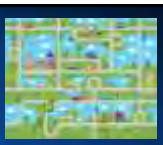



A Roadmap for Making the Diagnosis in Glaucoma

Michael Chaglasian, OD
Illinois College of Optometry
Chicago, IL

Eric Schmidt, OD
Omni Eye Specialists
Wilmington, NC

Disclosures

Michael Chaglasian, O.D.

- In the past 12 months Dr Schmidt has received honoraria or compensation from the following Companies:
  - Aerie- Advisory Board, Speaker Bureau
  - Allergan- Advisory Board, Speaker Bureau
  - B+L- Advisory Board, Speaker Bureau
  - Carl Zeiss
  - Equinox- Research
  - Heidelberg-Advisory Board
  - Topcon- Consultant
  - Optos- Research

Eric E. Schmidt, O.D.

- In the past 12 months Dr Schmidt has received honoraria or compensation from the following Companies:
  - Aerie – Advisory Board, Speaker Bureau
  - Allergan- Consultant, Advisory Board, Speakers Bureau
  - Carl Zeiss – Consultant, Advisory Board
  - Sun- Advisory Board
  - Eyenovia – Consultant
  - Kala – Speakers Bureau

Topics/Sections

1. Who is the Glaucoma Suspect?
   - Know the Key Risk Factors
2. How to evaluate the glaucomatous optic disc?
   - Yes, you still have to do this
3. Perimetry: The Essentials
   - No, they haven't gone away.
4. OCT Imaging: The Essentials
   - Really get know your device and what it's telling (or not!)

Who is the Glaucoma Suspect?

This starts with a Risk Factor Assessment.

Risk Assessment in Clinical Practice: (quick look at 3)

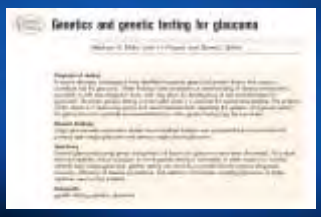
- Family History
- Diabetes
- Systemic Hypertension

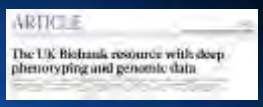
Risk Factors: Family History

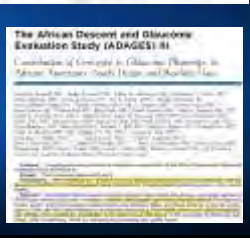
- POAG is a multi-factorial polygenetic disease
- Rotterdam Study:
  - the lifetime absolute risk of glaucoma at age 80 years was found to be almost 10 times higher for individuals having relatives with glaucoma, (22.0 versus 2.4%).
  - "family history alone cannot account for the observed proportion of the disease, suggesting that non-genetic factors play a significant role in the overall occurrence of glaucoma."

Ophthalmol 112(9) 2005

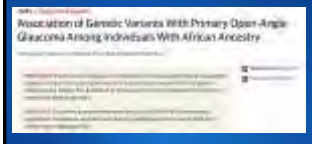
Genetics in Glaucoma

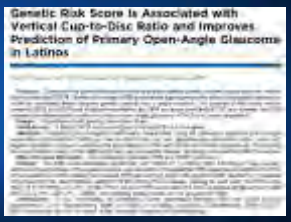

Genetics and genetic testing for glaucoma


ARTICLE
The UK Biobank resource with deep phenotyping and genomic data


The African Descent and Glaucoma Evaluation Study (ADAGES) II

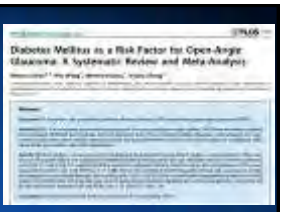
Genetics in Glaucoma


Association of Genetic Variants With Primary Open-Angle Glaucoma Among Individuals With African Ancestry


Genetic Risk Score Is Associated with Vertical Cup-to-Disc Ratio and Improves Prediction of Primary Open-Angle Glaucoma in Latinos

JAMA. 2019;322(17):1682-1691

Risk Factors: Diabetes


Diabetes Mellitus as a Risk Factor for Open-Angle Glaucoma: A Systematic Review and Meta-Analysis

- **Yes, a Risk Factor: ~1.35x greater risk**
  - **Just NOT very strong**
    - Beaver Dam Eye Study
    - Blue Mountains Eye Study
    - Nurses' Health Study
    - Los Angeles Latino Eye Study
- Progression Risk Yes:
  - EMGT and AGIS
- Progression NOT a Risk:
  - Barbados Eye Study
- Older Data:
- DM is NOT a risk factor:
  - Baltimore Eye Survey
  - Barbados Eye Study
  - European Glaucoma Prevention Study
  - Rotterdam Study
  - Visual Impairment Project

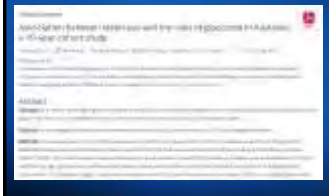
Diabetes Summary

- The current literature does not provide a definitive link between DM and POAG.
- Vascular dysregulation in diabetes likely has a component in glaucoma disease but is likely *NOT a sole, initiating cause* of glaucoma,
- Should only be considered as a *modest* RF compared to other RFs (eg family history and CCT)

Risk Factors: Systemic Hypertension

- No definitive link to elevated BP
  - NO association in several studies
  - High Blood Pressure may be "Protective"
  - **Low BP is a factor in Ocular Perfusion Pressure**
    - OPP=DBP-IOP
    - Increased at OPP of <50-55 mmHg
  - OVER treatment of HTN can be an issue (BP too low)
- Cardiovascular Disease
  - no solid evidence of RF link

Rosuvastatin (Crestor) : Increased Risk OAG



- "With respect to specific types of statins, participants taking rosuvastatin were more likely to suffer from glaucoma (OR 1.11, 95%CI 1.01 to 1.22). The use of other statins was not significantly associated with glaucoma onset."

Some Basic Guidelines:

Short Overview and Highlights

OHTS and Corneal Thickness

- For all IOP's, a *thinner cornea increased the risk* of developing glaucoma at 5 yrs

IOP	CCT Microns <555	>555-<588	>588
>25.75	36%	13%	6%
>23.75-<25.75	12%	10%	7%
<23.75	17%	9%	2%

OHTS & CCT: 3 Outcomes

- Thin: <555 µm — High Risk (thus treat!)
- Average: 555-588 µm — No change in Risk (treat or monitor, use other RFs)
- Thick: >588 µm — Low Risk

Applies to only to patients with ocular hypertension

Know this!

Diagnosis In The Glaucoma Suspect —When To Treat?

- Glaucoma suspects can be (broadly) categorized into two groups:
  1. Ocular hypertensive subjects with risk factors for the future development of glaucoma
     - **These patients are addressed by OHTS data and who to treat**
  2. Subjects with questionable glaucomatous findings that cannot definitely be distinguished from normal
     - e.g., suspicious appearance of optic disk, RNFL/GCA or VF and
     - IOP that is 21 mmHg or lower

Open Angle Glaucoma Suspect

- **The Decision Tree:**
  - The patient **without** OCT, VF or ONH damage
  - This may be someone with IOP >21 or <21 mmHg

Who do you treat? Options, Bias, Preferences

- Rather than a simplistic approach of treating everyone with an IOP of over 21 mmHg, treatment is held off until there is sufficient evidence of glaucoma damage at some level (OCT, VF,)
  - This is a practice philosophy that can be followed for ***low risk*** patients
- **Or, we elect to treat those with the most significant risk factors.**

Early Glaucoma or Not? Example findings

Pro

- Family history
- Elevated IOP

One Way to Organize and Sort Risk Factors

Mixed

- Suspicious optic nerve
- CCT = 570
- Unreliable VF

Con

- Normal OCT
- Younger age

What do you do?

Glaucoma Suspect: The Ocular Hypertensive

- ***IOP 21-30+ mmHg with***
  - Normal appearing or suspicious optic nerve, But NO definitive changes!
    - no visual field defects
  - some risk factors
  - **Follow OHTS Treatment Guidelines:**

Glaucoma Suspect: IOP under 21

- Management Options:
  - no single treatment plan nor guidelines, varies with every patient, must be individualized

1. Follow these patients every 3-6 months with observation and repeated: ONH, VF, OCT, IOP
   - Wait until confirmation of true OCT/VF defect, ONH *change*
2. Or, may initiate therapy for those with **3** or more risk factors:
   positive family history,
   - C/D ratio 0.8 or greater, asymmetry of the nerve heads
   - African American; diabetes, etc.
   - Questionable visual field defects, fluctuating IOP

Patients Who Require Therapy:

- At any IOP
  1. *Glaucomatous* ONH Changes
     - As identified by you or via photograph, OR
  2. Strongly abnormal, characterstic and *reliable* OCT
     - This must have some "clinical correlation"
     - Rarely do you treat based upon this *alone* (patient has other findings)
     - Watch out for "Red Disease"
  3. Characteristic/Confirmed Visual Field Loss
     - (***not required for diagnosis***)
- OHTN with IOP over 30 mmHg
  - Some exceptions; eg very, thick cornea

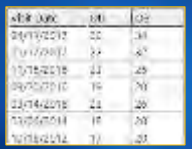
Glaucoma diagnosis can be a very complex puzzle:

- Requirements
  - Organized, step-by-step approach
  - Sort and organize the data
  - Identify good data
  - Ignore bad/unreliable data
  - Confirm data when necessary
  - Sort and organize again
  - No need to rush your decision
  - Individualize to your patient
- Begin therapy (later) or monitor

CASE EXAMPLE

56 yo
+ Fam Hx of Glaucoma
Systemic HTN (lisinopril/HCTZ)

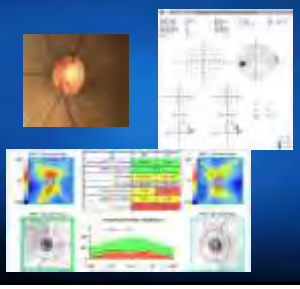
Discussion



OHTN?
Early Glaucoma?
Treat? Don't Treat?
Monitor? How Frequently?
Other Information?
Next Steps?

What is the future risk?

Back to our Patient: Treat or Observe?

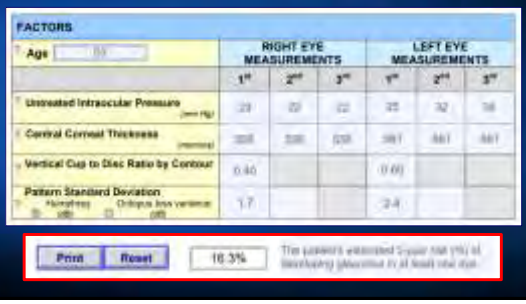


Can we get additional information?

How to Manage OHTN?

OHTS Risk Calculator (online)

OHTS Risk Calculator (online)



Polling Question:

What percentage risk of developing glaucoma from ocular hypertension, is considered reasonable/appropriate for starting treatment on a patient with OHTN?

(by expert panel consensus)

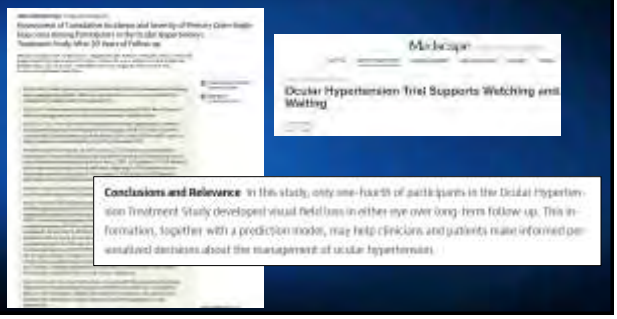
1. > 5%
2. > 10%
3. > 15%
4. > 20%

What does OHTS Risk Mean?

Expert Panel Recommendations	
< 5%	No treatment
5-15%	Treatment optional
>15%	Treatment recommended

- These are suggested guidelines only, treat every case individually
  - Must consider all and other factors (family Hx, Drance Heme, age.)

OHTS 20 Years: The difference is Risk Factors:



Ocular Hypertension: When is Therapy Indicated?

- When there are other (multiple) significant Risk Factors:
  - CCT under 555 microns
  - Family History
  - Disc Hemorrhage
  - Vertical CD ratio
  - Low Ocular Perfusion Pressure
- When Risk Calculation is over ~ 15%

CASE 2

44 yo, Black, Male
Last exam at Vision Center 1 month earlier
"large cupping"

History and Clinical Data

- VA = 20/20 OD, OS
- Entrance Tests = normal
- Slit Lamp Exam = unremarkable
- IOP
  - 16 OD mmHg @ 9:00 AM
  - 15 OS
- Family History
  - Mother with POAG
    - On topical meds
- Gonioscopy
  - Open to Ciliary Body 360 OU
  - Moderate Pigment

Discussion

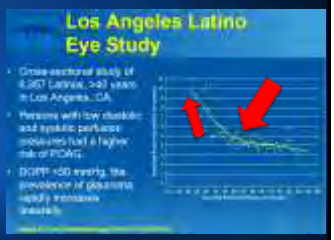
Glaucoma with IOP in the Normal Range (Normal Tension Glaucoma)

Nocturnal IOP and Glaucoma

- Most individuals spend 1/3rd of day asleep in recumbent position
- Habitual IOPs of most untreated glaucomas higher during nocturnal/sleep period than office hours
  - IOP measured sitting during day and supine position at night
- Important to understand and recognize this
  - May explain why glaucomatous damage occurring in certain individuals

Ocular Perfusion Pressure (OPP) = <50mmHg

- The differential between arterial (diastolic) BP and IOP
  - OPP = DBP-IOP
    - eg 65 mmHg - 20 mmHg = 45
  - Ocular perfusion is regulated to maintain constant blood flow to the optic nerve despite fluctuating blood pressure and IOP
  - The major cause of reduced blood flow is thought to be secondary to vascular dysregulation in susceptible patients, resulting from abnormal/insufficient autoregulation.



Clinical Control of OPP

- **Lower IOP improves OPP**
  - **Remains number 1 goal !!**
- **Measure blood pressure on your patients**
- **Higher systemic BP improves OPP, but you do not necessarily want to raise BP:**
  - **Stroke #3 cause of death in US behind CVD & CA!**
  - **Avoid drugs that lower systemic BP beyond patient's desired systemic control.**
  - **Avoid nocturnal hypotension.**
  - **Communicate with PCP**

To treat or not to treat? IOP Guidelines: Randomized Clinical Trials

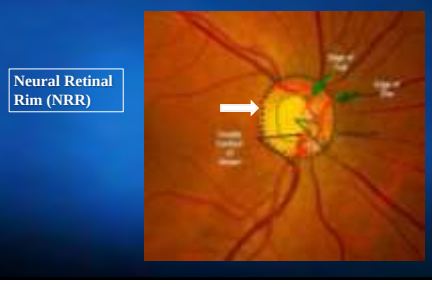
- IOP Is the Most Prominent and Consistent Glaucoma Risk Factor
  - Important Considerations and Facts
    - **Ocular Hypertension Treatment Study (OHTS)**
      - CCT of less than 555 µ has higher risk
      - IOP: every 1mmHg higher (>22) increased risk by 10%
    - **Early Manifest Glaucoma Trial (EMGT)**
      - Every 1mmHg of IOP reduction lowers risk of progression by 10%

To treat or not to treat? IOP Guidelines: Randomized Clinical Trials

- **Advanced Glaucoma Intervention Study (AGIS)**
  - Another IOP related factoid:
    - IOP always under 18mmHg, or keeps a mean of 12mmHg, has a lower risk of progression
- **Collaborative Normal-Tension Glaucoma Study**
  - 30% reduction of IOP reduces risk of progression
  - Note that many patients with NTG do not progress, while other with 30% IOP reduction continue to progress

Yes, you still need to look at the optic disc.

Optic Disc Defined



Glaucomatous Disc Features

Descriptive terms to know : examples coming up

- *increased* (meaning it changed) cup-to-disc ratio or significant cup asymmetry;
- decreased or documented change in neuroretinal rim area;
- *notch* of the neuroretinal rim;
- *saucerization* of neuroretinal rim;
- flame-shaped *disc hemorrhage*;
- nerve fiber layer loss;
- peripapillary atrophy
- Laminar dot sign (non-specific)

TIPS and PITFALLS

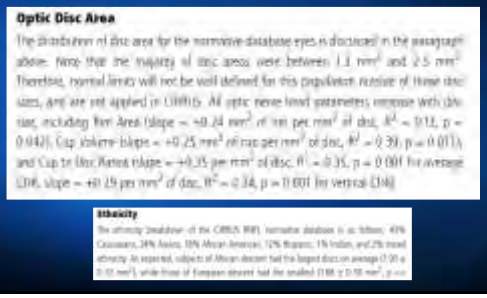
- Do not emphasize the C/D ratio
- Concentrate on the neural retinal rim
- Look for focal defects (notching) and and/or generalized thinning
- Evaluate symmetry between eyes
- Disc Hemes
- Peripapillary atrophy
- Baring of circumlinear vessels
  - Loss of NRR tissue

Examples of ONHs

CASE JM

54 YO, AA
IOP
IOP Range = 16- 20 OD; 16-19 OS
CCT= 462 OD 468 OS
CH = 8.8

Zeiss Cirrus HD-OCT RDB



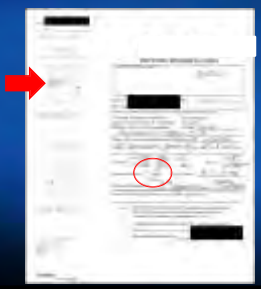
Management

- This patient was treated due to significant risk factors:
  - IOP high of 20 mmHg
  - Thin CCT
  - Low CH
  - OCT
  - There has been minimal progression over time
- But what can progression look like in other patients??

CASE LP

43 year old male
Referred for Possible Open Angle Glaucoma

Clinical Background: Referral



Clinical Background:

- BCVA: 20/20 OD and OS
- Entrance Tests: all normal
- Slit Lamp:
  - Normal anterior segment
- Gonioscopy:
  - Open angles, SS/CB, 360 OU
- IOP
  - First Visit:
    - 21 OD and 21 OS
  - Second Visit (AM appt)
    - 22 OD and 22 OS
- CCT / Pachymetry
  - 481 OD and 487 OS
- Corneal Hysteresis:

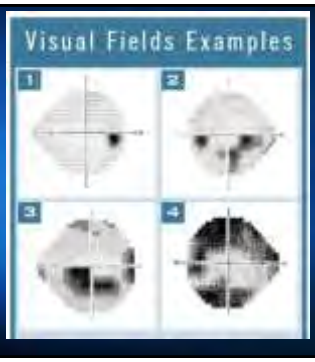
Visual fields: are still essential!

GLAUCOMA SEVERITY SCALE DEFINITIONS:

- **Mild Stage:**
  - optic nerve changes consistent with glaucoma but *NO visual field abnormalities on any visual field test*
- **Moderate Stage:**
  - optic nerve changes AND glaucomatous visual field abnormalities in hemifield and not within 5 degrees of fixation.
- **Severe Stage:**
  - optic nerve changes consistent with glaucoma AND glaucomatous visual field abnormalities in both hemifields and/or loss within 5 degrees of fixation in at least one hemifield.
- ***If both of the patient's eyes are glaucomatous, code for the more severe stage of the two eyes.***

American Glaucoma Society

Visual Fields Examples



Mild

Moderate

Severe

Severe

AGS def: Mild Stage Glaucoma

- Patient would have other definite signs of glaucoma:
  - ONH notching
  - OCT/RNFL loss
- "Pre-Perimetric" is another term that is sometimes used

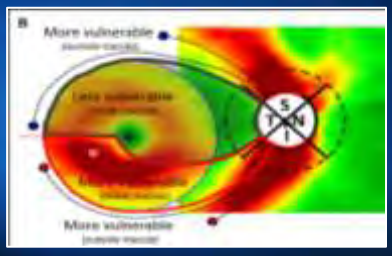
Perimetry: The Essentials

- Required at baseline for all patients (std of care)
  - but perhaps best clinical usefulness is for middle and late stage disease
  - Using software for Progression Analysis
- Faster Testing Options: new SITA Faster
  - SITA Faster testing takes about two-thirds of the time required by SITA Fast and about half the time required by SITA Standard.
- Central Visual Fields and Glaucoma
  - 50% of retinal ganglion cells are found within 4.5mm of fovea
  - Macula region comprises only 10% of overall visual field area though it is responsible for 60% of area of visual cortex
  - 10-2 grid pattern is best for detecting small, central defects

Perimetry: The Essentials

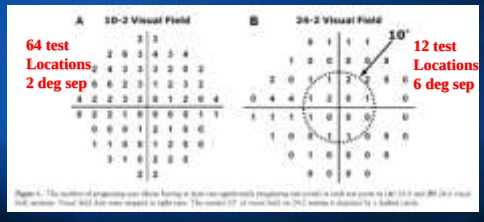
- Central VF Testing (cont.)
  - Rationale (Don Hood papers)
    - Macular Zone Vulnerability
- How and when use 10-2 VFs or the new 24-2C (adds 10 Central test points):
  - Good Test Takers, Younger patients
  - Minimal to no defects on 24-2
  - OCT Macula/Ganglion Cell scan is abnormal
  - High Risk Patients

Macular Zone Vulnerability. Don Hood, PhD.

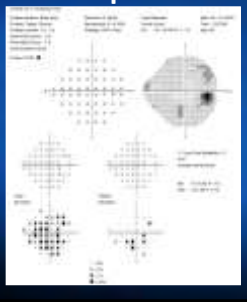


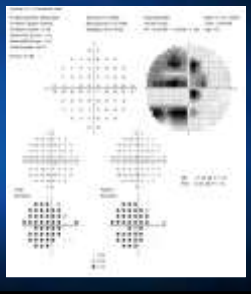
D.C. Hood et al. / Progress in Retinal and Eye Research 32 (2013) 1e21
D.C. Hood / 48 Progress in Retinal and Eye Research 57 (2017) 46e75
Departments of Psychology and Ophthalmology, Columbia University, New York,

Central Field Testing: 10-2 vs 24-2



One Example: 24-2 10-2





How and when use 10-2 VFs

- Good Test Takers, Younger patients
- Minimal to no defects on 24-2
- OCT Macula/Ganglion Cell scan is abnormal
- High Risk Patients
- Be Selective for High Risk Patients

New 24-2C pattern: 10 additional central points

Note:

- Runs new SITA-Faster algorithm
- Test time ~2.5 minutes
- Perhaps can avoid 10-2 VF
  - No published evidence for this yet
- Can be integrated with other tests for Progression Analysis
- Can have high False Positives (>15%)
  - Best for reliable/good VF test takers
- May not compare exactly to other tests
- May not be best for baseline tests
  - Note both baseline tests must be the same in order to start GPA

SITA Faster Considerations

- **Very short testing time (<2min)**
- **Higher False Positive Rate**
  - Give better, more clear instructions to the patient to be more discriminating when responding
  - **Excellent VF test for "good test takers"**
  - **Allows for more frequent tests to be completed**
- Not directly comparable on a "one to one" comparison
  - **Obtain a series of tests with Faster**

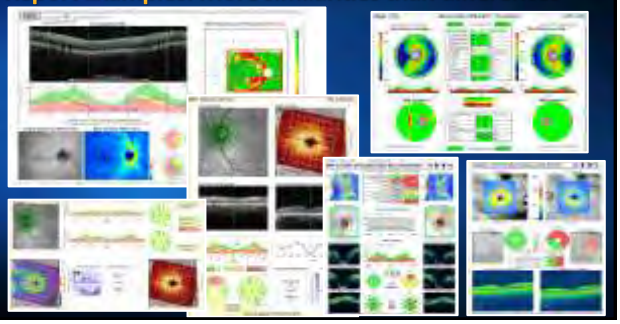
OCT, also Essential

Review of Key Points and Demonstrated on Case Examples

Tip #1:
Know your OCT and its Report

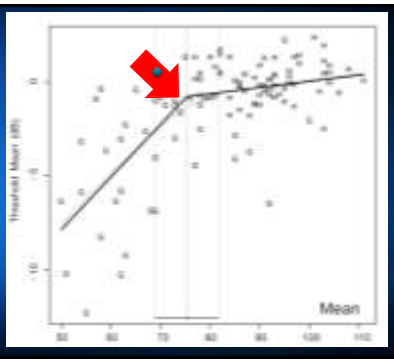
(too) Many Options!!

Report Examples: More similarities than differences



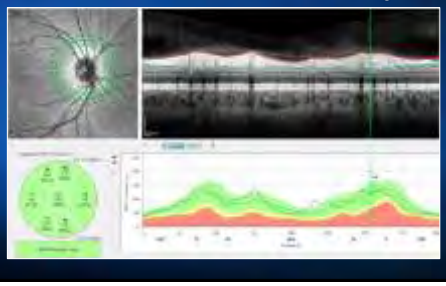
Tip #2:
Assure a Quality Image without an Artifact

Significant VF loss starts here:



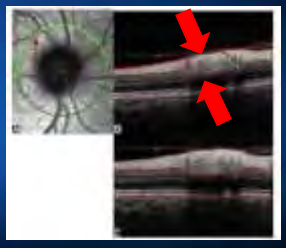
Start with a Good Quality B-Scan:

Dr. Fingeret will discuss further



Segmentation Failure:

Repeat the scan, should not use in management.

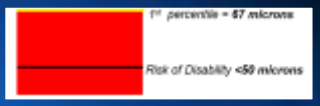


Common Forms of OCT B-Scan Segmentation Failure and Image Artifact

1. De-centration (28% of scans)
2. Error associated with posterior vitreous detachment (14%)
3. Posterior RNFL misidentification (8%)
4. Poor signal (5%)
5. High Myopia (2%)
6. Peripapillary atrophy associated error (1%)
7. Incomplete segmentation (1%)
8. Motion artifact (<1%)

- All have the potential of being misread by you as true disease, the so called "red disease"
- As any artifact is categorized as being outside the normative database, thus automatically depicted in red on the report
- Then leading to an erroneous diagnosis and possibly unnecessary treatment

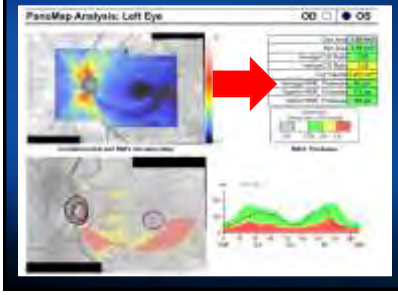
OCT: "Floor Effect"



In early to moderate glaucoma, progressive thinning of RNFL thickness measured by SD-OCT is a very useful tool to judge progression of disease. At advanced stages however, SD-OCT is less clinically useful due to a "floor effect" of RNFL thickness.

With advanced loss, RNFL thickness levels off, rarely falling below **50 µm** and almost never below 40 µm due to the assumed presence of residual glial or non-neural tissue including blood vessels. At this level of disease, serial **visual fields are more useful to judge progression**.

"Green Disease"

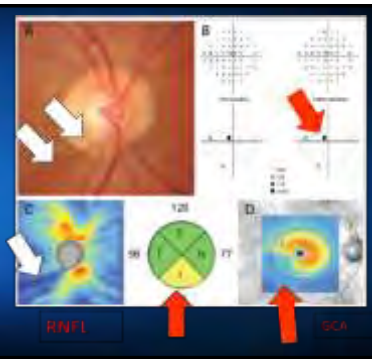


Tip #3:
Understand Structure-Function
Classic Confirmation vs. Normal Variability

Use this to confirm the presence of glaucoma vs other disease or artifact.

Classic S-F

All the pieces fit together.



Questions?

Michael Chaglasian, OD
Illinois College of Optometry
Chicago, IL

Eric Schmidt, OD
Omni Eye Specialists
Wilmington, NC