IMAGING IN GLAUCOMA

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IMPORTANCE OF IMAGING IN GLAUCOMA (ANALYSIS OF STRUCTURE)

There is an important role for ocular imaging in glaucoma although the full potential of that role is yet to be fully understood. There has been significant advancement in imaging technology over the last decade, especially in optical coherence tomography (OCT).

The use of an imaging device facilitates the assessment and management of glaucoma but it is important to note that there will never be a device that will replace clinical examination and evaluation.

One of the advantages to imaging is that it overcomes inter-observer and intra-observer variation to subjective assessment of the optic nerve head (ONH) and retinal nerve fiber layer (RNFL) assessment, to an extent. The devices usually provide reliable and objective measures of the optic disc and associated RNFL morphology. Several images are usually required to establish a baseline measure and one must be aware of the limitations of poor quality scans of an instrument.

The high resolution provided from objective measurements help to identify disease progression and help to determine statistically significant changes over time, usually before clinical examination or visual field assessment do.

IMAGING INSTRUMENTS AVAILABLE FOR GLAUCOMA ANALYSIS:

- Confocal Scanning Laser Tomography
    - Heidelberg Retinal Tomographer
- Optical Coherence Tomography (OCT)
- Scanning Laser Polarimetry

- GDx

CONFOCAL SCANNING LASER OPHTHALMOSCOPY

HEIDELBERG RETINAL TOMOGRAPHER (HRT)

The Heidelberg Retinal Tomographer provides objective and quantitative measures of the optic disc topography and has the potential for discriminating between glaucomatous and normal eyes (Miglior, Guareschi, Albe et al 2003).

The device measures the rim tissue of the optic nerve head (ONH) (Figure 16.1). Absolute values are assigned to the ONH analysis based on the operator's ability to subjectively identify outer limits of the nerve.

The device generates multiple 2D pictures (Figure 16.2) by moving the confocal aperture to create a 3D topography image of the nerve head. It takes three sets of raw image series (up to 64 images) then makes three topographical images. It then takes the mean and averages one resultant mean topographical image (Figure 16.3). Multiple sets of series improve the accuracy of the output image.

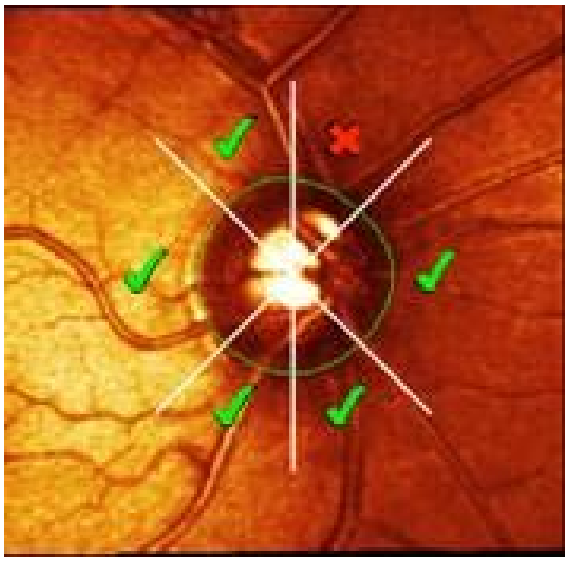


Figure 16.1: *Rim tissue analysis of the optic nerve head*

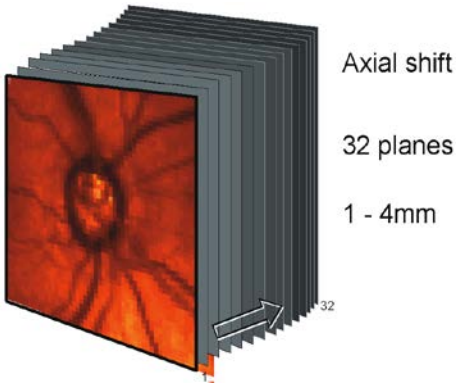
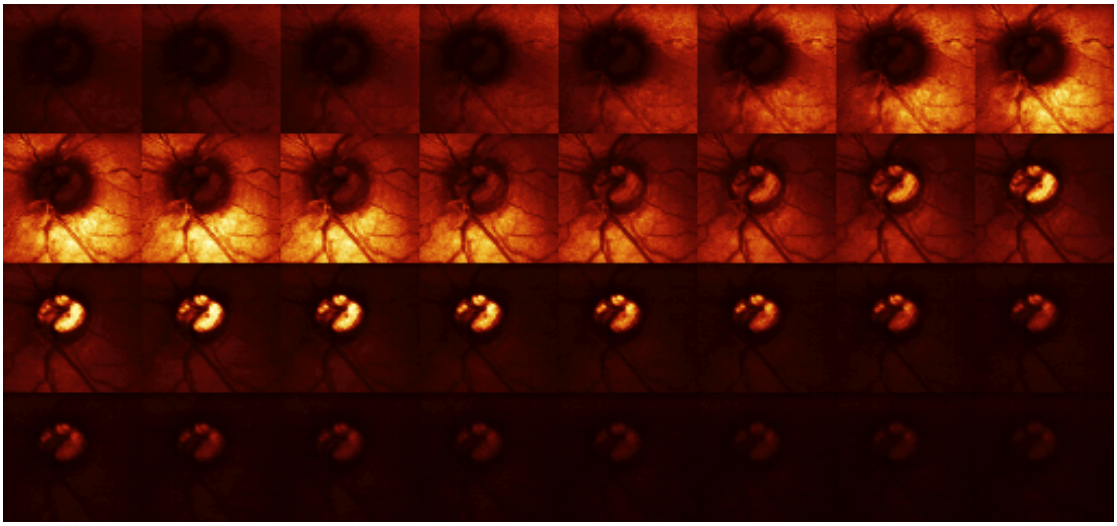


Figure 16.2: *Multiple 2D images*



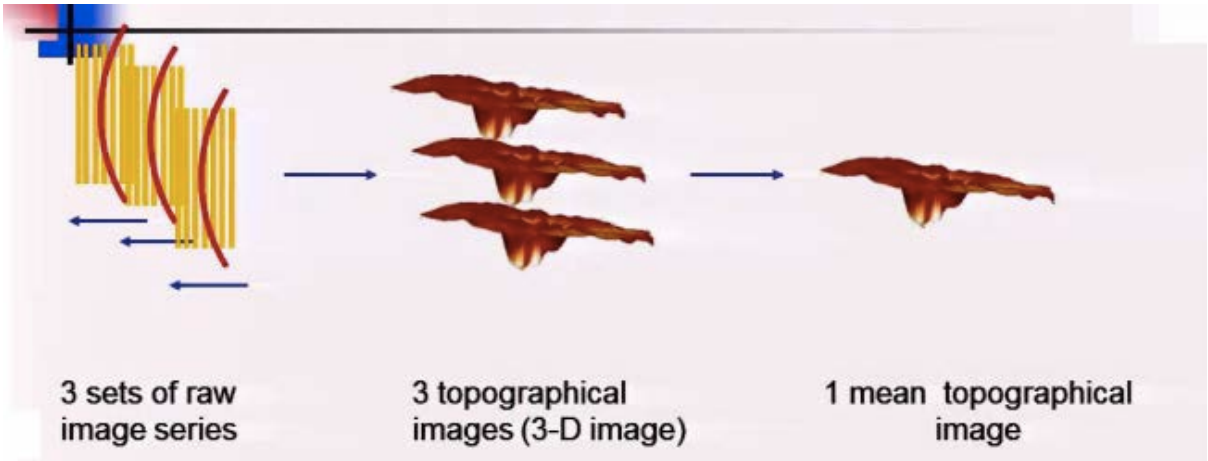


Figure 16.3: *Production of one mean topographical image*

OPTIC NERVE HEAD EVALUATION

The examiner draws a contour line defining the nerve margins and then a plane of reference is generated. This leaves room for subjective error if the examiner does not carefully identify the correct margin of the nerve.

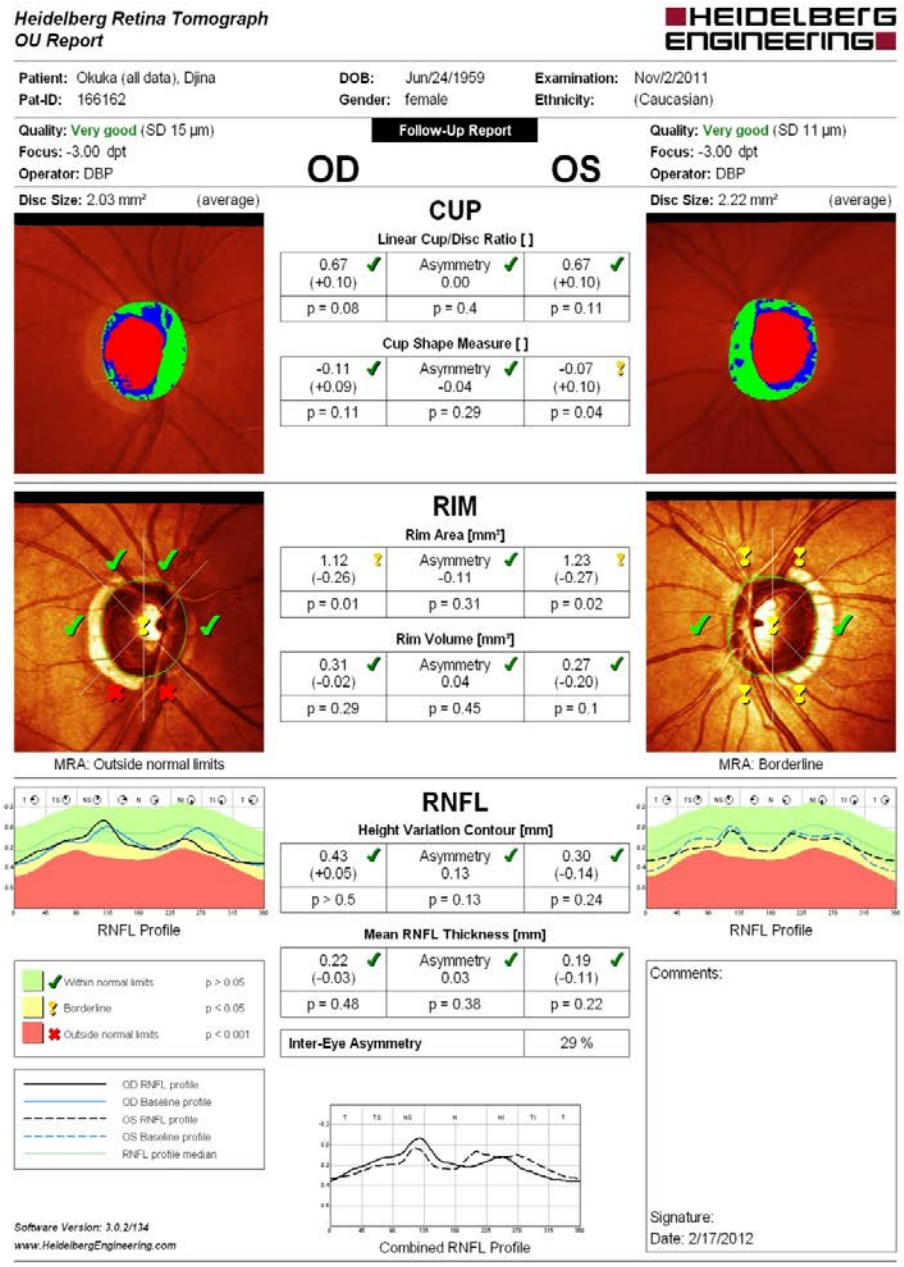
Stereometric parameters of optic nerve head topography are generated relative to the reference plane including the following:

- Rim area
- Rim volume
- Cup area
- Cup volume
- Cup-to-disc ratio
- Height variation contour
- Cup shape measure

Figure 16.4: *The 3D image generated by the HRT*

WHAT IS ON THE HRT PRINTOUT?

A typical print-out from the HRT device is shown in Figure 16.5.



Heidelberg Retina Tomograph
OU Report

HEIDELBERG ENGINEERING

Patient: Okuka (all data), Djina
Pat-ID: 166162
DOB: Jun/24/1959
Gender: female
Examination: Nov/2011
Ethnicity: (Caucasian)

Follow-Up Report

OD		OS
Quality: Very good (SD 15 µm)		Quality: Very good (SD 11 µm)
Focus: -3.00 dpt		Focus: -3.00 dpt
Operator: DBP		Operator: DBP
Disc Size: 2.03 mm² (average)		Disc Size: 2.22 mm² (average)

CUP

Linear Cup/Disc Ratio [ ]

0.67 (+0.10)	Asymmetry 0.00	0.67 (+0.10)
p = 0.08	p = 0.4	p = 0.11

Cup Shape Measure [ ]

-0.11 (+0.09)	Asymmetry -0.04	-0.07 (+0.10)
p = 0.11	p = 0.29	p = 0.04

RIM

Rim Area [mm²]

1.12 (-0.26)	Asymmetry -0.11	1.23 (-0.27)
p = 0.01	p = 0.31	p = 0.02

Rim Volume [mm³]

0.31 (-0.02)	Asymmetry 0.04	0.27 (-0.20)
p = 0.29	p = 0.45	p = 0.1

MRA: Outside normal limits

MRA: Borderline

RNFL

Height Variation Contour [mm]

0.43 (+0.05)	Asymmetry 0.13	0.30 (-0.14)
p > 0.5	p = 0.13	p = 0.24

Mean RNFL Thickness [mm]

0.22 (-0.03)	Asymmetry 0.03	0.19 (-0.11)
p = 0.48	p = 0.38	p = 0.22

Inter-Eye Asymmetry	29 %

RNFL Profile

RNFL Profile

Within normal limits p > 0.05
Borderline p < 0.05
Outside normal limits p < 0.001

OD RNFL profile
OD Baseline profile
OS RNFL profile
OS Baseline profile
RNFL profile median

Combined RNFL Profile

Comments:

Signature:
Date: 2/17/2012

Software Version: 3.0.2/134
www.HeidelbergEngineering.com

Figure 16.5: *Print-out from the HRT*

The main features of the analysis are as follows:

1. CUP

Cup shape

Topographic Image
Red = cup
Blue = sloped rim
Green= flat (neuro-retinal rim)

Cup parameters

- Cup/Disc ratio
- Symmetry

Quality Check

- < 10 = excellent
- 11-20 = very good
- 21-30 = good
- 31-40 = acceptable (but too noisy so avoid)
- > 40 = poor

2. RIM

The ONH rim analysis provides the best indicators for the presence of glaucoma.

The key components of the rim analysis are as follows:

Moorfields Regression Analysis (MRA)

- Analysis of the rim tissue in proportion to the optic nerve size
- Sectoral analysis of the structure of the rim against normative database
    - Outside normal limits: X
        - Less than 99.9% of normative database have this rim thickness
    - Borderline: !
        - Between 99 – 99.5% of normative database have this rim thickness
    - Within Normal Limits: ☐
        - Within the 95% of normal rim thickness

3. RNFL

The key components of the retinal nerve fiber layer analysis are as follows:

- Green = within 95% confidence-interval (ethnic specific, age and disc size adjusted)
- Lighter green solid line = average value for that specific age, race, optic disc size
- Yellow = 5th to 0.1 percentile of normal distribution - **borderline**
- Red <0.1 percentile of normal limits - **outside normal limits**

The RNFL is thickest supero-temporally and infero-temporally, giving a classic “double hump” (similar to other RNFL thickness printouts from other devices).

OPTICAL COHERENCE TOMOGRAPHY

Optical coherence tomography (OCT) works by measuring echoes from near infra-red light reflected back by retinal tissue. A beam of light is directed toward the eye and passed through a beam splitter which sends one ray to the eye and one to a reference mirror. Light is reflected back from both and re-combined, a detector analyzes the time delays of the two lights. The instrument measures 'time of flight' of light (time domain) and wavelengths of back reflected light (spectral domain). The time-domain OCT had limitations which decreased the resolution of the imaging. It was used clinically between 1990s and early 2000s. Spectral domain is now the main OCT used clinically (since around 2005). A more recent OCT, called swept-source, is also available.

OCT imaging can be used in many biological tissues but has gained significant popularity amongst eye care providers for imaging structures of the eye. The OCT is able to image the retina, optic nerve head, retinal nerve fiber layer (RNFL), and anterior segment. Time domain OCT was the first OCT used clinically.

OCT technology (Figure 16.6), when applied for ophthalmic clinical use, offers a non-contact, non-invasive, qualitative, quantitative and repeatable imaging option to make diagnoses, and observe and monitor *in vivo* details of biological tissues in the eye that are otherwise invisible to the clinician during standard ophthalmoscopy and slit-lamp examination.

Figure 16.6: *Optical coherence tomographer*

OCT may be the most useful to detect early glaucoma. Advanced software on newer OCT's allows for glaucoma progression analysis as well as analysis of the ganglion cell layer (Figure 16.7).

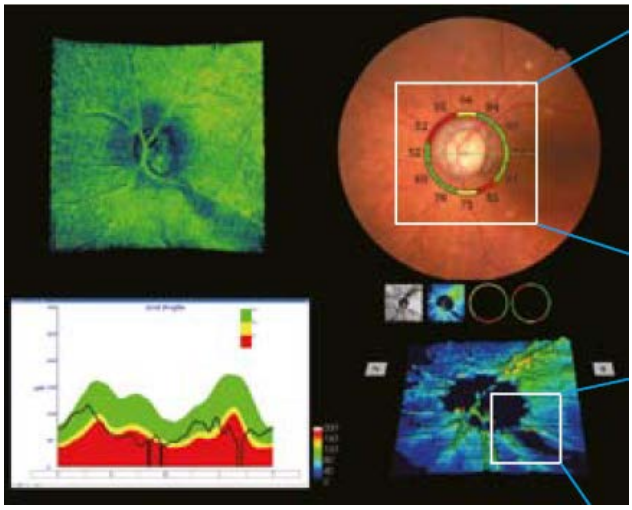


Figure 16.7: *Optic nerve head and retinal nerve fiber analysis with OCT*

COMMERCIALLY AVAILABLE OCTS FOR GLAUCOMA

A list of OCT devices are shown on Table 16.1.

Device	Company	Axial Resolution	Scanning Speed	Summary
Stratus TD-OCT	Carl Zeiss	10 µm	400 (A scans/sec)	More prone to motion artifacts Better for macula but can be used for RNFL thickness
Cirrus SD-OCT	Carl Zeiss Meditec Inc	5 µm	27 000 (A scans/sec)	RNFL, ONH GPA for glaucoma Compatible with Stratus data
3D-OCT 2000	Topcon Medical Systems	5 µm	50 000 (A scans/sec)	Combines SD-OCT with high-resolution fundus camera ONH, RNFL, asymmetry scans Trend and event analysis for progression
Spectralis	Heidelberg Engineering	4 µm	40 000 (A scans/sec)	SD-OCT with SLO RNFL, asymmetry scans Trend and event analysis for progression
RTVue-100 SD-OCT	Optovue Inc	5 µm	26 000 (A scans/sec)	RNFL analysis, ONH, GCC Event and Trend Analysis

Table 16.1: *Commercial OCT devices*

WHAT SD-OCT SCANS ARE USED IN GLAUCOMA?

The main glaucoma OCT scan protocols are as follows:

- ONH Analysis (weak)
- RNFL Analysis (strong)
- Asymmetry Thickness Analysis (weak)
    - Comparison of retinal thickness of posterior pole between individual hemispheres and between the two eyes

OPTIC NERVE HEAD AND RNFL ANALYSIS

A combined report using the Optic Disc 200x200 cube scan is shown in Figure 16.8.

The key components of the report are as follows:

1. Optic nerve head parameters
2. RNFL parameters

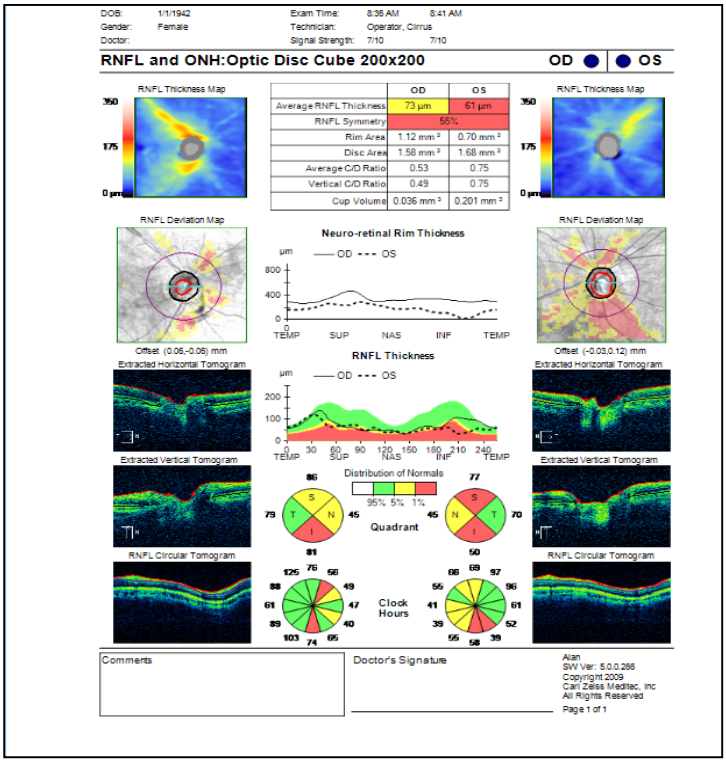


Figure 16.8: *RNFL and ONH analysis*

ONH ANALYSIS

The key features of the ONH analysis are as follows:

- High density scan (200 x 200 scan images)
- Covers 6 x 6 mm area centered on the ONH
- Image is analyzed using automated detection of optic disc's boundaries
    - Disc, cup, rim area; c/d area ratio; linear and vertical cup/disc ratio, cup volume, rim volume, horizontal and vertical disc diameter (DD)
    - No normative database

RNFL ANALYSIS

The key features of the RNFL analysis are as follows:

- Generated from the scanned cube or circular scan
- Circum-papillary analysis can be performed by sampling from the cube or circular scan along a 3.4 mm diameter scan centered on the ONH
- RNFL thickness is compared to normative database
    - Thickness profile (TSNIT)
    - Quadrant and clock hour thickness pattern

- Look for symmetry between the right and the left eye

For more information on OCTs, please refer to the Clinical Optometric Procedures 2 chapter *Ocular Coherence Tomography*.

SCANNING LASER POLARIMETER: GDX

The scanning laser HRT-3 is shown in Figure 16.9.

Figure 16.9: *The HRT-3 Scanning laser device*

GDx measures birefringence of retinal nerve fiber layer that yields relative retinal nerve fiber layer thickness data (Figure 16.10). Deeper layers of retinal tissue reflect light back to a detector. The degree of polarization change is recorded and yields a TSNIT curve.

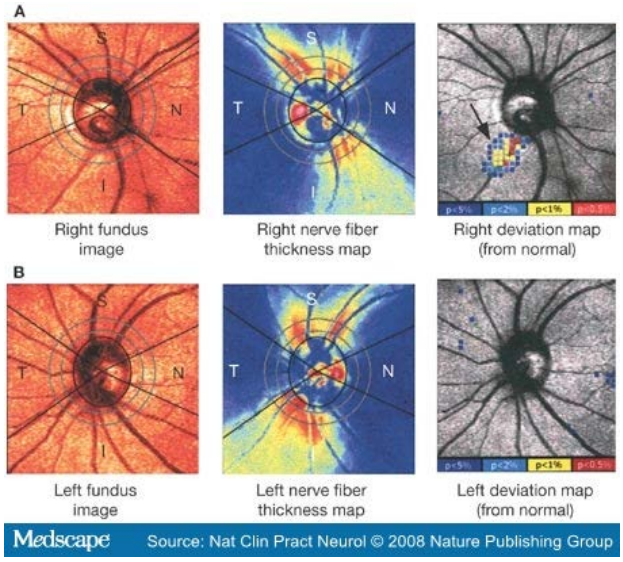


Figure 16.10: *Retinal nerve fiber layer thickness data*

CONFOCAL LASER SCANNING SYSTEM

The confocal system makes use of a laser light instead of a bright flash of light to illuminate the retina and captures the reflected light through a small aperture (Figure 16.11).

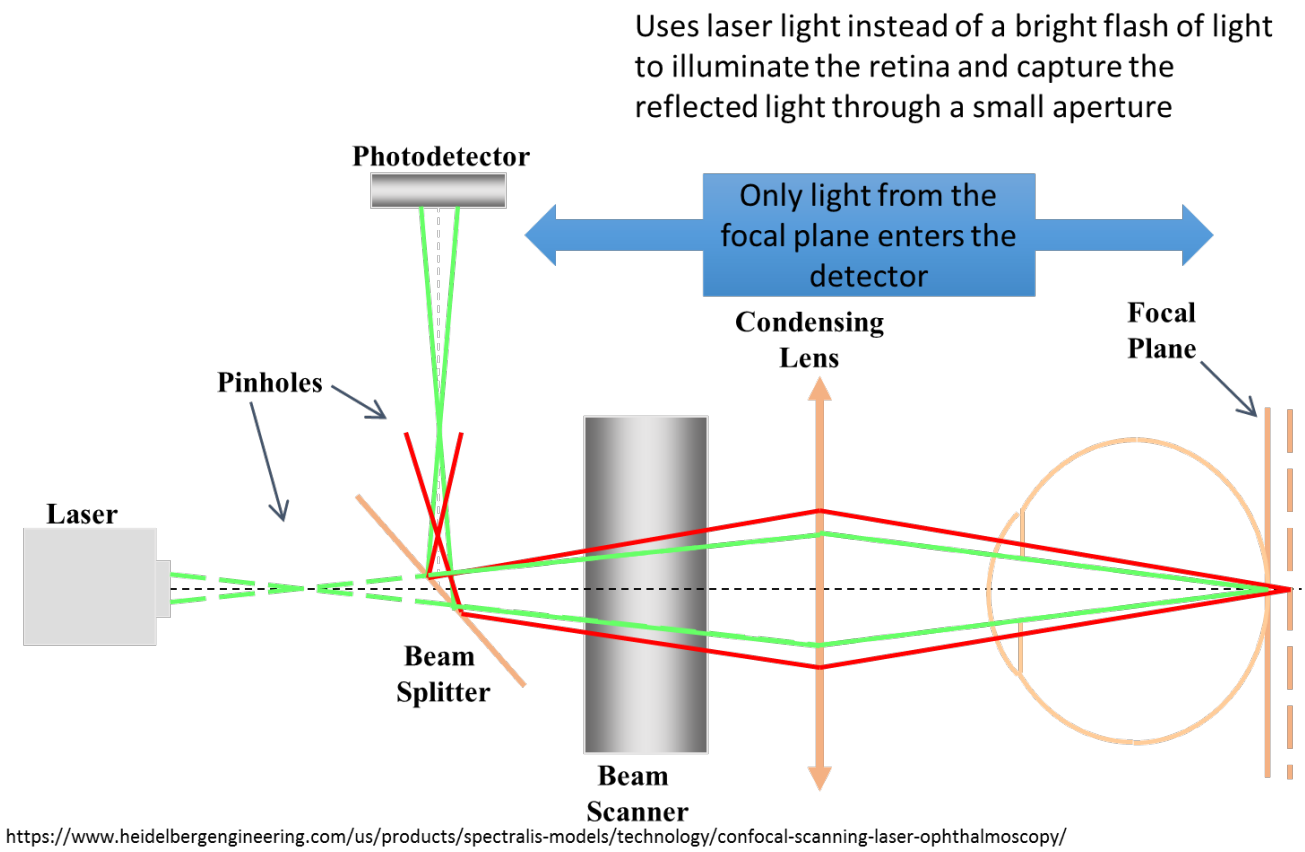


Figure 16.11: *Confocal scanning laser ophthalmoscope*

The main features of the device are as follows:

- Confocal imaging is the process of scanning an object point by point by a focused laser beam (670 nm diode laser) and then capturing the reflected light through a small aperture (a confocal pinhole)
- The emitted beam is redirected in the x-axis and y-axis along a plane of focus perpendicular to the optic axis using two oscillating mirrors to obtain a 2D image
- A luminance detector measures the light reflected from each point in the image after passing through the aperture
- The aperture limits the depth from which reflected light reaches the detector
- Light that is deeper or shallower than this focal plane is suppressed to provide an optical section of the posterior pole corresponding to this set focal plane
- The depth of the focal plane is automatically adjusted by shifting the confocal aperture to acquire multiple optical sections through the tissue of interest to create a layered three dimensional image

The RNFL maps are generated as follows:

- SLP passes polarized light through the RNFL and creates a high resolution map from over 32,000 data points
- A phase shift occurs because light polarized parallel to RNFL microstructures travels more slowly than light polarized perpendicular to them
- RNFL Integrity measurement:

- o Size of phase shift which is dependent on the thickness of the RNFL and the cumulative organization of its micro structures
- ECC = Enhanced Corneal Compensation – compensates for birefringence in the cornea

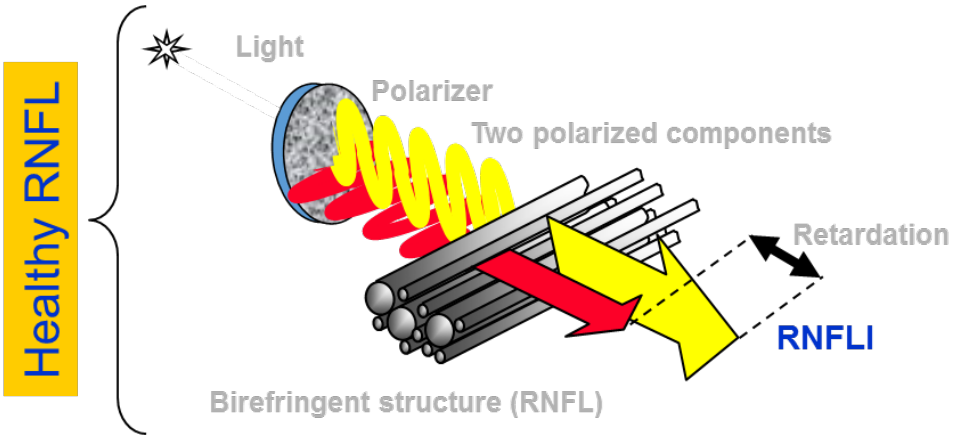


Figure 16.12: *Healthy RNFL*

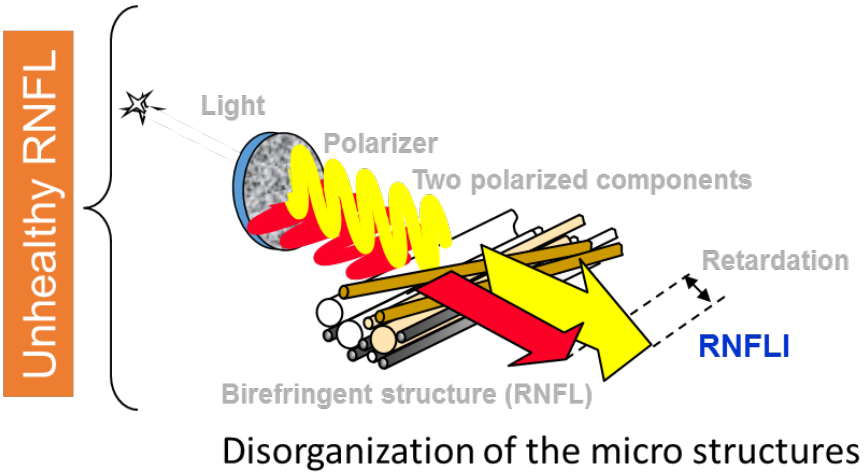


Figure 16.13: *Unhealthy RNFL layer - In diseased eyes, the phase shift difference gets smaller*

An example of a GDx analysis summary is shown in Figure 16.14.

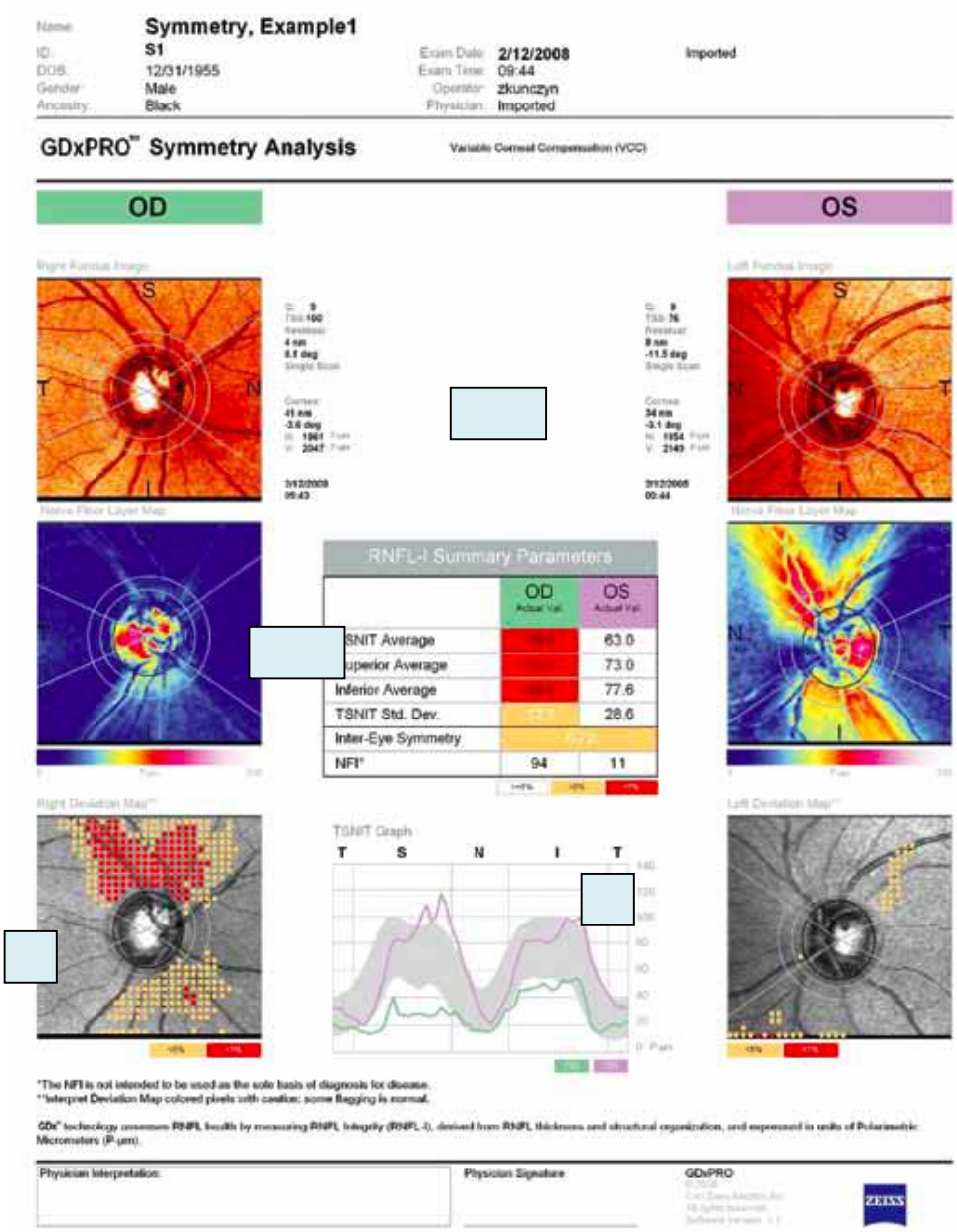


Figure 16.14: *A printout from a GDx measurement*

Some of the key considerations in GDx measurement are as follows:

1. **Fundus Photo**
    - Ensure illumination is even
    - Ensure scan is centered appropriately
2. **Quality Check**
    - Q $\geq$ 7 recommended
3. **Nerve Fiber Layer Map (Thickness map)**
    - Hour glass shape of yellow and red colours around the ONH is typical
    - Red = thicker
    - Blue = thinner
4. **RNFL-I Summary Parameters Table**
    - Only outputs 5 parameters for simplicity
    - Average thickness TSNIT, superior and inferior
    - NFI: The Nerve Fiber Indicator is related to the likelihood that the nerve fiber layer is abnormal
        - < 30 = normal
        - 30-50 = glaucoma suspect

        - >50 = probable glaucoma

5. **Deviation Map**
    - Colour coded indicating comparison to normative limits
    - Red = outside normal limits
6. **TSNIT graph**
    - Pattern generated by thickness pattern of RNFL (i.e. thickest superior and inferior sector)
    - Displays normal range and patient's values
        - High modulation = normal
        - Low modulation = abnormal