Glaucoma Detection using High-speed, High-resolution Fourier Domain Optical Coherence Tomography

Vikas Chopra MD

Assistant Professor

Doheny Eye Institute

USC Keck School of Medicine

Financial Disclosure

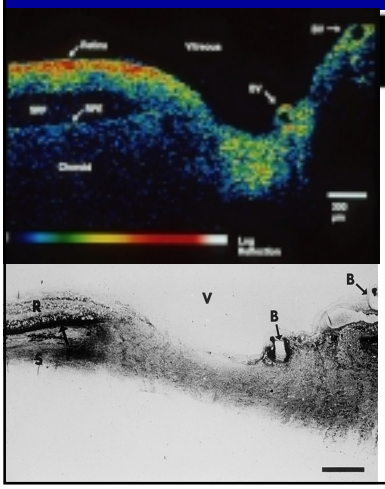
- The author acknowledges no financial interest.

Pathology of Glaucoma

- Loss of retinal ganglion cells (RGCs) and their axons (RNFL)
- Glaucomatous damage to RNFL precedes functional loss by up to 5 years

Quigley HA, Dunkelberger GR, Green WR. *Am J Ophthalmol* 1989;107:453-464.
Hoyt WF, Frisen L, Newman NM. *Invest Ophthalmol* 1973;12;814-29.
Quigley HA, Miller NR, George T. *Arch Ophthalmol* 1980;98:1564-71.
Sommer A, Katz J, Quigley HA, et al. *Arch Ophthalmol* 1991;109;77-83.
Quigley HA, Katz J, Derick RJ, et al. *Ophthalmology* 1992;99:19-28.
Airaksinen PJ, Drance SM, Douglas GR, et al., *Am J Ophthalmol* 1984;98;566-71.
Harwerth RS, Carter-Dawson L, Shen F, et al. *Invest Ophthalmol Vis Sci* 1999;40:2242-50.

- D Huang et al. *Science*, 254:1178 (1991). JG Fujimoto laboratory, MIT
- JA Izatt et al. *Arch Ophthalmol*, 112:1584 (1994). Corneal imaging
- MR Hee et al. *Arch Ophthalmol*, 113:325 (1995). Retinal Imaging
- JS Schuman et al. *Arch Ophthalmol*, 113:586 (1995). Glaucoma imaging



Reports

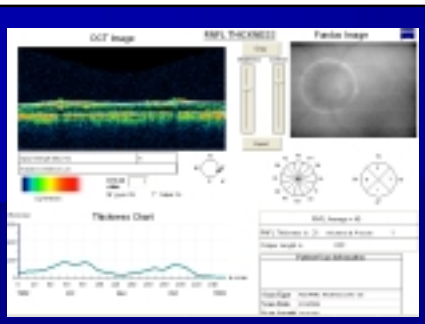
Science Vol. 254 (Nov. 22, 1991), 1178-1181

Optical Coherence Tomography

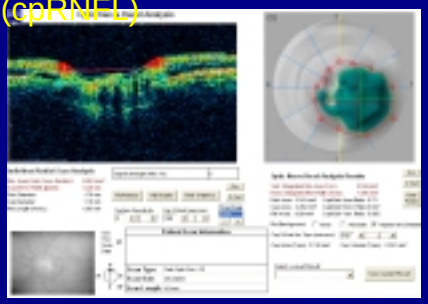
ERIC A. SWANSON, CHARLES P. LIN, JOEL S. SCHUMAN, WILLIAM G. STINSON, WARREN CHANG, MICHAEL R. HEE, THOMAS FLOTTE, KENTON GREGORY, CARMEN A. PULIAFITO, JAMES G. FUJIMOTO*

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.

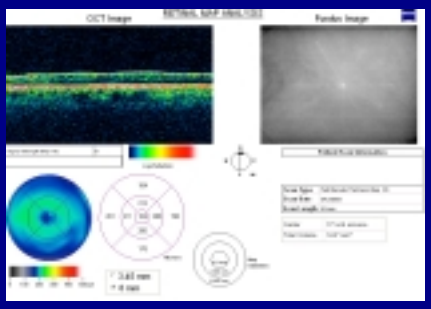
OCT in Glaucoma
3 Areas of Interest



Circumpapillary Nerve Fiber Layer (cpRNFL)



Optic Nerve Head



Macular Thickness

Looking for Glaucoma in the Macula

- RGCs and RNFL make up about 30-35% of macular thickness, where ganglion cells are most concentrated
  - RGC bodies are 10 to 20 times the diameter of their axons
  - RGC layer is more than one cell layer thick in macula (cell density up to 4-6 cell bodies thick)

Glovinsky Y, Quigley HA, Dunkelberger GR. *Invest Ophthalmol Vis Sci* 1991;32:484-91.
Glovinsky Y, Quigley HA, Pease ME. *Invest Ophthalmol Vis Sci* 1993;34:395-400.

Looking for Glaucoma in the Macula

- In glaucoma, loss of RGCs also occur at the posterior pole
  - Experimental glaucoma studies showed substantial loss of RGCs in zone surrounding fovea

Glovinsky Y, Quigley HA, Pease ME. *Invest Ophthalmol Vis Sci* 1993;34:395-400.
Frishman LJ, Shen FF, Du L, et al., *Invest Ophthalmol Vis Sci* 1996;37:125-41.

Using Macular Thickness for Glaucoma

- Reduced macular thickness can be used as a measure of glaucoma
- Visual function correlates with macular thickness

Zeimer R, Shahidi M, Mori M, et al. *Invest Ophthalmol Vis Sci*. 1996;37:1994-2001.
Giovanni A, Amato G, Mariotti C. *Acta Ophthalmol Scand Suppl*. 2002:236:34-6.
Greenfield DS, Bagga H, Knighton RW. *Arch Ophthalmol*. 2003;121:41-6.
Guedes V, Schuman JS, Hertzmark E, et al. *Ophthalmology* 2003;110:177-89.
Lederer DE, Schuman JS, Hertzmark E, et al. *Am J Ophthalmol*. 2003:135:838-43.
Wollstein G, Schuman JS, Price LL, et al. *Am J Ophthalmol* 2004;138:218-25.

OCT Circumpapillary vs. Macular Mapping

- cpRNFL thickness measurements outperform macular thickness in terms of magnitude of association with visual function

Wollstein G, Schuman JS, Price LL, et al. *Am J Ophthalmol* 2004;138:218-25.
Guedes V, Schuman JS, Hertzmark E, et al. *Ophthalmology* 2003;110:177-89.

<u>Problem</u> using Macular Thickness for Glaucoma

- Macular thickness represents *total* retinal thickness
  - Reduced macular thickness in glaucoma mainly due to RGC and RNFL loss
  - So, 65-70% macular thickness unchanged in glaucoma
- Retinal structures other than RGC confound the data so that the macular thickness not as sensitive as cpRNFL thickness measurement

Macular Thickness for Glaucoma

- Crucial to differentiate retinal layers so that only layers affected by glaucoma be measured for glaucoma discrimination

OCT Retinal Layer Segmentation

- Inner retinal complex thickness equal to cpRNFL for glaucoma detection
  - But , only 65% of glaucomatous eyes had good SNR to perform segmentation on Stratus OCT

Ishikawa H , Stein DM, Wollstein G, et al., *Invest Ophthalmol Vis Sci* 2005;46:2012-17.
Tan O, Huang D, et al., ARVO e-abstract, 2005

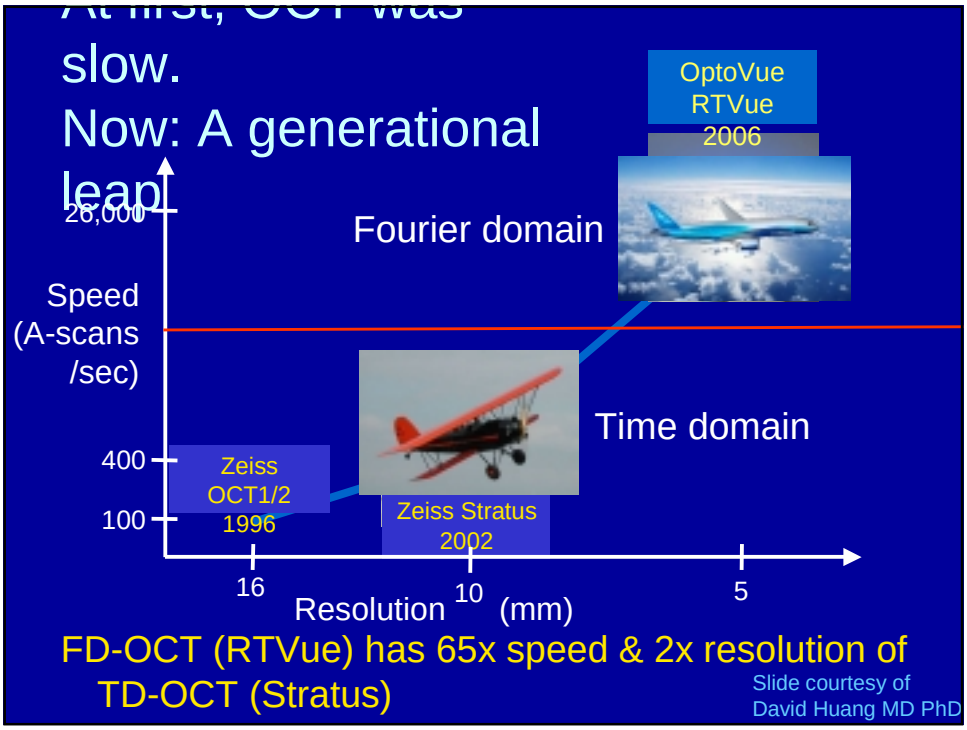
Stratus OCT Retinal Layer Segmentation

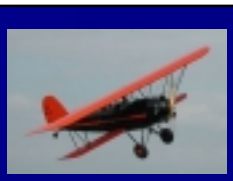
Macular Segmentation with Optical Coherence Tomography

Hiroshi Ishikawa,[1,2] Daniel M. Stein,[1] Gadi Wollstein,[1,2] Siobahn Beaton,[1,2] James G. Fujimoto,[3] and Joel S. Schuman[1,2]

Investigative Ophthalmology & Visual Science, June 2005, Vol. 46, No. 6

"...two approaches to minimize these factors [speckle noise and uneven tissue reflectivity]: higher resolution, and improved signal quality (signal-to-noise ratio)."



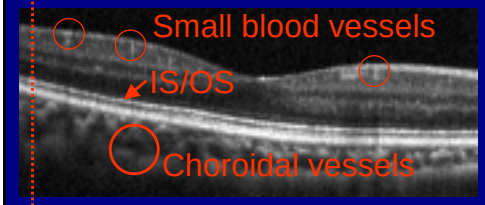


FD OCT

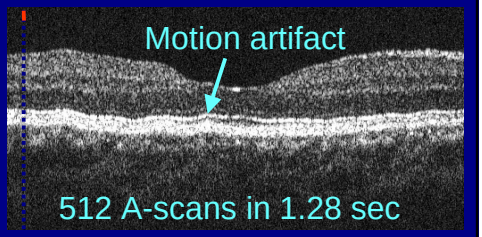
Simultaneous
2048 pixels at a time

TD OCT

Sequential
1 pixel at a time



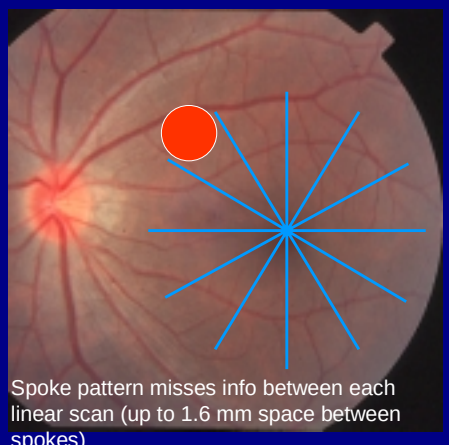
1024 A-scans in 0.04 sec



Higher speed, higher definition and higher signal.

Slide courtesy of
David Huang MD PhD

Slow OCT undersamples the macula



Spoke pattern misses info between each linear scan (up to 1.6 mm space between spokes)

6 lines, 768 A-scans, 1.9 sec

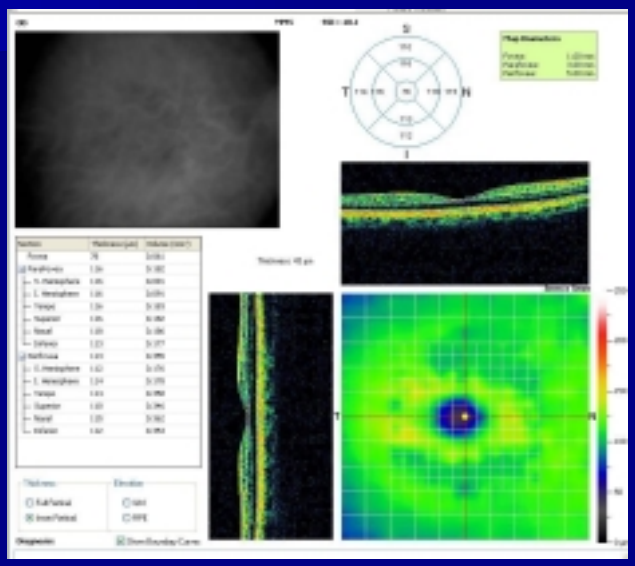
High speed improves macular mapping

5 mm grid

34 lines

19,496 A-scans

0.78 sec

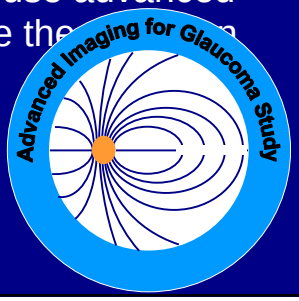


Purpose

- To evaluate the newly developed Fourier-domain optical coherence tomography in glaucoma detection

Study Design

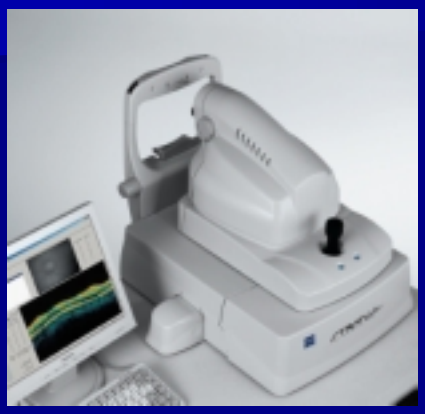
- Subset of Advanced Imaging for Glaucoma Study
- AIGS is a large, multi-center, prospective, longitudinal trial to develop and use advanced imaging technologies to improve the [illegible] and management of glaucoma
  - David Huang MD PhD (Director)
  - www.AIGStudy.net



Study Design

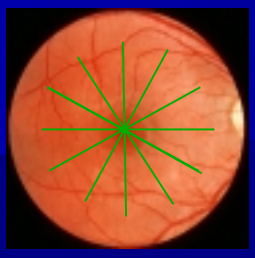
- AIGS cross-sectional cohort
  - 30 Normal eyes
    - Absence of glaucomatous optic nerve
    - Absence of risk factors for glaucoma
    - Absence of VF defects
  - 31 perimetric Glaucoma eyes
    - Characteristic optic nerve head abnormalities
    - Glaucomatous VF defects

Methods:
Circumpapillary and macular scans



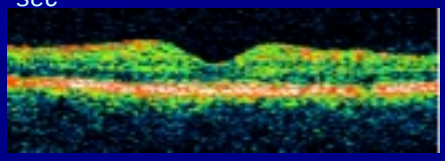
Stratus OCT, Zeiss Meditec
400 A-scan per-second
9-10 micron axial resolution

RTVue FD-OCT, OptoVue
26,000 A-scan per-second
5 micron axial resolution

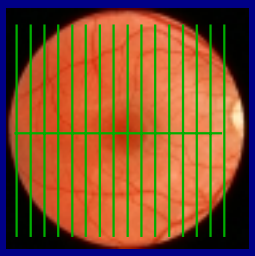


Stratus FMTM 6mm radial

Stratus TD-OCT
9-10 µ axial resolution; 400 axial scans / sec

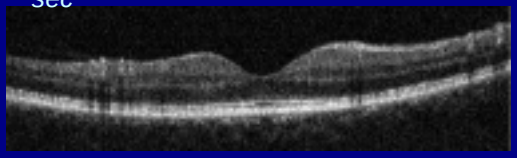


FMTM vertical scan, center at fovea, 128 a-scan, take 0.3s



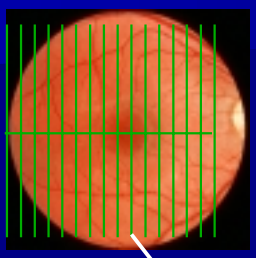
RTVue MM7 7mm rectangular

RTVue FD-OCT
5 µ axial resolution; 26,000 axial scans / sec



MM7 vertical scan, center at fovea, 933 a-scan, take 0.035s

Inner Retinal Layers Preferentially Affected by Glaucoma



Inner Retinal Layer (IRL)

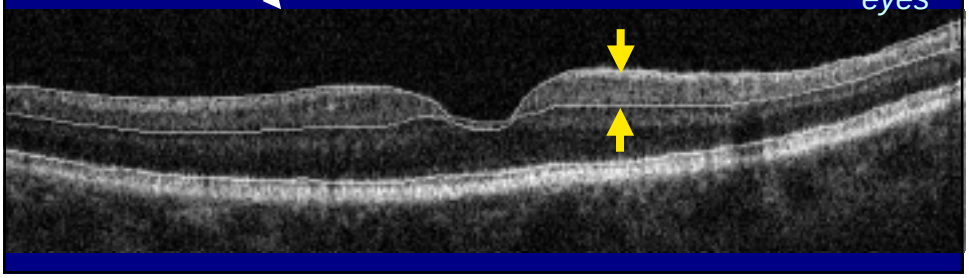
Ganglion cells:

Axons = nerve fiber layer

Body = ganglion cell layer

Dendrites = inner plexiform layer

Perform Retinal Layer Segmentation on all eyes



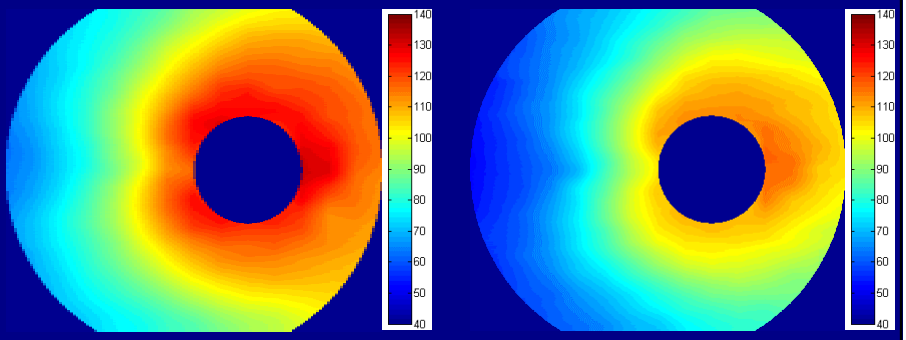
Results:

Average Thickness reduced in cpRNFL, Retina, IRL in Glaucoma

	Normal TD-OCT	Glaucoma TD-OCT		Normal FD-OCT	Glaucoma FD-OCT	
	Mean ± SD	Mean ± SD	p	Mean ± SD	Mean ± SD	p
cpRNFL	100.3 ± 8.6	76.0 ± 13.8	<0.001	91.0 ± 9.2	71.1± 11.7	<0.001
Retina	245.6 ± 12.1	224.5 ± 14.6	<0.001	223.2 ± 10.7	204.3 ± 10.9	<0.001
IRL	n/a	n/a	n/a	100.0 ± 4.5	84.8 ± 8.4	<0.001

Results:

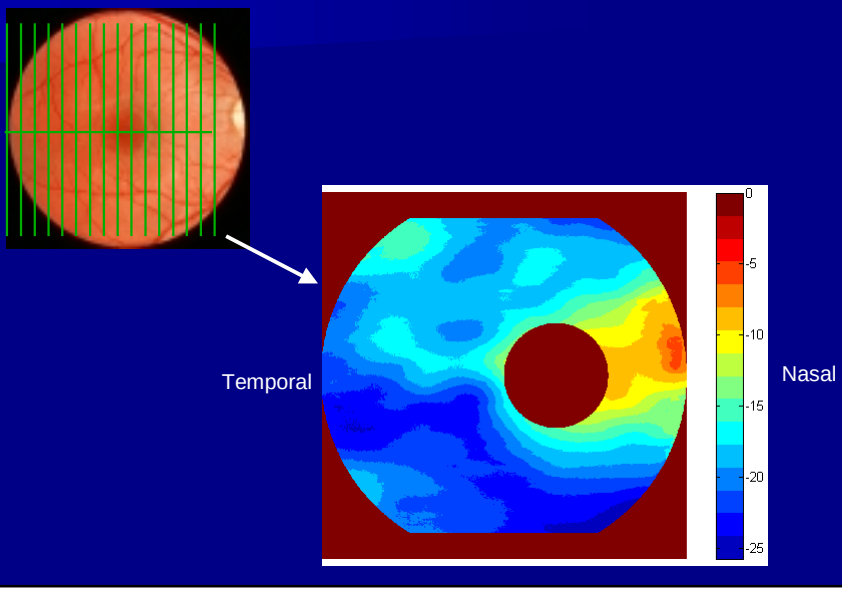
Reduced Average IRL Thickness maps in Glaucoma



Normal Glaucoma

Results:

Fractional Macular IRL Thickness Loss Map



Temporal Nasal

Results:
FD-OCT Capability for Glaucoma Discrimination

	Stratus OCT		FD-OCT	
	AROC	SE	AROC	SE
cpRNFL	0.94	0.04	0.90	0.04
Retina	0.87	0.06	0.90	0.05
IRL	n/a	n/a	0.96	0.02
cpRNFL + IRL	n/a	n/a	0.97	0.02

Discussion

- *Fourier-domain OCT (RTVue)* offers faster speed and higher resolution in-vivo retinal scans compared with Time-domain OCT (Stratus)

Discussion

- Like Stratus TD-OCT, the *Fourier-domain OCT* demonstrated the ability to differentiate glaucoma from normal eyes using cpRNFL thickness measurements

Discussion

- Unlike Stratus TD-OCT, *retinal segmentation analysis* with Fourier-domain OCT allowed determination of macular inner retinal layer thickness in all eyes
  - Demonstrated ability to objectively quantify damage to RGCs and RNFL to discriminate between glaucomatous and normal eyes

Conclusions:

Enhanced Glaucoma Detection using FD-OCT Macular Mapping

Good Total MT

Better IRL or cpRNFL

Best **IRL and/or cpRNFL**

MT = Macular Thickness
IRL = Inner Retinal Layer
cpRNFL = circumpapillary RNFL

Early results from our on-going prospective study shows that macular IRL thickness provided by Fourier-domain OCT can serve as an additional parameter for detection of glaucoma and may complement the cpRNFL thickness measurement for glaucoma discrimination

Acknowledgements

- David Huang MD PhD
- Ou Tan PhD
- Ake Lu PhD
- Rohit Varma MD MPH
- Advanced Imaging for Glaucoma Study Group

- NIH / NEI Grant R01 EY013516
  - "Advanced Imaging for Glaucoma" www.AIGStudy.net
- Carl Zeiss Meditec, Inc.