Spectral Domain Optical Coherence Tomography in the Diagnosis and Management of Glaucoma

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GUMS

- Optical coherence tomography is a noncontact , noninvasive imaging technique that can reveal layers of the retina by looking at the interference patterns of reflected laser light.
- Spectral-domain OCT (SD-OCT) which improved upon TD-OCT by capturing more data in less time at a higher axial image resolution, around 5 µm.

- Objective assessment of glaucomatous structural alterations due to fast and highly reproducible scan acquisition.
- OCT is now the imaging modality of choice for objective assessment of glaucomatous structural alterations due to fast and highly reproducible scan acquisition.

- the most common commercially available SD-OCT devices are:

  - Cirrus HD-OCT

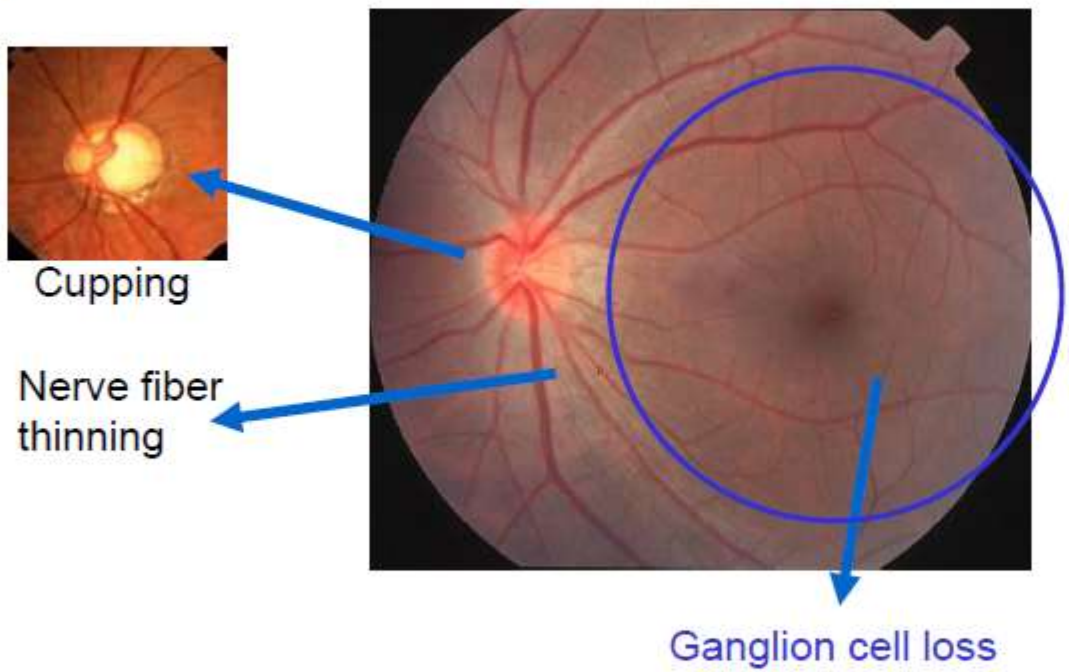
  -RTVue-100

  -Spectralis OCT

  -Topcon 3D-OCT 2000

Each machine has different glaucoma scan patterns, proprietary software segmentation algorithms

Glaucoma affects 3 areas in the posterior segment of the eye



SD-OCT Parameters IN Glaucoma

- There are three main parameters relevant to the detection of glaucomatous loss:

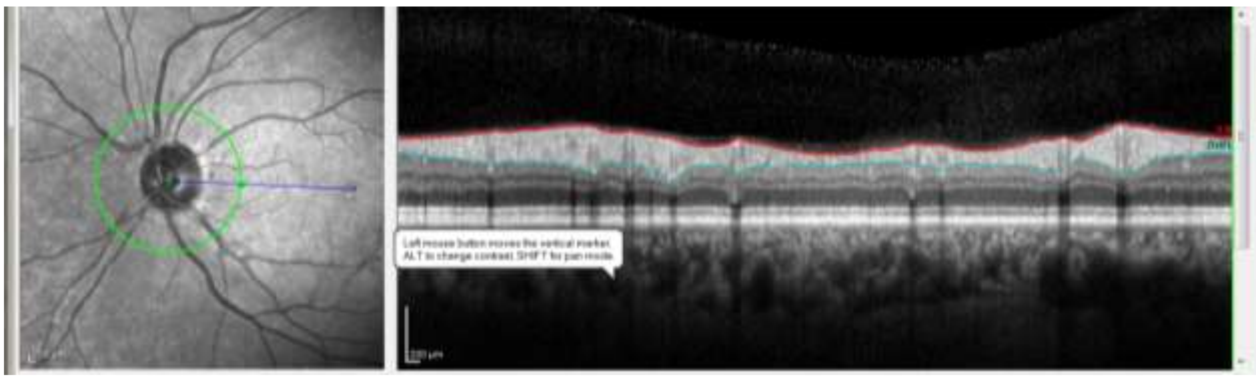
  - Retinal nerve fiber layer

  - Optic nerve head

  - Ganglion cell complex

Retinal Nerve Fiber Layer

- SD-OCT can directly measure and quantify RNFL thickness by calculating the area between the internal limiting membrane (ILM) and RNFL border.
- The Cirrus and Spectralis RNFL map represents a 6 x 6 mm cube of A-scan data centered over the optic nerve in which a 3.4 mm diameter circle of RNFL data is extracted to create what is referred to as the TSNIT map (temporal, superior, nasal, inferior, temporal).


Left mouse button moves the vertical marker.
ALT to change contrast, SHIFT for pan mode.

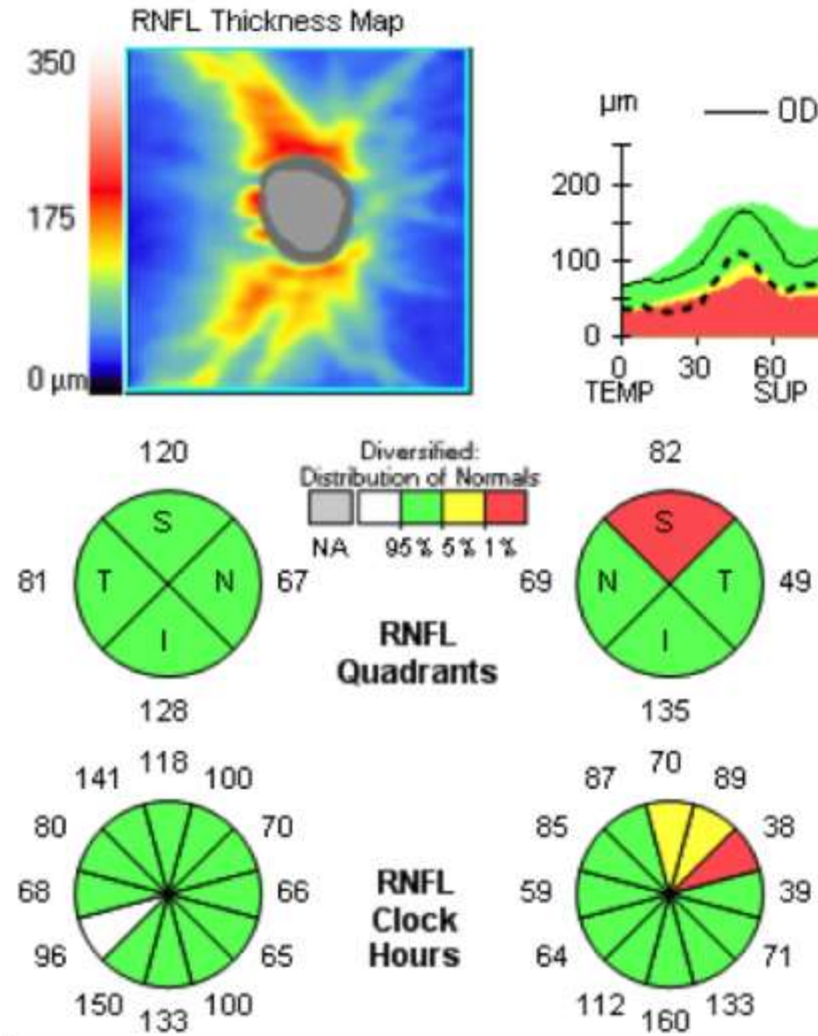
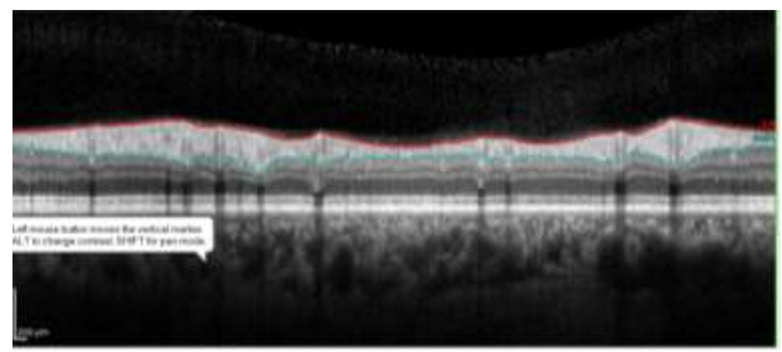


Figure 1:

(a) RNFL thickness map

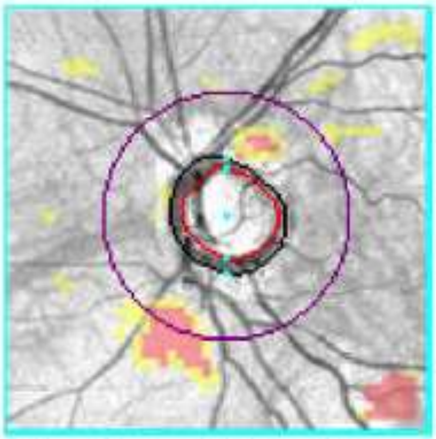
(b) TSNIT map

(c) RNFL quadrant map



Optic Nerve Head

RNFL Deviation Map



Disc Center (0.09,0.09) mm

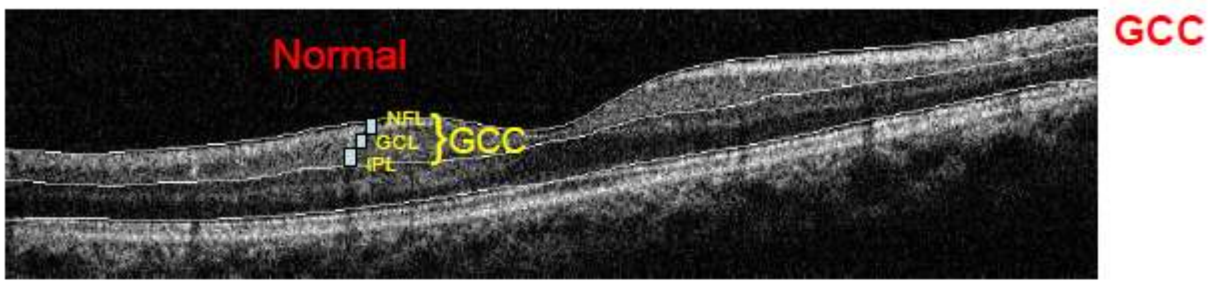
	OD	OS
Average RNFL Thickness	77 µm	80 µm
RNFL Symmetry	58%	
Rim Area	0.88 mm²	0.77 mm²
Disc Area	1.97 mm²	2.01 mm²
Average C/D Ratio	0.75	0.80
Vertical C/D Ratio	0.80	0.78
Cup Volume	0.472 mm³	0.616 mm³

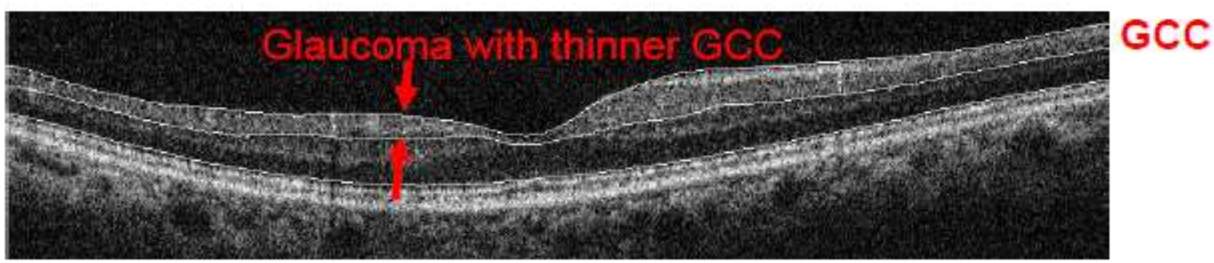
- The calculated ONH parameters, except for disc area, are compared to a normative database.
- The parameters found to have the greatest diagnostic capability are vertical rim thickness, rim area, and vertical cup to disc ratio.

Ganglion Cell Analysis

- The ganglion cell layer is thickest in the perimacular region and decreased total macular thickness has been observed in glaucomatous eyes likely due to thinning of the ganglion cell layer in this region.
- However segmenting the ganglion cell layer alone is very difficult based on reflectivity.
- Cirrus chose to measure its Ganglion Cell Analysis (GCA) consisting of the combined ganglion cell layer (GCL) and inner plexiform layer (IPL).
- Optovue's Ganglion Cell Complex (GCC) chose to include RNFL in their combined GCL and IPL layers.

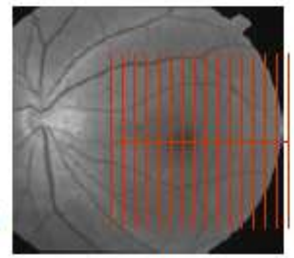
Glaucoma preferentially thins the <u>Ganglion Cell Complex (GCC)</u> which includes the axons, cell bodies, and dendrites of retinal ganglion cells





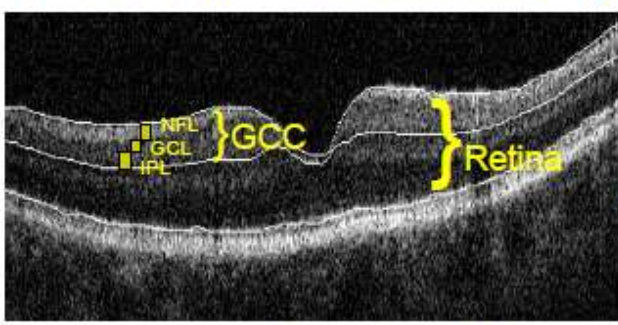
Glaucoma: Macular Ganglion Cell Mapping

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

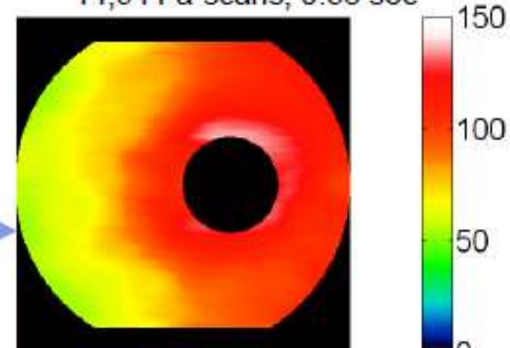


Ganglion Cell Complex (GCC)
7 mm scan area
14,944 a-scans, 0.58 sec

David Huang, MD, PhD www.AIGStudy.net



GCC = Ganglion Cell Complex



mGCC thickness map

micron

Use of SD-OCT in Diagnosis of Glaucoma

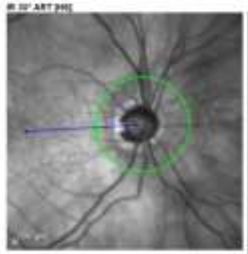
- It is well known that significant structural RNFL loss occurs prior to the development of functional visual field loss. In such preperimetric disease, SD-OCT RNFL is especially useful in helping to diagnose glaucoma prior to the onset of visual field loss.
- In the presence of perimetric disease, finding RNFL bundle loss on SD-OCT with a corresponding abnormality in the visual field served by those retinal ganglion cells can help confirm the diagnosis of glaucoma.

RNFL Single Exam Report OU
SPECTRALIS® Tracking Laser Tomography

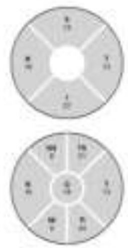
HEIDELBERG ENGINEERING

Patient:	Panjtan panah, Abolghasem	**DOB:**	Jan/1/1940	**Sex:**	M
Patient ID:	---	**Exam.:**	Dec/28/2014		

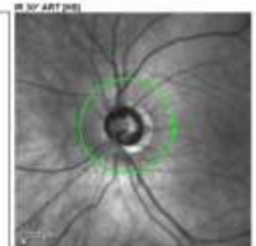
OD

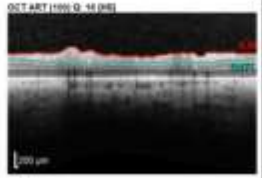


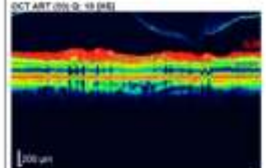
Asymmetry OD - OS

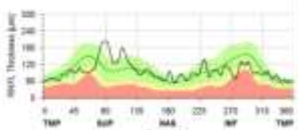


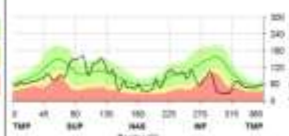
OS

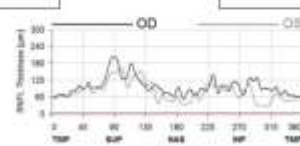












Classification OD

Borderline

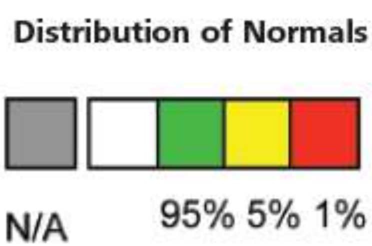
Classification OS

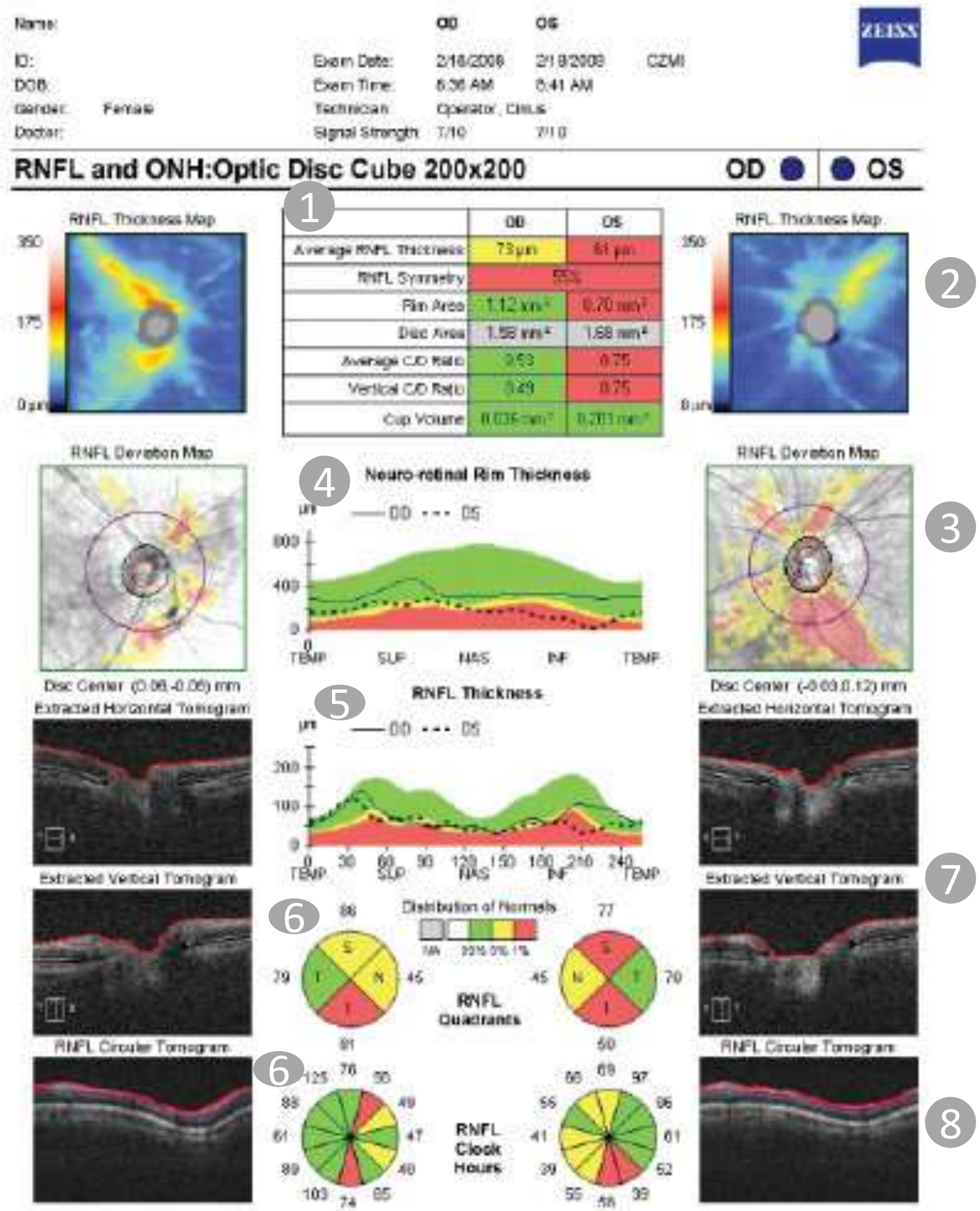
Outside Normal Limits

Notes:

Date: 2/16/2015 Signature:

1. **Key parameters**: compared to normative data
2. **RNFL thickness map**
3. **The RNFL Deviation Map**
4. **Neuro-retinal Rim Thickness**
5. **RNFL TSNIT graph**
6. **RNFL Quadrant and Clock Hour**
7. **Horizontal and vertical B-scans**
8. **RNFL calculation circle**





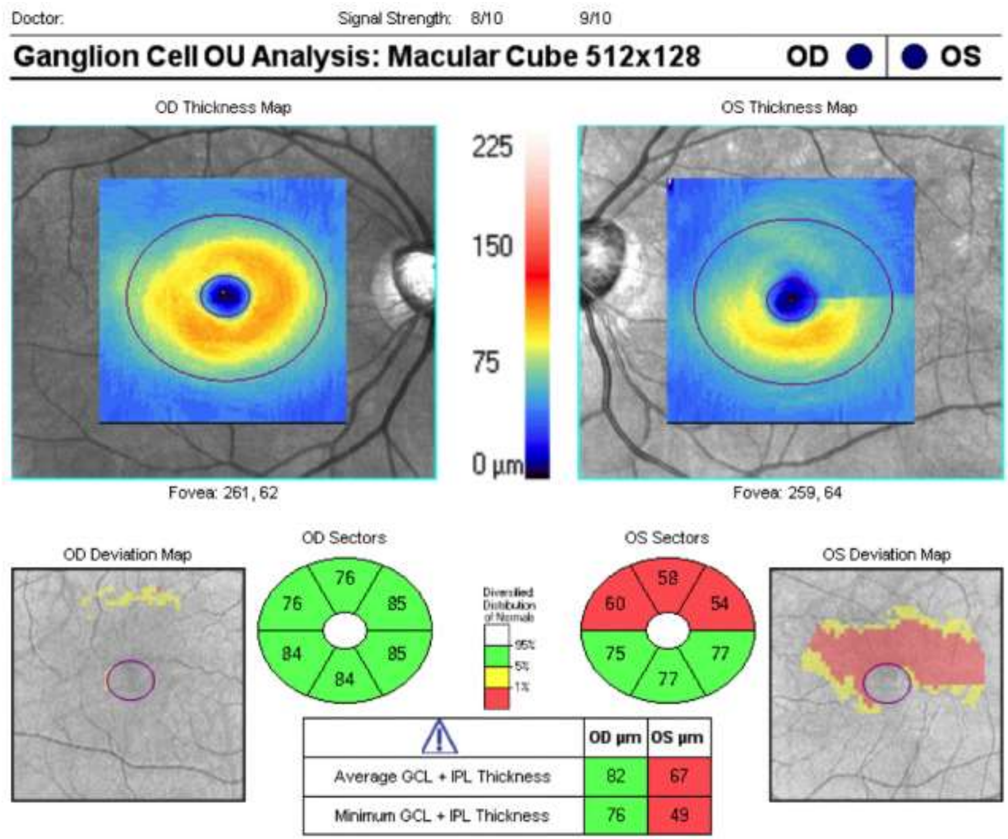
Macular OCT Imaging in Glaucoma

- Traditionally, images of the optic nerve head and the peripapillary area have been used to evaluate the structural changes associated with glaucoma.
- There is growing evidence in the literature supporting the use of macular OCT as complementary tool for clinical evaluation and research purposes in glaucoma.
- Containing more than 50% of retinal ganglion cells in a multilayered pattern, macula is shown to be affected even at the earliest stages of glaucomatous structural damage.

Macular OCT Imaging in Glaucoma

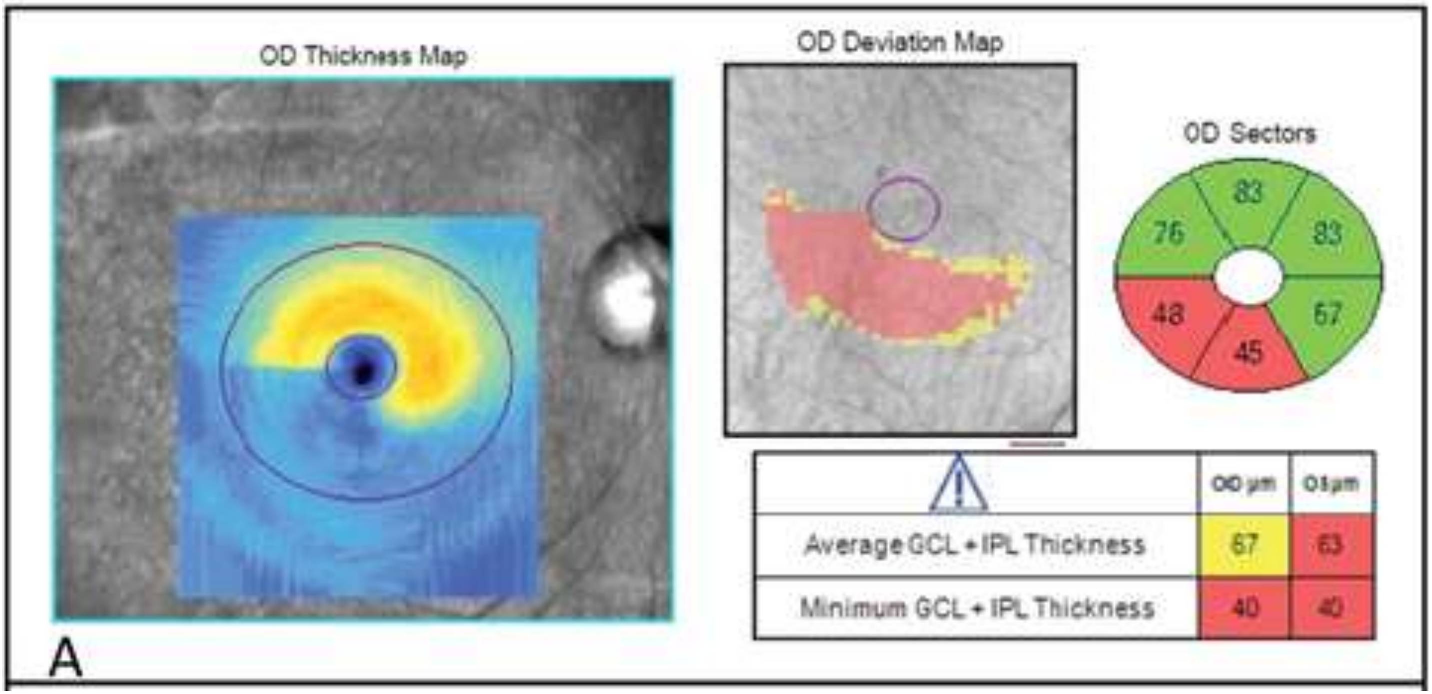
- **Utility in the Detection of Early Glaucoma**
- **Monitoring of Advanced Glaucoma**
- **Utility in the Detection of Glaucoma in Myopic Eyes**
- **Risk Assessment**

Ganglion Cell Analysis



The most diagnostically useful parameters are minimum, inferotemporal sector, average, superotemporal sector, and inferior sector ganglion cell complex thickness.

The temporal raphe sign



Use of SD-OCT in Detection of Glaucomatous Progression

Repeatability and Reproducibility of SD-OCT:

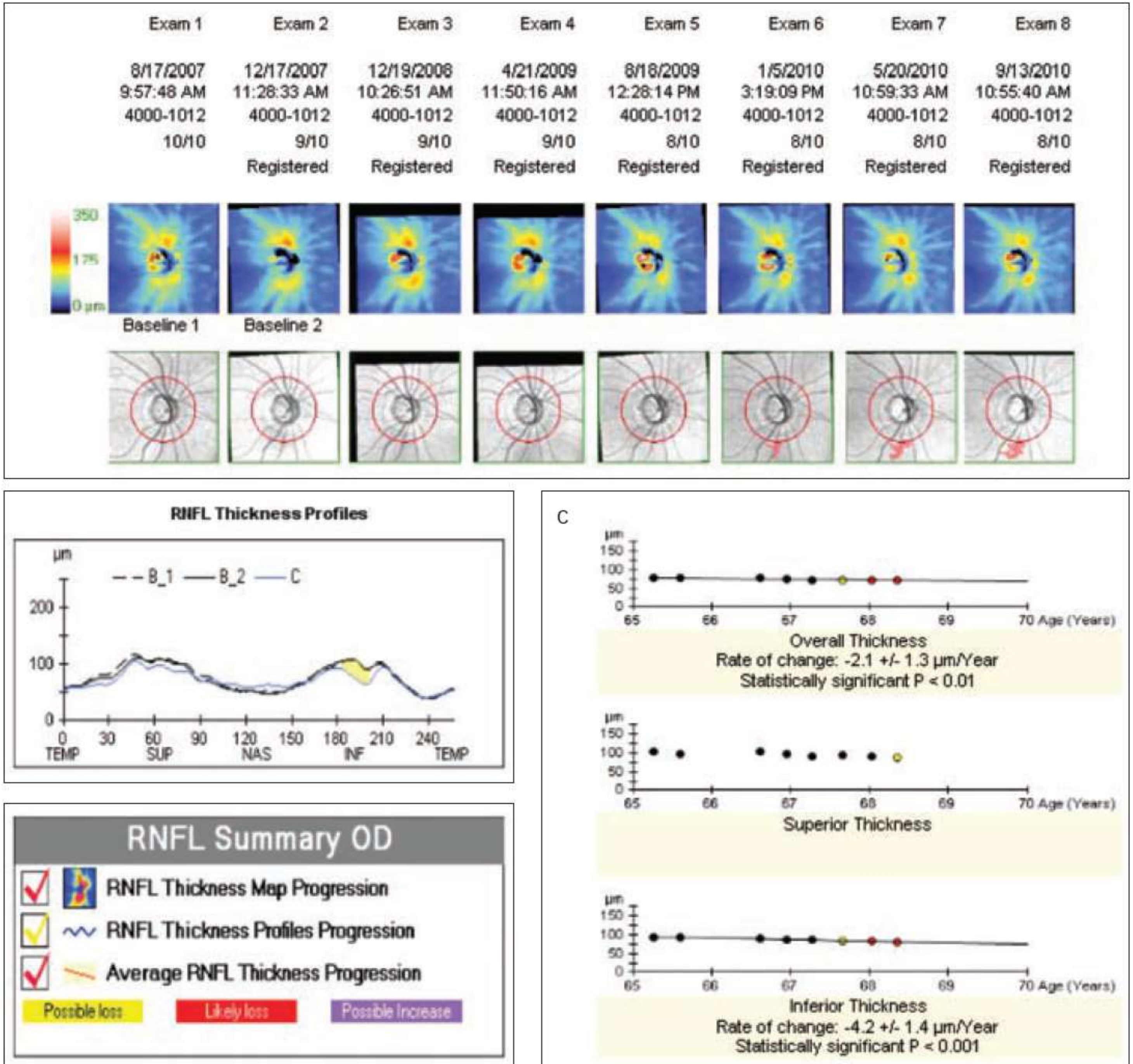
- The intervisit tolerance limit for average RNFL thickness was 3.89 µm in a study suggesting that a reproducible decrease of ≥4 µm may be a statistically significant change. A more cautious cutoff would be a 10 µm change.
- It is important to exclude any scans that are not of adequate quality.
- Scans with a signal strength less than 6, with eye movement or blinking artifacts within the 1.73-mm radius around the optic nerve head, or with segmentation errors should be repeated.

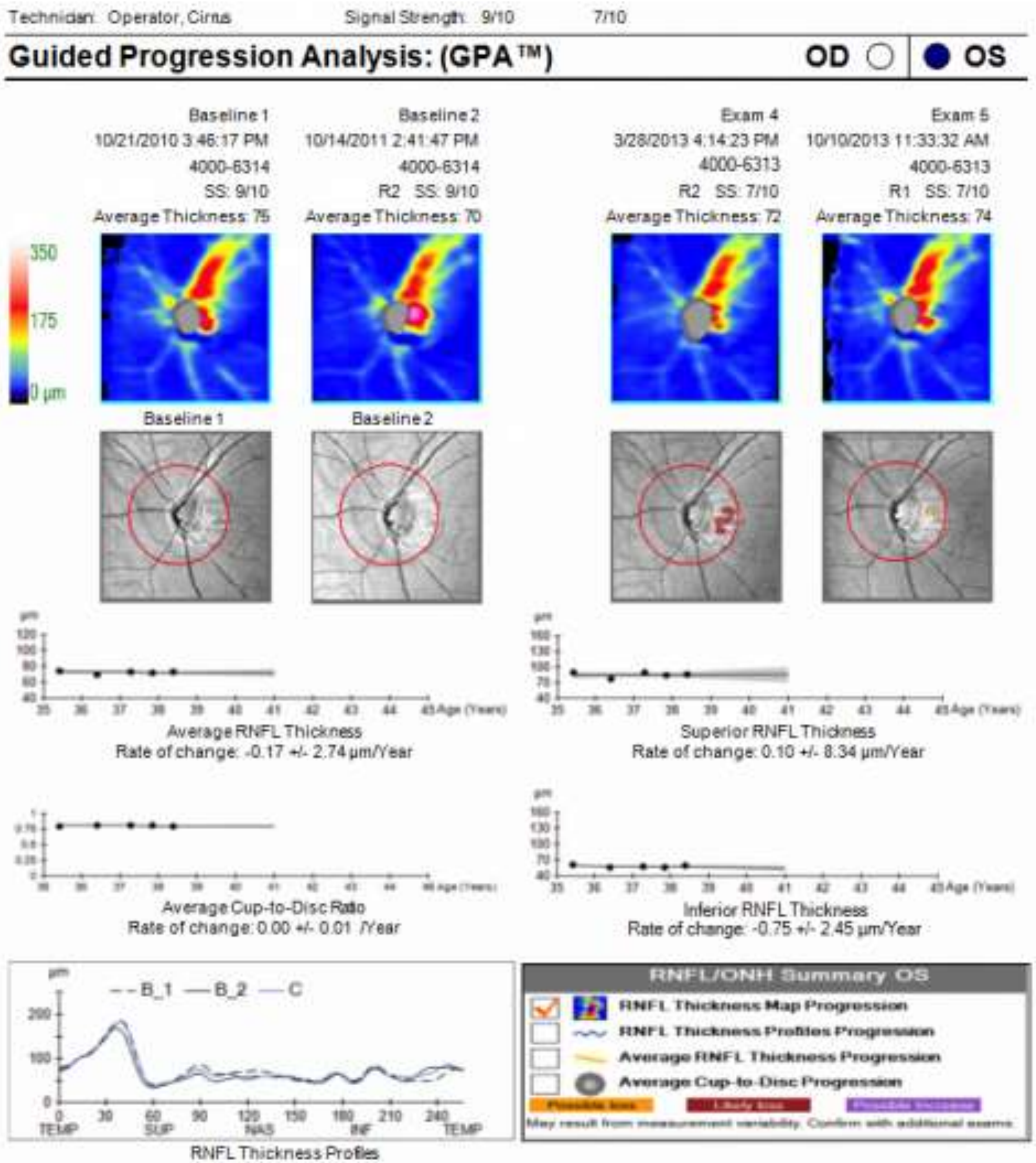
Glaucoma progression algorithms:

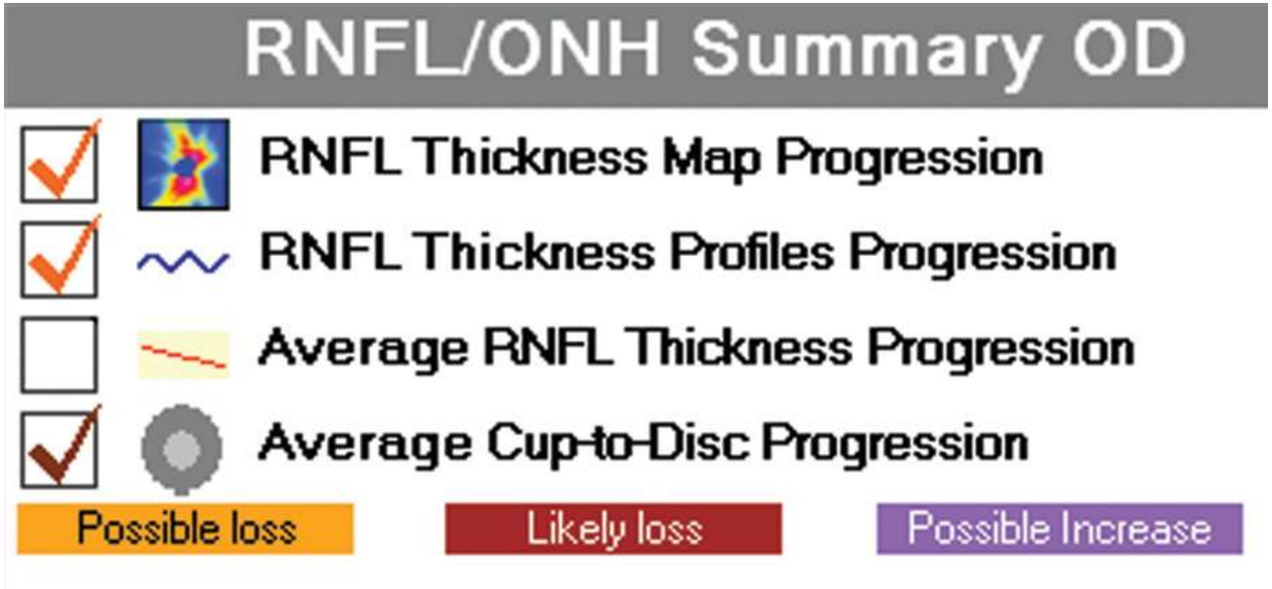
- Glaucoma progression algorithms can be divided into event-based and trend-based approaches
- Event-based analysis defines progressive change when a follow up measurement exceeds a pre-established threshold for change from baseline.
- Trend-based analysis defines progression by monitoring the change over time using regression analysis to provide a rate of progression and corresponding significance level.

Guided Progression Analysis (GPA)

- GPA introduced in 2009 on the Cirrus.
- Local pixels exceeding such test-retest variability are coded in yellow at the first event, and in red if the same changes are seen on three consecutive images.
- In order to generate an overall trend plot, two baseline scans with three follow up scans are necessary.
- This linear regression line in µm/yr, representing rate of change, is drawn with an estimated confidence interval carried forward.


Exam 1
Exam 2
Exam 3
Exam 4
Exam 5
Exam 6
Exam 7
Exam 8
8/17/2007
9:57:48 AM
4000-1012
10/10
12/17/2007
11:28:33 AM
4000-1012
9/10
Registered
12/19/2008
10:26:51 AM
4000-1012
9/10
Registered
4/21/2009
11:50:16 AM
4000-1012
9/10
Registered
8/18/2009
12:28:14 PM
4000-1012
8/10
Registered
1/5/2010
3:19:09 PM
4000-1012
8/10
Registered
5/20/2010
10:59:33 AM
4000-1012
8/10
Registered
9/13/2010
10:55:40 AM
4000-1012
8/10
Registered
350
175
0 µm
Baseline 1
Baseline 2
RNFL Thickness Profiles
µm
B_1
B_2
C
200
100
0
0
30
60
90
120
150
180
210
240
TEMP
SUP
NAS
INF
TEMP
RNFL Summary OD
RNFL Thickness Map Progression
RNFL Thickness Profiles Progression
Average RNFL Thickness Progression
Possible loss
Likely loss
Possible Increase
C
µm
150
100
50
0
65
66
67
68
69
70 Age (Years)
Overall Thickness
Rate of change: -2.1 +/- 1.3 µm/Year
Statistically significant P < 0.01
Superior Thickness
Inferior Thickness
Rate of change: -4.2 +/- 1.4 µm/Year
Statistically significant P < 0.001


Technician: Operator, Cirrus
Signal Strength: 9/10
7/10
Guided Progression Analysis: (GPA™)
OD
OS
Baseline 1
10/21/2010 3:46:17 PM
4000-6314
SS: 9/10
Average Thickness: 75
Baseline 2
10/14/2011 2:41:47 PM
4000-6314
R2 SS: 9/10
Average Thickness: 70
Exam 4
3/28/2013 4:14:23 PM
4000-6313
R2 SS: 7/10
Average Thickness: 72
Exam 5
10/10/2013 11:33:32 AM
4000-6313
R1 SS: 7/10
Average Thickness: 74
350
175
0 µm
Baseline 1
Baseline 2
Average RNFL Thickness
Rate of change: -0.17 +/- 2.74 µm/Year
Superior RNFL Thickness
Rate of change: 0.10 +/- 8.34 µm/Year
Average Cup-to-Disc Ratio
Rate of change: 0.00 +/- 0.01 /Year
Inferior RNFL Thickness
Rate of change: -0.75 +/- 2.45 µm/Year
B_1
B_2
C
TEMP
SUP
NAS
INF
TEMP
RNFL Thickness Profiles
RNFL/ONH Summary OS
RNFL Thickness Map Progression
RNFL Thickness Profiles Progression
Average RNFL Thickness Progression
Average Cup-to-Disc Progression



RNFL Summary summarizes Guided Progression Analysis (GPA) analyses and indicates with a check mark if there is possible or likely loss of RNFL:

RNFL Thickness Map Progression (best for focal change)

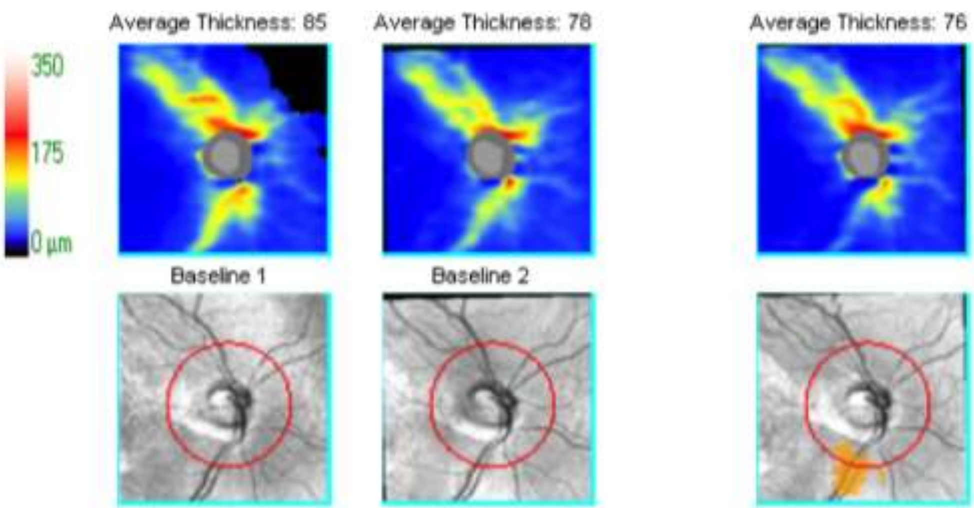
RNFL Thickness Profiles Progression (best for broader focal change)

Average RNFL Thickness Progression (best for diffuse change)

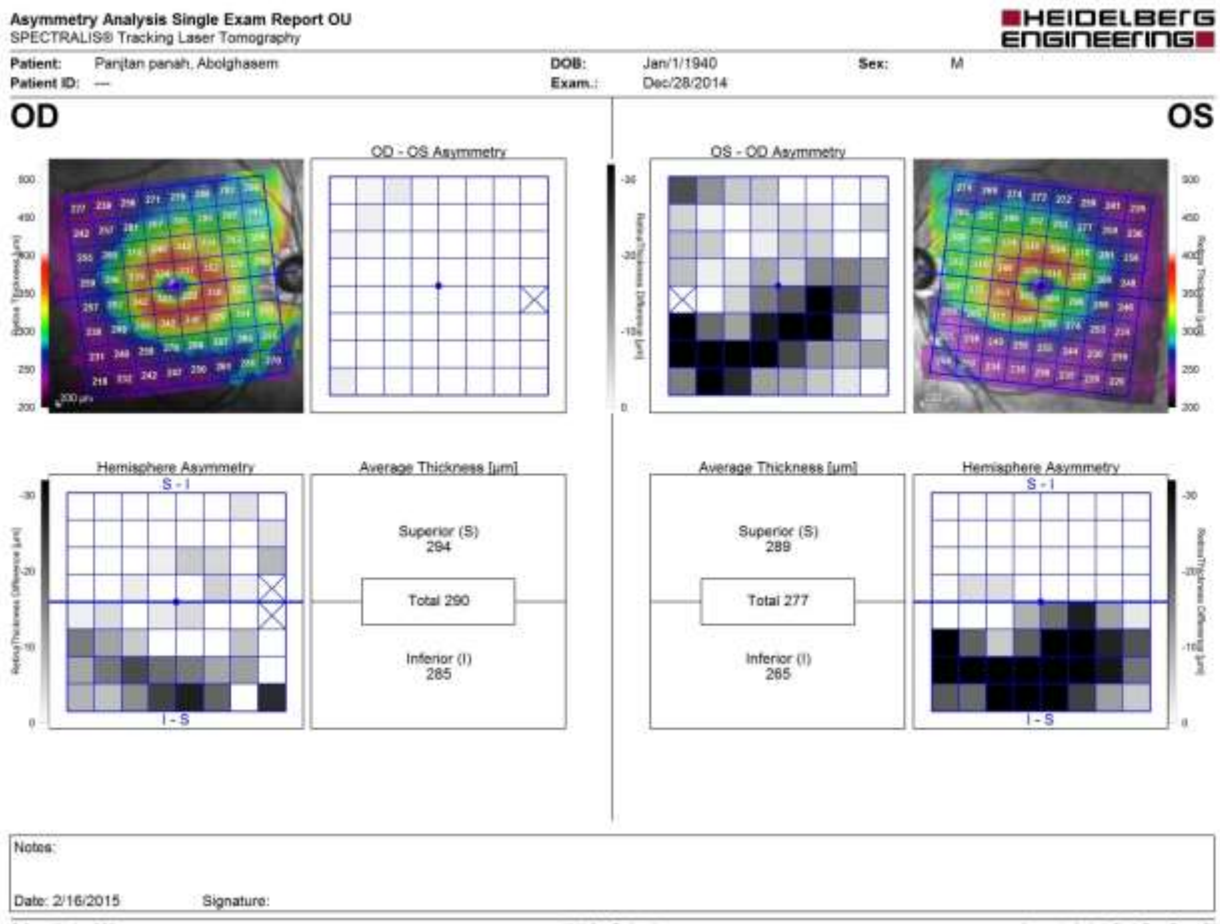
Progressive RNFL Thinning

- Progressive RNFL thinning measured on SD-OCT can often be used to detect progressive disease.
- The top three RNFL progression patterns are: widening of an existing RNFL defect, deepening without widening of an existing RNFL defect, or development of a new RNFL defect.
- The inferotemporal quadrant is the most frequent location for RNFL progression.

Progressive RNFL Thinning



Asymmetry analysis(P Pole)



Correlation of OCT with visual field and clinical findings

- Due to the variability or possible artifacts with SD-OCT measurements, all changes on OCT should be correlated with visual field changes and clinical findings before confirming definite progression.
- When such correspondence is not found, caution should be exercised and sources of erroneous measurements should be sought.

Floor Effect

- In early to moderate glaucoma, progressive thinning of RNFL thickness measured by SD-OCT is a very useful tool to judge progression of disease.
- At advanced stages, RNFL thickness levels off, rarely falling below 50 µm and almost never below 40 µm due to the assumed presence of residual glial or nonneural tissue including blood vessels (floor effect).
- At this level of disease, serial visual fields are more useful to judge progression.

Sources of Misinterpretation:

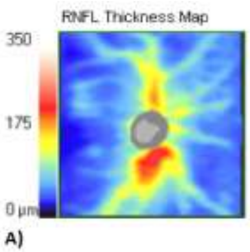
- **Normative Database**
- **Signal Quality**
- **Blink/Saccades**
- **Segmentation Errors**
- **Media Opacities**

Sources of Misinterpretation: Normative Database

- SD-OCT measurements are compared against an age-matched normative database.
- The normative database for the Cirrus SD-OCT consisted on 284 healthy individuals with an age range between 18 and 84 years (mean of 46.5 years).
- Ethnically, 43% were Caucasian, 24% were Asians, 18% were African American, 12% were Hispanic, 1% were Indian, and 6% were of mixed ethnicity.
- The refractive error ranged from -12.00 D to +8.00 D.
- Due to this relatively small normative database and wide variation of distribution of RNFL, many results obtained by SD-OCT may be flagged as abnormal statistically in patients who are not represented in the database and thus not necessarily representing real disease.
- Clinicians should use caution to avoid overtreating “red disease” in these situations.

OCT in high myopic eyes

- High myopes were not included in the Cirrus normative database.
- Myopic eyes have thinner RNFL measurements, which can confound comparisons to the normative database.
- Myopic eyes can have unique distributions of RNFL bundles.
- With increasing myopia, the superotemporal and inferotemporal RNFL bundles tend to converge temporally.This may result in the temporal shift of the superior and inferior RNFL bundle peaks of normal magnitude. Due to this shift, although the peaks are of normal magnitude, they can be interpreted as thinned due to having a different distribution from the normative database.
- Even in normal eyes, split RNFL bundles, both superiorly and inferiorly, have been found on histologic section, thus representing a true normal variant which may appear abnormal on SD-OCT.



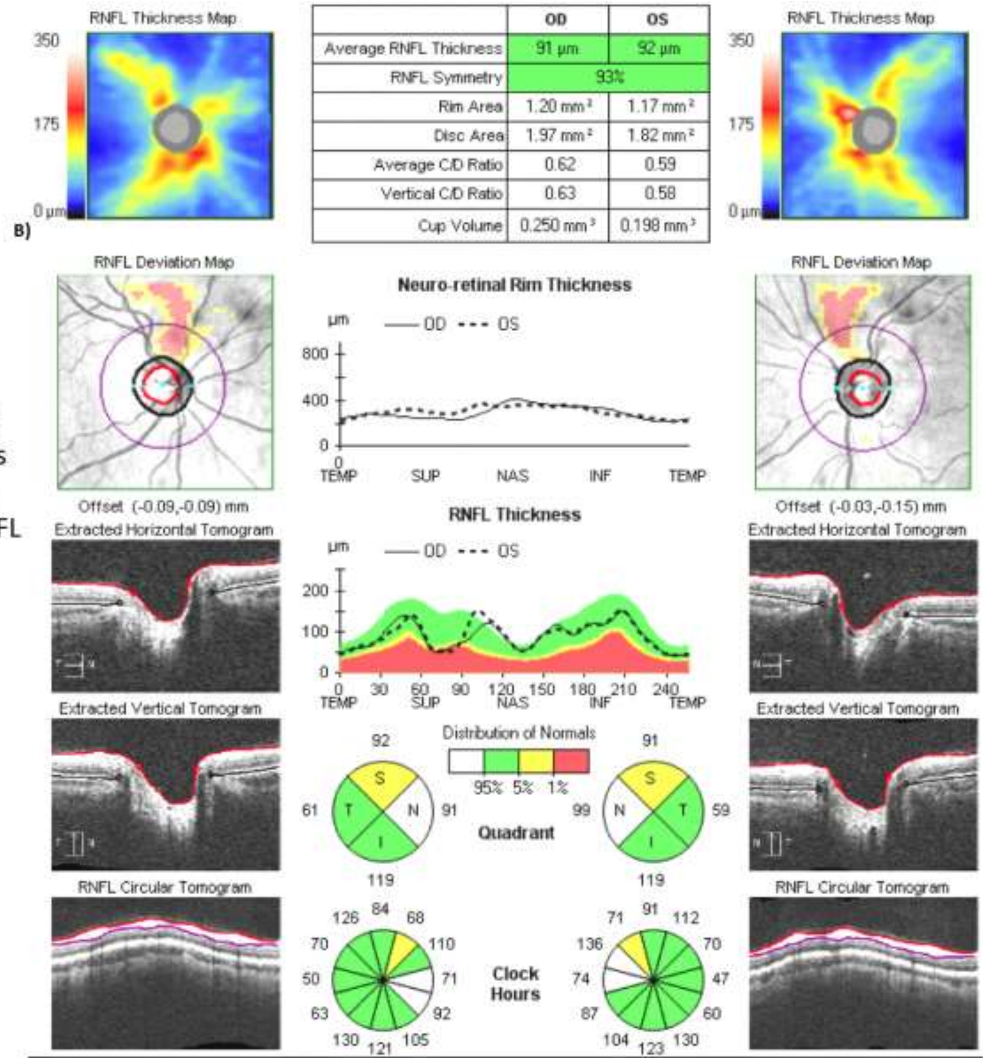
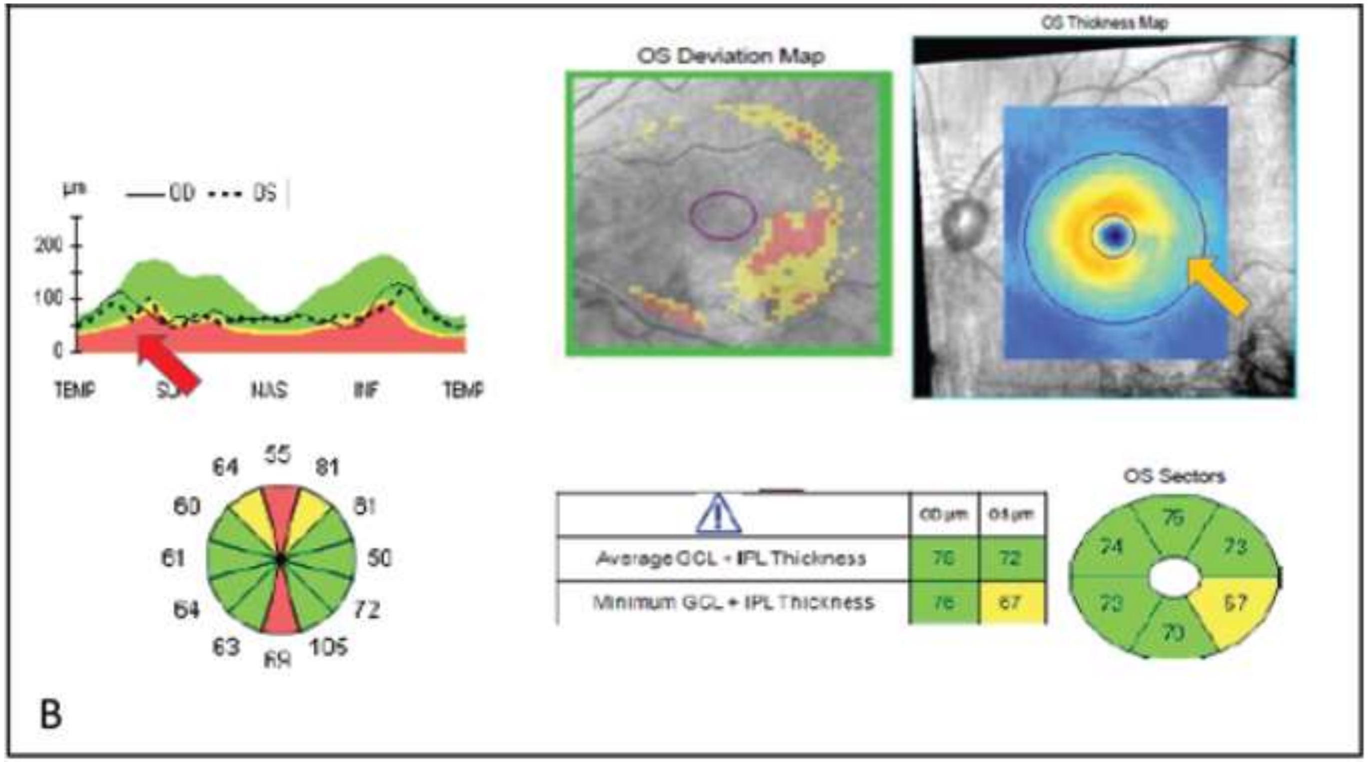


Figure 7:
(a) Normal classic superior and inferior RNFL bundles (b) Split superior RNFL bundles falsely interpreted as apparent superior RNFL thinning.


µm
OD
OS
200
100
0
TEMP
NAS
INF
TEMP
64
55
81
60
81
61
50
64
72
63
105
OS Deviation Map
OS Thickness Map
OD µm
OS µm
Average GCL + IPL Thickness
76
72
Minimum GCL + IPL Thickness
76
67
OS Sectors
76
74
73
73
67
70
B

- While the limitations of the normative database may hinder the utility of SD-OCT in diagnosing glaucoma using a single scan, serial SD-OCT scans can be very useful to judge glaucomatous progression by setting a baseline scan against which to judge progressive thinning on subsequent scans.
- Therefore, each patient can be his or her own “normative database” to diagnose glaucoma in such difficult settings as high myopia

- Clinician should be aware that RNFL thickness decreases with age in normal, healthy individuals.
- Based on a longitudinal study, the age-related rate of reduction in RNFL thickness has been estimated to be -0.52 µm/year, -1.35 µm/year, and -1.25 µm/year for average, superior, and inferior RNFL respectively

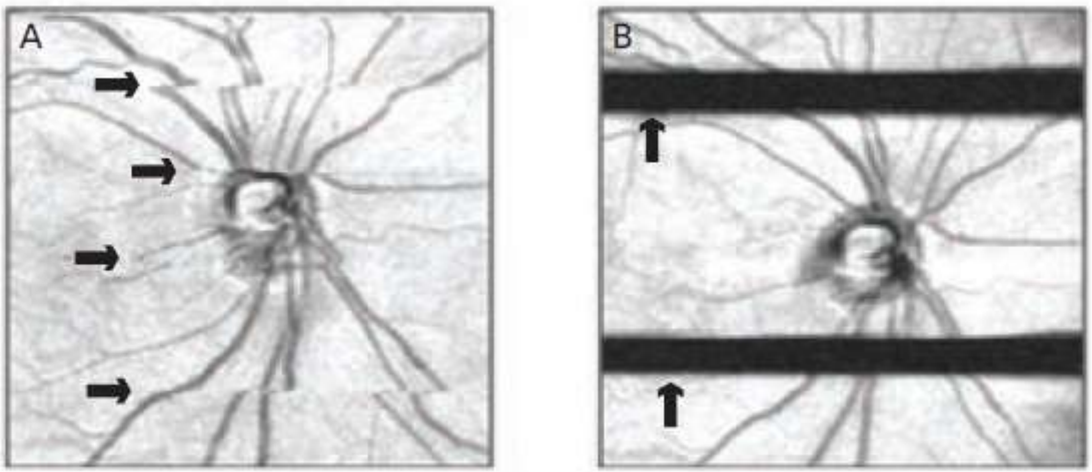
Sources of Misinterpretation: Signal Quality

- The signal strength, reported on a scale of 0 to 10, is defined as the averaged intensity value of the signal pixels in the OCT image.
- The best quality scans have SS> 8 (minimum acceptable scan > 6).
- In one study, artificially defocusing an image scan by +2 diopters resulted in an artifactual 10 µm thinning of the RNFL.
- Similarly, a 9.3% increase in mean average RNFL thickness was seen after cataract surgery in a study of 45 patients.

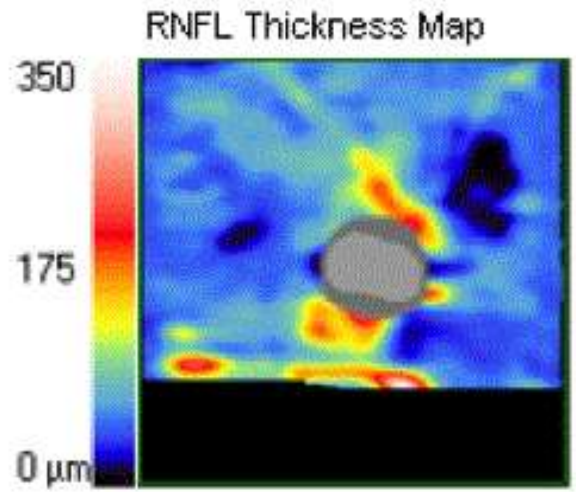
Sources of Misinterpretation: Blink/Saccades

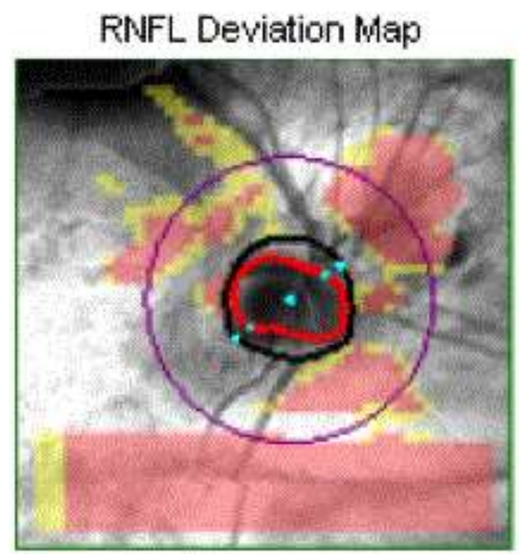
- An SD-OCT RNFL scan consists of multiple single A-scans side by side to represent a B-scan cube.
- With eye movement or blinking, these scans do not align correctly which can lead to an erroneous RNFL thickness measurement, which may be misinterpreted as progressive thinning.
- The new SD-OCT versions have a built-in eye tracking function which can help compensate for eye movement by relying on blood vessel registration or iris tracking.
- Using the eye tracker significantly improves the reproducibility of RNFL measurements

Sources of Misinterpretation: Blink/Saccades



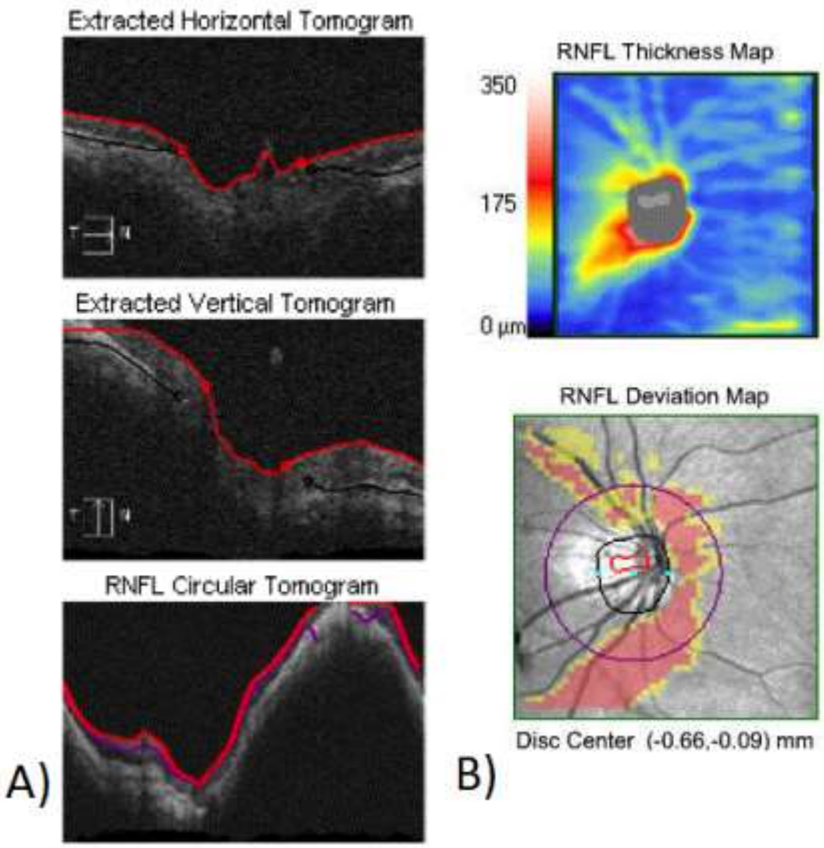
Discontinuities due to: eye movement during the scan (A); blinking (B).





Sources of Misinterpretation: Segmentation Errors

- It is important to look at the segmentation lines produced by any SD-OCT machine's software algorithm to ensure that they are appropriately placed.
- Lines should not come together (go to zero).
- Occasionally, one will find that the segmentation lines are misplaced along the retina leading to errors in the calculation of RNFL thickness .
- The segmentation errors are more common in the presence of poor signal strength, tilted discs, staphylomas, large peripapillary atrophy, epiretinal membranes, and posterior vitreous detachments.
- Studies have found a decreased incidence of such segmentation errors in SD-OCT compared to TD-OCT.



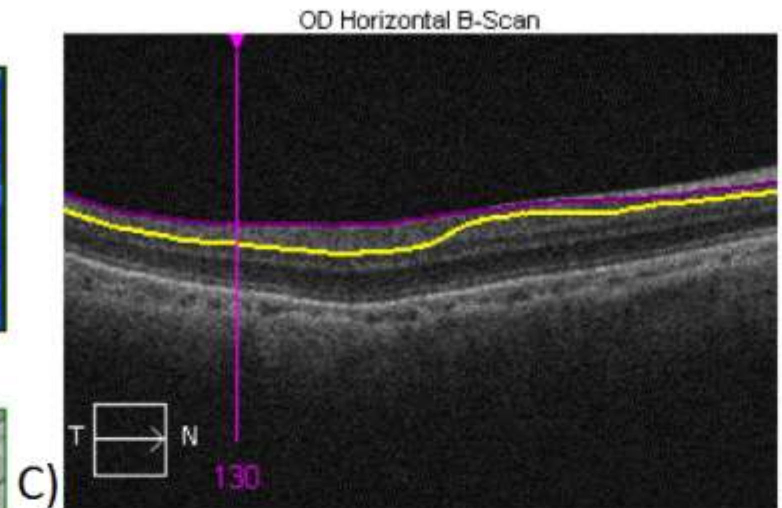


Figure 9: Examples of segmentation errors (a) in RNFL thickness map (b) in ONH borders and (c) in GCC layers

Sources of Misinterpretation: Media Opacities

- The en face scanning laser ophthalmoscope (SLO) image should be examined to ensure the absence of a media opacity, such as a PVD, within the circumpapipillary scan area.
- Areas in which data is missing due to an opacity are represented in black on the en face SLO image .In such a case, the overlying PVD can lead to a falsely thin RNFL measurement in the underlying area.
- Cataracts can affect RNFL thickness measurements. One study found a 4.8 µm increase in RNFL thickness measurement after cataract surgery.
- This effect was most pronounced in cortical cataracts, followed by posterior subcapsular cataracts. Interestingly, nuclear cataracts were not found to affect signal strength or RNFL thickness measurements.

Red & Green Disease

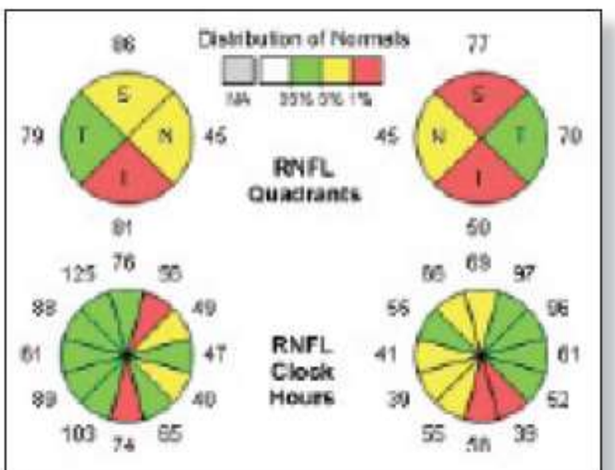
1

	OD	OS
Average RNFL Thickness	73µm	61 µm
RNFL Symmetry	55%	
Rim Area	1.12 mm²	0.70 mm²
Disc Area	1.58 mm²	1.68 mm²
Average C/D Ratio	0.53	0.75
Vertical C/D Ratio	0.49	0.75
Cup Volume	0.036 mm³	0.201 mm³

RNFL Quadrant and Clock Hour

2

3



The values below are based on a 69-year old patient.

1

Parameter	Normal Range*
Average RNFL Thickness	75.0 - 107.2
RNFL Symmetry	76% - 95%
Rim Area	1.015 - 1.615
Average C/D Ratio	0.618 - 0.169
Vertical C/D Ratio	0.594 - 0.165
Cup Volume	0.288 - 0.004

2

Parameter	Normal Range*
Temporal Quadrant	45.1 - 82.2
Superior Quadrant	88.9 - 136.7
Nasal Quadrant	50.0 - 86.2
Inferior Quadrant	89.4 - 138.3

3

Clock Hour	Normal Range*
9	36.4 - 67.4
10	52.7 - 100.5
11	87.2 - 154.6
12	70.7 - 155.7
1	72.6 - 133.9
2	52.4 - 109.7
3	41.7 - 70.4
4	44.8 - 89.0
5	61.9 - 125
6	85.7 - 163.2
7	84.8 - 159.4
8	42.2 - 90.2

Thank you for your attention