MAXIMIZING YOUR DIAGNOSTIC TECHNOLOGIES: SOMETHING OLD, NEW, BORROWED AND BLUE

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ASSESSING THE OPTIC DISC: IS PHOTOGRAPHY STILL NECESSARY IN THE OCT ERA?

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GLAUCOMA SUSPECT BASED UPON DISC APPEARANCE

Larger discs will have larger cups, but rims are intact

- Glaucoma is over-diagnosed in larger discs and under-diagnosed in smaller discs

CRITICAL DISC EVALUATION

- Size
- Rim color
- Focal rim defects (notching)
- Hemorrhages
- RNFL defects
- Parapapillary atrophy

You talk about glaucoma in cup-to-disc ratios

EVALUATING THE DISC IN GLAUCOMA

Characteristic glaucomatous neuropathy

- Focal rim damage, not generalized concentric enlargement
METHODS OF DISC ASSESSMENT

- Direct ophthalmoscopy
- Binocular indirect ophthalmoscopy
- Non-contact fundus lens biomicroscopy
- Wide-field imaging?
- Disc photography

OCT TO VERIFY GLAUCOMA—THE OPTIC NERVE HEAD?

Using OCT to Verify Early Glaucoma

A healthy 50-year-old Caucasian man was referred for evaluation for vision decrease. The patient had a moderately elevated cup-to-disc ratio of 0.5 to 0.6, as per his ophthalmologist’s report. The disc was asymmetrical, with inferotemporal notching.

To verify the OCT, I carefully examined his optic nerves and found that his cup-to-disc ratio was 0.85 x 0.85 OD and 0.85 x 0.80 OS.

ARE WE LOSING OUR ABILITY TO EXAMINE THE DISC?

ODDS OF USAGE

- Visual field utilization
  - Decreased from 65%-51% ophthalmologists
  - Decreased from 66%-44% optometrists
  - Overall decrease by 44%
- Imaging
  - Increased from 30%-46% ophthalmologists
  - Increased from 26%-47% optometrists
  - Overall increase by 147%
  - By 2008, pts cared for by ODs were more likely to undergo imaging than fields
- Disc photography
  - Only 16% likelihood
    - ODs more likely to use photos
Detection and Prognostic Significance of Optic Disc Hemorrhages during the Ocular Hypertension Treatment Study

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Purpose: To compare the rates of detection of optic disc hemorrhages by clinical examination and by review of optic disc photographs at the Optic Disc Reading Center, to assess the incidence of and the predictive factors for disc hemorrhages, and to determine whether optic disc hemorrhages predict the development of primary open-angle glaucoma.

Participants: Three thousand and twenty-five eyes of 1989 participants.

Methods: Both eyes were examined for optic disc hemorrhages every 6 months by clinical examination and by review of optic disc photographs at the Optic Disc Reading Center.

Stereophotography-confirmed glaucomatous optic disc hemorrhages were detected in 128 eyes of 123 participants before the POAG end point. Twenty-one cases (16%) were detected by both clinical examination and review of photographs, and 107 cases (84%) were detected only by review of photographs.

Review of stereophotographs was more sensitive at detecting optic disc hemorrhage than clinical examination.

Agreement of Retinal Nerve Fiber Layer Defect Location Between Red-Free Fundus Photography and Cirrus HD-OCT Maps

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ABSTRACT

Purpose: To investigate the agreement of retinal nerve fiber layer defects between red-free fundus photography and Cirrus High-Definition Spectral-Domain Optical Coherence Tomography (HD-OCT) maps in patients with glaucoma.

Methods: Retinal nerve fiber layer defects were defined as at least 20% loss of retinal nerve fiber layer thickness (RNFLt) compared to the fellow eye. The RNFLt was measured with Cirrus HD-OCT and compared with red-free photography. The area under the receiver operating characteristic curve (AUC) for red-free photography was 0.83, and the AUC for HD-OCT was 0.87. The correlation coefficient between the red-free photography and HD-OCT maps was 0.82, indicating good agreement for the RNFLt.

Conclusions: Red-free fundus photography and OCT RNFLt maps showed good agreement for the RNFLt. However, this was not the case for deviation maps, especially in young eyes. This finding should be considered when evaluating RNFL defects using OCT maps.
IDENTIFYING GLAUCOMA PROGRESSION

- Photographic comparisons
  - Not c/d ratio or written descriptions
  - Obtaining RNFL photographs with sufficient quality for interpretation is difficult.
  - Visualizing RNFL defects can be obscured in eyes with hypopigmented fundus and myopia in which background reflection is high and contrast is low.
- Sustained decrease in imaging
  - Measuring rate of progression with OCT is not so difficult and already is better than people recognize.
- Sustained decrease in visual field
  - Look at photos and imaging for support
  - Look at rate of change
    - requires good baseline fields and then careful follow-up fields, excluding inappropriate tests, none of which is easy.

Baseline 5 years later

Missed the disc hemorrhage, didn't you?

Baseline 5 years later
Yet another patient

- 17 YOF- glaucoma suspect at age 10 based upon disc appearance
  - Disc normal; OCT normal
- Peak IOP: 19 mm OD, 17 mm OS (2010)
  - 14 mm OD, 17 mm OS (2017)
- CCT 564 OU
- 20/15 OD, OS
- Color vision normal OU

Well, can’t I just use my OCT and be done with all this photo nonsense?

**ISSUES IN IMAGING**

- You cannot make a diagnosis of glaucoma based solely upon imaging results.
- The use and overemphasis of imaging technology to the exclusion of additional clinical findings and assessment of risk will put patients in peril.
- Exactly how much confidence should an OCT give you as to whether or not a patient has glaucoma?
  - Depends how much confidence you had before you imaged the patient.

**ISSUES IN IMAGING**

- Normative Database
- Signal Quality
- Blink/Saccades
- Segmentation Errors
- Media Opacities
- Axial Length
**DISPARITY IN IMAGING AND EXAMINATION**

- Things have to make sense. If the imaging findings do not fit with the anatomic and functional correlates of pathophysiologic change, trust your own knowledge and judgment.
- When in doubt, repeat the imaging study and the visual field or both.

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**RED DISEASE – A NEW CLINICAL NON-ENTITY**

A supratentorial, non-glaucomatous masquerade disease

Afflicts the educated patient (especially with internet access) with good health care plans and/or wealth

Debilitating to the patient and painful for the visual care provider to treat

2005. *Journal of Irreproducible Results and Senseless Studies*

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**SCANNING LASER OPHTHALMOSCOPY EXAMPLE OF RED DISEASE**

- First Visit
- Follow up visit #1
- Follow up visit #2

HRT3 Optic Nerve Head Changes
How long did this change take?

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**GREEN DISEASE – AN INSIDIOUS CLINICAL ENTITY**

A glaucomatous process masquerading as non-disease

Afflicts inexperienced, poorly-educated, and lazy doctors who simply want a machine to make all clinical decisions for them

Debilitating to the patient and painful for the visual care provider, but a boon for malpractice attorneys

2015. *Journal of Irreproducible Results and Senseless Studies*
Is this person really a glaucoma ‘suspect’?
A example of Green Disease

BELIEVE YOUR OWN EYES

Green Disease
ASSESSING THE OPTIC DISC

- Advantages:
  - Glaucoma is a primary optic nerve disease. Changes often occur here early and are clinically detectable.
  - No extra or expensive equipment needed
  - Still part of a comprehensive analysis

- Disadvantages
  - Patient cooperation
  - Hemorrhages and RNFL defects are easily and often missed.
    - Forget about the green filter

ASSESSING THE OPTIC DISC WITH PHOTOGRAPHY

- Advantages:
  - Allows for careful inspection
  - Identifies RNFL defects and disc hemorrhages
    - Actually most sensitive detection method (OHST)
  - Identifies optic disc pallor in comparison
  - Platform has been around for a long time
  - Ubiquitous in practice
  - No normative database
  - Complementary to OCT

- Disadvantages
  - No normative database
  - Learned skill

ASSESSING THE OPTIC DISC WITH PHOTOGRAPHY

- Optic disc photography has been around a long time
- Personal skill makes this a technique with fewer ‘errors’
- Allows you to see things missed by OCT and clinical exam
- The camera is your friend
- Take photos…and actually look at them.

ANTERIOR SEGMENT OCT IN ANGLE ASSESSMENT

- Cross-sectional view of the angle in a single plane
- Non-contact procedure
- May be performed in total darkness

LANDMARKS OF GONIOSCOPY

- Trabecular meshwork
- Scleral spur
- Ciliary body
QUANTITATIVE EVALUATION

Trabecular-iris angle
Angle opening distance

Where is the scleral spur?!

Pigmentation?
Recession?
Neovascularization?

What about the rest of the anterior chamber?

BOTTOM LINE

• Quantitative tools have a limited role in a clinical environment

• Adjunct to gonioscopy
  - AS OCT may be more likely to identify angle closure
  - May help to determine whether the angle open or closed

OCT: RNFL AND GCC ANALYSIS

• Objective structural assessment

• Used as an adjunct to clinical examination and automated perimetry

• Normative database provides comparative information

RETINAL NERVE FIBER LAYER VS. GANGLION CELL COMPLEX

• Analysis of both are recommended

• Ganglion cell complex (not just the cell layer)
  • Difficult to segment ganglion cell layer ONLY
  • Retinal ganglion cells most dense at the macula (more than 50%)
  • Lack of retinal blood vessels and support cells
  - Retinal nerve fiber layer contains non-neuronal elements
    • Thickness impacted by blood vessels, glial elements
    • BUT-contains all retinal ganglion cell axons

NORMATIVE DATABASES

• Cirrus
  - 284 eyes; 6 US sites, 1 China
    • 19-84 years of age

• RT-Vue
  - 600 eyes: 11 worldwide sites-USA, Japan, India, England
    • 19-84 years of age

• Spectralis
  - 201 patients; 1 site in Germany
    • Caucasian population
    • 18-78 years of age
**ERRORS IN ACQUISITION AND INTERPRETATION**

- Incorrect definition of boundaries on OCT
  - Segmentation error
  - Red vs. green disease
- Up to 1/3 of OCT images contain some form of artifact
- Floor effect

**GREEN DISEASE**

- Fondly referred to as an essentially normal RNFL and GCC with optic disc and functional abnormality

**GREEN DISEASE**

- 63 year old black male
- Angle recession glaucoma diagnosed in 2002
  - Blunt trauma OD with baseball bat
- Tmax
  - 37/14mmHg
- Travatan Z QHS OD
  - IOP last visit 18/13mmHg
- 1+ APD OD

**RED DISEASE**

- Normal GCC Parameters
**OPTIC DISC SIZE**

- SMALL <1.58mm²
- MED 1.58-1.88mm²
- LARGE >1.88mm²

**FLOOR EFFECT**

- When RNFL reaches approximately 50μm, even with further disease progression, thickness measurement will not change
  - Blood vessels and axonal support cells

**OCT AND GLAUCOMA MANAGEMENT**

- Early disease
  - Relatively thick retinal nerve fiber layer; (only) structural change
- Moderate disease (RNFL 75-90 μm)
  - Structural and functional change
- Advanced disease (RNFL <40-60 μm)
  - Functional change only
- Another way:
  - Once there is field loss, structure and function may change together

**IS THERE ONLY STRUCTURAL CHANGE IN EARLY DISEASE?**

- Progressive RNFL thinning without visual field defect
  - Four YEAR lead time (Weinreb 2012)
- This is not the case in all patients

- Some patients may have early functional change without significant structural change
  - Others have structural and functional change
**THE TIPPING POINT**

- Ultimate goal is earlier identification of pathology
- But what do we do with that information?
  - Earlier medical treatment?
  - Increased cost of healthcare
  - Earlier failure of medications?
  - Incisional surgical intervention
- How does this impact QOL?
- *Does earlier treatment reduce functional disability?*

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**OCT ANGIOGRAPHY**

- Imaging strategy that provides en face flow information
- The only thing that moves in the retina over time are red blood cells
- Take the difference between multiple B scans at the same location over time to produce a ‘decorrelation signal’
- Not a replacement for FA/OCT
  - Provides new information

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**CLINICAL USES OF OCTA**

- Driving force has been retinal disease
  - Choroidal neovascularization
  - Retinal vascular disease
  - Diabetic retinopathy
    - Microaneurysms
    - Macular ischemia
    - Retinal neovascularization
  - Non exudative lesions in eyes with intermediate AMD

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**OCT ANGIOGRAPHY IN GLAUCOMA**

- Reduced peripapillary perfusion with decreased vascular density

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**CLINICAL USES OF OCTA (continued)**

- Optic nerve disease
  - Glaucoma
- Neurological disease
  - Alzheimers disease
  - Parkinsons disease
  - Multiple sclerosis
WHAT HAPPENS FIRST?

- Does decreased ocular blood flow cause optic neuropathy—or does optic disc damage cause decreased blood flow?
- May allow for objective assessment of progression below typical ‘floor’ of GCC and pRNFL on SD-OCT

OCT IN NEURODEGENERATIVE DISEASE

- Ultimate goal is to determine imaging biomarkers for disease diagnosis and to monitor progression
- Retinal thickness parameters can be assessed to determine a relationship with traditional disease markers

THE OPTIC NERVE & RETINAL GANGLION CELLS

- Retinal ganglion cells are an anatomic extension of the CNS
  - Optic nerve is a white matter tract, surrounded by meninges within the BBB
  - RGC = cell body forms the ganglion cell layer
  - Axons extend to form the optic nerve, optic chiasm, and optic tract
  - Axons synapse at the LGN

MAGNITUDE OF DISEASE STATES

- Neurological disease
  - 10 million people living with Parkinson’s disease in the United States
  - 44 million with Alzheimer’s disease
  - Cost of Alzheimer’s disease more than $259B alone in 2017
    - Estimated to rise to more than $1T by 2050
  - Over a 20 year period, Pfizer sponsored at least 99 trials or 24 potential drugs—only one (Aricept) was FDA approved

NOW WHAT?

- Parallel to drug development in advanced macular degeneration (geographic atrophy)
  - Drugs may be administered too late in the disease course
- Shift towards early identification and treatment
- In neurological disease
  - Treatment of pre-clinical disease
ALZHEIMER'S DISEASE

- Progressive degenerative disease
  - Amyloid plaques & neurofibrillary tangles
- The most common cause of dementia
  - Affected population doubles every 20 years
  - By 2050, may be the most costly disease in the United States
- RNFL thinning and GCC thinning may be the earliest sign of damage
  - Even in the absence of hippocampal damage

ALZHEIMER'S DISEASE

- 1) Asymptomatic amyloidosis
  - Amyloid beta deposition-biomarkers detectable through SPECT, PET, and CSF analysis
- 2) Neurodegeneration
  - Progresses to hippocampal atrophy and cortical thinning on volumetric MRI
- 3) Cognitive decline
  - Mild cognitive impairment or Alzheimer's disease

MICROVASCULAR ROLE

- MV disease contributes to dementia
- Clinical examination:
  - Theoretically may be able to appreciate venous branching asymmetry
- Amyloid deposition from CNS to retina results in BV wall destruction
- Role of OCTA?

LOOKING AHEAD

- No longitudinal studies of disease process using OCT
  - Need for further validation and comparison with other biomarkers
- Caution is recommended in interpretation of OCT in patients with diagnosed or suspected neurodegenerative disease
- GCC and RNFL could potentially be used as biomarkers of choice for disease diagnosis, severity and progression in neurodegenerative disease

FINAL IMAGING PEARLS

- Always scan both eyes
- If there's something unexpected:
  - Re-scan
  - (Use a different device)
  - Watch the scan being performed
The way we detect disease is changing

In general, OCT allows earlier detection of disease

No “gold standard” to definitively determine who is getting worse

Correlate clinical and anatomical findings with imaging results

BRINGING LOVE BACK TO THE VISUAL FIELD

NORMAL VISUAL FIELD PARAMETERS

- 60° superior
- 60° nasal
- 75° inferior
- 100° temporal
- Macula the central 13°
- Fovea the central 3°
- Visual field is limited by the size of the retina and margins of the orbit

PEARLS ON STATIC VISUAL FIELDS

- Most visual fields test 0-51 decibels
  - 41-51 decibels is outside human vision
- 1 diopter of refractive blur in undilated patient
  - A little more than 1 decibel of depression of the hill of vision
  - With Goldmann III stimulus
- Leave cylindrical errors of less than 2 diopters uncorrected
  - Adjusted with spherical equivalent
  - Above 2 diopters correct the astigmatism with trial lens
- Background of a visual field illuminated (31.5 apostilbs)
  - Minimum brightness for photopic or daylight
  - Cones are isolated, test photopic system
  - Changes in pupil size, crystalline lens color and transparency have less effect on result

STATIC PERIMETRY IN EYE CARE

- Neurological disease
- Retinal disease
- Glaucoma
  - Perimetry is essential in diagnosis and management
  - Why test the central 24-30 degrees?
    - Only a small percentage of glaucomatous defects occur in the peripheral visual field alone
    - Testing the central 24-30 degree field is preferred in glaucoma management
    - Most of the retinal ganglion cells are within the 30 degrees of fixation

24-2 versus 30-2 Static Visual Field

- 30-2 tests 76 locations
- 24-2 tests 54 locations
  - Tests 30 degrees nasal
  - Little diagnostic information lost in 24-2
  - Time is saved
  - Fewer trial lens and lid artifacts
- 24-2 has become the VF for glaucoma
  - Only downside, 30-2 can sometimes find progression earlier due to more test points
SAP AND SITA

- SAP - Standard Automated Perimetry
  - Determines the threshold (how dim of light) can be seen at various points
  - Various algorithms have been developed to determine this threshold using few to numerous individual points in a single visual field test
- SITA - Swedish Interactive Thresholding Algorithm
  - Optimizes the determination of perimeter thresholds
  - Continuously estimating what the expected threshold is based on the patient's age and neighboring thresholds
  - Reduce the time necessary to acquire a visual field by up to 50%
  - Decreases patient fatigue and increases reliability
  - SITA mode is now widely used in many computerized automated perimeters
- SITA - can be applied to:
  - SAP - Standard Automated Perimetry
  - SWAP - Short Wavelength Automated Perimetry (SWAP)

Sita Standard versus Sita Fast

- Sita strategies are twice as fast as order strategies
- Sita fast takes 67% the time of Sita standard
  - Sita fast has larger retest variability
  - Primary difference is between the two strategies is the amount of certainty that is required before testing is stopped
- Sita standard
  - More precise
  - More tolerance of mistakes
  - Easier test as stimuli are brighter

- Stay tuned: “Sita-Faster” Coming Soon.

SITA FASTER

- Turns off False Negatives
- Turns off Blind Spot monitor
- Leaves on False Positives
- Leaves on Gaze Tracking
- Faster test with same reliability

FOVEAL THRESHOLD

FOVEA “ON” VERSUS “OFF”

- Instrument can do 51 db
  - Perfect macula and perimetrically trained young person = 40 db
- Visual acuity and foveal threshold should correlate
  - Each validate each other
  - Visual acuity is good and threshold is low
    - Possible early damage to fovea
    - Glaucoma
    - Macular toxicity
- 47% of patients with 20/20 had threshold better than 37db
  - This method may be useful to predict visual acuity in eyes with possible nonorganic visual acuity loss.

SHORT WAVELENGTH AUTOMATED PERIMETRY (SWAP)

- Blue-yellow perimetry
- Goldmann V stimuli on yellow background
- Thought to detect glaucomatous defect earlier than white on white
- Due to Sita standard strategy can find defect as early

GLAUCOMA VISUAL FIELD

- Need a current refraction
  - Cataracts cause refractive shifts
- 24-2
- Sita-Standard (not fast)
- Fovea “on”

- Sita Faster on the experienced VF test taker

INTERPRETING VISUAL FIELDS

- No longer reliable or unreliable
  - A continuum from highly reliable to marginally informative
- False positives
  - More destructive to interpretation than formerly believed
- False negatives
  - Expected to be abnormal in a glaucomatous visual field
  - Even in attentive tester
- Gaze tracker
  - Typically a better indicator than blind spot
- Progression is not present or absent
  - Is the rate of change acceptable

5 DECIBEL LOSS

- Read slower
- Don’t leave home as much
- Walk slower
- Increase in car accidents

INTERPRETING VISUAL FIELDS

- Diagnosis
  - Probability Plots
  - Glaucoma Hemifield Test
- Staging and following over time
  - Mean Deviation
  - Visual Field Index

PROBABILITY PLOTS
TOTAL DEVIATION TO PATTERN DEVIATION
WHAT WE EXPECT: RAISES THE HILL OF VISION

PROBABILITY PLOTS
TOTAL DEVIATION TO PATTERN DEVIATION
NOW WHAT HAPPENED?
**VISUAL FIELD INDEX-VFI**

- Part of the visual field indices
  - MD, PSD, and VFI
- Mean Deviation- zero indicates, no deviation
  - "How deep" is the defect (or elevated)
- Pattern Standard Deviation
  - "How localized" is the defect
- Visual Field Index
  - Enhanced Mean Deviation
    - Designed to be less affected by cataracts
    - More sensitive to changes in the center of the visual field
    - Better correlates with ganglion cell loss
  - Normal 100%
  - Panoramic blindness 0%
- VFI and MD helpful in:
  - Staging
  - Following over time

**THOUGHTS ON MEAN DEVIATION (MD)**

What is the Mean Deviation on a visual field of a blind eye?

Turn on your VF let it run

- 30 DB (decibel)
- 0-5 (1/6) 30% reduction
- 5-10 (1/3) 40% reduction
- >10 (1/2) 50% reduction

How many DB difference to reliable VF should cause a RAPD?

- 3 DB for a small AFD, the larger the difference the greater the AFD
Diagnosis
Probability Plots
Glaucoma Hemifield Test
Staging and following over time
Mean Deviation
Visual Field Index

54 YO WOMAN WITH POAG

59 YO MAN, SEVERE POAG (OVER 4.5 YEARS)
59 YO MAN, SEVERE POAG (OVER 4.5 YEARS)

STRUCTURE VERSUS FUNCTION DEBATE

48 YO MAN
TMAX 36/38
STRONG FAMILY HISTORY OF POAG

STRUCTURE AND FUNCTION

STRUCTURE (OKAY) AND FUNCTION

AT 48 YO I WILL TAKE MY GLAUCOMA SERIOUS

TMAX AT DIAGNOSIS 26/32
POOR COMPLIANCE FROM 44-48 YO

51 YO STAYING COMPLIANT
51 YO STAYING COMPLIANT

69 YO MAN WITH POAG
BE CAREFUL OD VF LOOKS RELIABLE WITH FL, FP, FN, AND GAZE MONITOR

69 YO- BE CAREFUL EVEN THE VF SAYS RELIABLE

69 YO- BE CAREFUL EVEN THE VF SAY RELIABLE