Maximizing OCT in Diagnosis and Management of Glaucoma

Danica J. Marrelli, OD, FAAO
AAO Diplomate, Glaucoma
University of Houston College of Optometry
Dmarrelli@uh.edu

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DIAGNOSIS:
CASES 1-2
IS THIS GLAUCOMA?
Case 1: Dennis, 65yo WM

- POH: (-) injury, (-) surgery
- PMH: (+) DM2, (+) Systemic HTN
- FH: (-) glaucoma
- Meds: metformin, HCTZ
- All: None

Case 1: Dennis, 65yo WM

- BVA: 20/25 OD 20/20 OS
- Pupils: 3mm, 3+ D/C OD/OS, (-) RAPD
- CVF: FTFC OD, OS
- Slit lamp: mild nuclear sclerosis OD>OS
- IOP: 31mmHg OD, 30mmHg OS
- See ONH and VF

Case 1: Dennis, 65yo WM

![Images of retina]
Case 1: Dennis, 65yo WM

Case 1: Is this glaucoma?
A. Yes  
B. No  
C. I need additional information

Case 2: Maria, 45 yo Hispanic female
- CC: referred for glaucoma evaluation
- POH: unremarkable, no trauma, no surgery
- PMH: unremarkable, no vascular disease
- FH: no known glaucoma, most family in Mexico
- Meds: None
- All: None
Case 2: Maria, 45 yo Hispanic female

- BVA: 20/20 OD, OS
- Pupils: 3mm, 3+ D/C OD/OS, (-) RAPD
- Slit Lamp: normal, no secondary signs, open angles
- Gonioscopy: open to CB, no secondary findings
- IOP: 24mmHg OD 23mmHg OS
- See ONH and VF
Case 2: Is this glaucoma?
A. Yes
B. No
C. I need additional information

Is this glaucoma?
• If there is characteristic optic nerve damage...
  – “Yes”
• If there are no characteristic optic nerve or VF changes ...
  – Usually “No”
  – This is changing a little with use of OCT and ability to detect earlier changes

Glaucoma Basics
• Glaucoma is a disease of ganglion cells
  – Damage occurs at level of the lamina cribrosa
  – Selective damage to superior and inferior poles of the optic nerve/RNFL
  – Asymmetry between sup/inf poles as well as OD/OS asymmetry
Characteristic Optic Nerve Changes

• Large C/D ratio FOR THE SIZE OF THE OPTIC NERVE
• Focal or diffuse rim thinning
• Focal or diffuse RNFL loss
• Optic disc hemorrhage
• Peripapillary atrophy

Case 1: Dennis, 65yo WM

Case 2: Maria, 45 yo Hispanic female
Case 2: Maria, 45 yo Hispanic female

EVALUATION OF RETINAL NERVE FIBER LAYER (RNFL)

- Defects in RNFL may precede glaucomatous visual field loss and structural changes in ONH
- Can help to differentiate physiologic cupping from glaucomatous cupping

ANATOMY OF THE NERVE FIBER LAYER

- RNFL is thickest (and brightest) in superior and inferior arcades
- RNFL is thinner (dimmer) in papillomacular bundle and nasal bundles
- “BRIGHT-DIMMER-BRIGHT” pattern
Retinal Nerve Fiber Layer

RNFL Drop Out

- Diffuse (More Common)

RNFL Drop Out

- Focal Loss (less common): slits and wedges
RNFL Drop Out

- Focal Loss: slits and wedges
Glaucoma Detection - Imaging

- ONH/RNFL photography
- Scanning laser ophthalmoscopy
- Scanning laser polarimetry
- Optical Coherence Tomography
  - Time Domain
  - Spectral Domain
  - New technology such as swept source
Quantifiable/Objective Imaging

- “Diagnostic capability”:
  - Good for early glaucoma
  - Excellent for moderate to severe glaucoma
  - Improved when more than one parameter is evaluated
- Many of us rely on imaging devices to identify glaucoma (and progression)
- Has imaging become “the answer”?
Is automated imaging the answer?

Spectral-Domain Optical Coherence Tomography for Glaucoma Diagnosis

Several different SD-OCT instruments are commercially available. Although these instruments do not appear to be interchangeable [4], they have been demonstrated to have similar diagnostic capabilities in cross-sectional investigations [26, 67]. Lima et al. [24] analyzed and compared the diagnostic accuracies of SLO-OCT, C-scanning OCT and ETDRS OCT (Optical Instruments, Fremont, CA, USA). Although SD-OCT instruments, Lima et al. [24] concluded that their ability to detect glaucoma is a new and important development that is superior to any other method.
• 75 eyes of 75 glaucoma suspects without visual field defects (control = healthy subjects)
• Significant differences in average RNFL thickness between groups seen up to 8 years before the development of visual field defects

What Information Do the Instruments Give Us?

• Optic Nerve Parameters
  – Disc Size
  – Rim Area
  – Rim Volume
  – Cup Volume
• Retinal Nerve Fiber Layer Parameters
  – TSNIT curves
  – Average RNFL thickness
  – Sectoral RNFL thickness
• Macular Thickness
  – Ganglion Cell Complex
  – Inner Retina
  – Total Macular Thickness
Systematic Strategy

• Quality
  – Signal Strength
  – Circle Placement
  – Movement?

Systematic Strategy

• Thickness Map
• Deviation Map

IMPORTANCE OF BLOOD VESSELS!!!!!
Systematic Strategy

• Thickness Profiles
  – Compared to normative data
  
  ![Thickness Profiles Image]

  Good at picking up notches in NRR

Systematic Strategy

• Quadrant and Clock
  Hour RNFL analysis

![Quadrant and Clock RNFL Image]

Systematic Strategy

• Quantitative Parameters
  – Average RNFL
    • Measures average thickness around calculation circle
    • Affected by blood vessels, astrocytes, glial cells
    • Global measure (will miss focal loss)
  – RNFL Symmetry

![Quantitative Parameters Image]
Systematic Strategy

• Quantitative Parameters
  – Rim Area
    • Uses Bruch’s membrane as edge of disc
    • Range 0.75-2.38mm (avg 1.31)
  – Disc Area
    • Range 1.06-3.38 mm² (avg 1.83)
    • Small: <1.63
    • Med 1.63-1.97
    • Large >1.97
  – C/D ratio
  – Cup Volume
Importance of Disc Size & Axial Length/Refractive Error

- Axial hyperope < 3.4 mm
- Axial emmetrope = 3.4 mm
- Axial myope > 3.4 mm

Case 3: Victor, 61 yo HM

- Referred for glaucoma evaluation ("big C/D")
- POH: unremarkable
- PMH: hypothyroid disease, pre-diabetes
- Fam Hx: No glaucoma
- Meds: thyroid replacement hormone
- Allergies: NKDA
Case 3: Victor, 61 yo HM

- BCVA: 20/20 OD, OS
- Pupils, EOMs, CVF: normal OU
- Slit lamp: normal, (-) secondary signs
- Gonioscopy: open to CB, normal
- IOP: 18mmHg OD, 15mmHg OS
- See ONH and VF
• Quality: Excellent
• Thickness Map: Lots of “thick” colors
• Quantitative Parameters:
  - Average RNFL: VERY THICK!
  - RNFL Symmetry: High
  - Rim Area: Thicker than average
  - Disc Area: VERY LARGE
  - C/D: Large (but large disc)

• Thickness Profiles
  - Neuro-retinal Rim?
  - RNFL: Super thick!

• Quadrant/Sector Analysis
  - All in green/white
Is this glaucoma?

Pitfalls of Imaging #1: Database

• "Normative Database"
  – "REFERENCE DATABASE"
    • Reference population WITHOUT DISEASE in question, to which an individual's data will be compared
    • Can be utilized to classify the patient's data as "normal" or "abnormal"
    • Can be utilized to measure reproducibility
  – Problem: "normal" and "healthy" are often used interchangeably
    • Does "abnormal" mean "unhealthy"?

Database Considerations

• Inclusion/exclusion criteria
  – Cohort should be representative of the population from which the suspects are drawn, except free of the disease in question
    • How do you define "un-diseased"?
  – Exclusion criteria should be minimized to avoid a "hyper-normal" database
    • Include co-morbidities that are often seen in population, so long as they don't interfere with the data in question
Database Considerations

• Covariates:
  – Some covariates are known to affect measurements (age, refractive error, axial length, etc)
  – When the effect of the covariate is known and is potentially large, adjustment for that covariate is preferred.

• Database Size:
  – Sufficient to adequately characterize the reference population, including covariates

OCT Database Information

• RTVue: 600 eyes (Largest database)
  – Age
  – Disc Size
  – Ethnic Group (African, Chinese, Japanese, Caucasian, Hispanic, Indian, "other")
• Cirrus: 284 eyes
  – Image quality 6 or above
  – Age 18-84
  – RE: -12D to +8D
  – Ethnic Groups: Caucasian (43%), Asian (24%), AA (18%), Hispanic (12%);
• Spectralis: 205 patients
  – All Caucasian
  – Age 18-78
  – RE: -7D to +5D
  – New “Premium Module” = more robust database (size and ethnicity)

“Normative” Distribution

WHAT DOES THIS MEAN?

• White = upper 5% normal (Cirrus)
• Green = middle 90% (Cirrus) or upper 95% (Spectralis)
• Yellow = Lower 5%
• Red = Lowest 1%
• Gray = not in database
**REVIEW**

**Glaucoma versus red disease: imaging and glaucoma diagnosis**

Dennis T. Cheng and Richard K. Lee

Glaucoma imaging is an integral part of the glaucoma management armamentarium for glaucoma screening, diagnosis, and follow-up, that is red disease.

Glaucoma imaging results can be easily misunderstood without a good understanding of the underlying technology limitations and results in false-positive results.

The normative databases for the different imaging technologies have limitations in defining what is a normal versus a glaucomatous optic nerve head.

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**KEY POINTS**

- Glaucoma imaging is an integral part of the glaucoma management armamentarium for glaucoma screening, diagnosis, and follow-up, that is red disease.
- Glaucoma imaging results can be easily misunderstood without a good understanding of the underlying technology limitations and results in false-positive results.
- The normative databases for the different imaging technologies have limitations in defining what is a normal versus a glaucomatous optic nerve head.

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**REVIEW**

**Green disease in optical coherence tomography diagnosis of glaucoma**

Mohamed A. Saad, Michael Mauer, and Richard K. Lee

Purpose of study: Optical coherence tomography (OCT) has become an integral component of modern glaucoma practice. OCT enables the non-invasive glaucoma diagnosis and follow-up, and helps to identify normal variants,疑似, and progressive disease.

Recent findings: OCT is the only imaging modality that can image both the choroid and the retina simultaneously. OCT is a non-invasive imaging modality that can be used to assess the thickness of the retinal layers, the macula, and the anterior segment of the eye. OCT can be used to assess the thickness of the retinal layers, the macula, and the anterior segment of the eye.

Synopsis: OCT is a powerful tool for the early detection and monitoring of glaucoma.

Responsible: Mohamed A. Saad, Michael Mauer, and Richard K. Lee.

Optical coherence tomography.
Pitfalls of OCT #2: Operator Error/Artifacts

- Circle Placement
- Segmentation Errors

*Review Article*
Factors Affecting Cirrus-HD OCT Optic Disc Scan Quality: A Review with Case Examples

Joshua S. Hardin, Giovanni Taibbi, Seth G. Nelson, Elana Chao, and Giovanni Vittori
Misc Errors – Floater, Motion Artifact

Misc. Errors – Blink
Misc Errors – Motion Artifact

BARRIERS TO QUALITY

- Spectralis artifacts 28.2% MT and 19.9% in RNFL\(^1\)
- Stratus 16.9% MT and 15.7% RNFL\(^2\)
- 8.2-49.5% total error frequency in study of 6 OCTs\(^3\) (Stratus worst)
- Cirrus vs Swept source
  - Optic Disc= 35.9% SS vs 42.2% cirrus
  - Macular area= 24.2% vs 22.7%\(^4\)
- Artifacts can affect the Red/Green!!!!

4. Lee SY. Current Eye Research 2015

Pitfalls of OCT#3: Non-glaucoma

- NAION
- Retinal Dystrophies
- Vein Occlusion (hemi/branch)
- Optic Neuritis
- Toxic/nutritional/infectious optic neuropathies
- Posterior Vitreous Detachment
- High Myopia
Key Points Regarding ONH/RNFL Scans

- Need clinical correlation
  - NEVER interpret OCT printout in isolation
- In situations where the disc is anomalous (e.g. very large, very small, tilted), the normative/reference database will classify the patient as abnormal, when they may be normal
  - Can still use these scans for progression/change over time

Newest Addition to Glaucoma Diagnosis Arsenal: Macular Imaging

- 1998: Zeimer et al reported on macular thickness loss in patients with known glaucomatous damage
- 2003: Greenfield reported correlation between total macular thickness and MD on VF in glaucoma patients (time domain OCT)
- 2013: Hood et al – extensive investigation of segmented "RGC+" (RGC + IPL) layer and description of the "Macular Vulnerability Zone" (MVZ)
FLV% quantifies the graphical representation

Quantifies level of Irregularities

FLV% and GLV%
Why are these numbers so powerful?
• Reported at the recent AGS conference by the AIG study group (www.AIGStudy.net)
  – Looked at conversion and progression rates at 6 years
  – When baseline GCC-FLV was within normal limits
    • 10% of suspects convert to VF defects
    • 30% of glaucoma patients convert to VF defects
  – When baseline GCC-FLV was borderline or outside normal limits
    • 41% of suspects convert to VF defects
    • 60% of glaucoma patients convert to VF defects


Cirrus OCT
Advantages of Macular Analysis

- Macula contains ~50% of retinal ganglion cells
  - Glaucoma is a disease of these cells
  - Macular thinning/irregularity cannot be detected during clinical exam
- More reproducible measure (if not using retinal nerve fiber layer) than peripapillary RNFL
  - Fewer blood vessels and other cell components
  - Less anatomic variation compared to optic disc/peripapillary region
- Better superior/inferior symmetry and symmetry between eyes than peripapillary RNFL
Disadvantages of Macular Imaging

- Macular imaging is not helpful in glaucoma cases in which patients have concurrent macular disease
  - AMD
  - ERM
  - CME
  - DME
  - Macular hole

What are the most important parameters?

Most Important Diagnostic Parameters

- Intereye (OD/OS) macular thickness asymmetry 5 microns
- Intraeye (sup/inf of same eye) macular thickness 9 microns
- Intereye (OD/OS) average RNFL thickness 9 microns
- Total RNFL thickness 78 microns or less
Intereye (OD/OS) asymmetry of global RNFL = 11 microns (9*)

Intereye (OD/OS) macular thickness asymmetry = 12 microns (5*)

Intra eye (sup/inf) asymmetry OD = 14 microns (9*)
Intra eye (sup/inf) asymmetry OS = 0 microns (9*)

Minimum Rim Width
Case: Leo

- 71yo AAM
- Referral for glaucoma suspicion, based on age/race/IOP
- POH: Unremarkable
- PMH: (+) DM2 and HTN
- FOH: Unremarkable
- VA: 20/20 OD, OS
- SLE: Normal OU, mild cataract OU
- IOP: 23mmHg OD, OS
- CCT: 587 microns OD 582microns OS
AVERAGE RNFL THICKNESS
OD = 94 microns
OS = 87 microns
OD/OS difference = 7 microns
Case: Tony

- 51yo hypertensive HM
- FH: (+) glaucoma – grandmother
- BCVA: 20/20 OD, OS
- Pupils, motility, CVF: Full OD, OS
- Slit Lamp Exam: LASIK flaps OU, otherwise nl
- Angles: open to CB 360 OU
- Tmax: 17mmHg OU
- CCT: 523 OD 489 OS
What about the 10-2 VF?

- Central 8 degrees from the center of the foveal contains more than 30% of retinal ganglion cells
- 24-2 and 30-2 test strategies use a 6 degree test grid pattern; these points fall outside of the densest region of ganglion cells
- 10-2 test strategy uses a 2 degree test grid
- Recent research has shown that in some patients with small regions of macular ganglion cell loss, 10-2 testing may be better able to detect VF loss

Back to Tony...
Macular Damage in Glaucoma
(Take Home Message)

- Glaucoma damage to the macula is common
- Glaucoma damage to the macula can occur early in the disease
- Glaucoma damage to the macula is not visible on CLINICAL exam
- Glaucoma damage to the macula can be missed and/or underestimated by the standard 24-2 or 30-2 test grid
- ***Watch for new test patterns by perimetry manufacturers!!!

Glaucoma Progression

“Once the diagnosis of glaucoma has been made, the MOST IMPORTANT remaining question is whether the disease is stable and the therapy/compliance are sufficient, or whether the disease is progressive and the therapy in relation to the life expectancy has to be intensified.”

Glaucoma Progression, World Glaucoma Association, 2011 Kugler Publications
Progression of Glaucoma

“Although most glaucoma patients will show some evidence of progression if followed long enough, the rate of deterioration can be highly variable among them. While most patients progress slowly, others have aggressive disease with fast deterioration which can eventually result in blindness or substantial impairment unless appropriate interventions take place.”

WGA Consensus Statements on Structure & Function

• Both ON structure and function should be evaluated for detection of progression
• Currently, no specific test can be regarded as the perfect standard for determination of progression
• Progression detected by functional means will not always be corroborated using structural tests, and vice-versa
• The use of standard automated perimetry as the sole method for detection of change may result in failure to detect or underestimation of progression in eyes with early glaucoma damage.
• Progressive structural changes are often but not always predictive of future development of or progression of functional deficits in glaucoma.
Detection & Measurement of Change (Structure & Function)

- Event Analysis (EA): change that exceeds a certain predefined threshold compared to the baseline value; generally determined by measurement reproducibility
- Trend Analysis (TA): change over a designated time period using regression analysis. Generally takes more exams to obtain a reliable slope
Cirrus GPA™ Analysis

- TSNIT values from baseline and current exams are plotted.
- Areas of statistically significant change are color-coded yellow when first noted and then red when the change is sustained over consecutive visits.
Something to Consider

- There is normal age-related attrition of RNFL
  - Positive correlation between baseline RNFL thickness and rate of loss with age
  - Cross-sectional and longitudinal studies differ in the amount of loss per year in NORMALS
    - Cross-sectional (RNFL): -0.2 microns/year
    - Longitudinal (RNFL): -0.5 microns/year

- Changes seen over time may be age-related, related to diseases other than glaucoma, or true glaucoma progression
“Green Is Clean” Case

- 68yo WM, H/O Ocular Hypertension
- IOP (untreated):
  - 18-30mmHg OD (avg 26)
  - 20-31mmHg OS (avg 26)
- CCT 580 OD 578 OS
- C/D 0.4v OD 0.35v OS

Provided by Andrew Rixon, OD

2012 Photos.....2015 same

Risk Calculator
TTT Calculator

2015 cp-RNFL

2015 VF
Cp-RNFL 2012-2015

"ALL QUADS GREEN"

"OCT RNFL showing questionable Progression OD. Still remains in normal Range."

"POAG – MILD STAGE"!!!!

LOOK CLOSER

2010 2012 2014 2015

Global Trend Analysis OD
It Sector Trend Analysis OD

Global Trend Analysis OS

Range of values, wide in normal range. SDOCT measurements are highly reproducible.

90% in the Green

- We can measure multiple steps of statistically significant change while a glaucoma suspect still is in the green normal range.

Normal significance limits for average RNFL:

- 50th percentile = 89 microns
- 5th percentile = 75 microns
- 95th percentile = 107 microns

Risk of Disability <50 microns

Values shown are for a 69 year old normal.

Courtesy of Dr. John McSweeney
**What This Means For Everyday Clinical Care**

*Implication 1: SD-OCT can now measure 2 to 4 statistically significant RNFL progression steps for the typical glaucoma suspect. If still in the green zone.*

*Implication 2: It may be possible to view SD-OCT change from baseline as an early detection strategy in glaucoma suspects.*

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**What is Significant Change?**

Contingent on Intra and Intervist Instrument Repeatability

- Global RNFL (G) = 4-5 μm repeatable
- Sectors = 9-14 μm repeatable

5) 410K clearance data for cirrus and spectralis

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**What is fast change?**

- -2.54 μm/yr cp-RNFL is significant rate of progression (Baseline of 100 μm)
- -4 μm/yr in RNFL sectors (95% CI)


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NEW Case: Has OS Progressed?

Has OS progressed?

Change = -17um in 10 months???
Post Resegmentation

NO CHANGE!!!

NOV 2015  SEPT 2016

NO CHANGE!!!
WGA Recommendations

• For patient management decisions, clinicians should review quality of images included in the progression assessment

• If progression is SUSPECTED, it should be CONFIRMED with repeat testing
  – Is it TRUE change or artifact?
  – IF TRUE change – is it consistent/typical for glaucoma?

Example 1
Let’s VERIFY...
When to Cut Bait

Re-setting Baseline

• Once progression has been CONFIRMED and
treatment has been augmented (new target IOP, new meds/surg), you must RE-SET BASELINE so that you can see if there is additional progression
Final Case: SR 36yo Indian Female

- POH: 5D myope, SCL wearer
- FOH: (+) glaucoma (mother)
- Medical History: Anxiety
- BCVA: 20/15 OD, OS
- Motility: Full
- Pupils: Normal, (-) RAPD
- Slit Lamp: Unremarkable OU
- IOP: 18-23 mmHg OD, OS (multiple readings)
- Pach: 535 OD/OS
- Gonioscopy: Open to CB, normal OU
Is this glaucoma?
Summary

- OCT has significantly added to our ability to diagnose glaucoma and detect progression
- OCT technology is not perfect, and the clinician must be aware of pitfalls and caveats
- OCT should be considered one of many tools in the toolbox of the glaucoma practitioner.
Thank you for your attention!

Questions?

Email me: Dmarrelli@uh.edu