Glaucoma Progression

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Disclosures

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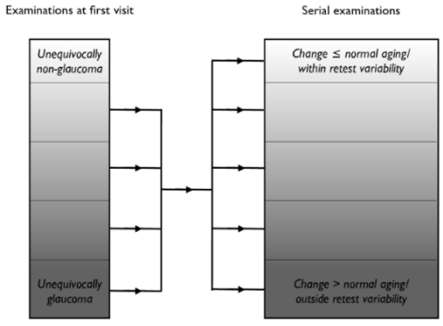
Managing glaucoma or glaucoma suspects Summary

- For patients diagnosed or at risk of glaucoma
  - Stage disease
  - Risk assessment
  - Asses for progression
  - Treatment plan
  - Surveillance
    - Establish adequate baseline
      - IOP
      - VF
      - Imaging

Glaucoma Progression

- Ability to discriminate true change, over and beyond measurement variability, is recognized as central requirement for any progression technique
  - Perimetry or Imaging
- Progression may be measured by
  - Structural changes at the optic nerve head, retinal nerve fiber layer and macula
  - Functional changes such as deterioration in the visual field or with electro-diagnostic testing (PERG)



Glaucoma Progression

- Evolving methods to assess change :
  - Better understanding of who and when progression occurs
    - EMGT, EGS guidelines
  - Imaging instruments have improved
    - Spectral OCTs have < 5um resolution
  - Computerization and software have improved
    - Recent introduction of GCC GPA
  - Visual field and imaging instruments allow quantification of data to recognize change using sophisticated mathematical principles
    - Single points and global indices
- The Future
  - Software that integrates imaging and visual field results
  - Neural network approach using artificial intelligence
  - Currently machines provide only spatial correlation between visual fields and imaging

Glaucoma Progression

- Glaucoma progresses slowly with high variability
  - Change is often non-linear
- Perimetry and OCT are complimentary methods to detect change
- Stereo photography and 2-D photography may detect early change but difficult to use
  - Difficult to see cup/disc ratio change when it is large
- Imaging provides quantitative measurements that may improve ability to detect progression

Glaucoma Progression

- Tools
  - Structural - Optic Disc and RNFL and Macula
    - Photographs
    - Imaging - OCT
      - RNFL and C/D ratio
      - RNFL and Macula GCC Guided Progression Analysis (GPA)
  - Functional
    - Perimetry
      - Glaucoma Progression Analysis (GPA)
      - Overview printouts
    - Electro-diagnostic testing (PERG)
- The best method to detect progression varies depending upon the stage of disease
  - Early (Mild) – Structure
    - Floor effect at approximately 55um
  - Moderate to Advanced- Function

Glaucoma Progression

- Historically progression determined by
  - Evaluating optic nerve in real time and comparing with old photographs
    - Decide if most recent picture indicative of change
  - OR
  - Evaluating visual field printouts, either single field or overview, by inspection to see if more points flagged on most recent field

Glaucoma Progression

- Ability to measure structural change with imaging devices, that is occurring over time to optic nerve and RNFL removes subjectivity associated with perimetry
- Imaging
  - Accuracy and reproducibility of imaging devices is excellent
  - Ability to detect glaucoma with devices may exceed trained clinicians
  - Improved resolution, reproducibility and speed of image acquisition allow better alignment
  - Allow smaller changes to be detected
  - Beware of signal strength image to image
- Advantages of imaging devices
  - Ease of use
  - Documentation

Glaucoma Progression

- Compared with glaucoma diagnosis, validation of what is glaucoma progression is more complicated
  - A reference standard is not available
  - Current guidelines define progression in general terms
  - Consensus on more objective and precise definition not been reached
  - Different studies use different criteria to define progression, making comparison of reported performance difficult

Top Five Risk Factors for Progression
EMGT

- Age
- Bilaterality
  - EMGT 72% progressed if bilateral vs. 45% unilateral
- Intraocular Pressure
- Diurnal Variation in IOP
- Pseudoexfoliation
  - EMGT 83% progressed
- Baseline Visual Field Defect
  - -4dB greater risk

What is an Acceptable Rate of Change? United Kingdom Glaucoma Treatment Study

- You can see progression in as little as one year but it requires extensive visual field testing
  - Not doable in today's practice environment
- Still can modify this since some people will progression quickly and need intervention

Glaucoma Progression

- Where does progression occur first? Optic Nerve or Visual Fields?
  - OR is it a matter of where we are best able to detect change clinically?
- Do all tests detect Progression?
  - Imaging vs. Visual Fields
- Does any one test do a better job than another?
  - Tests Perform Differently from person to person
    - Reasons are not clear
  - One test may detect change and the another does not in one patient and just opposite occurs in a different patient
  - How a test performs depends upon the severity of glaucoma

Visual Field Progression

- Visual field progression reflects the functional status of a patient with glaucoma or suspected of developing glaucoma by estimating whether the visual field is improving, remaining stable, or getting worse
- This assessment determines the management of the patient and the potential impact of visual field loss on quality of life and activities of daily living
- The rate of visual field change provides important predictive and prognostic information about the future visual state and management strategy for the patient

What methods are used to evaluate visual field progression ?

- Clinical Judgment
- Classification systems
- Event Analysis
- Trend (regression) analysis

What types of visual field progression can occur ?

- Defects become larger in size
- Defects become deeper
  - Most common
- New defects appear
- Diffuse (widespread) loss

Glaucoma Progression

- How often should we do the test
  - At Baseline and Once per Year?
  - At Baseline and Twice Per Year?
  - At Baseline and Three Times Per Year?
- When can we reduce our testing interval?
- Concept of bundling tests at beginning and several years later – Crabb et al
- Can a person get worse after being stable for a period of time?

If you think the field is worse, repeat it It probably isn't

- What indicates that a field is worse?
  - Relentless downhill course
  - 4 or more fields
  - Not a sudden worsening
  - 0.5dB per year in MD or PSD
- Classify patients into two groups
  - Stable = 0.1 dB/year change
  - Progressive = 0.9 dB per year

Do 5-6 years in first 2 years

- 3 fields in first year
  - At Diagnosis, 6 months, 12 months
- Then every 6 months for next 12 months
- Allows good identification of fast, severe progressor
- Scale back to 1/year if stable

GPA tends to overcall change

- This is OK because would like to be alerted to any question of change
- If you are not sure if fields are changing, do fields every 4 months
  - You cannot judge with only 2 fields
  - Do fields until pattern is clear
- Always repeat field to confirm a change before instituting a change in management

Progression Event Analysis

- Event analysis asks "Has this changed?"
  - Evaluation on point by point basis looking for a pre-determined amount of change
  - Points are compared to baseline
  - Identify progression when a measurement exceeds a predetermined criterion for change (or an event)
  - Assumed any change below the criterion represents measurement variability and that changes above the criterion represent true disease change
- Such changes can be identified earlier in the course of follow up management than can rates of progression
- If such events are observed, consider additional testing with the same instrument sooner rather than later to confirm the apparent event
  - also to provide a better idea of whether the associated rate of progression is unacceptable

Progression Event Analysis

- Identify changes that exceed expected test-retest variability
  - in perimetry and imaging
- The standard approach is to identify changes that would be expected from random variability in fewer than 1 out of 20 patients
- 5% of the time that amount of variability happens randomly, but 95% of the time it does not
- We call these changes statistically significant, although it is up to you to decide if they are clinically significant

What are the advantages and disadvantages of these procedures ?

- Event Analysis
  - Advantages
    - Direct comparison of current test to baseline
    - May detect progression earlier
  - Disadvantages
    - Ignores data obtained from intermediate sessions.
    - Suspected changes must be confirmed

Trend Analysis

- Trend analysis asks "Is the rate of change significant"?
  - Uses all the data with pointwise logistical regression formula
  - Identifies progression by monitoring the behavior over time

What are the advantages and disadvantages of these procedures ?

- Trend (regression) analysis
  - Advantages
    - Preferred method of determining visual field progression and rate of progression
    - Fast versus slow
  - Disadvantages
    - Requires at least 6 visual field exams over 2-3 years minimum

What is the OCT floor effect?

- The RNFL layer is composed of glial and other structural tissue
  - 40% of its makeup
- With advancing damage, never goes to 0
- The floor varies with OCT device but is between 50-60 um

OCT Glaucoma Progression

- Using OCT progression analysis in glaucoma suspects and in early disease is important
- Progression event analysis is central to the whole idea when using the OCT
  - trend analysis may be useful, but people are prone to misinterpret the data
  - they over-react when minimal but statistically significant rates are detected, or
  - they under-react when they see minimal progression in bad disease, not realizing that they have just bottomed out

Structure-Function Detection of Change

- Approximately 28% of RNFL is lost at the time that visual field loss is detected
- OCT Cirrus – 95% confidence limits for change is 4.5 microns which will improve with eye tracking
- HFA perimeter – 2 dB is limit to show that change has occurred with GPA

Life Expectancy Data – People are living long

(*USA, 2002, all persons, median)*

Current Age	Years	Life Expectancy
45 yrs	34.8	79.9 yrs
65 yrs	18.3	83.3 yrs
85 yrs	6.1	91.1 yrs

DHHS. National Center For Health Statistics
http://www.cdc.gov/nchs/data/nvsr/nvsr53/nvsr53_06.pdf