Decision making in Glaucoma

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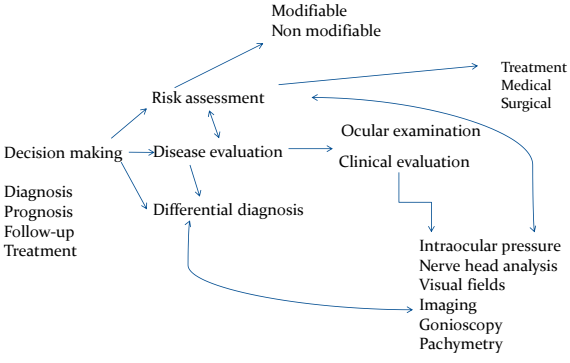
Disclosures

- **Speakers bureau** Optovue, Bausch and Lomb, Haag Streit
- **Consultant** Haag-Striet, ZeaVision, VectorVision, Optovue
- **Research** ZeaVision, Optovue, VectorVision

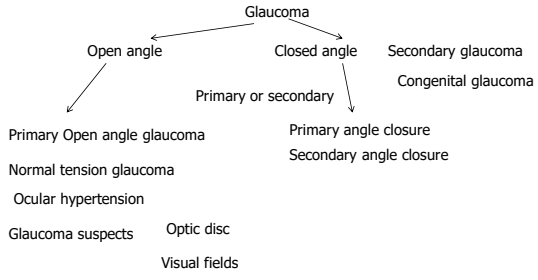
Outline



What is glaucoma?

- Definition:
  - "Ocular tissue damage at least partially related to intraocular pressure"
  - Where glaucoma is concerned agreement is limited among clinicians and scientists.

Types of glaucoma



Prevalence studies

- Prevalence in different studies varies
  - Different populations
  - Different methods used to obtain a sample
  - Definition of glaucoma

Prevalence of POAG in Caucasians

Study	Age range	Prevalence %
• Roscommon	Over 50	1.9
• Beaver Dam	43-84	2.1
• Rotterdam	Over 55	1.1
• Dalby	55-69	0.9
• Blue Mountain	Over 49	2.4
• Barbados Caucasians	40-84	0.8
• Baltimore Caucasians	Over 40	1.3

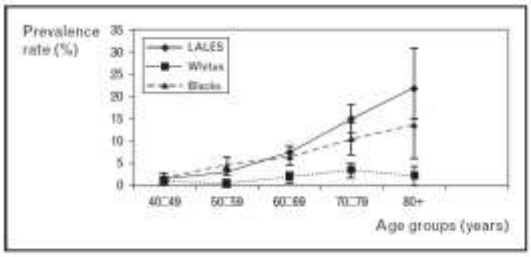
Prevalence of POAG in African American & African Caribbean

Study	Age range	Prevalence %	
• Barbados		40-84	7.1
• Baltimore		Over 40	4.2
• St Lucia		Over 30	8.8
• London		Over 35	3.9
African-Caribbean			

Prevalence of OAG in LALES

Age group (years)	Number who received on examination	Total	
		n (%)	95% CI
40–49	2363	31 (1.32)	0.90–1.86
50–59	1863	54 (2.92)	2.18–3.80
60–69	1195	88 (7.36)	5.90–9.08
70–79	584	86 (14.72)	11.78–18.18
≥80	147	32 (21.76)	14.90–30.72
Total	6142	291 (4.74)	4.22–5.30

Figure 2 Comparison between the Los Angeles Latino Eye Study (LALES) and the Baltimore Eye Study (blacks and non-Hispanic whites) in age-specific prevalence of open-angle glaucoma



Risk factors for glaucoma examined in population based studies

- Demographic
  - Age
  - Gender
  - Race
- Ocular
  - IOP
  - Optic nerve head
  - Myopia
  - Hypermetropia
- Systemic
  - Diabetes
  - Systemic hypertension
- Genetic
  - Family history
- Other
  - Cigarette smoking
  - Alcohol intake
  - Socio economic factors

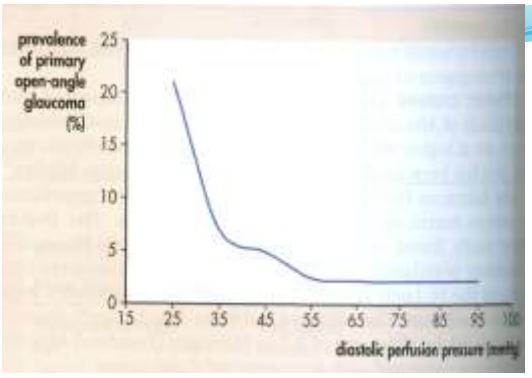
Intraocular pressure

- Major risk factor
  - Not as fundamental as once thought.
- Prevalence increases with increase in IOP
- Visual field loss slows down with decrease in IOP
- Even if both eyes have IOP lower than 21. The eye with greater IOP will lose field quicker.

Systemic hypertension and glaucoma

- Blood pressure and pathogenesis of glaucoma
  - Hospital based study
- Baltimore Eye Survey examined perfusion pressure
- Ocular Perfusion pressure= Blood pressure-IOP

(Systolic or Diastolic or mean pressure)



Tielsch et al Hypertension perfusion pressure and primary open angle glaucoma Arch ophthalmol 1995

Genetic factors

- Positive family history
- Bias:
  - + ve Family history makes a person have frequent check ups
  - Recall bias
    - Sibling with glaucoma odds ratio 3.69
    - Parents with glaucoma odds ratio 2.67
    - Children with glaucoma odds ratio 1.12

Summary

- Prevalence of POAG is Caucasians over 40 years of age 2% and in African American and African Caribbean is "four times" that.
- Hispanics greater risk than African American as they grow older
- Overall quite underdiagnosed- 50% unknown
- Glaucoma suspects- increases need for care dramatically

Intraocular pressure

- Diagnosis- not helpful
- Treatment- only proven method
- Progression- very closely associated with IOP
- Risk factor- without a doubt most important risk factor
- In fact only alterable risk factor!

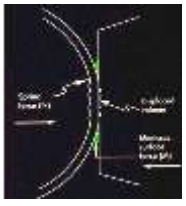
Corneal thickness and IOP issues

Modified Imbert-Fick law

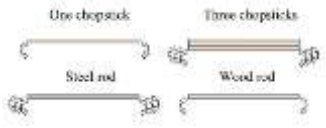
W + S = P x A +B

Where

1. S = Surface tension
2. B = Force required to bend the cornea



Understanding biomechanics of cornea



Liu J & Roberts CJ (2005)
Influence of corneal biomechanical properties on intraocular pressure measurement - Quantitative analysis.
J Cataract Refract Surg 31:146-155

Intraocular pressure

Pascal dynamic contour tonometer

Ocular Response Analyzer

Goals

- Document status of optic nerve structure and function
- Target pressure- so damage is unlikely to happen
- Maintain IOP below target pressure
- Monitor status of the optic nerve and visual function and reset target pressure if deterioration occurs.
- Minimize side effects of management and impact on vision and general health and quality of life.
- Educate and engage the patient in management

Nerve head evaluation

Measure Disc Size

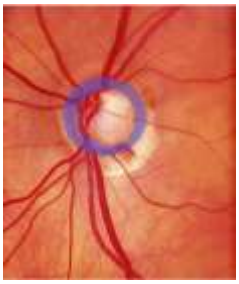
- Observe the scleral ring to identify the limits of the optic disc and evaluate its size.
  - 66D 1 X magnification
- Cup size is associated with disc size
- Effects any casual observer for cup to disc ratio measurement
- Rim thickness varies with disc size

Disc size

- Small < 1.5 mm ^{2}
- Medium > 1.5 but <2.5 mm ^{2}
- Large > 2.5 mm ^{2}

Neuroretinal rim characteristics

- Color of rim- pale rims not good
- Width of rim in all sectors
- ISNT rule
- ISNT rule is accurate about 70% of times

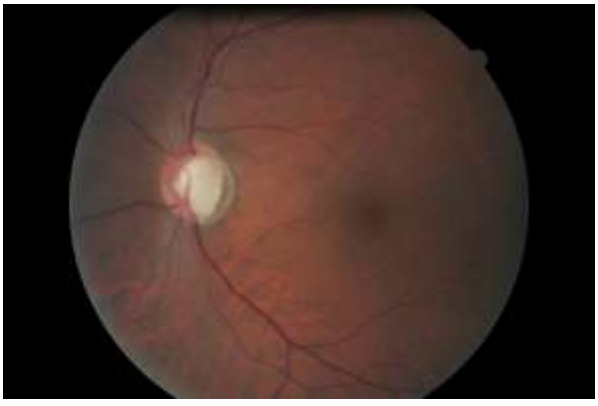


RNFL

- Healthy eye has striations
- A certain amount of NFL is required for visibility
- RNFL loss can be diffuse, localized or mixed

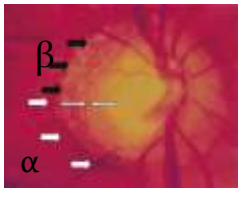
RNFL cont…

- Diffuse – reduction in RNFL brightness
- Localized – wedge shaped defect
- Localized RNFL defects should traced back the disc



Peripapillary atrophy

- Where
- How large
- *1/8, ¼, ½ , ¾, 1, > 1 DD*



Optic disc hemorrhages

- Transient
- Inferior temporal or superior temporal regions mainly
- Record present or absent
- If present where

Retinal vessels

Look for this in patients that you suspect NTG

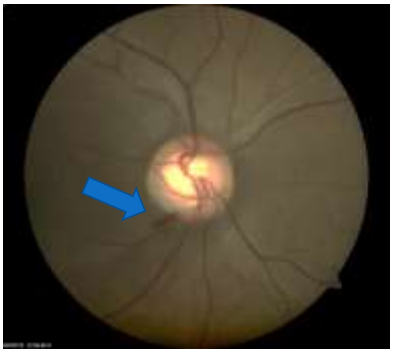
CD ratio

- Vertical
- Horizontal
- Largest
- CD ratio of imaging devices will not match your findings!

Focal atrophy of neural rim

Focal atrophy of neural rim-2

Optic disc hemorrhages



Optic disc hemorrhages-3

3 years later

Barring of circumlinear vessels

- Vessels that runs along margin between cup and neural rim.
- Found supero and infero temporally

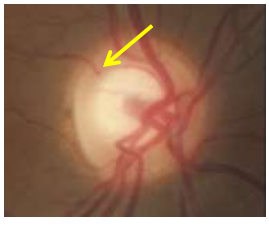
Barring of circumlinear vessels

- As rim becomes thinner it leaves an area of pallor between the rim and the circumlinear blood vessel.

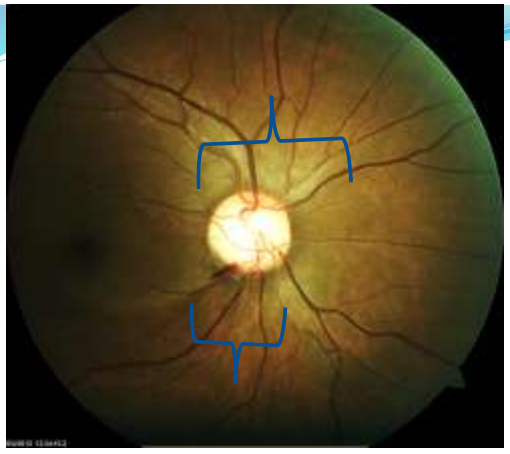
Barring of circumlinear vessels

Laminar dot sign

Bayonetting



- Double angulation of blood vessel.



Lab worksheet

Dr. Pinakin Davey

Disc size

Circle appropriately

Small < 1.5 mm^2, Medium > 1.5 but <2.5 mm^2, Large > 2.5 mm^2

OD = OS, OD > OS, OS > OD

Neuro retinal rim

Circle appropriately

1) Color
2) Follows ISNT rule
3) The thinnest clock hours

1) Pallor, Not well perfused (pale ish), pink
2) Yes/ NO
3)

Retinal nerve fiber layer

Circle appropriately

Diffuse NFL loss

Localized loss

Peripapillary atrophy

1) Where
2) How much disc diameter

1/8, ¼, ½ , ¾, 1, > 1

CD ratio

Vertical -------

Horizontal -------

Largest ----------

Signs present/ absent and where (what clock hour)

Focal atrophy of neural rim

Bayonetting sign

Barring of circumlinear vessels

Lamina dots sign

Optic disc hemorrhage

Nasal cupping

Proximal constriction of retinal arterioles

Advanced glaucomatous neuropathy

Shunt vessels

Complete glaucomatous optic neuropathy

Functional evaluation in glaucoma

Visual fields

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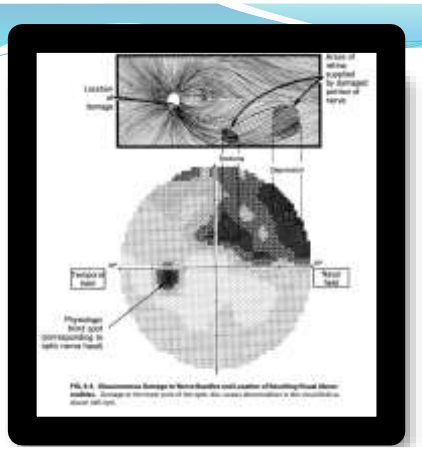

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Best perimetry

- If threshold is performed in all possible locations that can see in retina but it is not possible.

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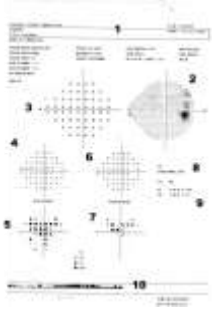
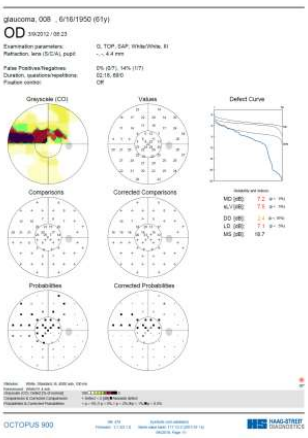
Visual fields – don't like them; cant live without them.

Humphrey "Gold standard" ?

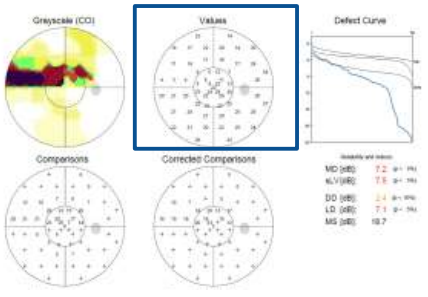


Single field analysis

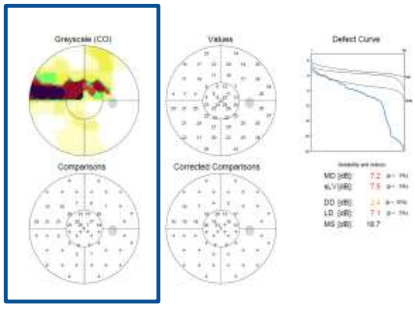


Reliability indices

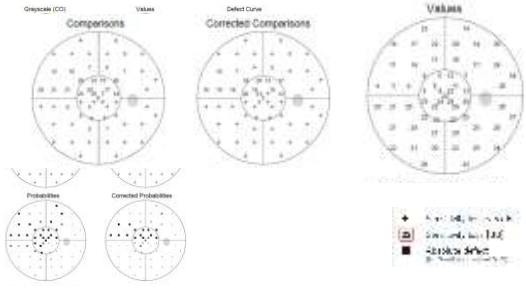
Raw data



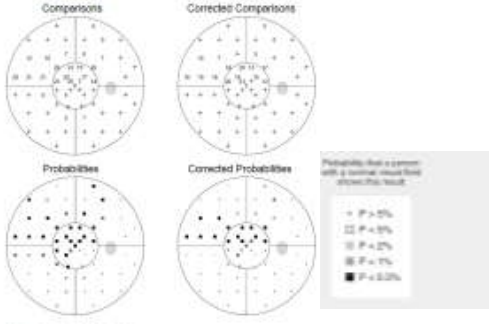
Grayscale



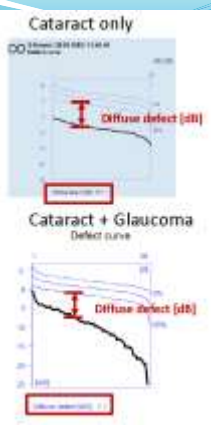
Comparisons and corrected comparisons



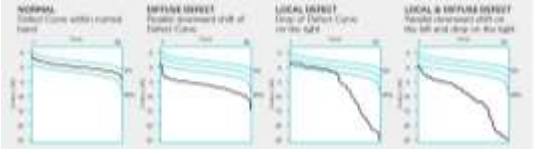
Probabilities plot



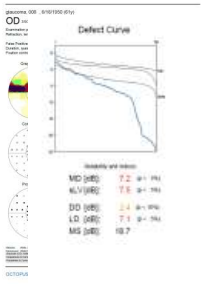
Bebie curve



Bebie curve examples

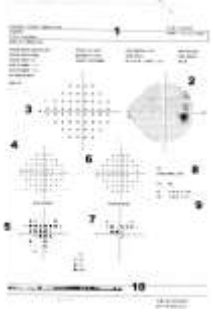


Global summarized indices



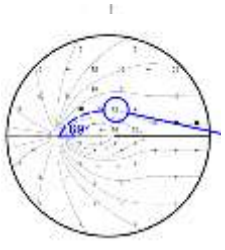
- MD = Mean Defect
- sLV= squareroot of Loss Variance
- DD- Diffuse defect
- LD- Localized defect
- MS Mean Sensitivity

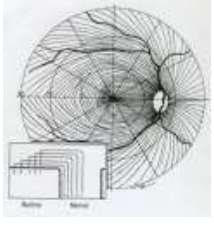
Humphrey visual fields



Some problems with HFA

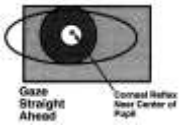
- Points spread evenly
- Data not representative of RNFL





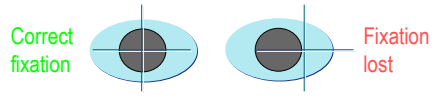
Problems continued

- No real blind spot monitoring



Octopus Features: Fixation Control

True Fixation Control



- No stimuli during fixation loss
- Automatic repetition of stimuli after blinking or darting
- Most accurate test possible

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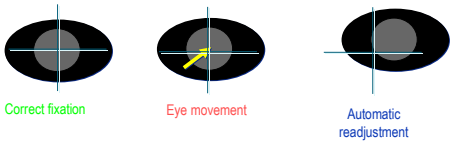
Octopus Features: Auto Eye Tracking



- The perimeter centers the patient automaticaly to the optical axis
- Less interrupts, less time to finish

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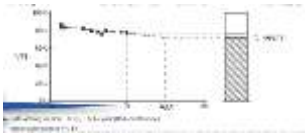
HFA II versus HFA 3

- Larger touch screen
- Liquid crystal lens -8 to +8 only sph correction

Visual Field Index

- Percentage of normal age adjusted field
- Greater the number more normal
- Trend over time is given with a probability values as well



- Should work in theory; in reality does not!

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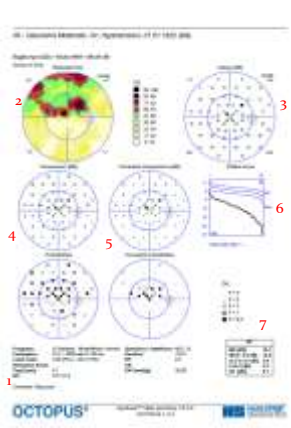
Octopus



Unique features of Octopus

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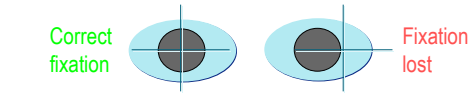
Octopus Features: Fixation Control

True Fixation Control



- No stimuli during fixation loss
- Automatic repetition of stimuli after blinking or darting
- Most accurate test possible

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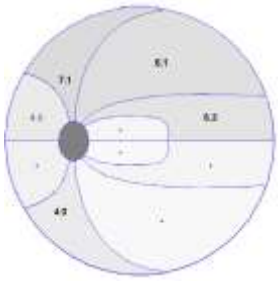
Cluster analysis



Why cluster analysis?

- Individual points may vary
- Overall clusters are more stable
- Also close representation to various bundles of RNFL
- So in some respect better structure function relationship.

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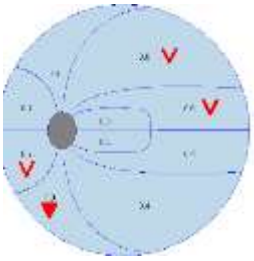
Trend analysis



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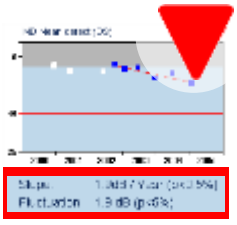
Global rate of progression



Progression rate

Color codes

Worsening at the 5% ,1% level

Improvement at the 5% ,1% level

Fluctuation at the 5% ,1% level

Scale

Grey: Normality

15dB: Seriously impaired vision

25dB: Considered legally blind

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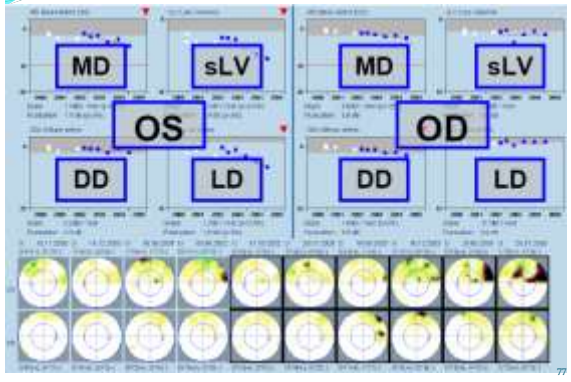
Global trends



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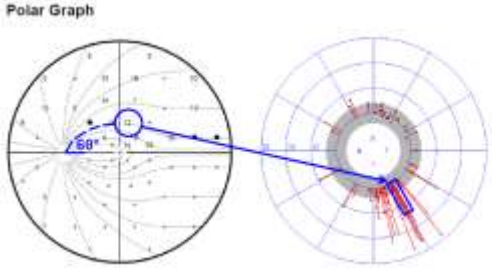
Polar graph



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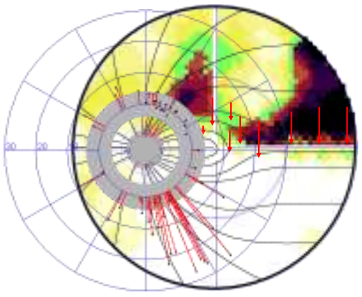
OCTOPUS Polar Diagram Principle



The bridge [illegible] structure:

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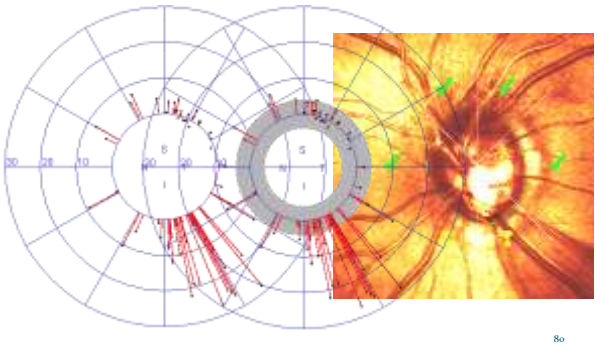
OCTOPUS Polar Diagram Bridging structure & function



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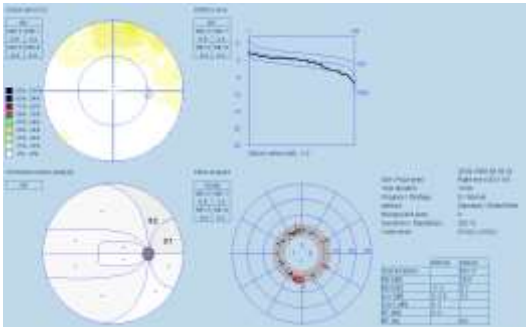
The 4-in-1 screen



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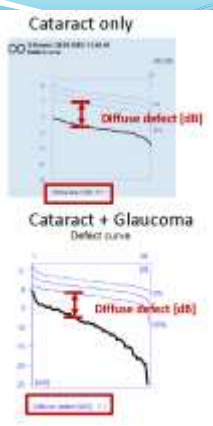
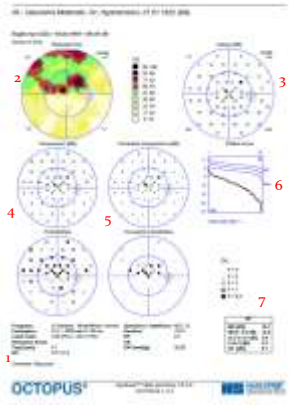
Bebie curve



Octopus



Is this defect a sign of "early glaucoma"

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Criteria for glaucomatous damage

1) GHT outside normal limits

2) PSD < 5% of normal individuals

3) A cluster of three or more **non-edge** points (pattern deviation plot) all of which are depressed at a p<5% and one of which is depressed at a p<1% on two occasions (respecting horizontal meridian)

- This criterion was written for 30-2, if 24-2 field is analyzed edge points are included.
- Criteria should be met on 2/3 issues mentioned above
- Confirmed on two occasions!

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Staging of disease

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Why is staging important?

- Treatment issues
- Management issues
- Prognosis
- Research

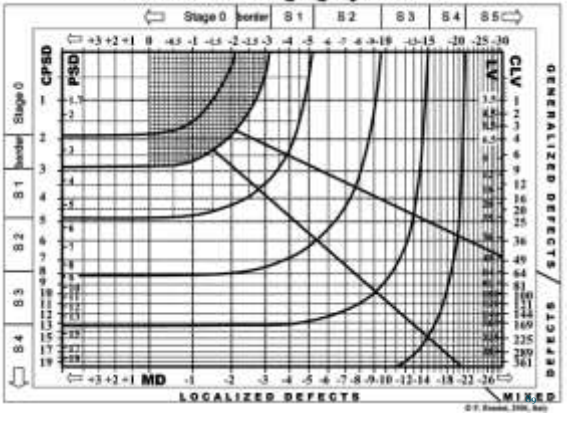
87

Glaucoma staging system- Brusini

GSS -2

88

Glaucoma Staging System 2

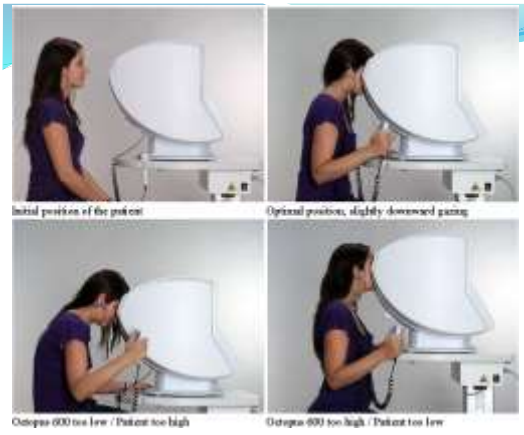


Clear text analysis

Stages

•normal VF
•borderline VF
•early VF defects (Brusini stage 1)
•moderate VF defects (Brusini st. 2)
•advanced VF defects (Brusini st. 3)
•severe VF defects (Brusini stage 4)
•most severe VF defects (Brusini st. 5)

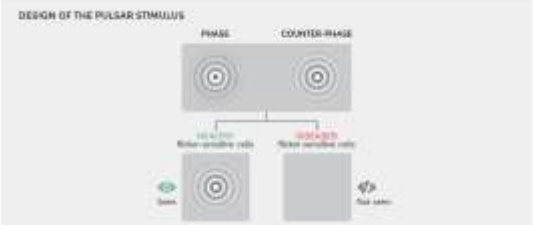
Octopus -600



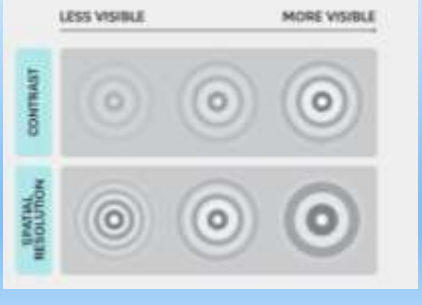
Pulsar perimetry

Why does it help targeting specific ganglion cells?

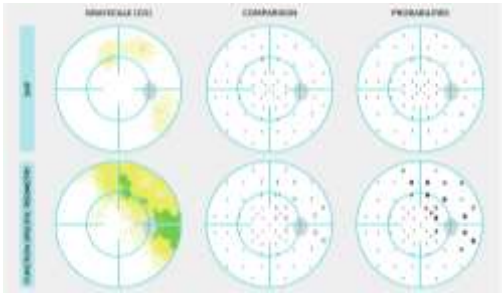
Design of the PULSAR stimulus



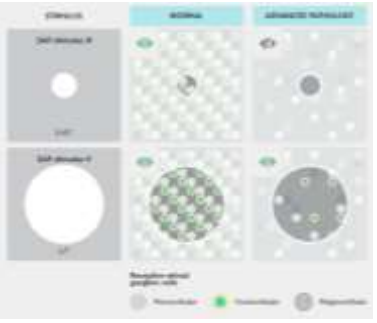
Sensitivity thresholds with PULSAR perimetry



Example of SAP and function-specific perimetry in the same eye

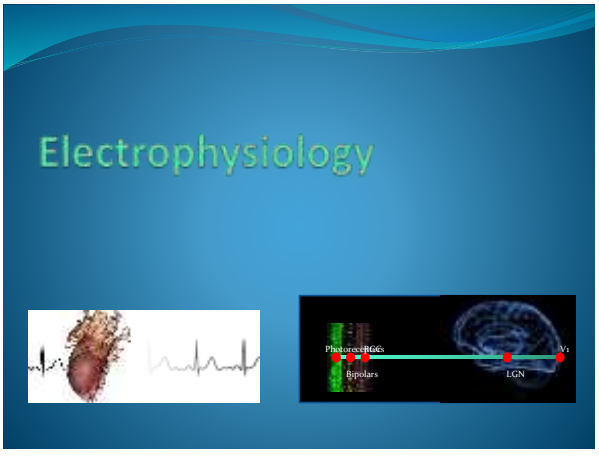


Principle of using stimulus V for low vision patients

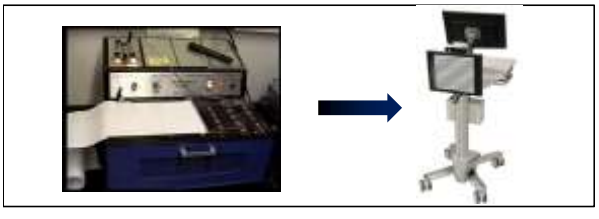


Summary

- Time for change is here.
- Doing what we have always done is unlikely to yield progress.
- Great programs that make a lot of sense clinically
- New technology may identify glaucoma early and easier to follow

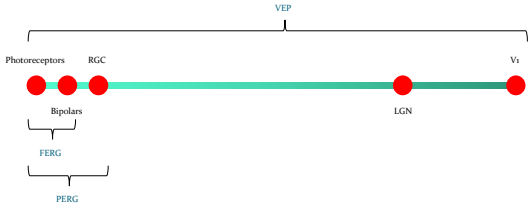


Electrophysiology has come a long way



Electrodes have come a long way

Which test when?



Structure

Fundus Photograph

(*Subjective*)

Function

Visual Field

(*Subjective*)

Structure

Coherence Tomography

(*Objective*)

Function

ERG

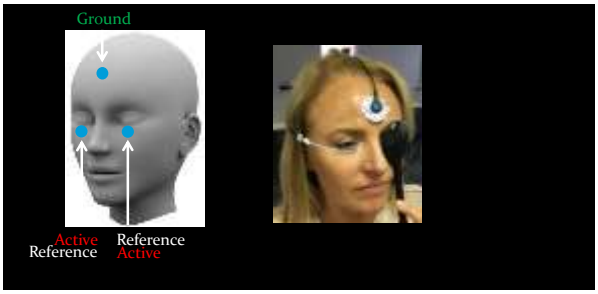
(*Objective*)

PERG Indications

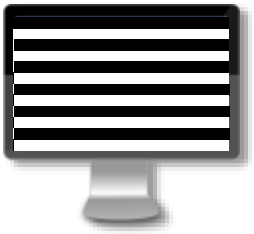
- Glaucoma
- Maculopathies

  AMD
  ERM
  DME
  etc.

ERG sensors



Pattern Electroretinogram (PERG)



Stimulus Monitor

Retinal ganglion cell signal recorded at the lower lid in response to pattern stimuli

Retinal Ganglion Cells

So where are the a, b, c waves?

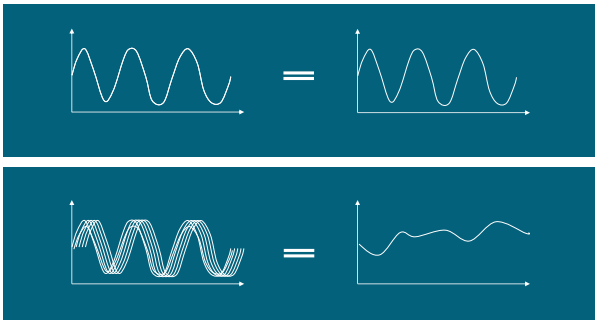
- Transient ERG that are less in frequency produce them.
- Variable and very much laboratory dependent.
- Difficult to obtain clinically.

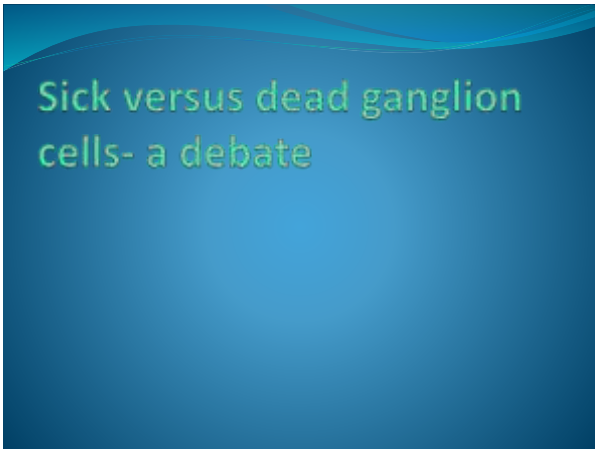
Steady sate- clinical state

Pattern ERG Flicker ERG

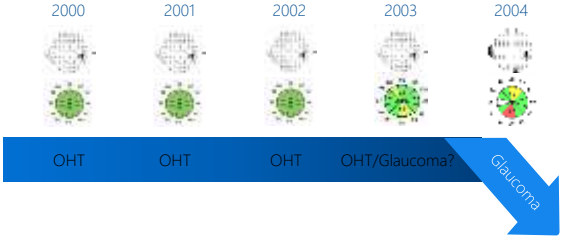
Steady state response
(high frequency)

Greater amount of information in shorter time:
300 responses

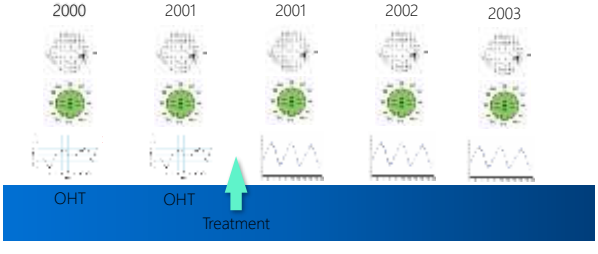




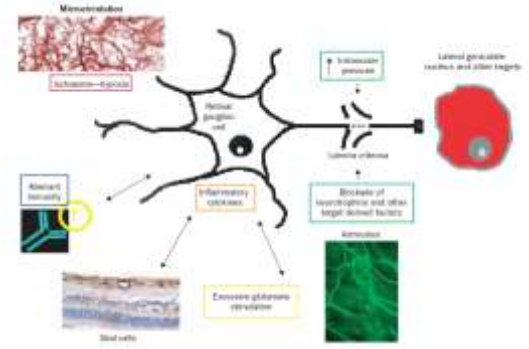
Current assessment of glaucoma suspect



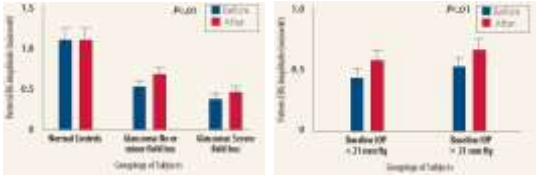
Suggested assessment of glaucoma suspect (AAO)



What are sick ganglion cells?



Changes in ERG post treatement



Ventura LM, Porciatti V. Restoration of retinal ganglion cell function in early glaucoma after intraocular pressure reduction: a pilot study. *Ophthalmology*. 2005;112:20-27.

Optical Coherence tomography

Glaucoma evaluation

- Anterior chamber evaluation
  - Angle evaluation
  - Corneal thickness
- Macula evaluation
- Retinal Nerve fiber layer
- Optic disc photography
- Visual fields

Anterior segment OCT

Gonioscopy

Iris insertion

A = Above Schwalbe line, totally occluded angle.
B = Behind the Schwalbe line, peripheral iris is in contact with TM.
C = Scleral spur Iris root at the level of scleral spur
D = Deep anterior ciliary body seen.
E = extremely deep

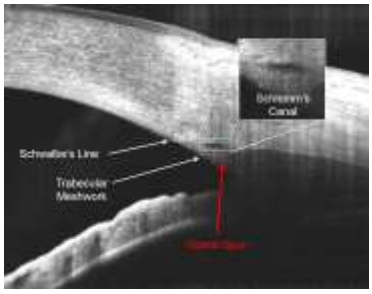
Angle approach

Guidelines recommend once a year procedure

Curvature of periheral iris

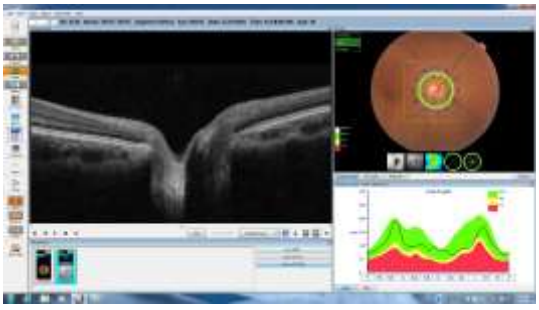
Angle Measurement with Quantification

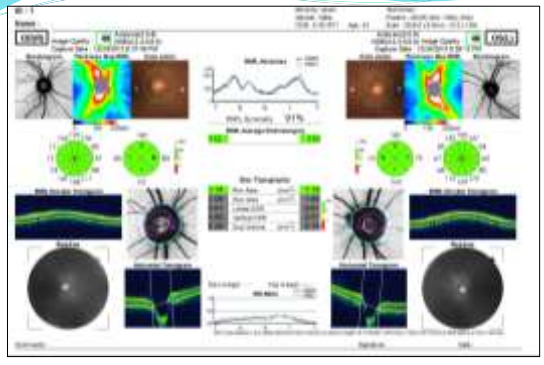
Anterior segment Angle Analysis



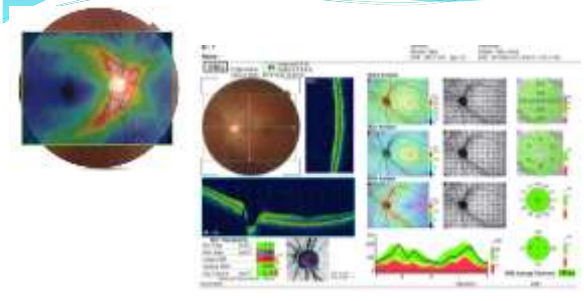
Optic Disc and Nerve fiber layer

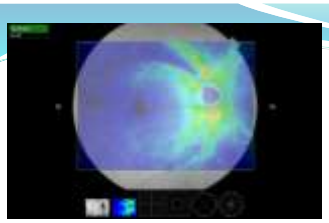
6 x 6 mm scan, Disc



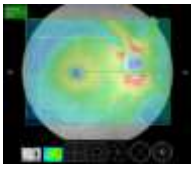


12x9mm Widefield scan, Report

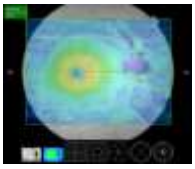




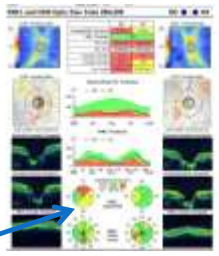
RNFL Thickness Map



GCL + IPL + RNFL

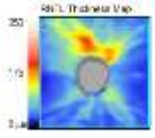


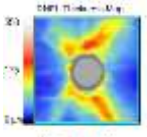
GCL + IPL



Best diagnostic parameter in identifying glaucoma using OCT is- Inferior average thickness

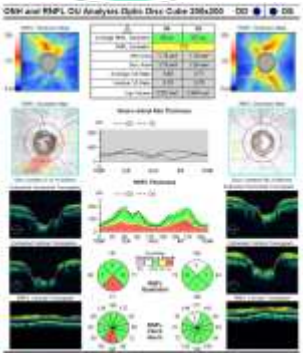
Thickness map



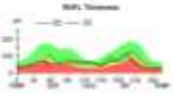


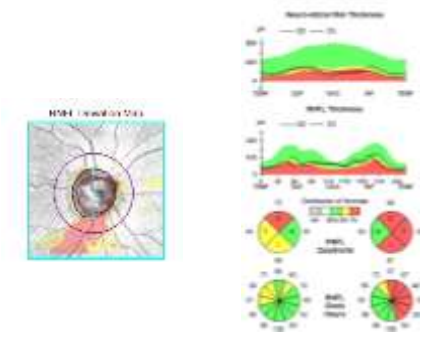
Deviation Map

Tomogram



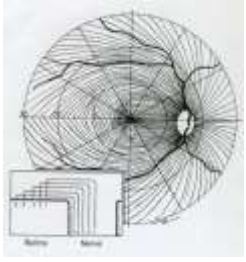
Global parameters





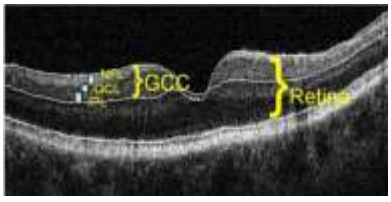
Macula analysis

Axonal facts



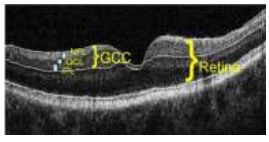
- 700,000 to 1.2 million
- Large variation
- Count of axons increase with increase in area.
- 50% of axons to the macula

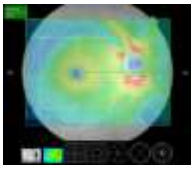
Ganglion Cell Complex (GCC)



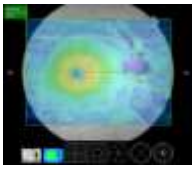
Macula analysis

- Optovue
  - NFL+ GCL + IPL
- Zeiss Ganglion Cell analysis- GCL+ IPL
- Topcon Maestro gives both
  - NFL+ GCL+ IPL
  - GCL+IPL
- Spectralis gives individual layers.



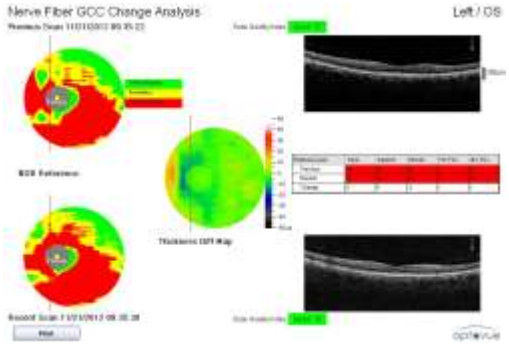


GCL + IPL + RNFL



GCL + IPL

GCC Change



Can "Macula Analysis" be used as an independent parameter to diagnose glaucoma?

The Applicability of Ganglion Cell Complex Parameters Determined From SD-OCT Images to Detect Glaucomatous Eyes

Paramasivan Arintawati, MD, Takashi Sone, MD,* Tomoyuki Akita, PhD,† Junko Tanaka, PhD,† and Yoshiaki Kiuchi, MD, PhD**

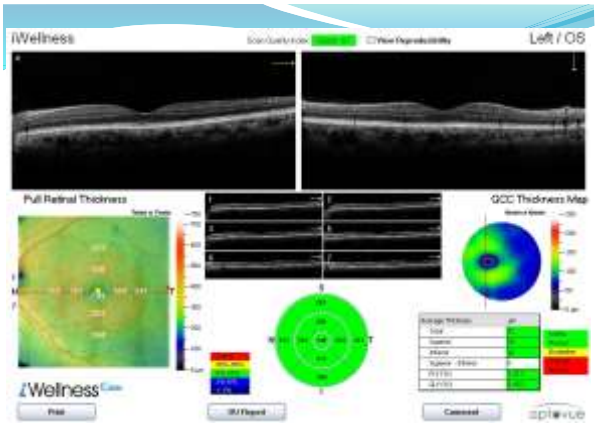
(*J Glaucoma* 2013;22:713–718)

Methods: Two hundred sixty-one eyes, including 68 normal eyes and 32 preperimetric glaucoma, 81 early glaucoma, and 80 advanced glaucoma were analyzed in the present study. The thicknesses of the GCC and retinal nerve fiber layer were measured using RTVue spectral-domain optical coherence tomographic (SD-OCT) images. The area under the receiver operating characteristic (AUROC) curve and sensitivities at fixed specificities were calculated for each parameter. A logistic regression analysis was used to determine the risk factors for glaucoma.

Evaluation of the OCT Parameters as Diagnostic Tests With the AUROC Curve

	N vs. PG	N vs. EG	N vs. AG
GCCa	0.795 (0.667-0.882)	0.806 (0.727-0.866)	0.902 (0.838-0.942)
GCCs	0.754 (0.617-0.853)	0.761 (0.678-0.828)	0.880 (0.809-0.928)
GCCi	0.815 (0.690-0.897)	0.795 (0.714-0.858)	0.915 (0.851-0.953)
FLV	0.745 (0.622-0.839)	0.789 (0.709-0.851)	0.948 (0.888-0.977)
GLV	0.806 (0.679-0.891)	0.816 (0.740-0.874)	0.929 (0.871-0.961)
RNFLa	0.740 (0.620-0.832)	0.734 (0.647-0.806)	0.910 (0.846-0.949)
RNFLs	0.748 (0.626-0.840)	0.725 (0.636-0.798)	0.889 (0.817-0.935)
RNFLi	0.723 (0.605-0.816)	0.700 (0.611-0.776)	0.912 (0.838-0.947)

Arintawati et al / Glaucoma • Volume 22, Number 9, December 2013



Eye and Brain

ORIGINAL RESEARCH

Sensitivity and specificity of the iVue iWellnessExam™ in detecting retinal and optic nerve disorders

Catherine Awad
Samantha Slotnick[1,2]
Sanjeev Nath[1]
Jerome Sherman[1,3]

Sensitivity and specificity were calculated for identifying normal and abnormal individuals

99 % Specificity
95.5% sensitivity in identifying retinal diseases
90% identifying optic nerve disease

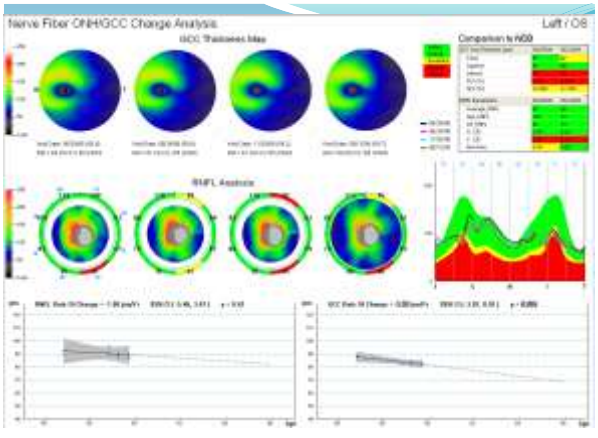
Summary

- OCT is a must in clinics that would like to manage any chronic diseases
- Particularly when monitoring change overtime
- Good quality data is a must in getting the best clinical outcome

Progression and glaucoma

Progression

- Consensus is limited
- Visual fields tend to fluctuate in early glaucoma
- Reliable and repeatable structural measurements is very valuable
  - Fourier domain OCT 5 microns accuracy.



Beware of RED and Green Syndrome!

OCT

Red syndrome

- False positive

Green Syndrome

- False neagtive

SD-OCT image quality at varying Z depths

Image quality decreases at deeper Z depths

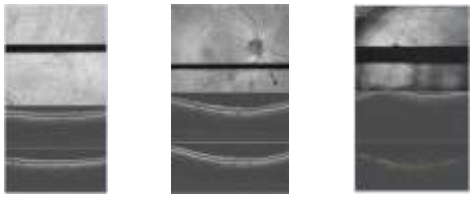
Image Acceptance Criteria

1. Image Quality Score (TopQ Score)
2. Eye Blinks
3. Eye Movement
4. Clipping
5. Fixation/Centration
6. Localized weak signal

Factors influencing OCT images

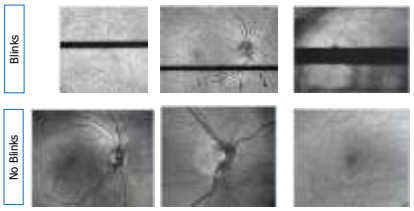
- Dirty objective lens
- Subject's head and/or chin not in proper position
- B Scan too high or too low in scanning area
- Improper focus
- Pupil too small
- Media opacity
- Reduced tear film on cornea
- These suggested steps should be used in order to improve the image quality score

Eye Blinks

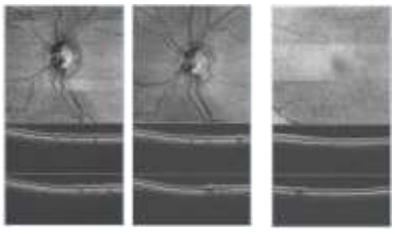


View on Instrumnt

Eye Blinks

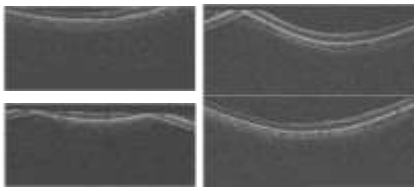


Eye Movements- Unacceptable



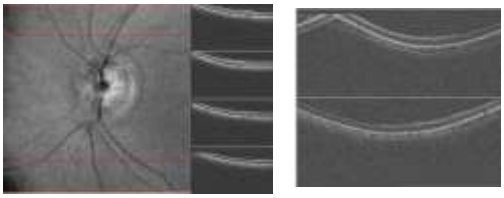
View on Instrument

Clipping- Unacceptable



View on Instrument

Clipping- Acceptable



View on Instrument

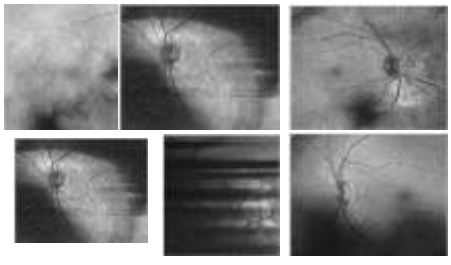
Fixation/Centration- not acceptable

6mm x6mm - Macula

6mm x6mm - Disc

View on PC

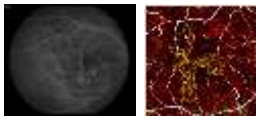
Localized Weak Signal



Whats new with OCT

OCT Angiography: A New Approach to Protecting Vision

- **Non-invasive** visualization of **individual layers of** retinal vasculature
- Pathology **not obscured** by fluorescein staining or pooling
- Image acquisition requires **less time** than a dye-based procedure
- Reduced patient burden allows more frequent imaging to **better follow disease progression and treatment response**



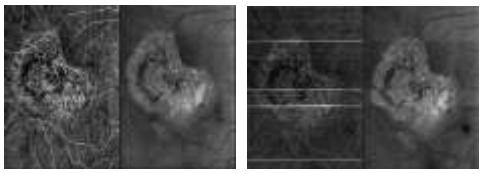
FA of CNV OCTA of CNV

How Does AngioVue Work?

Principles of AngioVue OCTA

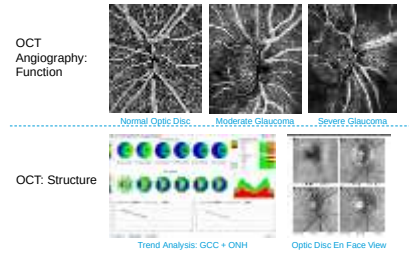
- Uses motion contrast to detect blood flow
- Rapidly acquire multiple cross-sectional images from a single location on the retina
- Flow is the difference between two sequential scans
  - Flow = Frame #1 – Frame #2

Motion Correction Technology (MCT™): Minimizes Saccadic Motion to Enhance Image Intensity



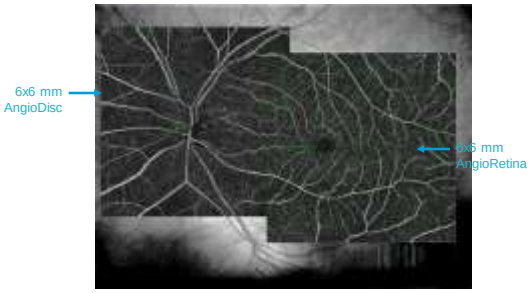
With MCT | Without MCT

Glaucoma

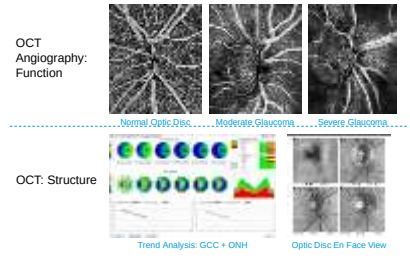


Previously diagnosed patient. Images courtesy of Michel Puech, MD, FRCS

AngioMontage Provides a Wider Field of View

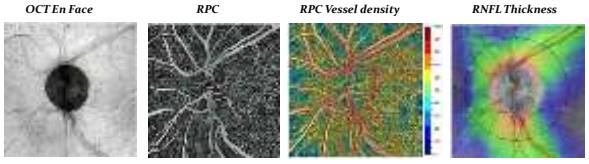


Glaucoma



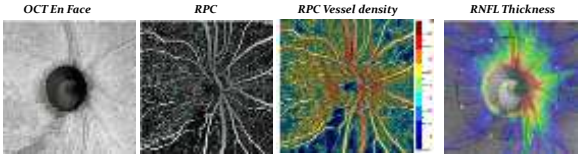
Previously diagnosed patient. Images courtesy of Michel Puech, MD, FRCS

Normal Eye



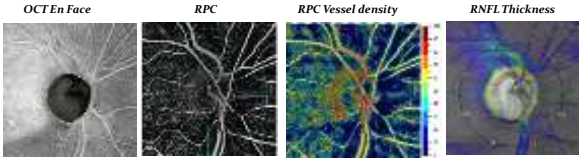
Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

Moderate Glaucoma



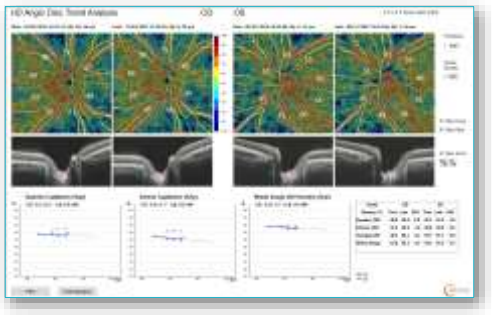
Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

Advanced Glaucoma

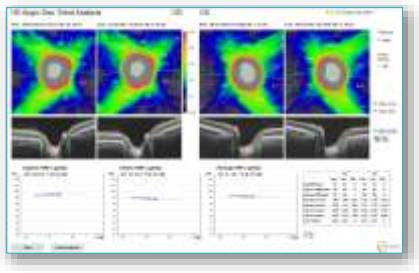


Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

AngioDisc Trend Analysis



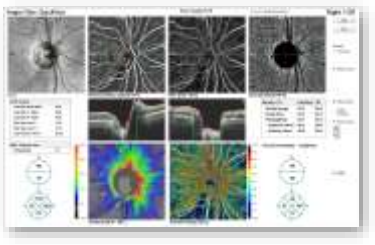
RNFL Thickness Trend Analysis



Overview Report Provides Disc Health at a Glance

One scan generates report showing:

- OCT Intensity
- RPC
- RPC Density
- RNFL
- Cup/Disc



Disc Overview Report Brings New Information to Glaucoma Management

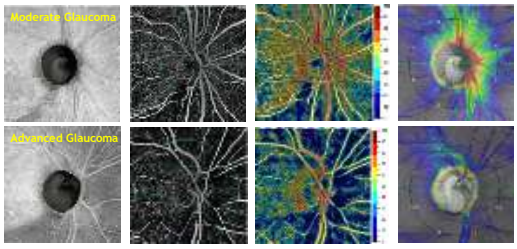


Image Courtesy: Drs. Weinreb, Nudleman, Goldbaum, Zangwill, UCSD, San Diego, CA (USA)