OCT in the Diagnosis and Management of Glaucoma

Murray Fingeret, OD

OCT in Glaucoma

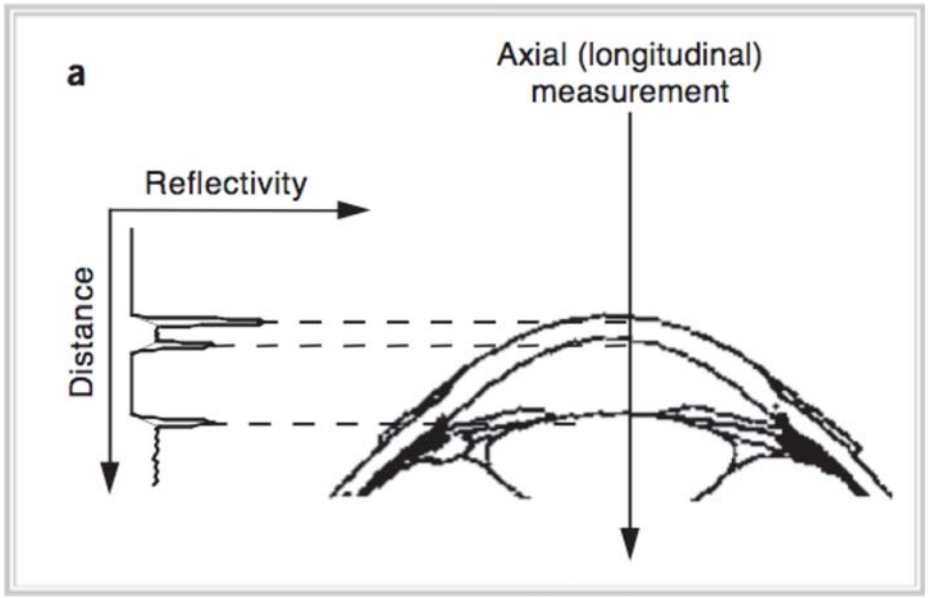
- An overview
  - How it works
- Interpretation of the printout
- Image artifacts
- Examples of OCT loss
- Progression

OCT: AN OVERVIEW

- Optical coherence tomography is a rapidly emerging biomedical imaging technology
- Obtains high-resolution, cross-sectional images of biological microstructures
- Images are provided ***in situ*** and in real-time
- Non-invasive
  - does not require excision and processing of specimens

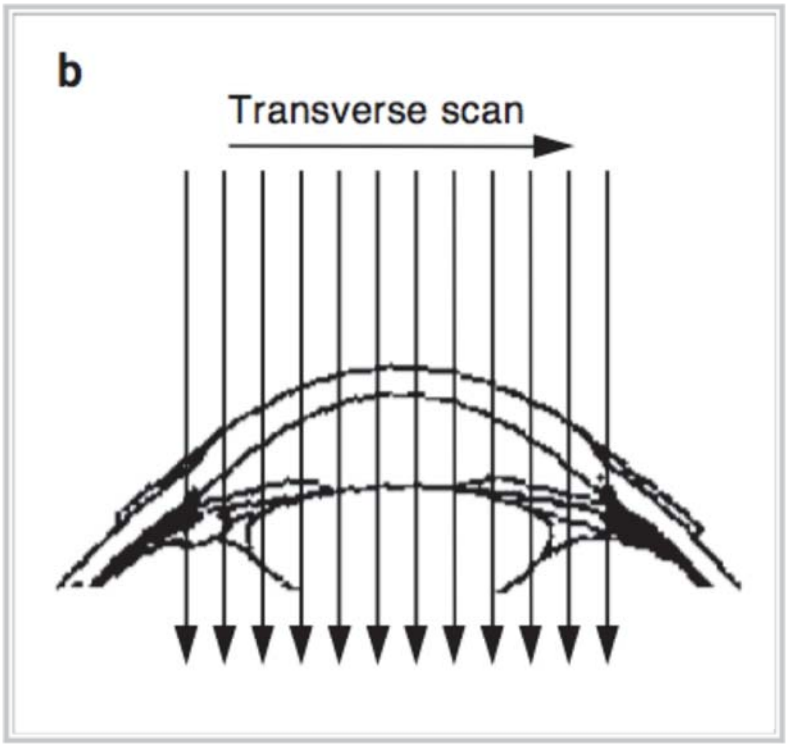
THE TECHNOLOGY BEHIND OCT

- OCT is analogous to ultrasound, but uses light instead of sound
- A beam of light is directed at the retina, and the echo time delay and magnitude of back-reflected and back-scattered light is measured (similar to A scan)



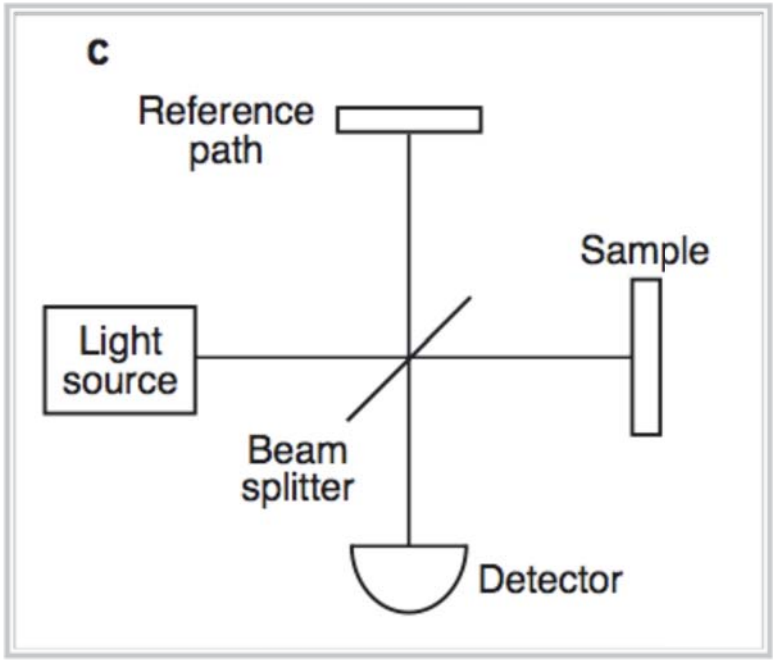
THE TECHNOLOGY BEHIND OCT

- The light beam then scans the tissue in the transverse direction to form a cross-sectional image (similar to B scan)



THE TECHNOLOGY BEHIND OCT

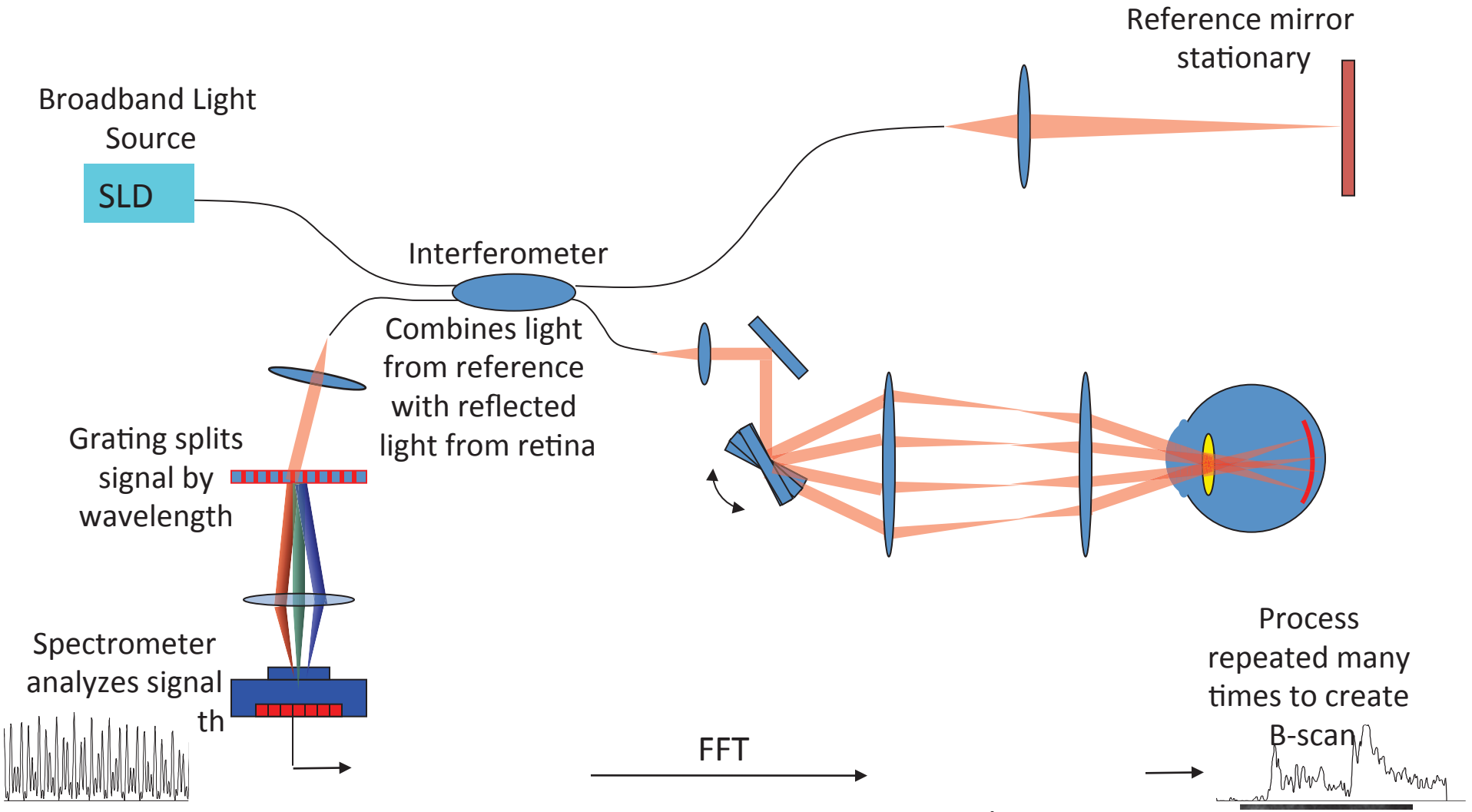
- The velocity of light is too great to measure optical echoes directly
- Instead, the light that is reflected back from inside the sample is measured indirectly, by correlating it with light that has traveled a known reference path
- This technique is called low coherence interferometry



OCT TECHNOLOGY: SPECTRAL DOMAIN

- Spectral domain OCT (also called Fourier-domain or high-definition OCT) was FDA approved in 2006
- Spectral domain OCT uses a stationary reference arm and eliminates the need for a moving mirror; it does so by using a spectrometer as a detector

Fourier Domain OCT



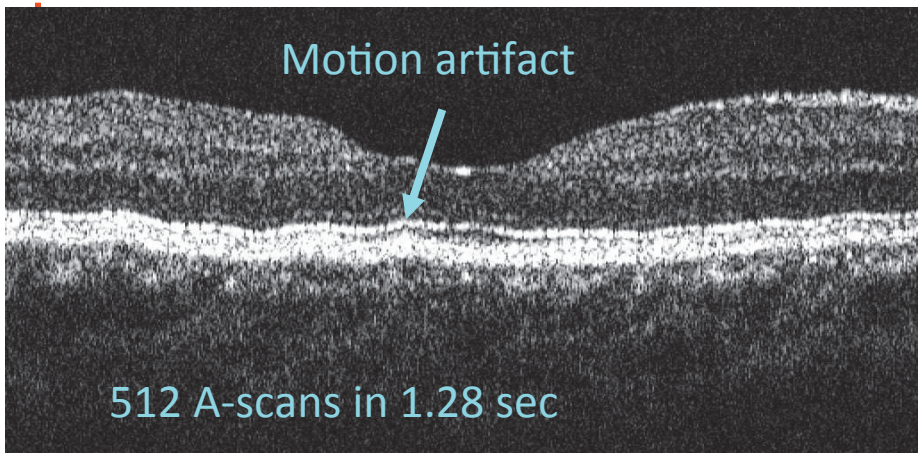
Slide courtesy of Dr. Yimin Wang, USC

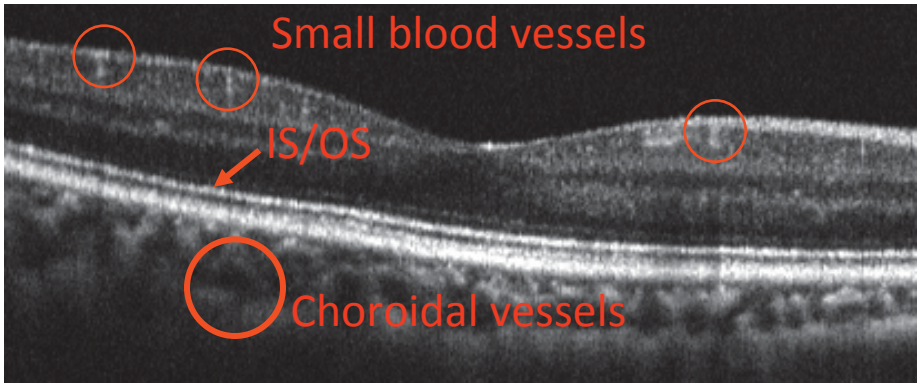
Time Domain OCT

- Sequential
- 1 pixel at a time
- 1024 pixels per A-scan
- .0025 seconds per A scan
- 512 A-scans in 1.28 sec
- Slower than eye movements

Fourier Domain OCT

- Simultaneous
- Entire A-scan at once
- 2048 pixels per A scan
- .00000385 sec per A scan
- 1024 A-scans in 0.04 sec
- Faster than eye movements



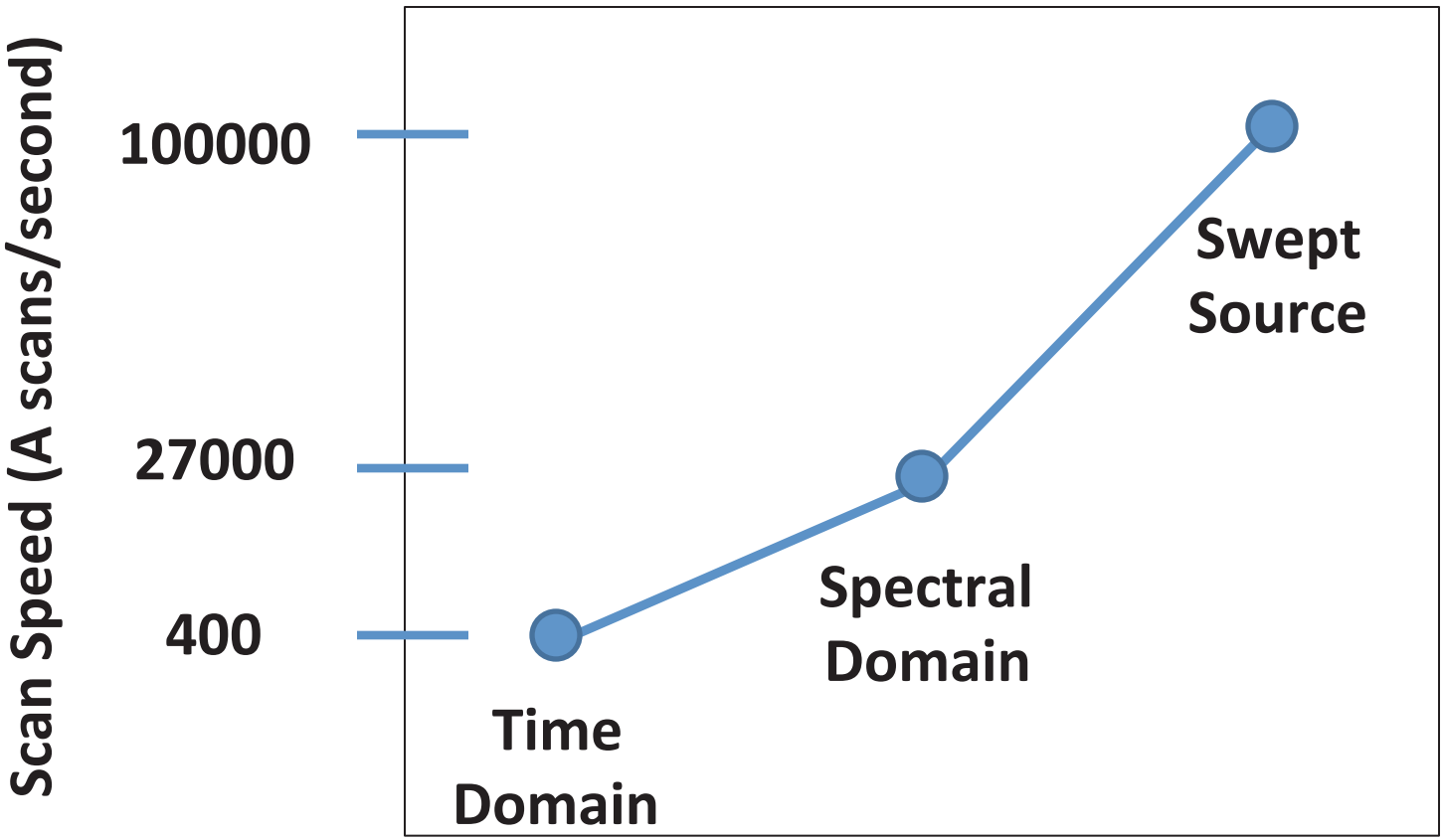


1024 A-scans in 0.04 sec

Higher speed, higher definition and higher signal.

Slide courtesy of Dr. David Huang, USC

Evolution of OCT



Swept Source OCT

- Swept-source (SS) OCT is a next-generation Fourier domain OCT that demonstrates less signal decay over depth compared with the current SD OCT.
- Faster speed
- Probe light with a center wavelength of 1040 to 1060 nm, which allows high-penetration imaging deep retinal tissues such as Choroid and Sclera
- SS OCT improves visualization of the deep structures of the optic disc
- Compared with SD OCT, SS OCT is characterized by a higher speed scan rate and relatively lower sensitivity roll-off versus depth

Swept Source OCT

- 100,000 A scans per second w 1 micron wavelength lightsource (1050 nm)
- Deep Tissue Imaging
  - Penetrates deeper into retina for choroid and lamina assessment
- Images through cataracts
- Swept source OCT is faster because:
  - No spectrometer
  - No line-scan camera (for detector)
  - Utilizes tunable laser source
  - 'Sweeps' across spectrum rapidly
  - Photodiode detector (near instantaneous)

OCT is Being Used More Often!!!

Trends in Use of Ancillary Glaucoma Tests for Patients with Open-Angle Glaucoma from 2001 to 2009

Joshua D. Stein, MD, MS, Nidhi Talwar, MA, Alejandra M. LaVerne, BS, Bin Nan, PhD, Paul R. Lichter, MD

Purpose: To assess trends in the use of ancillary diagnostic tests in the evaluation of patients with open-angle glaucoma (OAG) and glaucoma suspects over the past decade.

Design: Retrospective, longitudinal cohort analysis.

Participants: A total of 169 917 individuals with OAG and 395 721 individuals with suspected glaucoma aged ≥40 years enrolled in a national United States managed care network between 2001 and 2009.

Methods: Claims data were analyzed to assess trends in visual field (VF) testing, fundus photography (FP), and other ocular imaging (OOI) testing for patients with OAG or suspected glaucoma between 2001 and 2009. Repeated-measures logistic regression was performed to identify differences in the odds of undergoing these procedures in 2001, 2005, and 2009 and whether differences exist for patients under the exclusive care of optometrists versus ophthalmologists.

Main Outcome Measures: Odds and annual probabilities of undergoing VF testing, FP, and OOI for OAG from 2001 to 2009.

Results: For patients with OAG, the odds of undergoing VF testing decreased by 36% from 2001 to 2005, by 12% from 2005 to 2009, and by 44% from 2001 to 2009. By comparison, the odds of having OOI increased by 100% from 2001 to 2005, by 24% from 2005 to 2009, and by 147% from 2001 to 2009. Probabilities of undergoing FP were relatively low (13%–25%) for both provider types and remained fairly steady over the decade. For patients cared for exclusively by optometrists, the probability of VF testing decreased from 66% in 2001 to 44% in 2009. Among those seen exclusively by ophthalmologists, the probability of VF testing decreased from 65% in 2001 to 51% in 2009. The probability of undergoing OOI increased from 26% in 2001 to 47% in 2009 for patients of optometrists and from 30% in 2001 to 46% in 2009 for patients of ophthalmologists. By 2008, patients with OAG receiving care exclusively by optometrists had a higher probability of undergoing OOI than VF testing.

Conclusions: From 2001 to 2009, OOI increased dramatically whereas VF testing declined considerably. Because OOI has not been shown to be as effective at detecting OAG or disease progression compared with VF testing, increased reliance on OOI technology, in lieu of VF testing, may be detrimental to patient care.

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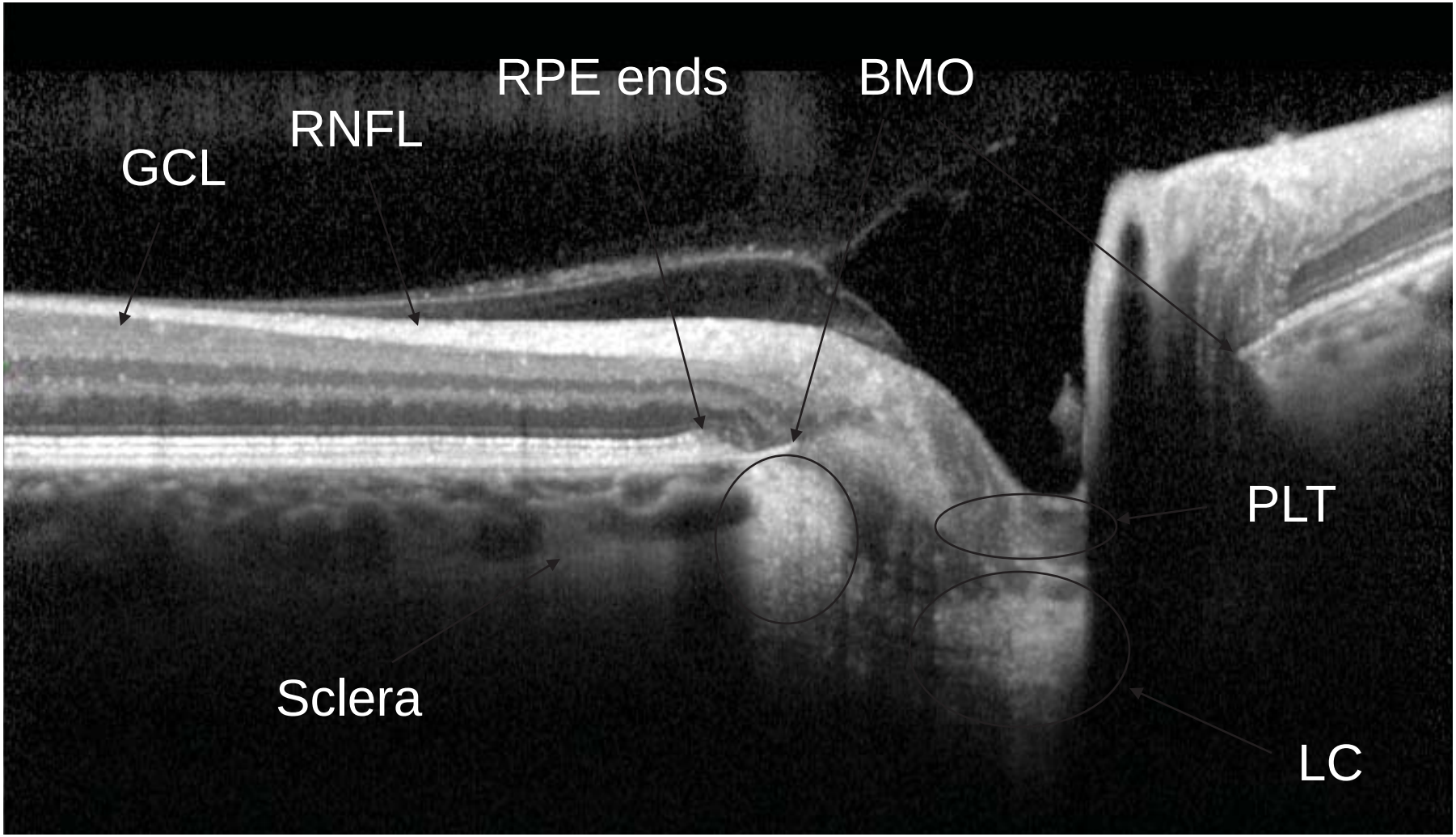
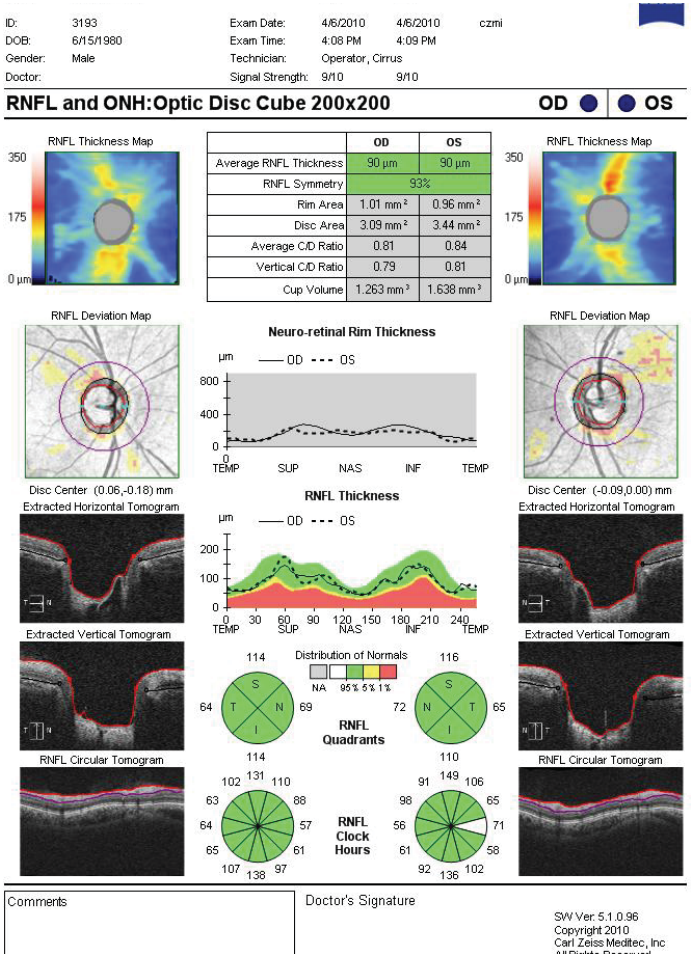
Optic Nerve Head – Detail



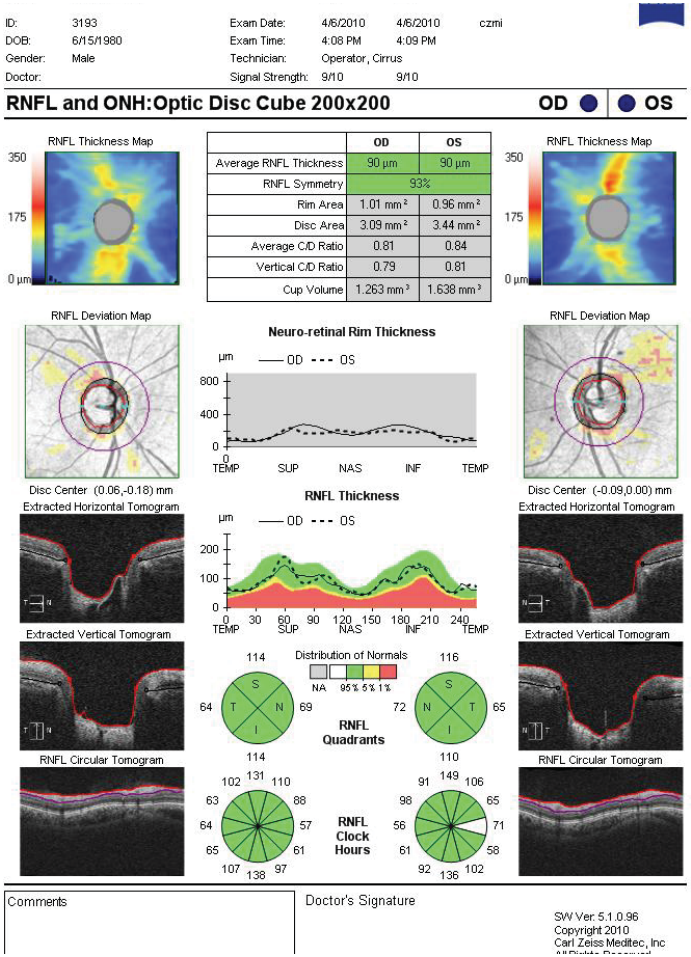
What Do You Look For When You Evaluate a Scan

- Quality score
- Illumination
- Focus OK
- Image centered
- Any signs of eye movement
- Segmentation accuracy
- B Scan Centration



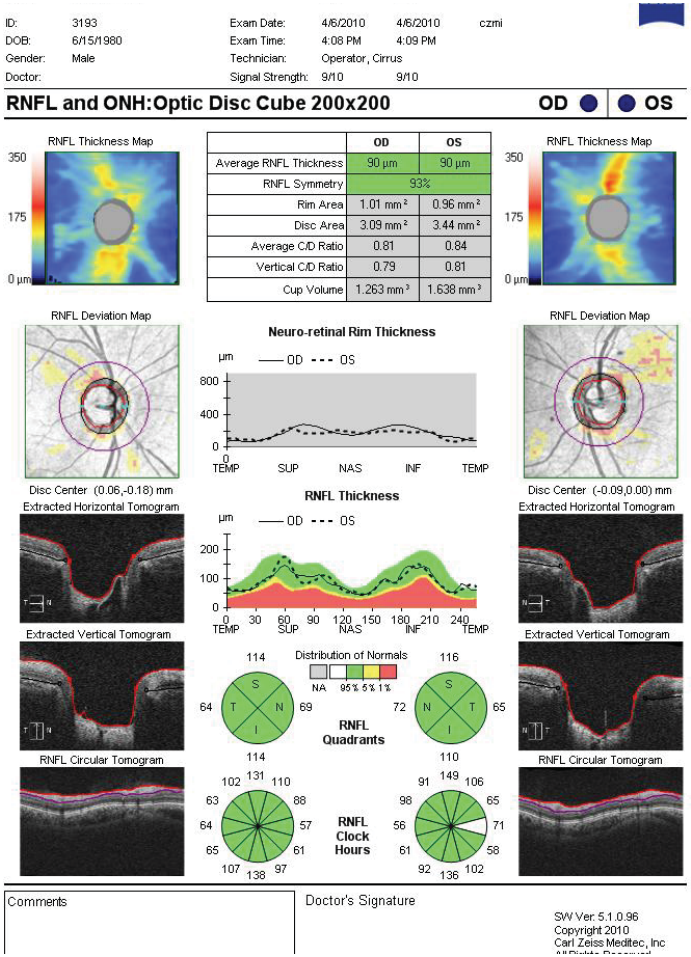
What Do You Look For When You Evaluate a Scan

- RNFL Thickness Map
  - Hot colors present?
  - Any areas in yellow or red?
  - What areas?
  - Do they correlate to other sections of printout?
- RNFL Deviation Map
  - Any areas flagged?
  - Is so, yellow or red?
  - How large?
  - Location of area flagged



What Do You Look For When You Evaluate a Scan

- Sector and quadrant map
  - Any areas flagged?
  - How many?
  - Yellow or red?
- Parameters
  - Which ones flagged?
  - One eye or both?
  - Yellow or red?
  - How many?
  - Any gray areas?



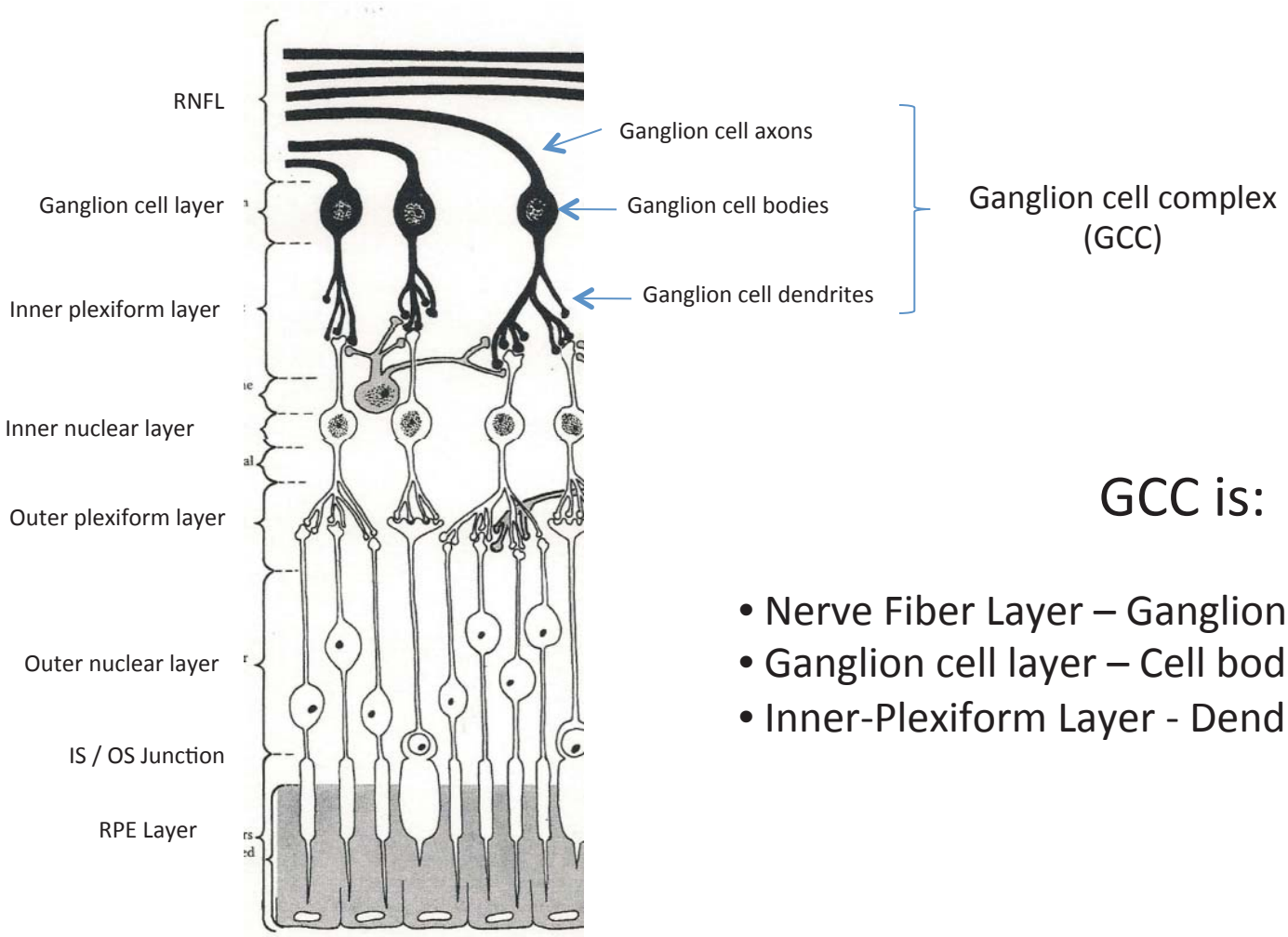
Macula Testing in Glaucoma

- Imaging to detect glaucoma damage has concentrated around RNFL and optic nerve evaluation
- Complicating the assessment of the optic nerve when evaluating for glaucoma damage is:
  - High variability of the ONH size and shape
    - Even among healthy individuals
  - Wide range of optic cup shapes and sizes
  - Variable size and configuration of blood vessels
  - Variable angle of penetration into the eyeball of the optic nerve (tilted disc)
  - Parapapillary changes such as atrophy
- These are the reasons why it is difficult to detect early glaucomatous damage

Macula Testing in Glaucoma

- Imaging allows measurement of features that are not possible otherwise
  - Imaging can detect changes in the macular region
  - The eye has about 1 million retinal ganglion cells, and their numbers are densest in the macula
    - about six cells deep
  - About 50% of ganglion cells are in the central 4.5 mm of the retina
    - an area that represents only 7% of the total retinal area
  - This area is not well covered in most visual field testing

Retinal Ganglion Cells extend through three retinal layers



GCC is:

- Nerve Fiber Layer – Ganglion cell axons
- Ganglion cell layer – Cell bodies
- Inner-Plexiform Layer - Dendrites

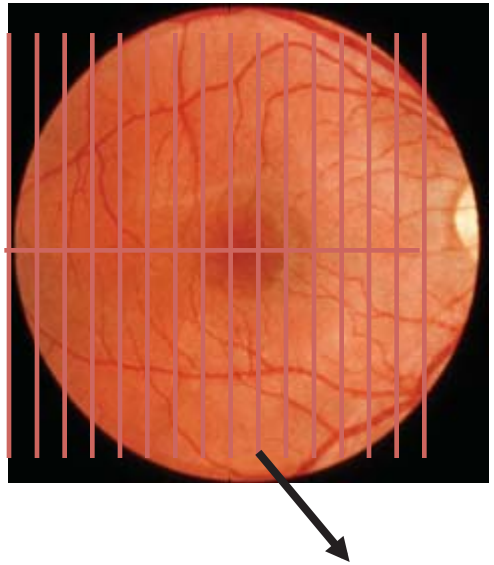
Macula Testing in Glaucoma

- Compared to the optic nerve, the macula is a relatively simple structure
  - Devoid of large vessels
  - Has multiple cellular and plexiform layers with central depression (fovea) devoid of retinal ganglion cells
  - The RGC layer (shape) within the macula is generally less variable in healthy individuals than RNFL or ONH
    - Perhaps reduction may offer better sensitivity in recognizing glaucoma damage

Macula Testing in Glaucoma

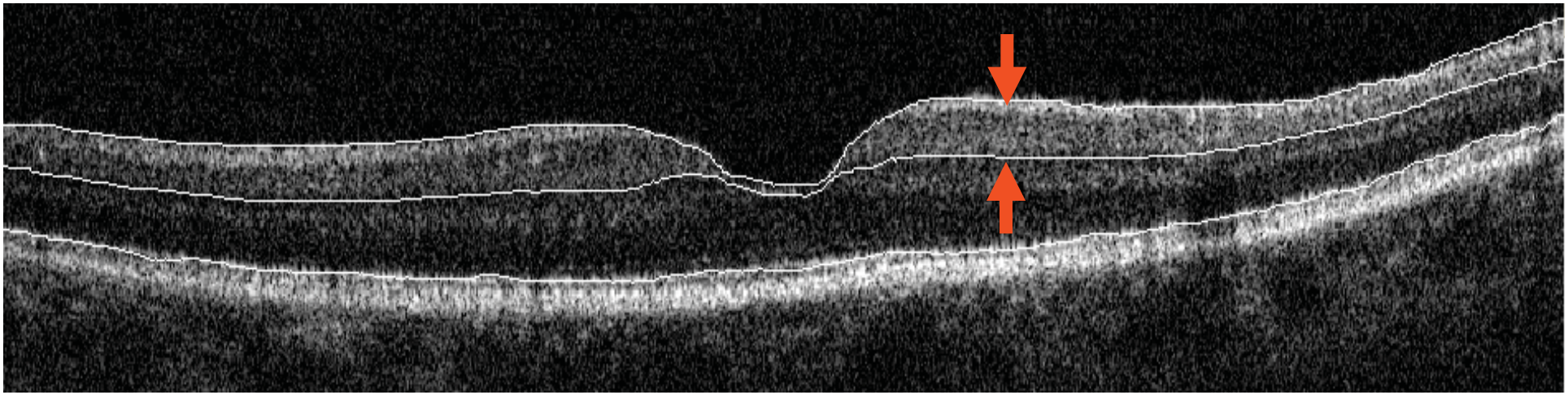
- The inner layer of the retina is composed of the nerve fiber layer (the ganglion cell axons), the ganglion cell layer (the cell bodies), and the inner plexiform layer (the dendrites)
- Spectral-domain optical coherence tomography (SD-OCT) can measure the thickness of the ganglion cell complex so the clinician can evaluate it over time to determine progression of glaucoma
- Importantly, analysis of the ganglion cells might allow clinicians to detect damage before there are changes in the retinal nerve fiber layer

Measuring the ganglion cell complex directly (ILM – IPL)



Inner retinal layers and provides complete Ganglion cell assessment:

- Nerve fiber layer (g-cell axons)
- Ganglion cell layer (g-cell body)
- Inner plexiform layer (g-cell dendrites)



Macula Testing in Glaucoma

- Other advantages of macula testing
  - Easier for patient to perform since involves central, not eccentric fixation
  - Measurement variability is less with macula testing
    - Macula thickness in healthy eyes – 280-300 um
    - RNFL – 80-100 um

Macula Testing in Glaucoma

- RTVue OCT
  - Segments Ganglion Cell Complex (GCC) from 3 innermost retinal layers
    - Retinal nerve fiber layer, retinal ganglion cell layer, inner plexiform layer
  - Measures over 7 mm^2 area, centered 1 mm temporal to fovea
  - Color coded thickness map
    - Thicker colors are yellow or orange
  - Has normative database
  - Concern is whether there is noise when including RNFL in this measurement

Macula Testing in Glaucoma

- Heidelberg Spectralis
  - Measures total retinal thickness, does not segment by layers
  - Scanned area is 8 x 8 mm grid containing 65 3^0 x 3^0 cells
  - Does NOT have normative database
  - Uses asymmetry analysis
    - Between eye (intra eye)
    - Between eyes (inter eye)
  - Has eye tracking that may improve test-retest variability

Macula Testing in Glaucoma

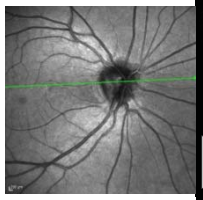
- Cirrus OCT
  - Segments ganglion cell and inner plexiform layer (GC-IPL) into Ganglion Cell Analysis (GCA)
  - Uses 14.13 mm^2 elliptic annulus area centered on fovea
    - Area of annulus corresponds to thickest area of retinal ganglion cell area in normals
  - Removes RNFL from measurement b/c this layer may show high variability

What is EDI?
Enhanced Depth Imaging

- For spectral domain, sensitivity is highest at top of window (vitreous) and declines with depth
- With EDI, sensitivity in window is flipped and now sensitivity is higher on bottom (lamina or choroid)
  - Loss of sensitivity at top (vitreous)
  - Advantage of swept source is less drop off in sensitivity with depth of imaging
- All OCTs have ability to shift sensitivity with depth

Enhanced Depth Imaging (EDI)

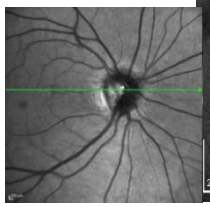
Without EDI



Vitreous / Retinal interface highlighted

Bruch's membrane opening (Neural Canal Opening - NCO)

With EDI



Posterior surface of lamina cribrosa

Enhanced depth imaging (EDI)

- Enhanced depth imaging (EDI) was developed for SD OCT to improve image quality of the deep structures of the posterior segment
- However, although EDI is an effective method for visualizing the deep structures of the optic disc, it is disadvantageous for observing axially extended structures in highly myopic eyes in their entirety because its signal intensity decays with axial distance.

Focal Lamina Cribrosa Defects Associated With Glaucomatous Rim Thinning and Acquired Pits

Jae Young You, MD; Sung Chul Park, MD; Daniel Su, BS; Christopher C. Teng, MD; Jeffrey M. Liebmann, MD; Robert Ritch, MD

Importance: Considering the potential clinical importance of focal lamina cribrosa (LC) defects as a characteristic structural feature in glaucoma and a risk factor for glaucomatous visual field progression, it may be helpful to know the structure of focal LC defects and the spatial relationship between them and glaucomatous optic disc changes such as neuroretinal rim thinning/notching and acquired pits of the optic nerve (APON).

Objective: To investigate structural and spatial relationships between focal LC defects and glaucomatous neuroretinal rim thinning/notching and APON.

Design: In a cross-sectional analysis of data from an ongoing, prospective, longitudinal study, serial enhanced-depth imaging (EDI) optical coherence tomographic (OCT) images of the optic nerve head were obtained from patients with glaucoma and reviewed for focal LC defects (laminar holes or disinsertions). Anterior laminar insertion points and edges of laminar holes or disinsertions were marked in EDI-OCT images, reconstructed 3-dimensionally, and superimposed on optic disc photographs.

Setting: A glaucoma referral practice.

Participants: Two hundred thirty-nine eyes (120 patients) were examined. Fifty-four eyes were excluded because of an incomplete horizontal or vertical set of serial EDI-OCT images or poor-quality EDI-OCT images owing to media opacity, irregular tear film, or poor patient cooperation. Among the remaining 185 eyes, 40 (from 31 patients) had laminar holes or disinsertions and were included for analysis.

Main Outcome Measures: Presence, extent, and location of laminar holes or disinsertions.

Results: Among 185 eyes, 11 laminar holes and 36 laminar disinsertions were found in 40 eyes. Superimposed images of the 3-dimensionally reconstructed focal LC defects and disc photographs showed that the outline of the LC defect corresponded almost precisely to that of clinical APON for 6 laminar holes and that the LC defect was much larger than and enclosed APON for 10 laminar disinsertions. The remaining 5 laminar holes and 26 laminar disinsertions corresponded to focal neuroretinal rim loss, with no evidence of APON in disc photographs.

Conclusions and Relevance: Focal LC defects (laminar holes or disinsertions) are associated with neuroretinal rim loss and APON. The extent of LC defects can be visualized more effectively on EDI-OCT images than by clinical examination.

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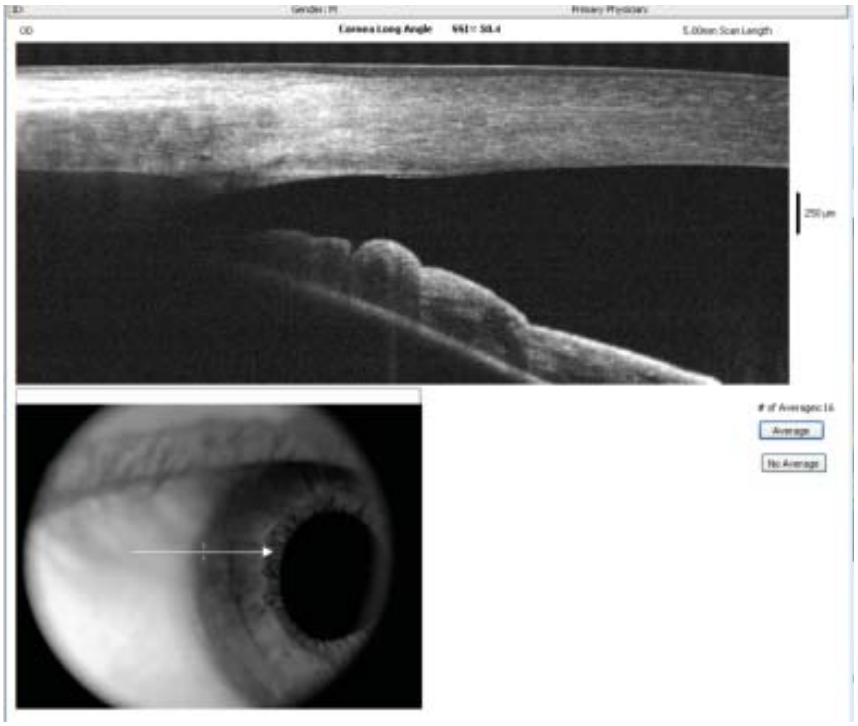
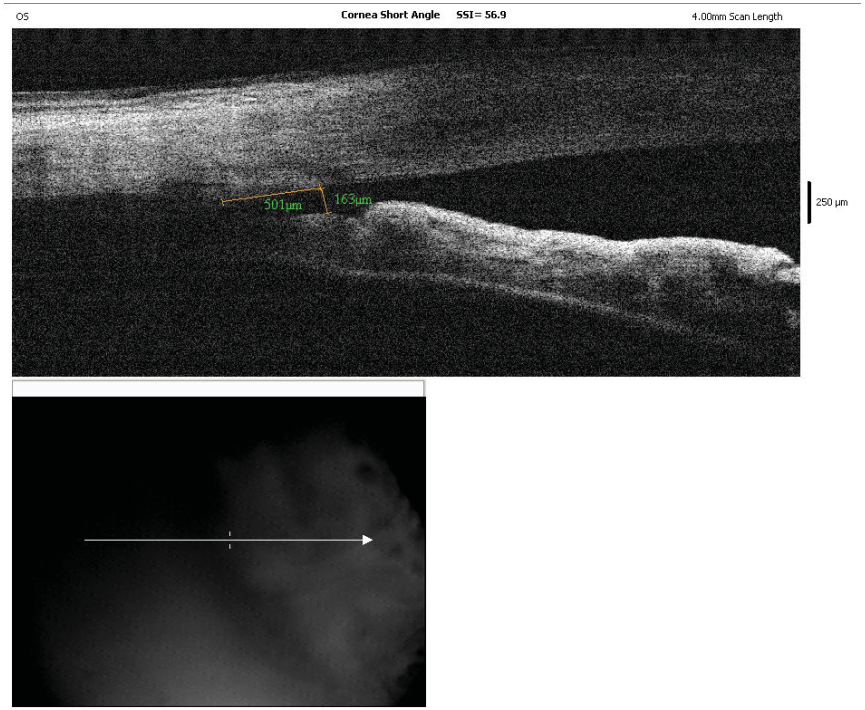
Anterior Segment Imaging

Angle Measurements



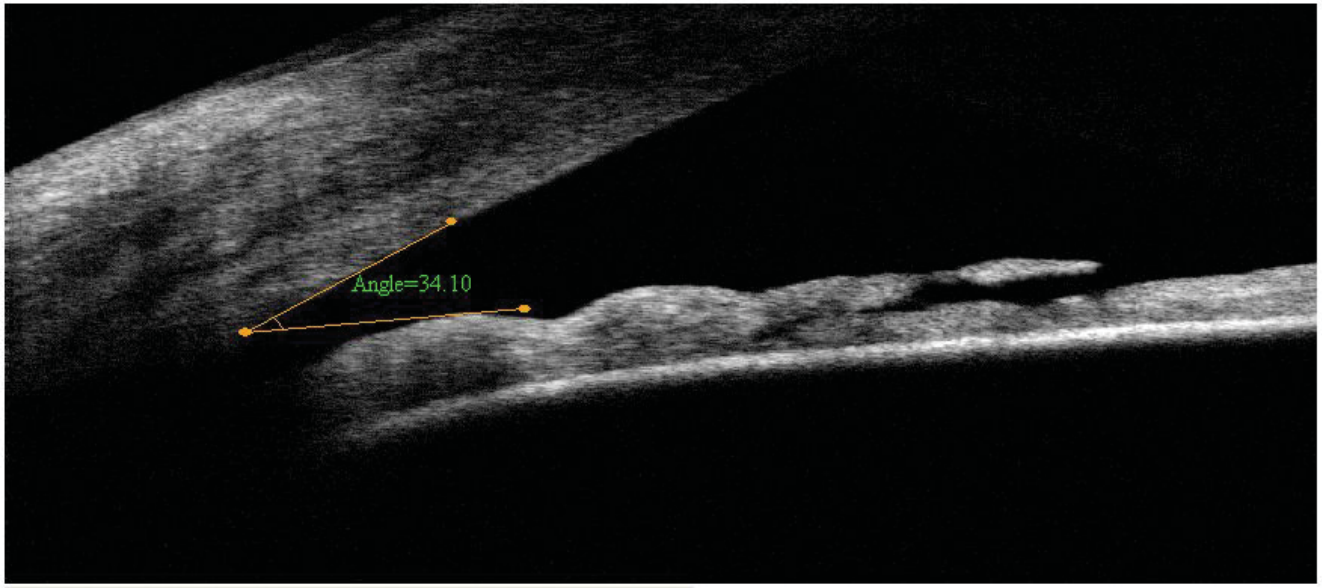
Normal

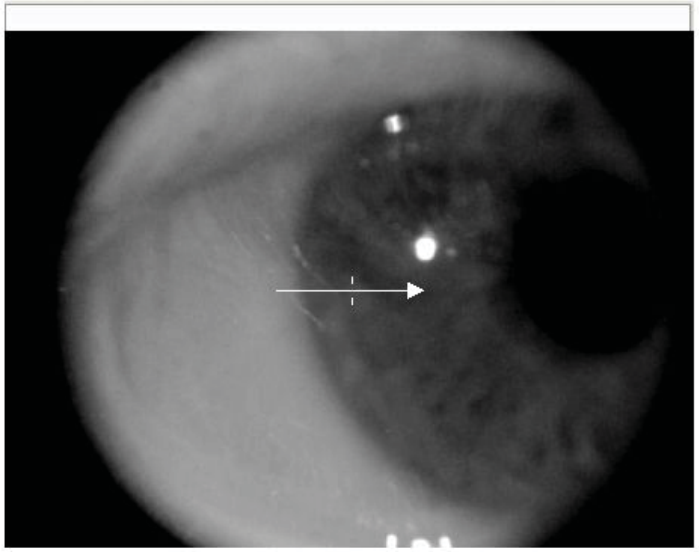


Narrow

DOB (age): 01/01/1960 (48) ID:	Algorithm Version: A2, 0, 2, 6 Gender: M	Examine Date: 02/06/2008 Primary Physician:

OD **CL - Angle** **SSI= 61.8** 3.00mm Scan Length





# of Averages:6

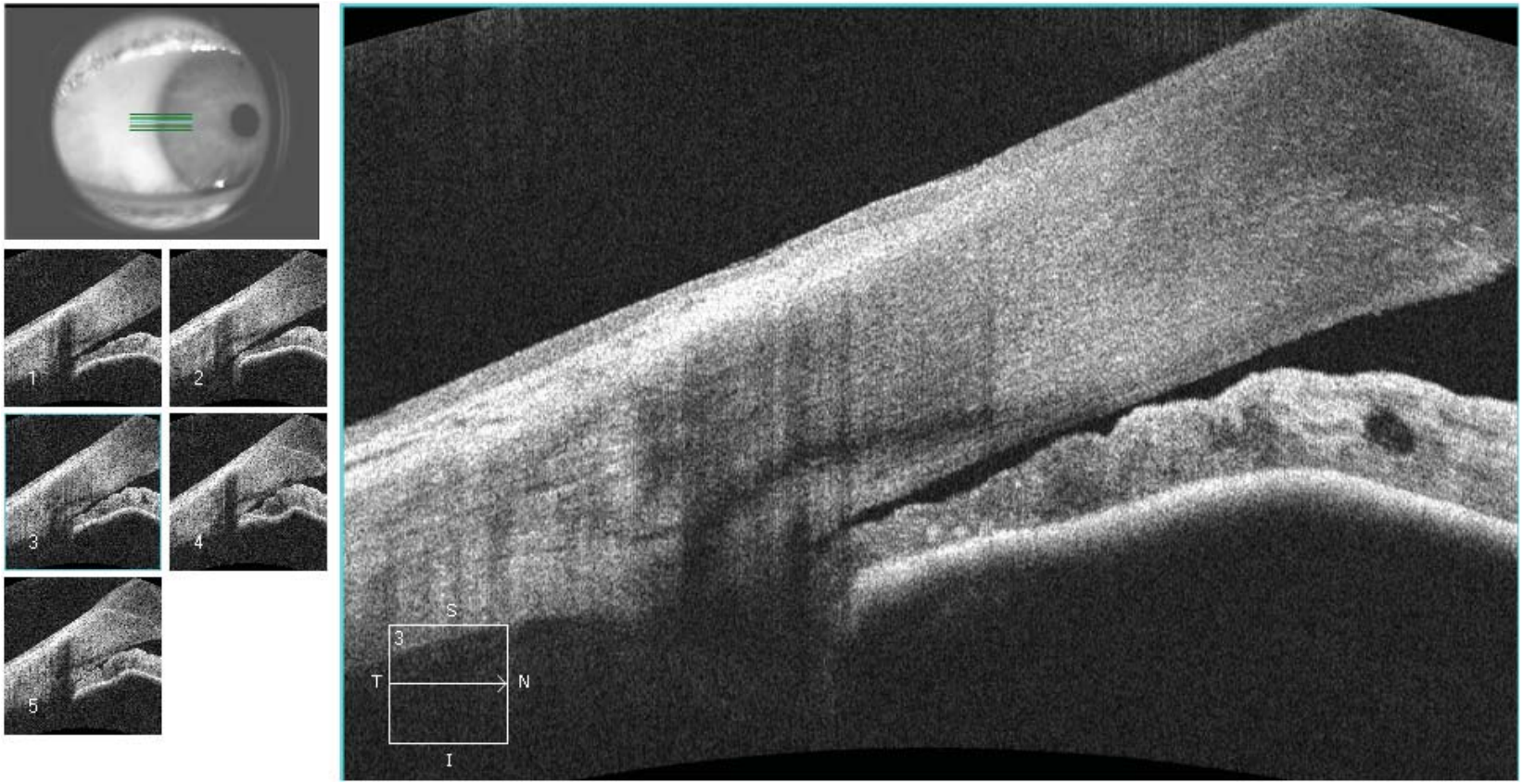
Average

No Average

Diagnosis:

Report Date: Thursday February 07 09:01:24 2008

Anterior segment imaging using the Cirrus HD-OCT, showing multiple scans of a narrow angle



Images courtesy of Martha Leen, M.D. & Paul Kremer M.D. Achieve Eye and Laser Specialists, Silverdale, WA

Artifacts in Taking OCT Images

- Each OCT image/printout needs to be carefully analyzed
- Some may not be of sufficient quality and should be evaluated with caution
  - may mislead the clinician
- There are different reasons why an OCT image may not of adequate quality
- Poor quality images may appear to be abnormal and glaucomatous when an artifact is the cause of the problem

Artifacts in Taking OCT Images
Poor Quality Images

- Out of focus
- Reduced illumination
  - Not properly illuminated
- Reduced signal strength
  - Dry eye, cataracts, other media opacities or small pupils
- There is a relationship between signal strength and RNFL thickness

Artifacts in Taking OCT Images
Poor Quality Images

- Want signal strength to meet manufacturer's recommendations
- Use carefully any image in which quality scores are below recommendations
- Even if Quality score is acceptable, there may still be problems with image

Image Artifacts

- Blink cutting off image
- Scan too high or too low cutting off image
- Eye movement
- Hi Myopia
- Large optic disc and / or PPA
  - RNFL circle too small - encroahces on optic disc/PPA
- Floaters obscuring tissue underneath
- Pathologies such as epiretinal membrane or chorioretinal scar

Artifacts in Taking OCT Images

- Algorithm failure
  - Segmentation errors
  - B scan segmentation inaccurate
  - Retinal assessment (RNFL, GCC, Retina thickness)
  - Disc margin error
    - Throws off disc size
  - Cup not properly outlined (material in cup throwing segmentation off)
    - Can not over ride this with Cirrus

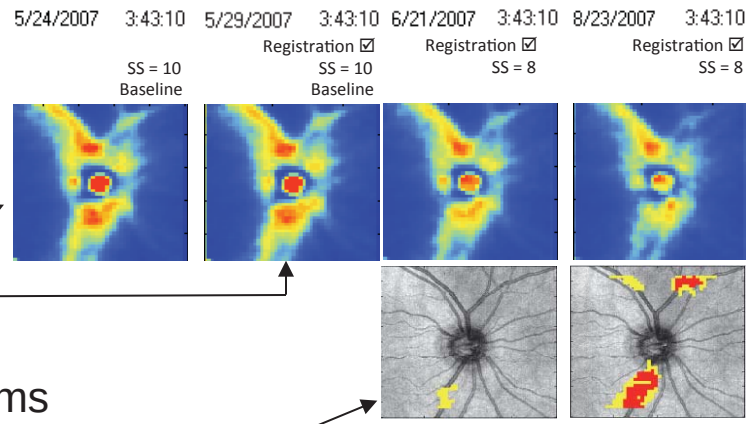
Artifacts in Taking OCT Images

- Any of these problems can lead to inaccurate images
  - Possibly giving the sense of an abnormal scan and a glaucoma diagnosis when the problem is with the scan and not the eye

Progression

Cirrus HD-OCT GPA Analysis

IMAGE PROGRESSION MAP

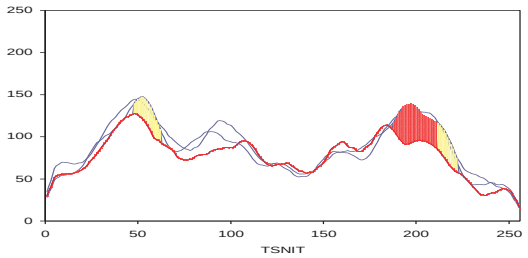


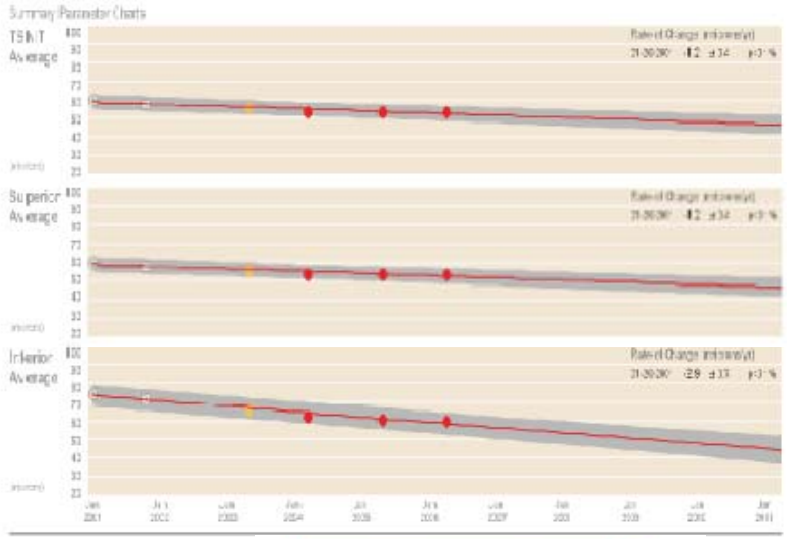
- Two baseline exams are required*. Follow up exams are registered to the baseline to ensure accurate comparison.
- Third exam is compared to the two baseline exams
- Sub pixel map demonstrates change from baseline. Yellow pixels denote change from both baseline exams
- Third *and* fourth exams are compared to both baselines. Change identified in three of the four comparisons is indicated by red pixels; yellow pixels denote change from both baselines

Change refers to statistically significant change, defined as change that exceeds the known variability of a given pixel based on a study population.

*with software version 5.0, the two baseline exams can be obtained on the same day

Cirrus HD-OCT GPA Analysis





TSNIT PROGRESSION MAP

- TSNIT values from each exam are shown
- Significant difference is colorized yellow or red
- Yellow denotes change from baseline exams
- Red denotes change from 3 of 4 comparisons

SUMMARY PARAMETER TREND ANALYSIS

- Rate and significance of change shown in text
- RNFL thickness values for Overall Average, Superior Average, and Inferior Average are plotted for each exam
- Yellow marker denotes change from both baseline exams
- Red marker denotes change from 3 of 4 comparisons
- Confidence intervals are shown as a gray band

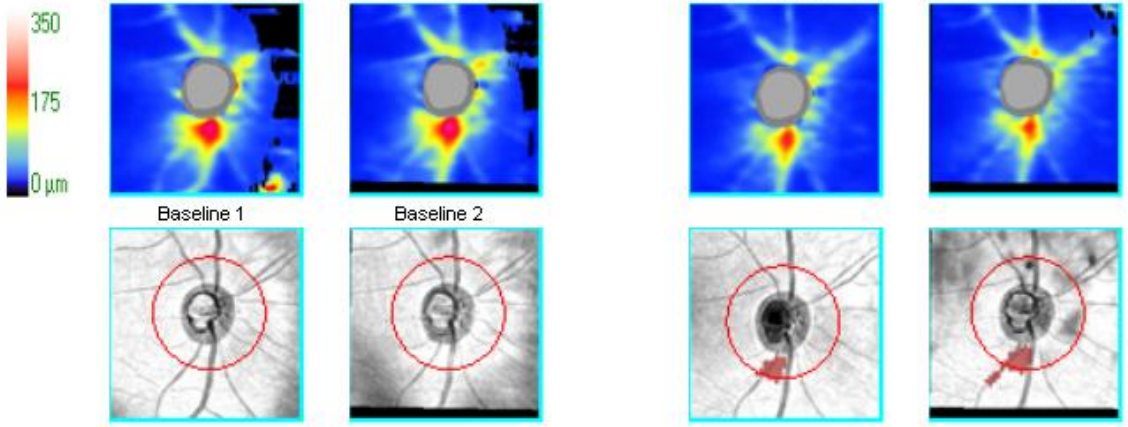
- Legend summarizes GPA analyses and indicates with a check mark if there is possible or likely loss of RNFL

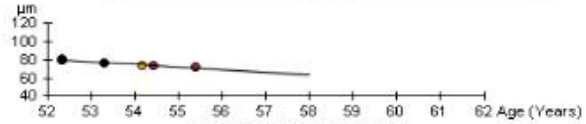
Doctor: Signal Strength: 10/10 9/10

Guided Progression Analysis: (GPA™)

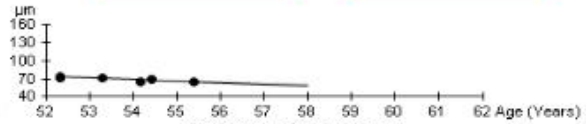
OD ● | ○ OS

Baseline 1	Baseline 2	Exam 5	Exam 6
9/24/2009 12:07:51 PM	9/24/2009 3:07:08 PM	10/24/2011 2:54:51 PM	10/17/2012 2:57:15 PM
400-10004	4000-2202	4000-7488	4000-7488
SS: 10/10	R2 SS: 8/10	R1 SS: 9/10	R2 SS: 9/10
Average Thickness: 80	Average Thickness: 82	Average Thickness: 74	Average Thickness: 72

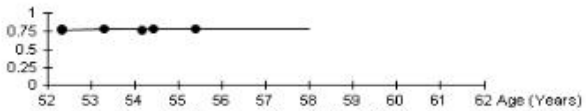




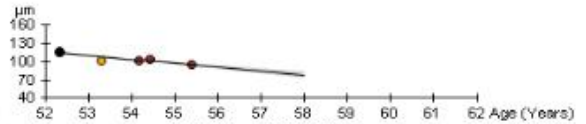
Average RNFL Thickness
Rate of change: -3.04 +/- 1.25 µm/Year



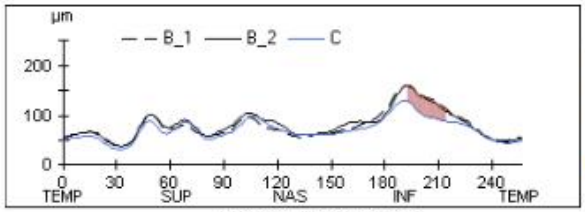
Superior RNFL Thickness
Rate of change: -2.41 +/- 2.44 µm/Year



Average Cup-to-Disc Ratio
Rate of change: 0.00 +/- 0.00 /Year



Inferior RNFL Thickness
Rate of change: -6.26 +/- 3.70 µm/Year

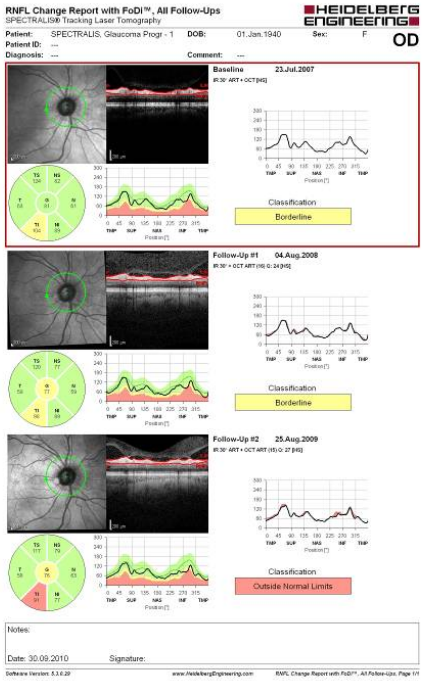


RNFL Thickness Profiles

Heidelberg Spectralis RNFL trend report

- Shows change over time for each sector.
- Compares measurement to normative database.
- Results are displayed numerically and as a trend graph.

Trend Report (new in 5.3)



RNFL Progression Report (already in 5.1)