OCT in the Diagnosis and Follow-up of Glaucoma

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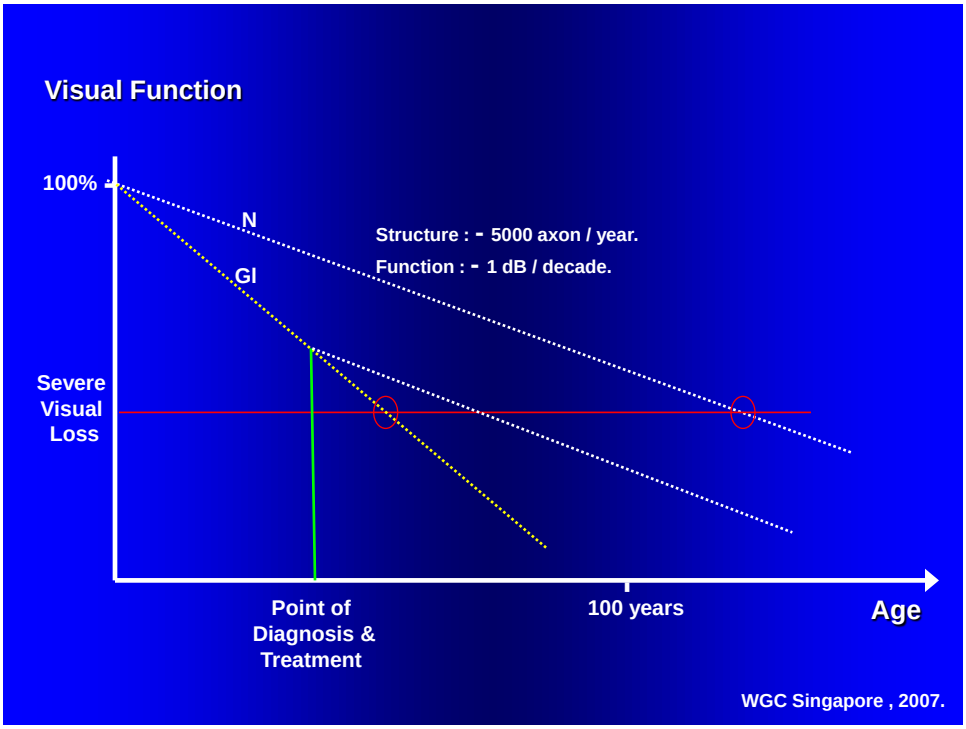
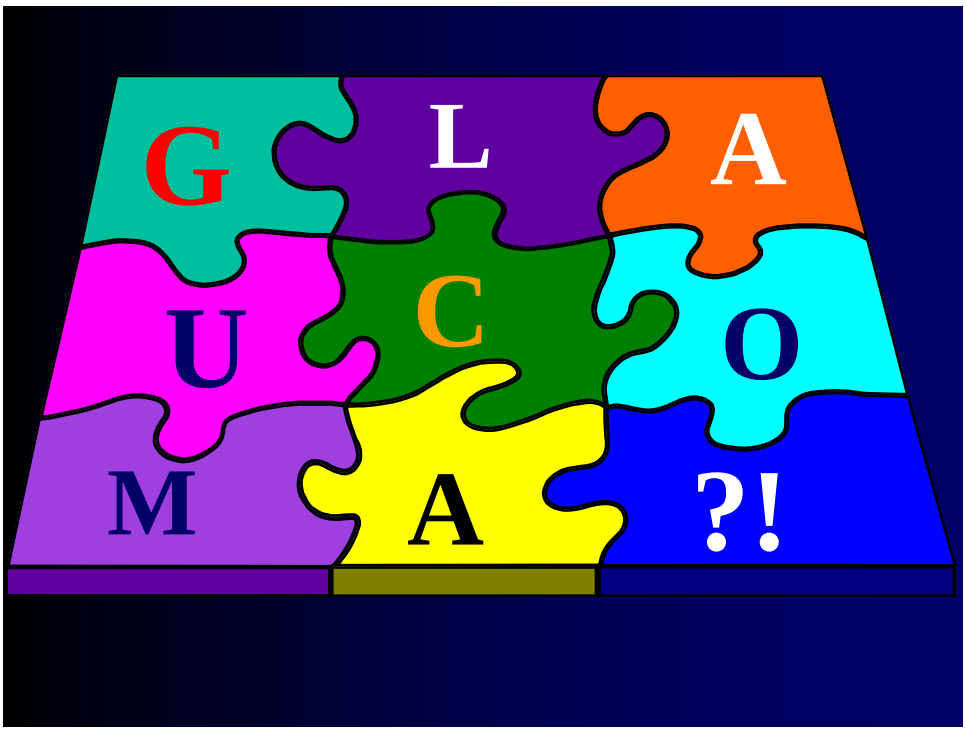
Cairo University


Visual Function
100%
N
GI
Structure : - 5000 axon / year.
Function : - 1 dB / decade.
Severe Visual Loss
Point of Diagnosis & Treatment
100 years
Age
WGC Singapore , 2007.


G
L
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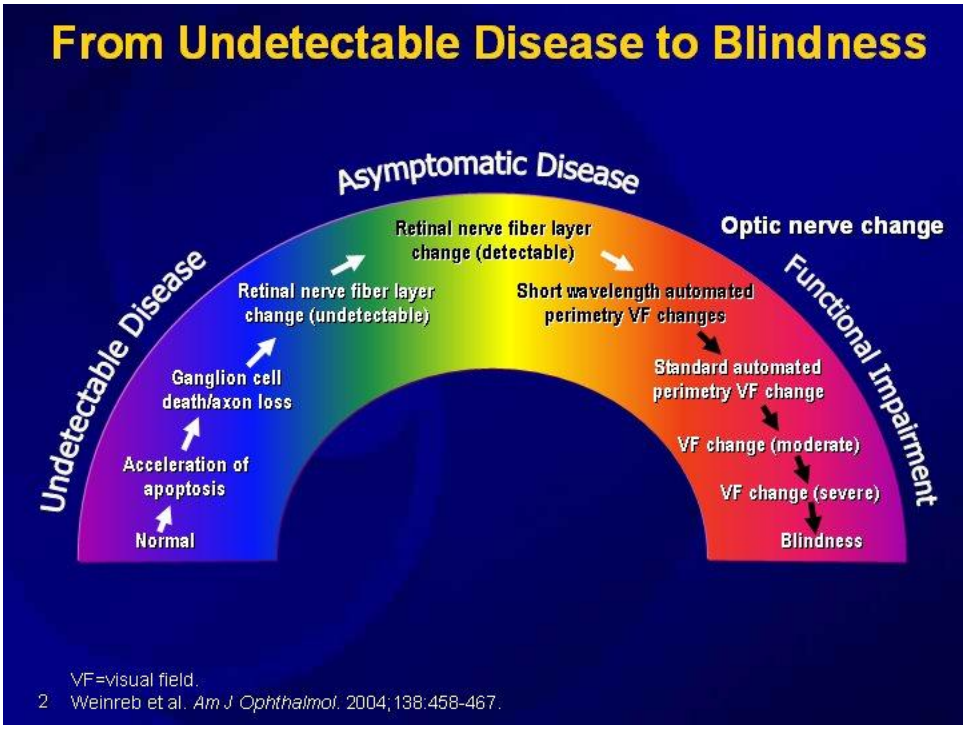
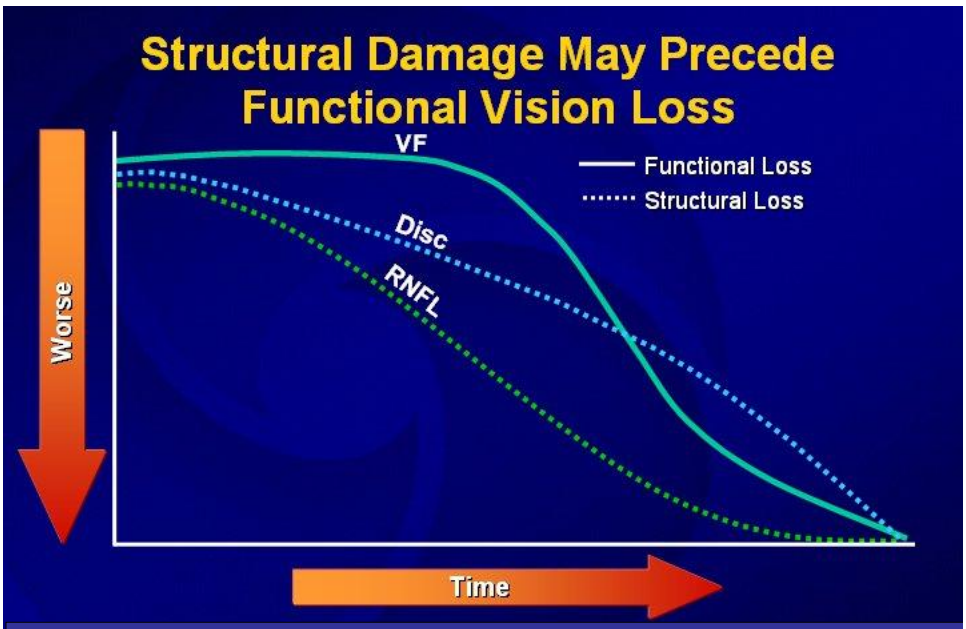
?!


From Undetectable Disease to Blindness
Asymptomatic Disease
Undetectable Disease
Functional Impairment
Optic nerve change
Retinal nerve fiber layer change (detectable)
Retinal nerve fiber layer change (undetectable)
Short wavelength automated perimetry VF changes
Ganglion cell death/axon loss
Standard automated perimetry VF change
Acceleration of apoptosis
VF change (moderate)
VF change (severe)
Normal
Blindness
VF=visual field.
2 Weinreb et al. Am J Ophthalmol. 2004;138:458-467.


Structural Damage May Precede Functional Vision Loss
VF
Functional Loss
Structural Loss
Disc
RNFL
Worse
Time
Glaucoma Progression is *Individual* and *variable*

- Glaucoma suspect.
- Glaucoma workup. → Damage at presentation
- Initiate therapy.
- Follow-up. → Rate of progression.; Progressive change of optic disc or visual field is the hallmark of glaucoma diagnosis.
- Modify/Change treatment.

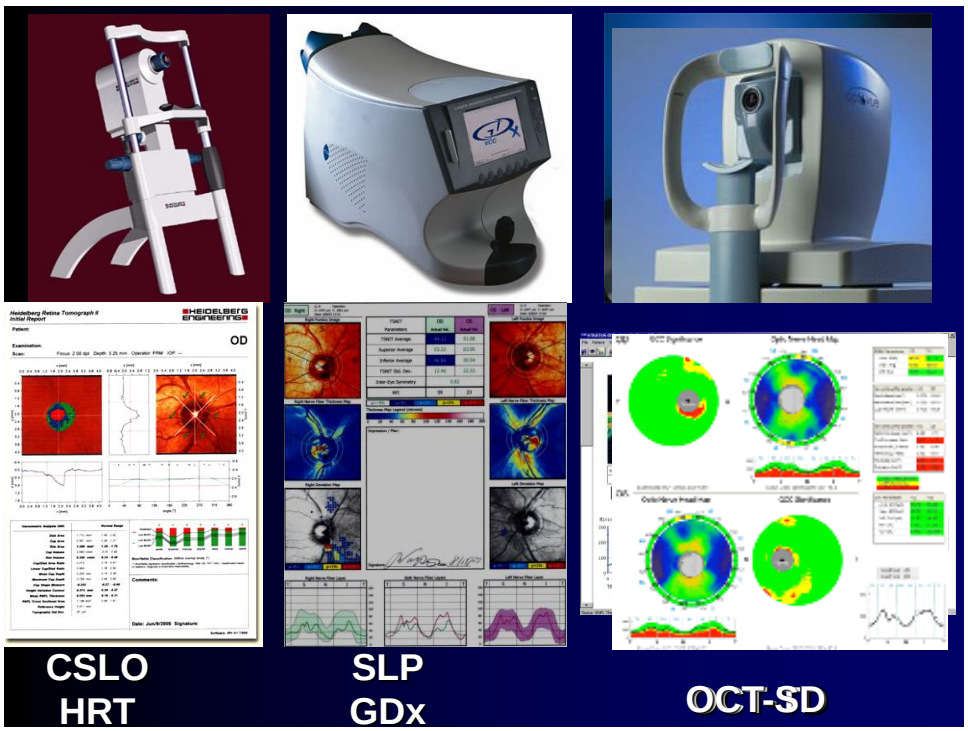
"The decision to initiate anti-glaucoma therapy is a *very serious* one that has far-reaching consequences".

Geroge Spaeth

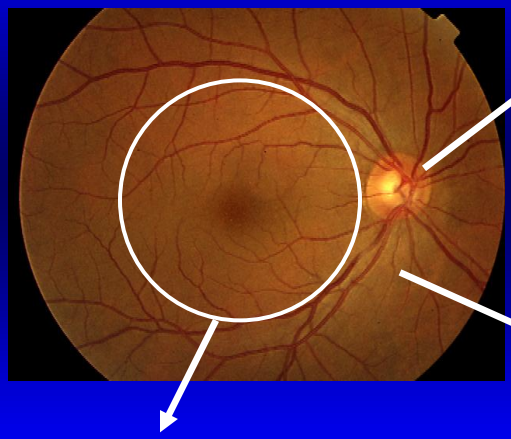
- Side effects
- Significant cost
- Altered QoL

Rationale for Quantitative Imaging in Glaucoma

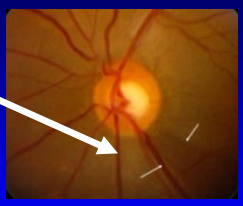
- Visual field : subjective , 3 consecutive fields are required to reliably confirm glaucoma.
- Structural loss precedes functional loss :
  6 years in 60% of eyes.
- As much as 30-50% of RNFL may be lost before Standard Automated Perimetry (SAP) VF changes.
- Change in the cup represents loss of *thousands of axons*.



Glaucoma affects *3 areas* in the posterior segment of the eye.



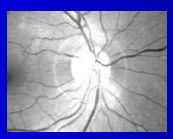
Cupping

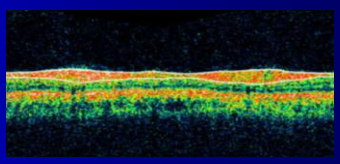


Ganglion Cell Loss

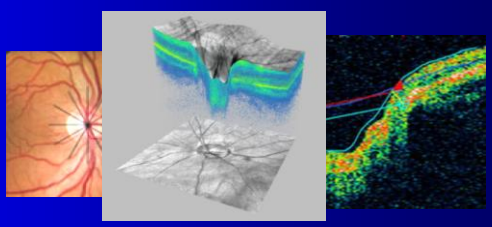
Nerve fiber thinning

Peri-papillary RNFL Thickness



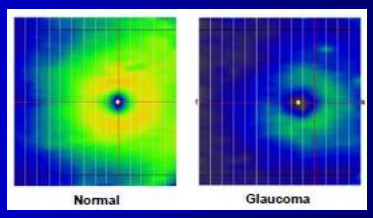


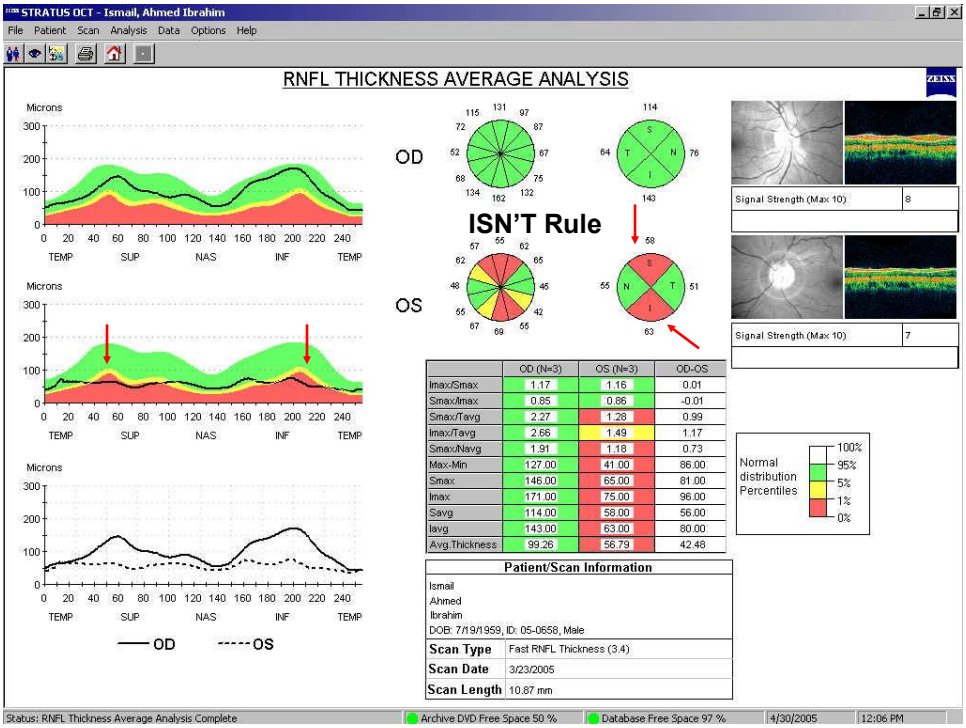
ONH Analysis

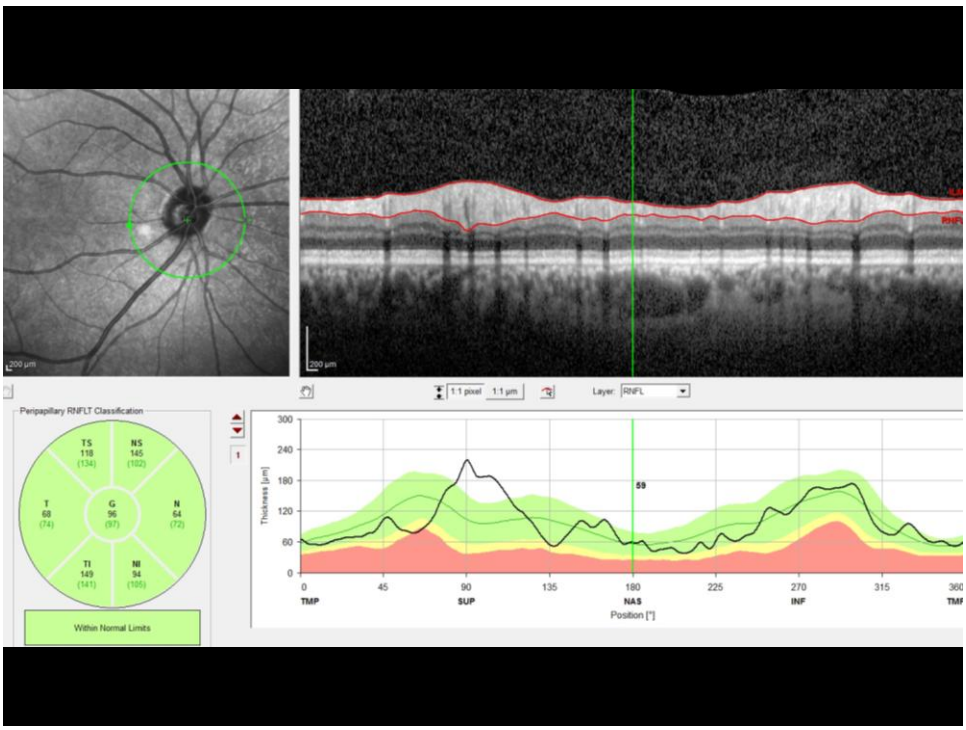


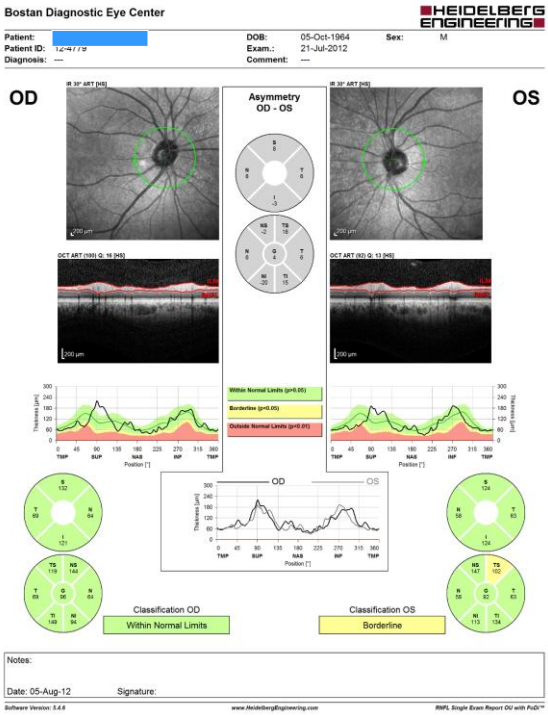
Macular GCC Measurement

SD-OCT




STRATUS OCT - Ismail, Ahmed Ibrahim
File Patient Scan Analysis Data Options Help
RNFL THICKNESS AVERAGE ANALYSIS
ZEISS
Microns
TEMP SUP NAS INF TEMP
OD
OS
ISN'T Rule
Signal Strength (Max 10) 8
Signal Strength (Max 10) 7
Normal distribution Percentiles
100%
95%
5%
1%
0%
OD (N=3) OS (N=3) OD-OS
Imax/Smax 1.17 1.16 0.01
Smax/Imax 0.85 0.86 -0.01
Smax/Tavg 2.27 1.28 0.99
Imax/Tavg 2.66 1.49 1.17
Smax/Navg 1.91 1.18 0.73
Max-Min 127.00 41.00 86.00
Smax 146.00 65.00 81.00
Imax 171.00 75.00 96.00
Savg 114.00 58.00 56.00
Iavg 143.00 63.00 80.00
Avg.Thickness 99.26 56.79 42.48
Patient/Scan Information
Ismail
Ahmed
Ibrahim
DOB: 7/19/1959, ID: 05-0658, Male
Scan Type Fast RNFL Thickness (3.4)
Scan Date 3/23/2005
Scan Length 10.87 mm
Status: RNFL Thickness Average Analysis Complete
Archive DVD Free Space 50 %
Database Free Space 97 %
4/30/2005
12:06 PM

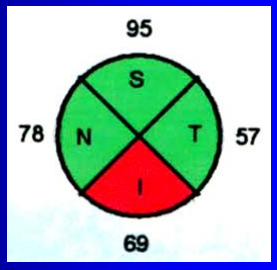

Peripapillary RNFLT Classification
Within Normal Limits
Thickness [µm]
Position [°]
TMP SUP NAS INF



"Does any RNFL loss mean Glaucoma ?

Inferior Average :

- Least affected by age-decay.
- Significantly thinner in glaucoma than in normal.
- Highest sensitivity and specificity in early glaucoma diagnosis.
- Discriminates progressors from non-progressors.

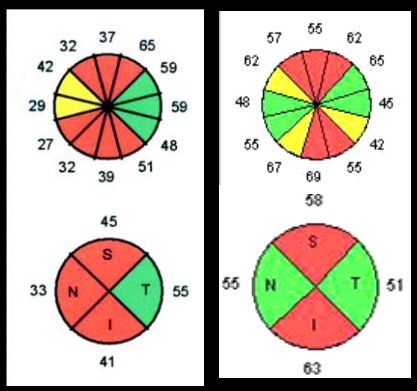


ISN'T Rule

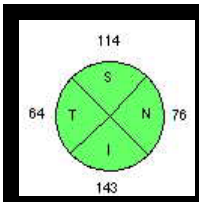
Inferior Average :

the best to discriminate healthy from glaucomatous eyes

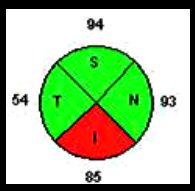
Sensitivity 84%
Specificity 90%

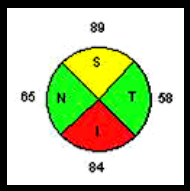


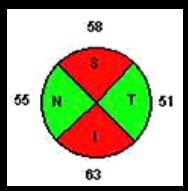
ISN'T Rule



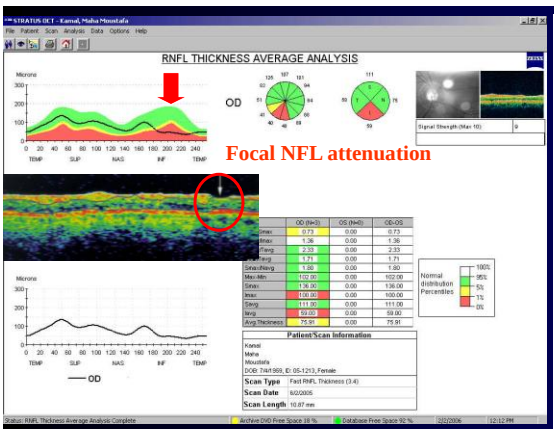
- **Established diagnosis** -- uncontrolled disease -- therapy advancement.
- **Glaucoma suspect** – confirm diagnosis.

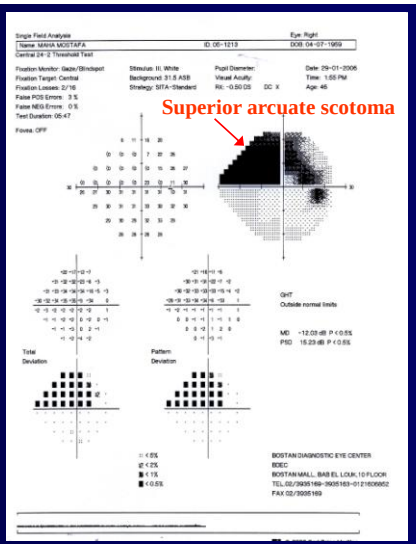






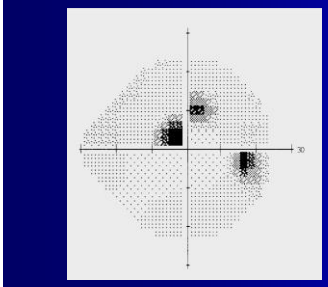
Glaucoma Progression

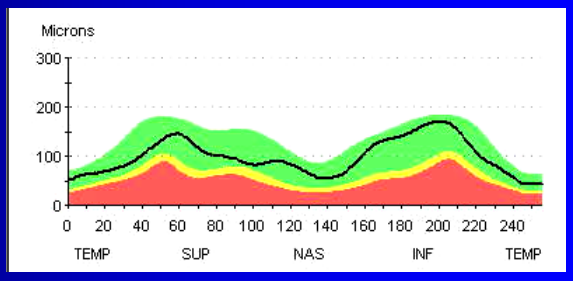


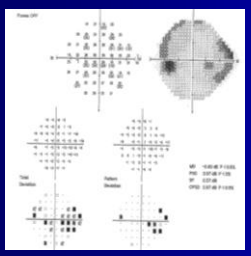


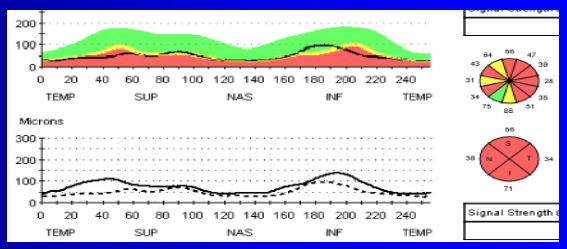
ISN'T Rule

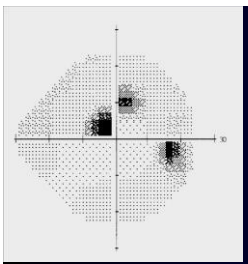
Perimetric Glaucoma



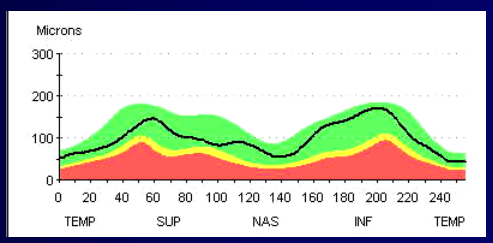






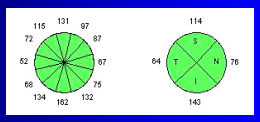


Structural Damage Precedes Functional Damage?!



Glaucoma Visual Field Loss, *NO* corresponding RNFL Defects.

- 1-clock hour is "*too wide*" for detection of localized loss.

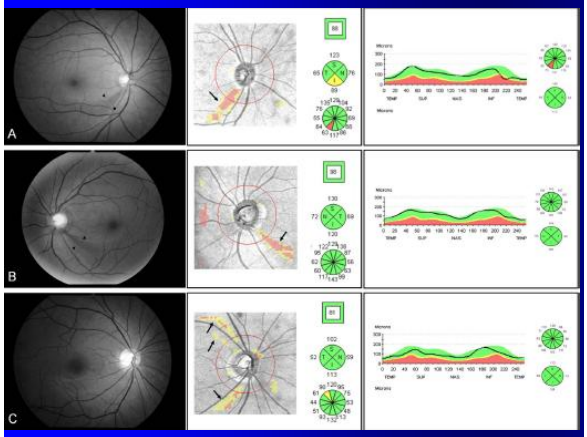


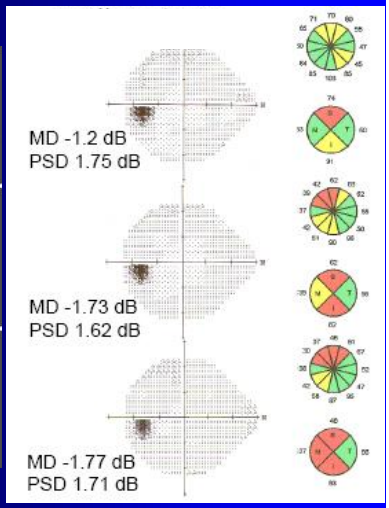
- RNFL defects "*not always*" result in reduction of RNFL thickness.
- Reduction of RNFL thickness not exceed *"normal variation".*

Glaucoma Visual Field Loss, *NO* corresponding RNFL Defects.

- Order of Glaucomatous Damage vary from patient to patient.
- Localized RNFL defects limited to deeper layers while most superficial layers being intact.
- Physiologic age-decay of the RNFL.
- Diffuse component of RNFL loss so large to mask localized defects.

Pre-perimetric Glaucoma





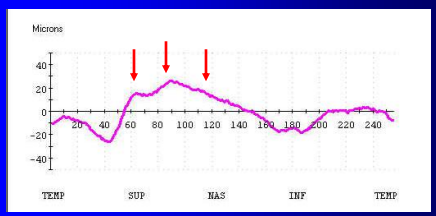
Quantitative Imaging may detect glaucoma at an earlier stage.

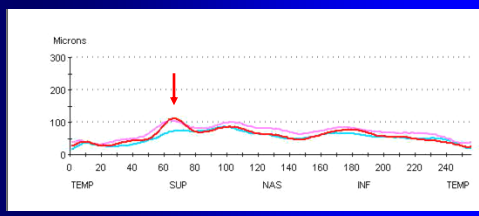
Jeoung et al , IOVS 2010.

RNFL thickness after IOP reduction

- **IOP reduction (medical or surgical) ---- *significant increase* of mean RNFL thickness .**
- **Correlated to the IOP reduction**
- **0.5 µ increase of mean NFL thickness/ mmHg decrease of IOP**
- **Least evident in inferior quadrant**

Recovery of the compressed NFL , Retinal swelling , Restoration of normal axoplasmic flow to the RNFL , Changes in the axial length of the globe.





Clinical implication : obtain new OCT measurements as a baseline for follow up after glaucoma surgery .

OCT & Early Glaucoma

Moderate Sensitivity and High Specificity

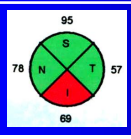
Diagnostic Test

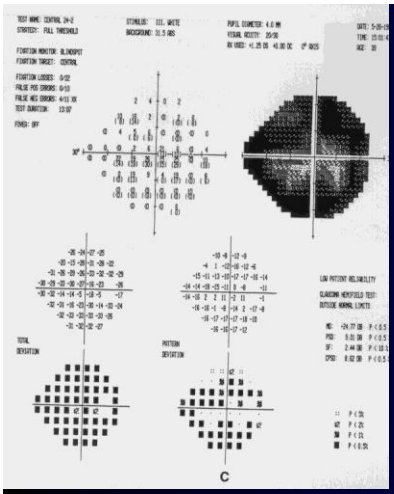
- **Highly specific** : if +ve ----- Rule ***IN*** the disease.
- **Highly sensitive** : if -ve ---- Rule ***OUT*** the disease.

OCT (esp inferior RNFL thickness) rule *IN* early glaucoma when +ve but can *not* rule *OUT* when -ve

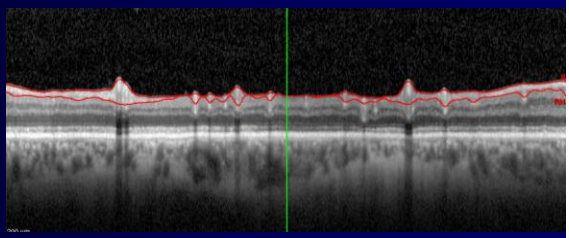
Inferior Quadrant RNFL Thickness

- ≤ 92.5 µ → 100% Glaucoma
- > 92.5 µ and ≤ 119 µ → 56% Normal, 44% Glaucoma
- > 119 µ → 88% Normal, 12% Glaucoma



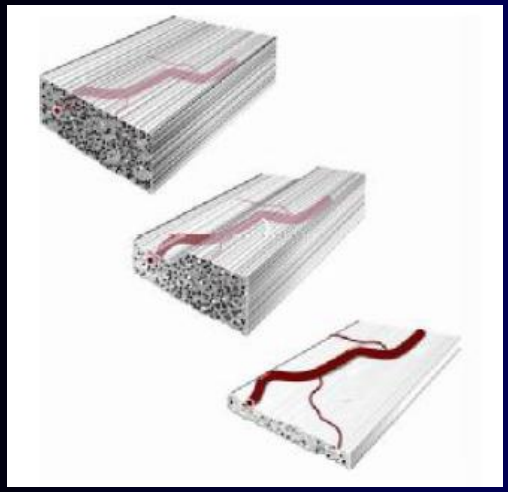


Advanced Glaucoma



OCT has little role!

Location of 2nd order blood vessels within RNFL

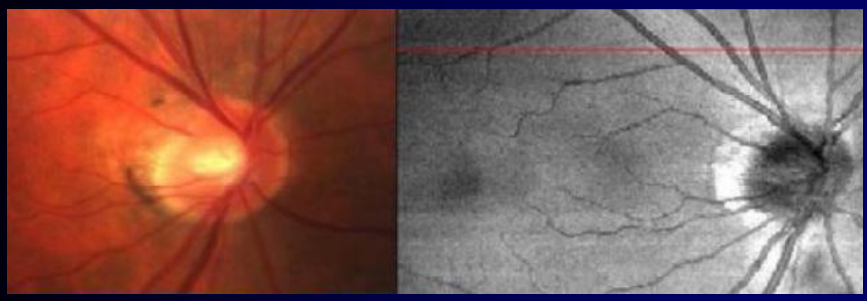


Normal

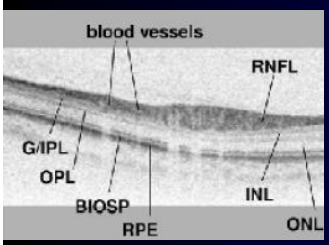
Focal RNFL loss

Diffuse RNFL loss

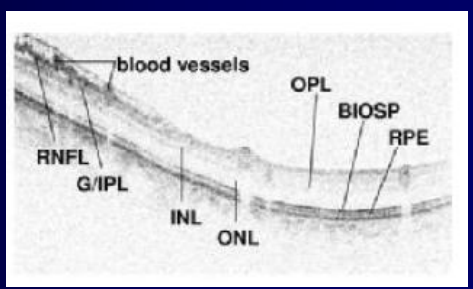
Location of 2nd order blood vessels within RNFL



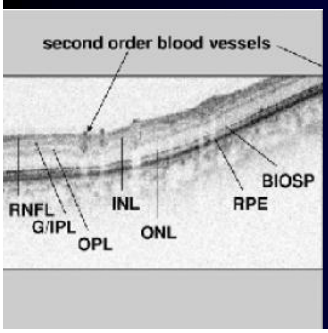
Location of 2nd order blood vessels within RNFL



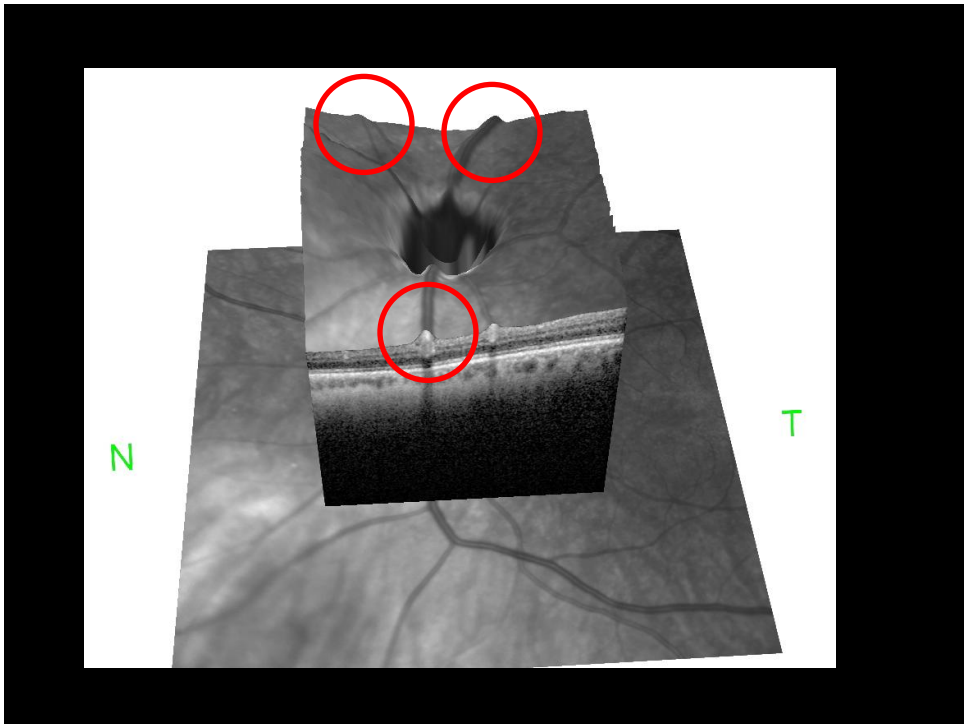
Normal

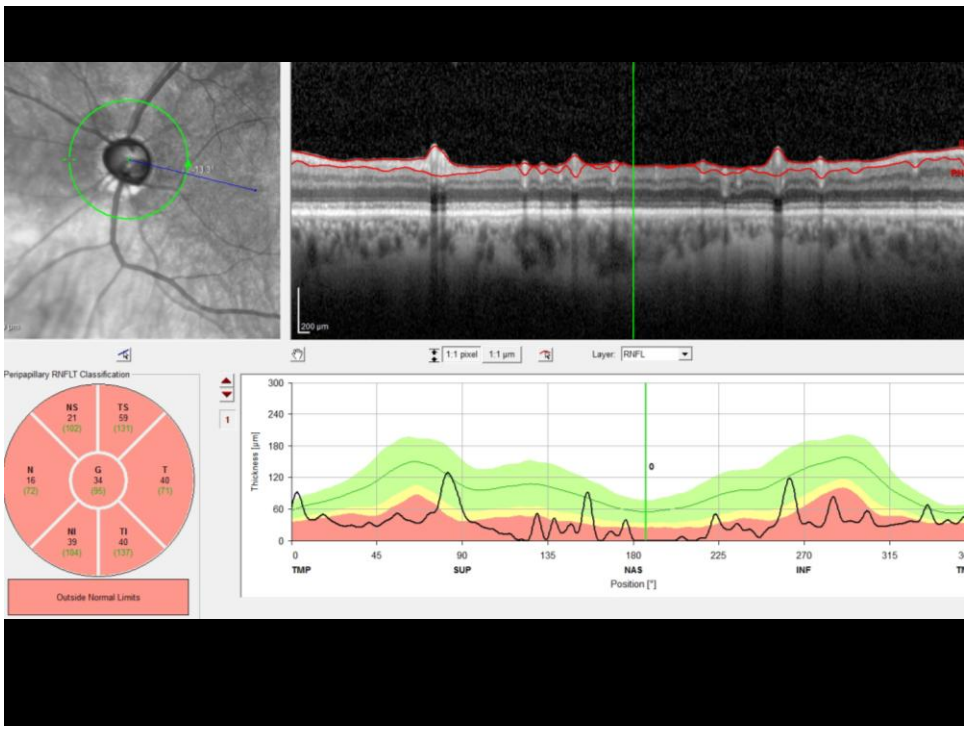


Mild RNFL loss

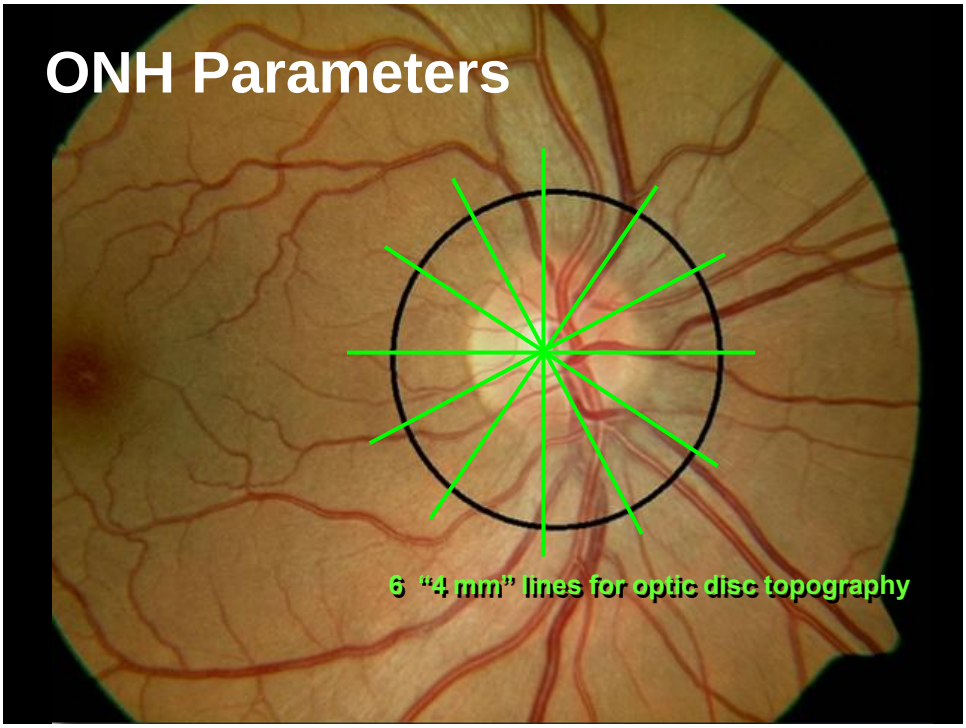


Severe RNFL loss


N
T


200 µm
1:1 pixel
1:1 µm
Layer: RNFL
Peripapillary RNFLT Classification
NS 21 (102)
TS 59 (131)
N 16 (72)
G 34 (95)
T 40 (71)
NI 39 (104)
TI 40 (137)
Outside Normal Limits
Thickness [µm]
300
240
180
120
60
0
0
45
90
135
180
225
270
315
TMP
SUP
NAS
INF
Position [°]

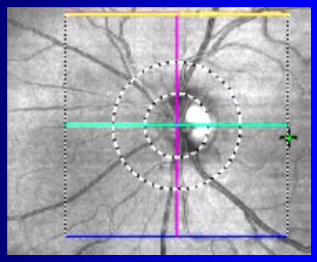
ONH Parameters



TD-OCT

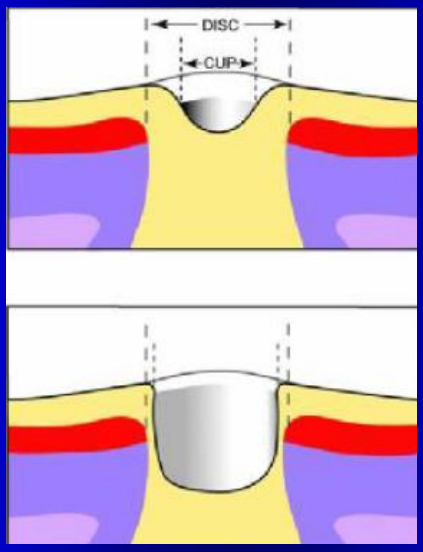
- 3.4 mm circle
- 512 A-scan
- Interpolation : localized RNFL defects can be missed.

SD-OCT



- 6 X 6 mm cube
- 512 X 128 B-scan
- Much higher number of measurements.

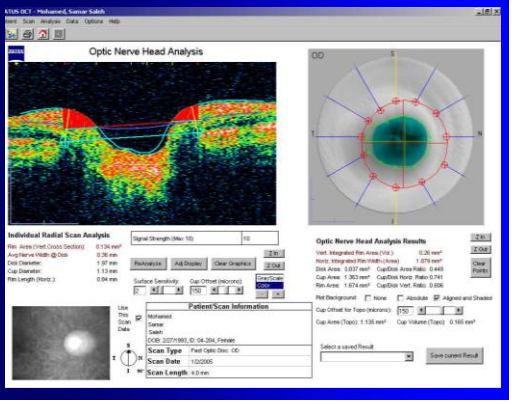
Can *not* be compared : different tech spcs, imaging protocols and thickness measurement algorisms



ONH Parameters :

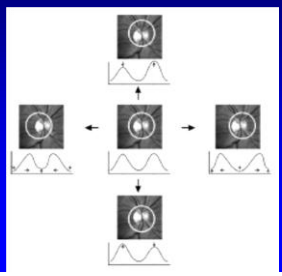
Poor sensitivity for glaucoma progression :

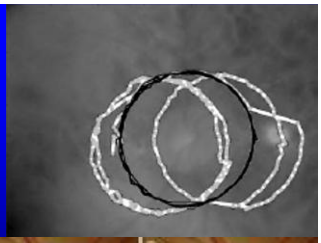
- Interpolation .
- Progressive para papillary atrophy in glaucoma.

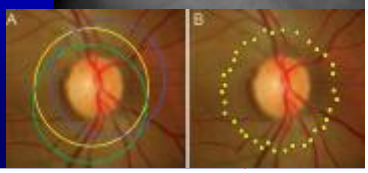


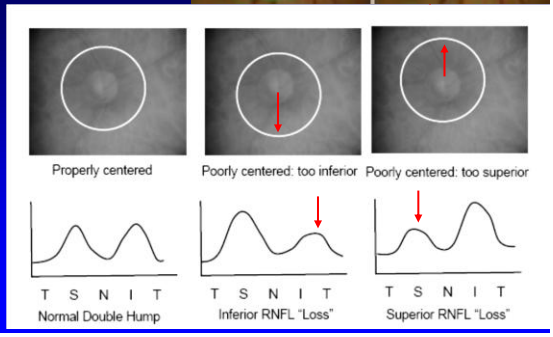
TD-OCT susceptible to eye movements – scattering of sampling locations.

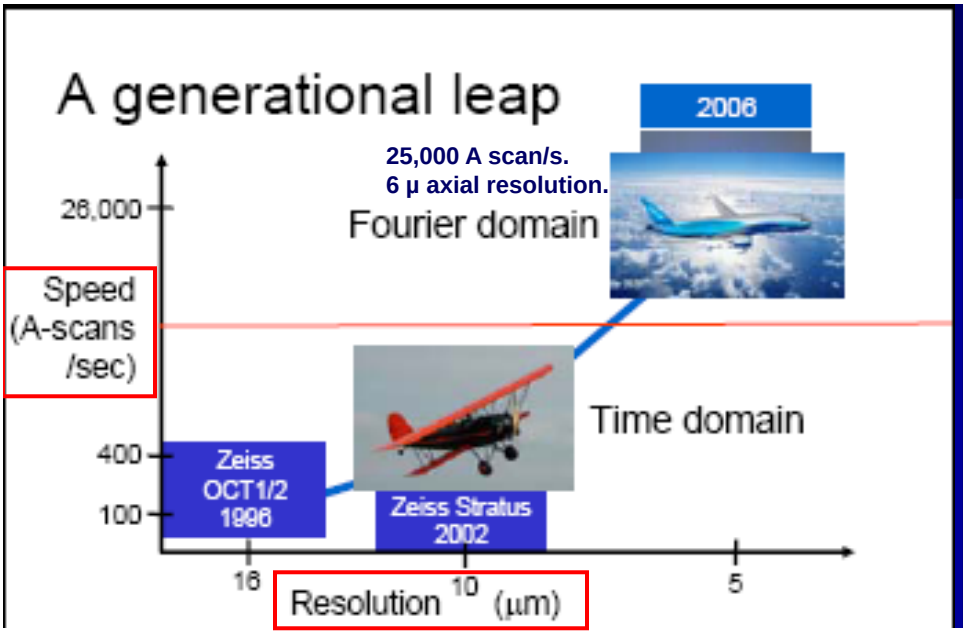
Manual placement: scan location affects results.





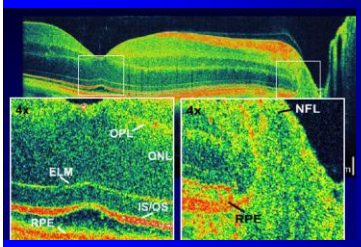




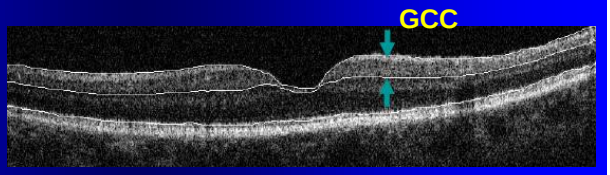


Higher acquisition speed (X100) , Higher axial resolution (X2)

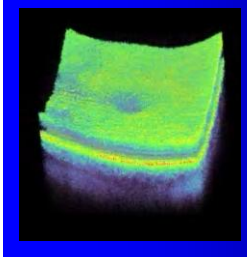
How to use speed and resolution to advantage?



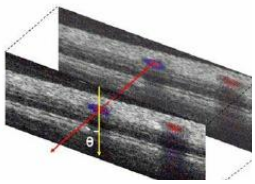
Microstructure identification



3-D Reconstruction

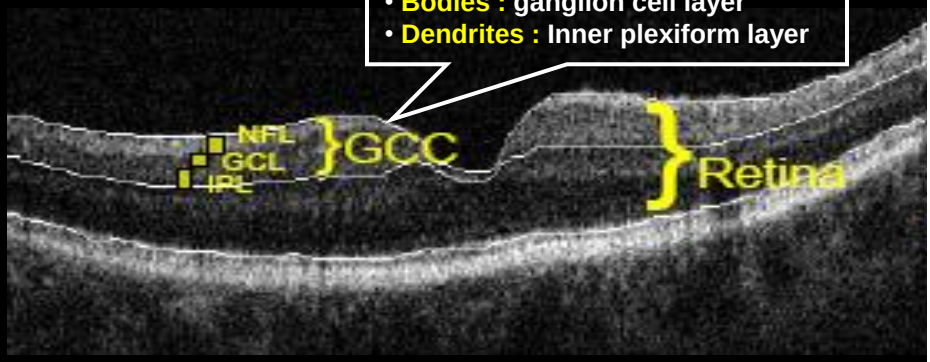


Function (Blood Flow)

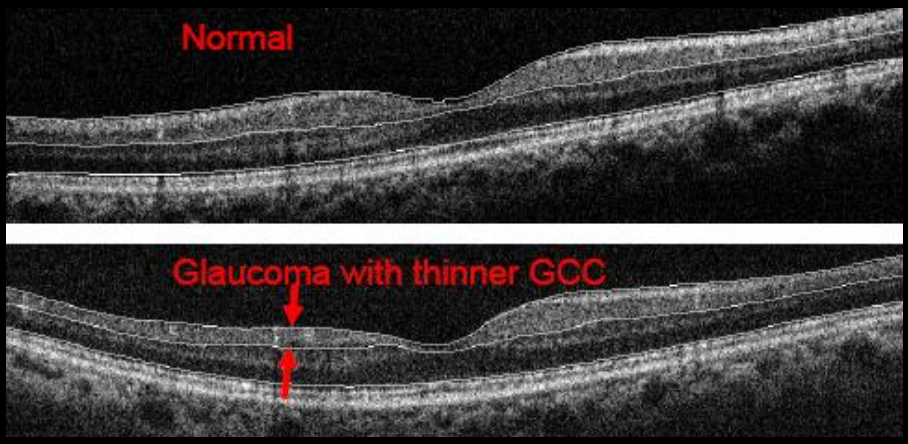


Ganglion Cell Complex (GCC)

- **Axons :** NFL
- **Bodies :** ganglion cell layer
- **Dendrites :** Inner plexiform layer



Glaucoma primarily damages the ganglion cell complex (GCC)

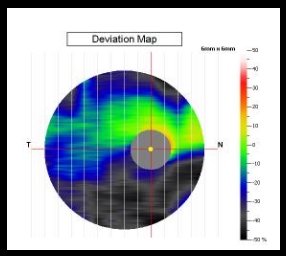


Retinal thickness mapping is not sensitive for detecting glaucoma because glaucoma preferentially affects the *inner* retinal layers (GCC).

GCC Deviation Map

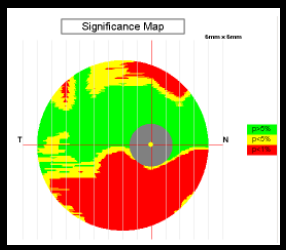
$$\% \text{ Loss} = \frac{\text{actual - normal}}{\text{normal}}$$

Blue : 20-30% loss
Black : > 50% loss

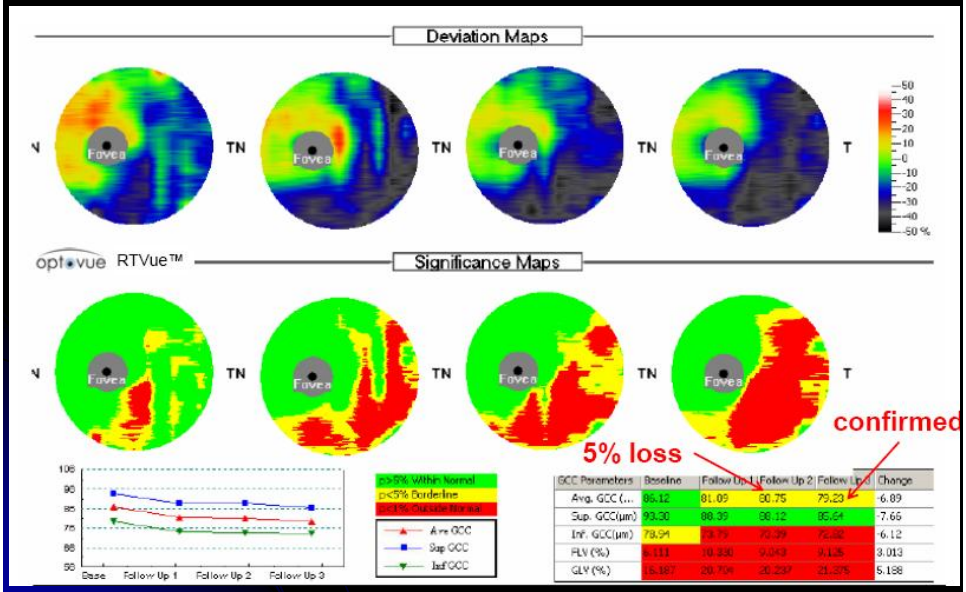


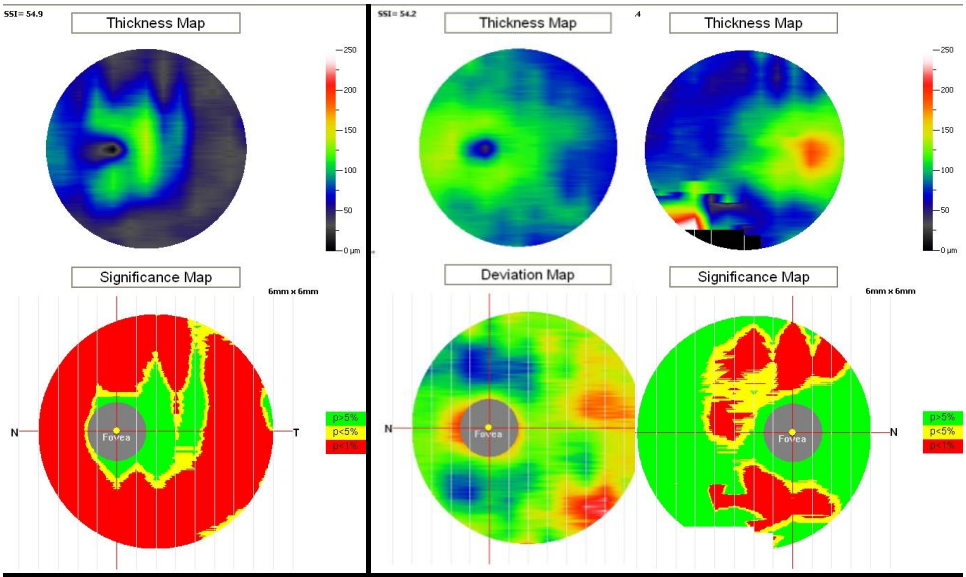
GCC Significance Map

Green : within normal limits.
Yellow : Borderline.
Red : outside normal limits.

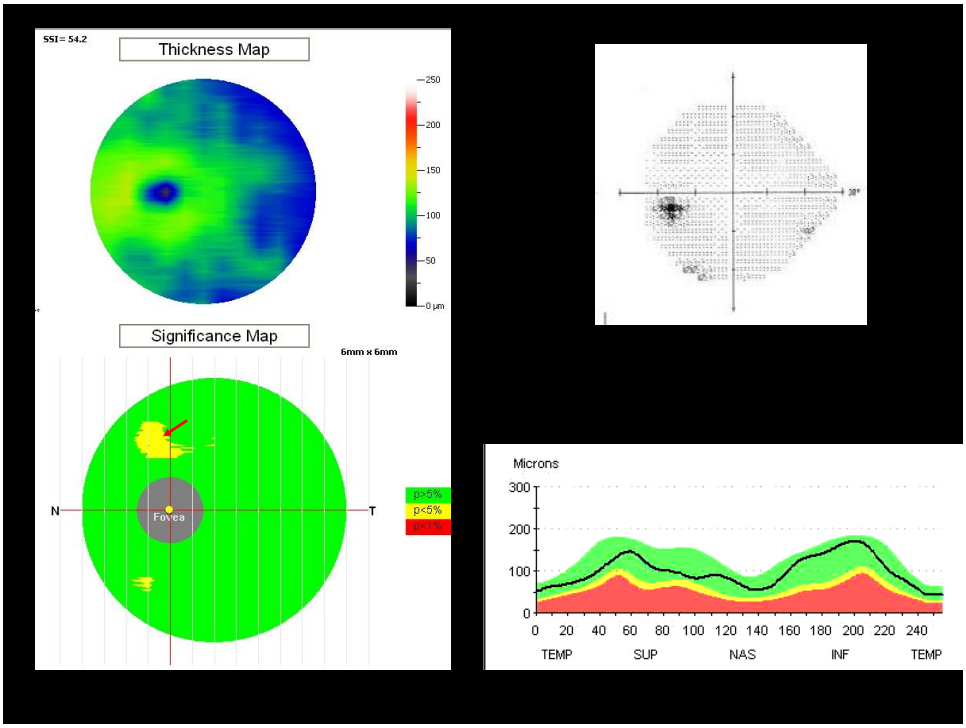


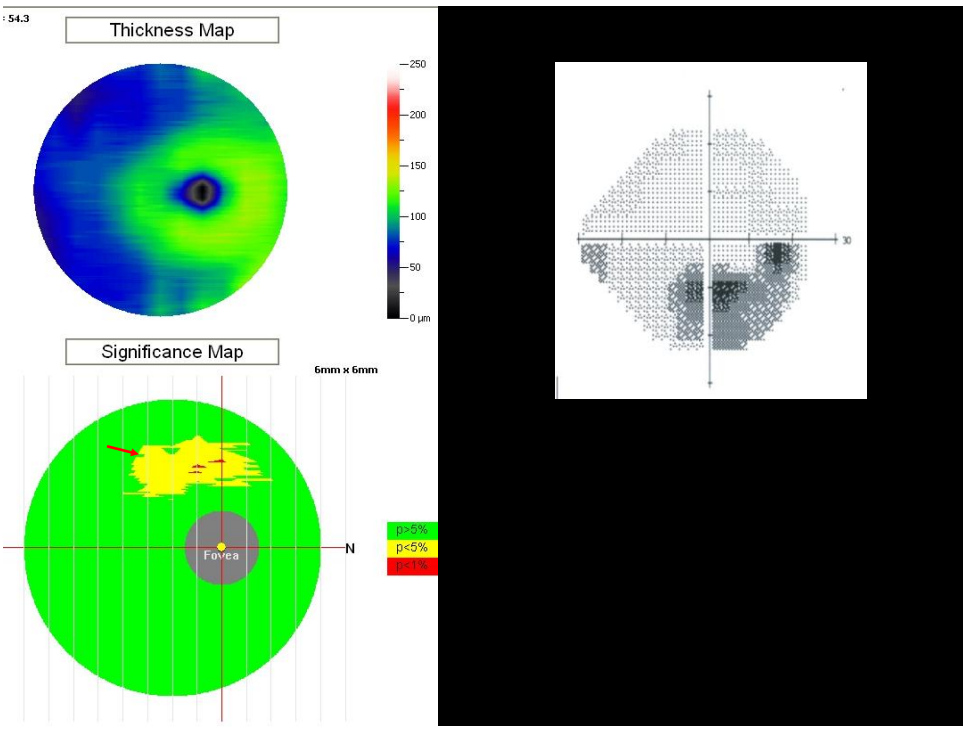
GCC Progression Analysis (visit every 6 months)

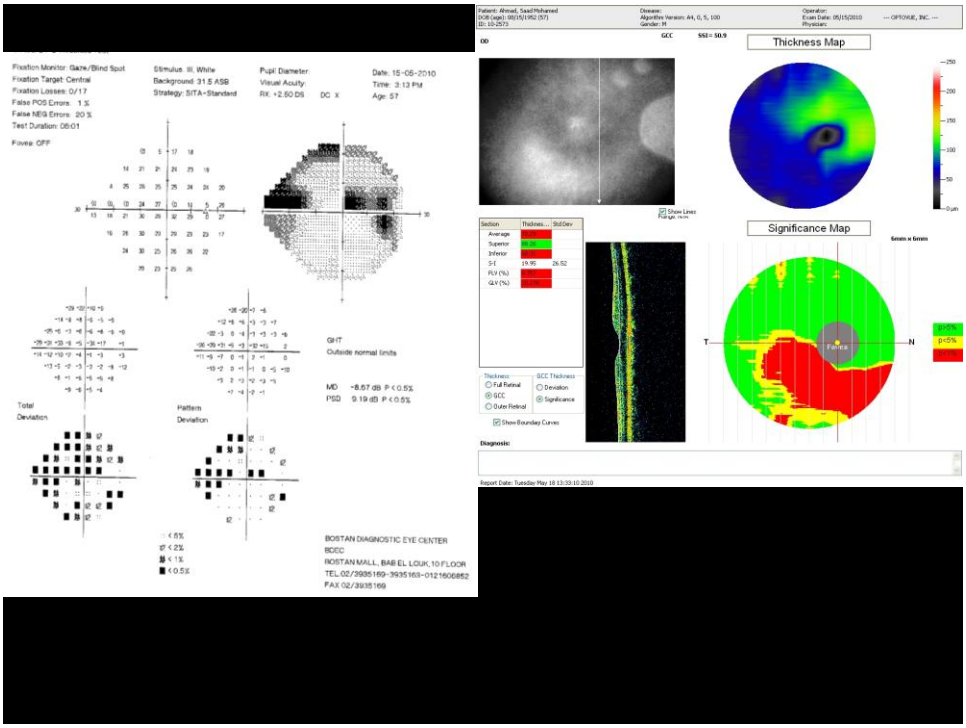


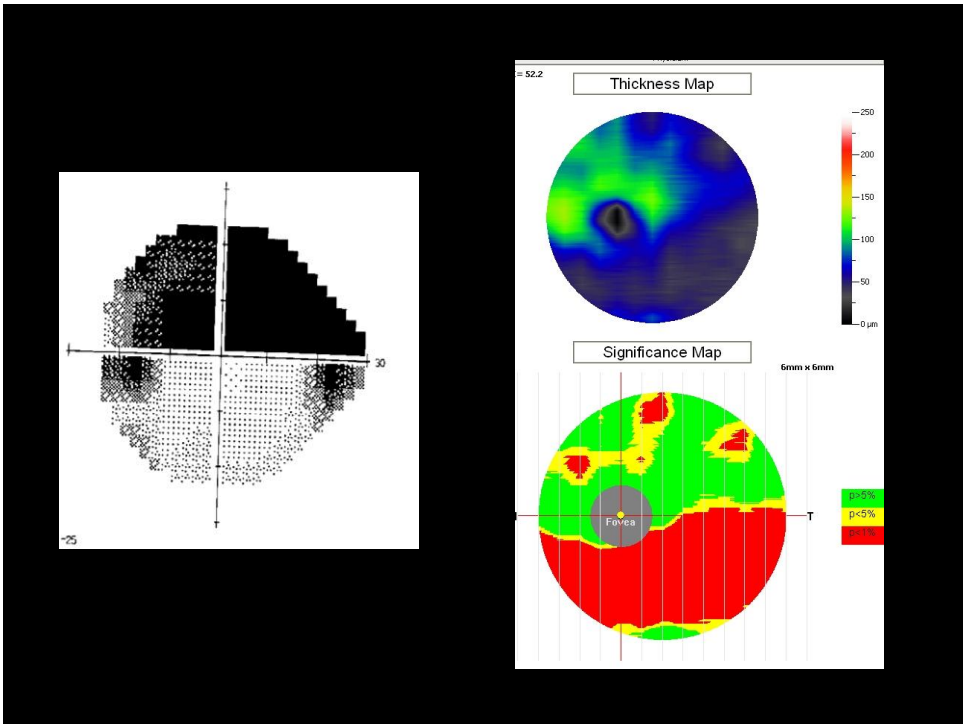


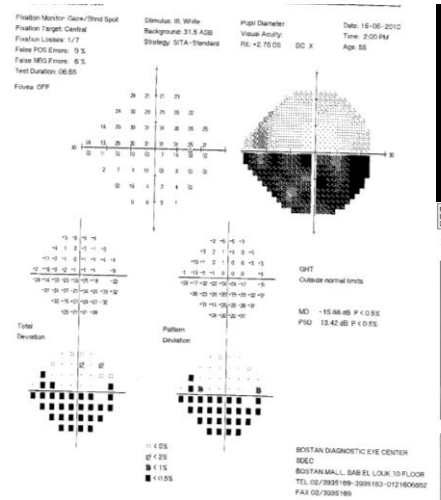
Generalized loss **Localized loss**

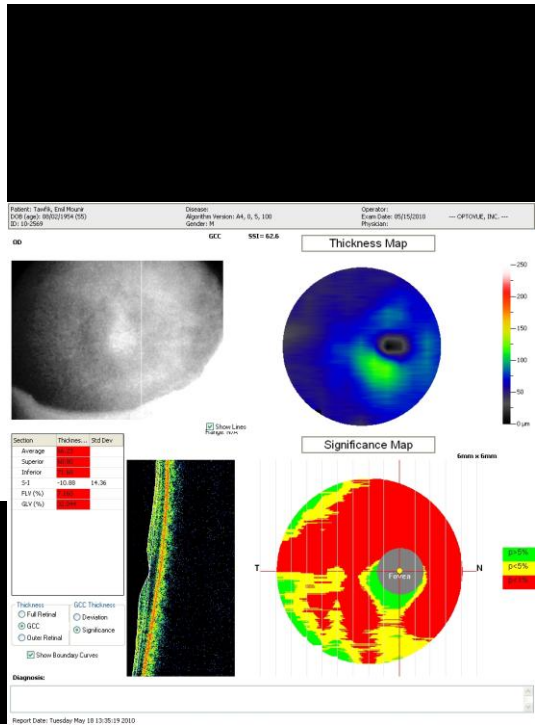

SSI= 54.2
Thickness Map
250
200
150
100
50
0 µm
Significance Map
6mm x 6mm
N
T
Fovea
p>5%
p<5%
p<1%
Microns
300
200
100
0
0 20 40 60 80 100 120 140 160 180 200 220 240
TEMP SUP NAS INF TEMP

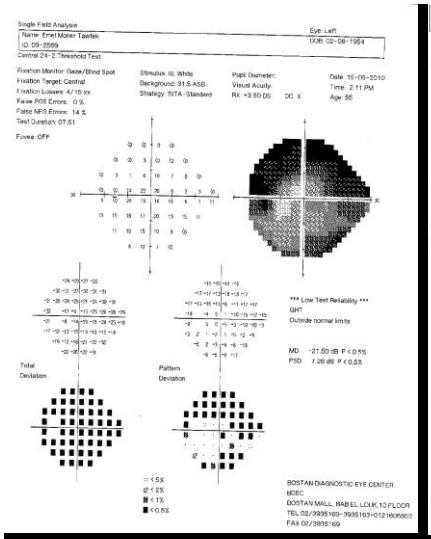

54.3
Thickness Map
250
200
150
100
50
0 µm
Significance Map
6mm x 6mm
N
Fovea
p>5%
p<5%
p<1%

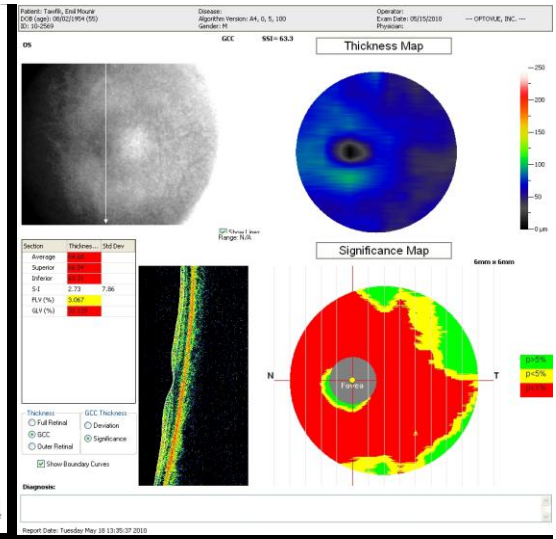

Thickness Map
Significance Map
Fovea
Total Deviation
Pattern Deviation
BOSTAN DIAGNOSTIC EYE CENTER


Thickness Map
Significance Map
6mm x 6mm
Fovea

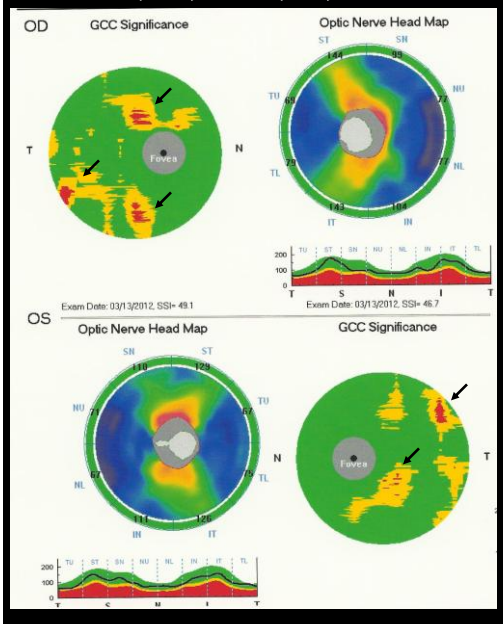


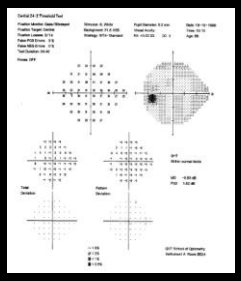

Thickness Map
Significance Map
Diagnosis:

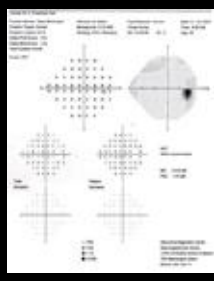



Thickness Map
Significance Map
Diagnosis:

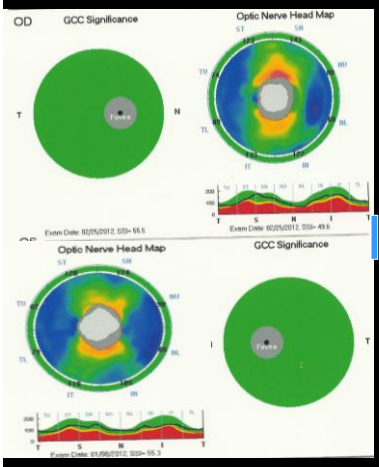
Male , 58 years-old , IOP 27 mmHg (OD) , 26 mmHg (OS)
C/D 0.4 (OD) , 0.3 (OS).



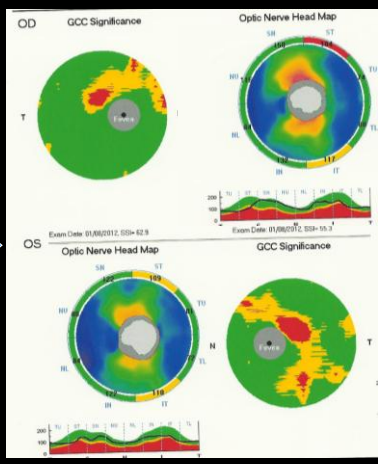




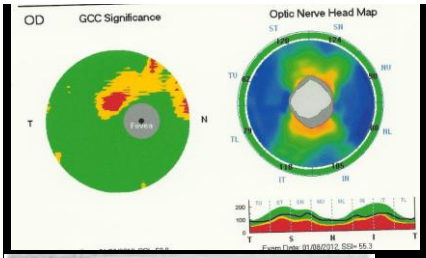
Ocular Hypertension



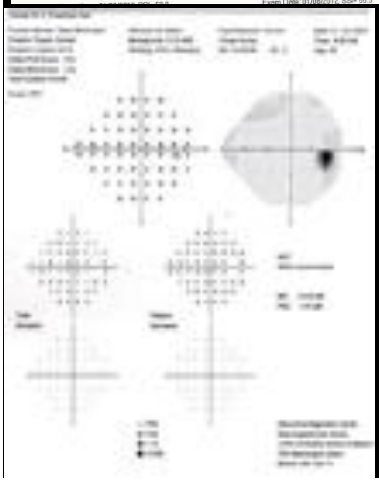
9 Months later



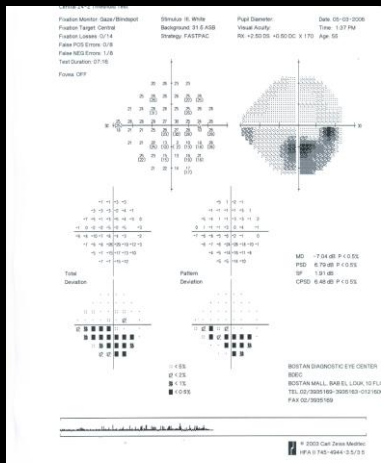
Pre-perimetric Glaucoma

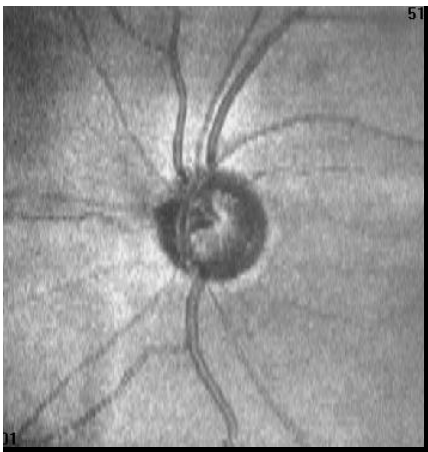


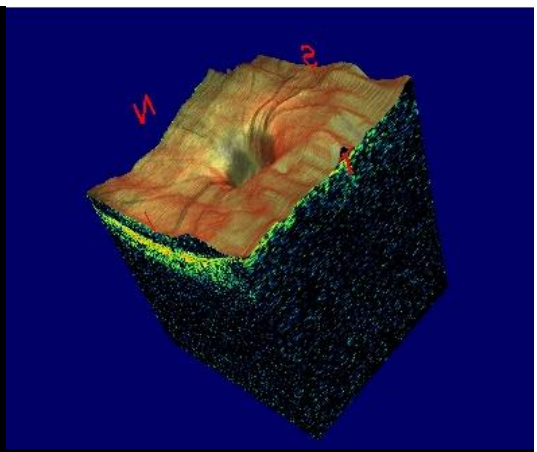
Predict future visual field loss

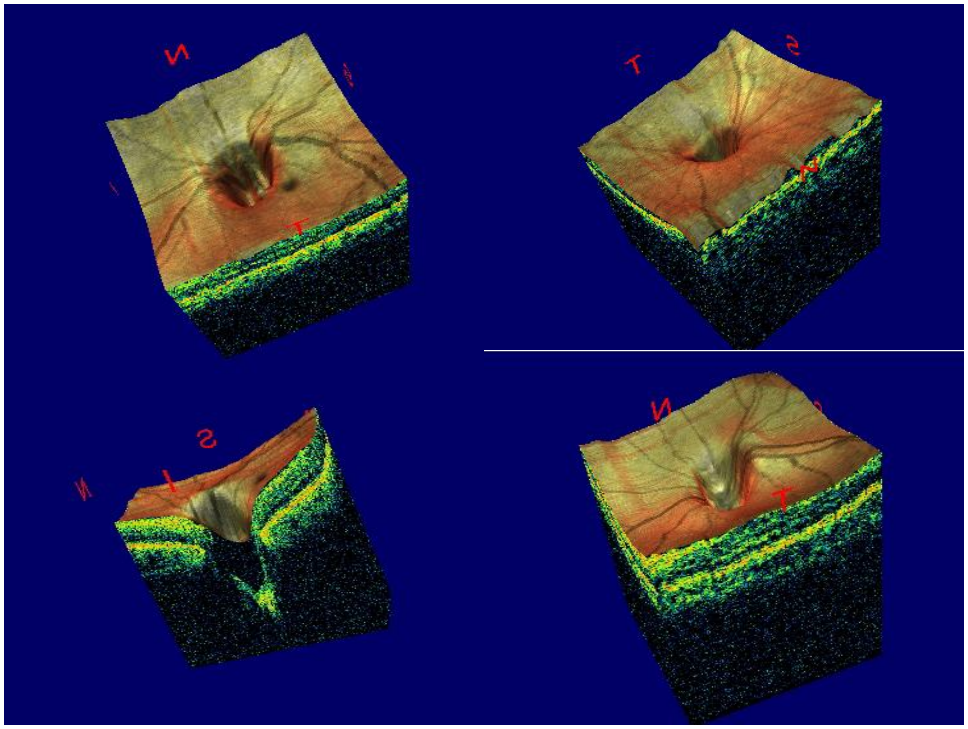


9 months

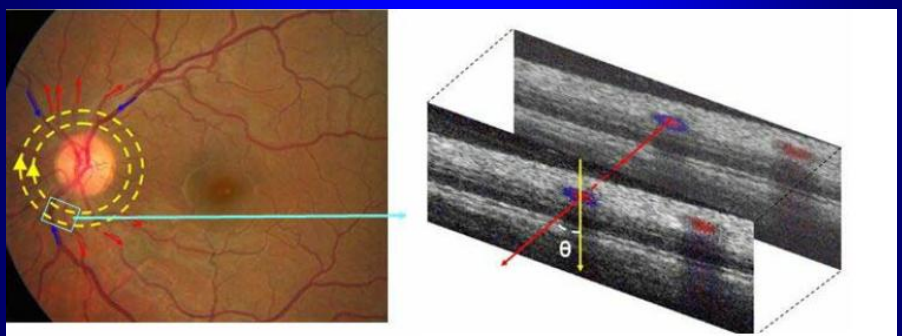








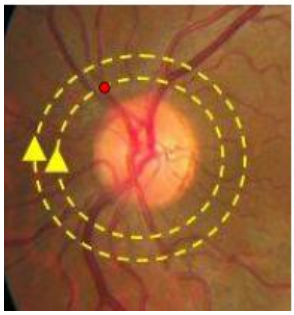
Near-future : Doppler OCT measurement of Retinal Blood Flow

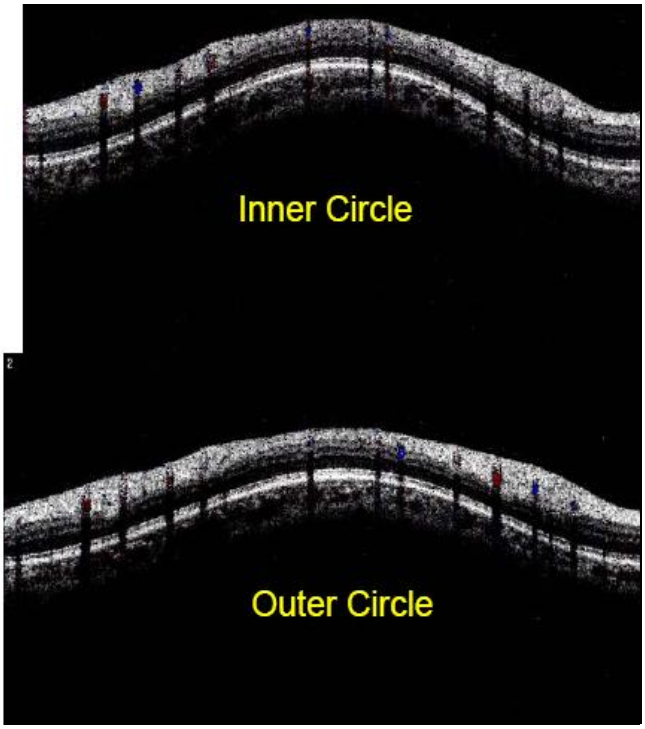


Double circular scan

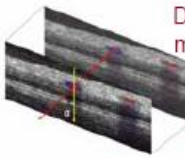
Flow profile and direction determined on parallel sections*

Double circular scan transects all retinal branch vessels 6 times per second

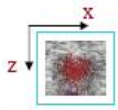




Algorithm for Total Retinal Blood Flow



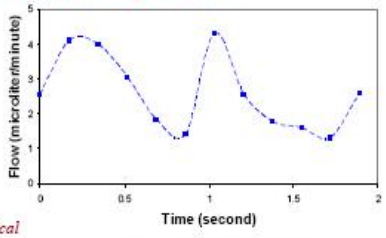
Doppler angle measurement



vessel velocity cross section

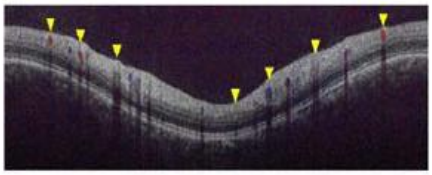
$$\iint \frac{\Delta v}{2\cos\alpha} dxdz$$

Flow in a single vessel



Y. Wang, et. al., Journal of Biomedical Optics 13, 064003, (2008)

Average flow over 2 seconds for each vessel



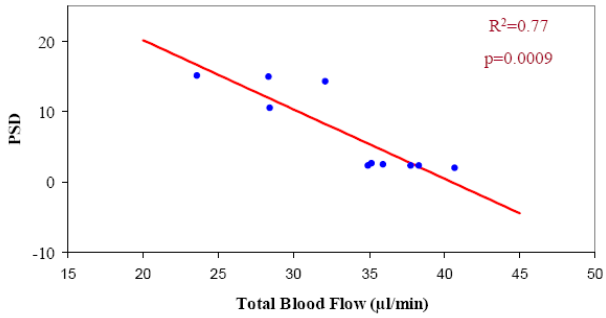
$\sum$ Flow in Veins

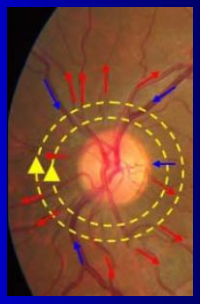
Total Retinal Blood Flow

Flow value : 40.8 to 52.9 μl/min, CV: 10.5%

Glaucoma reduces retinal blood flow

Group	Number of Subjects	Total retinal blood flow (µl/min)	
		Average	*Range*
Normal	8	45.64	40.73-52.91
Perimetric Glaucoma	10	33.54 **P < 0.003**	23.6-40.88





Thank You