Introduction

- UC Berkeley School of Optometry 2008
- San Francisco VA Residency 2009
- VA Staff Optometrist – teaching
- Regular lecturer at AAO and other meetings
- No conflicts of interest

Today's Goals

- Visual field analysis and interpretation
- OCT analysis and interpretation
- Touch on research about HVF and OCT for diagnosis and progression
- Case examples with OCT and HVF to help improve glaucoma care

Case #1 - 68 year old AA male

Ocular Findings:

- BCVA: 20/30-2 OD, 20/20-2 OS
- Pupils: ERRL, No APD OU
- Slit Lamp: 1+ NS and cortical cataracts OU
- IOP: 16/17 mmHg @ 0838
- Pachy: 589 μm OD, 579 μm OS
- Gonio: Ciliary Body 360°, 2+ Pig. OU

Family Ocular Hx: POAG – maternal aunt

Case #1: Optic Nerves

Glaucoma or not?

- IOP
- Advanced age
- Race
- Family history
- Pseudoxefoliation
- Pigment dispersion
- Disc hemorrhages
- Diabetes
- Glaucoma syndromes
- Corneal thickness
- Gender: NTG, POAG
- Migraines: NTG
- History of Trauma
- History of Steroid Use
- Peripapillary atrophy
- Myopia
- Raynaud’s phenomenon
- Ocular Biomechanics

Glaucoma Continuum

Most cases detected

Glaucoma Risk Factors

- Not detected
- Late detection

HVF Glaucoma Questions

- How does Humphrey VF work?
- What defines a glaucomatous visual field?
- What are the stages of glaucoma?
- How fast does glaucoma progress?
- How often are visual fields necessary?

Understanding the Humphrey Visual Field Analyzer
- Testing Strategies
- Evaluating Reliability
- Glaucoma Hemifield Test
- Visual Field Indices (MD/PSD)
- Total and Pattern Deviation

Testing Strategies
- Full Threshold
- FastPAC
- SITA Standard
- SITA Fast
- Decrease test time
- Maintain sensitivity and specificity

Test Patterns
- Central 30-2
  - 76 test points
  - 30 degrees each quad
- Central 24-2
  - 54 test points
  - 30 degrees nasal
  - 24 degrees sup/inf/temp
- Points 6 degrees apart
- Pick one and stick with it

HVF: Reliability
- Fixation Losses: <20-33%
- False Positives: <15-33%
  - “Trigger Happy”
  - SITA Stand may underestimate
  - Current: <5% likely unreliable, reject >10%
- False Negatives: <33%
  - Status of eye, not patient
  - 84% of pts had TFN in eye with more defects
  - Age, testing order had no effect

If Pattern > Total = Unreliable
Numerical and Probability Plots

Case #2 - Consistently Elevated FP
- 8% FP
- 5% FP
- 7% FP

Switched to 24-2
- 16% FP
- 15% FP
- 6% FP

Case #2

Glaucoma Hemifield Test (GHT)
- Compares local defects in 5 distinct zones
  - "Outside Normal Limits" – p<0.01
  - "Borderline" – p<0.03
  - "Generalized Depression" – under 0.5%
  - "Abnormally High Sensitivity" – over 0.5%
  - "Within Normal Limits"
- High sensitivity and specificity
- Good for early loss

Probability Plots

- Total Deviation
  - Corrects for age
  - Highlights abnormal areas
- Pattern Deviation – Most Important
  - Corrects for general depressions (cataracts)
  - 7th most sensitive point on total = pattern baseline
  - Highlights localized loss (glaucoma)
VF Indices (MD and PSD)

- **Mean Deviation (MD)**
  - Weighted average of dB values from total deviation plot
  - Shows average amount of change from age matched normal subjects for entire VF
  - Can be affected by cataract

- **Pattern Standard Deviation (PSD)**
  - Low PSD = smooth hill of vision
  - High PSD = pt variability or irregular VF

Variations in MD and PSD

- Low MD, normal PSD = diffuse loss
- Normal MD, higher PSD = local defect
- Normal MD, lower PSD = irregularity

Using HVF for Glaucoma

Basic Glaucoma VF Rules

1. Asymmetric across horizontal midline (early/mod)
2. Midperipheral (early/mod)
3. Clustered points
4. Reproducible 2x or more
5. Not explained by other diseases
6. Representative of pt's functional status (FPs, FLs)

Common Glaucoma VF Patterns

- Arcuate scotoma
- Bjerrum/Seidel
- Nasal step
- Paracentral
- Temporal wedge
- Overall depression
- Transient changes

**Glaucoma VF Definition (HAP)**
- GHT “Outside Normal” on at least 2 VFs OR
- Cluster of 3+ contiguous non-edge points p< 5% on PD and 1+ points p< 1% OR
- Corrected PSD <5% on 2 VFs

(2 consecutive VFs for last 2 definitions)


**New Glaucoma VF Definition (HAP2)**
- Any of the following must be reproducible on two consecutive 24-2 VFs:
  - GHT “Outside Normal Limits”
  - A cluster of 3+ points in a location typical for glaucoma, all of which are depressed at a p<5% level on the pattern deviation plot and one of which is depressed at a p<1% level
  - PSD that occurs in <5% of normal VFs


**Case #3 – Optic Nerves**

**Case #3 - 62 year old Asian male**

**Ocular Findings:**
- BCVA: 20/25 OD and 20/30 OS
- Pupils: ERRL, No APD OU
- Slit Lamp: 1-2+ NS and cortical OU
- IOP: 12/12 mmHg @ 0835
- Fundus: Unremarkable OU
- Family Ocular Hx: Unremarkable
- Medical Hx: DM, hyperlipidemia, sleep apnea

**Baseline HVF**
Repeat HVF – 1 month later

- 2 consecutive VFs with GHT outside normal limits
- Cluster 3+ points in typical location p<5% on PD with 1+ points p<1%

3rd HVF – 6 months later

Staging Glaucoma

- Has evolved in last 25 years
- Now part of ICD-10
- Baseline = 2 HVFs

Staging: ICD-10

- Mild or early: pre-perimetric (normal VF)
- Moderate: ONH abnormalities w/ glaucoma and VF abnormalities in 1 hemifield, but not within 5° of fixation

Staging: ICD-10

- Severe: ONH abnormalities w/ glaucoma and VF abnormalities in both hemifields and/or loss within 5° of fixation in 1 hemifield
- Indeterminate: ONH abnormalities w/ glaucoma without VF data

HAP2 Staging Criteria

- Early defect – neither extensive nor near fixation
- Must meet all 3 criteria:
  1. MD: >-6 dB
  2. No central pts <15db
  3. PD: 1-12 pts <5% and 1-4 pts <1%

HAP2 Staging Criteria

- Severe defect – Only 1 necessary:
  1. MD: <-12 dB
  2. More than 50% (27+ points) are <5% level and more than 25% (14+ points) are <1% on PD
  3. Any point in central 5° is 0 dB
  4. Both hemifields have points <15db within central 5°

HAP2 Staging Criteria

- Moderate (need 1)
  - MD: 6 to 12dB
  - No central pts 0db
  - PD: 13-26 pts <5%
  - PD: 5-13 pts <1%

HAP2 Staging Criteria

- Severe (need 1)
  - MD: < -12dB
  - Any central pts 0db
  - PD: 27+, pts <5%
  - PD: 14+ pts <1%
  - Both hemifields central pts <15dB
**HAP2 Staging Criteria**

- **Moderate defect** – any VF defect that is neither early nor severe

- At least one of the following is present:
  1. MD is between -6 dB and -12 dB
  2. 26-50% (13-26 points) are <5% level and 10-25% (5-13 points) are <1% level on PD
  3. No point in central 5° is 0 dB
  4. Only 1 hemifield has a point of <15 dB within central 5°


**Moderate Defect**

- **Mild** (need all 3)
  - MD: >-6 dB
  - No central pts <15db
  - PD: 1-12 pts <5% and 1-4 pts <1%

- **Moderate** (need 1)
  - MD: -6 to -12dB
  - No central pts 0db
  - PD: 13-26 pts <5%
  - PD: 5-13 pts <1%


**VF Progression**

- **NO WIDELY ACCEPTED STANDARD!**

- Most authors agree:
  - Deepening or expansion of an existing scotoma
  - New defect in a previously normal area

- **Risk factor analysis**
  - Methods for determination only agree about 50-60% of the time
  - Variability is huge amongst populations
  - Rates of VF change are not constant
  - No consensus among major investigators


**Major Challenges**

- Every clinical trial has different criteria
- Large differences in testing analyses
  - Methods for determination only agree about 50-60% of the time
  - Suspected changes have to be confirmed
  - Variability is huge amongst populations
  - Rates of VF change are not constant
  - No consensus among major investigators


“Disease progression rates in glaucoma vary very much among patients – and cannot be predicted even taking risk factors into account.”
- Andor Hjøll, 2011

**Determining Progression**

- **Clinical judgment**
- **Defect classification systems**
  - HAP, HAP2, AGIS, CIGTS
- **Event analysis**
  - Greater change than expected (GPA)
- **Trend analysis**
  - Rate over time (MD, VFI, etc)

- All have pros and cons
- Be consistent and evidence-based in your decisions


**VF Progression: HAP2**

- Requires at least 2 consecutive VFs
- New defects in previously normal area:
  - 1 point ↓>15dB
  - Within central 10° – any point ↓>10dB
  - Outside central 10° – 3 points ↓>5dB


**VF Progression: HAP2**

- Within preexisting defects:
  - 1 point ↓>15dB
  - Within central 10° – any point ↓>10dB
  - Outside central 10° – 3 points ↓>5dB on 2 consecutive VFs or ↓>5dB on 3 consecutive

- Either of these on GPA:
  - Slope of p<1% on VFI or “Likely Progression” on GPA

Classic Progression

At 5 years, 90.5% of untreated patients showed no ONH or VF progression. 9.5% in the observation group progressed, and 4.4% in the treatment group progressed.

85.9% of eyes with initial VF defects had normal repeat VF.

Change in MD of \(-0.08\) dB/yr.

Confirming Progression

AGIS – 12,746 VFs over 10-13 years
- Sustained decreased VFs (SDVF)
- Can temporarily recover
- 55% with SDVF on 2 visits, 40% on 3 visits showed recovery

Repeat VF at least once!

Progression - OHTS

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Visual Field Index (VFI)

Summary index on 24-2 and 30-2 tests
- Calculated by all test points in pattern dev'n
- Normal points (p>5%) = 100%, 0 dB points = 0%
- Eccentricity-weighted mean of scores

Gives visual function as % of normal age VF
- Resistant to cataract
- Used to judge rate of progression
Guided Progression Analysis (GPA)
- Calculates rate of progression from VFI
- 1-2 page summary report
  - Baseline exams at top
  - VFI trends in middle
  - Current exam at bottom
- Uses oldest 2 exams as baseline
  - Can and should be changed

How many VFs are needed?
- OHTS: 3 consecutive, abnormal, reliable
  - Originally 2 VFs, but 66% then were WNL
- HAP and HAP2: 2 reliable for baseline
- WGA: 2 reliable baseline in 6 months, then 2 more within 18 months
- CIGTS: 2+ for confirmation
- CNTGS: 2-3 in 1st month & 2-3 at 3 months
- HVF algorithms: 2 to 6 for analysis

Assessment of Visual Function in Glaucoma
A Report by the American Academy of Ophthalmology

"Advances in technology and analytical tools over the past decade have provided us with more and varied ways of assessing visual function in glaucoma, but they have yet to produce definitive guidance on the diagnosis of glaucoma or its progression over time."
VF Progression: Quick Review

- No single definition of progression exists
  - Pick an evidence-based approach that works for your patient population
- Repeat VF when a change is suspected
  - Set new baselines as needed
- Use software to your advantage
  - VFI and GPA are fast and easy to use
- Rates of progression vary
  - Determine an acceptable rate for each patient

OCT INTERPRETATION

Today's Goals

- Discuss analysis of optic nerve OCTs
- Review strengths and weaknesses of OCT for glaucoma management
- Review recent research about OCT for diagnosis and judging progression
- Provide tips for improved use of OCT in clinical practice

Available OCTs

- Zeiss Cirrus
- Heidelberg Spectralis
- Nidek 3000
- Canon Copernicus
- RTVue
- Opko/OTI Spectral OCT/SLO
- Topcon 3D-OCT
- Zeiss Stratus (Time Domain)

Spectral vs. Time Domain

- Similarities/differences in databases
- Color codes do not agree well
- Progression between instruments?
- SD-OCT advantages:
  - Higher resolution, decreased scanning time
  - Better repeatability of RNFL measurements
  - More data – peripapillary scans with RNFL thickness maps, macular GC analysis, etc
  - Better for diagnosis and progression

Jeoung, Park. IOVS, 2010;51:938–945.
Influential Factors?

- Normative databases
- Media
- ONH size
- ONH distance to foveola
- PPA
- Retina
- Axial length
- Interocular symmetry
- Refractive error
- Age
- Sex
- Race

Stratus Database
- 328 subjects
- 48% male, 52% female
- Mean age 47.4 ± 11.8 yrs, range 18-85
- Rx: -11.75 to +6.75, mean -0.54
- 63% Caucasian, 24% Hispanic, 8% African American, 1% Asian
- No eye surgery except cataract (9 pts), no ocular disease, IOP <22, normal and reliable VF, normal ONH, BCVA >20/32

Cirrus Database
- 284 subjects
- 47% male, 53% female
- Age range 19-84
- Only 3 pts >80 and 28 pts between 70-79
- Rx: -12 to +8
- 43% Caucasian, 18% African American, 12% Hispanic, 1% Indian, 6% mixed
- All normal subjects

Spectralis Database
- 201 subjects, all Caucasian
- 55% male, 45% female
- Mean age 46.2 ± 14.5 yrs, Range 18-78
- Only 1 pt <20 and only 13 pts >70
- Rx: -7 to +5
- No glaucoma, normal IOP, normal VF, normal optic nerve, etc

RTVue Database
- 861 subjects, various ethnicities
- Largest available database
- Mean age 50 ±/− 15.5 yrs, Range 19-82
- Rx: -8 to +8 sphere, -2 to +2 cylinder
- No glaucoma, normal IOP, normal VF, normal optic nerve, etc

Average RNFL Thickness

- Stratus: 99-100um in Caucasian/Japanese
- Spectralis: 98-97.3um ± 8.8 to 18.83um
- Cirrus: 94-94.9um ± 13.9um
- RTVue: 107.8 ± 10um
- Topcon: 102um

Red-Green Disease

- Color code determined by the database of the instrument
- Based on probability of that population only
- 15-36% of OCTs for glaucoma may contain artifacts that influence red-green analysis
Disc Area Measurements
- **Cirrus**
  - Small: <1.66mm²
  - Medium: 1.66-1.97mm²
  - Large: >1.97mm²

- Only 5% of eyes in normal database were <1.33mm² or >2.5mm² with Cirrus
- Stratus: 2.26mm² mean disc area
- RTVue: Range 1.86-2.1mm²

**Media and Eye Mvmts**
- RNFL Deviation Map
- ONH Size/Disc Area
  - Larger ONH means OCT scan is closer to ONH
  - RNFL decreases as measurement diameter increases
  - Overestimates RNFL in some studies but not others
  - Thicker RNFL measurements in larger ONH
  - 3.3um per 1mm² (Budenz 2007)
  - RNFL thickness correlates with disc area
    (Hirasawa 2010, Japanese)
  - No association between ONH size and RNFL thickness (AIGS 2012)

**ONH Size/Disc Area**
- Larger ONH means OCT scan is closer to ONH
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**Stratus**
- 2.26mm² mean disc area

**RTVue**
- Range 1.86-2.1mm²

PPA
- Present in 15% of normals but 62-84% of glaucoma patients
- Stratus overestimates disc size in glaucoma patients and controls
- Cirrus performs well compared to clinical disc evaluation

Axial Length
- Variable relationship in the literature
  - No correlation of axial length and RNFL, myopia (2010)
  - RNFL thickness ↓ with ↑ axial length (Ueda 2015)
- If temporal quadrant is thick, superior and inferior thinning could be due to refractive error (Alasil 2012, Ueda 2015)
- Be cautious of thinning in myopic Caucasians

**OCT: GLAUCOMA DIAGNOSIS**

**Other Factors**
- Rx:
  - RNFL thinner by 1.2 μm/diopter of myopia
- Race:
  - RNFL decreases from Hispanics > Asians > African Americans > Caucasians
  - Differences in ONH area, ave C/D, vert C/D, cup volume also
- FOHx:
  - Patients with FOHx of glaucoma have thinner RNFL and GCC than normals

**Utility of OCT in glaucoma**
- RNFL loss precedes VF loss by 6 years in 60% of eyes
- In OHTS, HRT showed glaucomatous change 8 years before VF defects
- 17% RNFL loss before VF detection
- Progressive optic disc changes may not correspond to RNFL thinning in the same eyes with glaucoma progression

**Glucoma Detection**
- Both TD and SD have high sensitivity and specificity for glaucoma when >1 clock hour is <5% level (yellow)
- Both TD and SD may be inadequate in detecting preperimetric RNFL defects
  - Worse when defects <10 degrees
- Cirrus can discriminate mild glaucoma from normal using ONH parameters
  - Vertical rim thickness (VRT), Rim area, Vertical C/D

**Abnormal RNFL Thickness**
- Average RNFL <5th percentile
  - Yellow or red
- Any quadrant <5th percentile
  - Yellow or red
- Any clock hour <1st percentile
  - Red

**Abnormal RNFL Contour (TSNIT)**
- Any focal thinning superior or inferior
  - Especially if yellow or red
- Any significant asymmetry between contour of OD and OS, especially superior or inferior

**Glaucoma Detection**
- RNFL parameters:
  - Average/global RNFL thickness*
  - RNFL thickness at infero-temporal* (3, 4, 9 o'clock are most variable)
  - RNFL thickness inferior quadrant
- Additional useful information:
  - Cirrus – RNFL deviation-from-normal map
  - Stratus – TSNIT
  - Asymmetry

**Case #4 - 45 year old Caucasian male**

**Ocular Findings:**
- BCVA: 20/20 OD, 20/25+2 OS
- Pupils: ERRL, no APD
- Slit Lamp: trace NS, no PXF OU
- IOP: 22/23 mmHg @ 0841
- C/D: 0.35 OD and OS
- Fundus: normal OU
Interocular symmetry

- Increasing age is not associated with increased RNFL asymmetry
- Spectralis: 6.6x greater asymmetry in glaucoma vs. normal
  - Difference of 6um for RNFL global average had high sensitivity and specificity to detect POAG

Detection: Quick Review

- OCT is a validated technology for glaucoma detection
  - Variations exists between instruments
  - Average RNFL thickness = ~84-108um
- Use caution when interpreting OCTs
  - Normal eyes can appear glaucomatous

OCT: GLAUCOMA PROGRESSION
Progression: Considerations
- Variable nature of glaucoma
- Event-based vs. trend-based analyses
- Changing technology – longitudinal flu
- Instrument variability
- No consensus on limit of RNFL thinning that equals progression; no reference standard
- Eyes without VF loss?

Reliability and Reproducibility
- Inter-visit repeatability is good for most SD-OCT
- Signal strength: 7 or greater desired
- Dilation: may not effect repeatability
- Variability vs. progression?

Assumptions To Remember
- Progressive RNFL thinning occurs with increased glaucoma severity
- Abnormal (thinner) RNFL may show less inter-visit variability than normal (thicker) RNFL
- Severe glaucoma can potentially have more functional loss with smaller RNFL changes

Variability vs. Progression
- Stratus
  - Test-retest variability of ~4-10um per quadrant
  - Be suspicious of changes over 10um
- Cirrus
  - Ave RNFL thinning of >4-6um between visits is suspicious
- Spectralis
  - Clinically appears to have very low fluctuation
  - Global 5-14um intra- and inter-visit variation

Suspected Progression
- Variability:
  - Average RNFL: ~5um
  - By quadrant: ~5um
  - By clock hour: ~10-12um
- Thinning of >10um (or maybe 20um) are more concerning, especially I/T and S/T
- Suspicious OCTs should be repeated

Case #5 - 68 year old male

Case #5
**Case #5**

**4/12/17**

**Recommendations**

- Repeat OCTs before making treatment decisions
  - 41-56% of abnormal scans were not duplicated on follow-up exams
- Consider abnormal if 2 of 3 RNFL or GCIPL scans are borderline or ONL
  - Some suggest up to 5 tests (linear regression)

**HAP2 Recommendations**

- Serial, good quality OCTs can help detect progression
  - For patients who can NOT do VFs:
    - Early glaucoma: average RNFL ↓ 8µm
    - Mod/severe glaucoma: ave RNFL ↓ 4µm

**Types of RNFL Change**

- Inter-temporal is most common in glaucoma
  - Widening of RNFL defect (85.7%)
  - Development of new RNFL defect (17.9%)
- Other optic neuropathies can cause RNFL thinning, but patterns are different

**Age-Related RNFL Loss**

- Average rate: -0.10 to -0.52µm/yr or 1.5 - 2µm/decade
- Greater baseline thickness = faster rate of change
- No significant change in nasal and temporal quadrants with age
- Rate in glaucoma is faster
  - ➤ > -2.54 µm/yr is significant

**GPA**

- Cirrus: GPA available for OCT or HVF or combined analysis for both

**Pros:**
  - OCT GPA on Cirrus is useful to judge progression when VF detect is mild

**Cons:**
  - Agreement between OCT GPA and disc photos or VF analysis can be poor
  - Subject to artifacts in scans

**Age-Related RNFL Loss**

- Average rate: -0.10 to -0.52µm/yr or 1.5 - 2µm/decade
- Greater baseline thickness = faster rate of change
- No significant change in nasal and temporal quadrants with age
- Rate in glaucoma is faster
  - ➤ > -2.54 µm/yr is significant

**HAP2 Recommendations**

- For patients who can do reliable VFs:
  - No VF defect: average RNFL ↓ 10µm
  - New VF defect or disc heme: RNFL ↓ 5µm
- If severe glaucoma with RNFL < 60µm, a stable OCT does NOT rule out progression
Macular OCT

- Useful in advanced glaucoma
  - Papillomacular bundle preservation
- Early glaucoma detection
  - High discriminating power
  - High reproducibility


Ganglion Cell Analysis (GCA)

- Macular RGC complex is 1-7 cells thick: RNFL, GCL and IPL
  - Contains 50% of retinal RGCs
- Average RGC count is lower in eyes with early VF defects: 652K vs 911K
  - RGC loss of 7877 per year
- RGC counts were better than average RNFL thickness for detecting glaucoma with early/minimal VF loss

Ganglion Cell Analysis

- Macular RGC counts can be affected by drusen and AMD
- GCIPL thinning with thinner RNFL, older age, longer axial length, and males
- GCIPL and total macular thickness (TMT) have similar sensitivity in detecting glaucoma progression
  - Average RNFL was better in diagnosis
- Minimum GCIPL is best parameter for early perimetric glaucoma detection and is similar to best RNFL or ONH parameters (Mwanza, Jeoung)

- Glaucoma is likely when:
  - Intereye macular thickness asymmetry >5 um
  - Intraeye macular thickness asymmetry >9 um
  - Intereye RNFL thickness asymmetry >9 um
  - Global RNFL thickness ≤78 um

* Spectralis

OCT: Conclusions

- OCT is great technology but it isn’t perfect
  - Correlate HVF and OCT findings
- Evaluate scan data and not just colors
  - Remember artifacts, instrument capabilities, etc
- No set standard for OCT progression
  - Research studies vs. clinical care
- Repeat OCTs and correlate with other findings before making treatment decisions