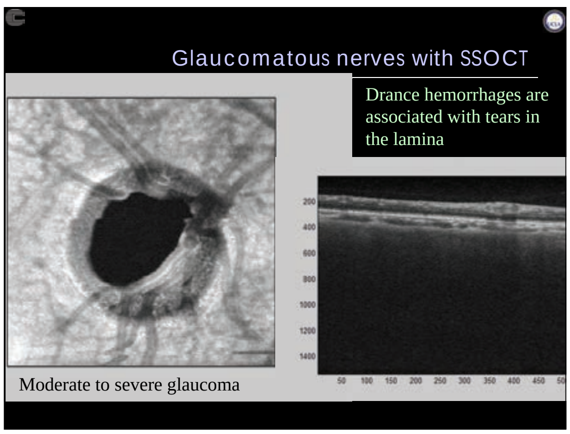

En face imaging through retina and choroid
Zeiss SS-OCT prototype (investigational device, not FDA cleared)

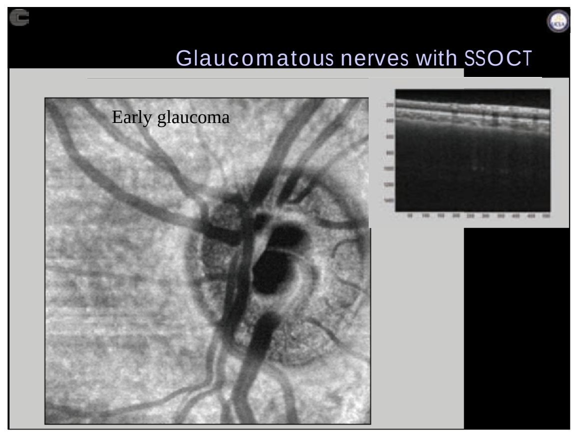

Serous PED
Zeiss SS-OCT prototype (investigational device, not FDA cleared)

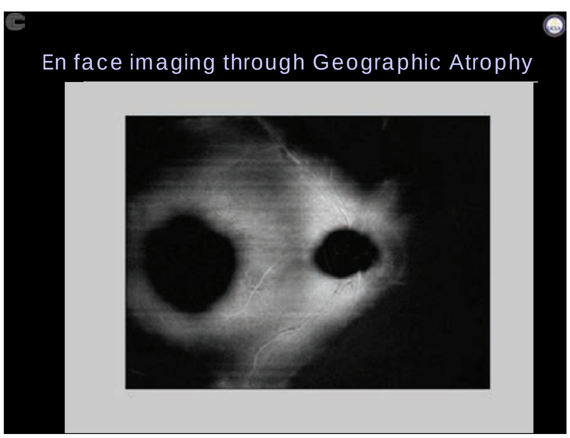

En face imaging through CNV
Zeiss SS-OCT prototype (investigational device, not FDA cleared)

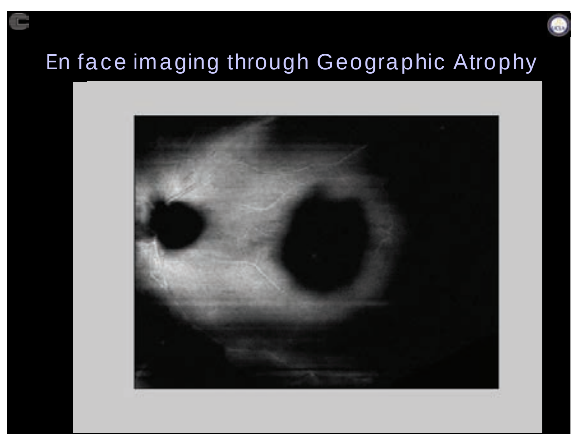

En face imaging through CNV
50
100
150
200
250
300
350
400
450
500


Optic Nerve Head Imaging with SSOCT
EXPERT REVIEWS
Improved visualization of deep ocular structures in glaucoma using high penetration optical coherence tomography


Glaucomatous nerves with SSOCT
Drance hemorrhages are associated with tears in the lamina
Moderate to severe glaucoma

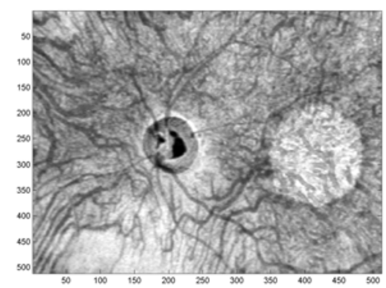

Glaucomatous nerves with SSOCT
Early glaucoma


En face imaging through Geographic Atrophy

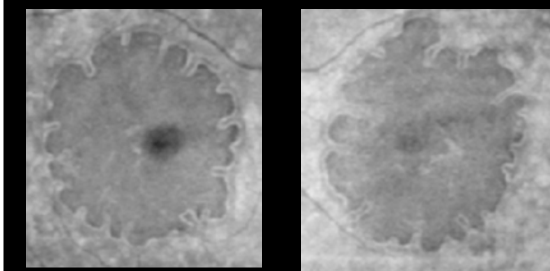

En face imaging through Geographic Atrophy

High-resolution en face OCT

En face slabs can be extracted from any layer of interest

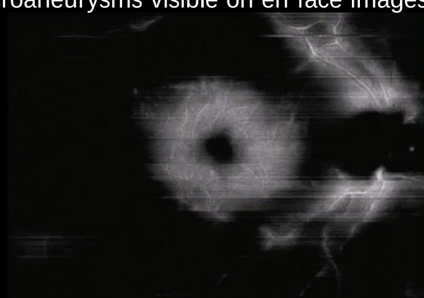


En Face slabs at photoreceptor - RPE level



Non-proliferative Diabetic Retinopathy

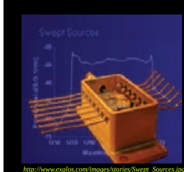
- Microaneurysms visible on en face images

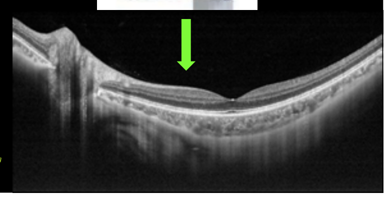


Zeiss SS-OCT prototype (investigational device, not FDA cleared)

Swept Source OCT and wavelength

- Most future commercial swept source OCT devices will likely operate in the long wavelength (>1 micron) regime
- Deeper Penetration





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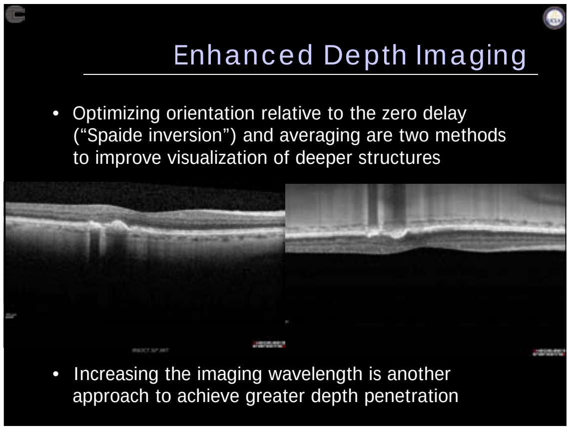
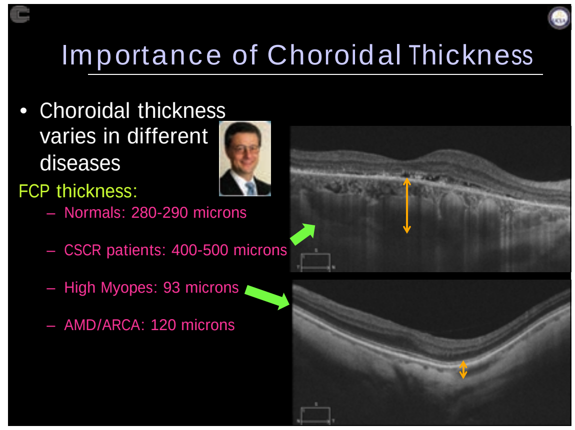
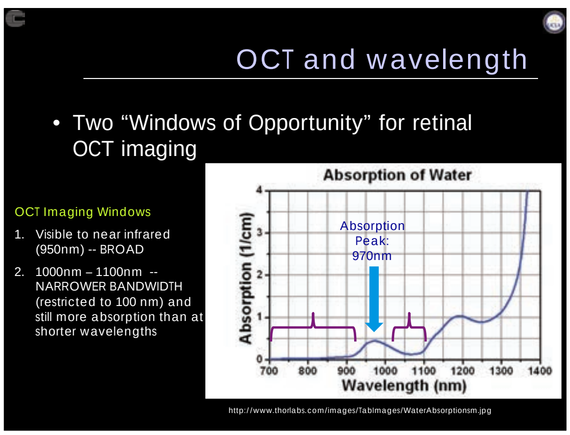
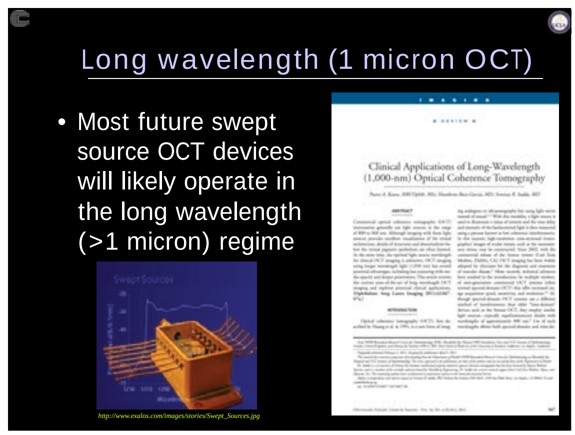
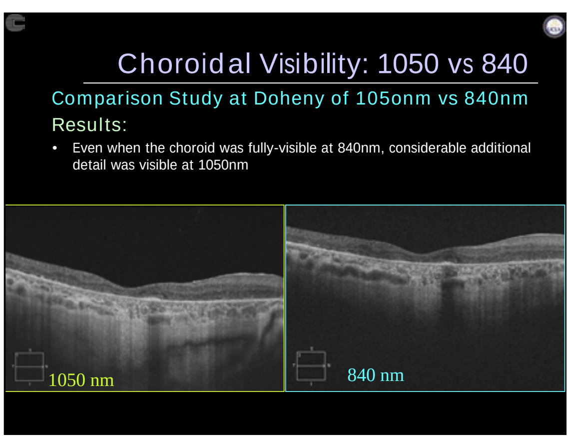
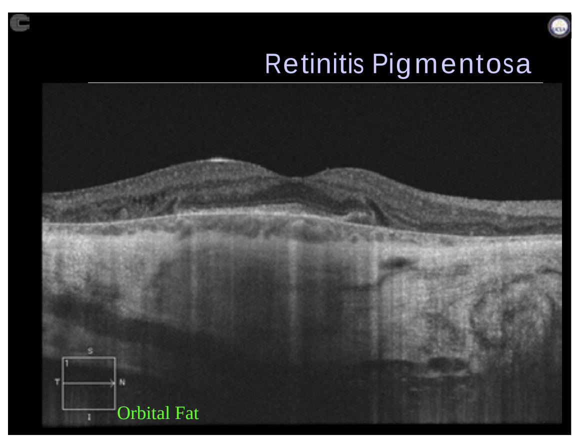

Enhanced Depth Imaging
• Optimizing orientation relative to the zero delay ("Spaide inversion") and averaging are two methods to improve visualization of deeper structures
• Increasing the imaging wavelength is another approach to achieve greater depth penetration


Importance of Choroidal Thickness
• Choroidal thickness varies in different diseases
FCP thickness:
– Normals: 280-290 microns
– CSCR patients: 400-500 microns
– High Myopes: 93 microns
– AMD/ARCA: 120 microns

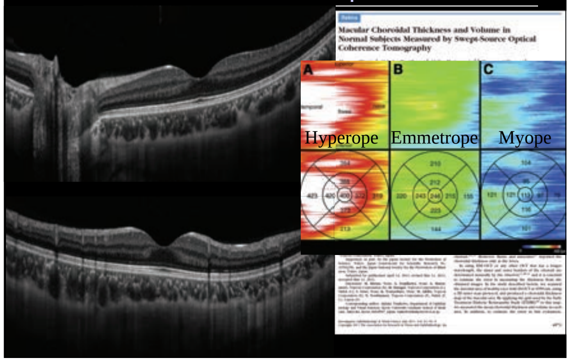

OCT and wavelength
• Two "Windows of Opportunity" for retinal OCT imaging
OCT Imaging Windows
1. Visible to near infrared (950nm) -- BROAD
2. 1000nm – 1100nm -- NARROWER BANDWIDTH (restricted to 100 nm) and still more absorption than at shorter wavelengths
Absorption of Water
Absorption Peak: 970nm
Absorption (1/cm)
Wavelength (nm)
700 800 900 1000 1100 1200 1300 1400
http://www.thorlabs.com/images/TabImages/WaterAbsorptionsm.jpg


Long wavelength (1 micron OCT)
• Most future swept source OCT devices will likely operate in the long wavelength (>1 micron) regime
Clinical Applications of Long-Wavelength (1,000-nm) Optical Coherence Tomography
http://www.exalos.com/images/stories/Swept_Sources.jpg


Choroidal Visibility: 1050 vs 840
Comparison Study at Doheny of 105onm vs 840nm
Results:
• Even when the choroid was fully-visible at 840nm, considerable additional detail was visible at 1050nm
1050 nm
840 nm


Retinitis Pigmentosa
Orbital Fat

Choroidal volume quantification



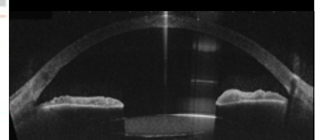
Better Anterior Segment Imaging with 1050 nm OCT

- Anterior Segment
  - Superior visualization of angle recess and trabecular meshwork

Better Anterior Segment Imaging with 1050 nm OCT

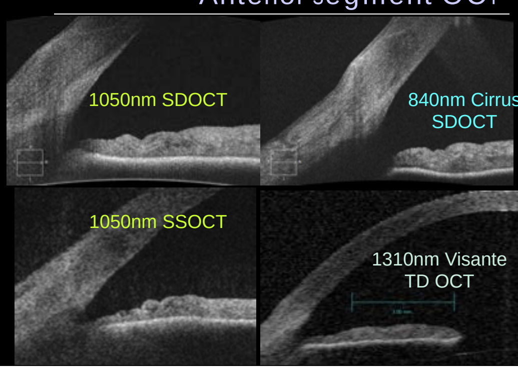
- Anterior Segment
  - Superior visualization of angle recess and trabecular meshwork, corneal endothelium

Anterior segment imaging with SS-OCT



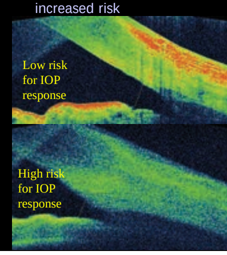
Deep penetration (1050nm) and high sensitivity of SSOCT allows visualization of full extent of lens/ IOL and angle recess

Anterior segment OCT



Why should you care about OCT of the angle?

- Singer et al., Retina 2012
- Angle configuration on OCT was highly predictive of steroid response
  - Narrower angle opening distance (termed "angle recess width" in the paper) increased risk

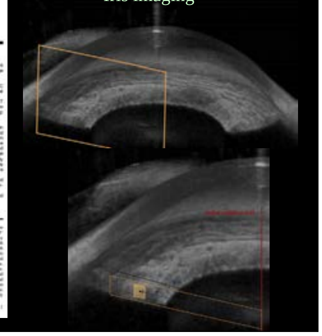


- Courtesy of Michael Singer, MD

Anterior segment imaging with SS-OCT


Imaging the Iris with Swept-Source Optical Coherence Tomography: Relationship between Iris Volume and Primary Angle Closure

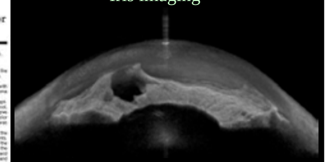
Iris imaging



Anterior segment imaging with SS-OCT


Anterior Chamber Angle Imaging with Swept-Source Optical Coherence Tomography: Measuring Peripheral Anterior Synechia in Glaucoma

Iris imaging



Evaluation of the trabecular outflow system, Schlemm's canal, and collector channels is an area of current interest

Future OCT Technologies

OUTLINE

- Improved Resolution
- Improved Speed
- Improved Penetration
- Functional Information
- Vascular/Molecular Imaging
- Increased Automation

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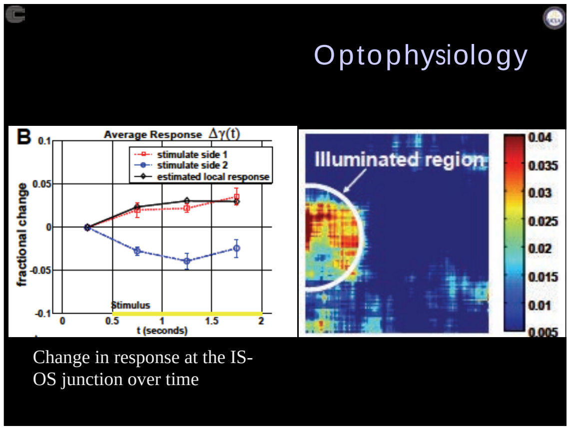
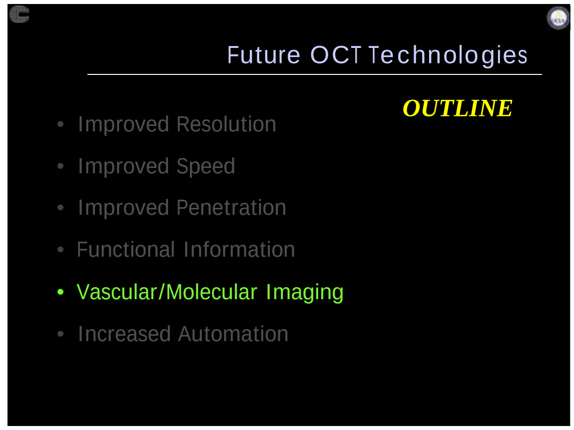
Optophysiology

- Dual laser approach
- High-speed long wavelength used to obtain repeated OCT scans from same location over time, without stimulating photoreceptors
- Separate visible light laser used to activate photoreceptors


In Vivo Functional Imaging of Intrinsic Scattering Changes in the Human Retina with High-speed Ultrahigh Resolution OCT


Optophysiology
B
Average Response Δγ(t)
stimulate side 1
stimulate side 2
estimated local response
fractional change
Stimulus
t (seconds)
Illuminated region
Change in response at the IS-OS junction over time


Future OCT Technologies
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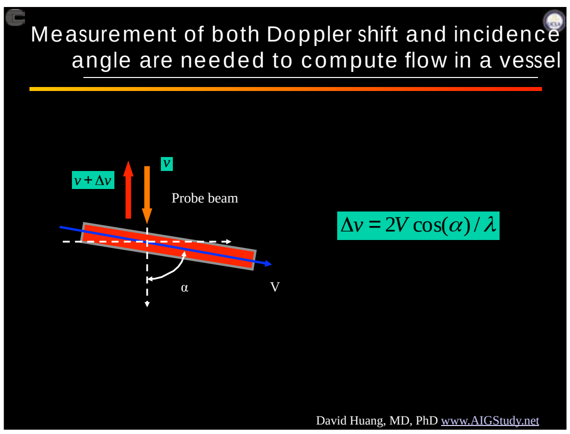
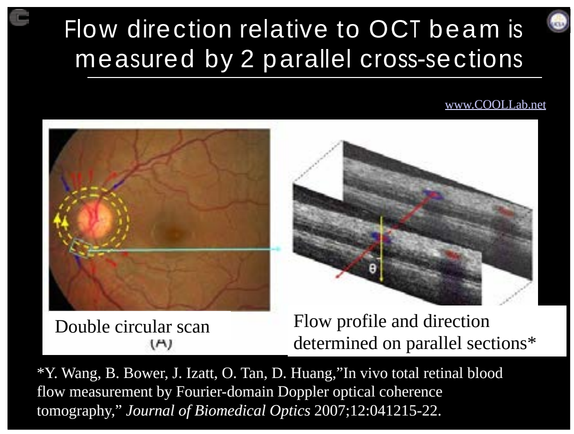
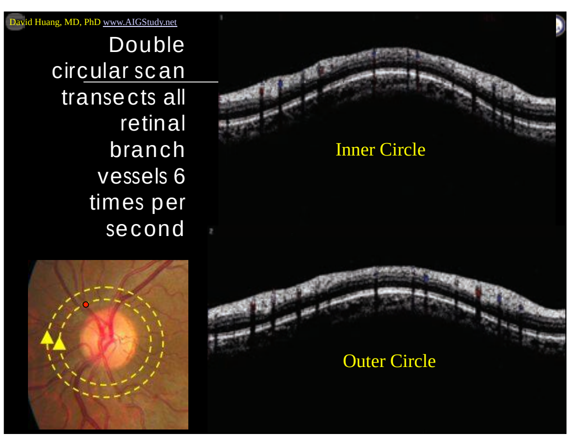
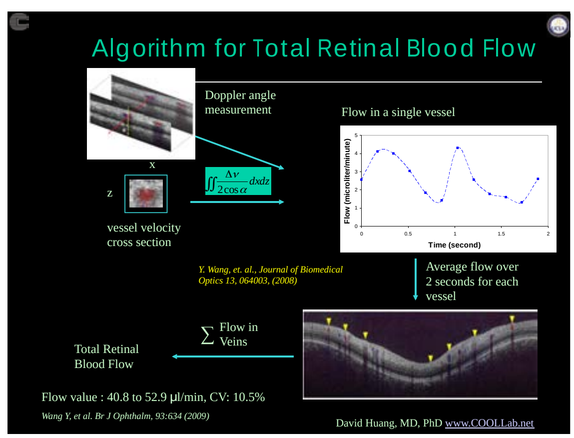
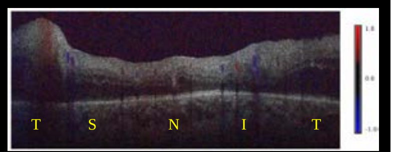

Measurement of both Doppler shift and incidence angle are needed to compute flow in a vessel
v + Δv
v
Probe beam
α
V
Δv = 2V cos(α) / λ
David Huang, MD, PhD www.AIGStudy.net


Flow direction relative to OCT beam is measured by 2 parallel cross-sections
www.COOLLab.net
θ
Double circular scan
Flow profile and direction determined on parallel sections*
*Y. Wang, B. Bower, J. Izatt, O. Tan, D. Huang,"In vivo total retinal blood flow measurement by Fourier-domain Doppler optical coherence tomography," Journal of Biomedical Optics 2007;12:041215-22.


David Huang, MD, PhD www.AIGStudy.net
Double circular scan transects all retinal branch vessels 6 times per second
Inner Circle
Outer Circle


Algorithm for Total Retinal Blood Flow
Doppler angle measurement
Flow in a single vessel
x
z
vessel velocity cross section
Time (second)
Y. Wang, et. al., Journal of Biomedical Optics 13, 064003, (2008)
Average flow over 2 seconds for each vessel
Σ Flow in Veins
Total Retinal Blood Flow
Flow value : 40.8 to 52.9 µl/min, CV: 10.5%
Wang Y, et al. Br J Ophthalm, 93:634 (2009)
David Huang, MD, PhD www.COOLLab.net

Superior Branch Vein Occlusion & Proliferative Diabetic Retinopathy

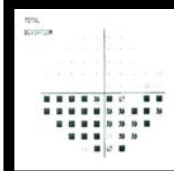


Amani Fawzi, MD

Venous Flow	Superior (µl/min)	Inferior (µl/min)
Case	8.2	12.1
Normal mean±SD (Range)	23.5 ± 3.0 (19.2-27.5)	22.2 ± 2.6 (19.6-27.4)

Non-Arteritic Anterior Ischemic Optic Neuropathy

Inferior altitudinal visual field defect matched with lower superior blood flow in 3/3 cases.



Venous Flow	Superior (µl/min)	Inferior (µl/min)
Case	12.99	19.47
Normal mean±SD (Range)	23.5 ± 3.0 (19.2-27.5)	22.2 ± 2.6 (19.6-27.4)

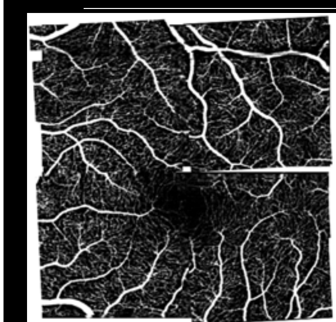
Alfredo Sadun, MD, PhD

OCT Angiography

Phase variance OCT

- Using the complex data encoded within the OCT images (complex data is generally discarded by most commercial devices), structures with motion may be selectively isolated.
- After eliminating Brownian motion and fixation artifact, most of the residual motion in the eye is blood flow.

Phase Variance OCT



"OCT Angiography"

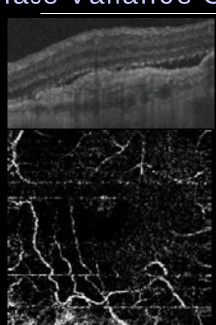
ADVANTAGES

- No Dye
- Depth Resolved

Composite image – Sadda's Eye Undilated

Collaborative work with Scott Fraser and Jeff Fingler (Caltech)

Phase Variance OCT for imaging CNV



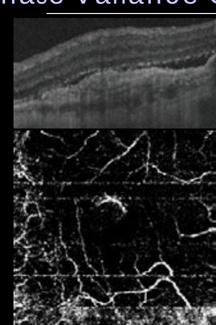
Neovascular AMD, FVPED s/p >30 ranibizumab injections

Old lesion – mature vessels within membrane

Deep Retinal Capillary Plexus

Courtesy of Jeff Fingler, Scott Fraser

Phase Variance OCT for imaging CNV

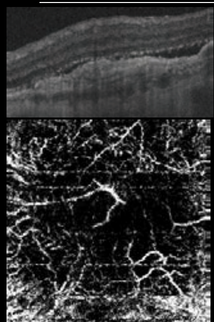


Neovascular AMD, FVPED s/p >30 ranibizumab injections

Retinal – Choroidal Anastomosis

Courtesy of Jeff Fingler, Scott Fraser

Phase Variance OCT for imaging CNV



Neovascular AMD, FVPED s/p
>30 ranibizumab injections

Retinal – Choroidal Anastomosis

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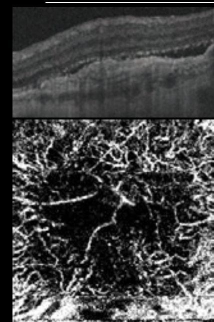
Phase Variance OCT for imaging CNV

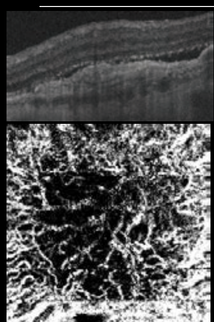


Neovascular AMD, FVPED s/p
>30 ranibizumab injections

Superficial vessels of CNV

Courtesy of Jeff Fingler, Scott Fraser

Phase Variance OCT for imaging CNV

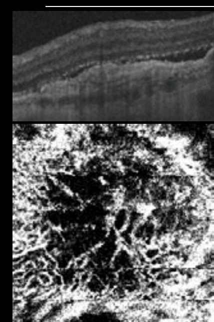


Neovascular AMD, FVPED s/p
>30 ranibizumab injections

Larger CNV Vessels

Courtesy of Jeff Fingler, Scott Fraser

Phase Variance OCT for imaging CNV



Neovascular AMD, FVPED s/p
>30 ranibizumab injections

Larger CNV Vessels

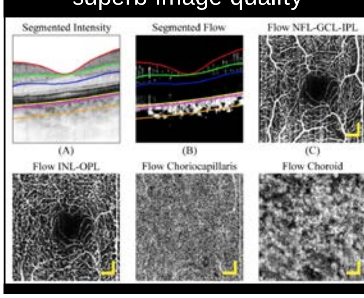
Courtesy of Jeff Fingler, Scott Fraser

PV OCT pitfalls

- Motion artifact can be a problem for obtaining high-quality images in some patients.
- Fixation tracking may be a key requirement for optimal imaging

PV OCT

- Eye tracking can yield superb image quality

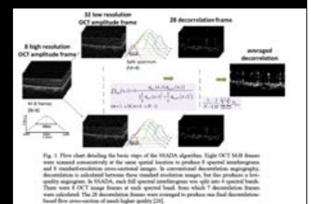


OCT Angiography

Split-Spectrum Amplitude Decorrelation Angiography

SSADA

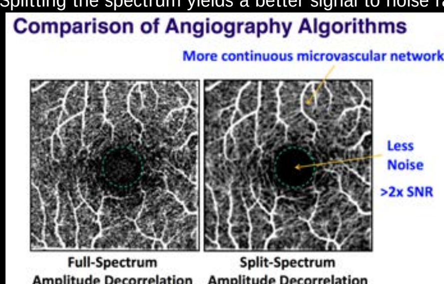
- "Decorrelation" refers to fluctuating values of OCT intensities
- Blood flow results in fluctuation in the amplitude of the OCT fringes as RBCs enter and exit a particular voxel
- Greater fluctuation means greater flow



Jia et al, Biomed Opt Exp 2012

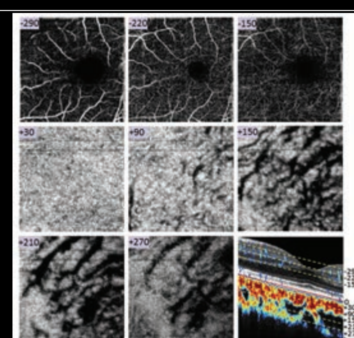
SSADA

- Splitting the spectrum yields a better signal to noise ratio



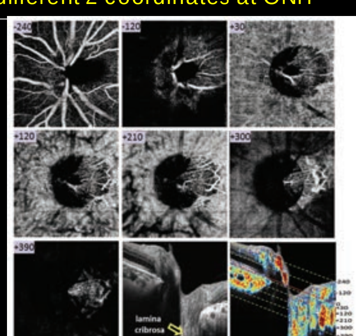
Jia et al, Opt Exp 2012

En face retinal and choroidal angiograms at different Z coordinates at macula



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

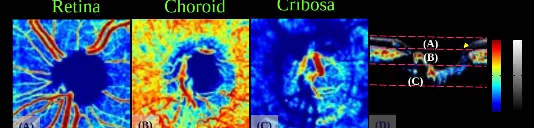
En face retinal and choroidal angiograms at different Z coordinates at ONH



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

En face ONH angiograms separately showing the microcirculation within retina , choroid and lamina cribrosa

Slab Level



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

Quantitative OCT Angiography

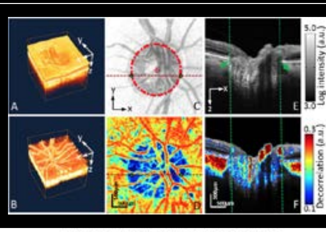


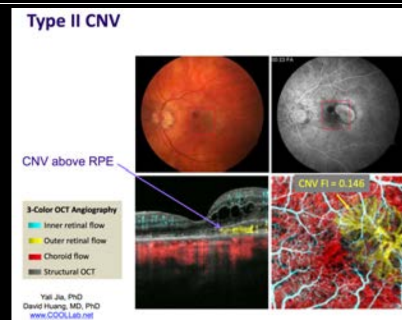
Table 1. OCT disc perfusion measurements on the whole disc region[a]

Parameters	Normal	PPG	p-value	CV (%)
Flow index (dimensionless)	0.180 ± 0.031	0.104 ± 0.009	0.040	6.81
Vessel density (%)	74.2 ± 14.3	49.1 ± 5.20	0.043	6.23

[a]PPG, preperimetric glaucoma; CV, coefficient of variation of repeated measurements; p-values based on unpaired t-tests.

Flow and vessel density was reduced in glaucoma patients

Depth – resolved angiography

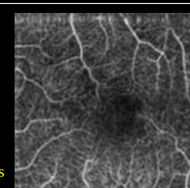


Courtesy: David Huang, MD PhD

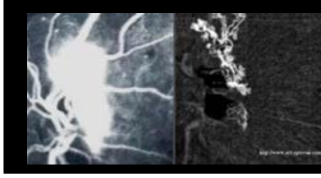
Near-commercial OCT Angiography

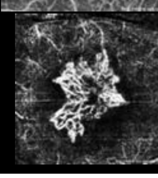
Near-commercial OCT Angiography

- SSADA-based
  - Optovue Avanti XR



- SD-OCT - based
- Resolution not as good as research prototypes



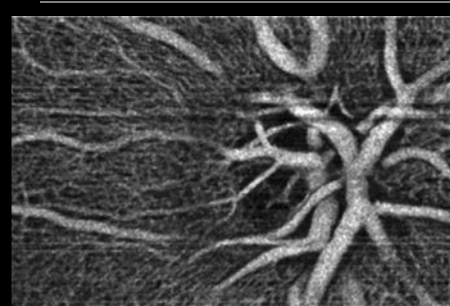


Vascular Detail with OCT Angiography

Swept-source OCT
OMAG - Based

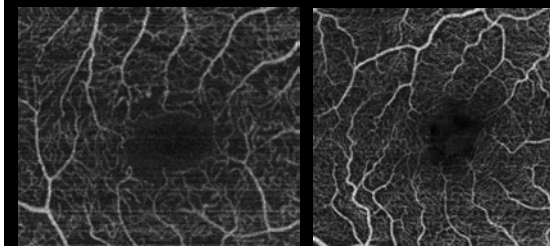
Zeiss SS-OCT prototype (investigational device, not FDA cleared)

Vascular Detail with OCT Angiography



Zeiss SS-OCT prototype (investigational device, not FDA cleared)

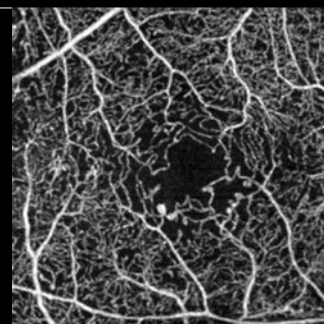
Diabetic Retinopathy



2 patients with NPDR --- note microaneurysms and enlarged foveal avascular zone

Zeiss SS-OCT prototype (investigational device, not FDA cleared)

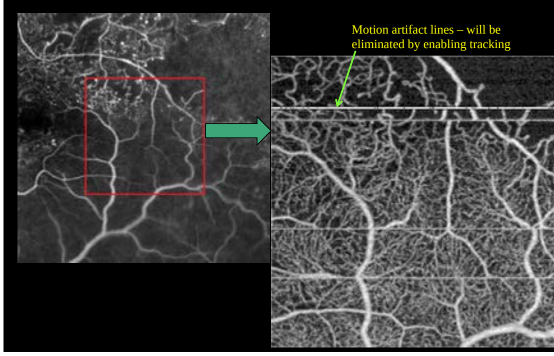
Diabetic Retinopathy



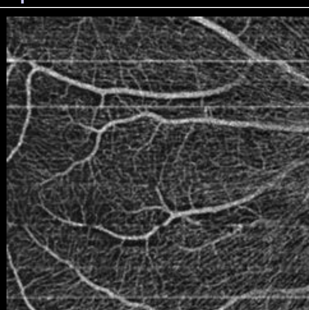
Zeiss SS-OCT prototype (investigational device, not FDA cleared)

Branch vein occlusion

Branch vein occlusion – OCT Angiography



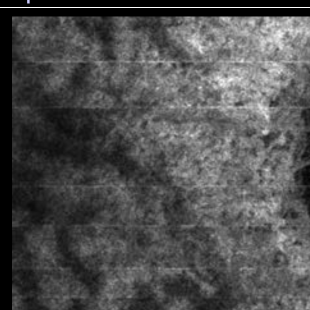
Depth resolved vascular imaging



Superficial Retinal Capillary Plexus Level

Zeiss SS-OCT prototype (investigational device, not FDA cleared)

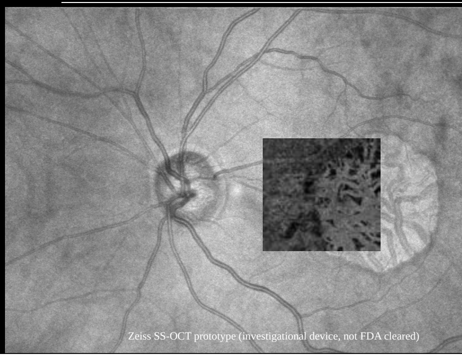
Depth resolved vascular imaging



Choriocapillaris Level!

Zeiss SS-OCT prototype (investigational device, not FDA cleared)

Depth resolved vascular imaging



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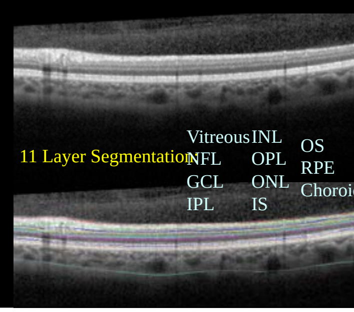
Advanced Automated Analyses

- Many groups developing algorithms for segmenting various retinal layers

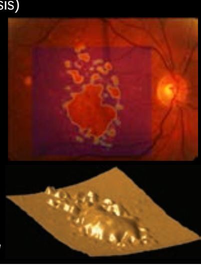
Doheny Image Analysis Laboratory

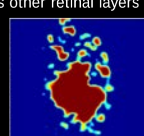
(Jewel Hu)



Advanced Automated Analyses

- Algorithms for segmenting specific pathologic structures already becoming available in commercial OCT software (e.g. drusen, GA analysis)
- In the near future we can expect automated algorithms to segment PEDs, subretinal fluid, retinal cysts and various other retinal layers





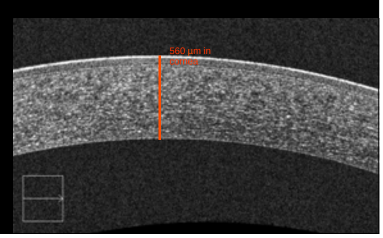
Area: 5.21 mm^2
Volume: 0.899 mm^3

Courtesy of Phil Rosenfeld

Anterior Segment Analyses

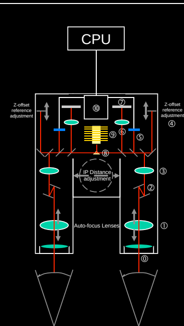
OCT pachymetry

- Automated tools now available
- Individual corneal layer thickness and volume quantification in development



Automated Acquisition

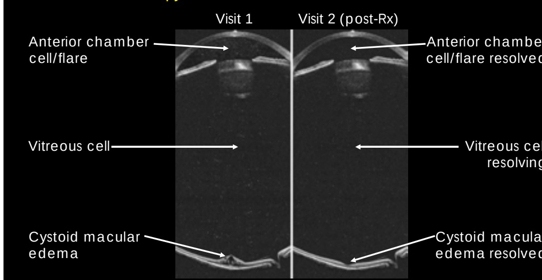
- Binocular self-administered OCT
  - Prototype in development (Walsh/Updike)



  - Scan both eyes simultaneously from cornea to posterior pole with high-speed SS-OCT

Automated Acquisition

- OCT Biomicroscopy



May facilitate rapid and remote assessments which may be of use in pharmacotherapy era

Summary

- Advances in OCT technology continue to proceed at a rapid pace.
- These advances are addressing many of the limitations of existing devices.
- Applications of OCT in our diagnosis and treatment of patients can be expected to continue to expand.

Thank You!