The Clinicians' Guide to Glaucoma: Optic Disc and Visual Field Analysis

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> **Despite the multifaceted nature of glaucoma and the array of diagnostic technologies available, the single most important aspect of glaucoma diagnosis and management is evaluation of the optic disc and nerve fiber layer. It is the goal of every good glaucoma practitioner to be able to diagnose glaucoma and judge disease stability or progression based solely upon the appearance of the optic disc.**

Optic Nerve Head:
- 1 million retinal ganglion cell axons
- Blood supply: mostly short posterior ciliary arteries (SPCA)
  - Central core blood supply is the small branches of the central retinal artery.
  - Peripheral prelaminar supply is the centripetal branches of the peripapillary choroid arising from the short posterior ciliary arteries.
  - The laminar portion is nourished by the Circle of Zinn-Haller, an anastamoses arising within the sclera of adjacent SPCA's.
  - The peripheral part of the retro-laminar nerve is supplied by branches from the pia mater's vascular plexus. This plexus is formed by branches from muscular arteries, the ophthalmic artery, and recurrent branches from the peripapillary choroid and the Circle of Zinn-Haller. SPCA supplies some extent of all portions of the nerve; the CRA supplies only the NFL and central core of the nerve.
- Average disc size ranges from 1.7 and 2.0 mm vertically and 1.6 to 1.8 horizontally (1.9 mm x 1.7 mm is a good average)
  - Physiologically large nerves have large cups
    - Occur more commonly in patients with normally large chorioscleral canals and large discs
    - Megalopapillae
    - Causes over diagnosis of glaucoma
  - Physiologically small nerves have small cups
    - Moderate cupping can indicate significant loss of tissue
    - Causes under diagnosis of glaucoma

The Glaucomatous Nerve:

ONH: Cupping
- Neural tissue vs. non-neural tissue (donut vs. hole)
- 'cupping' is a poor way to think about the glaucomatous process and C/D ratios are nearly meaningless in glaucoma
- Axon, glial tissue, capillaries
  - Direct ophthalmoscopy has limited value due to magnification and monocularity.
- Current teaching*:* the point of deviation of small blood vessels on the surface of the ONH should be used to determine the size of the cup (contour technique) rather than the area of pallor in the center of the disc (color-contrast technique)
  - Reality*:* the area of pallor in the center of the disc frequently corresponds well with the area of the cup. Use both techniques together. However, contour always wins out over color
- Average cupping: 0.4
  - As disc area increases, so does the average size of the C/D ratio
    - Due to inter-individual variation in disc size and cup size, the C/D ratio in normal patients can range from 0.0 to 0.9
    - Large discs have larger cups and smaller discs have smaller cups
- Symmetrical C/D ratio in most of normal population
- Symmetrical increase in C/D ratio not common in glaucoma
- Difficult to distinguish from physiological cupping
  - Considerable overlap in C/D ratio of normals, physiological cups, and glaucoma patients.
- Rim thinning: generalized loss of tissue
- Notching: focal loss of tissue. Corresponds well with field loss in most cases
  - Very characteristic of glaucoma
- Saucerization:
  - Shallow cupping- very hard to detect in some cases, hence the need for contour judging rather than color judging. Leads to misdiagnosis often
- Bean potting
  - Deep cupping
  - Occurs in normals

Clinical Pearl: Increasing excavation and enlargement of the optic cup occurs most commonly in glaucoma, but can occur in arteritic anterior ischemic optic neuropathy and compressive lesions of the optic nerve such as sphenoid wing meningioma. However, in these last two cases, the neuroretinal rim typically will have pallor and potentially decreased acuity whereas glaucoma will not.

Clinical Pearl: If you *think* that you see a relative afferent pupil defect and the visual acuity is 20/20, you are likely wrong. If you are sure that you see a relative afferent pupil and the vision is 20/20, then it is likely to be asymmetric glaucoma. The reason is that glaucoma is the optic neuropathy most likely to preserve good vision.

Clinical Pearl: Glaucoma is over-diagnosed in large discs and under-diagnosed in small discs. Size does matter.

ONH: Rim Tissue
- Pink coloration due to axons and capillaries
- Glaucoma: rim is always pink (except in very endstage disease)
- Pale cupping (pallor exceeding cupping): compressional lesion, ischemic vascular accident, neurological event. No rim pallor - if this occurs, it is <u>not</u> glaucoma (alone)
  - Rim pallor can only be accepted as glaucomatous once other potential causes have been ruled out
  - Other diseases can cause "cupping", though there will be other features inconsistent with glaucoma such as central acuity loss and disc pallor. Non-glaucomatous cupping include arteritic anterior ischemic optic neuropathy and possibly some others:
    - Compression
    - Inflammation
    - Trauma
    - Hereditary

ONH: Notching
- Focal loss of tissue-87% specific for glaucoma
- Highly indicative of glaucoma
- While other conditions can cause optic atrophy and increased in cup, they don't notch the nerve like glaucoma.
- Inferior, Superior, Nasal, Temporal (ISNT) rule. Any disc that breaks this rule of rim thickness is suspect.
- Vertical elongation
  - Axons loose in inferior and superior lamina- this is the reason for vertical elongation
  - Look for narrowing of neuroretinal rim superiorly and inferiorly
    - Inferior temporal or superior temporal (usually)
      - Inferior or superior in 2/3rds of cases
- NFL defect often associated
- Hemorrhage may be present or an antecedent event
- Typically associated with (dense) field defect
- Occurs only from inside cup to inner rim. There may be patients who have an irregularity of the outer rim-this is not notching
- This aspect of disc analysis is the most compelling in diagnosing glaucoma.

> **Clinical pearl: Notching does not occur commonly on the temporal or nasal aspect of the disc. Temporal thinning of the disc is most commonly an anomaly of disc insertion and not glaucoma. The term "temporal thinning", in the absence of other glaucomatous disc changes, is meaningless.**

ONH: Hemorrhages
- Names: NFL hemorrhages, splinter hemorrhages, Drance hemorrhages, disc hemorrhages
- Inferior, inferior temporal, superior, superior temporal regions of the disc most susceptible and account for virtually all true disc hemorrhages

- Hemorrhages at other areas of the disc (nasal and temporal) tend to not be associated with glaucoma
- Typically occurs where notches occur
- Resides in the retinal nerve fiber layer, not in the cup
- Small and contiguous with the neuroretinal rim
- Resolves within about 6 weeks. This is the reason that the incidence is difficult to determine. Also, many disc hemorrhages are missed in clinical observation
  - Remarkably, in the OHTS study, 16% of disc hemorrhages were detected by both clinical examination and review of photographs, and 84% were detected *only by review of photographs* following clinical examination.
    - Thus, review of stereophotographs was more sensitive at detecting optic disc hemorrhage than clinical examination.
    - The occurrence of an optic disc hemorrhage was associated with an increased risk of developing POAG (as defined by the OHTS end points), though it must be acknowledged that 87% of eyes in which a disc hemorrhage developed have not converted to POAG to date.
- Can be recurrent and, if it recurs, it typically is in the same place on the disc each time
- Precedes notching, NFL defect, field loss. Perhaps the earliest change in glaucoma (if it happens)
- More common in patients with large IOP variations
- Disc hemorrhages do not constitute a diagnosis of glaucoma nor a progression or conversion to glaucoma or an endpoint for any major glaucoma
- Meaning is unclear- probably bad stuff. Seems to indicate progression of the disease
  - Anemia, posterior vitreous detachment, vascular occlusion, subarachnoid hemorrhage (Terson's syndrome) can cause hemorrhages of the disc that are mistaken for glaucomatous disc hemorrhages
  - Ischemic or mechanical
  - Probable infarction of the blood supply to the ONH
- Major studies: EMGT, OHTS, and collaborative normal tension glaucoma study indicated that disc hemorrhages were strongly associated with progression
  - Curiosities:
    - OHTS: majority of eyes with disc hemorrhages have not converted to glaucoma
    - EMGT: While disc hemorrhages were predictive of progression, IOP-reducing treatment was unrelated to the presence or frequency of disc hemorrhages. Disc hemorrhages were equally common in both the treated and untreated groups of patients. The results may suggest that disc hemorrhages cannot be considered an indication of insufficient IOP-lowering treatment, and that glaucoma progression in eyes with disc hemorrhages cannot be totally halted by IOP reduction. The results also suggest that disc hemorrhages do not occur in all patients with glaucoma.
    - Normal Tension Glaucoma Study: while disc hemorrhages predicted progression, treating eyes with disc hemorrhages did not benefit the patient or affect the clinical course of the disease

ONH: Laminar dot sign
- Exposure of laminar tissue secondary to loss of neural tissue
- Round pores in normals and slit pores in glaucoma

- Weak finding- can occur in normal nerves as well
- Posterior deformation of the anterior laminar cribrosa surface (ALCS) preceded or was concurrent with changes in pore geometry & RNFL thickness in early glaucomatous eyes (experimental glaucoma)
    - Laminar pores initially become more oval before becoming elongated in early glaucoma

Parapapillary Observations
- A ratty looking atrophic peripapillary retina should make you suspect glaucoma
- Often due to tissue misalignment
- Possible shifting of tissues
- May change over time
- Susceptibility to damage or the result of damage
- Unclear if this is a cause of glaucoma or an epiphenomenon of glaucoma
- Zone beta
    - Adjacent to nerve
    - Scleral tissue
    - More associated with glaucoma
- Zone alpha - pigment adjacent to zone beta

Nerve Fiber Layer Evaluation
- Normal NFL- striate appearance- underlying vessel obscured as if transparent tape was over them
- Alteration in appearance of normal striated pattern of NFL around ONH
    - Diffuse or focal
- Selective damage
- Precedes field loss (in one study, 50% showed NFL loss 5 years prior to field loss)
- NFL loss is 85% specific for glaucoma (in certain patterns)
- Precedes disc changes
- Often appears as a dull area to the fundus which allows a better observation of the underlying choroidal details

NFL Defects
- Slit
- Wedge (bigger than slit)
- Diffuse
- NFL defects must meet two criteria
    - They are at least the same caliber as an arteriole
    - They must extend to the disc
        - Anything that doesn't meet these criteria are pseudodefects

Compressive Lesions vs Glaucoma
- Patients with optic nerve tumors tend to be younger than 50 years, have vision less than 20/40; have disc pallor, and have vertically aligned field defects
- Patients with glaucoma tend to be older, have less disc pallor, more focal defects of the

neuroretinal rim, more frequent disc hemorrhages, and have horizontally aligned visual field defects

> **Clinical Pearl: While other conditions can cause increased cupping, nothing notches the neuroretinal rim like glaucoma.**

Summary: "-Omas" vs. Glaucoma

-Oma	Glaucoma
Reduced VA	Normal VA
Color defect	Normal color
RAPD more likely	RAPD less likely
Field doesn't match disc	Field matches disc
Rim pallor	Rim defect
Central and cecocentral scotoma	Arcuate defects

Visual Field Analysis in Glaucoma

- Damage may be extensive or focal
- Relative scotomas
- Fluctuating scotomas
- Absolute scotomas
- Paracentral scotomas (5-15°)
- Nasal steps
- Arcuate scotomas (Bjerrum's scotomas)
- Altitudinal defects
- General depression and overall depression in sensitivity (diffuse loss) is actually very rare in glaucoma and more indicative of cataract, miosis, or other media/refractive issues.

> **Clinical Pearl: The earliest visual field defect in glaucoma is increased short term fluctuation. However, it is not practical to measure this on contemporary visual fields. The next is a shallow fluctuating scotoma, which can be measured practically, though is often not recognized clinically as a true defect.**

> **Clinical Pearl: President George H.W. Bush repeatedly referred to "*a thousand points of light*" in several speeches such as when he accepted the presidential nomination as well as in other addresses. It is widely believed that his affinity for this phrase comes from undergoing threshold perimetry for his exfoliative glaucoma.**

The Four "R" of Visual Fields
- Reliable
  - Reliability parameters vs. gaze tracker vs. perimetrist's comments
  - Reproducible
    - Reproducibility is perhaps the greatest indicator of reliability

- o Reproducibility increases the likelihood that "insignificant" defects are indeed significant.
- Relatable
  - o Objective interpretation important
  - o Must then correlate field to anatomy to support or refute "defects"
- Recognizable
  - o As glaucomatous defects rather than something else

Swedish Interactive Thresholding Algorithm (SITA)
- Threshold strategy which reduces threshold test time down to 3-5 minutes from original 15 – 18 minutes (Full Threshold algorithm) without sacrificing accuracy
  - SITA standard threshold field is a good routine test for diagnosing and following glaucoma
  - SITA Fast is a good *screening* test and for those patients who can not maintain attention for long
- Error Related Factor (ERF)
  - SITA algorithms employ ERF.
  - Perfect determination of threshold (that is, the sensitivity where the patient will see the stimulus 50% of time) is impractical. SITA allows for some "error" based upon known data and patient responses. SITA fast differs from SITA Standard in that there is decreased test time because the ERF is greater. That is, SF allows for a greater degree of uncertainty about threshold when deciding to end the test.

Clinical Pearl: SITA Standard 24-2 is the most widely accepted and accurate visual field for glaucoma.

Clinical Pearl: You cannot compare results from different test strategies and testing algorithms. You cannot judge stability or progression if you switch between FT, SS, and SF

Reading and Interpreting the Printout: Single Field Analysis

Reliability Parameters:
- **Fixation losses (FL):**
  - High values occur if:
    - The patient's gaze had often drifted from fixation so that the stimulus falls on a seeing point of the retina
    - The presumed location of the blind spot is incorrect (pseudo-loss of fixation).
    - The patient readjusted head position after the blind spot had been plotted, yet still maintains good fixation (pseudo-loss of fixation).
- Eye tracking system (gaze monitor) in SITA tells, by deviation above or below a horizontal line, the exact instances when a patient closes their lids (excluding blink) or makes a saccadic deviation from fixation.

Clinical Pearl: A high degree of fixation losses does not necessarily mean that the results are invalid.

- **False Negative Rate (FN):**
  - This may indicate that the patient is fatigued and falling asleep, has changed personal criteria for response, or is a true indicator of actual field loss where sensitivities are variable. A high FN rate is more indicative of the state of the eye rather than the state of the patient, i.e., it is more likely to indicate true visual field loss rather than a patient's degree of alertness.

- **False Positive Rate (FP):**
  - A high false positive rate indicates an unreliable field. This is seen as the patient becomes "trigger happy". High FP rate is most devastating to interpretation. High FP rates will be accompanied by:
    - Suprathreshold levels
    - MD has a high (+) value
    - Fixation losses high
    - Patchy loss on grayscale
      - White scotoma
    - Pattern Deviation is worse than Total Deviation
  - SITA: The computer knows how long that it minimally takes in order to respond to a stimulus. A response faster than the preset criteria is determined to be an aberration and is considered a false positive response
  - Likewise, the time of the patient's responses are monitored. The average time to respond is determined as is the range of response time. It determines an "acceptable interval" of response time. Any response falling beyond this interval is perceived as a response to something other than the stimulus and is deemed a false positive response
    - SITA strategies have no published criteria that indicate when a field is unreliable based upon false positive responses, but most believe that anything exceeding 10% is unreliable.

Visual Field Analysis

- **Raw data:** threshold sensitivity values (in decibels – tenth of log unit)
- **Grayscale:** interpolated raw data
- **Total deviation:**
  - General depression
  - Numeric values: deviation from normal values for age.
  - Probability display symbols indicate frequency of that particular value within a normal population, derived as a percentile by non-gaussian statistics.
- **Pattern deviation:**
  - Localized depression
  - Deviation is corrected for the overall height of the hill of vision (if the best portion of the field tends to be above or below the average normal values by virtue of normal variation or depression). The computer ranks the total deviation values from best to worst and then looks at the value of the point that represents the 85th percentile of non-edge points (also excluding some points around the optic disc/physiological blind spot). This point is used to determine the "general height indicator". The difference between the obtained threshold

value for the general height indicator and its expected value is then added to all points in the visual field. If the point used for the general height indicator is depressed, all threshold values in the visual field will be raised. By raising the values of the patient's actual threshold, the effects of cataracts or miosis can be minimized, allowing for the detection of focal defects. Conversely, the general height indicator may be elevated rather than depressed. This will occur in patients who have truly supersensitive threshold values (rare). This will lower the hill of vision and reduce the visual field threshold measurements by a few decibels. This is important because shallow scotomas may be missed otherwise. This will also occur in those who have a high degree of false positive responses and the field may be lowered by some absurd factor, which is physiologically impossible and a sign of unreliability.

- Probability display is provided equivalent to the total deviation probability plot after removing any deviation from normal that affects the entire field equally. This subtracts out the field defects that occur from aging, i.e., cataracts, media opacity, etc.
  - For both the total deviation and the pattern deviation probability displays, the low probability refers to the probability of the value at that point, i.e., the occurrence of that particular sensitivity value in a normal population. However, when points are analyzed, a normal field may contain a few scattered points that have, by chance, an abnormal value. The finding of an abnormal point is not sufficient to conclude that a field is abnormal, especially if the clinical picture does not correlate. Abnormality of a field as a whole must be judged on the basis of finding sufficient abnormality in a cluster of points in a pattern that is typical of the associated clinical findings.
  - The probability symbols are probably the most important feature of the single field analysis. This analyzes the deviation from normal of the patient's threshold values and displays then individually as probability symbols. Each symbol corresponds to the occurrence of that threshold value in a normal individual within a normal population. It allows us to see the degree of departure from expected values in a normal population and the pattern of field loss (as it is).

Clinical Pearl: The Pattern Deviation is the best representation of the true retro-lenticular visual field defect.

Global Indices:
- **Mean deviation (MD):**
  - *Weighted Average* of the numbers on the total deviation plot each value weighted according to the magnitude of the normal range at that point (points with low variation, i.e., closer to fixation, are weighted more heavily).
  - Signifies the overall severity of the field loss, interpreting the severity of the field loss at individual locations and the area of the field involved. Thus, a MD of -4 db depression may indicate a 4 db depression everywhere in the field or a depression of -8 db over half of the field.
  - A positive number indicates that the average sensitivity is above the normal for age, and a negative number indicates that the average sensitivity is below the average age-matched normal.
  - If the MD is outside the normal range, the probability that such a value would occur in a normal population is given, determined by non-Gaussian stats stored in a computer look-up

table.
- Abnormalities may indicate:
  - Widespread damage
  - General depression
  - Many small depressions
- Mean Deviation is affected by cataracts

- **Pattern standard deviation (PSD):**
  - Weighted standard deviation of the difference of each sensitivity value from the value expected, based on normal values and the MD index. This is a measure of how different points are from one another within the field. This is the "averaged" amount that each point in the field deviates from the expected STAT-PAC value after it has been adjusted for a general depression or suprasensitvity. This is a weighted average of the pattern deviation. Conceptually, the PSD is supposed to indicate how evenly the visual loss is spread across the visual field. It is minimally influenced by cataract. One would expect similar values in adjacent points in a normal field. In an abnormal field, contiguous points may vary widely as a sign of field loss. In a normal field, or a field in which all points are equally abnormal, the PSD will be low. The PSD becomes larger as some points become more affected, and is thus an index of localized change in the field. If the PSD is outside the normal range, the probability that such a value could exist in a normal person is given.

Glaucoma Hemifield Test (GHT):
- In glaucoma, the upper and lower hemispheres of the field are often significantly different.
- Points within the visual field are grouped together into 5 smaller zones with mirror images of one another above and below the horizontal meridian. Probability values are used rather that threshold values. The mirror images are compared to one another. There are 5 possible interpretations of the results that are printed.

1. GHT outside normal limits*:* A score is assigned to each member of the pair of mirror image matched zones based on the percentile deviation from normal. This message will appear if one of the matched zones that are compared yields a score that is found in less than 1% of normals, or if each zone in a matched pair is outside the 0.5% level of probability. Put another way, if the difference between the mirror image zones would be expected in less than 1% of the normal age-matched population, this message will appear. If both mirror image zones are depressed more or less equally, but to a degree found in less than 0.5% of the normal age-matched population, this message will appear.

2. GHT borderline: Zone pairs differ by a degree greater than that seen in less than 3% of the normal population, but more than 1% of the normal population (doesn't meet the criteria for "Outside Normal Limits".

3. General reduction of sensitivity: The GHT looks at the "elevator" factor (the general height indicator as described above) used in the analysis of pattern deviation. If the value is positive and occurs in less than 0.5% of normals, this message will appear. Criteria for a localized depression are absent and the general height adjustment yields a result in which the best part of the field is depressed to a degree that would be expected in less than 0.5% of the age-matched population.

This message will be superseded by either of the above two messages if those conditions are met.

4. Abnormally high sensitivity: If the patient's threshold values are higher than those occurring in less than 0.5% of age-matched normals, this message will appear. The best part of the field is more sensitive than that of 99.5% of the normal age-matched population. This will supersede all other messages and indicates that the patient's responses are unreliable.

5. Within normal limits: None of the above criteria are met

Clinical Pearl: If you could look at just one aspect of the visual field printout, it should be the pattern deviation.

Clinical Pearl: Each diopter of blur (under-correction) can cause a 1 dB depression in retinal sensitivity.

Clinical Pearl: A 3-dB decrease in retinal sensitivity generally represents a 50% loss of vision.

Guided Progression Analysis: (GPA)
- Formerly known as "Glaucoma Progression Analysis"
- Used with Humphrey HFA perimeter
- Uses algorithm developed for Early Manifest Glaucoma Trial
- Designed to help identify clinically significant progression of visual field loss in patients with glaucoma
  - Differentiates from normal physiological variability
- Highlights changes from selected baseline examinations that are larger than typical clinical variability in patients with similar degrees of glaucoma.
- Identifies consistent and repeated patterns of loss
- Corrects for ocular media effects
- Analysis based upon detailed empirical knowledge of variability found at all stages of glaucomatous visual field loss
- Can be used on full threshold (as baseline only), SITA Standard, and SITA Fast strategies
  - However, once strategy is chosen, only similar strategies will be used in GPA
- Visual fields that repeatedly and consistently show changes exceeding what is known to represent typical variability are identified as having "possible" or "likely" progression

GPA: Clinical Considerations
- Baseline is established
  - Either by machine or by operator
    - Machine picks two earliest similar strategies
- Small triangles on printout (following baseline) identify statistically significant change
- Open triangles
  - Denotes a point that has changed (beyond normal variability) at least one time
  - Identifies any point that has worsened by an amount that exceeds the variability expected in all but the most variable 5% ($p<0.05$) of glaucoma patients having similar visual fields status. This symbol is shown if the change is greater than 95% of the variability seen in

that exact test location in fields having a similar mean threshold deviation from normal values. This can occur on the first follow-up (after 2 baseline fields have been performed) exam
- Half-filled triangle
  - Identifies points changing as described above (p<0.05) in two consecutive follow-up (after baseline) exams. (Possible Progression)
- Filled triangle
  - Identifies points changing as described above (p<0.05) in three consecutive follow-up (after baseline) exams. (Likely Progression)

GPA Alert: Possible Progression, Likely Progression, and No Progression Detected
- Combines the knowledge of clinical variability with the demand that the change be consistent and repeatable.
- Judging progression should involve all clinical data
  - However, if solely using perimetric data, the significant change should be present in at least two follow-up tests and must be found consistently in the same area of the visual field
  - Before changing therapy based upon this information, care should be made to ensure that the baseline exams are appropriate and the follow-up exams are reliable.
- When significant degradation is present in the same three or more points (on the same side of the horizontal meridian) on two consecutive follow-up exams (after baseline), the GPA software will alert you to "Possible Progression". The minimal total number of fields to get this alert is four (2 baseline and 2 follow-ups). If this trend is present on three consecutive follow-up exams, the GPA software with alert you to "Likely Progression". The minimal total number of fields to get this alert is five (2 baselines and 3 follow-ups).
- On newest version, if none of the above criteria are met, the message "No Progression Detected" will be displayed
- Visual Field Index (VFI) is a new summary measurement of the visual field status as a percent of a normal age-adjusted visual field.
  - VFI is optimized for progression analysis
  - It is less affected by cataract or media changes than earlier indices
  - VFI is used to quantify the rate of progression where it is plotted relative to the patient age to calculate the rate of functional loss
  - The VFI plot provides a linear regression analysis of the VFI over time
    - Minimum of 5 exams over 3 years is required to have VFI plot (Trend analysis)
  - Slope of Mean Deviation from all exams is determined using a regression analysis. This allows one to determine the rate of progression
  - An outstanding concept, but it ignores the fact that progression isn't necessarily linear.

Progression Possibilities: Event Analysis vs. Trend Analysis
- Progression can be categorized as event analysis or trend analysis
  - Event analysis- compares baseline to most recent data; change as dictated by criteria has occurred or not
  - Trend analysis looks at the significance of rate of change over time.

- Identifies progression by looking at patient behavior over time.
- Uses all data points and a linear regression formula
- Weakness- progression is not necessarily linear
- Glaucoma progression rate is the most important determinant of therapy and future visual impairment
- Past progression rate is the most influential determiner of future progression rate
- Measuring rate of progression is difficult as it is hard to differentiate true change from variation in testing.