STRUCTURAL ASSESSMENT OF OPTIC DISC AND RETINAL NERVE FIBER LAYER

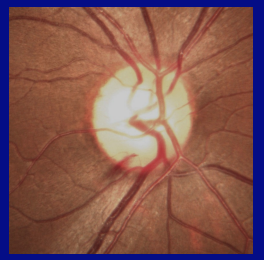
Detecting glaucoma

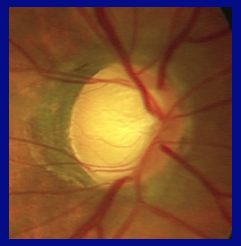
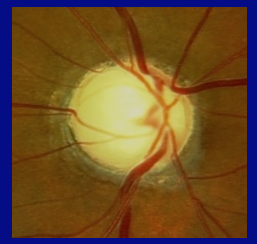
Internal use

Glaucomatous Optic Neuropathy

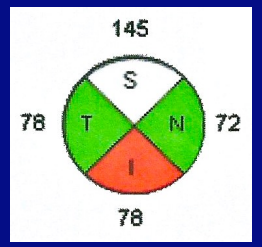
STRUCTURE

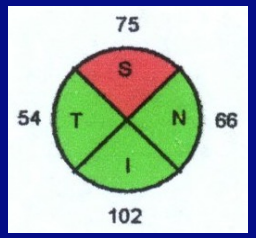
- Qualitative

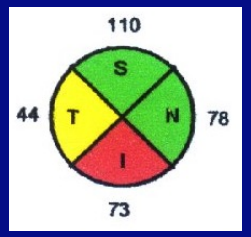


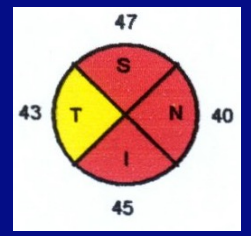



- Quantitative
(e.g.,OCT)









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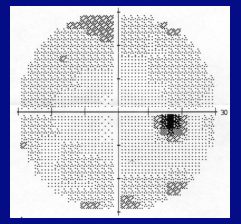
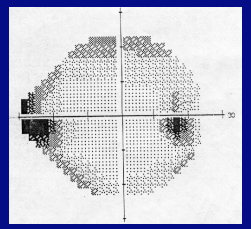
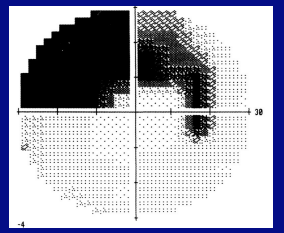
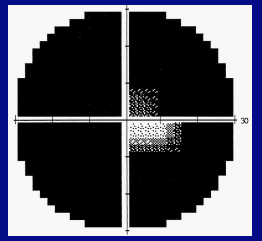

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Internal use

QUALITATIVE STRUCTURAL ASSESSMENT OF THE OPTIC DISC AND RNFL

Detecting glaucoma

Internal use

Outline

I. Five rules for assessment of the optic disc in glaucoma

II. Detecting glaucoma

III. Examples

IV. Test your skills

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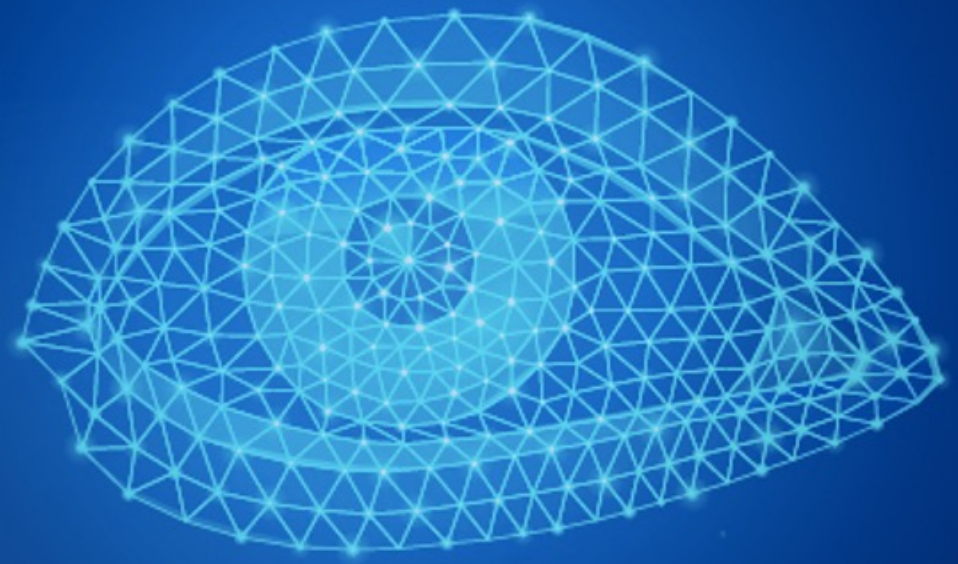
Internal use



FIVE RULES FOR ASSESSING THE OPTIC DISC IN GLAUCOMA

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Internal use

Five rules for assessing the optic disc in glaucoma (1)

1. Observe the scleral Ring to identify the limits and size of the optic disc
2. Identify the size of the Rim
3. Examine the Retinal nerve fibre layer
4. Examine the Region of peripapillary atrophy
5. Look for Retinal and optic disc haemorrhages

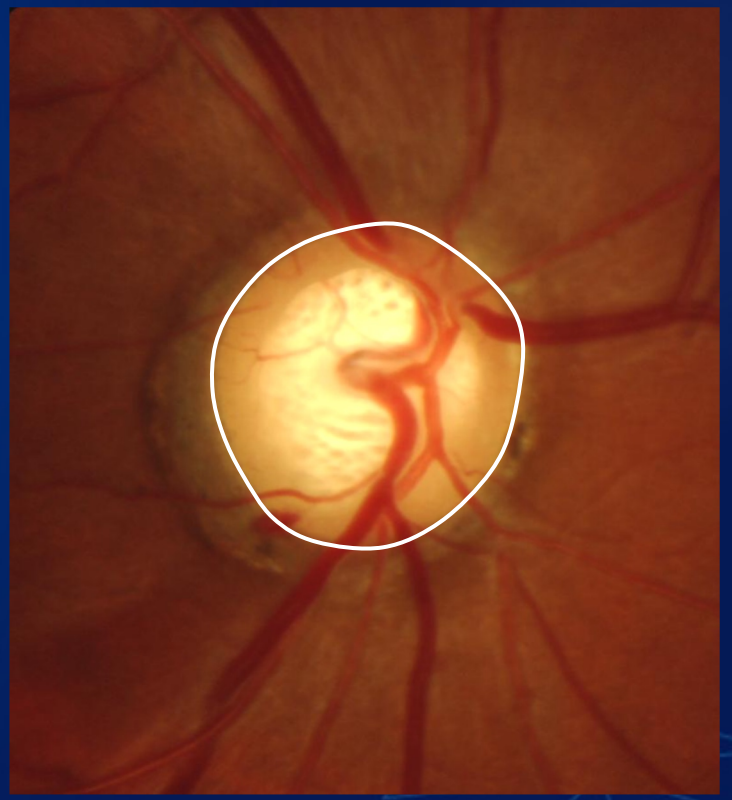

Photo courtesy of Ki Ho Park

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Internal use

Five rules for assessing the optic disc in glaucoma (2)

1. Observe the scleral Ring to identify the limits and size of the optic disc
2. Identify the size of the Rim
3. Examine the Retinal nerve fibre layer
4. Examine the Region of peripapillary atrophy
5. Look for Retinal and optic disc haemorrhages

Photo courtesy of Ki Ho Park

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Internal use

Five rules for assessing the optic disc in glaucoma (3)

1. Observe the scleral Ring to identify the limits and size of the optic disc
2. Identify the size of the Rim
3. Examine the Retinal nerve fibre layer
4. Examine the Region of peripapillary atrophy
5. Look for Retinal and optic disc haemorrhages

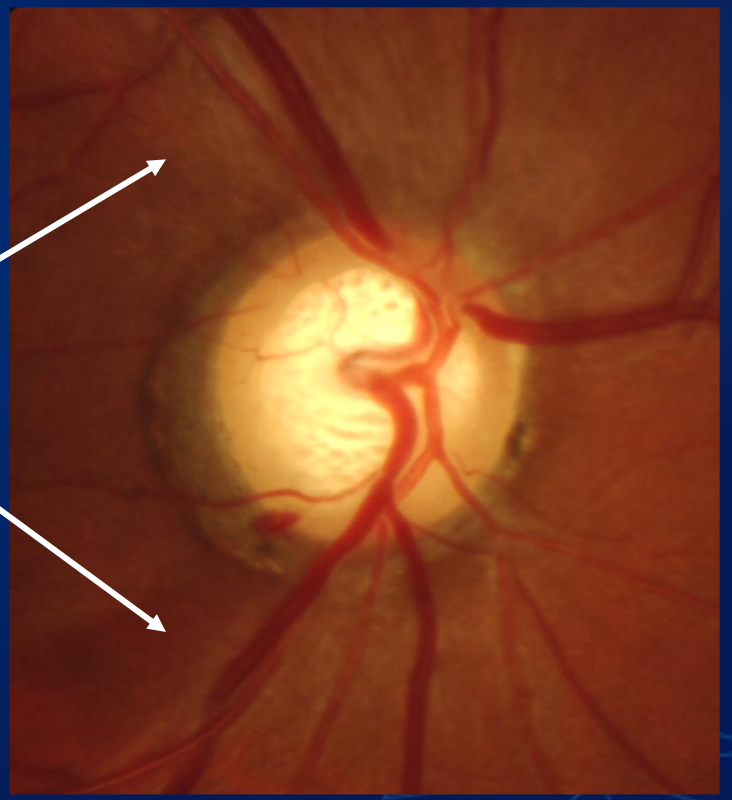

Photo courtesy of Ki Ho Park

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Internal use

Five rules for assessing the optic disc in glaucoma (4)

1. Observe the scleral Ring to identify the limits and size of the optic disc
2. Identify the size of the Rim
3. Examine the Retinal nerve fibre layer
4. Examine the Region of peripapillary atrophy
5. Look for Retinal and optic disc haemorrhages

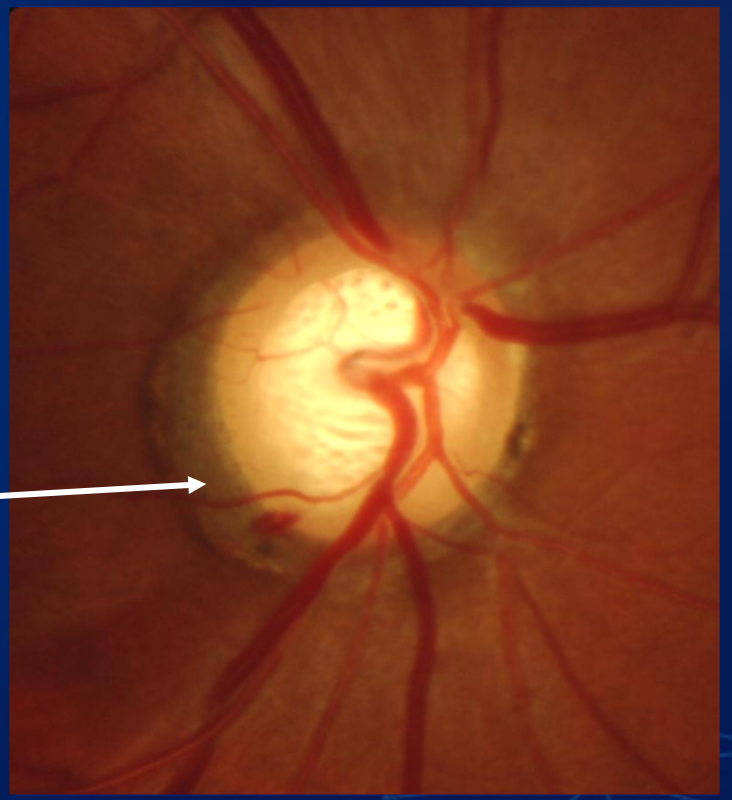

Photo courtesy of Ki Ho Park

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Internal use

Five rules for assessing the optic disc in glaucoma (5)

1. Observe the scleral Ring to identify the limits and size of the optic disc
2. Identify the size of the Rim
3. Examine the Retinal nerve fibre layer
4. Examine the Region of peripapillary atrophy
5. Look for Retinal and optic disc haemorrhages

Photo courtesy of Ki Ho Park

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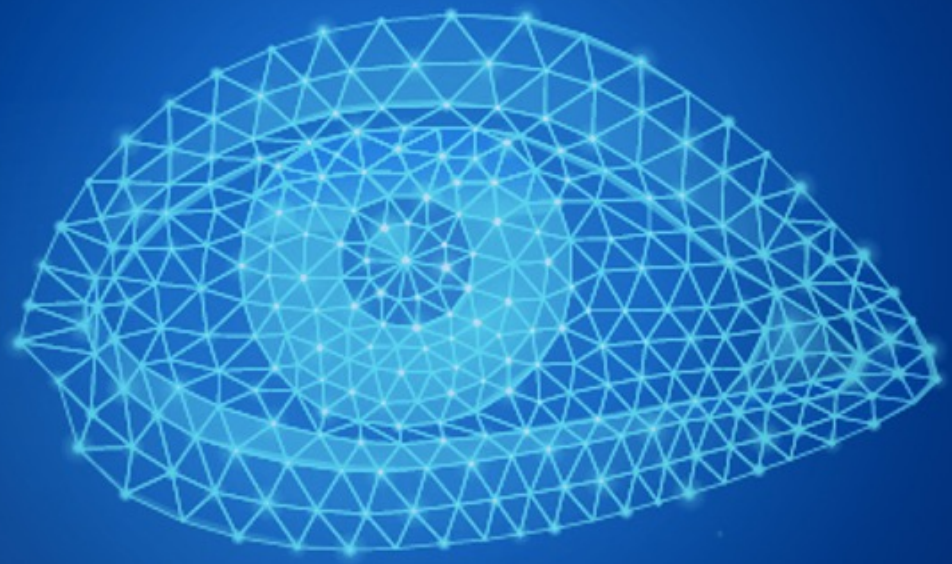
Internal use



Rule 1

Observe the scleral Ring to identify the limits and size of the optic disc

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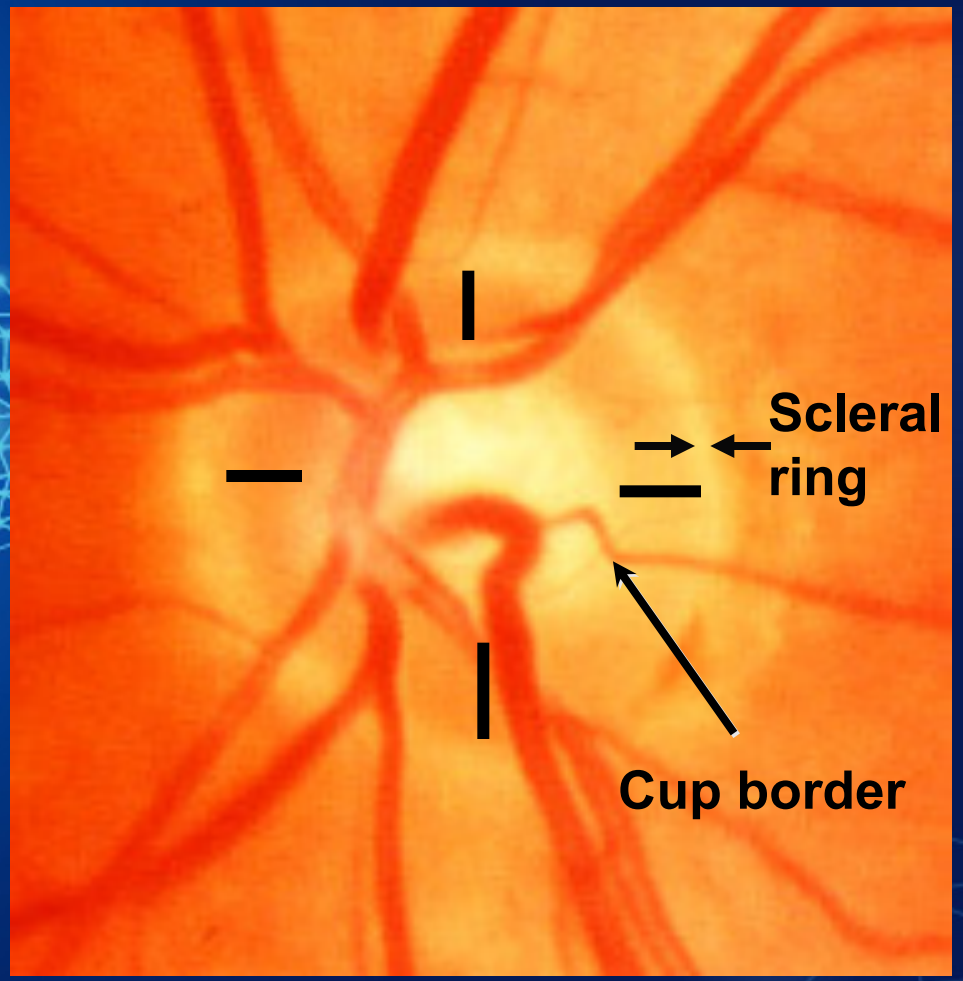
Internal use

The scleral ring (1)

Rim width = distance between the scleral ring (disc border) and the location where the vessel is bent (cup border)



One may note a change in color or light reflection of the vessels as it beds into the cup

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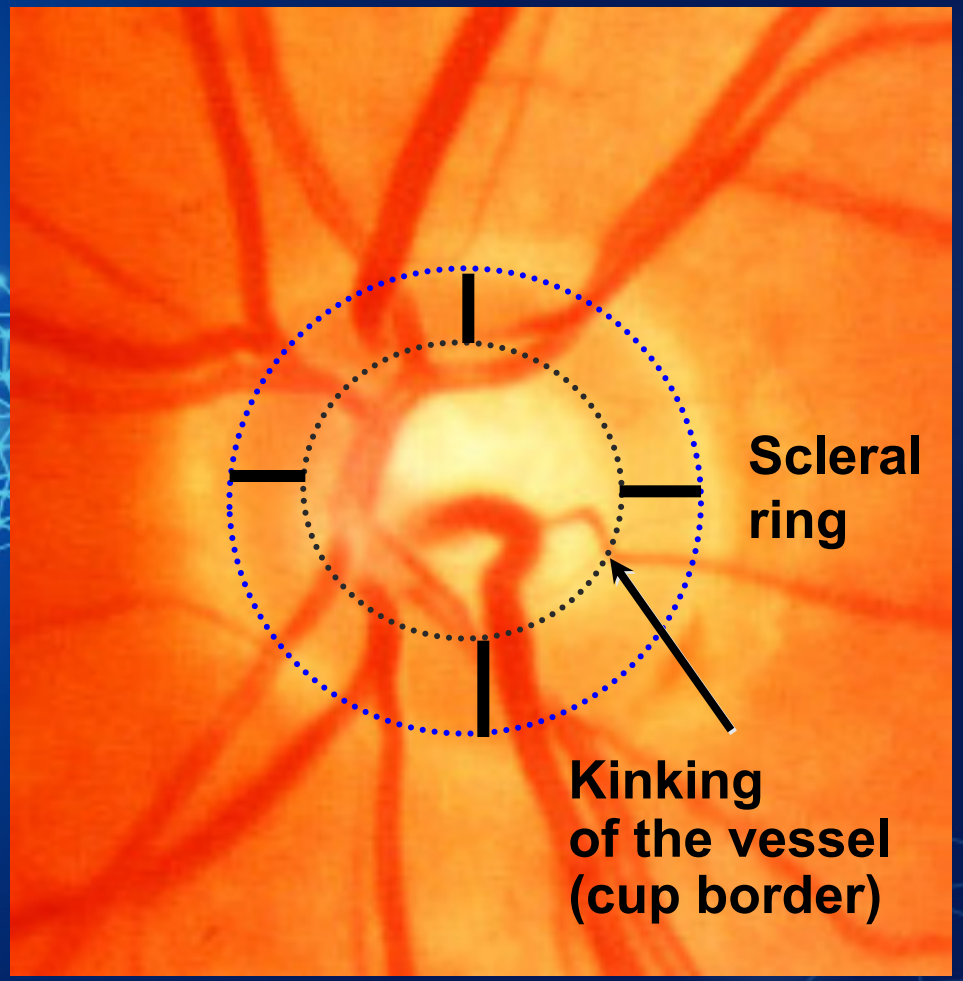
Internal use

The scleral ring (2)

Rim width = distance between the scleral ring (disc border) and the location where the vessel is bent (cup border)

One may note a change in color or light reflection of the vessels as it beds into the cup



Internal use

Optic disc size (1)

Extremely variable

A large cup–disc ratio is not necessarily pathological

Large discs have large cup–disc ratios,

even though the area of the neuroretinal

rim is normal

Pathological rim loss can be missed in a small disc,

especially if generalised

Asia Pacific Glaucoma Guidelines 3rd ed. 2016.

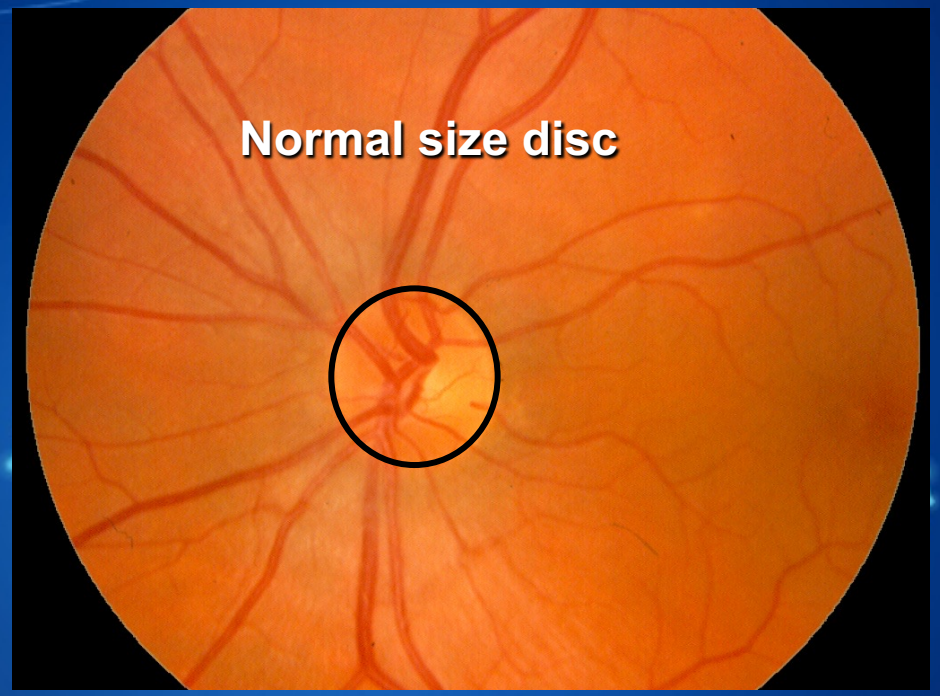
Internal use

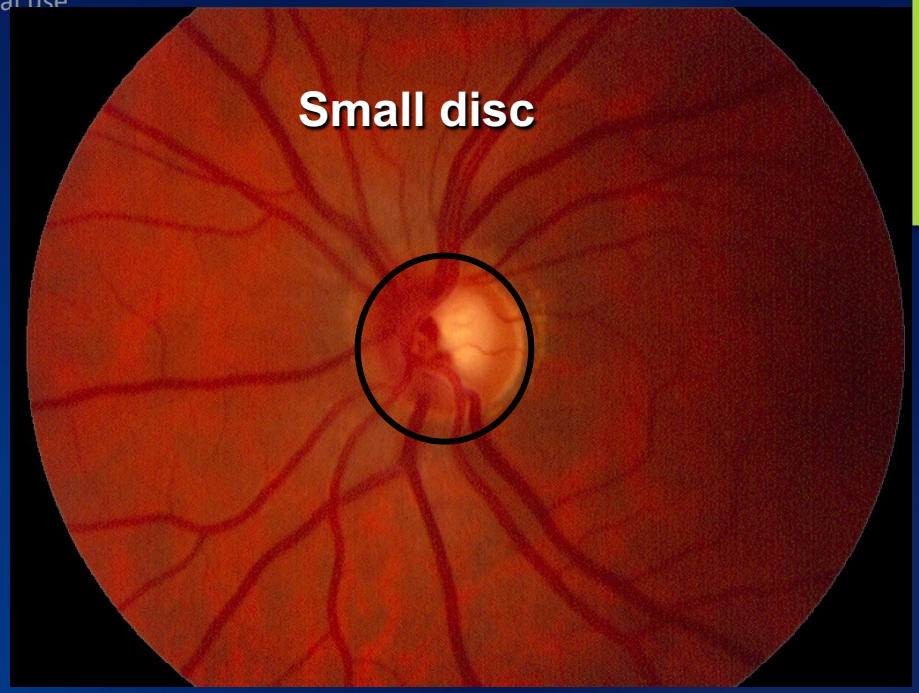
Optic disc size (2)

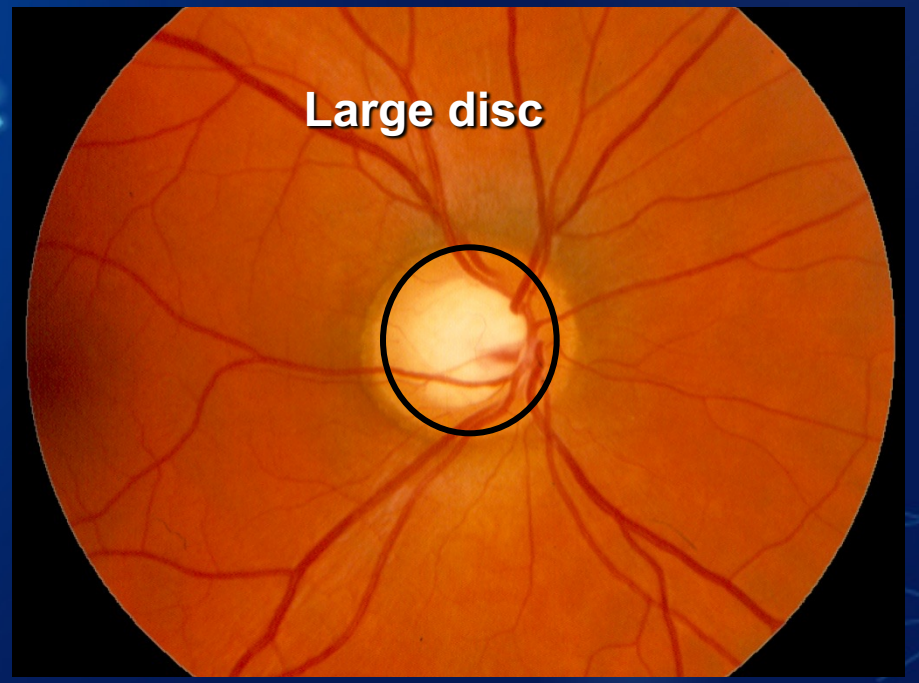
- Can be measured using the small light spot of a direct ophthalmoscope
  - The spot size can be used to estimate whether a disc is larger or smaller than average
- Other forms of evaluation
  - conventional photographic means with an overlay grid
  - optic nerve head analysis

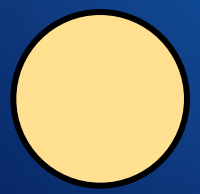
Asia Pacific Glaucoma Guidelines 3rd ed. 2016.

Internal use









Small aperture (5 degree) of Welch-Allen direct ophthalmoscope

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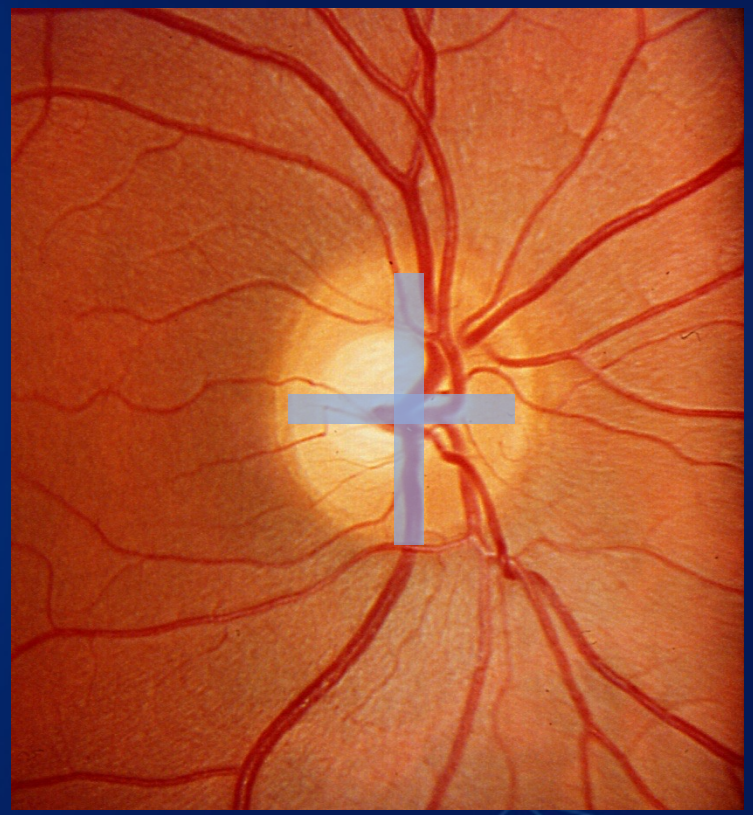
Internal use

Optic disc size (4)

- Indirect ophthalmoscopy and slit lamp examination
  - Use Volk slit lamp biomicroscopy lenses
  - Measure size of slit beam
- Correction factors
  - Volk 60D: × 1.0
  - Volk 78D: × 1.1
  - Volk 90D: × 1.3



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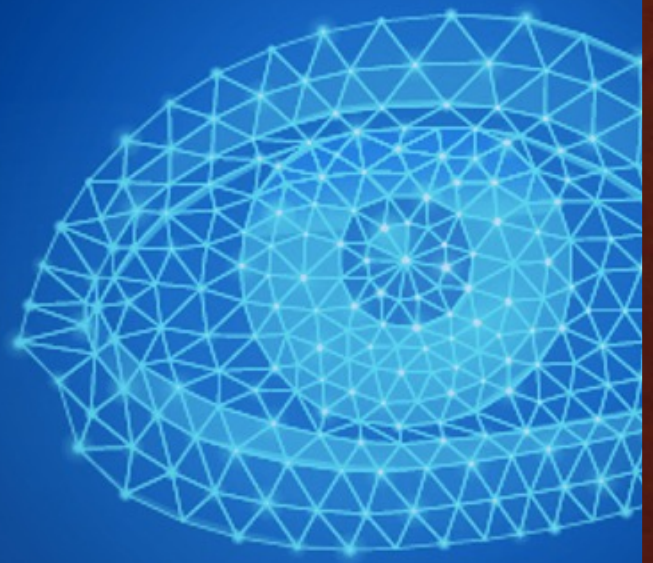
Internal use

Optic disc size (5)



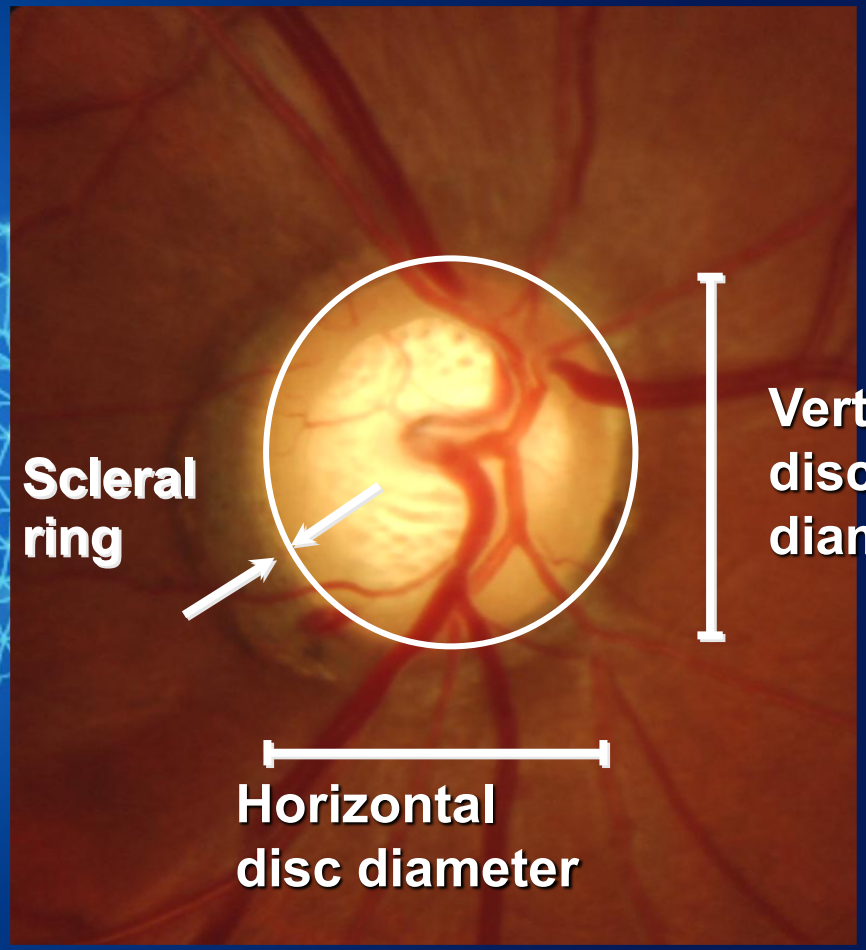


Photo courtesy of Ki Ho Park

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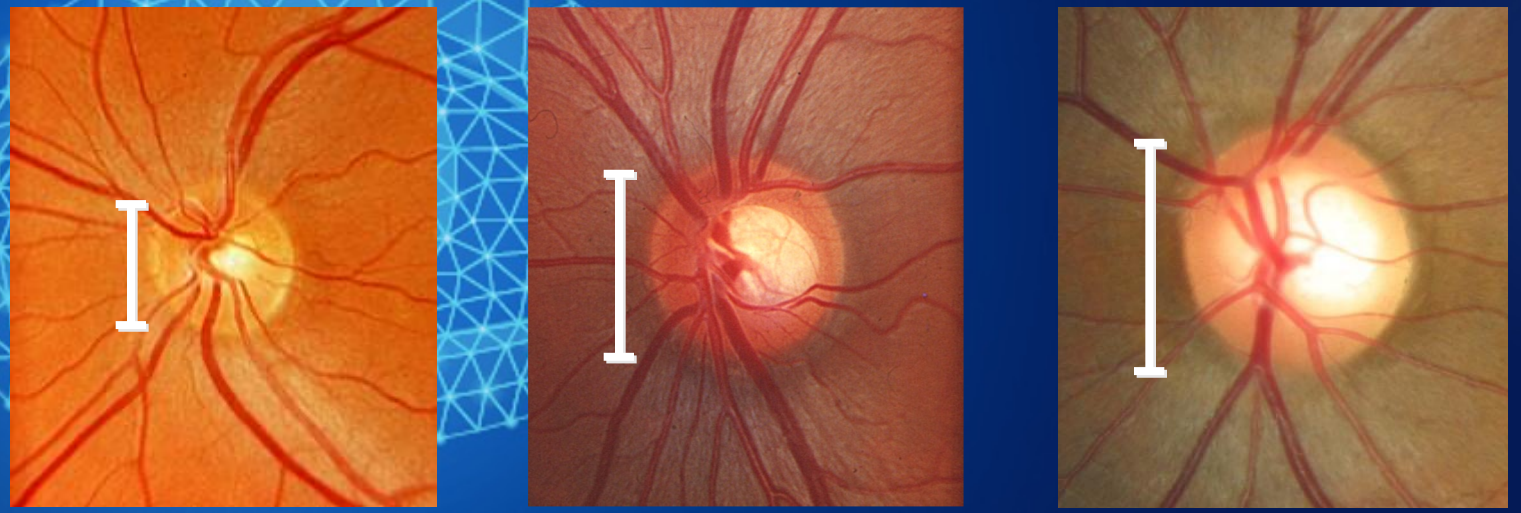
Internal use

Optic disc size (6)

- The size of the cup varies with the size of the disc
- Optic disc size varies between ethnic groups



Small **Average** **Large**

Cup size is proportional to disc size in normal eyes

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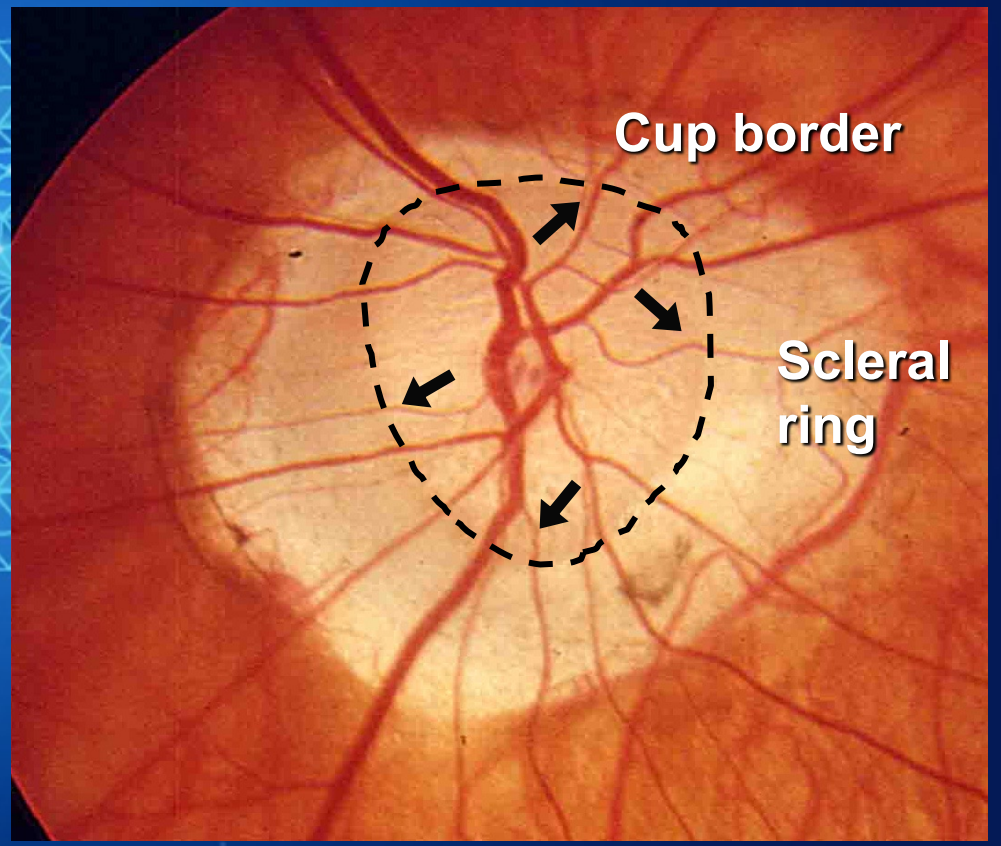
Right photo courtesy of Ki Ho Park

Internal use

Optic disc size (7)

Be cautious with myopic discs



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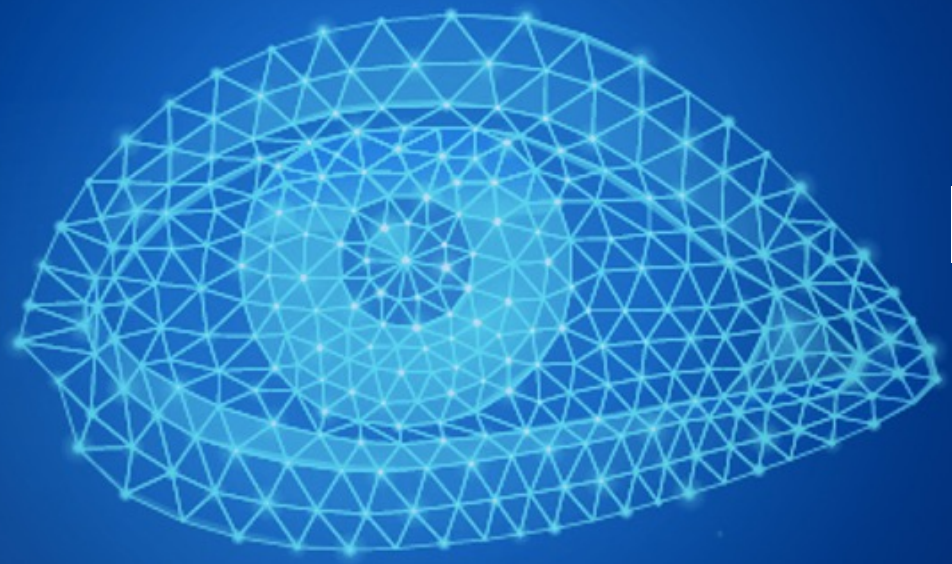
Internal use



Rule 2

Identify the size of the neuroretinal Rim

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Internal use

The neuroretinal rim (1)

- More important than the cup
  - The cup defines the inner edge of the rim where most signs of glaucoma appear
- Defining the rim width
  - Extends from the scleral ring to where the rim width falls below the level of the scleral ring
- Loss of tissue from the inner edge of the rim is the cardinal feature of glaucomatous optic neuropathy

Asia Pacific Glaucoma Guidelines 3rd ed. 2016.

Internal use

The neuroretinal rim (2)

- Features indicating that glaucomatous damage has already occurred
  - Notching (focal loss) of the neuroretinal rim, especially at the vertical poles
  - Haemorrhage crossing the rim
  - Undercutting of the rim
  - Asymmetry of rim width between the eyes in the absence of asymmetric disc size
  - Abnormally thin rim in one or two sectors

Asia Pacific Glaucoma Guidelines 3rd ed. 2016.

Internal use

The neuroretinal rim (3)

- A vertical cup–disc ratio (CDR) of > 0.7, or loss of rim outside the temporal sector, strongly suggests glaucoma
  - May not apply if the disc is extremely large or very tilted
- Asymmetry in the CDR of > 0.2 between two eyes is suspicious unless disc size is similarly asymmetrical

Asia Pacific Glaucoma Guidelines 3rd ed. 2016.

Internal use

The ISNT rule (1)

- Normally, the thickest to thinnest parts of the neuroretinal rim of the optic disc follow the ISNT rule:[1]*

  Inferior > Superior > Nasal > Temporal

- Any variation from this rule may help to detect glaucomatous damage

* The ISNT rule is followed in approximately 50–80% of normal discs, depending on the population[2,3]

1. Jonas JB *et al. Invest Ophthalmol Vis Sci* 1988; 29: 1151–8;
2. Harizman N *et al. Arch Ophthalmol* 2006; 124: 1579–83;
3. Wang Y *et al. Am J Ophthalmol* 2007; 144: 462–4.

Internal use

The ISNT rule (2)

Rim width = distance between border of disc and position of blood vessel bending (border of the cup)

ISNT rule

Inferior > Superior > Nasal > Temporal

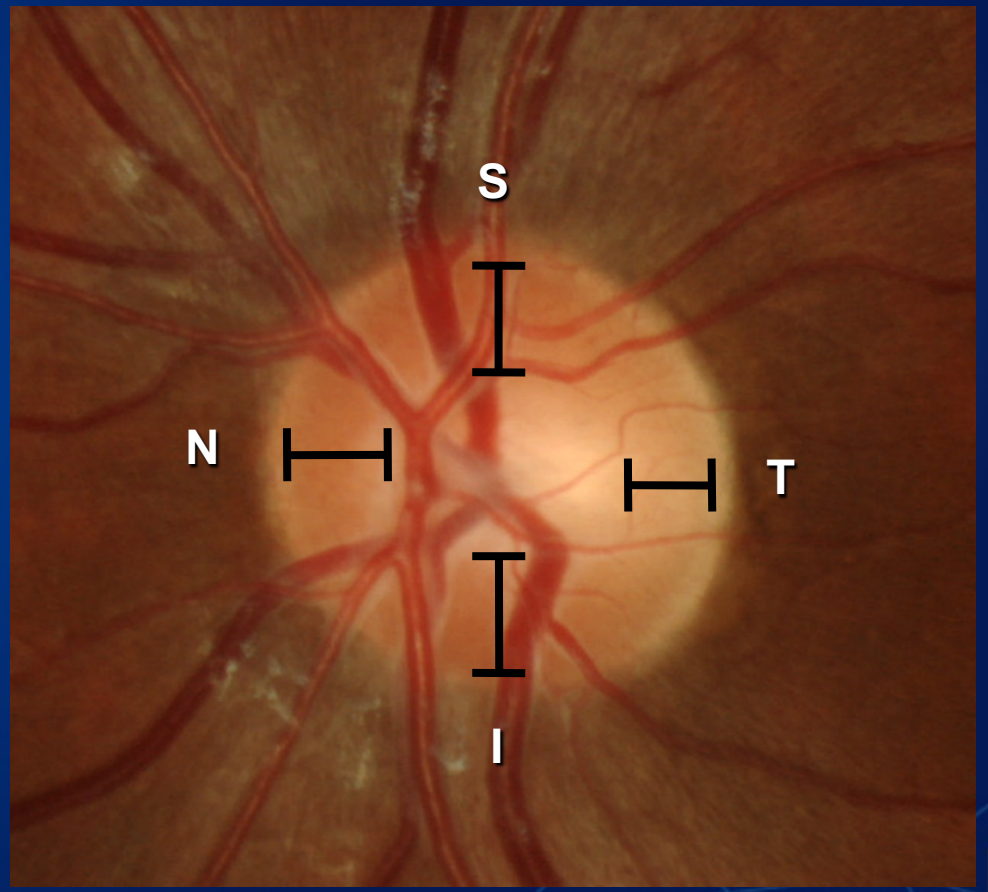

Photo courtesy of Ki Ho Park

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Internal use

Localised rim thinning/notching (1)

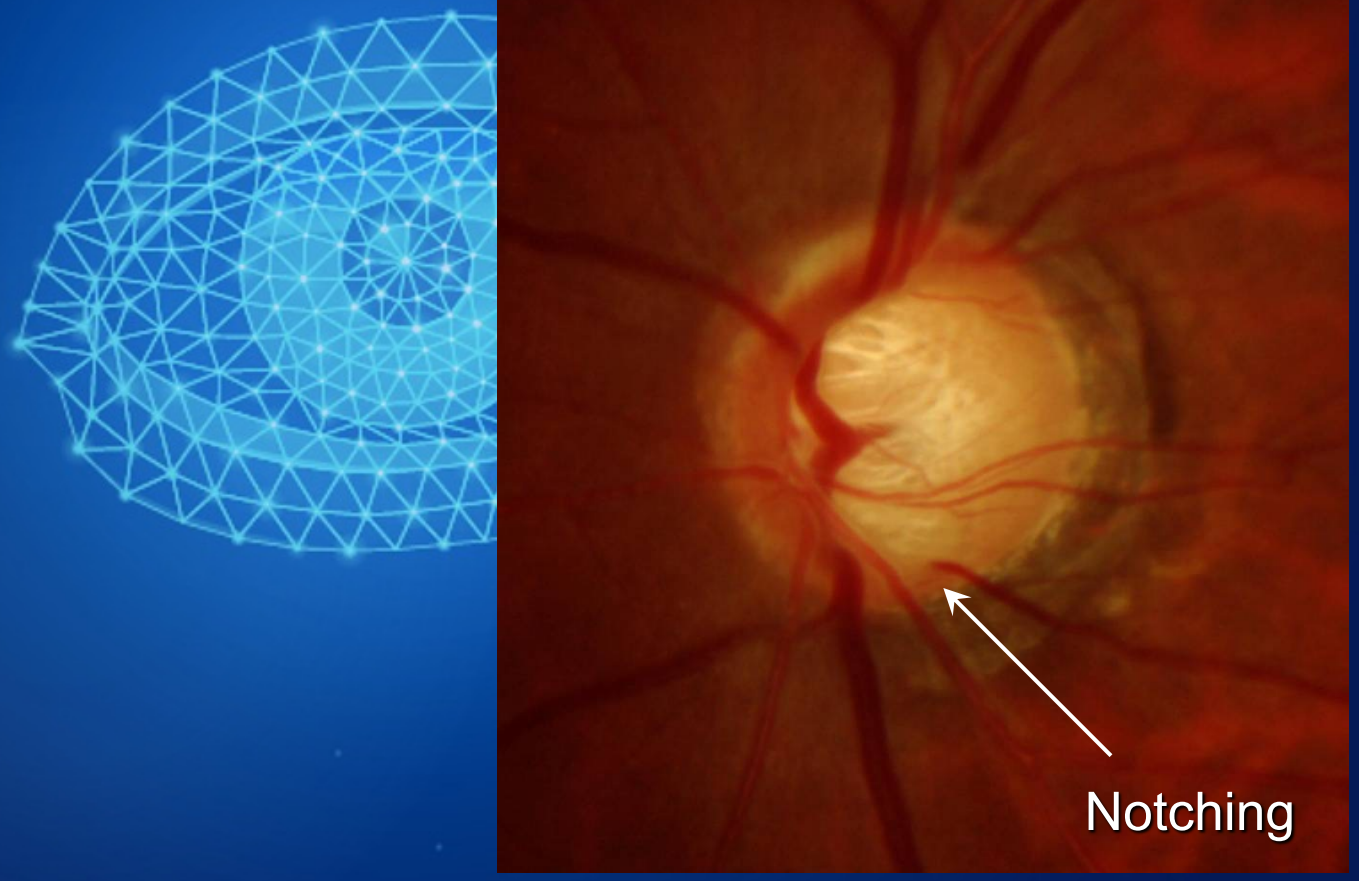

Photo courtesy of Ki Ho Park

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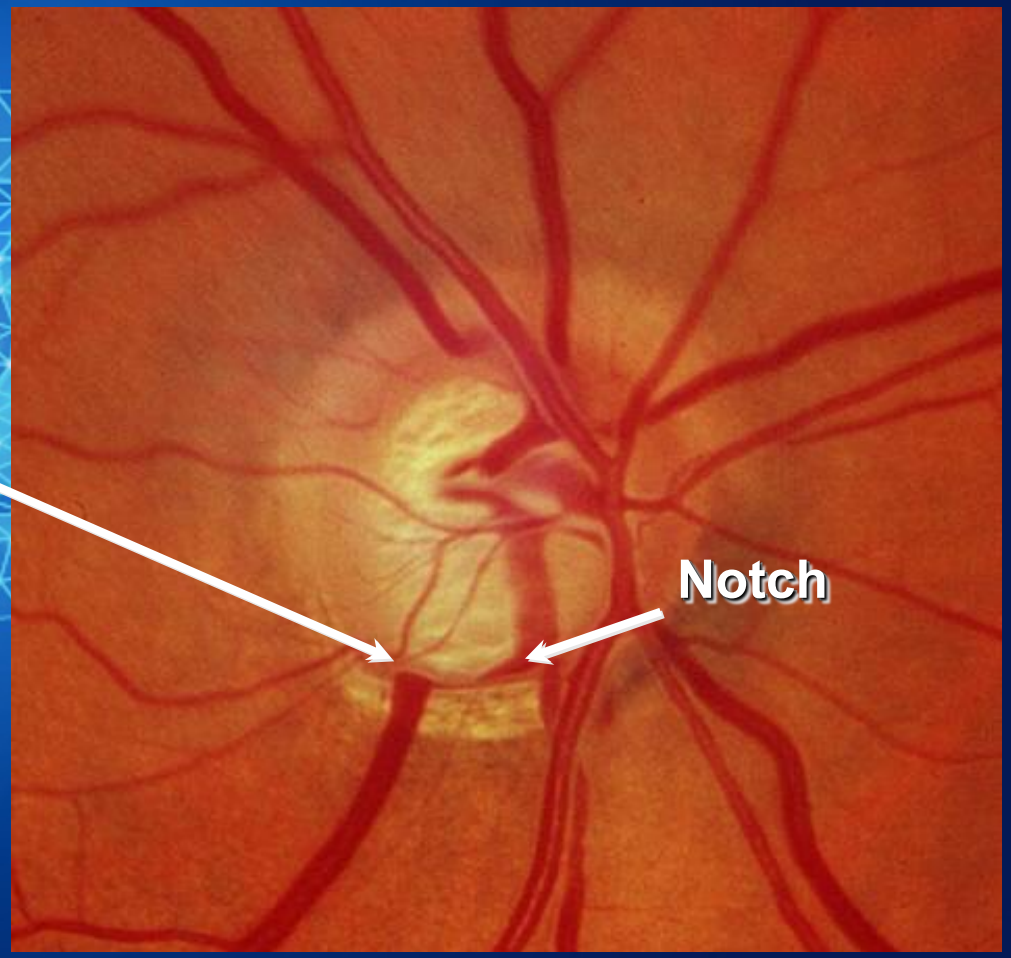
Internal use

Localised rim thinning/notching (2)

Bayonetting of vessels and undercutting of the rim



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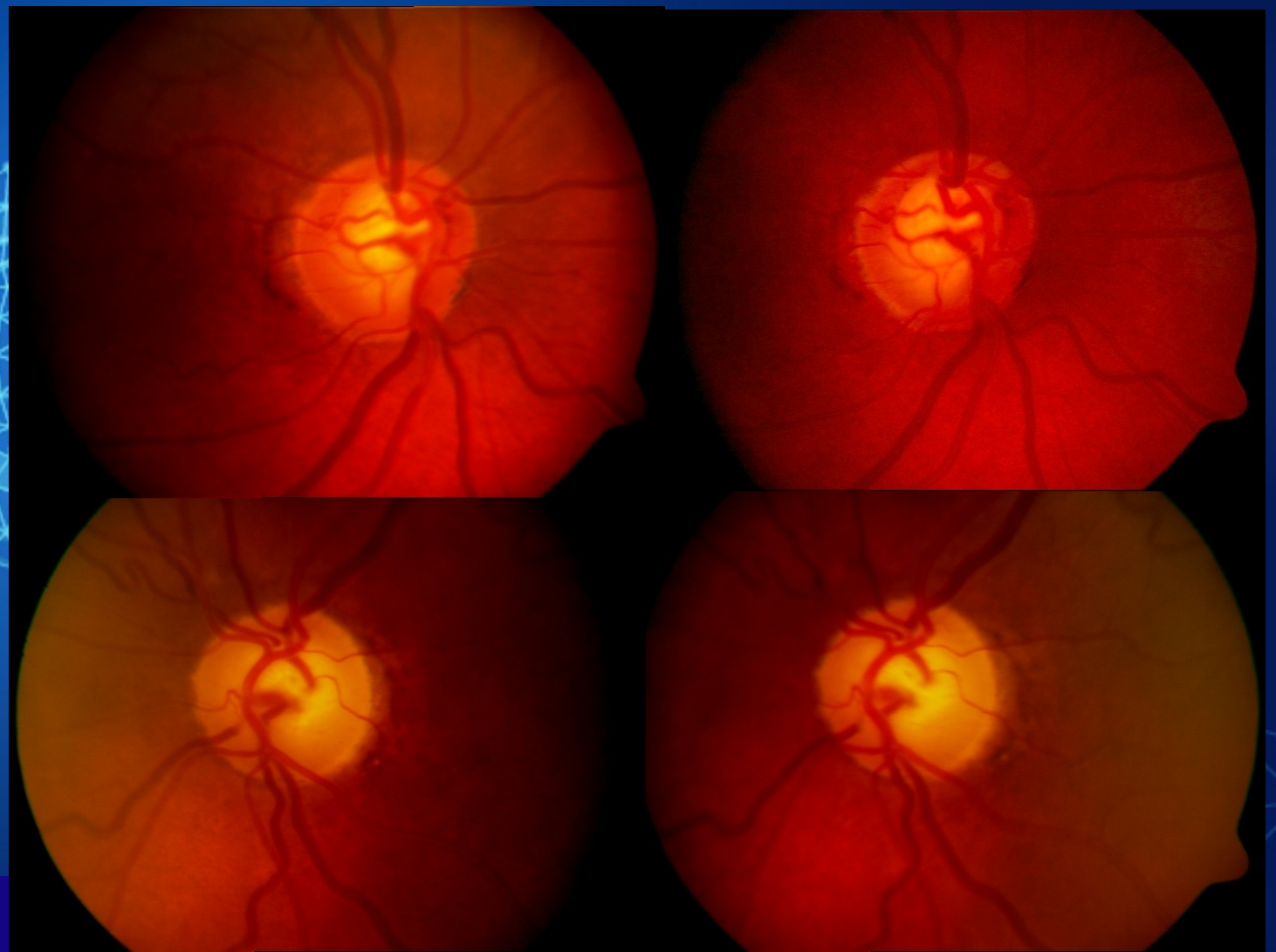
Internal use

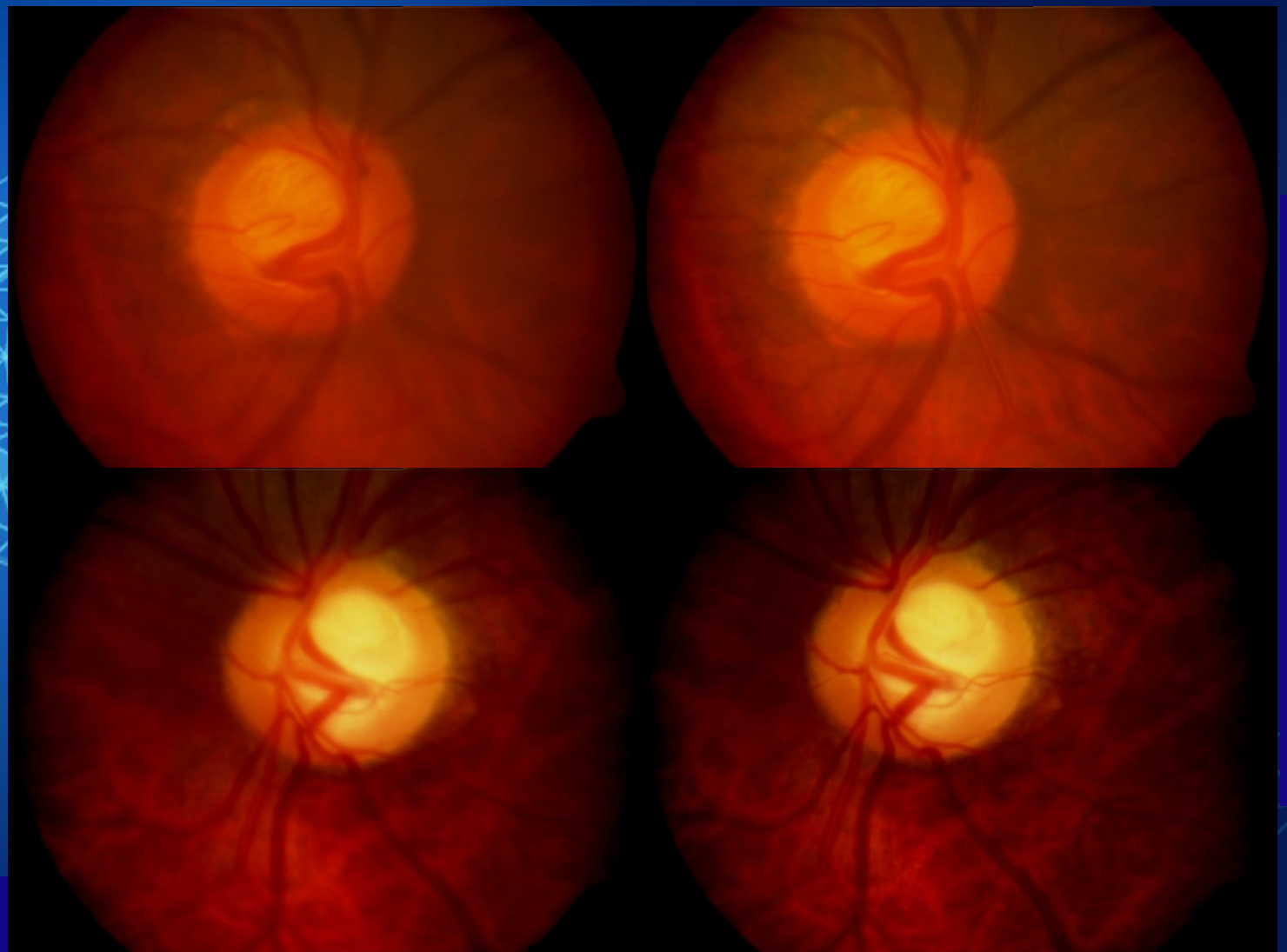
Localised rim thinning/notching (3)



Photos courtesy of GT Sunil and L Vijaya

Internal use

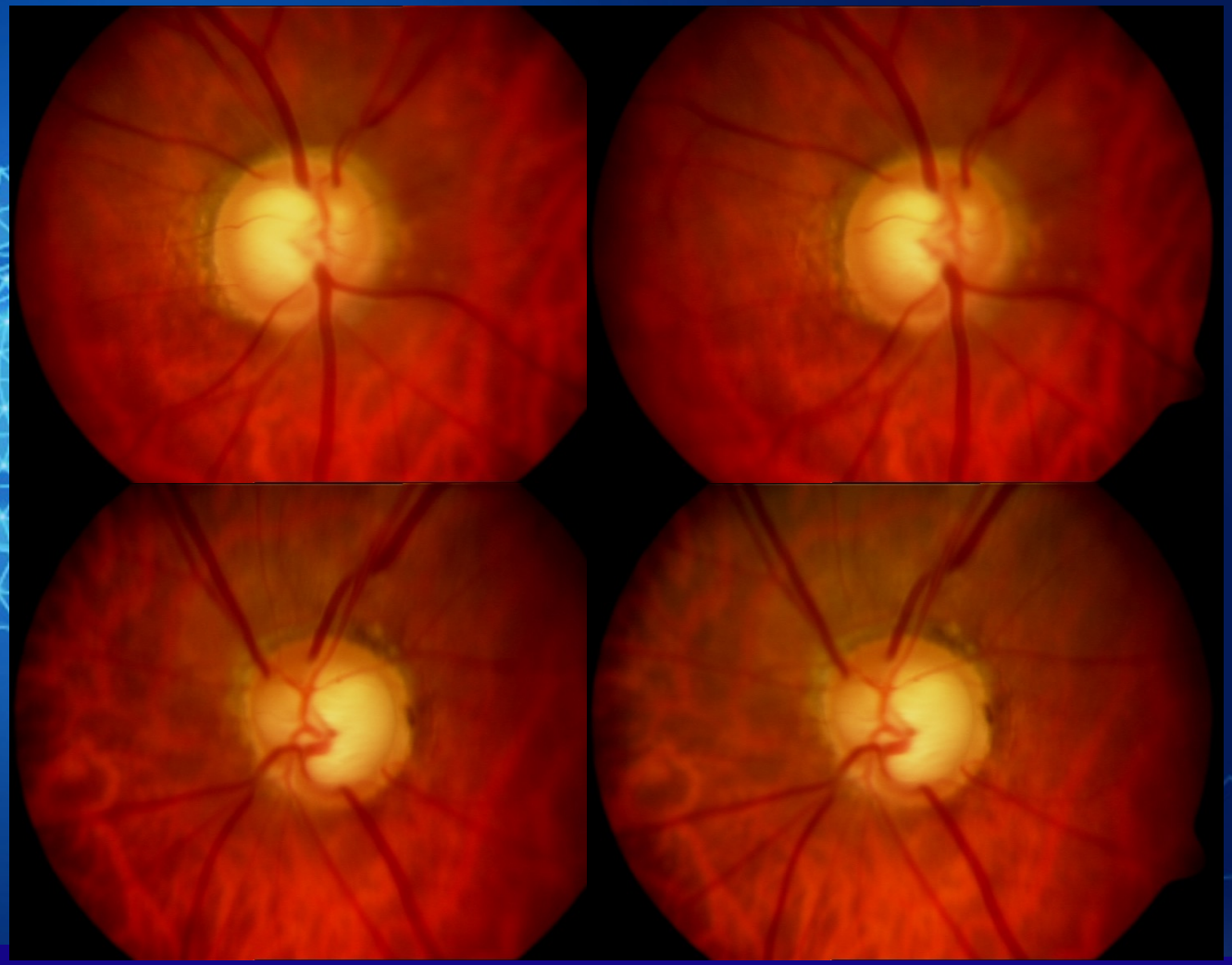
Localised rim thinning/notching (4)



Photos courtesy of GT Sunil and L Vijaya

Internal use

Diffuse neuroretinal loss



Photos courtesy of GT Sunil and L Vijaya

Internal use

Pallor (1)

- Observe the colour of the rim to identify pallor
  - A pale rim increases the likelihood of a non-glaucomatous optic neuropathy

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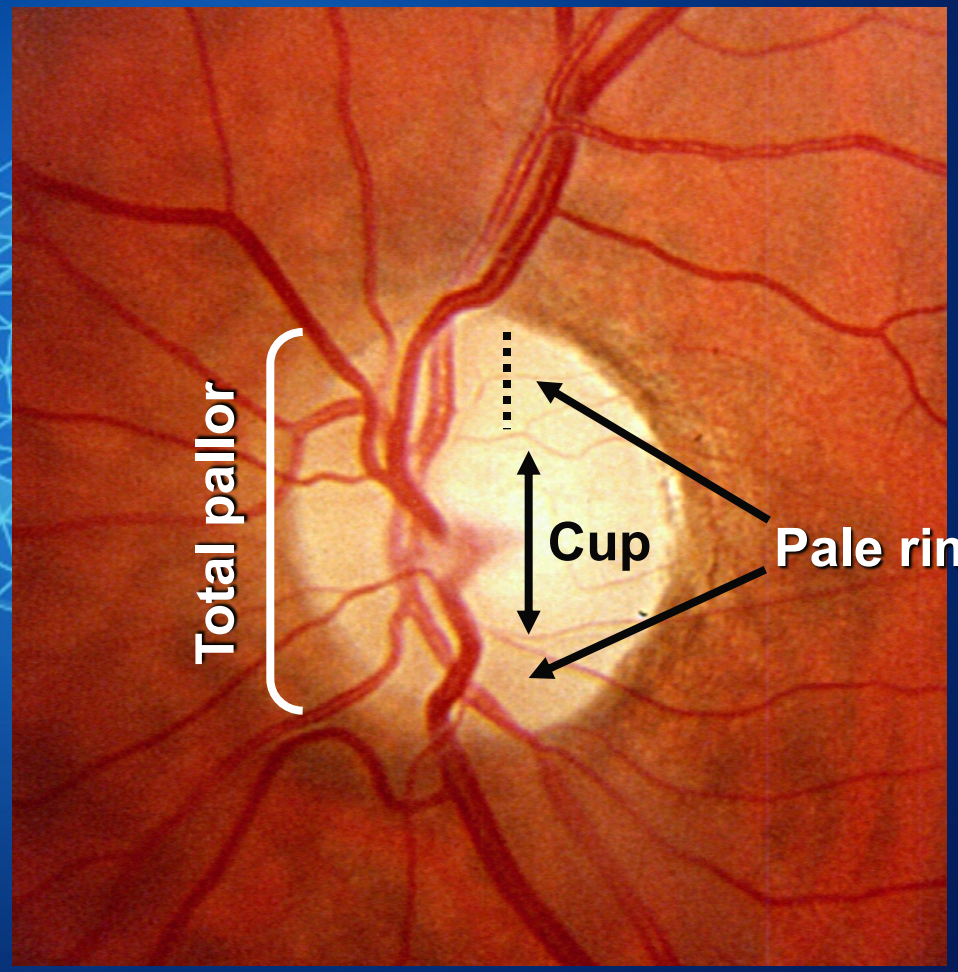
Internal use

Pallor (2)



Pallor > cup

Non-glaucomatous neuropathy

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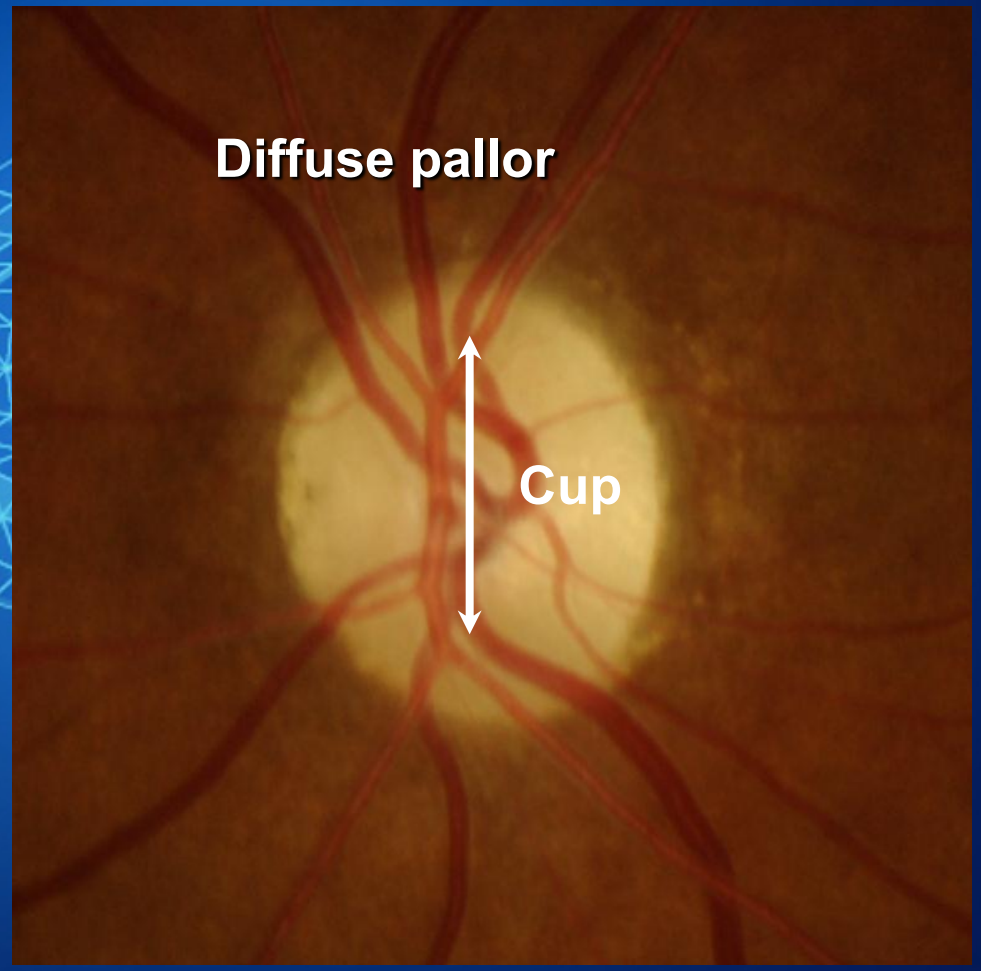
Internal use

Pallor (3)



Pallor > cup

Non-glaucomatous neuropathy

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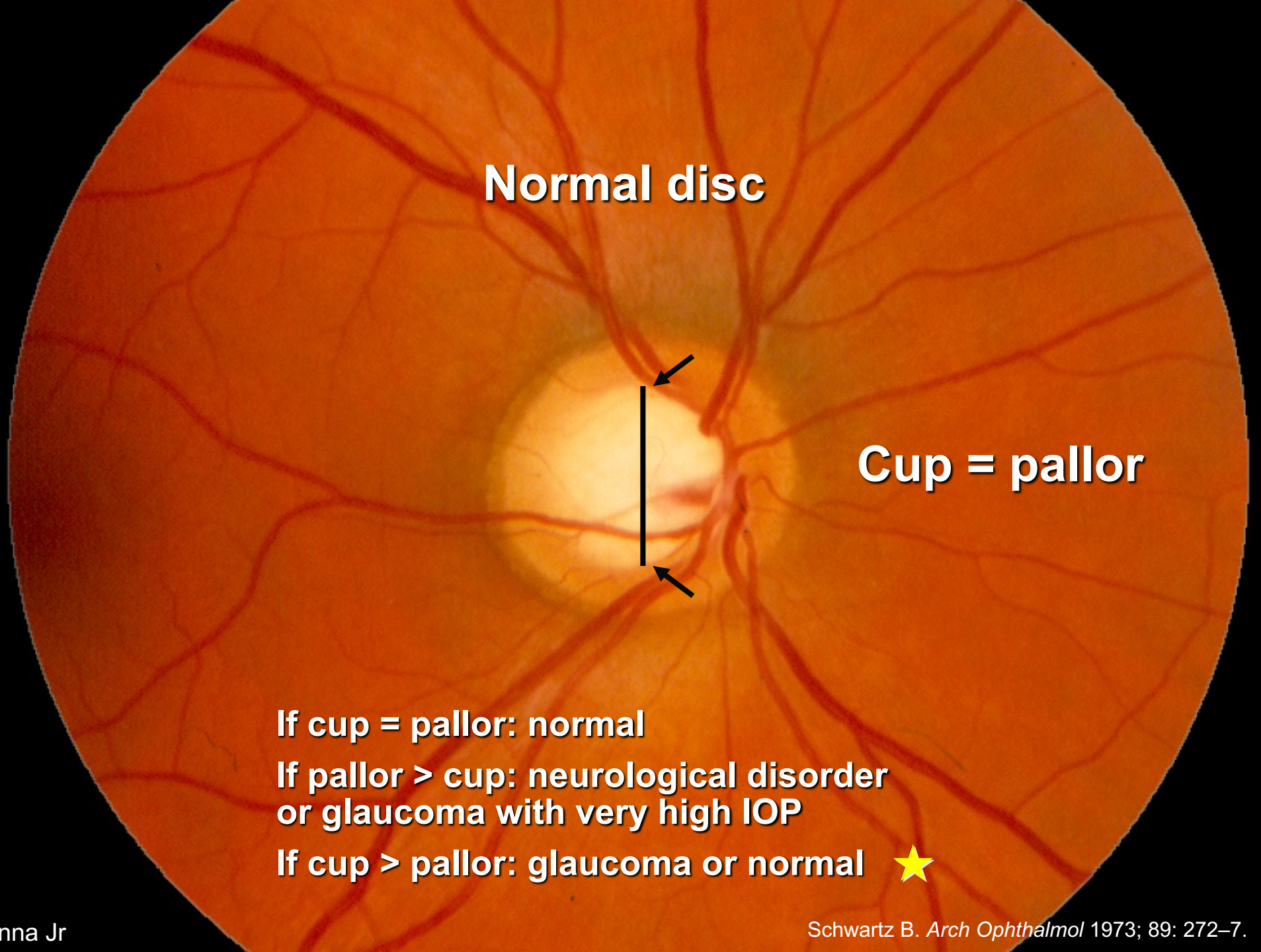
Normal disc



Cup = pallor

If cup = pallor: normal

If pallor > cup: neurological disorder or glaucoma with very high IOP

If cup > pallor: glaucoma or normal ★

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Schwartz B. *Arch Ophthalmol* 1973; 89: 272–7.

Internal use

Pallor (4)

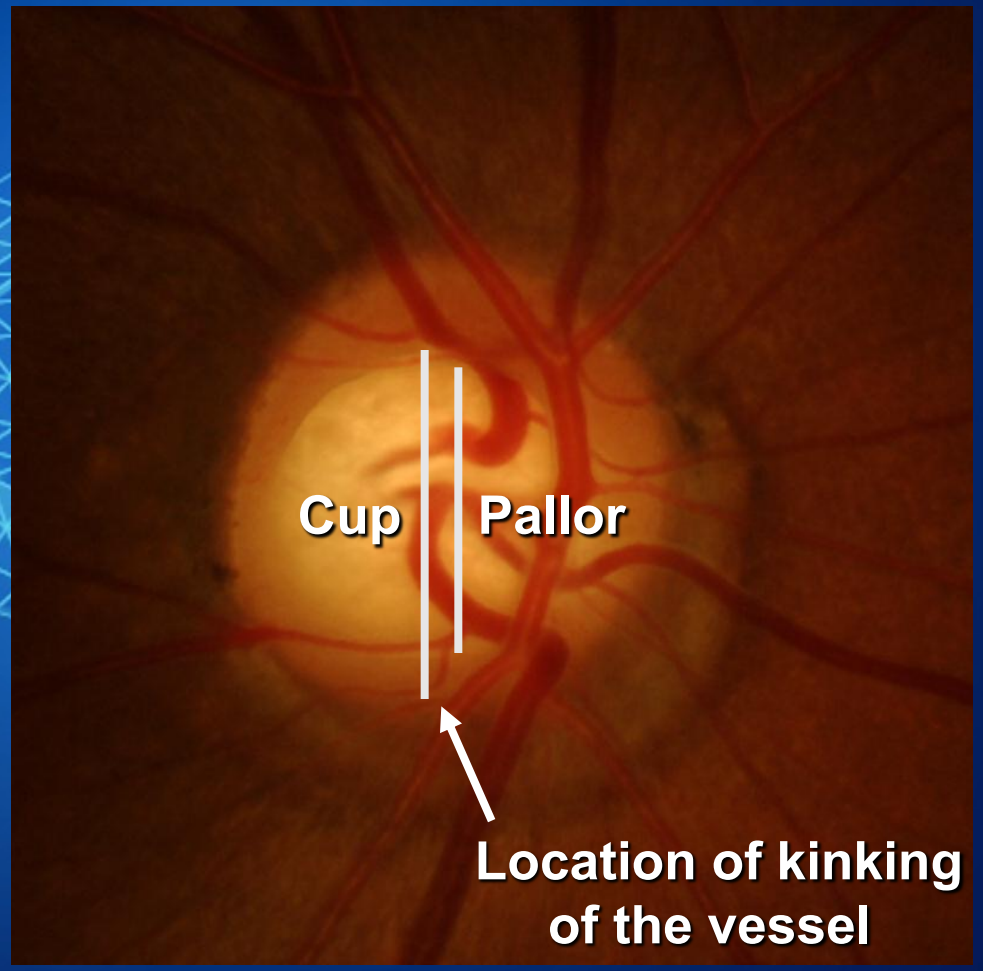


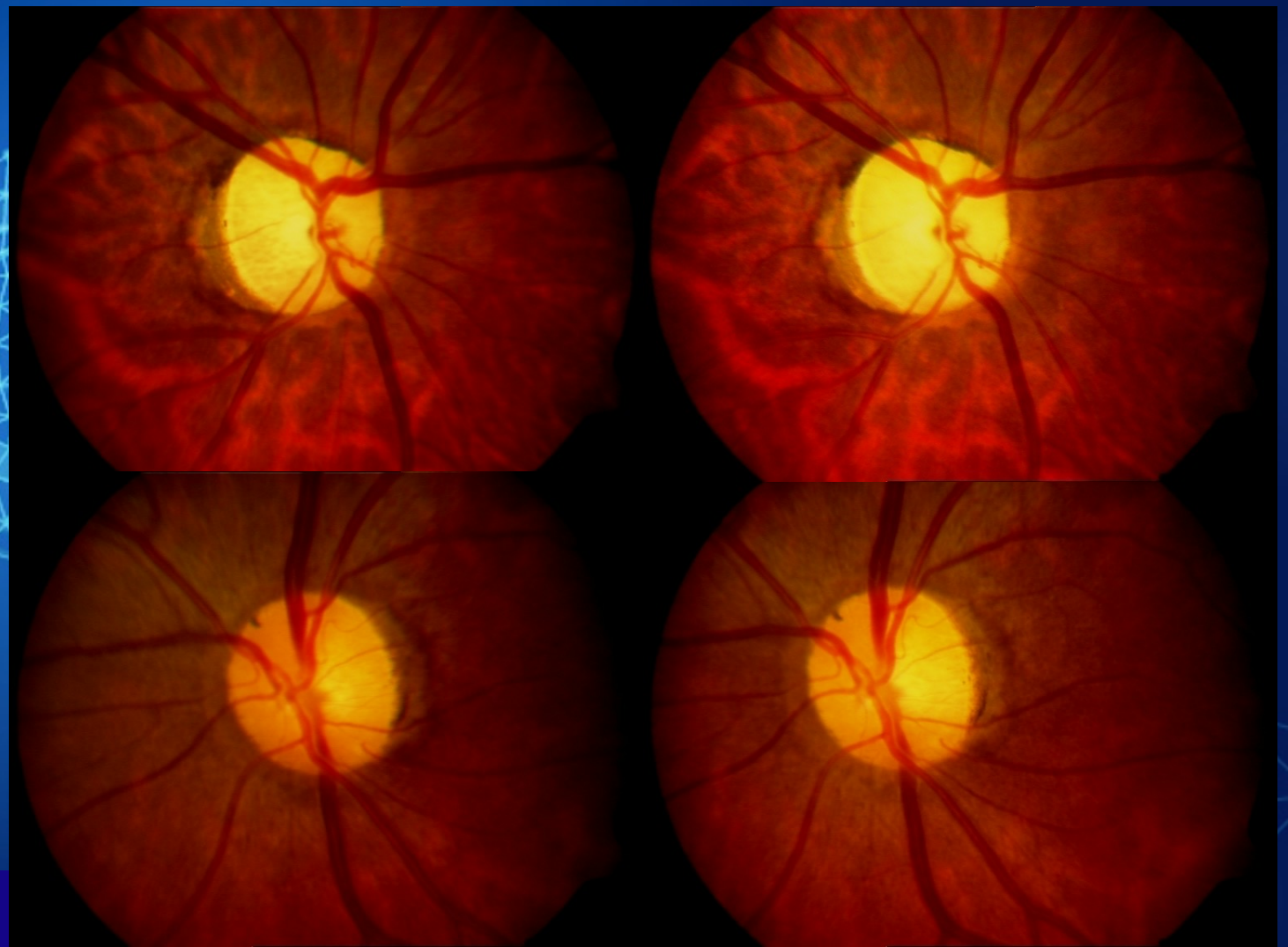
Photo courtesy of Ki Ho Park

Cup > pallor

Suspect glaucoma

Internal use

Pallor (5)



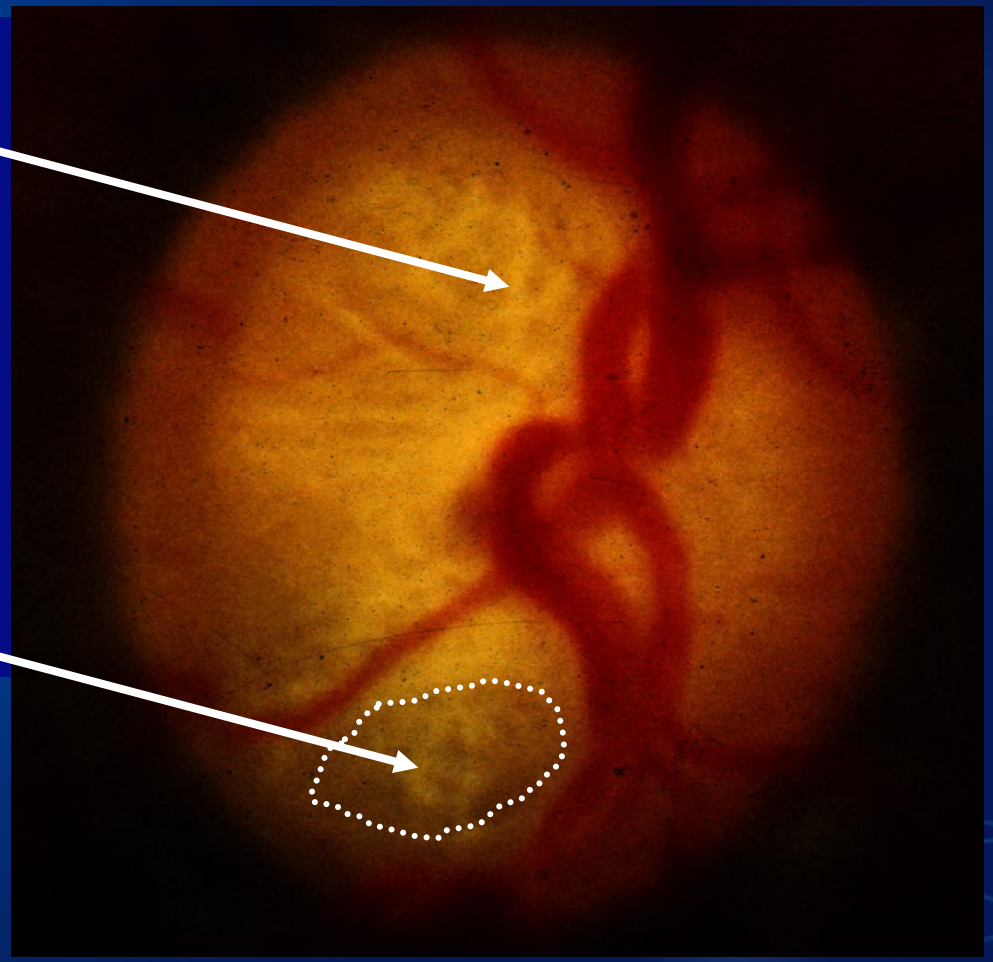
Photos courtesy of GT Sunil and L Vijaya

Internal use

Lamina cribrosa

Striated pattern
(Susanna 1983)
★

Acquired optic pit
(Radius *et al*. 1978)
★ ★ ★



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Internal use

Congenital pit of optic nerve

Photo courtesy of GT Sunil and L Vijaya

Internal use

Acquired pit of optic nerve

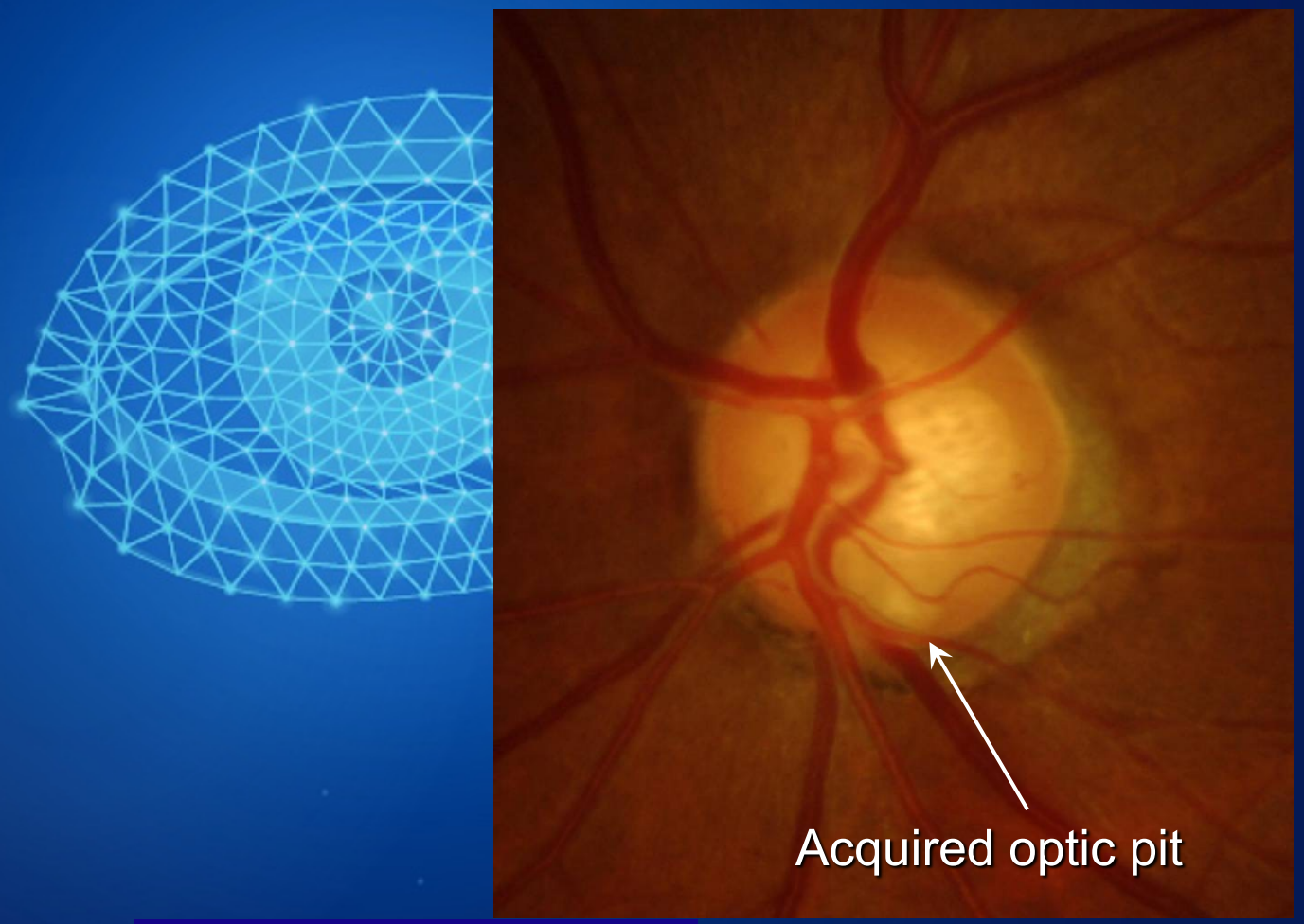
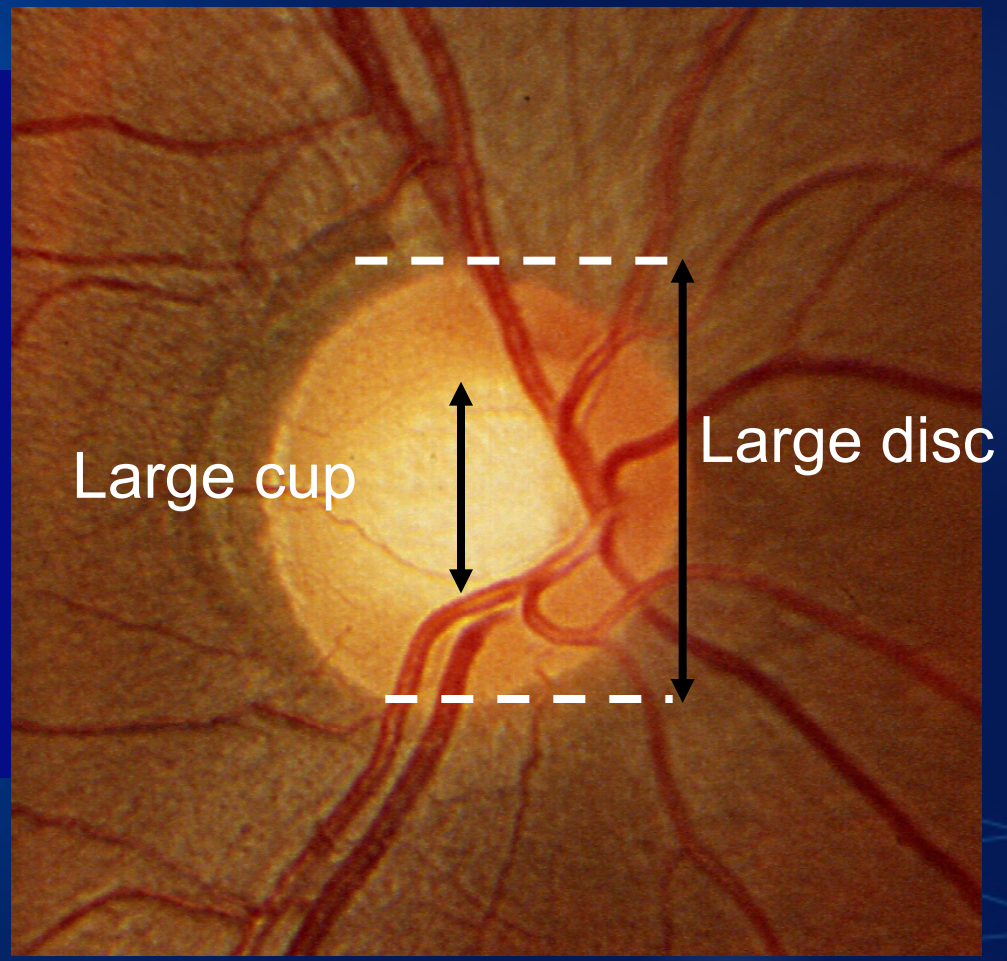


Photo courtesy of Ki Ho Park

Internal use

Normal optic nerve head

- Remember that a normal large disc has a large cup
  - ISNT rule obeyed
  - Cup = pallor



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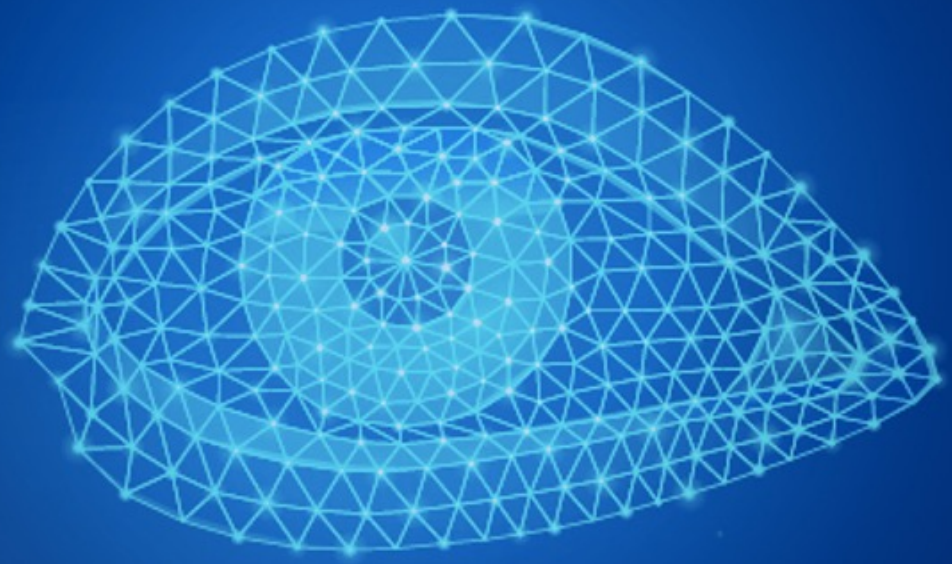
Internal use



Rule 3

Examine the

Retinal nerve fibre layer

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Internal use

RNFL examination

- Best performed using red-free light (red-free photographs or green light)
- Look at
  - Striations
  - Brightness
  - Visibility of peripapillary retinal vessels
- Look for diffuse and localised RNFL loss

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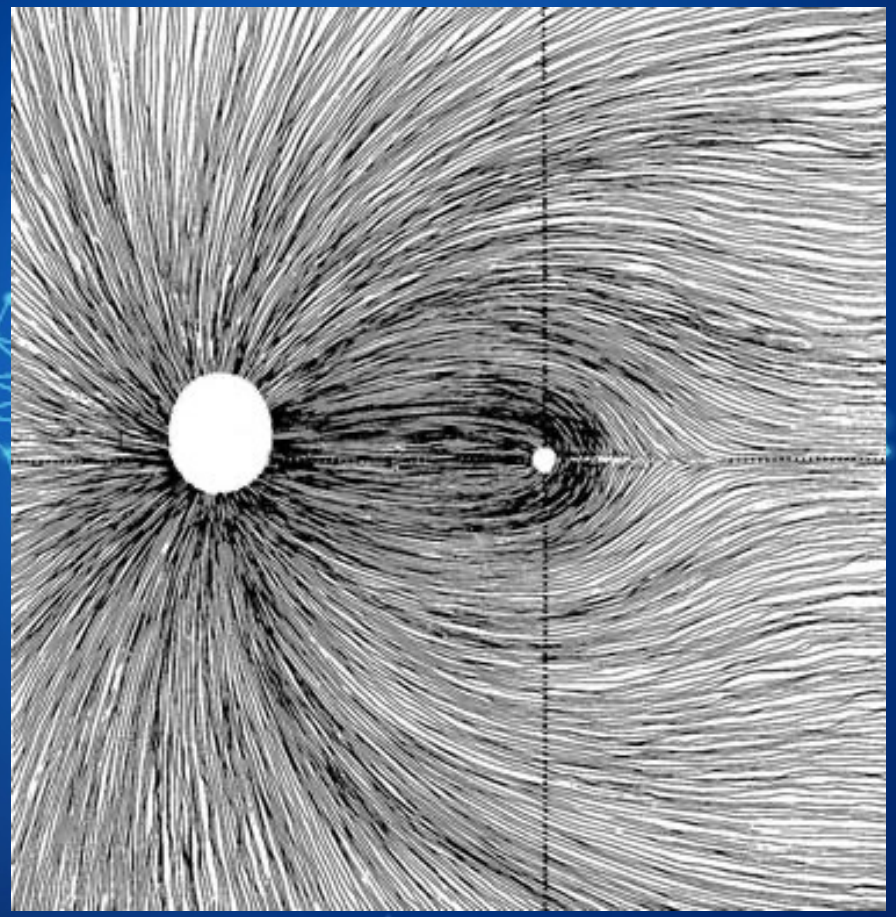
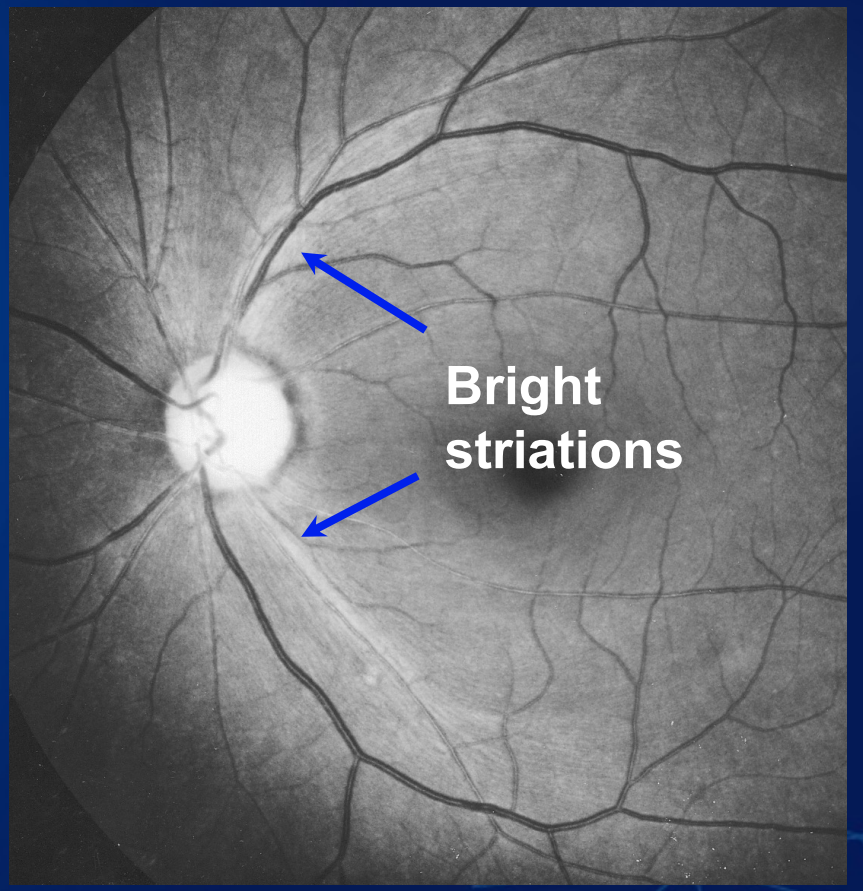
Internal use

Red-free photography





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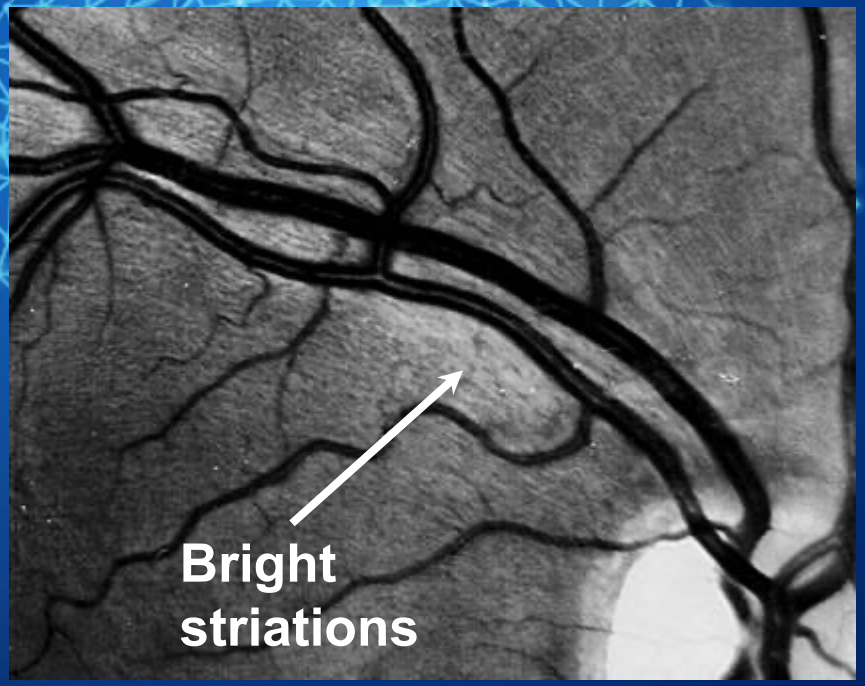
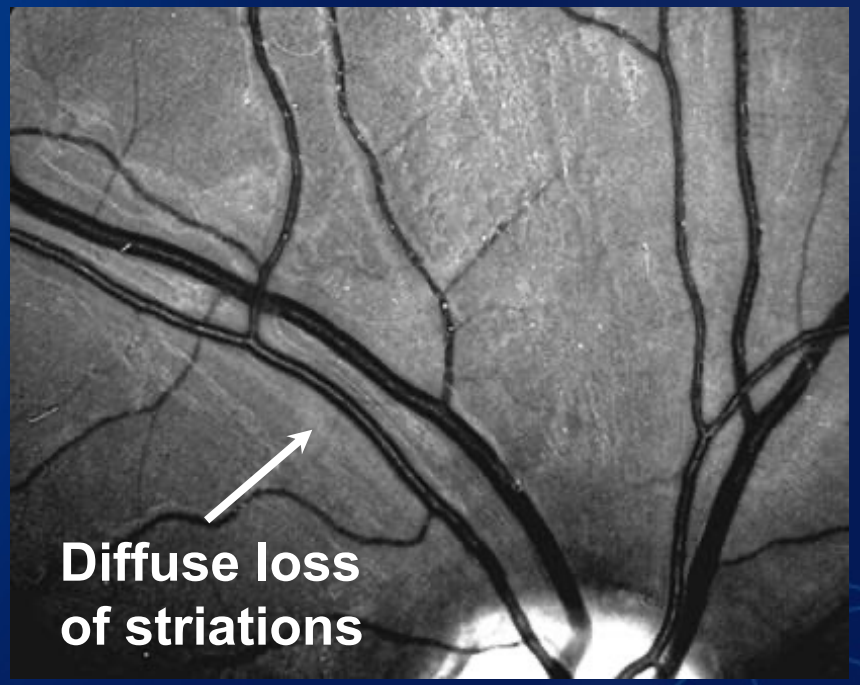
Right photo courtesy of Ki Ho Park

Internal use

Diffuse RNFL loss (1)

- Diffuse loss of striate pattern
- Increased visibility of retinal vessel borders



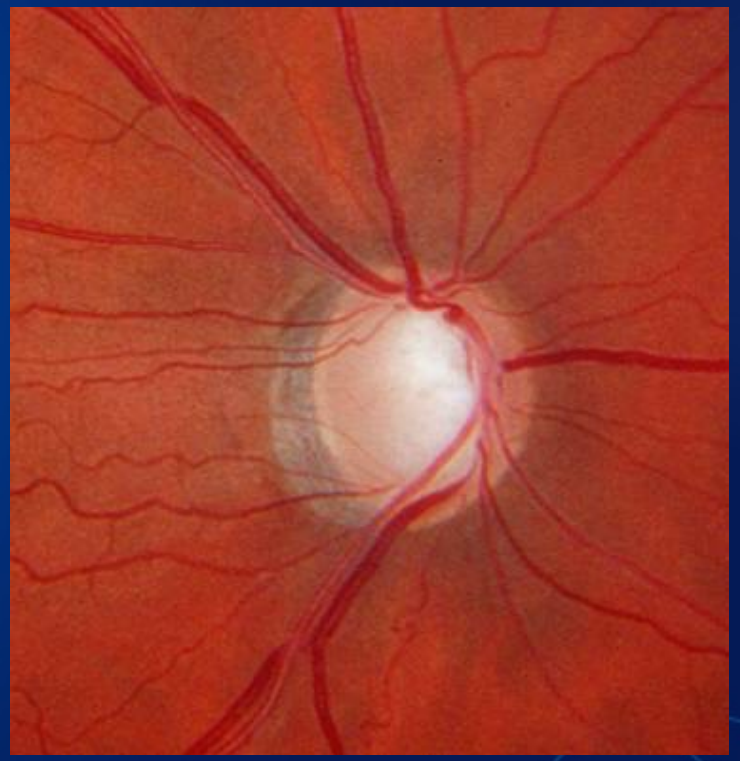


Internal use

Diffuse RNFL loss (2)

Normal RNFL

★ ★ ★

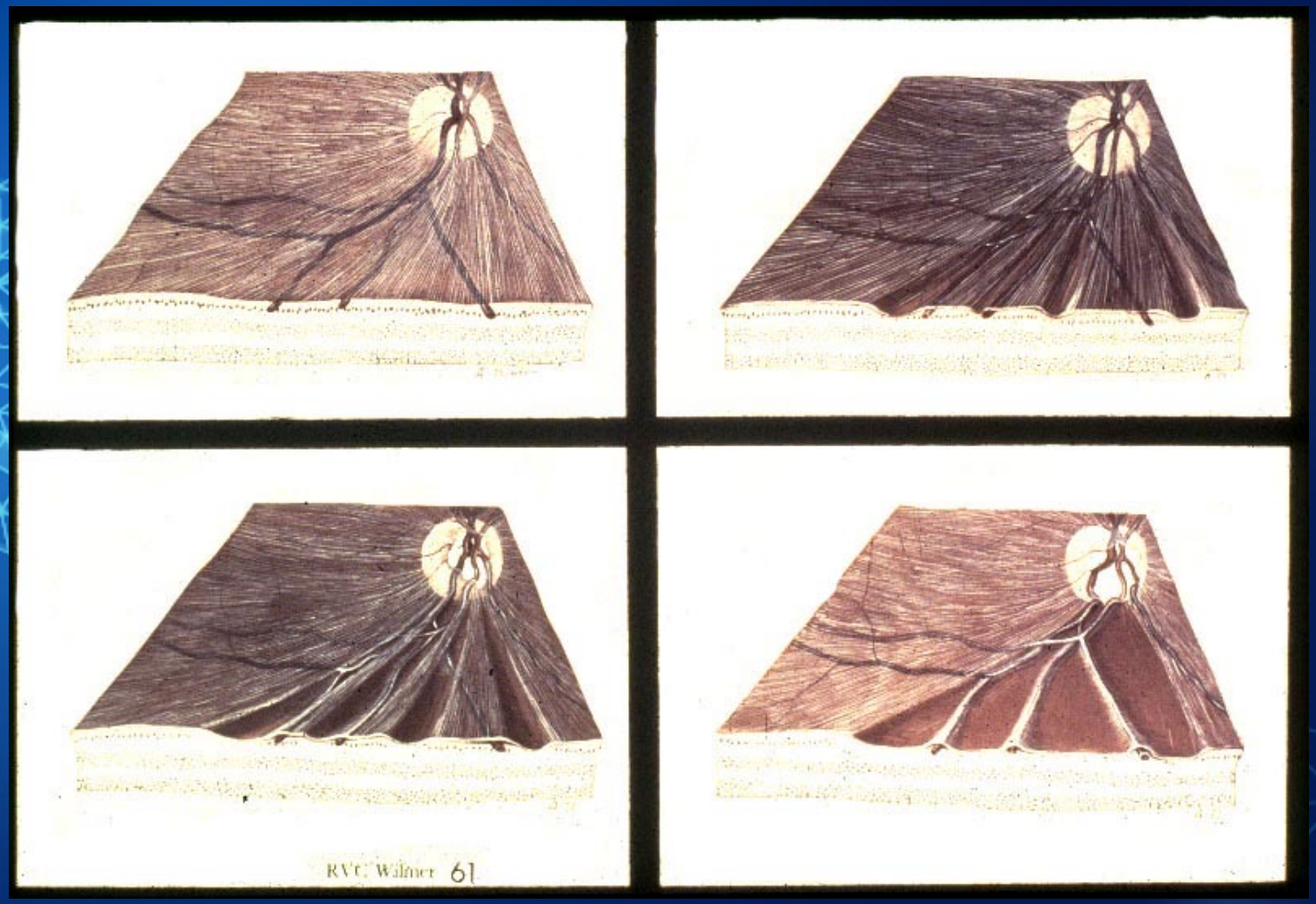


Diffuse RNFL loss

©2004 Remo Susanna Jr

Internal use

Localised RNFL loss (1)



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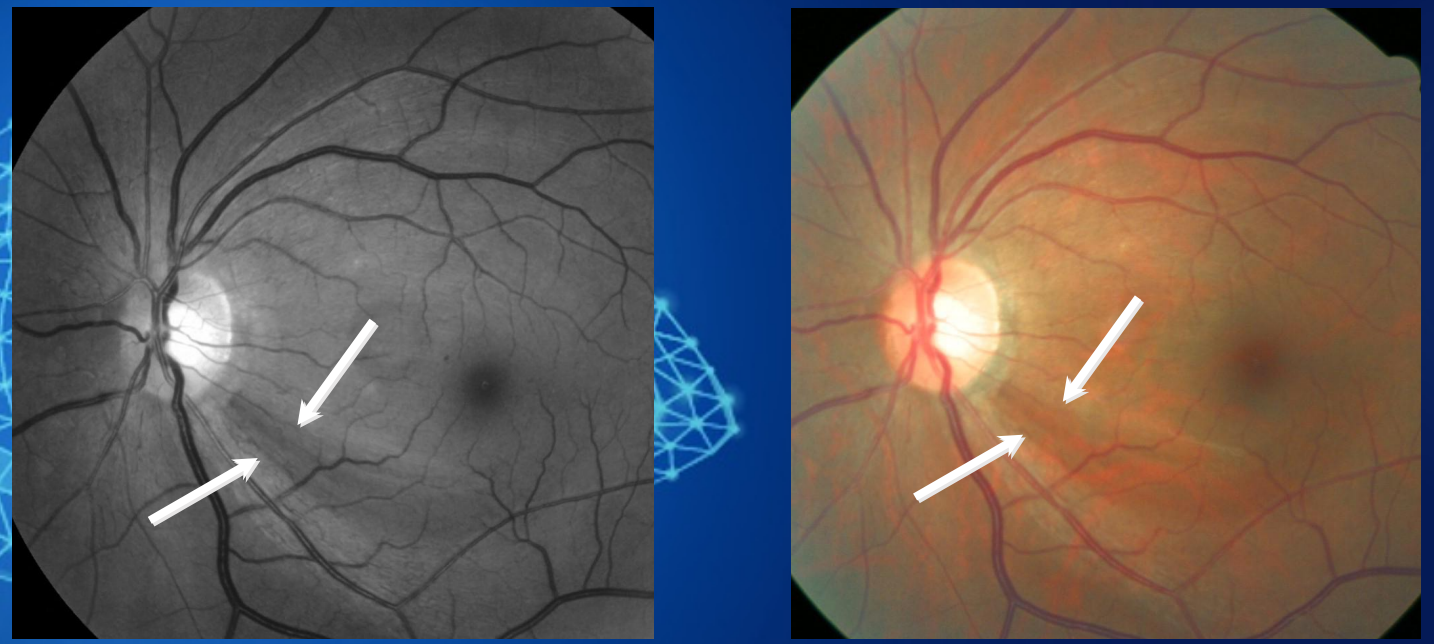
Internal use

Localised RNFL loss (2)



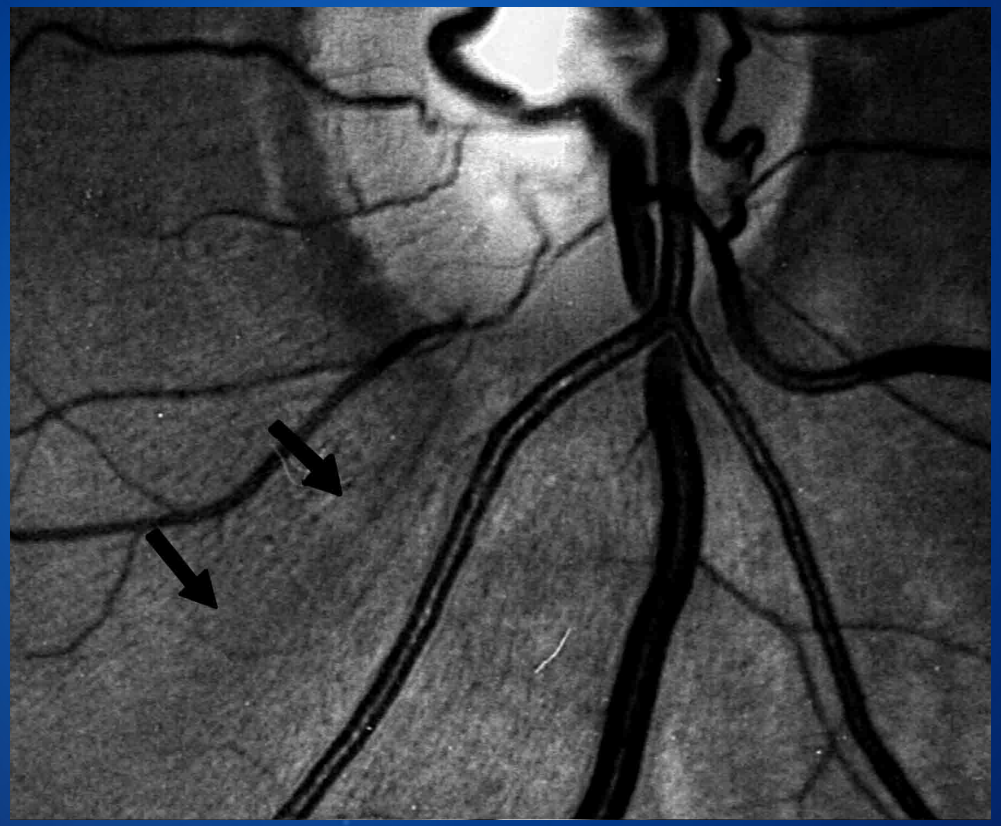
Localised RNFL defect

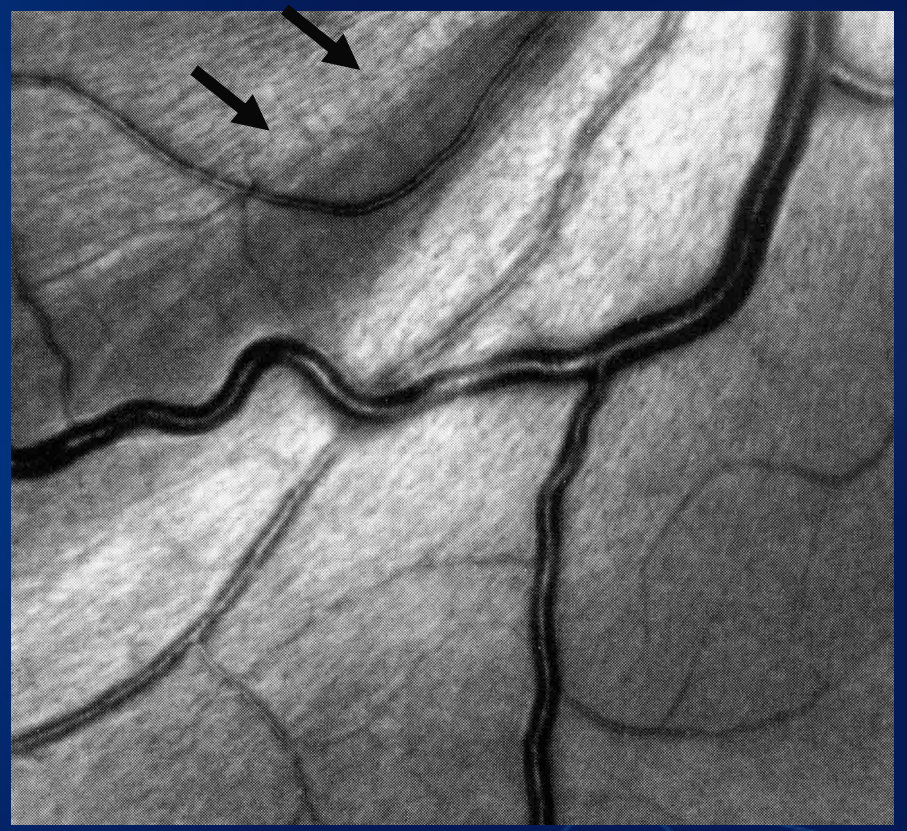
Wedge-shaped dark area

Photos courtesy of Ki Ho Park

Internal use

Localised RNFL loss (3)





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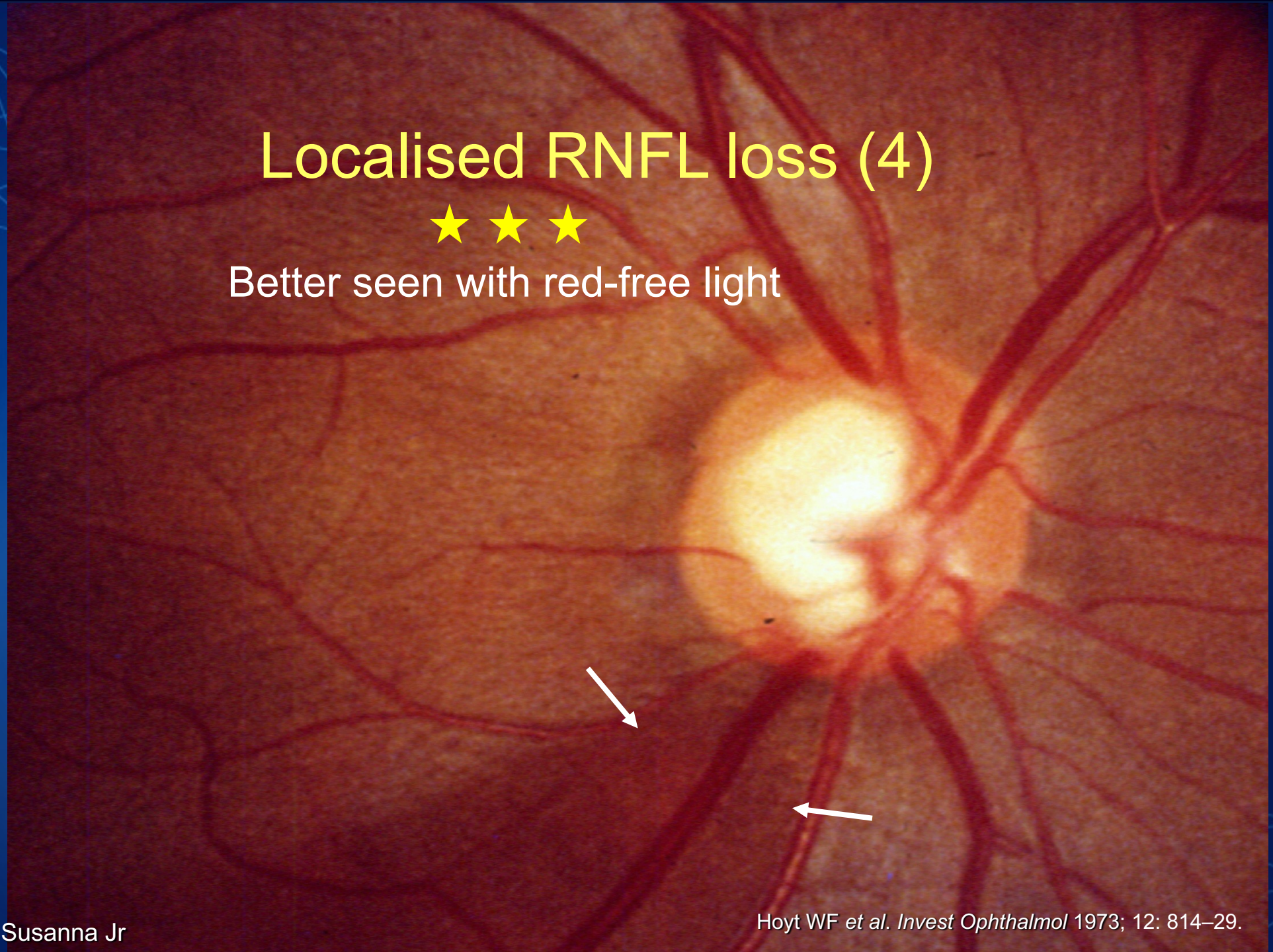
Localised RNFL loss (4)

★ ★ ★

Better seen with red-free light



Hoyt WF *et al. Invest Ophthalmol* 1973; 12: 814–29.

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Internal use

Localised RNFL loss (5)

Wedge-shaped dark area

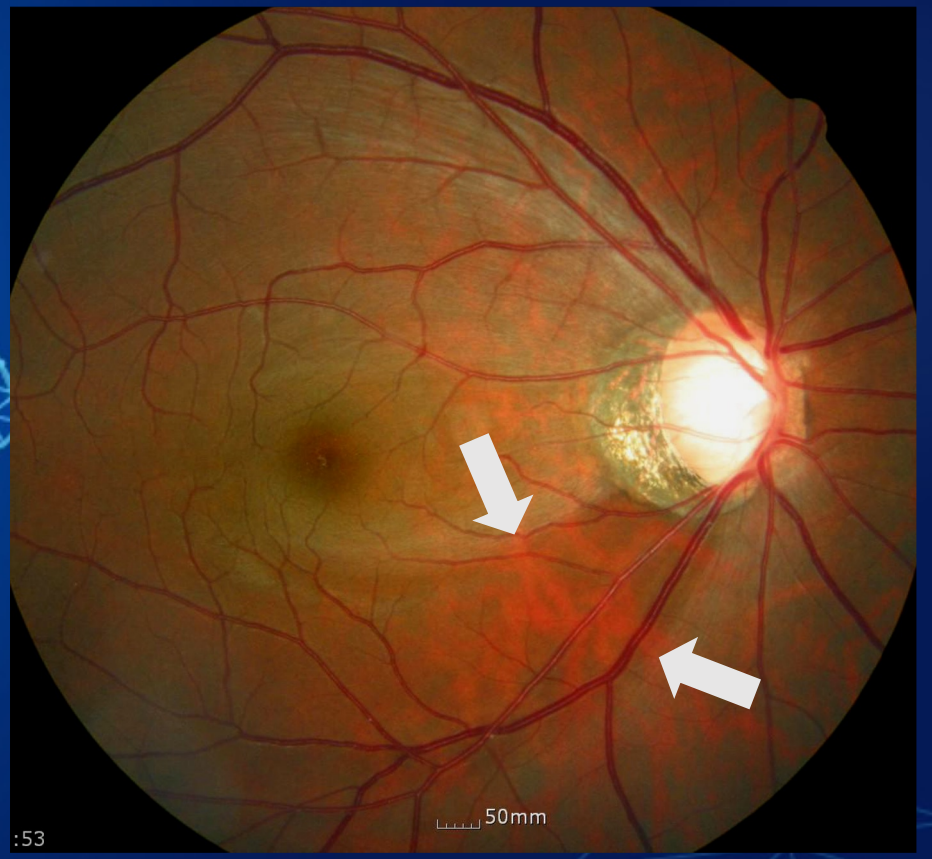
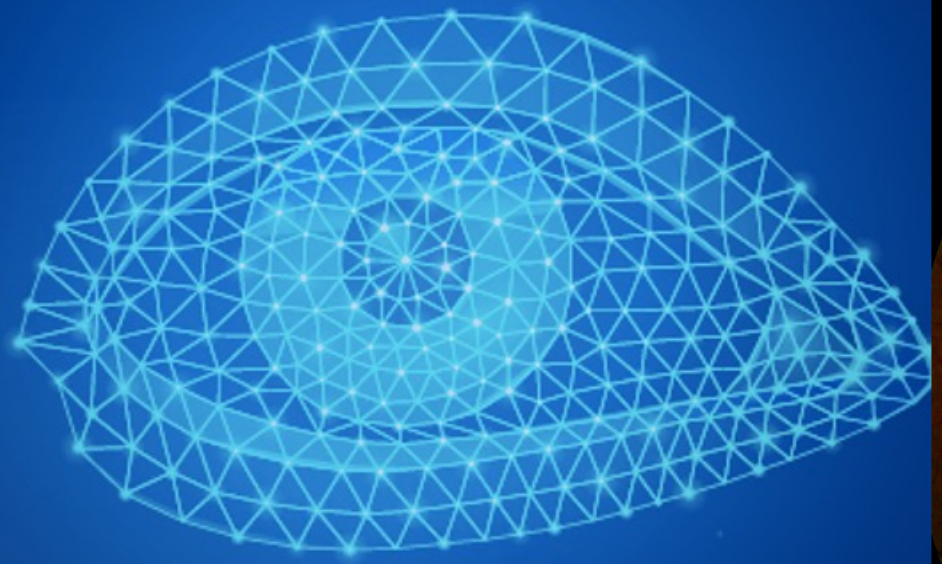


Photo courtesy of Ki Ho Park

Internal use

Localised RNFL loss (6)



Wedge-shaped dark area

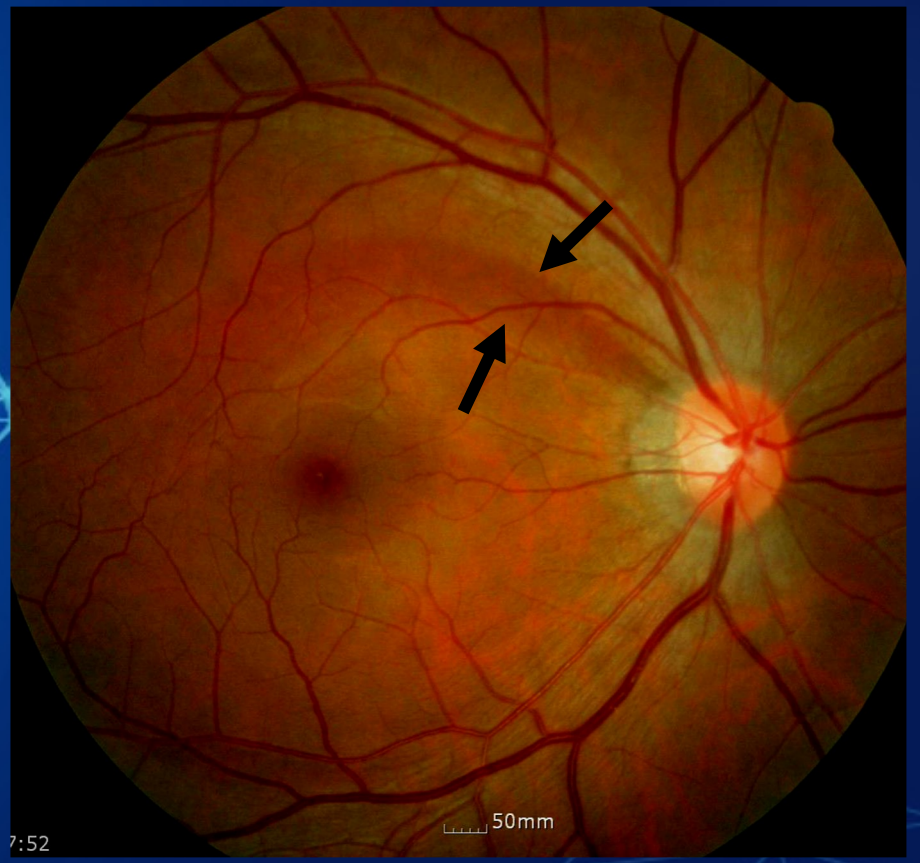
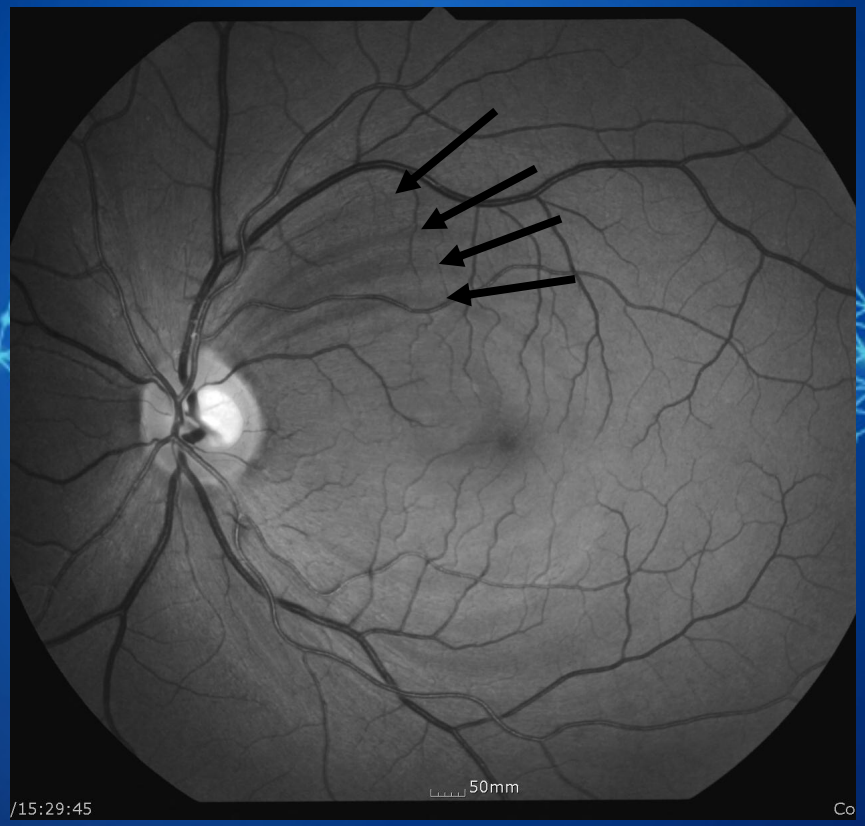
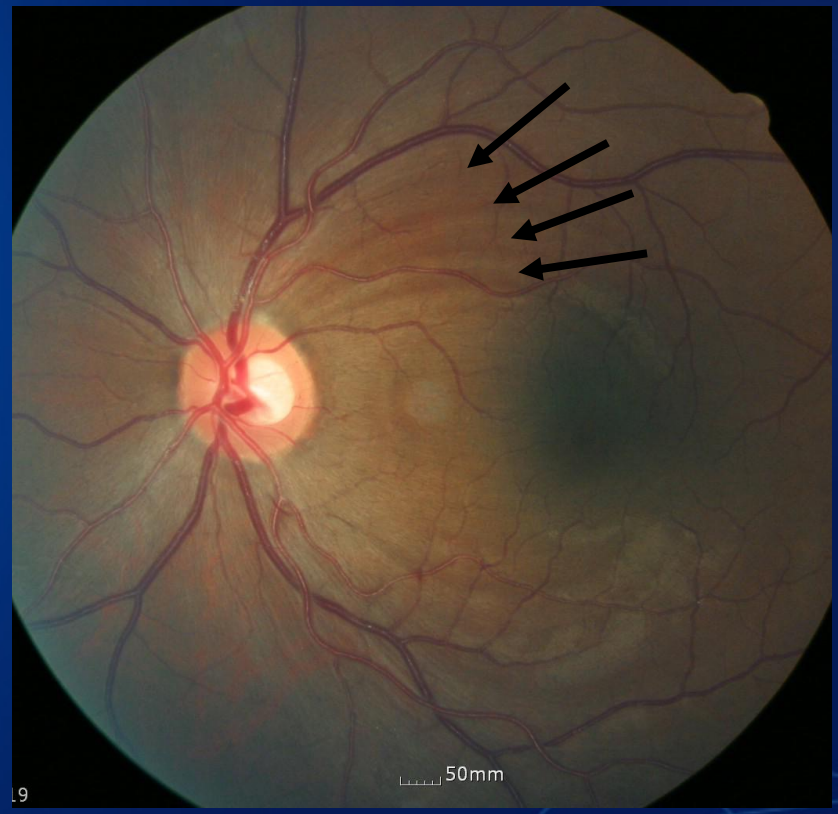


Photo courtesy of Ki Ho Park

Internal use

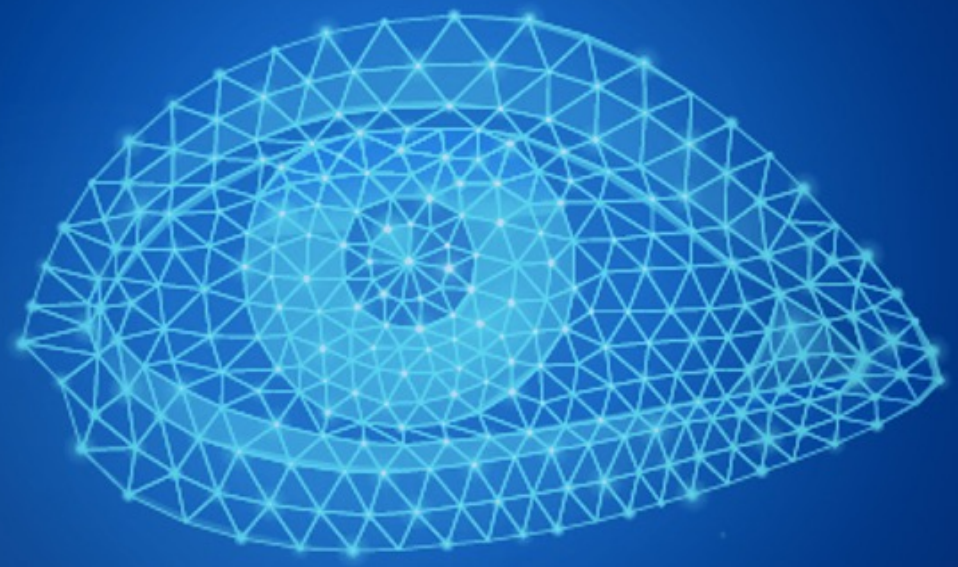
Localised RNFL loss (7)





Photos courtesy of Ki Ho Park

Internal use



Rule 4

Examine the Region of peripapillary atrophy

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Internal use

Peripapillary atrophy (1)

Alpha zone

Hypo- and hyper-pigmented areas

Present in normal as well as in glaucomatous eyes

Beta zone

Atrophy of the retinal pigment epithelium and choriocapillaris

Large choroidal vessels become visible

More common in glaucomatous eyes

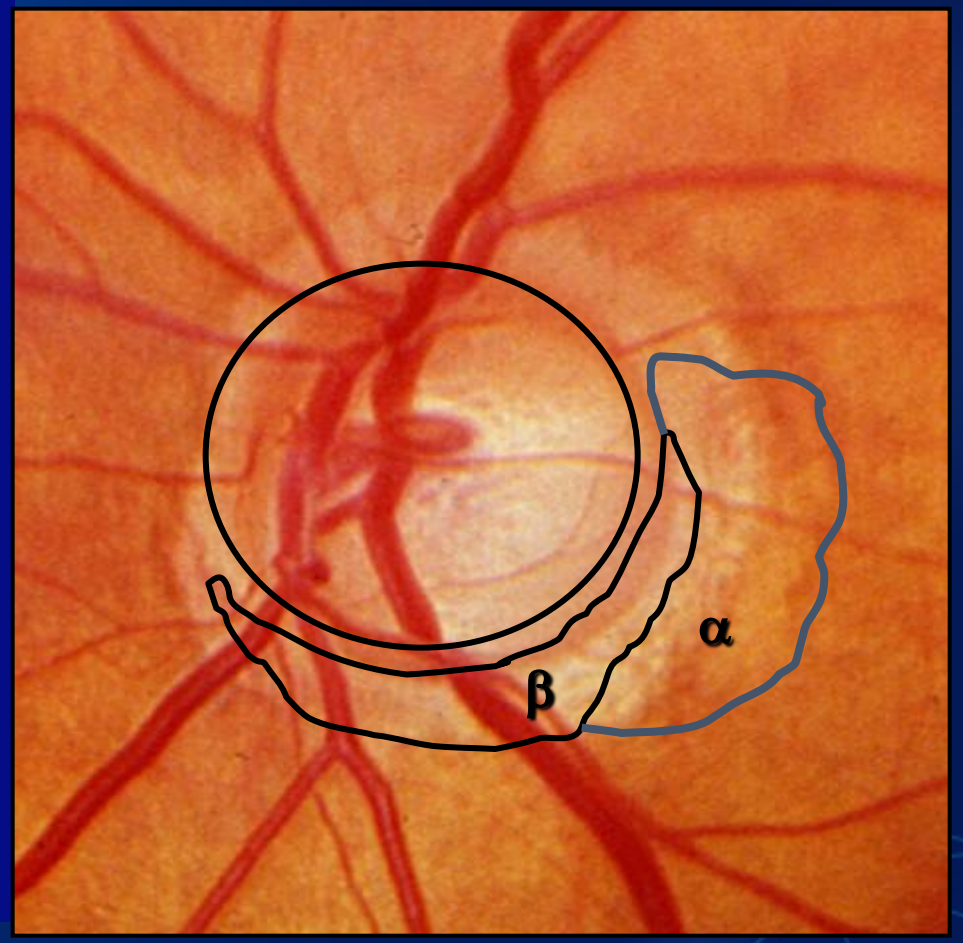

Photo courtesy of Ki Ho Park

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Internal use

Peripapillary atrophy (2)

Alpha zone

Beta zone ★

- Sensitivity 20–30%
- Specificity 80%
- 360º ring –normotensive senile sclerotic glaucoma

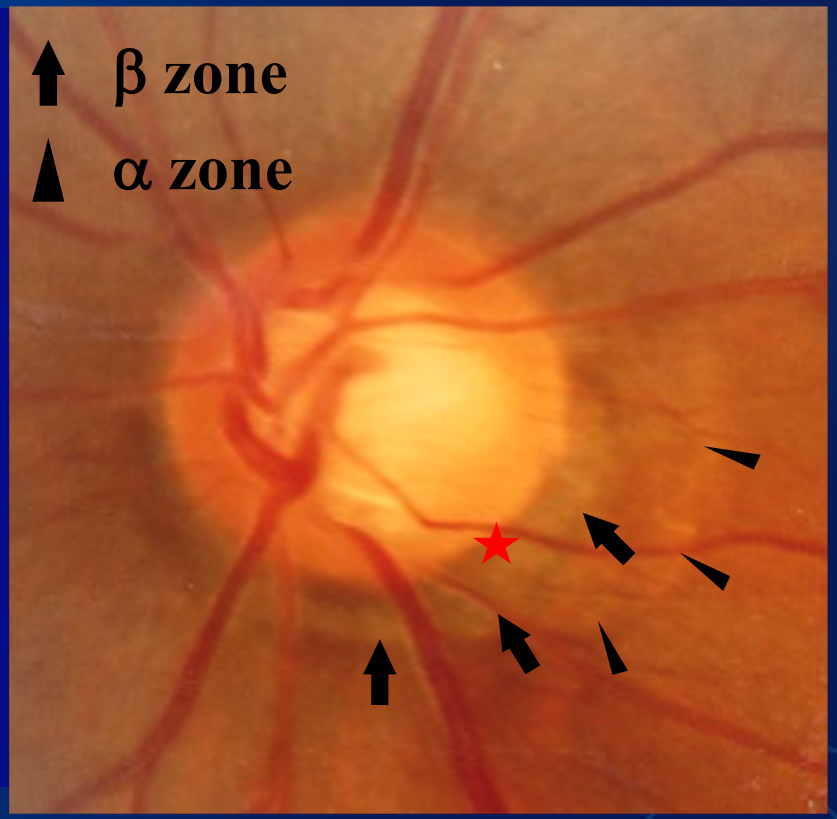

Photo courtesy of Ki Ho Park

Jonas JB *et al*. *Invest Ophthalmol Vis Sci* 2000; 41: 1764–73.

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Internal use

Peripapillary atrophy (3)

Beta zone

- Width of beta zone inversely correlates with rim width at same area
- Larger beta zone → thinner rim
- Progression of beta zone associated with progressive glaucoma

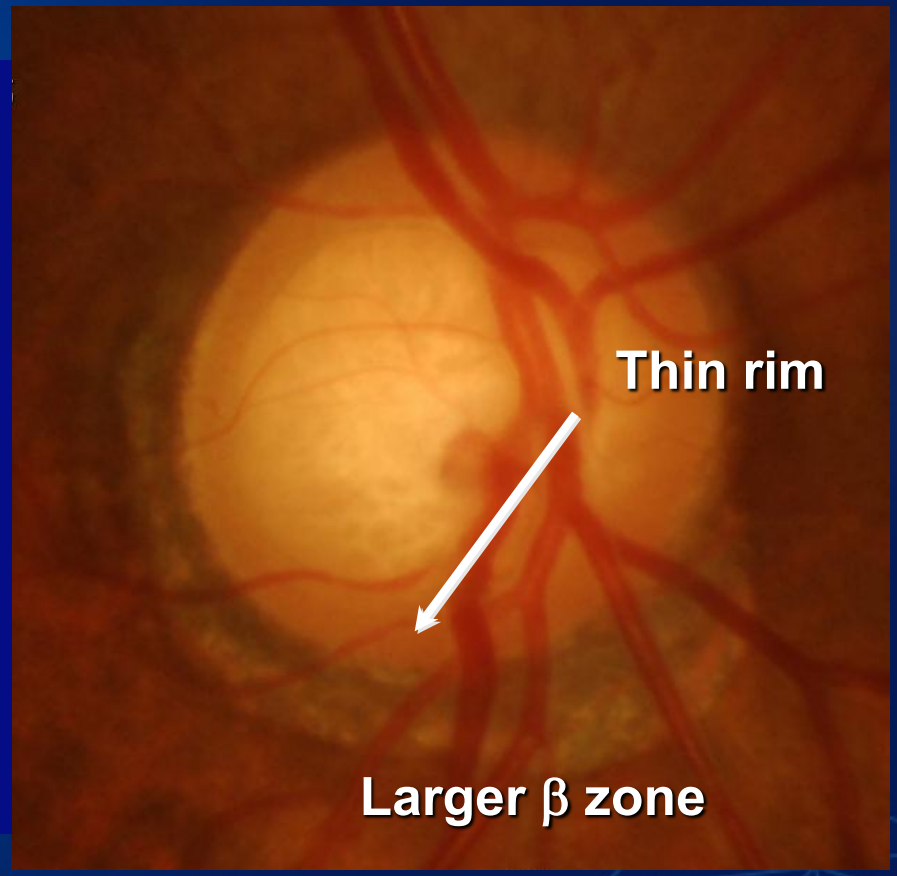

Photo courtesy of Ki Ho Park

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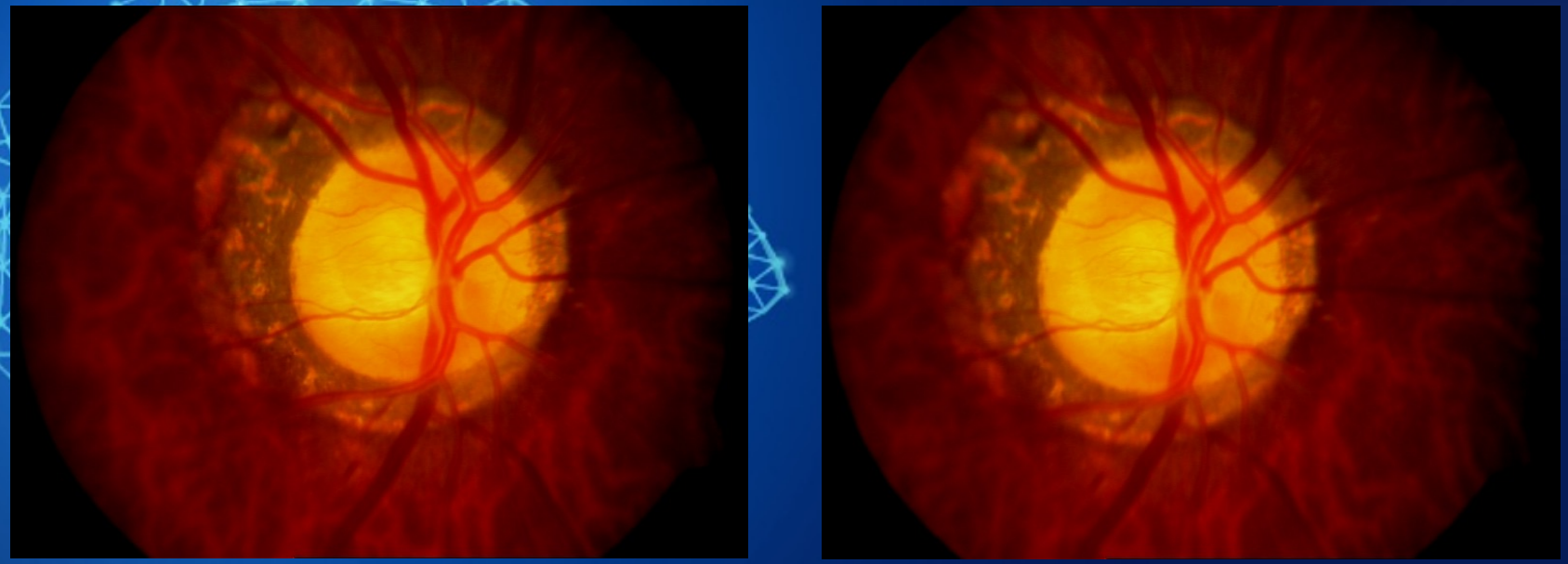
Internal use

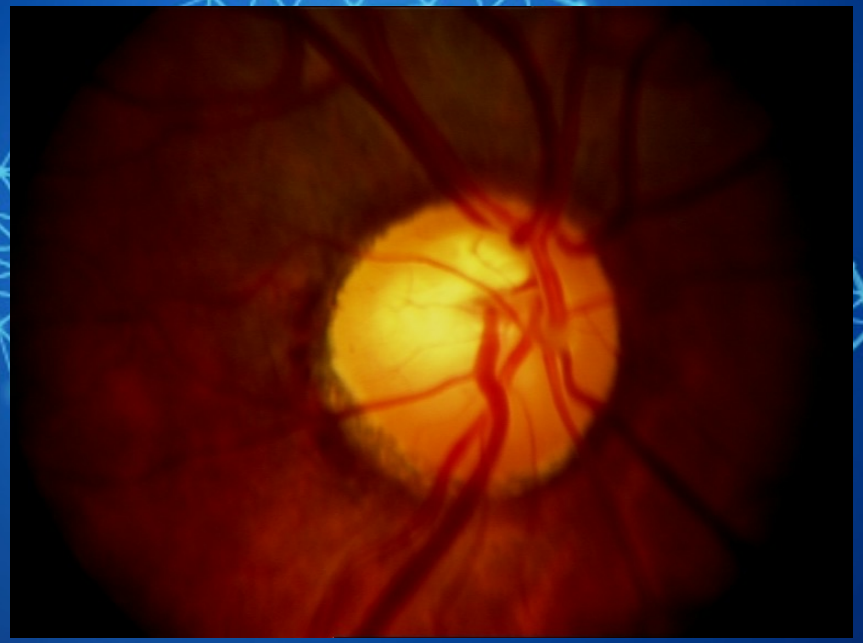
Peripapillary atrophy (4)



Photos courtesy of GT Sunil and L Vijaya

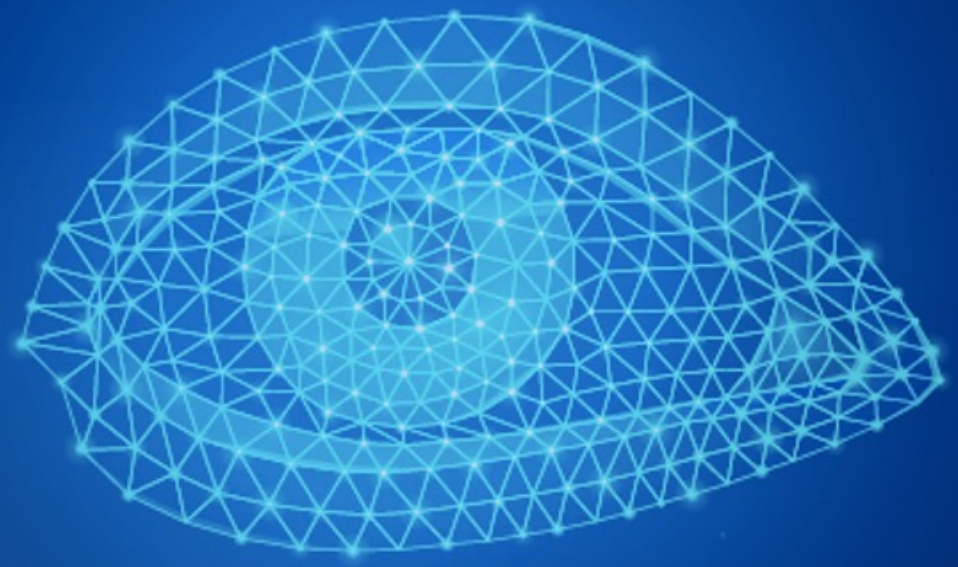
Internal use

Peripapillary atrophy (5)



Photos courtesy of GT Sunil and L Vijaya

Internal use



Rule 5

Look for Retinal and optic disc haemorrhages

★ ★ ★

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Internal use

Optic disc haemorrhage (1)

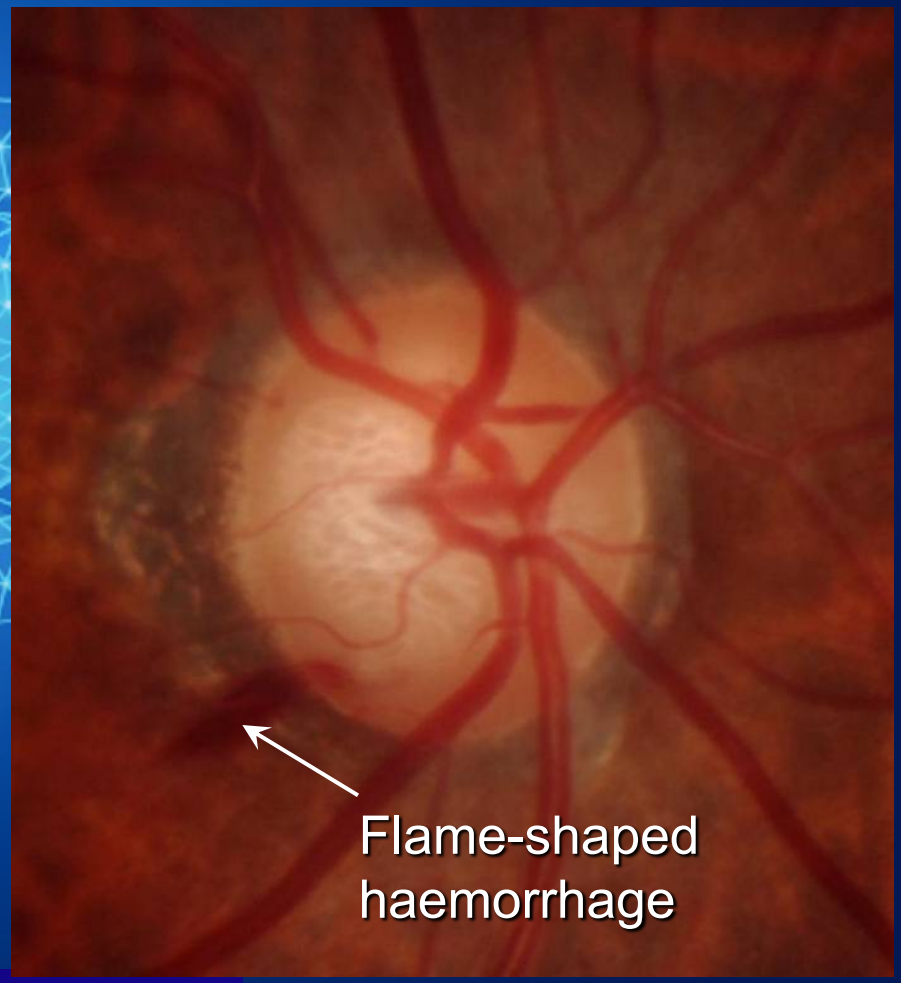


Photo courtesy of Ki Ho Park

Internal use

Optic disc haemorrhage (2)

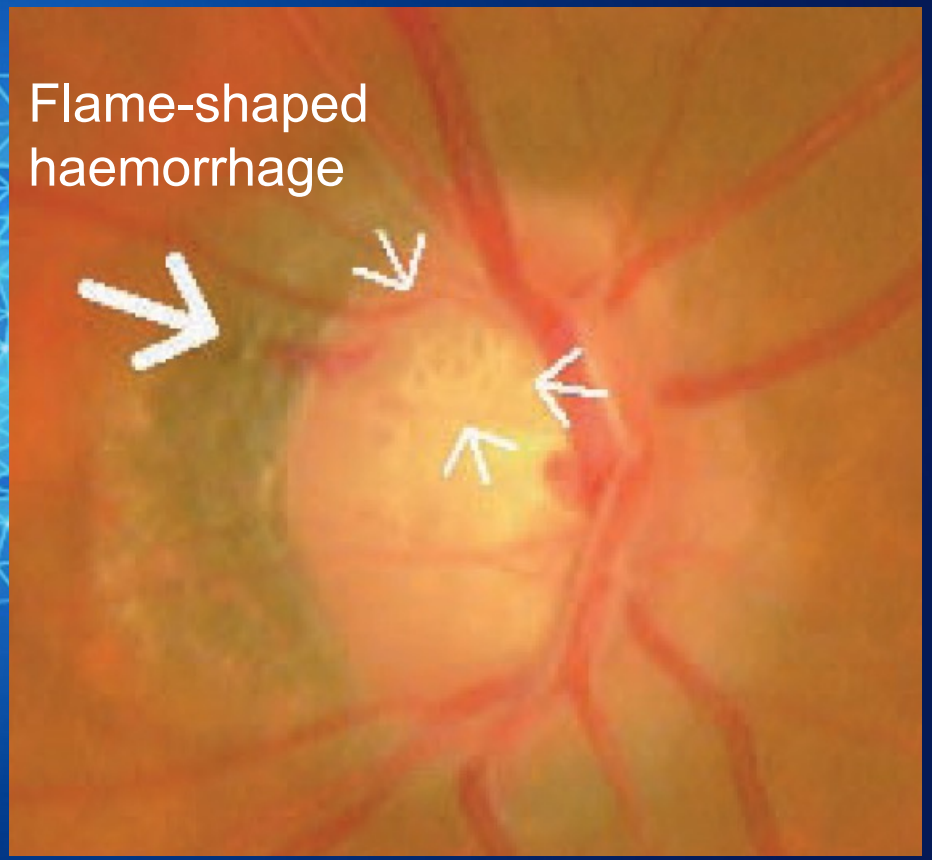


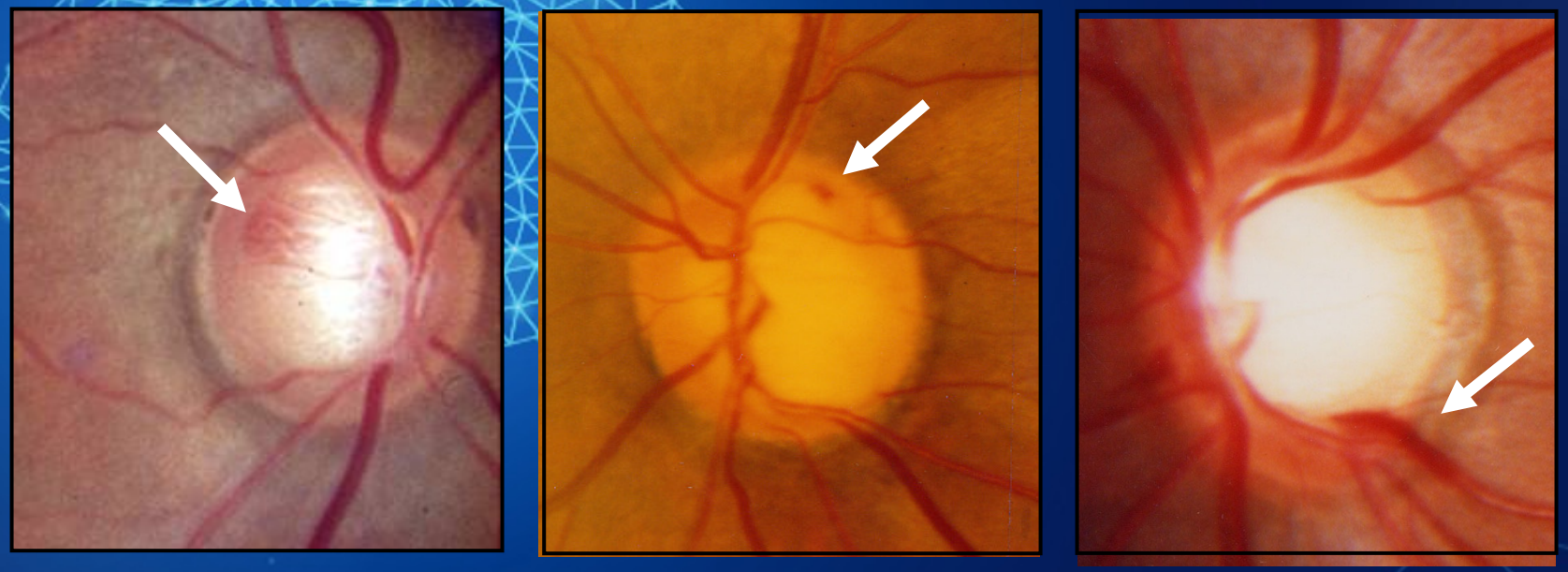
Photo courtesy of Prin Rojanapongpun

Splinter, superficial, flame-shaped haemorrhage at the disc margin (large arrow).
Localised loss of neuroretinal rim is evident at the corresponding area and laminar dots are also visible. The small arrows highlight a pit-like notch at the superotemporal rim.

Internal use

Optic disc haemorrhage (3)

Detection of disc haemorrhages requires careful optic disc examination



Middle and right photos courtesy of Ki Ho Park

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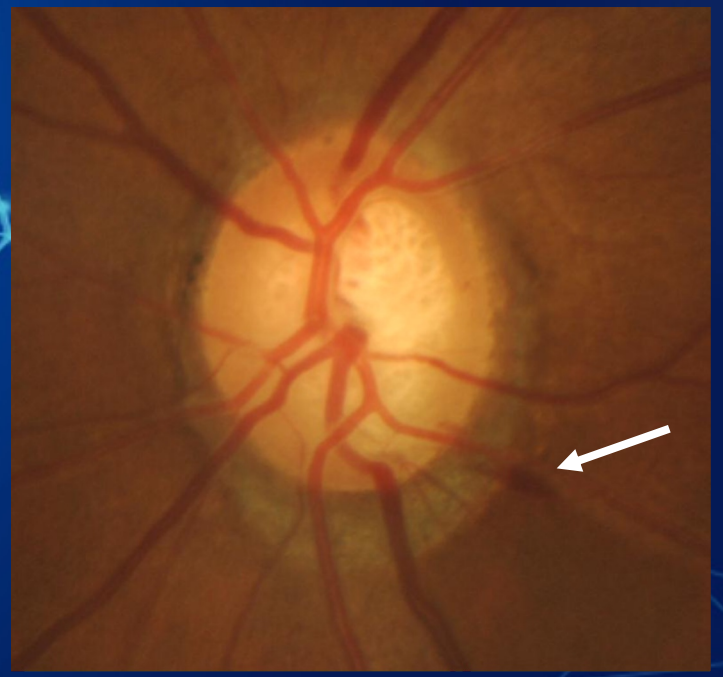
Internal use

Optic disc haemorrhage (4)

Detection of disc haemorrhages requires careful optic disc examination

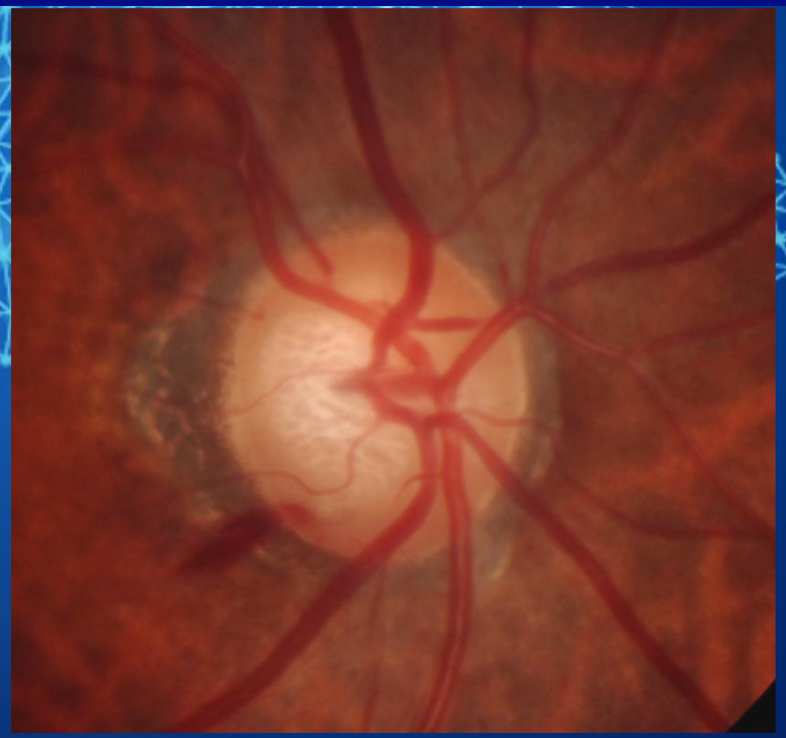


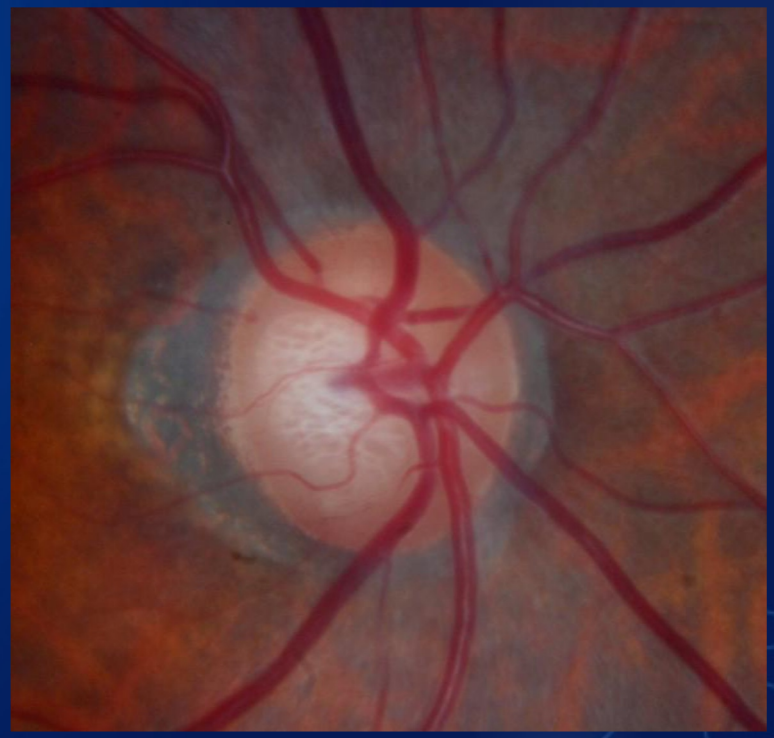
Photos courtesy of Ki Ho Park

Internal use

Optic disc haemorrhage (5)

- Normally disappears after 1–3 months
- Indicative of glaucomatous progression



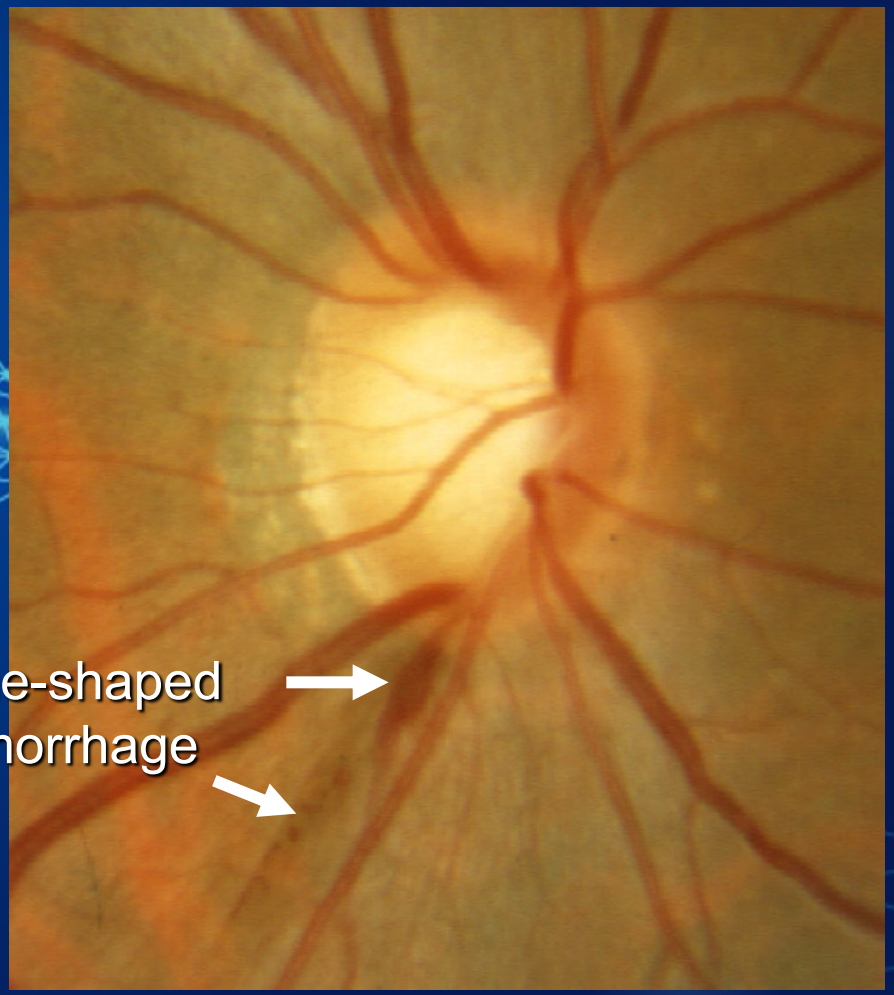


Photos courtesy of Ki Ho Park

Internal use

Optic disc haemorrhage (6)

- Normally disappears after 1–3 months
- Indicative of glaucoma progression



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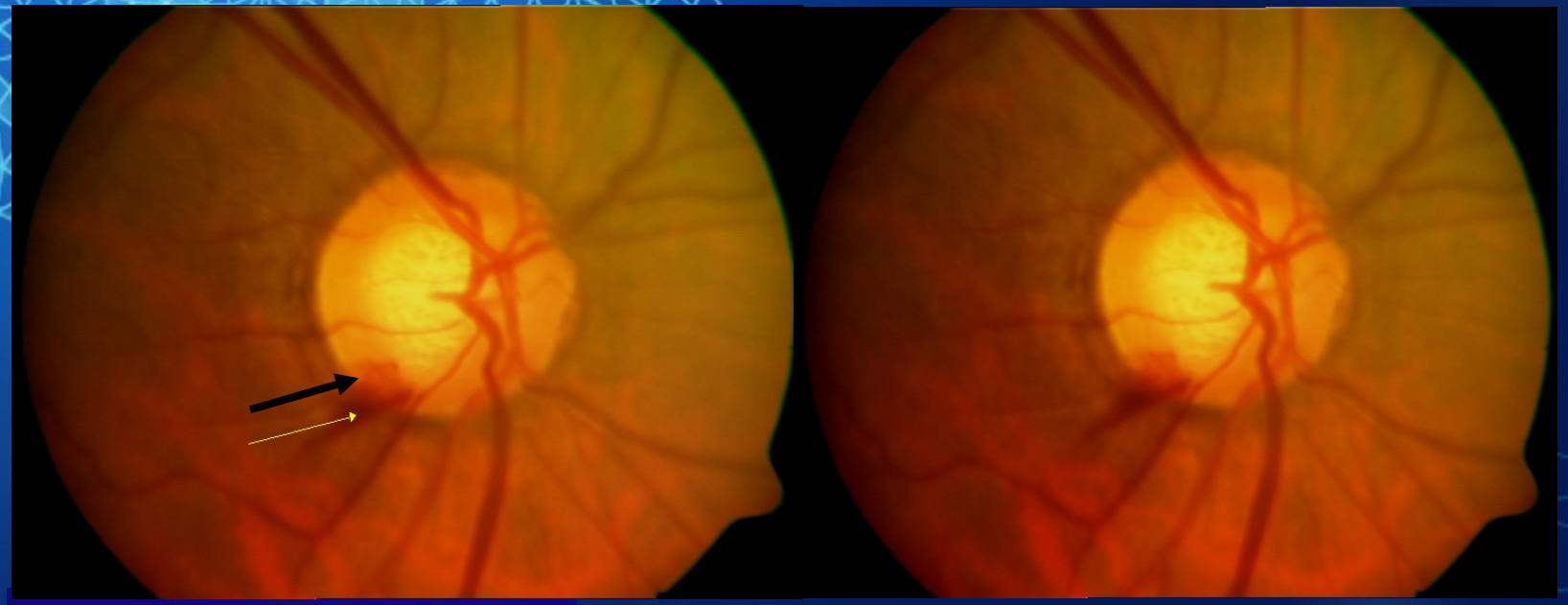
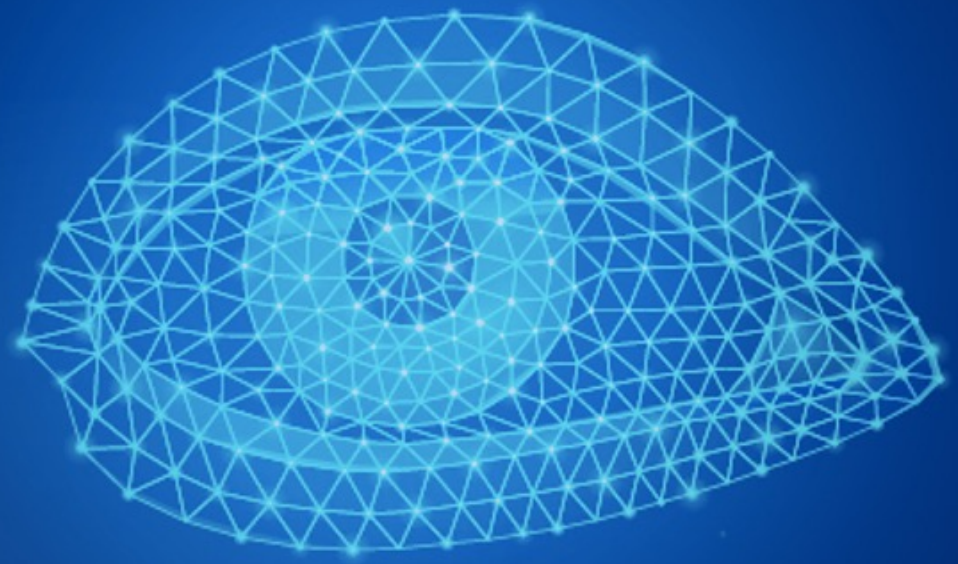
Internal use

Optic disc haemorrhage (7)



Photos courtesy of GT Sunil and L Vijaya

Internal use



DETECTING GLAUCOMA

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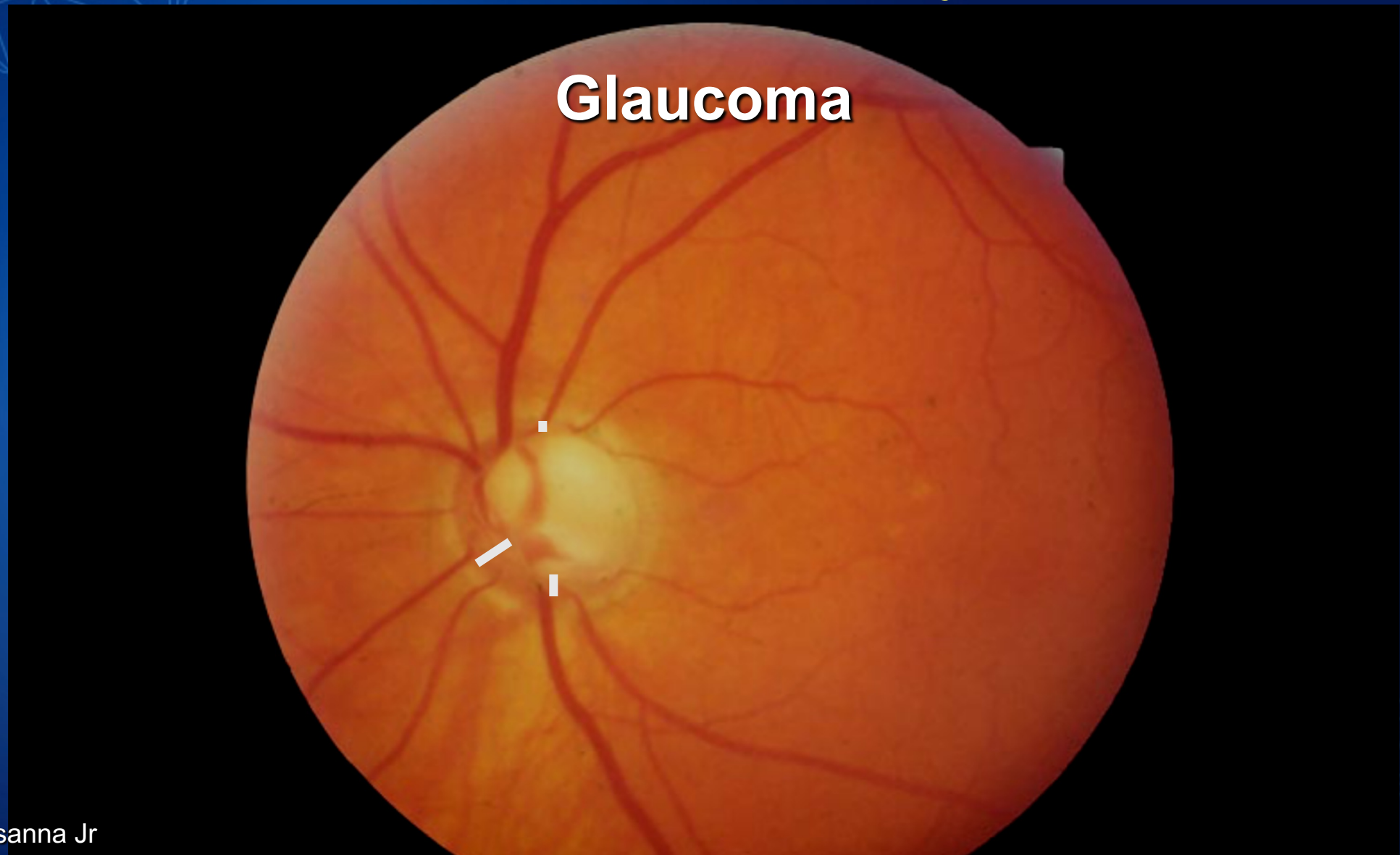
Internal use

ISNT rule is not obeyed ★★



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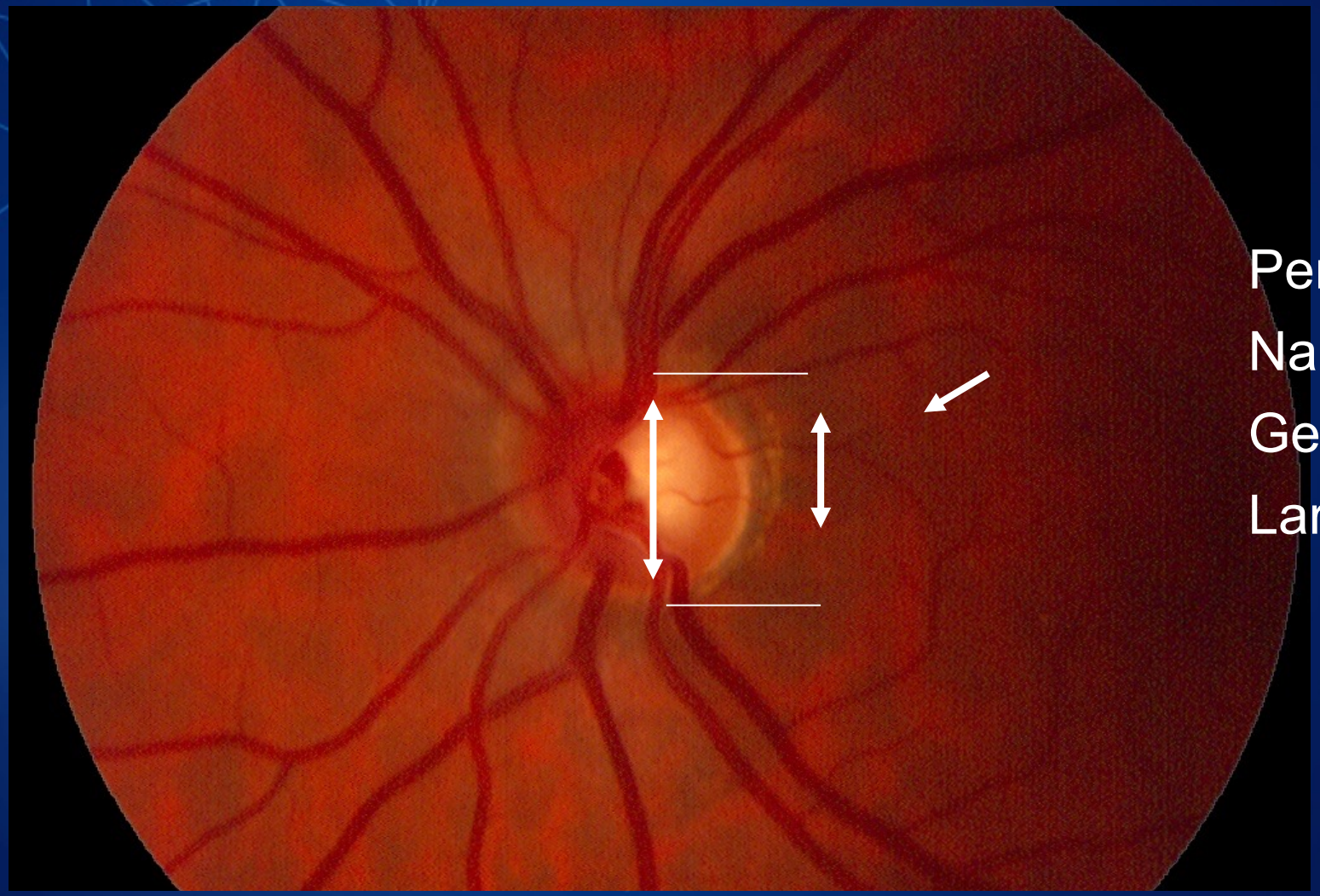
Internal use

Glaucoma – small disc



- Peripapillary atrophy ★
- Narrowing of retinal arteries ★
- Generalised RNFL loss ★★★
- Large cup for a small disc ★★★

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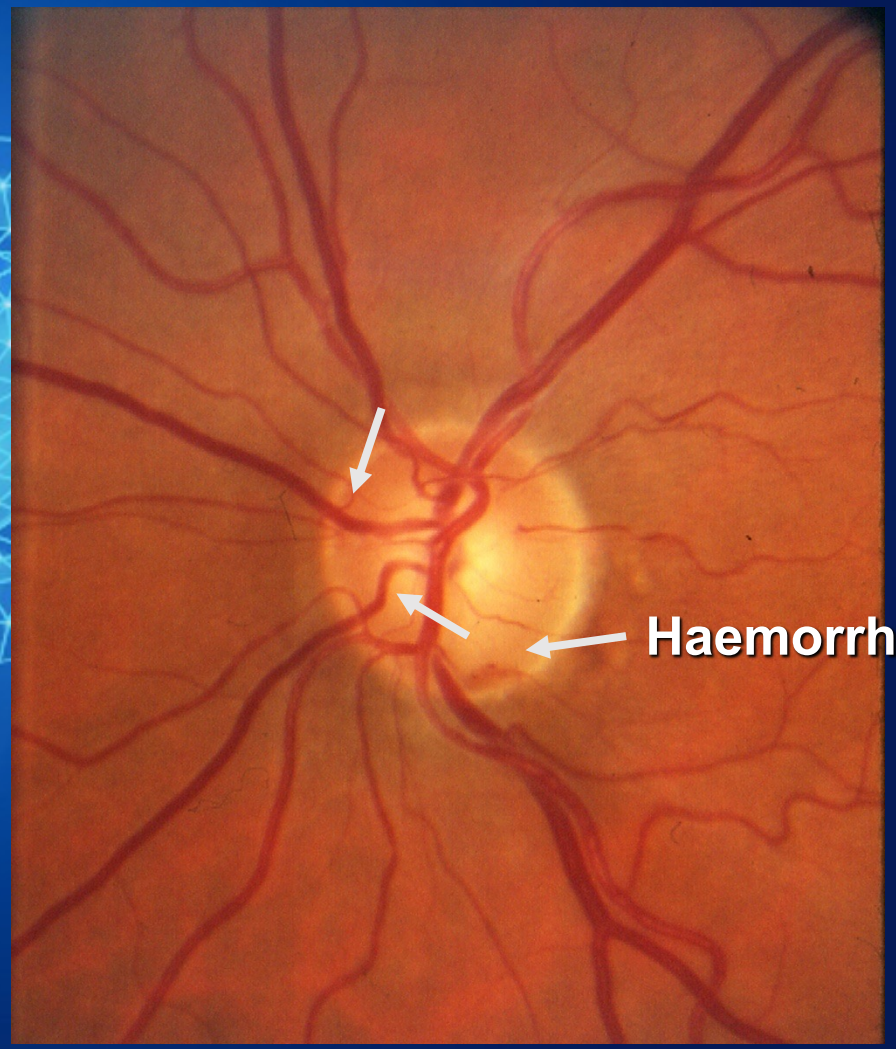
Internal use

Nasal cupping ★ ★ ★

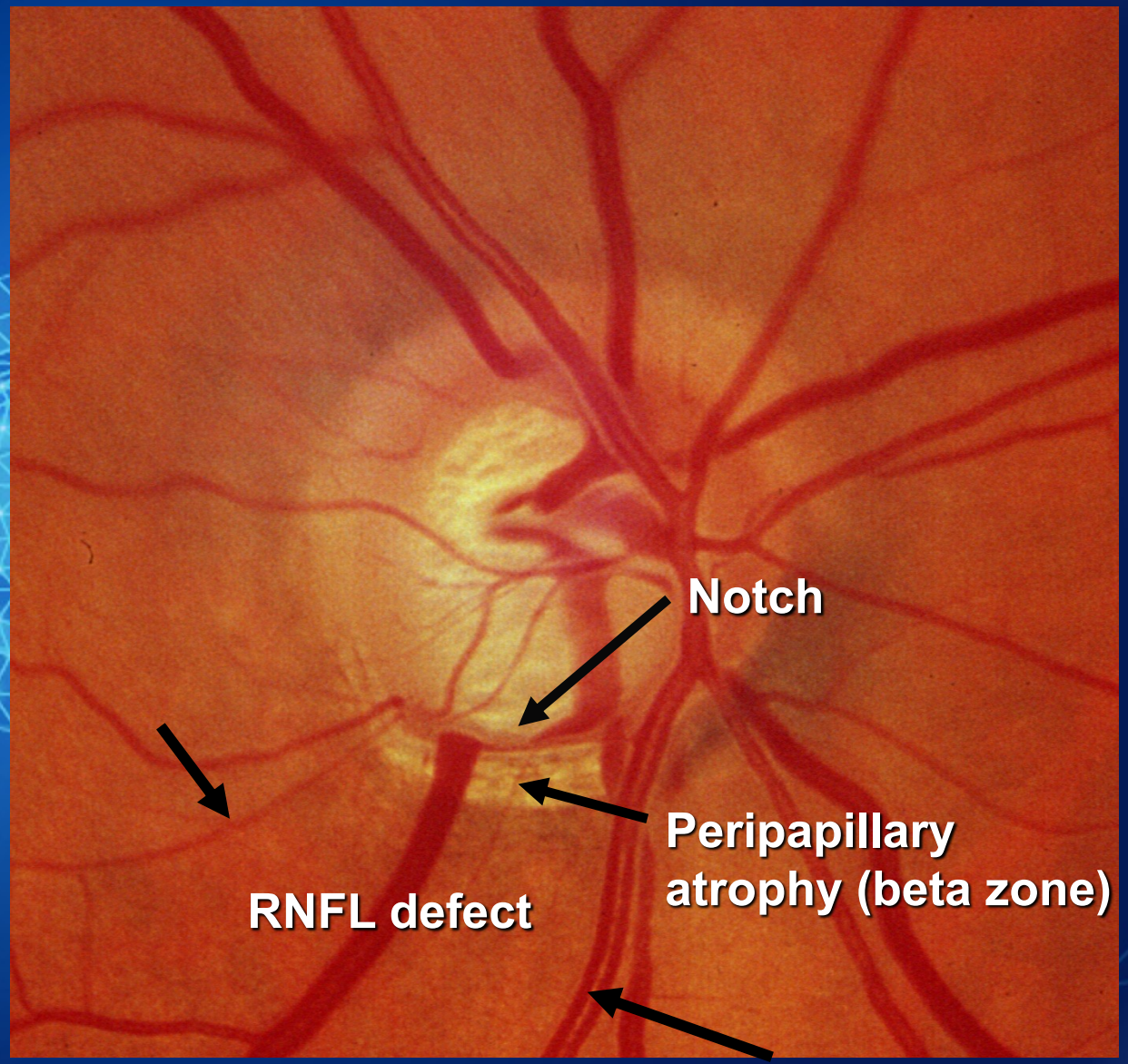


Read RM, Spaeth GL. *Trans Am Acad Ophthalmol Otolaryngol* 1974; 78: OP255–74.

©2004 Remo Susanna Jr

Internal use

Notch (1) ★ ★ ★



Hitchings RA, Spaeth GL. *Br J Ophthalmol* 1976; 60: 778–85.

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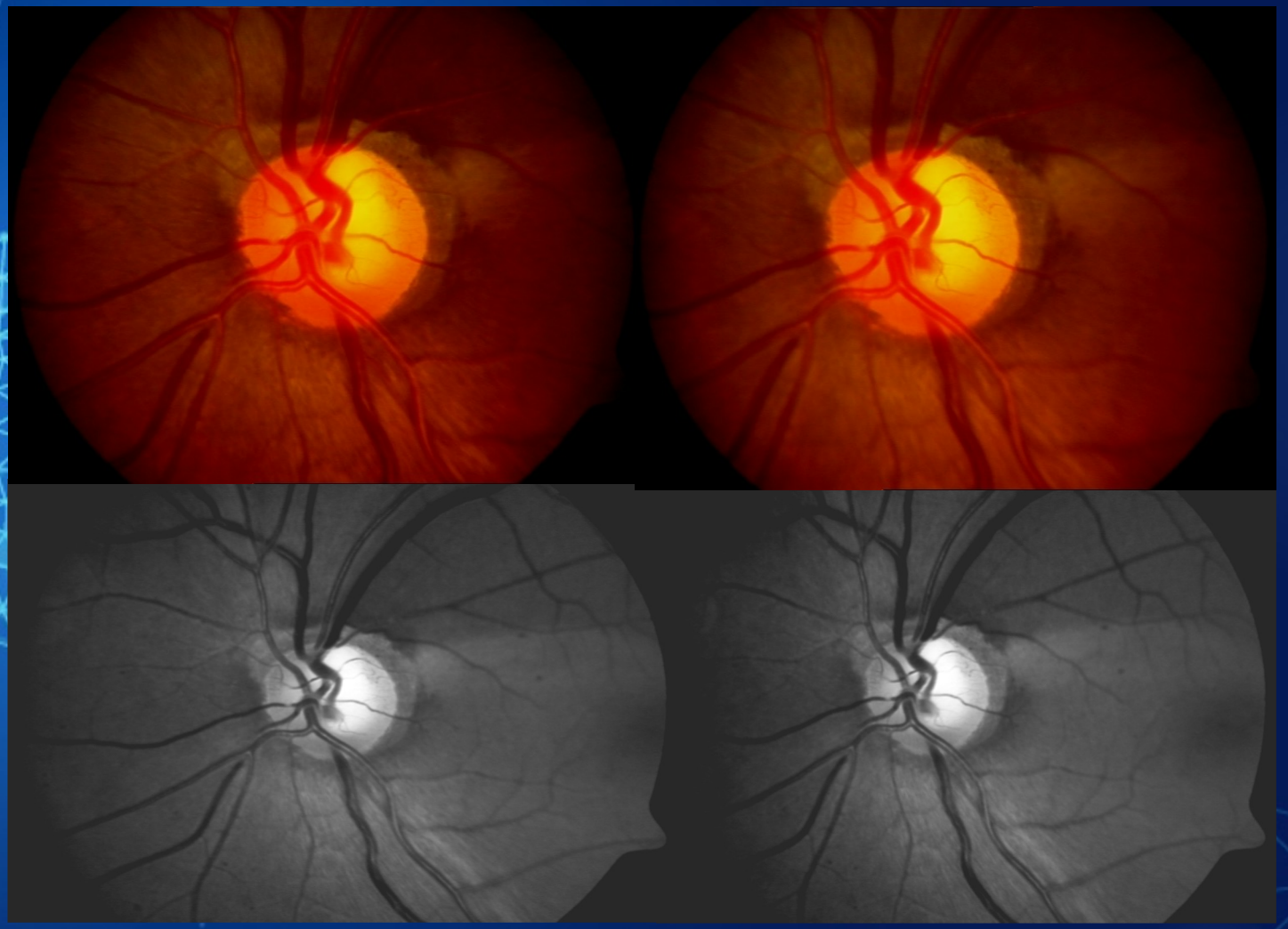
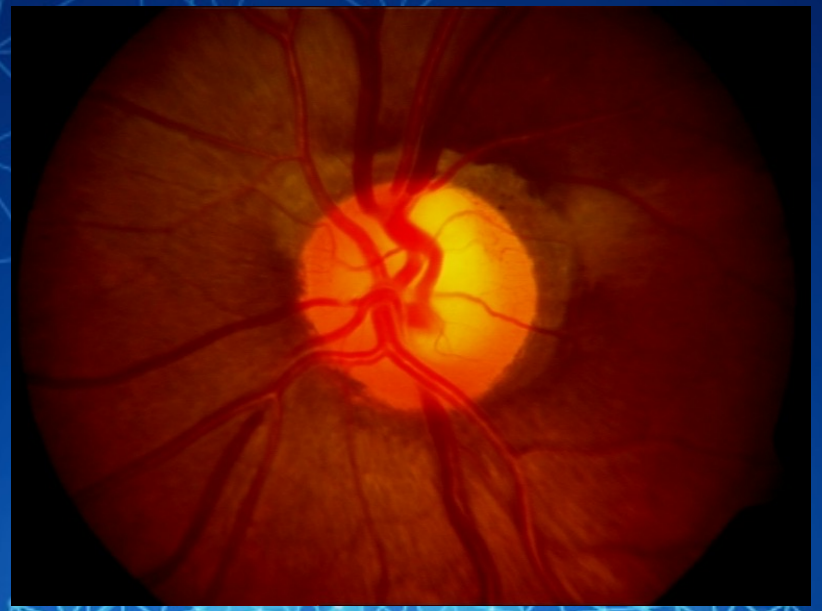
Internal use

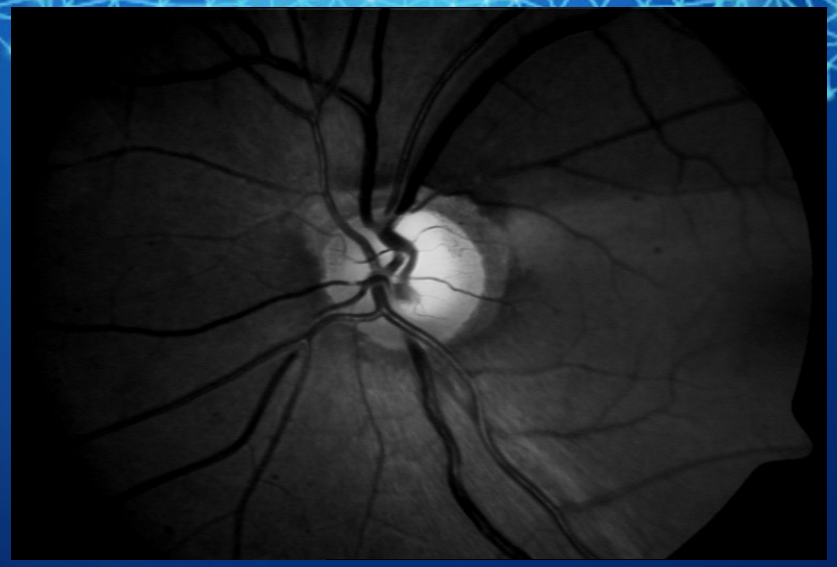
Notch (2) ★ ★ ★



Photos courtesy of GT Sunil and L Vijaya

Internal use





Single Field Analysis

Eye: Left

Name: [redacted] ID: 733971 DOB: 06-11-1958

Central 30-2 Threshold Test

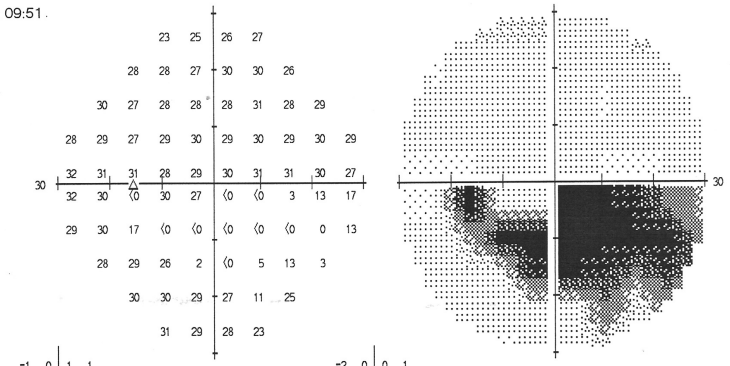
Fixation Monitor: Blindspot
Fixation Target: Central
Fixation Losses: 4/21
False POS Errors: 9 %
False NEG Errors: 0 %
Test Duration: 09:51

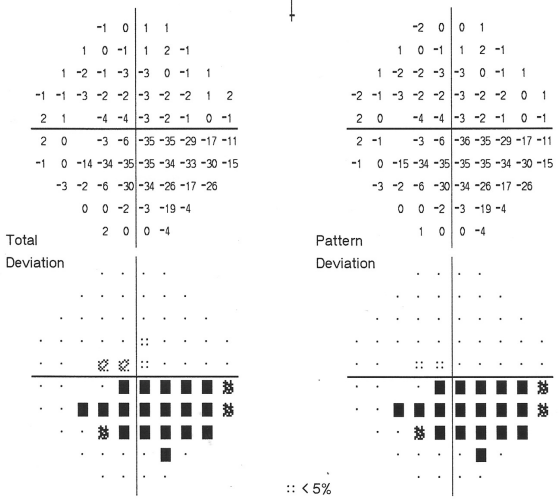
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard

Pupil Diameter: 4.5 mm
Visual Acuity: 6/6
RX: +1.50 DS DC X

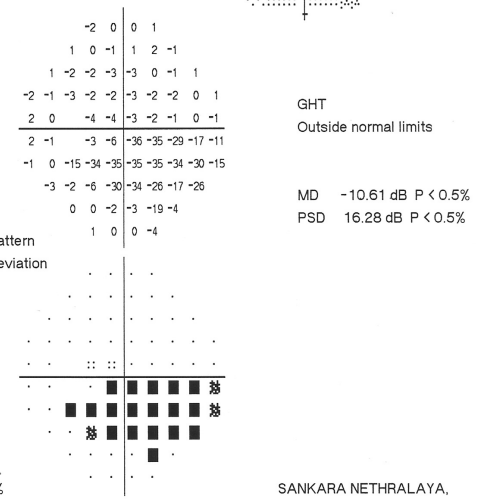
Date: 22-07-2003
Time: 12:15 PM
Age: 44

Fovea: 37 dB





Total Deviation



Pattern Deviation

GHT
Outside normal limits

MD -10.61 dB P < 0.5%
PSD 16.28 dB P < 0.5%

:: < 5%
▨ < 2%
▩ < 1%
■ < 0.5%

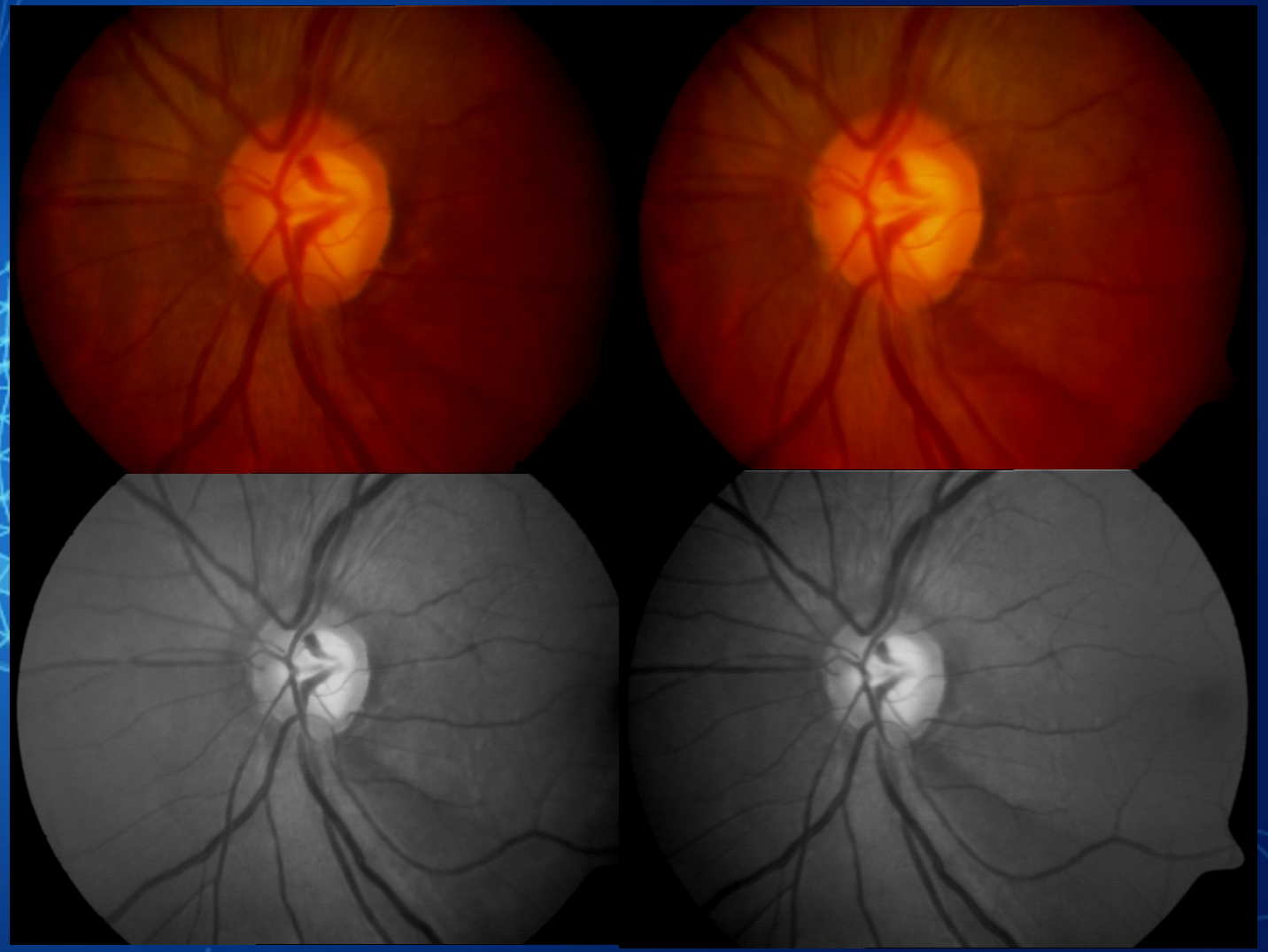
SANKARA NETHRALAYA,
18,COLLEGE ROAD
CHENNAI 600 006

© 1994-2000 Humphrey Systems
HFA II 720-5828-3.4/3.4

Images courtesy of GT Sunil and L Vijaya

Internal use

Notch (3) ★ ★ ★



Photos courtesy of GT Sunil and L Vijaya

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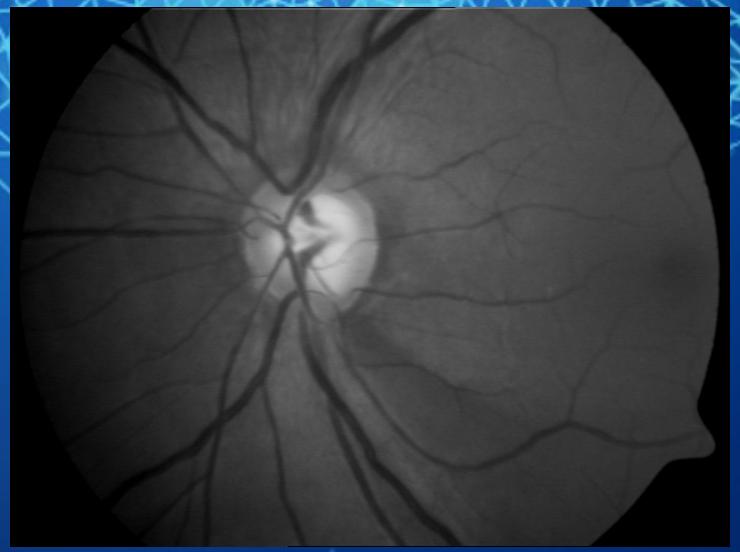
Internal use



Single Field Analysis — Eye: Left

Name: — ID: 960420105 — DOB: 01-01-1949

Central 24-2 Threshold Test

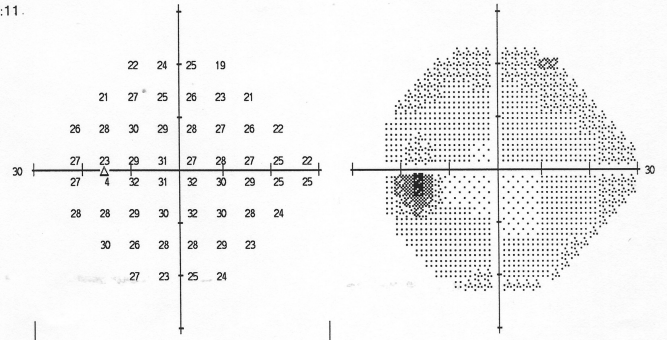
Fixation Monitor: Gaze/Blindspot
Fixation Target: Central
Fixation Losses: 2/15
False POS Errors: 4 %
False NEG Errors: 2 %
Test Duration: 05:11

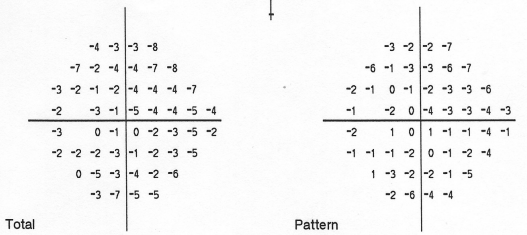
Fovea: 34 dB

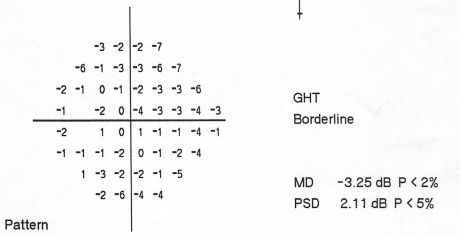
Stimulus: III, White
Background: 31.5 ASB
Strategy: SITA-Standard

Pupil Diameter: 4.8 mm
Visual Acuity: 6/7.5
RX: +4.50 DS -2.00 DC X 100

Date: 09-15-2005
Time: 10:37 AM
Age: 56



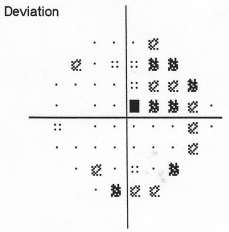




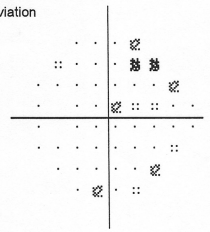
GHT
Borderline

MD -3.25 dB P < 2%
PSD 2.11 dB P < 5%

Total Deviation

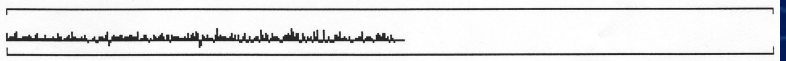


Pattern Deviation



:: < 5%
▒ < 2%
▓ < 1%
■ < 0.5%

CHENNAI GLAUCOMA STUDY
SANKARA NETHRALAYA
21,PYCROFTS GARDEN ROAD
CHENNAI-600006



© 2003 Carl Zeiss Meditec
HFA II 750-9584-3.5/3.5

Images courtesy of GT Sunil and L Vijaya

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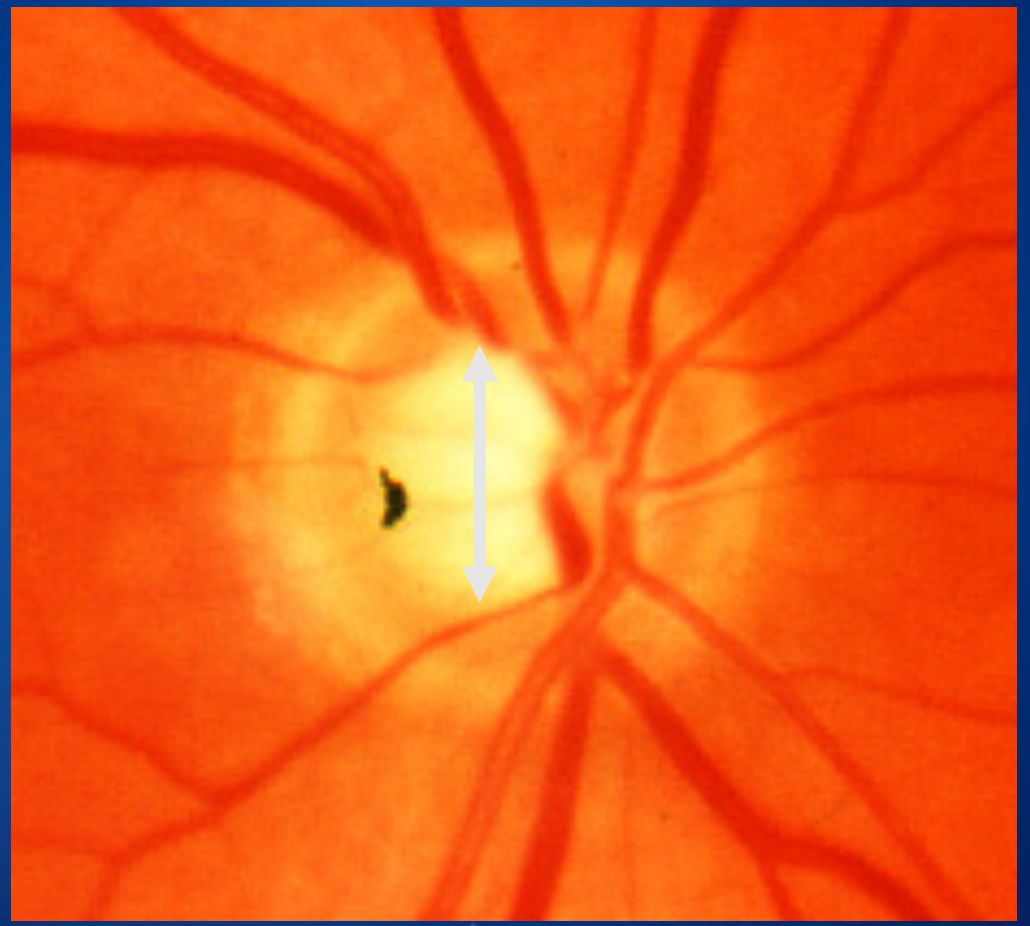
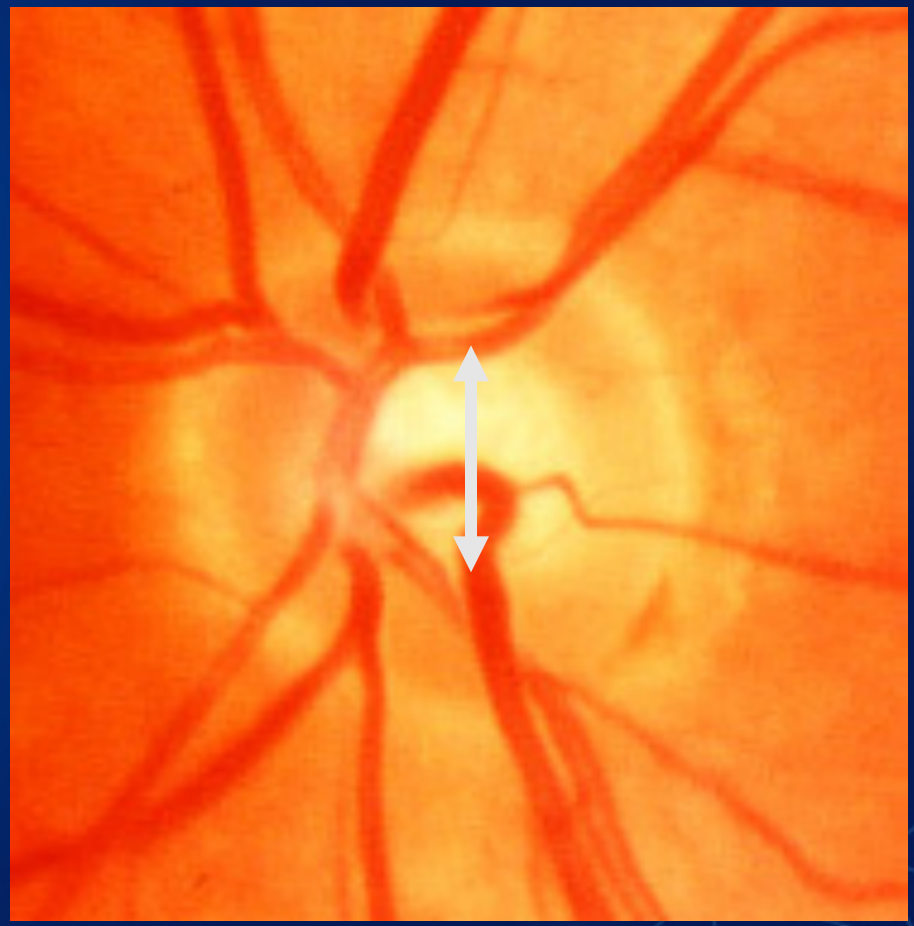
Internal use

Cup–disc ratio asymmetry > 0.2*

★ ★ ★





*After accounting for disc size asymmetry.

Armaly MF. *Arch Ophthalmol* 1967; 78: 5–43.

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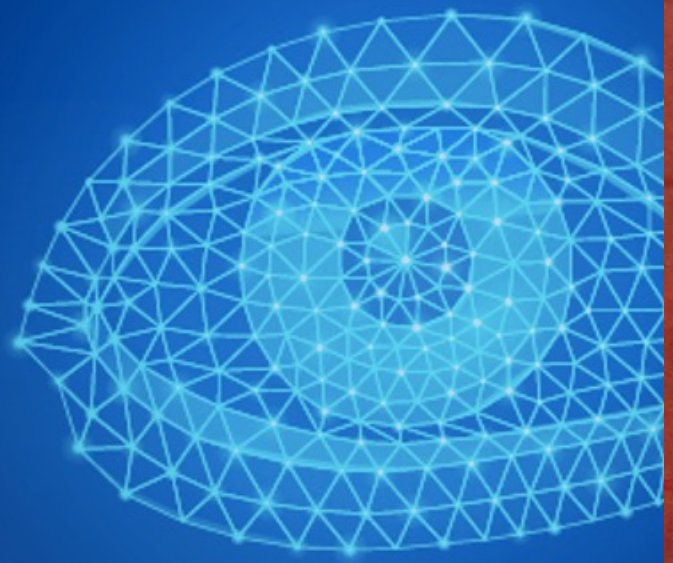
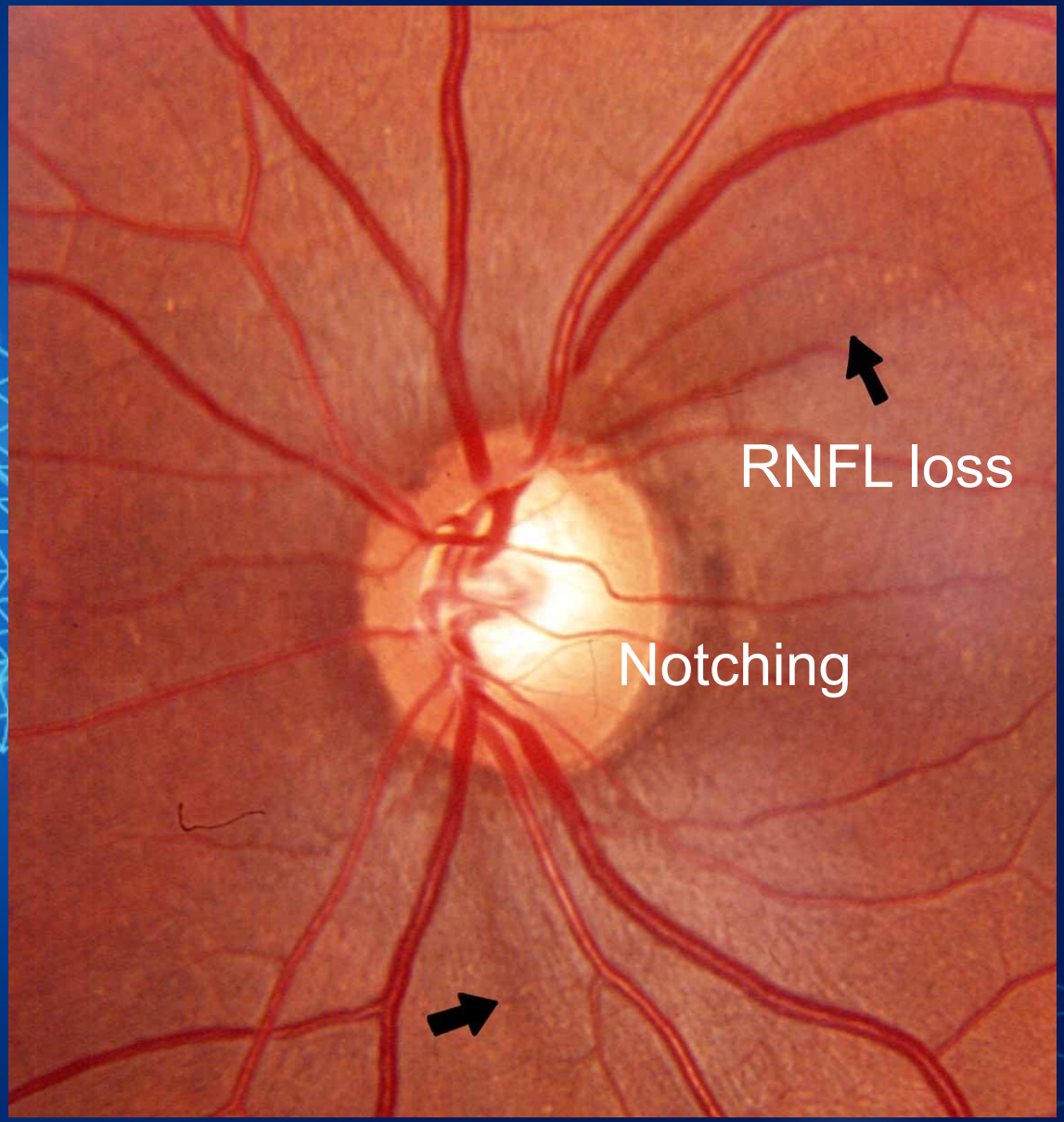
Internal use

Glaucoma (1)





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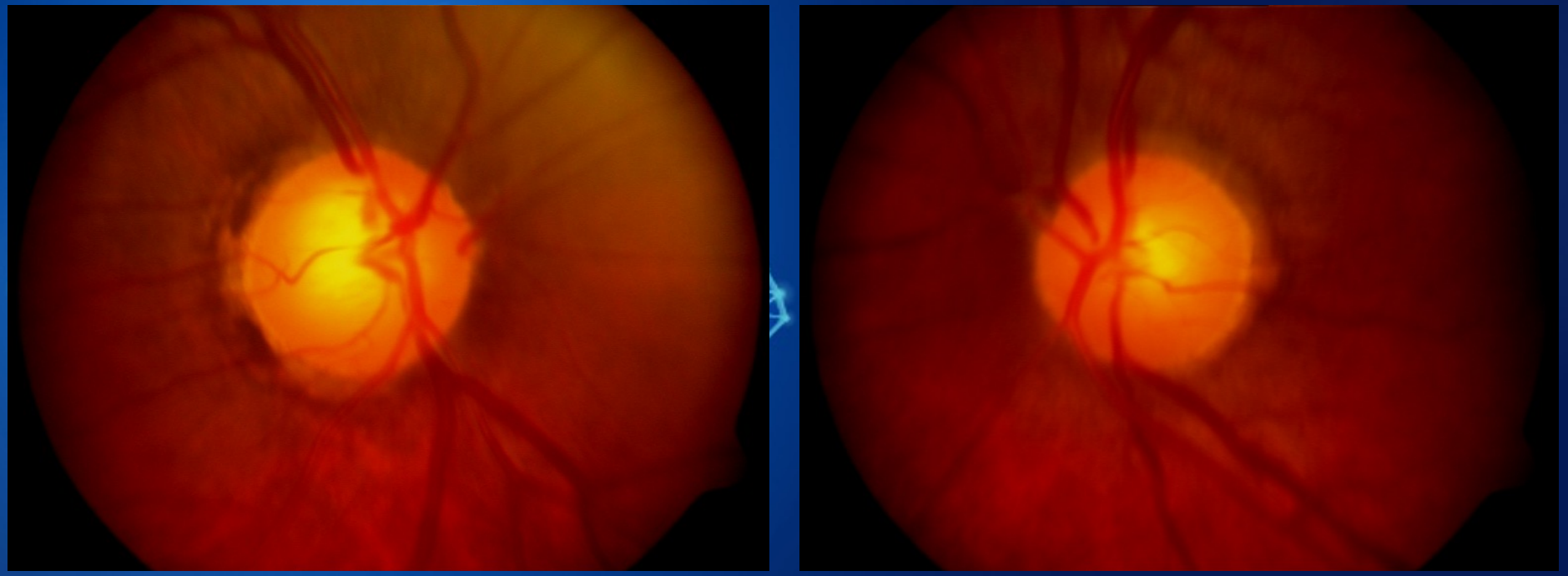
Internal use

Glaucoma (2)



Cup asymmetry exceeds disc asymmetry

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Internal use

Glaucoma (3)

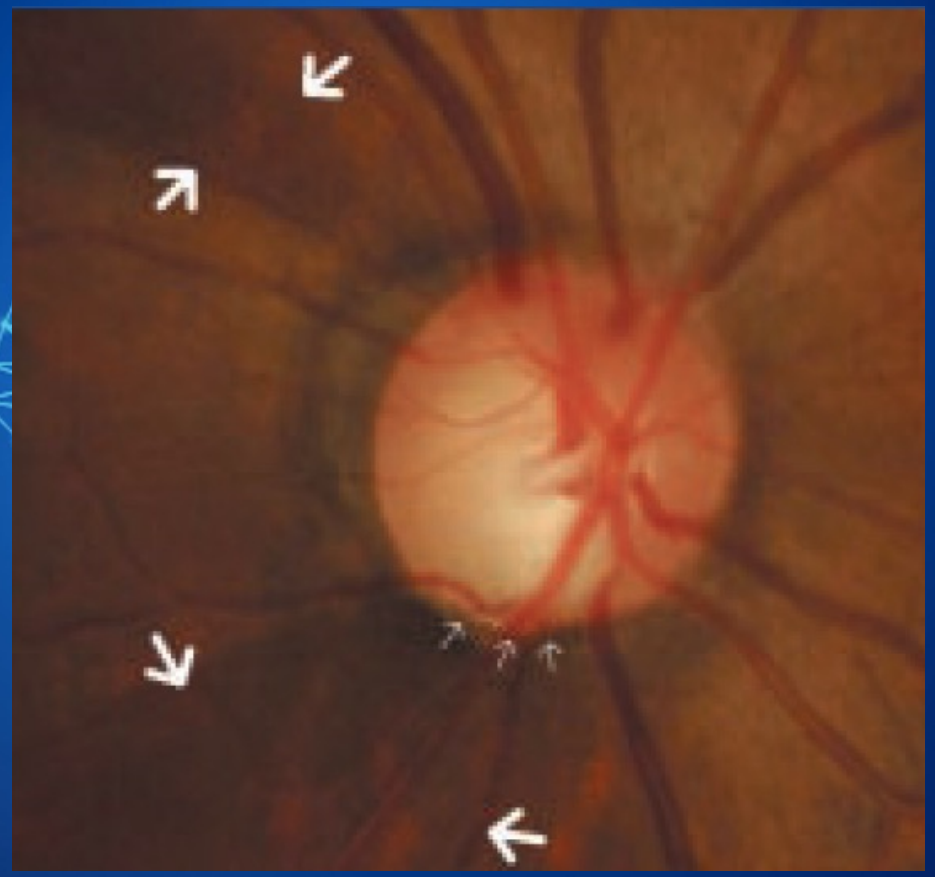

Photo courtesy of Prin Rojanapongpun

- Localised loss of both inferior and superior neuroretinal rim
- Classic inferior notch (small arrows)
- RNFL defect in superior and inferior arcuate area (large arrows)

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Internal use

Glaucoma (4)

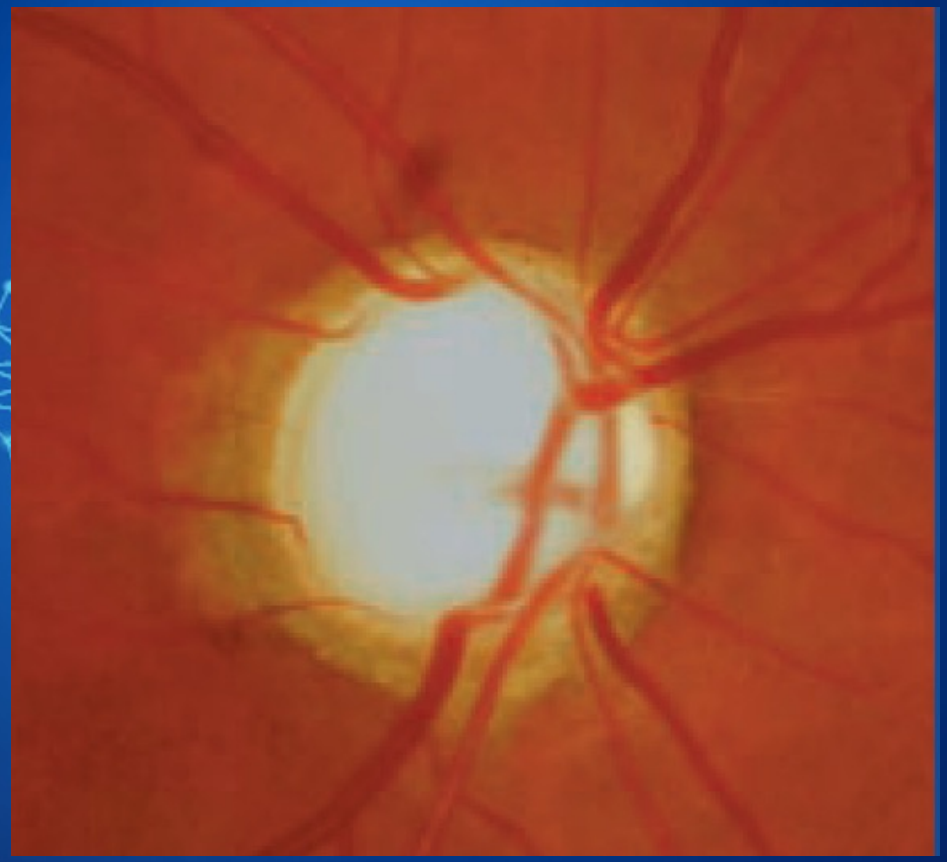

Photo courtesy of Prin RojanaPongpun

- Neuroretinal rim thinning
- The cup extends to the disc rim
- Circumlinear blood vessel baring
- Bayoneting of the blood vessels
- Peripapillary atrophy

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Internal use

Glaucoma progression

Features of glaucoma progression:

- disc haemorrhage
- focal rim notching
- change in vessel position
- wedge-type nerve fibre layer defects
- generalised rim thinning
- increased cup–disc ratio
- increase in peripapillary atrophy

Asia Pacific Glaucoma Guidelines 3rd ed. 2016.

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Internal use

Detecting progression

- Progression usually occurs over a long period of time, which can make detecting change difficult
- Serial photographs of the optic nerve head may be the most reliable way to detect progression
- For details, see *Module 9: Monitoring for progression*

Asia Pacific Glaucoma Guidelines 3rd ed. 2016.

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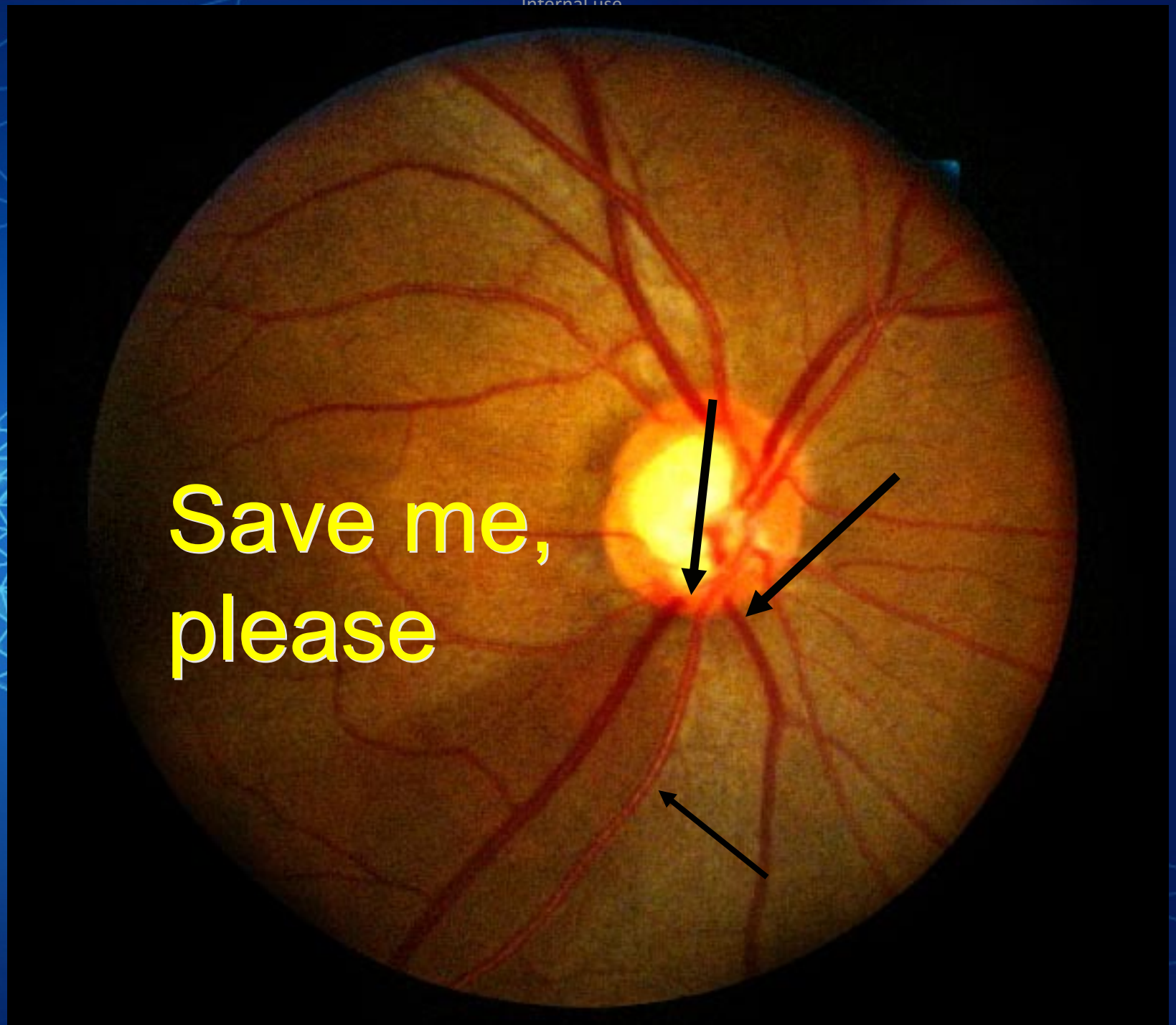
Internal use



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QUANTITATIVE STRUCTURAL ASSESSEMENT USING OPTICAL COHERENCE TOMOGRAPHY (OCT)

Internal use

Cirrus™ OCT Retinal Nerve Fiber Layer (RNFL) and Optic Nerve Head (ONH) Analysis

Patient and Examination Data – Include signal strength value ranging from 0 (weak) to 10 (strong). OCT scans with signal strength below 6 should not be used for analysis.

RNFL Thickness Map – Uses a color-pattern, where cool colors (blues, greens) represent thinner areas and warm colors (yellows, reds) represent thicker areas.

RNFL Deviation Map – Reports the results of a statistical comparison against the age-matched normative database for each pixel, overlaid on the OCT fundus image. Borderline and abnormally thin areas are highlighted in yellow and red, respectively. This map also contains the placement of the 3.46-mm purple RNFL calculation circle where quadrant and clock hour RNFL measurements are based.

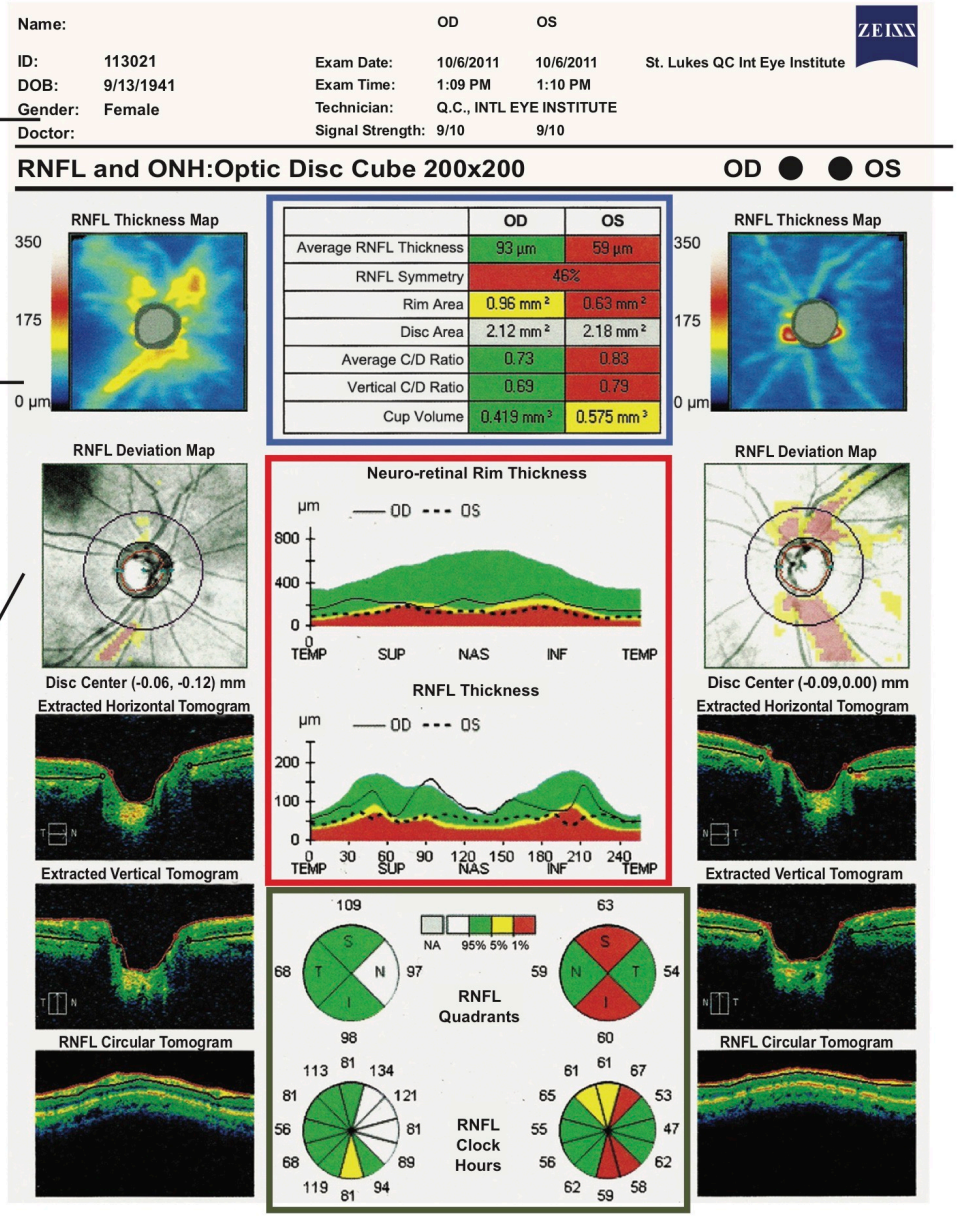


Table – Includes average RNFL thickness, RNFL symmetry, and five optic disc parameters. Except for the disc area, each value is compared to the age-matched normative database and is indicated with stoplight color scheme. Optic disc parameters will be gray or not applicable if the disc area is < 1.33 mm² or > 2.5 mm².

Neuroretinal Rim and RNFL Thickness TSNIT Profiles – The neuroretinal rim thickness and the RNFL thickness measurements along the calculation circles are plotted in TSNIT format. Color bands demonstrate the range of normative data.

RNFL Quadrant and Clock Hour Values – These report average thickness along the RNFL calculation circle by quadrants and clock hours. The color associated with each measurement is derived from its comparison to the age-matched normative data.

Chung AN. Quantitative structural imaging of the opetic nerve head and retinal nerve fiber layer. In: Aquino MV, Tumbocon JA, De Guzman MHP eds. Glaucoma Handbook. Quezon City: St. Luke's Medical Center; 2012

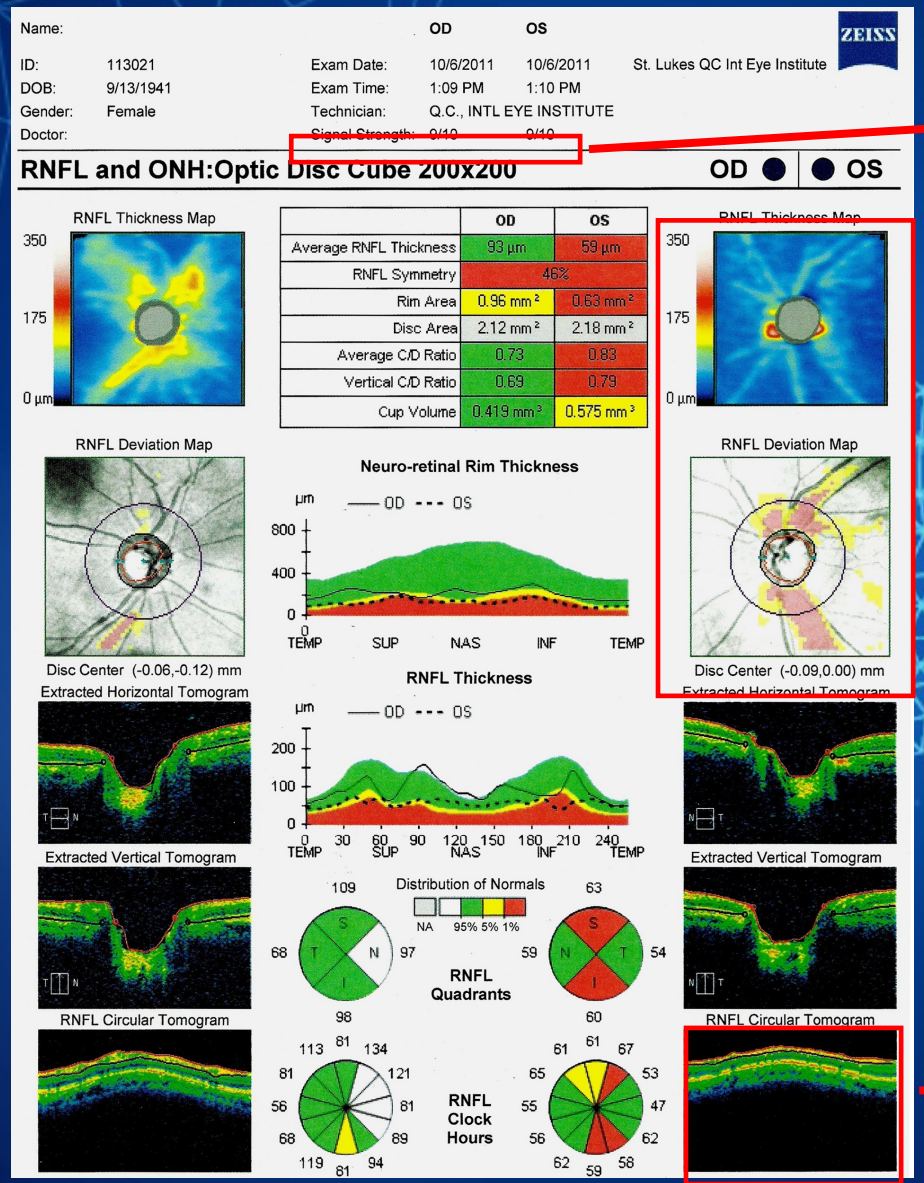
Figure 4-7. Cirrus (spectral domain) OCT ONH and RNFL analysis (*SW 5.1.1.4*) in a patient with manifest glaucoma on the left eye and a narrow area of suspiciously thin RNFL inferiorly on the right eye.

Internal use

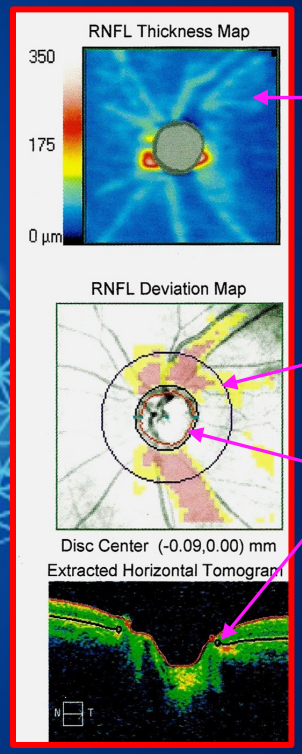
OCT circumpapillary Retinal Nerve Fiber Layer (cpRNFL)

Acceptable scan quality indicators

Signal strength ≥ 6



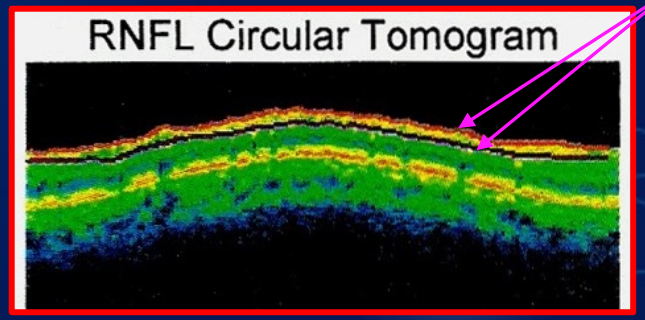
Signal Strength: 9/10 9/10



Absence of signal “drop out” (black regions) in the scan area, especially involving the calculation circle

Proper delineation of optic disc borders

Correct segmentation of the RNFL



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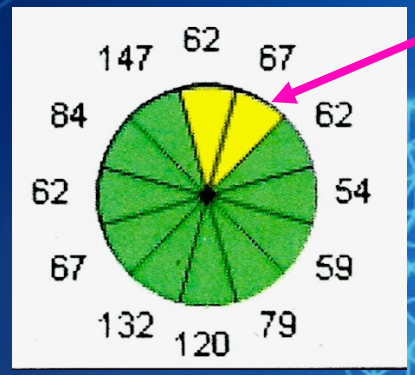
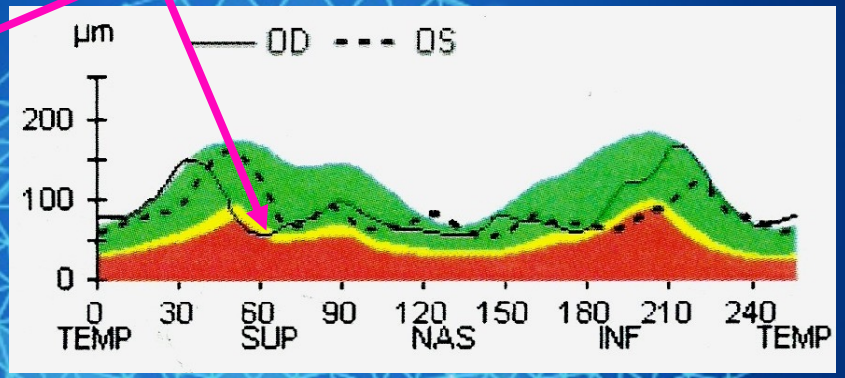
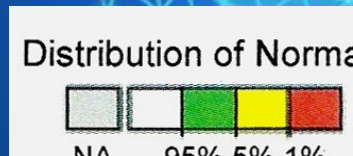
Internal use

Be aware of the reliability of the examinations, “artifacts”, statistical outliers, “normal variants” and other causes

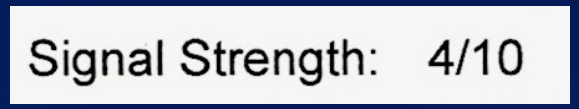
Normal variant: Thicker regions are located more temporal than usual:
“Yellow /red disease”



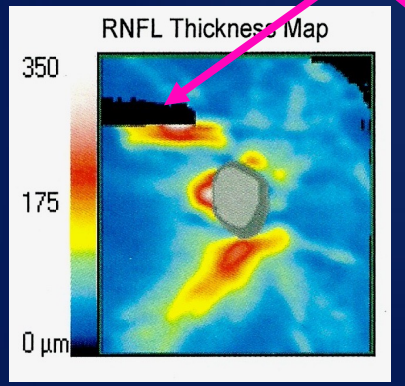


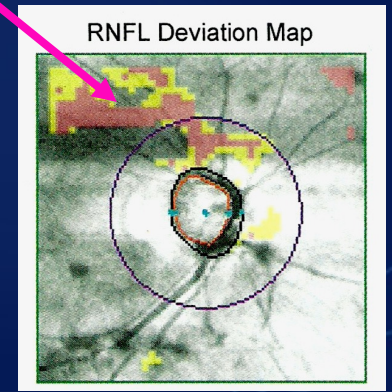


Low signal strength

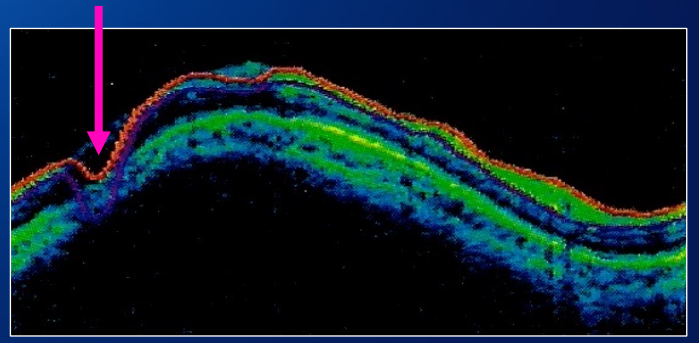


”Signal drop-out”





Incorrect RNFL segmentation



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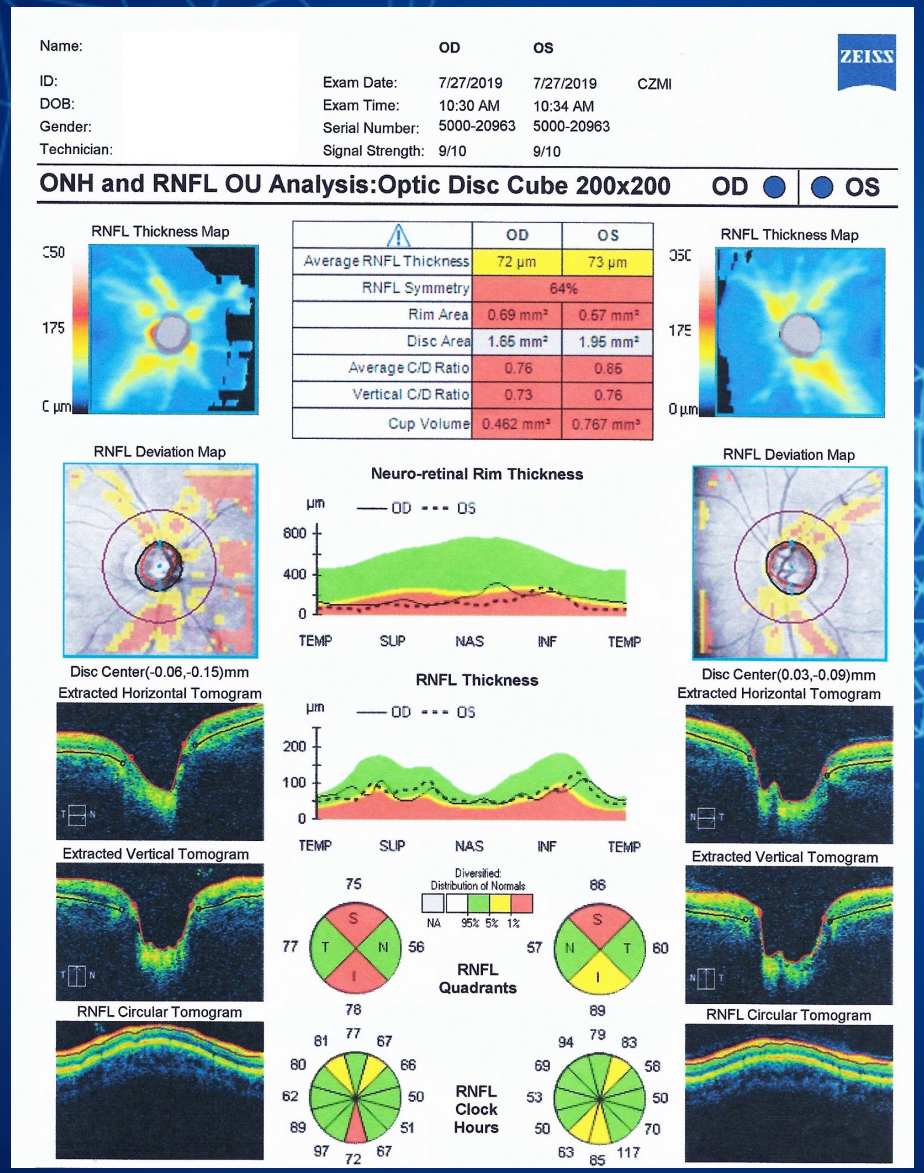
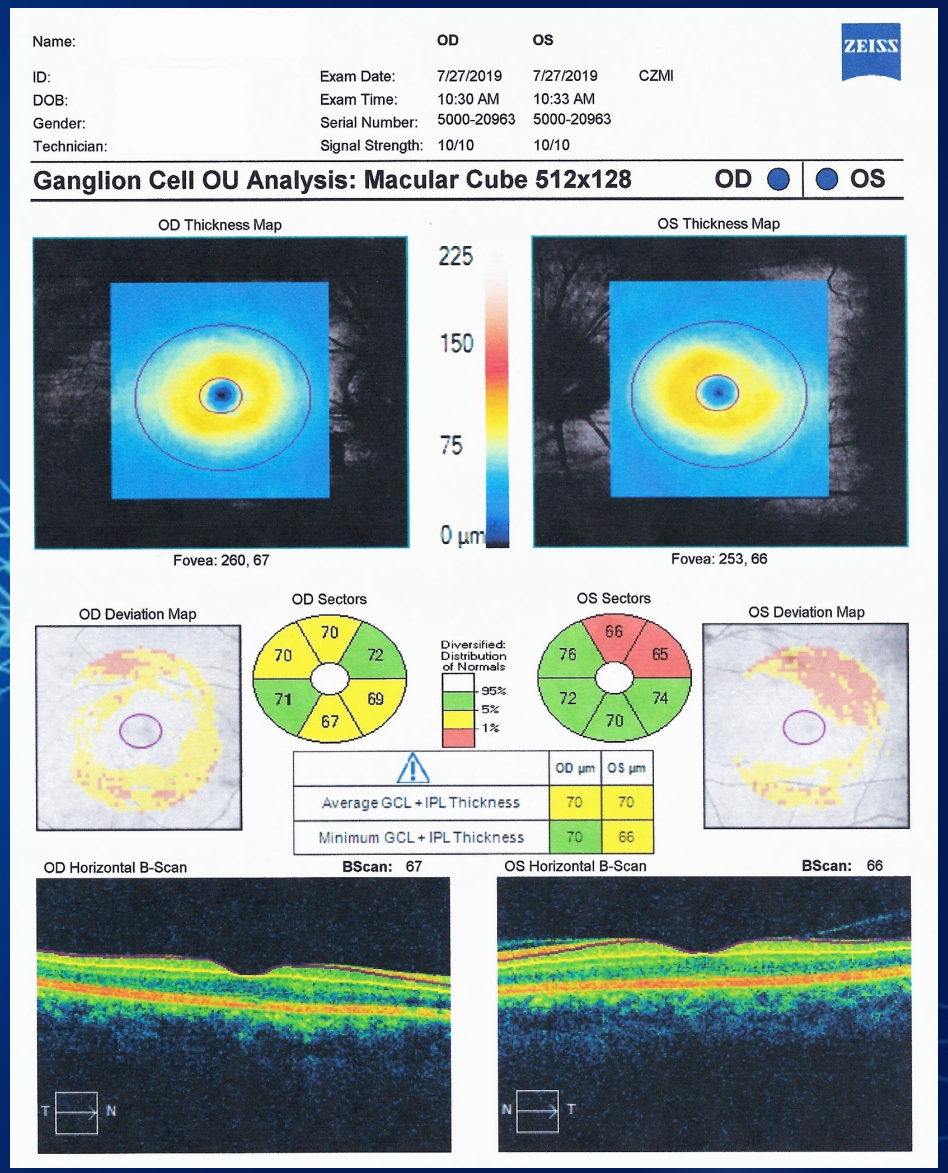
Internal use

OCT RNFL and ONH



OCT Macular Ganglion Cell Layer + Inner Plexiform Layer (GCL+IPL)



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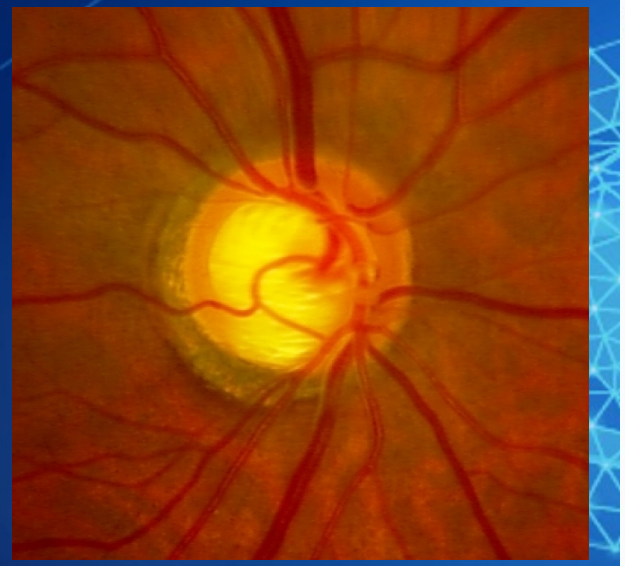
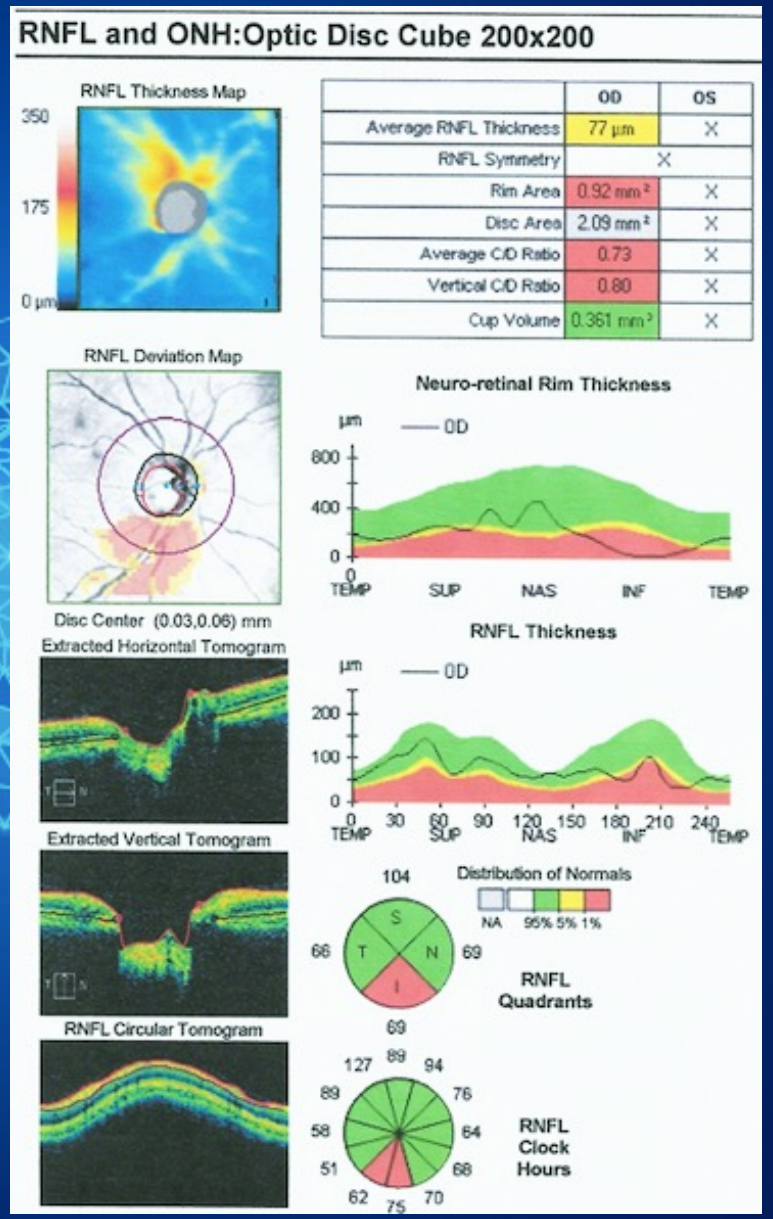
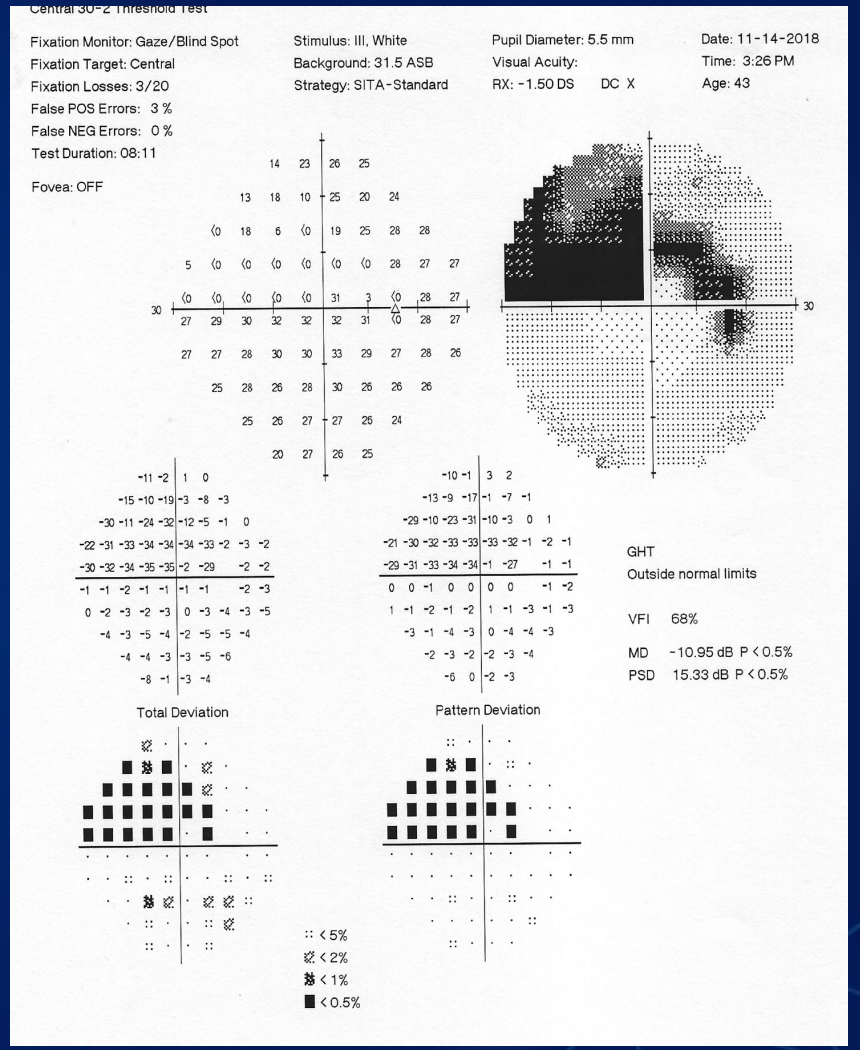
Internal use

Correlate OCT examination with optic nerve head and automated perimetry findings







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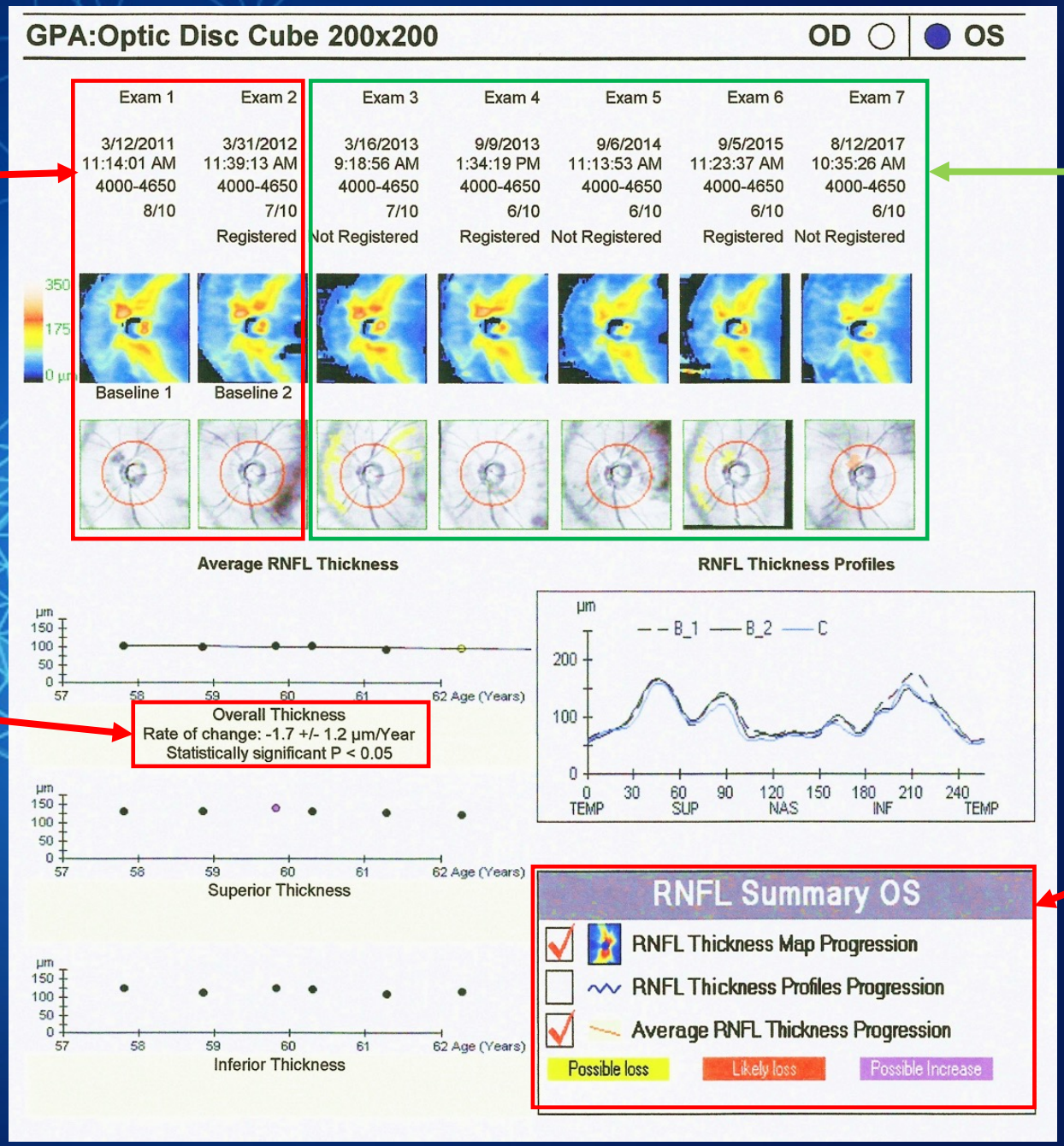
Internal use

Cirrus™ OCT Guided Progression Analysis (GPA)

Baseline tests

Follow-up tests



Rate of Change
(Trend analysis)

Cirrus OCT Guided Progression Analysis (GPA) compares RNFL thickness measurements over time and determines if statistically significant change has occurred. The analysis includes a chronological display of RNFL thickness maps, RNFL thickness change maps, average RNFL thickness graphs , and RNFL thickness profiles comparing the current exam to the baseline exams.

Statistically significant changes are summarized with flags for possible or likely RNFL thinning *(Event analysis)*

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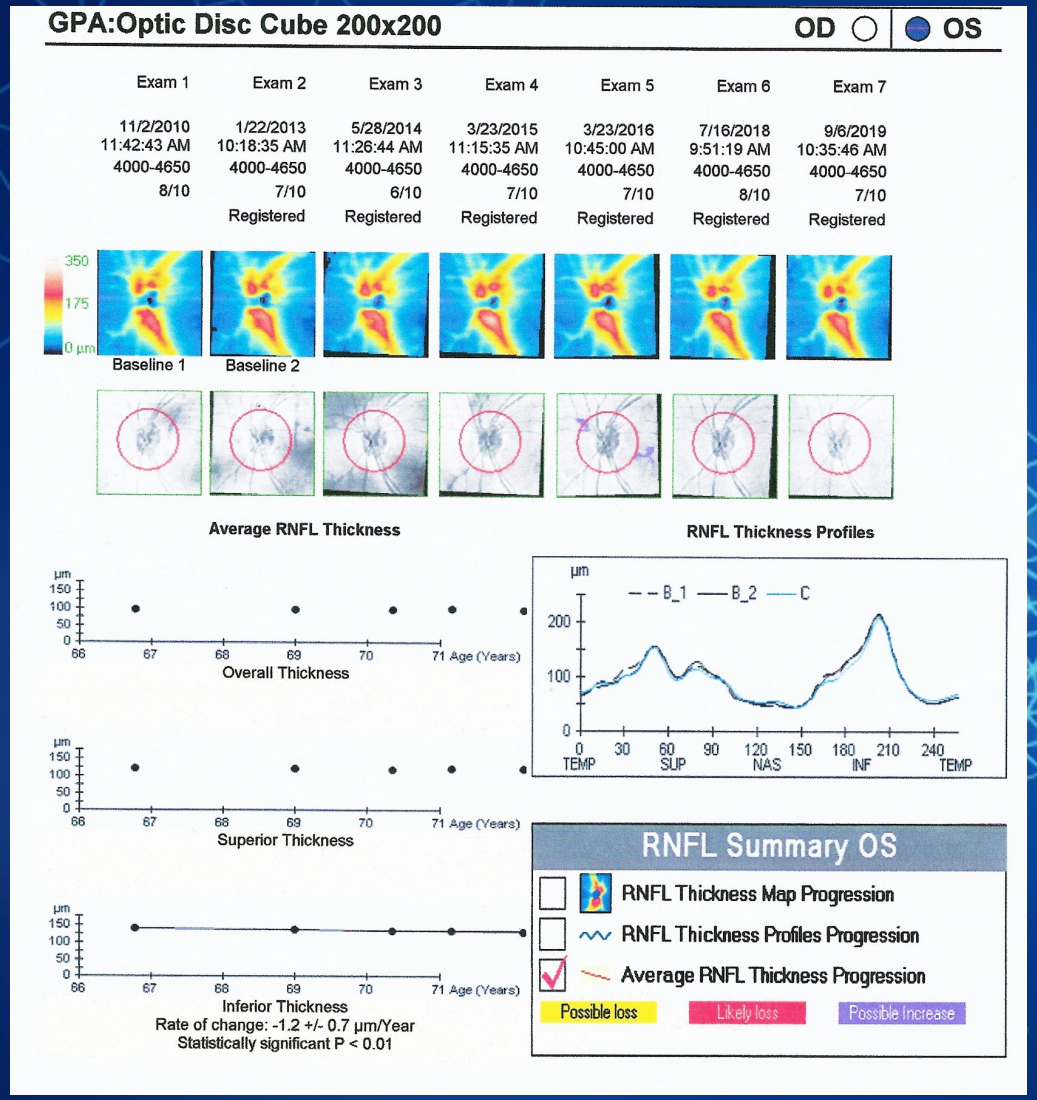
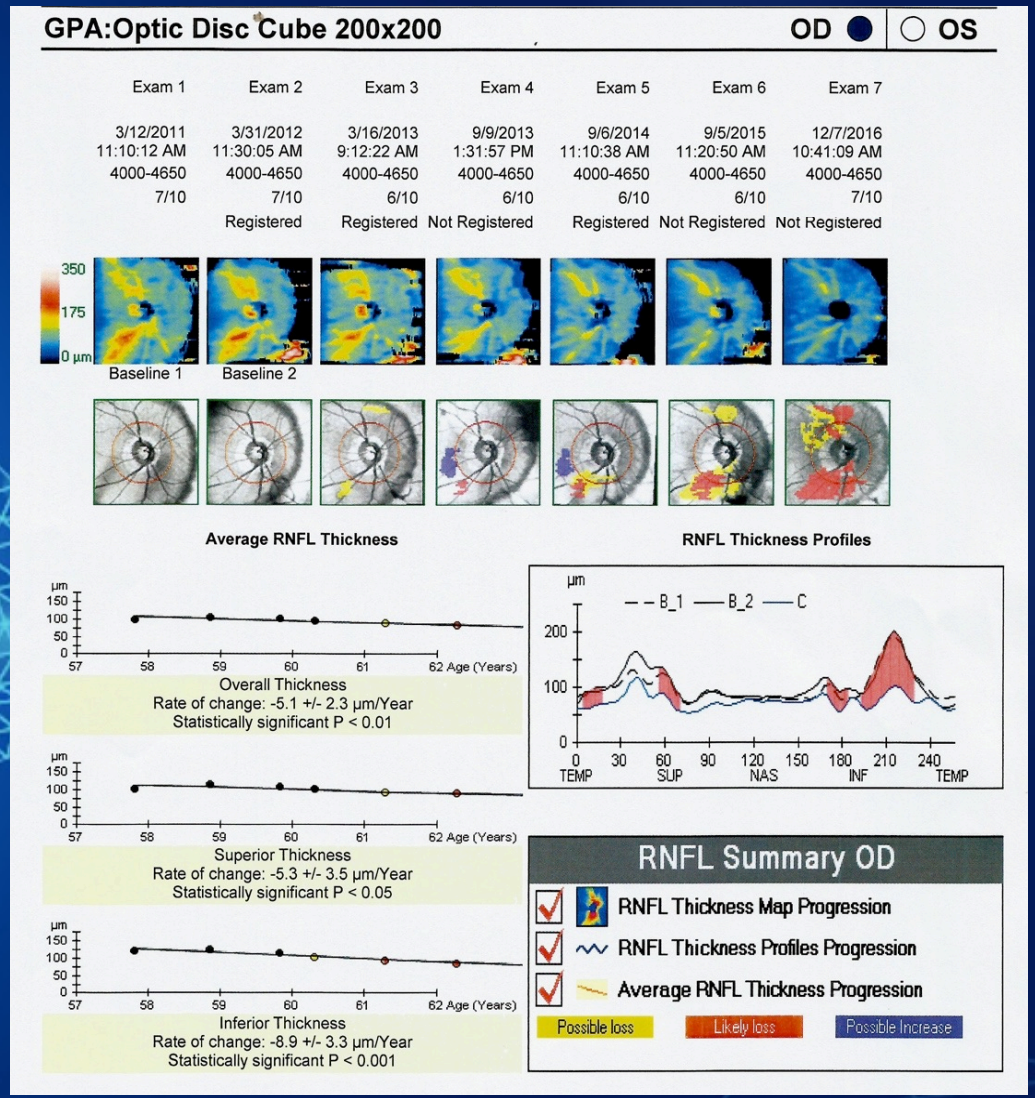
Internal use

Cirrus™ OCT Guided Progression Analysis (GPA)



Relatively STABLE RNFL thickness



Significant RNFL **THINNING**

Note: OCT-RNFL thickness analysis has a "floor effect" and may be less valuable for monitoring advanced glaucoma

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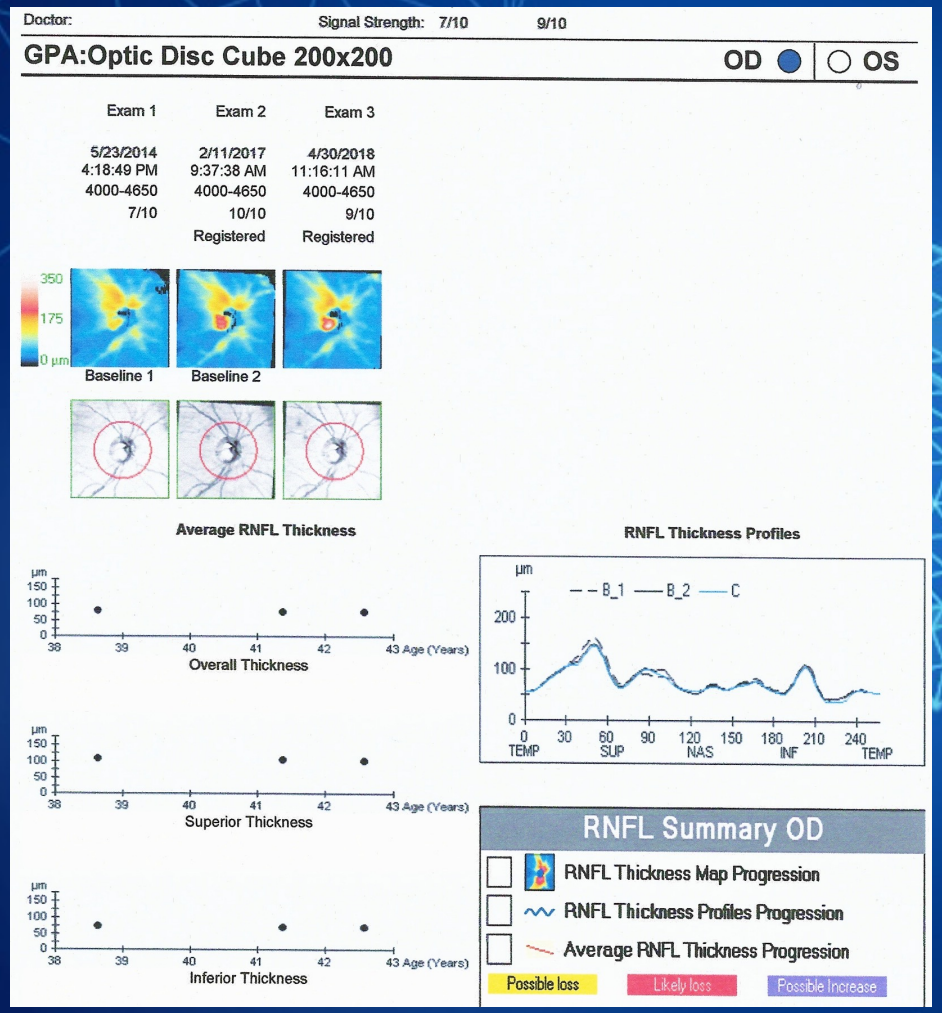
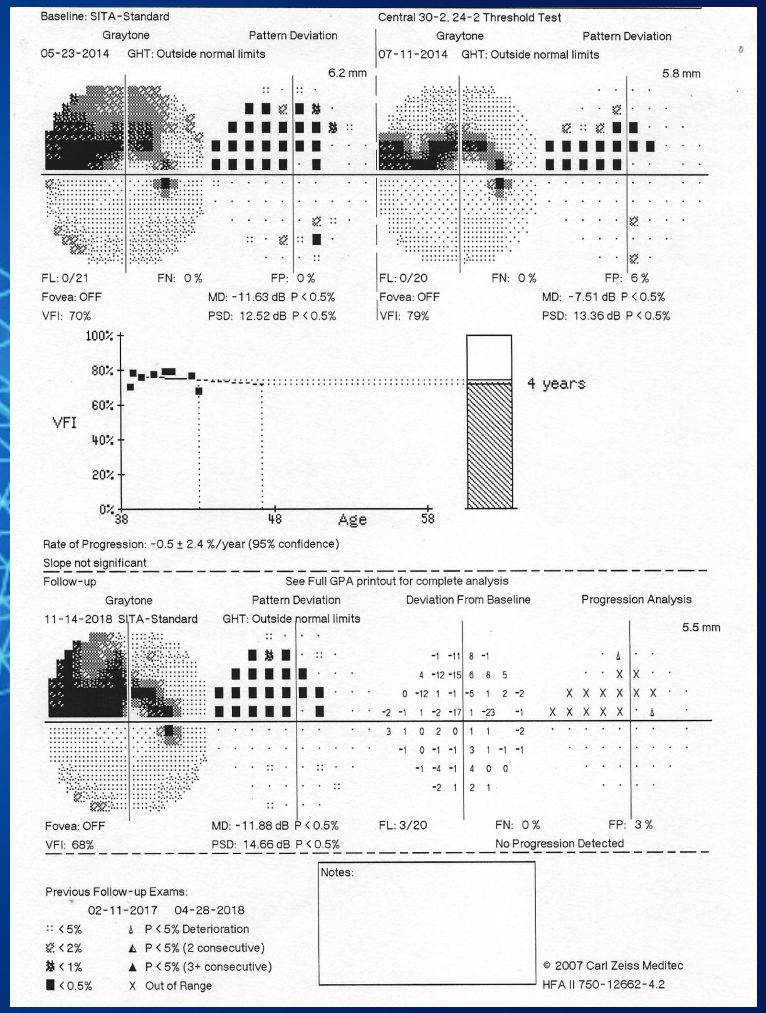
Monitor both structural and functional parameters to monitor for glaucomatous progression





Utilize trend and event analyses

- Recommended manner for monitoring glaucomatous progression
- Defines progression as changes larger than expected from random variability
- Progression can be measured with both high sensitivity and specificity

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Internal use

Guidelines

- Correlate the structural examinations with functional tests to properly diagnose, stage and monitor glaucoma
- All available clinical information about a patient must be taken into account before treatment decisions are made

For more information, see *Module 9: Monitoring for progression*

Internal use