

Glaucoma- Making the diagnosis

Pinakin G Davey PhD, OD, FAAO

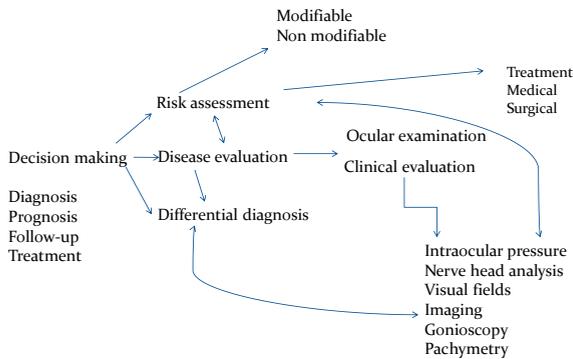
Professor



Disclosures

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

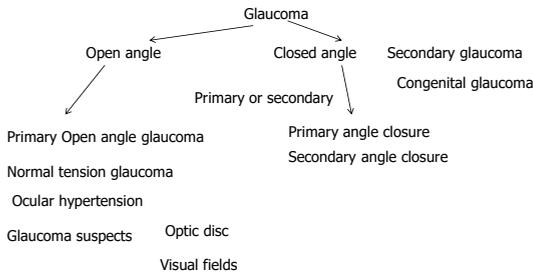
Outline



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

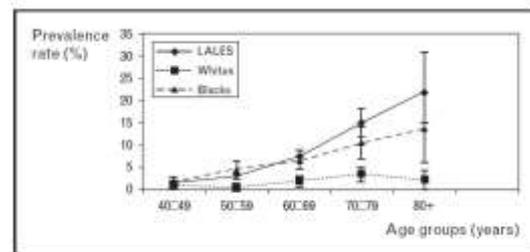
Prevalence of POAG in African American & African Caribbean

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

Prevalence of OAG in LALES

Age group (years)	Number who received on examination	Total	
		n (%)	95% CI
40-49	2363	31 (1.32)	0.90-1.88
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 (21.78)	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

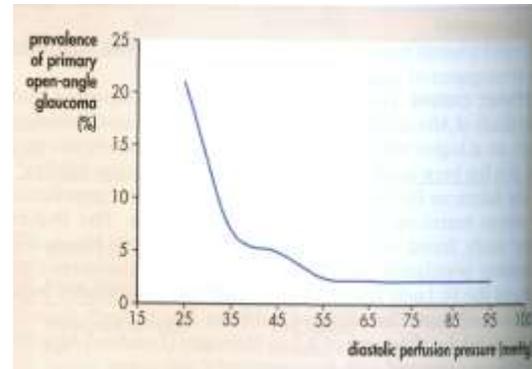
- Demographic
 - Age
 - Gender
 - Race
- Ocular
 - IOP
 - Optic nerve head
 - Myopia
 - Hypermetropia
- Systemic
 - Diabetes
 - Systemic hypertension
- Genetic
 - Family history
- Other
 - Cigarette smoking
 - Alcohol intake
 - Socio economic factors

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!

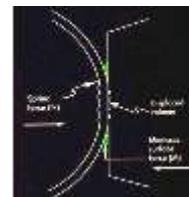
Corneal thickness and IOP issues

Modified Imbert-Fick law

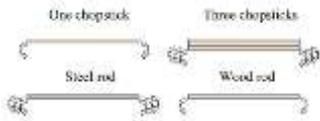
$$W + S = P \times A + B$$

Where

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



Understanding biomechanics of cornea



Liu J & Roberts CJ (2006)
Influence of corneal biomechanical properties on intraocular pressure measurement - Quantitative analysis.
J Cataract Refract Surg 32:48-55

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

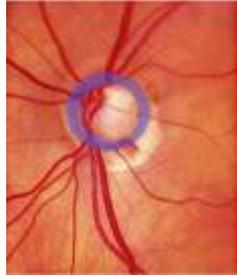
- Observe the scleral ring to identify the limits of the optic disc and evaluate its size.
 - 66D 1 X magnification
- Cup size is associated with disc size
- Effects any casual observer for cup to disc ratio measurement
- Rim thickness varies with disc size

Disc size

- Small < 1.5 mm²
- Medium > 1.5 but < 2.5 mm²
- Large > 2.5 mm²

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



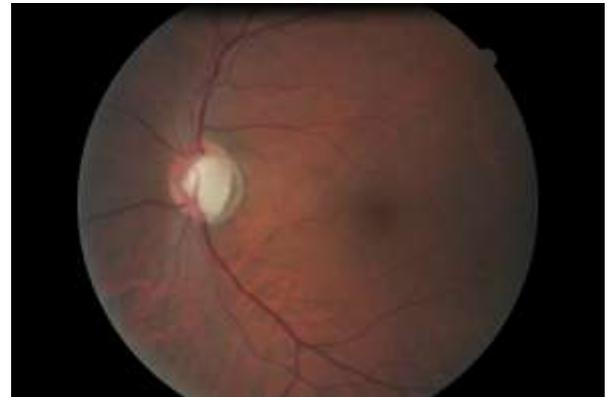
RNFL

- 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 be traced back to the disc



Peripapillary atrophy

- Where
- How large
- $1/8, 1/4, 1/2, 3/4, 1, > 1 DD$



Optic disc hemorrhages

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



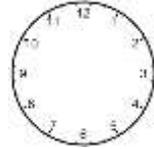
Retinal vessels



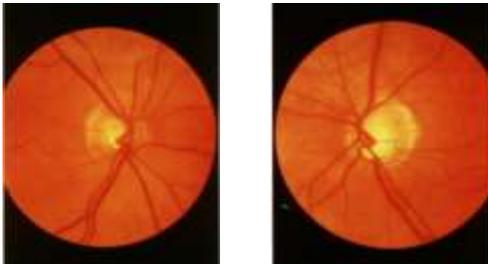
Look for this in patients that you suspect NTG

CD ratio

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



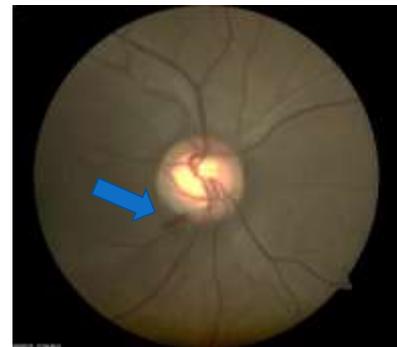
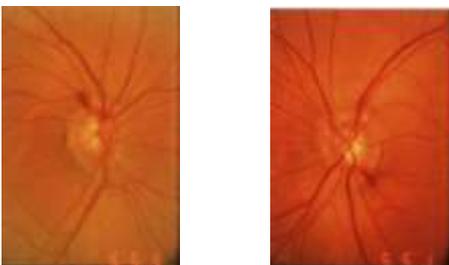
Focal atrophy of neural rim



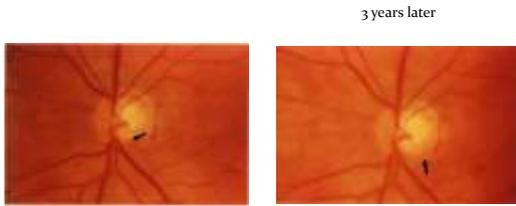
Focal atrophy of neural rim-2



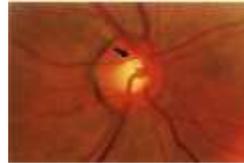
Optic disc hemorrhages



Optic disc hemorrhages-3

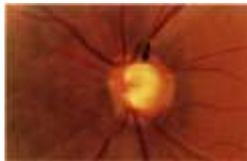


Barring of circumlinear vessels



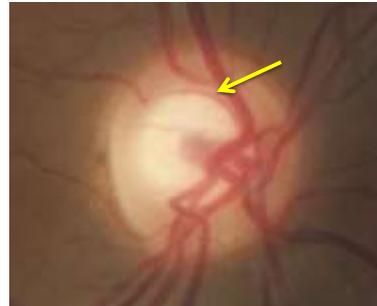
- Vessels that runs along margin between cup and neural rim.
- Found supero and infero temporally

Barring of circumlinear vessels

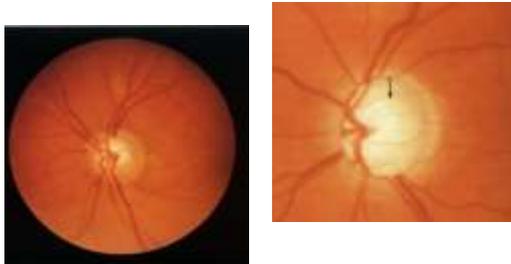


- As rim becomes thinner it leaves an area of pallor between the rim and the circumlinear blood vessel.

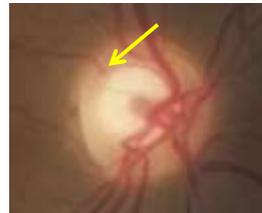
Barring of circumlinear vessels



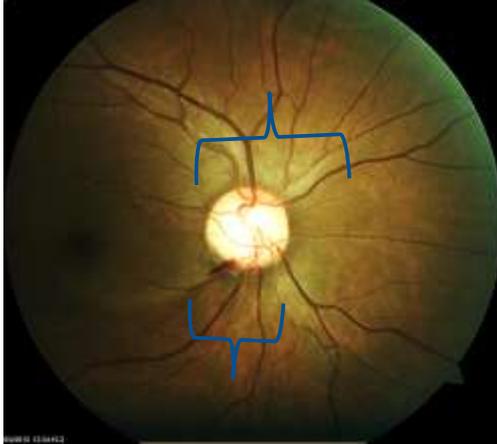
Laminar dot sign



Bayonetting



- Double angulation of blood vessel.



Lab worksheet

Dr. Pinakin Davey

Disc size
Circle appropriately

Small < 1.5 mm², Medium > 1.5 but < 2.5 mm², Large > 2.5 mm²
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, 1/4, 1/2, 3/4, 1, > 1

CD ratio

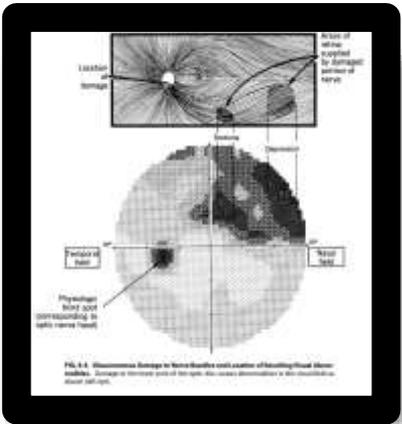
Vertical -----

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



Best perimetry

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

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

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Which perimeter shall I buy?

Very difficult question and very important



Features to consider

- Size of the device
 - Space is a premium
- Cost of the device
 - Ideally not an issue but..
 - A practice focused on managing disease needs a lot of equipment

Do you perform screening ?

- Who does not ?
- Headaches, disease specific like glaucoma



Central or a land far, far away...

- What tests are you interested in ?
 - central or far peripheral



Other important considerations

- Do you need kinetic perimetry ?
- Disability testing ?



Multimodal testing

- Screening tests
- White on White – SAP
- Specific Ganglion cell testing- M Cell, K Cell



Data interchangeable

- It is very important to maintain and old data
- Glaucoma is progressive disease and losing baseline is like losing your coordinates in a galaxy!



Software and analysis

- Various analysis techniques
- Structure function correlation plots
- Progression plots
- Customizable printouts to your need
- Electronic health record transfer

Summary

- Choose wisely !



Which test shall I select?

Threshold tests -standard of care in glaucoma

- Central threshold tests are standard of care in glaucoma
- Central 30 degrees
- Tests like 24-2, 30-2, G- Protocol, 32



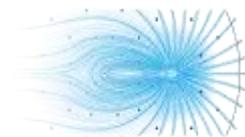
Is Glaucoma a peripheral disease ?

- Yes
- So why don't we measure visual fields from 30-60 degrees from center ?

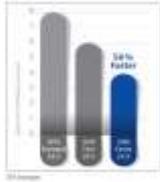


Is central retina and visual field more protected?

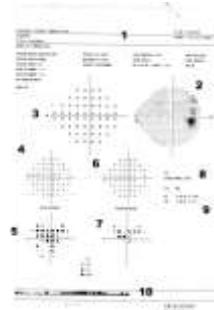
- Yes there is some truth to that
- But not as much as once considered...
- Lots of OCT studies identify macular damage early in glaucoma!



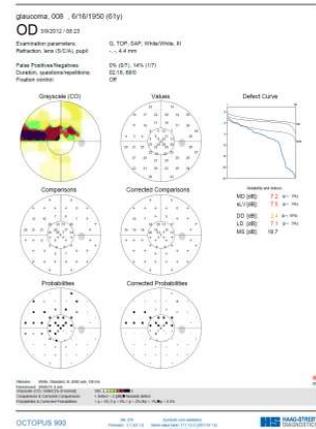
What strategy should I use?



Humphrey "Gold standard" ?



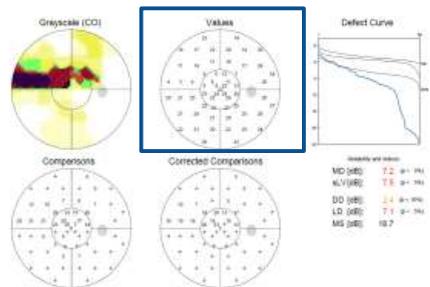
Single field analysis



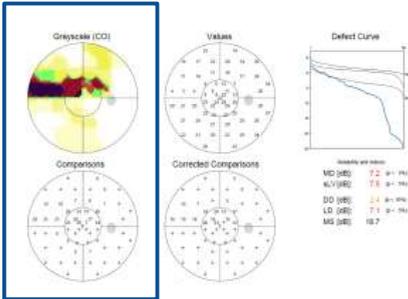
Reliability indices



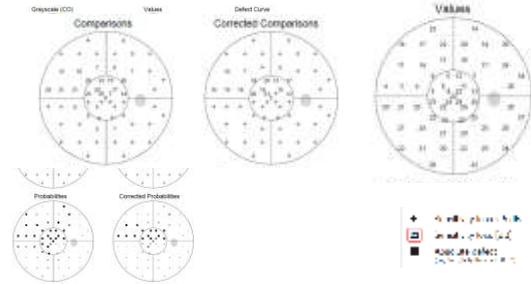
Raw data



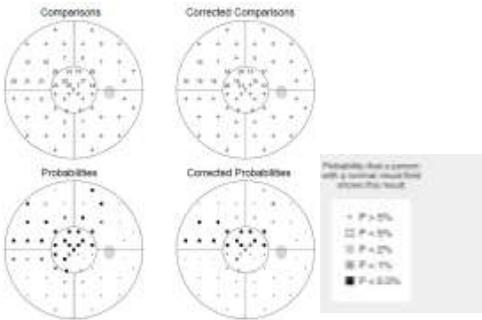
Grayscale



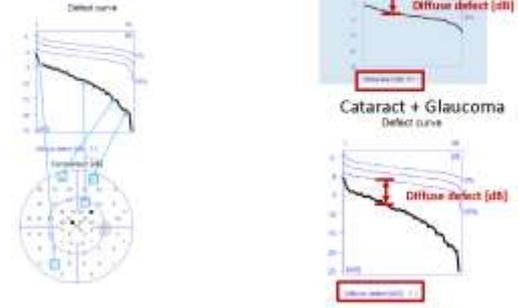
Comparisons and corrected comparisons



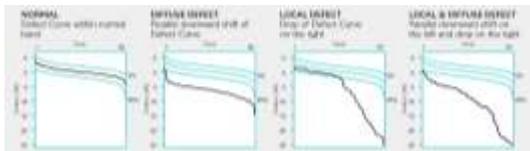
Probabilities plot



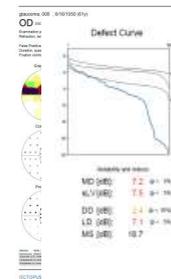
Bebie curve



Bebie curve examples

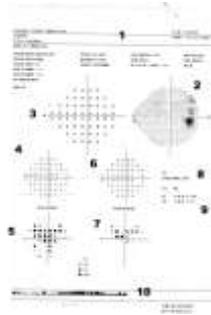


Global summarized indices



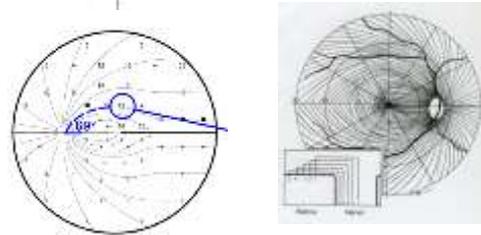
- MD = Mean Defect
- sLV= squareroot of Loss Variance
- DD- Diffuse defect
- LD- Localized defect
- MS Mean Sensitivity

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

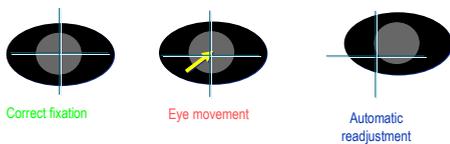
True Fixation Control



- 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 automatically to the optical axis
- ❖ Less interrupts, less time to finish

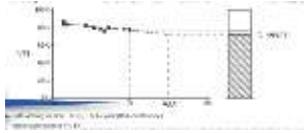
HFA II versus HFA 3

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

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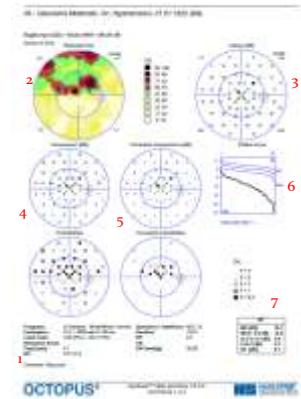
Visual Field Index

- 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

Octopus Features: Fixation Control

True Fixation Control



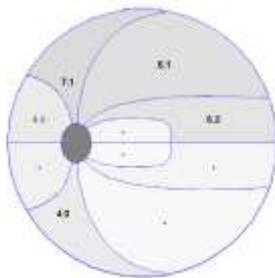
- No stimuli during fixation loss
- Automatic repetition of stimuli after blinking or darting
- Most accurate test possible

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Cluster analysis

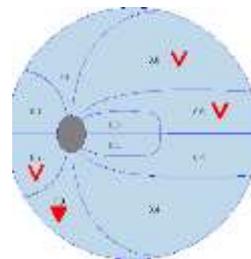
Why cluster analysis?



- 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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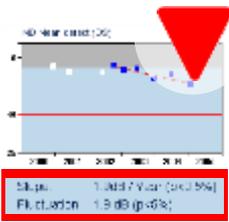
Trend analysis



- Numbers: Progression of size of field
- Red triangle: worsening at 1% probability
- Green triangle: recovery at 1% probability
- Blue triangle: fluctuation at 1% probability
- Orange triangle: fluctuation at 5% probability

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Global rate of progression



Progression rate

Color codes

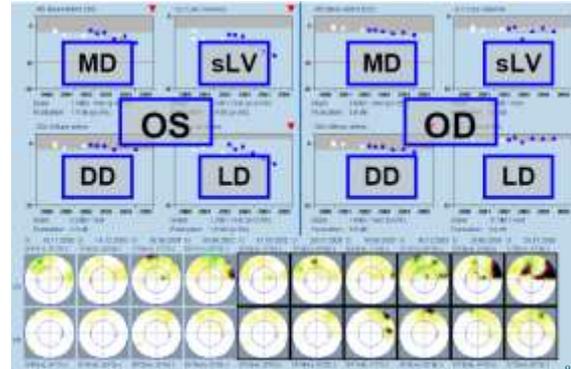
- Worsening at the 5%, 1% level
- Improvement at the 5%, 1% level
- Fluctuation at the 5%, 1% level

Scale

- Grey: Normality
- 15dB: Seriously impaired vision
- 25dB: Considered legally blind

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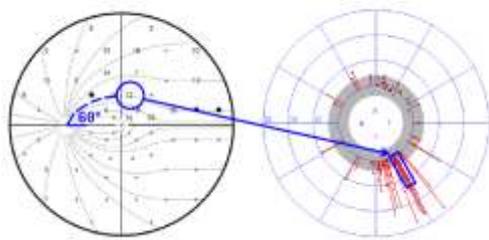
Global trends



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Polar graph

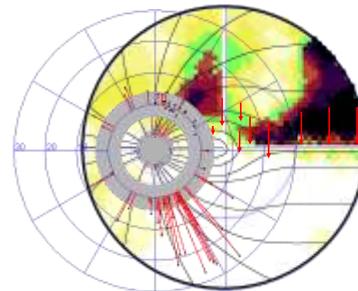
Polar Graph



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OCTOPUS

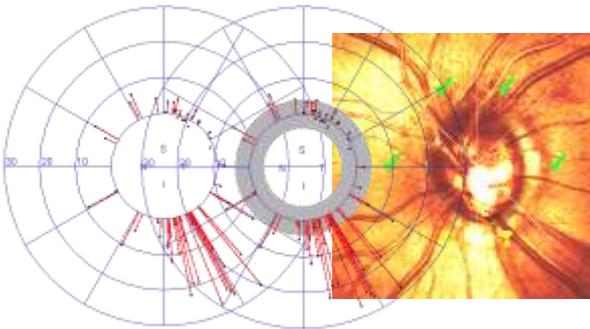
Polar Diagram Principle



The bridge structure of the polar diagram:

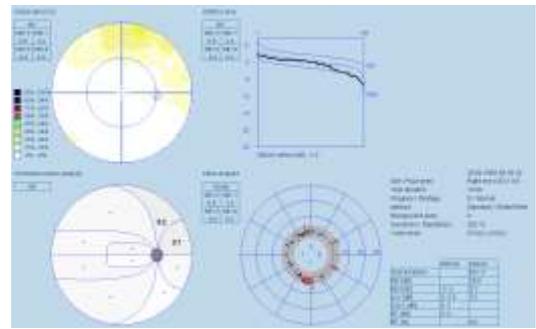
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OCTOPUS Polar Diagram Bridging structure & function



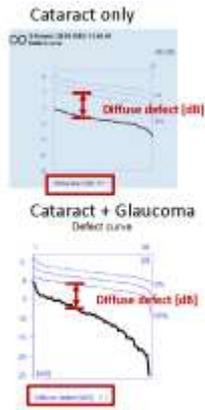
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The 4-in-1 screen

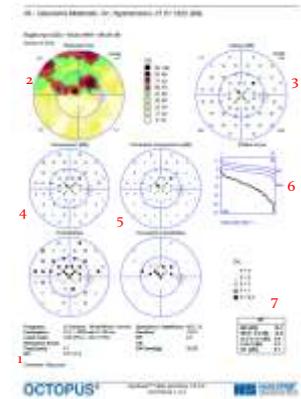


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Bebie curve



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

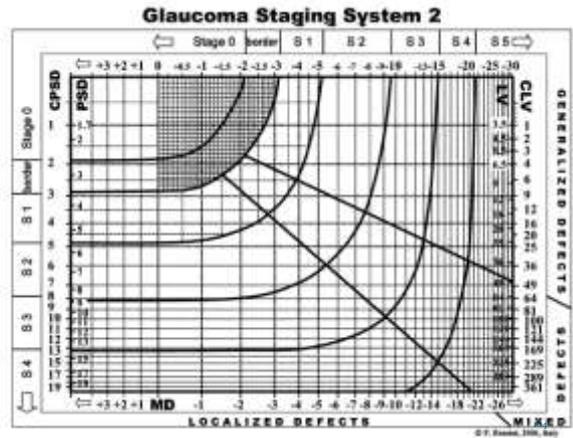
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Why is staging important?

- Treatment issues
- Management issues
- Prognosis
- Research

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Glaucoma staging system- Brusini GSS -2



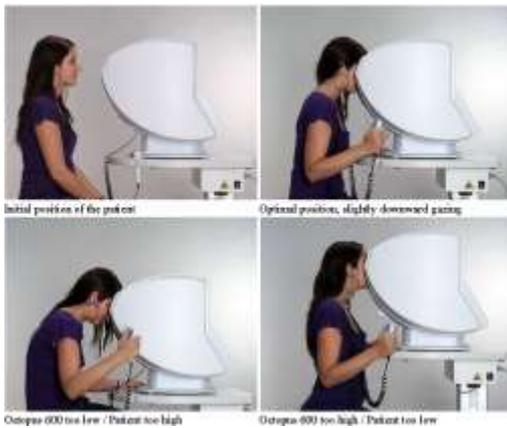
Clear text analysis



Stages

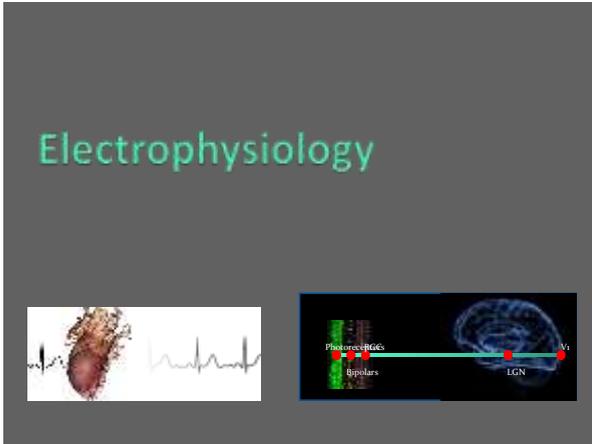
- normal VF
- borderline VF
- early VF defects (Brusini stage 1)
- moderate VF defects (Brusini st. 2)
- advanced VF defects (Brusini st. 3)
- severe VF defects (Brusini stage 4)
- most severe VF defects (Brusini st. 5)

Octopus -600

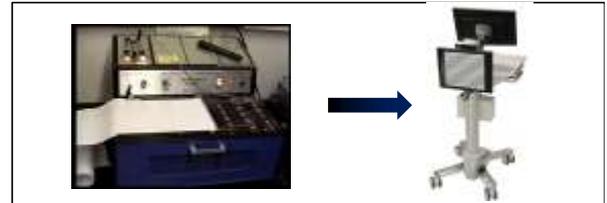


Pulsar perimetry





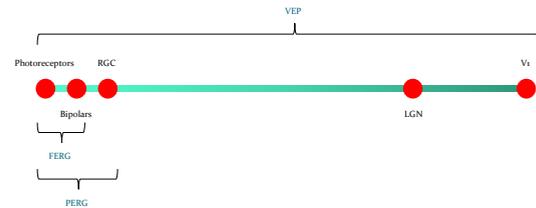
Electrophysiology has come a long way



Electrodes have come a long way



Which test when?



Structure
Fundus Photograph
(Subjective)



Function
Visual Field
(Subjective)



Structure
Fluorescein Tomography
(Objective)



Function
ERG
(Objective)



PERG Indications

- Glaucoma
- Maculopathies

AMD
ERM
DME
etc.



ERG sensors



Pattern Electretinogram (PERG)



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



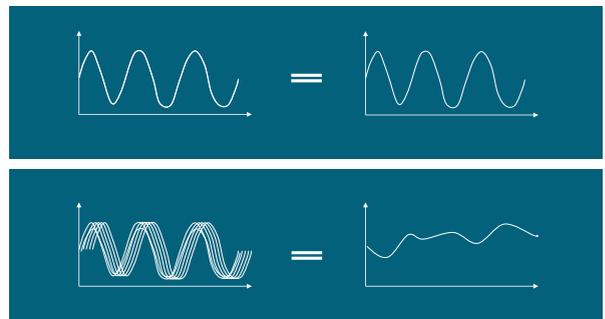
So where are the a, b, c waves?

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

Steady state- clinical state

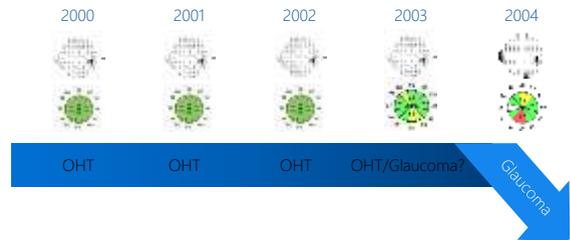


Greater amount of information in shorter time:
300 responses

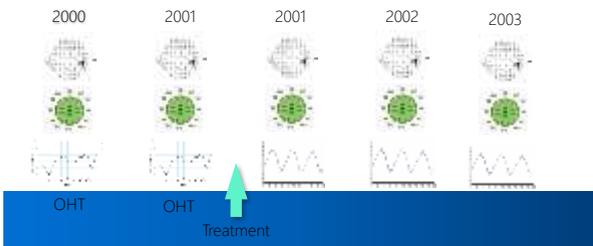


Sick versus dead ganglion cells- a debate

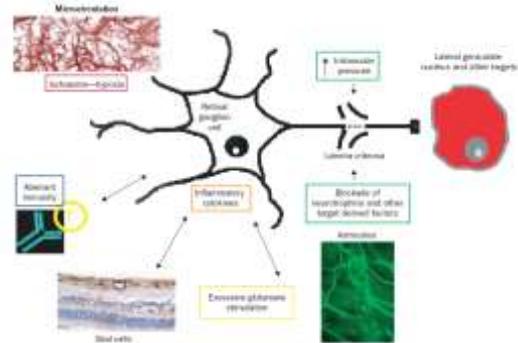
Current assessment of glaucoma suspect



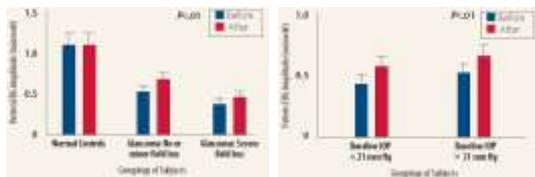
Suggested assessment of glaucoma suspect (AAO)



What are sick ganglion cells?

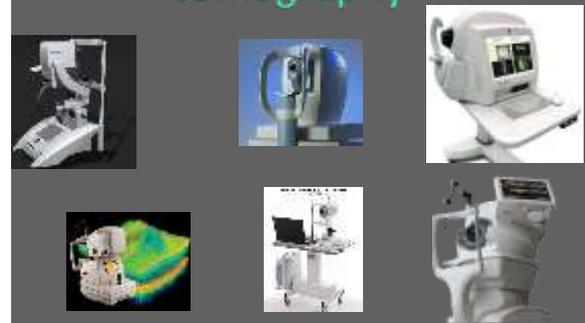


Changes in ERG post treatment



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

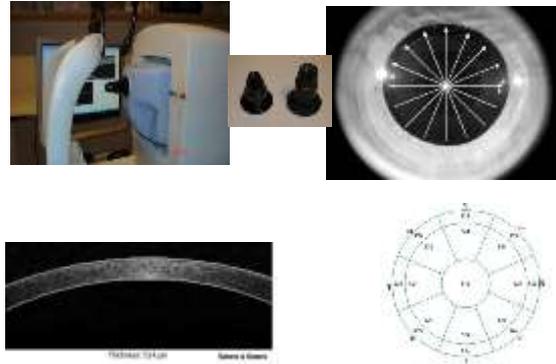
Optical Coherence tomography



Glaucoma evaluation

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

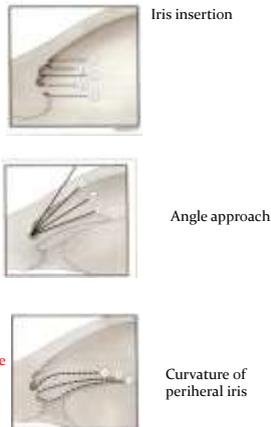
Anterior segment OCT



Gonioscopy

- 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

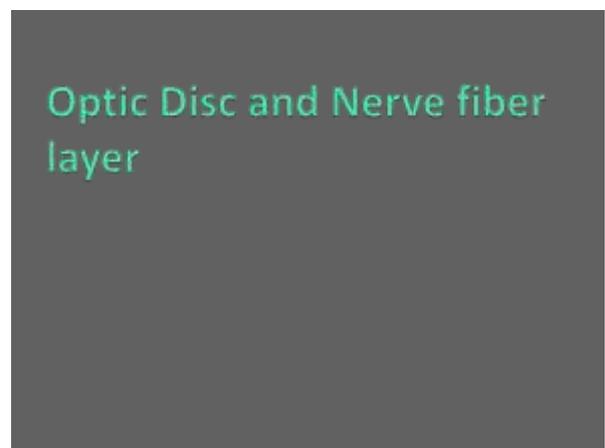
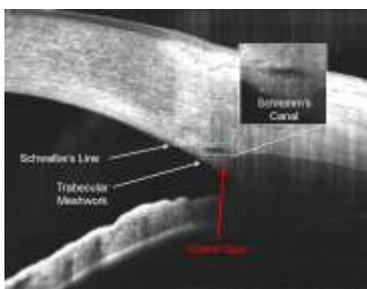
Guidelines recommend once a year procedure



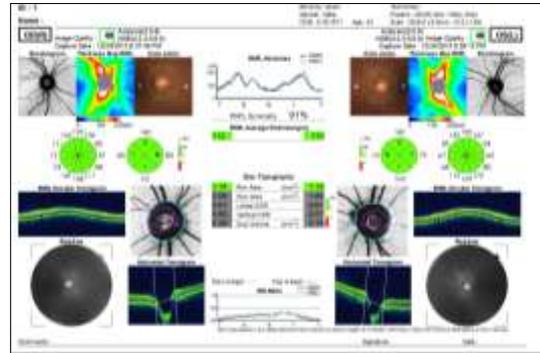
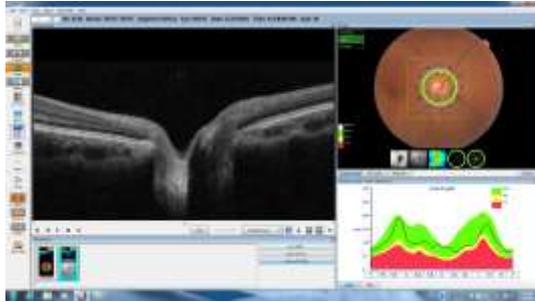
Angle Measurement with Quantification



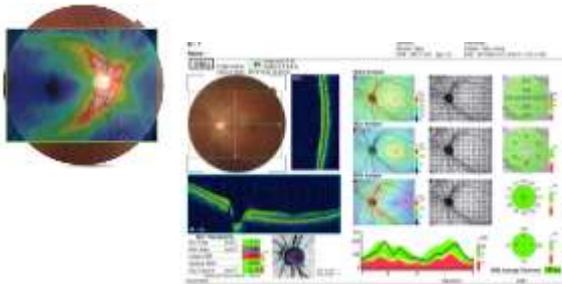
Anterior segment Angle Analysis



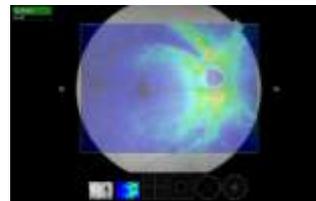
6 x 6 mm scan, Disc



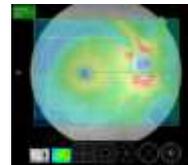
12x9mm Widefield scan, Report



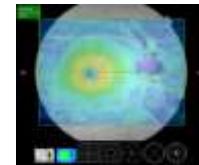
Best diagnostic parameter in identifying glaucoma using OCT is- Inferior average thickness



RNFL Thickness Map

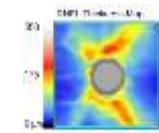
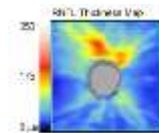


GCL + IPL + RNFL

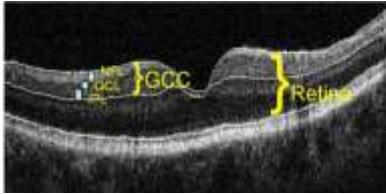


GCL + IPL

Thickness map

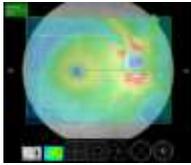
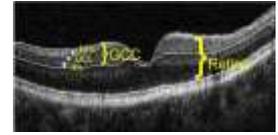


Ganglion Cell Complex (GCC)

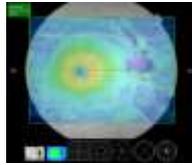


Macula analysis

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

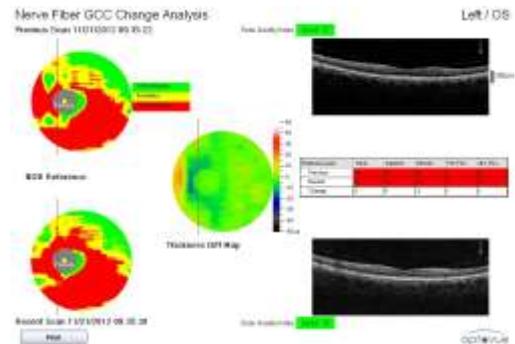


GCL + IPL + RNFL



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

Parasmiti Agrawal, MD,* Takashi Saito, MD,* Tomoyuki Akita, PhD,† Junko Tomika, PhD,† and Yoshiko Kishi, MD, PhD*

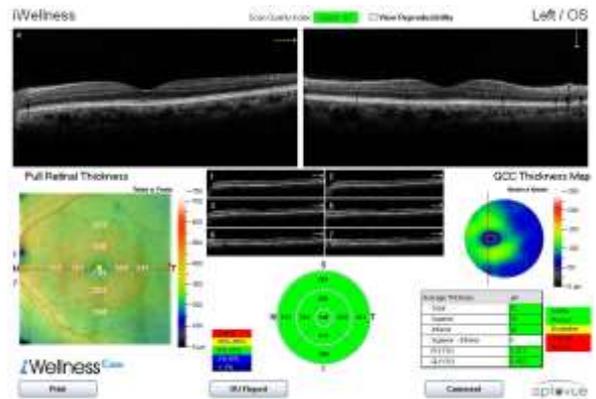
(*J Glaucoma* 2013;22:713–718)

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)
GCCt	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)
RNFLt	0.723 (0.605-0.816)	0.700 (0.611-0.776)	0.912 (0.858-0.947)

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



Eye and Brain

Development

ORIGINAL RESEARCH

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

Caroline Awwad,
Samantha Stenick,¹
Sanjeev Narsh,²
Jerome Sherman,³

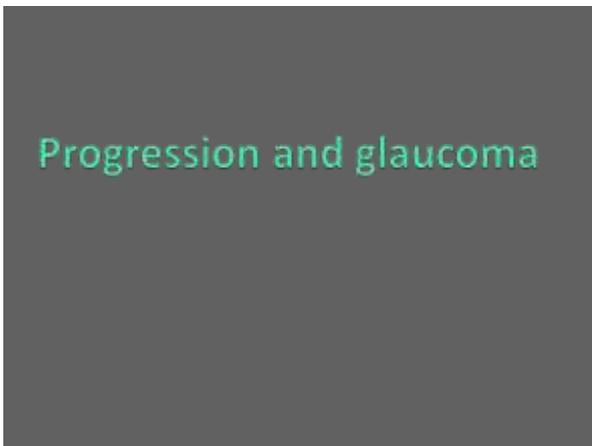
¹Mount Sinai School of Medicine,
Department of Ophthalmology, New York, NY, USA
²Department of Ophthalmology,
New York University School of Medicine,
New York, NY, USA
³Department of Ophthalmology,
New York University School of Medicine,
New York, NY, USA

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

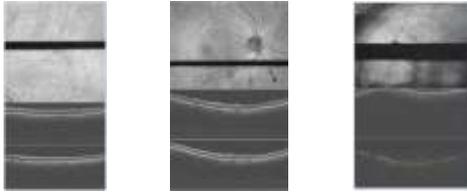
- OCT is a must in clinics that would like to manage any chronic diseases
- Particularly when monitoring change overtime
- Good quality data is a must in getting the best clinical outcome



Progression

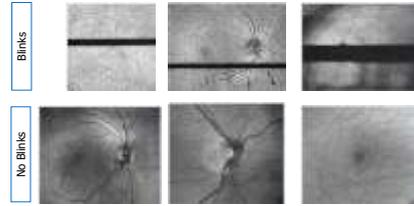
- Consensus is limited
- Visual fields tend to fluctuate in early glaucoma
- Reliable and repeatable structural measurements is very valuable
 - Fourier domain OCT 5 microns accuracy.

Eye Blinks

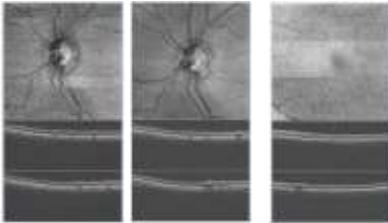


[View on Instrument](#)

Eye Blinks

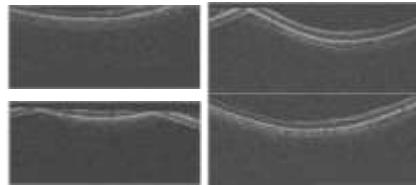


Eye Movements- Unacceptable



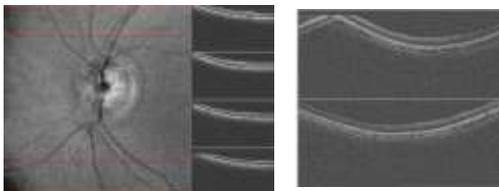
[View on Instrument](#)

Clipping- Unacceptable



[View on Instrument](#)

Clipping- Acceptable



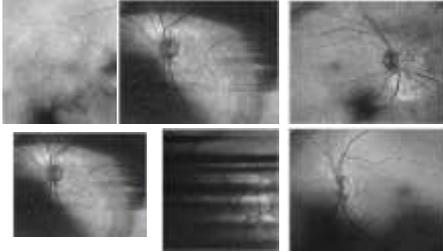
[View on Instrument](#)

Fixation/Centration- not acceptable



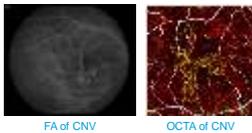
[View on PC](#)

Localized Weak Signal



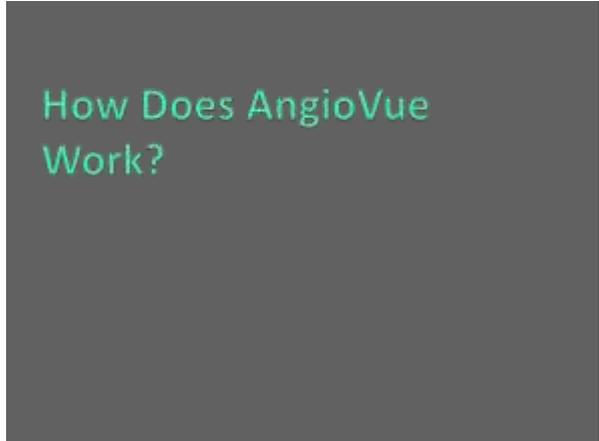
OCT Angiography: A New Approach to Protecting Vision

- **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

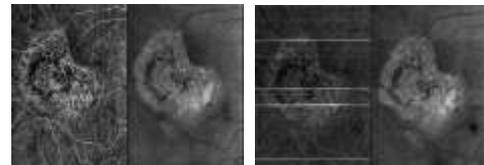


Principles of AngioVue OCTA

- 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



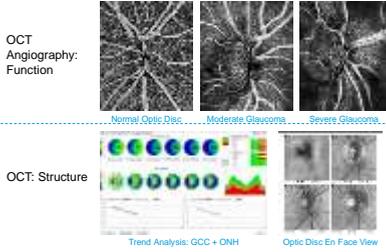
Motion Correction Technology (MCT™): Minimizes Saccadic Motion to Enhance Image Intensity



With MCT

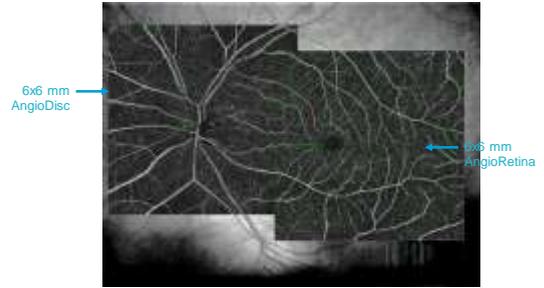
Without MCT

Glaucoma

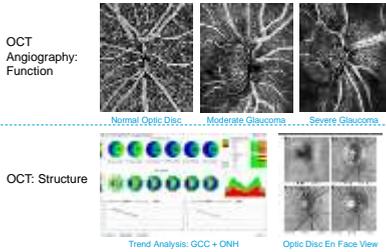


Previously diagnosed patient. Images courtesy of Michel Puauch, MD, FRCS

AngioMontage Provides a Wider Field of View

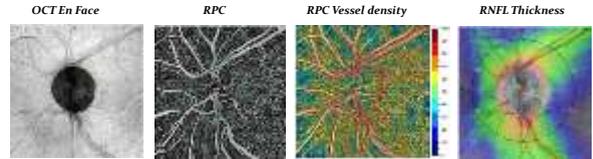


Glaucoma



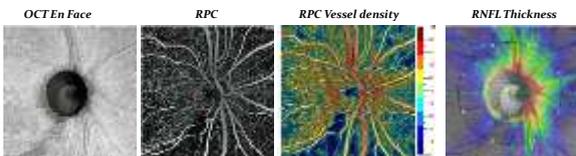
Previously diagnosed patient. Images courtesy of Michel Puauch, MD, FRCS

Normal Eye



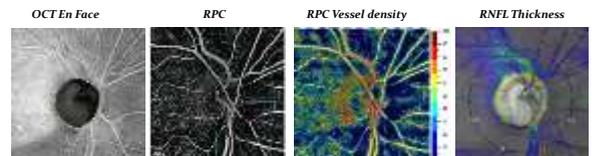
Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

Moderate Glaucoma



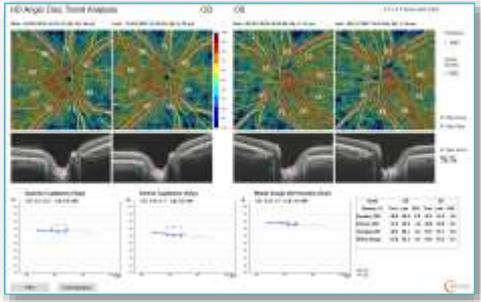
Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

Advanced Glaucoma

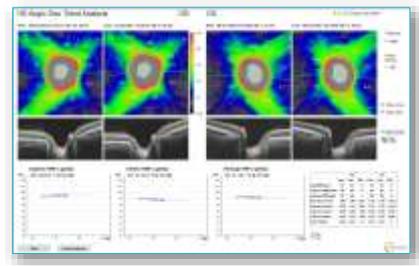


Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

AngioDisc Trend Analysis



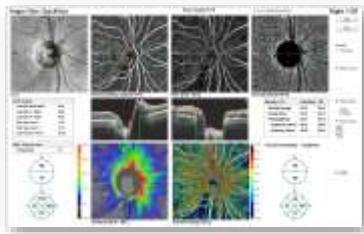
RNFL Thickness Trend Analysis



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

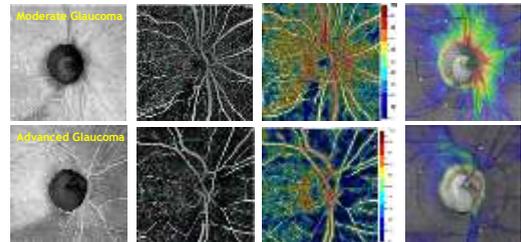


Image Courtesy: Drs. Weireb, Nuchim, Goldbaum, Zangwill, UCSF, San Diego, CA (USA)