A Roadmap for Identifying and Managing Progression in Glaucoma

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(previously presented jointly with Murray Fingeret, OD)

1

Disclosures

Michael Chaglasian
- Aerie, Allergan, B+L, Equinox, Carl Zeiss Meditec, Ivantis, Heidelberg Engineering, Optos, Topcon

2

Risk Factors for Progression

- For patients diagnosed or at risk of glaucoma
  - Stage disease
  - Assess risk for progression
  - Develop treatment plan
  - Surveillance
    - Establish adequate baseline testing
      - IOP
      - Visual fields
      - Imaging
      - Photographs

3

Risk Factors for Progression

- Once the diagnosis of glaucoma is made, the challenge is to prevent further deterioration
- If change does occur, detect it quickly
- Understanding which individual is at increased risk to get worse allows the clinician to individualize management such as:
  - Monitor closer
    - See at earlier intervals and do more frequent testing
  - Be more aggressive such as having a lower target IOP
  - Be quicker to advance therapy

4

Risk Factors for Progression

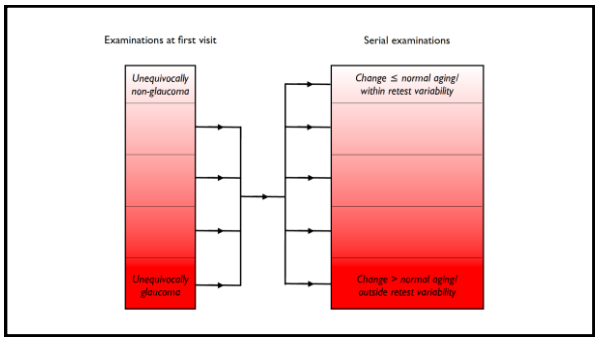
- Detecting change is a difficult task requiring periodic testing (photos, imaging, visual fields) performed over time
- Change may occur at any time
- Change does not occur at the same rate over the patient's lifetime
- Due to test variability, just because a test is different (worse) from the previous one does not mean the person got worse
  - Need to always confirm that change has occurred

5

Risk Factors for Progression

- Ability to discriminate true change, over and beyond measurement variability, is a 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 noted as deterioration in the visual field

6

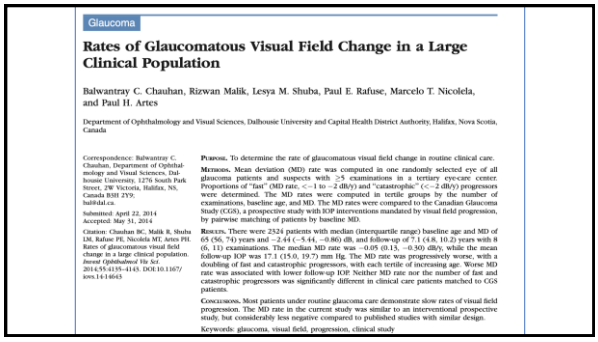


7

How Often Do Patients Get Worse Quickly?

Identify those as risk.
Treat them more aggressively.

22



Glaucoma

Rates of Glaucomatous Visual Field Change in a Large Clinical Population

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Purpose. To determine the rate of glaucomatous visual field change in routine clinical care.

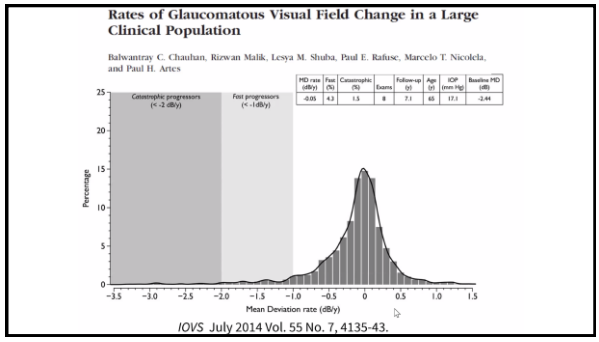
Methods. Mean deviation (MD) rate was computed in one randomly selected eye of all glaucoma patients and suspects with ≥5 examinations in a tertiary eye-care center. Proportions of "fast" (MD rate, <−1 to −2 dB/y) and "catastrophic" (<−2 dB/y) progressors were determined. The MD rates were computed in tertile groups by the number of examinations, baseline age, and MD. The MD rates were compared to the Canadian Glaucoma Study (CGS), a prospective study with IOP interventions mandated by visual field progression, by pairwise matching of patients by baseline MD.

Results. There were 2324 patients with median (interquartile range) baseline age and MD of 65 (56, 74) years and −2.44 (−5.44, −0.86) dB, and follow-up of 7.1 (4.8, 10.2) years with 8 (6, 11) examinations. The median MD rate was −0.05 (0.13, −0.30) dB/y, while the mean follow-up IOP was 17.1 (15.0, 19.7) mm Hg. The MD rate was progressively worse, with a doubling of fast and catastrophic progressors, with each tertile of increasing age. Worse MD rate was associated with lower follow-up IOP. Neither MD rate nor the number of fast and catastrophic progressors was significantly different in clinical care patients matched to CGS patients.

Conclusions. Most patients under routine glaucoma care demonstrate slow rates of visual field progression. The MD rate in the current study was similar to an interventional prospective study, but considerably less negative compared to published studies with similar design.

Keywords: glaucoma, visual field, progression, clinical study

23



24

Risk factors for Progression

- Older age
- Extent of damage at time of diagnosis
  - Based upon fields, optic nerve & RNFL appearance and OCT results
- Higher IOP (peak)
- Bilateral loss – damage in both eyes
- Disc hemorrhage - is this a risk factor or a sign of damage?
- Central visual field loss – within central 10^0
- Cornea hysteresis – reduced < 9.5
- Family history of progression
- Pseudoexfoliaton glaucoma
- Higher Myopia - > -6D

25

Risk factors for progression - EMGT

- Treatment and follow-up IOP
- Age
- Bilateral loss
- PXE glaucoma
- Disc hemorrhages
- Thinner central corneal thickness
- Lower systolic perfusion pressure
- Lower systolic blood pressure
- Cardiovascular disease

28

Predictive Factors for Glaucomatous Visual Field Progression in the Advanced Glaucoma Intervention Study

Kouros Nouri-Mahdavi, MD,[1] Douglas Hoffman, BA,[1] Anne L. Coleman, MD, PhD,[1] Gang Liu, MS,[2] Gang Li, PhD,[2] Douglas Gaasterland, MD,[3] Joseph Caprioli, MD[1]

Purpose: To investigate the risk factors associated with visual field (VF) progression in the Advanced Glaucoma Intervention Study (AGIS) with pointwise linear regression (PLR) analysis of serial VFs.
Design: Prospective, multicenter, randomized clinical trial.
Participants: Five hundred nine eyes of 401 patients from the AGIS with a baseline VF score of ≤16, ≥7 VF examinations, and ≥3 years of follow-up were selected.
Main Outcome Measure: Visual field progression.
Methods: This is a cohort study of patients enrolled in a prospective randomized clinical trial (AGIS). Worsening of a test location on PLR analysis was defined as a change of threshold sensitivity of ≥1.00 decibels a year, with $P \leq 0.01$. Visual field progression was defined as worsening of at least 2 test locations within a Glaucoma Hemifield Test cluster with PLR analysis. Multivariate logistic regression was used to determine risk factors associated with VF worsening. Intraocular pressure (IOP) fluctuation was defined as standard deviation of the IOP at all visits after the initial surgery.
Results: The mean (± standard deviation) follow-up time and baseline AGIS score were 7.4 (±1.7) years and 7.7 (±4.4), respectively. Visual field progression was detected with PLR analysis in 151 eyes (30%). Older age at the initial intervention ($P = 0.0012$; odds ratio [OR], 1.30; 95% confidence interval [CI], 1.11–1.50), larger IOP fluctuation ($P = 0.0013$; OR, 1.31; 95% CI, 1.12–1.54), increasing number of glaucoma interventions ($P = 0.01$; OR, 1.74; 95% CI, 1.14–2.64), and longer follow-up ($P = 0.02$; OR, 1.19; 95% CI, 1.03–1.38) were associated with increased odds of VF progression. When regression analyses were repeated in eyes with and without a history of cataract extraction, IOP fluctuation was the only variable to be consistently associated with VF progression.
Conclusion: Both increasing age and greater IOP fluctuation increase the odds of VF progression by 30% (for each 5-year increment in age and 1-mmHg increase in IOP fluctuation). The higher risk conferred by IOP fluctuation was consistently observed in eyes with and without a history of cataract extraction. *Ophthalmology 2004;111:1627–1635 © 2004 by the American Academy of Ophthalmology.*

29

Predictive Factors for Glaucomatous VF Progression - AGIS

- Increasing age and greater IOP fluctuation increase odds of VF Progression by 30%
  - For each 5-year increase or 1 mm Hg increase

30

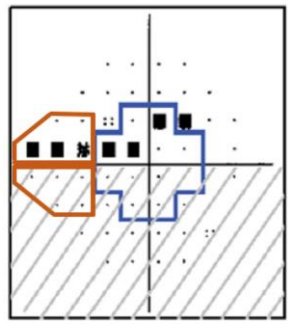
Baseline 24-2 Central Visual Field Damage Is Predictive of Global Progressive Field Loss

ANIRUDH GARG, C. GUSTAVO DE MORAES, GEORGE A. CIOFFI, CHRISTOPHER A. GIRKIN, FELIPE A. MEDEIROS, ROBERT N. WEINREB, LINDA M. ZANGWILL, AND JEFFREY M. LIEBMANN

• PURPOSE: Central visual field (VF) damage in glaucoma patients can significantly hinder daily activities. The present study investigates whether the presence of localized baseline damage to the central 10 degrees of the VF is predictive of faster global mean deviation (MD) progression.
• DESIGN: Prospective cohort study.
• METHODS: Eyes from the multicenter African Descent and Glaucoma Evaluation Study (ADAGES) with established glaucoma and VF loss and a minimum of 5 24-2 VFs were eligible. Baseline central 24-2 damage was defined as any of the 12 central-most points with total deviation (TD) values at $P < 0.5\%$ on 2 consecutive examinations. Progression was determined using trend-based and event-based criteria: (1) rates of MD change significantly faster than zero and (2) ≥ −5 dB MD loss over the entire follow-up.
• RESULTS: A total of 827 eyes of 584 patients were studied. Mean rate of MD change of the entire sample was −0.15 dB/year (95% CI: −0.19 to −0.12, $P < .001$). Eyes with baseline central damage progressed faster than those without (difference: $\beta_{central}$ = −0.07 dB/year, 95% CI: −0.11 to −0.03, $P = .011$) and were more likely to experience MD loss greater than 5 dB (hazard ratio = 3.0 [95% CI: 2.1–4.1, $P < .001$]). These differences remained significant after adjusting for confounders.
• CONCLUSION: The presence of central VF damage at baseline is significantly associated with more rapid global progression. Detection of central VF damage aids in stratification of high-risk patients who may need intensive surveillance and aggressive treatment. (Am J Ophthalmol 2018;187:92–98. © 2018 Elsevier Inc. All rights reserved.)

31

Risk factor for progression - Central visual field loss found at baseline



32

Risk Factors for Fast Visual Field Progression in Glaucoma

JI HYUN KIM, ALESSANDRO RABELLO, ESTEBAN MORALES, TE YU, ABDELMONEM A. ANIS, KOURO NOURI-MAHDAVI, AND JOSEPH CAPRIOLI

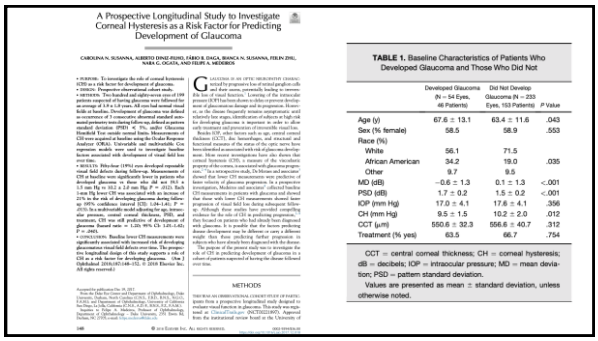
• PURPOSE: To identify baseline and longitudinal risk factors for fast visual field (VF) decay in patients with open-angle glaucoma.
• DESIGN: Retrospective cohort study.
• METHODS: Patients with open-angle glaucoma with ≥6 VFs and ≥4 years of follow-up were included. VF decay rates were measured with the following methods: mean deviation (MD) rates, VF index (VFI) rates, and the Glaucoma Rate Index (GRI). The relationship between VF rates and clinical variables were investigated with linear mixed models. Logistic regression analysis was performed to determine which factors were associated with fast progression.
• RESULTS: A total of 1317 eyes of 745 patients with a mean (± SD) age of 63.3 (±10.9) years and a median (interquartile range) MD −2.4 (−0.7 to −5.6) dB at baseline were analyzed. The median (interquartile range) number of VFs was 12 (9 to 16), and mean follow-up duration was 11.5 (±3.7) years. Older age ($P < .001$), higher peak intraocular pressure (IOP) ($P < .001$), and glaucoma surgery during the study period ($P < .001$) were associated with faster rates of progression regardless of the method used. Worse baseline MD was associated with MD rate ($P = .02$), but neither with VFI rate ($P = .37$) nor GRI ($P = .31$); whereas pseudoexfoliative glaucoma was associated with faster rates of progression with MD ($P = .008$) and VFI ($P = .01$) rates, but not with GRI. Higher peak IOPs ($P = .005$) was a significant predictor for fast progression.
• CONCLUSIONS: In this cohort, older age, peak IOP, pseudoexfoliative glaucoma, and baseline MD were associated with the rate of glaucomatous VF worsening. Fast progressors had a higher peak IOP than non-fast progressors. The identification and appropriately aggressive treatment of fast progressors would reduce visual disability from glaucoma. (Am J Ophthalmol 2019;207:168–178. © 2019 Elsevier Inc. All rights reserved.)

33

Risk factors for Fast VF progression

- Older age
- Higher baseline IOP
- PXE Glaucoma
- Baseline MD on visual fields

34



A Prospective Longitudinal Study to Investigate Corneal Hysteresis as a Risk Factor for Predicting Development of Glaucoma

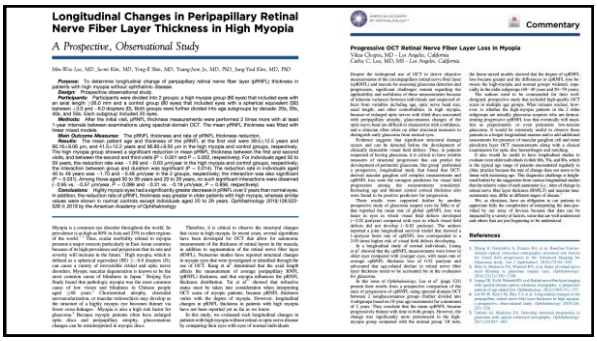
CAROLINA N. SUSANNA, ALBERTO DINIZ-FILHO, FABIO B. DAGA, BIANCA N. SUSANNA, FELIPA ZHU, NARA C. OGATA, AND FELIPE A. MEDEIROS

TABLE 1. Baseline Characteristics of Patients Who Developed Glaucoma and Those Who Did Not

	Developed Glaucoma (N = 54 Eyes, 46 Patients)	Did Not Develop Glaucoma (N = 233 Eyes, 153 Patients)	*P* Value
Age (y)	67.6 ± 13.1	63.4 ± 11.6	.043
Sex (% female)	58.5	58.9	.553
Race (%)			
White	56.1	71.5	
African American	34.2	19.0	.035
Other	9.7	9.5	
MD (dB)	−0.6 ± 1.3	0.1 ± 1.3	<.001
PSD (dB)	1.7 ± 0.2	1.5 ± 0.2	<.001
IOP (mm Hg)	17.0 ± 4.1	17.6 ± 4.1	.396
CH (mm Hg)	9.5 ± 1.5	10.2 ± 2.0	.012
CCT (μm)	550.6 ± 32.3	556.6 ± 40.7	.312
Treatment (% yes)	63.5	66.7	.754

CCT = central corneal thickness; CH = corneal hysteresis; dB = decibels; IOP = intraocular pressure; MD = mean deviation; PSD = pattern standard deviation.
Values are presented as mean ± standard deviation, unless otherwise noted.

35



Longitudinal Changes in Peripapillary Retinal Nerve Fiber Layer Thickness in High Myopia

A Prospective, Observational Study

Commentary

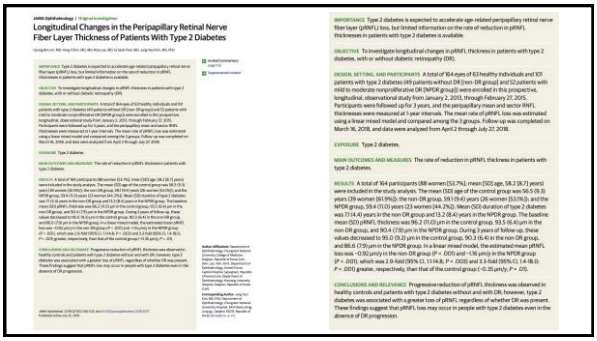
Progressive OCT Retinal Nerve Fiber Layer Loss in Myopia

38

Risk factors progression – non glaucoma

- Higher myopia
- Older age

39



Longitudinal Changes in the Peripapillary Retinal Nerve Fiber Layer Thickness of Patients With Type 2 Diabetes

40

Risk factors

- Diabetes associated with RNFL thinning over time
- Over 3 years , RNFL change in part related to aging and in part related to having diabetes
  - Controls 96.2 > 95.0 um
    - -0.4um/year
  - Diabetics wo retinopathy 93.5 > 90.3 um
    - -0.92um/year
  - Diabetics with NPDR 90.4 > 86.6 um
    - -1.16um/year

44

How Quick Will Progression Appear in a Glaucoma Patient?

47

Latanoprost for open-angle glaucoma (UKGTS): a randomised, multicentre, placebo-controlled trial

Procedures

We did visual field testing, intraocular pressure measurement, and imaging at 11 scheduled visits over 24 months, with clustering of the tests at baseline, 18 months, and 24 months; 16 visual fields test were scheduled over 24 months. We measured vision function through testing of the visual field. The visual field test

48

Summary

Background Treatments for open-angle glaucoma aim to prevent vision loss through lowering of intraocular pressure, but to our knowledge no placebo-controlled trials have assessed visual function preservation, and the observation periods of previous (unmasked) trials have typically been at least 5 years. We assessed vision preservation in patients given latanoprost compared with those given placebo.

Methods In this randomised, triple-masked, placebo-controlled trial, we enrolled patients with newly diagnosed open-angle glaucoma at ten UK centres (tertiary referral centres, teaching hospitals, and district general hospitals). Eligible patients were randomly allocated (1:1) with a website-generated randomisation schedule, stratified by centre and with a permuted block design, to receive either latanoprost 0·005% (intervention group) or placebo (control group) eye drops. Drops were administered from identical bottles, once a day, to both eyes. The primary outcome was time to visual field deterioration within 24 months. Analyses were done in all individuals with follow-up data. The Data and Safety Monitoring Committee (DSMC) recommended stopping the trial on Jan 6, 2011 (last patient visit July, 2011), after an interim analysis, and suggested a change in primary outcome from the difference in proportions of patients with incident progression between groups to time to visual field deterioration within 24 months. This trial is registered, number ISRCTN96423140.

Findings We enrolled 516 individuals between Dec 1, 2006, and March 16, 2010. Baseline mean intraocular pressure was 19·6 mm Hg (SD 4·6) in 258 patients in the latanoprost group and 20·1 mm Hg (4·8) in 258 controls. At 24 months, mean reduction in intraocular pressure was 3·8 mm Hg (4·0) in 231 patients assessed in the latanoprost group and 0·9 mm Hg (3·8) in 230 patients assessed in the placebo group. Visual field preservation was significantly longer in the latanoprost group than in the placebo group: adjusted hazard ratio (HR) 0·44 (95% CI 0·28–0·69; p=0·0003). We noted 18 serious adverse events, none attributable to the study drug.

Interpretation This is the first randomised placebo-controlled trial to show preservation of the visual field with an intraocular-pressure-lowering drug in patients with open-angle glaucoma. The study design enabled significant differences in vision to be assessed in a relatively short observation period.

49

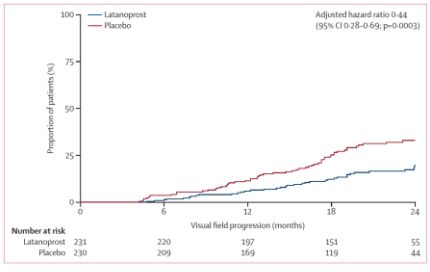


Figure 2: Kaplan-Meier failure estimates for visual field progression

50

Interpretation

To our knowledge, the United Kingdom Glaucoma Treatment Study (UKGTS) is the first randomised, triple-masked, placebo-controlled trial to assess the benefit of topical medical treatment (eye drops) for reduction of loss of vision in patients with open-angle glaucoma. Our findings provide strong evidence for the vision-preserving benefit of lowering of intraocular pressure, supporting evidence from previous randomised trials that were not masked or placebo-controlled. The study also provides evidence of the vision-preserving benefits of topical prostaglandin analogues. The trial design meant a fairly short observation period was needed to show treatment effects on vision, with the difference between treatment groups evident at just 12 months compared with typical observation periods of roughly 5 years in previous trials. The short trial duration will have a major beneficial effect on development and assessment of new treatments, increasing the likelihood of these treatments being made available for patient benefit.

51

UKGTS

- 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

52

UKGTS

- 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

53

CLINICAL SCIENCES

ONLINE FIRST

Influence of Visual Field Testing Frequency on Detection of Glaucoma Progression With Trend Analyses

Kouros Nouri-Mahdavi, MD, MSc; Reza Zarei, MD; Joseph Caprioli, MD

Objective: To explore whether increased frequency of visual field testing leads to earlier detection of glaucoma progression with trend analyses.

Methods: The visual fields of 468 eyes (381 patients) from the Advanced Glaucoma Intervention Study with 10 or more reliable visual field tests and 3 or more years of follow-up were studied. Starting at year 1, every other visual field examination was deleted to create a low-frequency data set, and the original group was kept as the high-frequency data set. The proportion of progressing eyes and the time to progression were compared between the 2 data sets with global and pointwise linear regression criteria.

Results: The median number of visual field examinations was 20 and 12 for the high- and low-frequency data sets, respectively. Based on primary mean deviation criteria, 209 eyes (43.6%) in the high-frequency data set and 160 eyes (34.2%) in the low-frequency data set progressed ($P < .001$), whereas 185 eyes (39.3%) in the high-frequency data set and 167 eyes (35.7%) in the low-frequency data set progressed according to pointwise linear regression ($P = .02$). The high-frequency data set was more likely to detect progression with mean deviation (hazard ratio [HR], 1.69 [95% confidence interval [CI], 1.36-2.10]) or pointwise linear regression criteria (HR, 1.52 [95% CI, 1.21-1.90]). A similar number of improving eyes were detected with mean deviation criteria (HR, 0.95 [95% CI, 0.58-1.60]), but pointwise linear regression criteria were more likely to detect improvement in the high-frequency data set (HR, 2.27 [95% CI, 1.43-3.62]). The results did not significantly change after censoring data at 5 years.

Conclusions: Increasing the frequency of visual field testing leads to earlier detection of glaucoma progression, especially with global trend analyses. This finding has significant implications for the care of patients with glaucoma.

Arch Ophthalmol.
Published online August 8, 2011.
doi:10.1001/archophthalmol.2011.224

58

What are the recommendations for determining progression and rate of progression ?

- Perform sufficient examinations to detect change (usually 6 or more)
  - European Glaucoma Society
- Six visual field examinations should be performed in the first 2 years
- Measure the rate of visual field progression
- Use the same threshold test
- Pay attention to examination quality

60

How many fields per year? And When?

- At 1 field/year, > 10 years to detect progression
- At 3 fields/year, find average los in 4 years, catastrophic in 2 year

Table 1 Time period (years) required to detect various rates of MD change with 80% power in visual fields with low, moderate and high degrees of variability with one (a), two (b) and three (c) examination per year

(a) 1 examination/year	Variability		
Progression rate (dB/year)	Low	Moderate	High
−0.25	13	19	30
−0.5	9	13	19
−1.0	6	9	13
−2.0	5	6	9
(b) 2 examinations/year	**Variability**		
Progression rate (dB/year)	**Low**	**Moderate**	**High**
−0.25	6.5	8.5	15
−0.5	4.5	6.5	8.5
−1.0	3	4.5	6.5
−2.0	2.5	3	4.5
(c) 3 examinations/year	**Variability**		
Progression rate (dB/year)	**Low**	**Moderate**	**High**
−0.25	4.3	6.3	10
−0.5	3	4.3	6.3
−1.0	2	3	4.3
−2.0	1.7	2	3

61

Tip= Do 5-6 tests 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

62

Glaucoma Progression

- The Future
  - Software that integrates imaging and visual field results
  - Neural network approach using artificial intelligence
  - Currently machines only provide spatial correlation between visual fields and imaging
  - OCT Angiography

63

ELSEVIER

American Journal of Ophthalmology

Volume 182, October 2017, Pages 107-117

Original article

Progressive Macula Vessel Density Loss in Primary Open-Angle Glaucoma: A Longitudinal Study

Takuhei Shoji [a, b], Linda M. Zangwill [a], Tadamichi Akagi [a, c], Luke J. Saunders [a], Adeleh Yarmohammadi [a], Patricia Isabel C. Manalastas [a], Rafaella C. Penteado [a], Robert N. Weinreb [a]

67

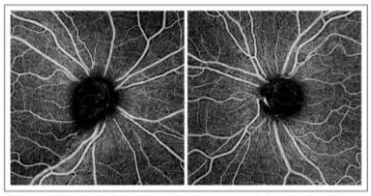


FIGURE 1. (a and b) In a patient with mild-moderate POAG, the circumpapillary OCTA maps show retinal vascular density (RVD) loss around ONH inferior-temporally and inferiorly in the right eye (Fig. 1a) vs relatively preserved RVD in the contralateral left eye (Fig. 1b) of the same patient. ONH, optic nerve head.

69

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 and tedious to use
  - Difficult to see cup/disc ratio change unless large change has occurred
- Imaging provides quantitative measurements that improves ability to detect progression

71

What is the pattern of optic nerve change?

72

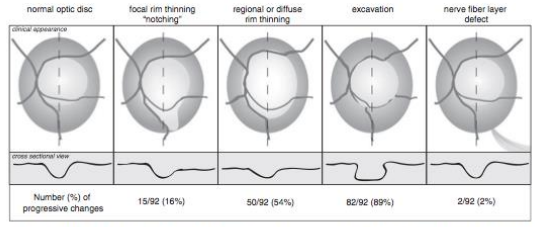


FIGURE 1. Schematic describing disc change with glaucoma. Optic discs were evaluated for the presence of rim thinning (could be focal, regional or diffuse), excavation, or a new nerve fiber layer defect compared with baseline photos. The line contours at the bottom of the image represent the changes in cross-sectional appearance (z axis) of the optic disc.

75

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)
    - OCTA – The Future
  - Functional
    - Perimetry
      - Glaucoma Progression Analysis (GPA)
      - Overview printouts
    - Electro-diagnostic testing (PERG)

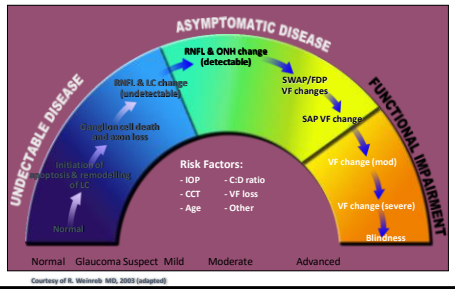
76

Glaucoma Progression

- 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

77

The Glaucoma Continuum



78

Glaucoma Progression

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

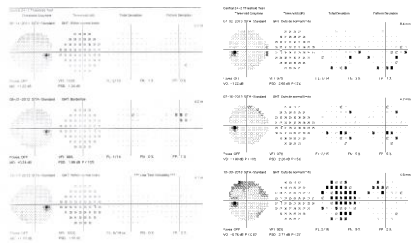
79

It is difficult to detect progression with fundus photographs

There is often not agreement among clinicians about who is getting worse

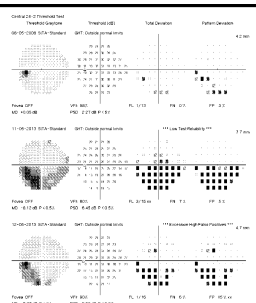
83

Field Variability is also a problem



87

Progression with some variability



88

Is One Test Better than Another to Detect Change?

Structure vs. Function

90

Using the Proper *Tools* for Monitoring Glaucoma with Progression Analysis

Michael Chaglasian, OD

58

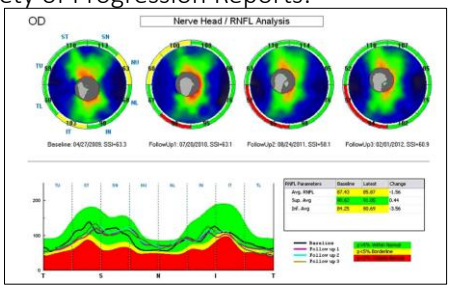
Monitoring for Progression

- **Essential Elements**:
  1. Series of good quality Visual Field tests
  2. Series of good quality RNFL and GCA tests
  3. Variety of Progression/Serial Reports

Must use both of these together

59

Variety of Progression Reports:



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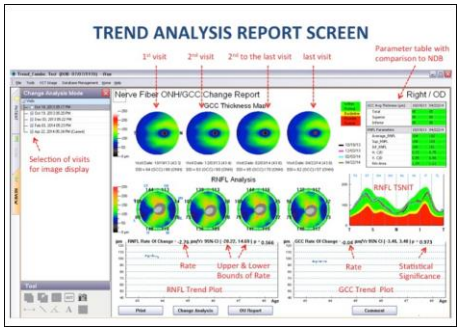
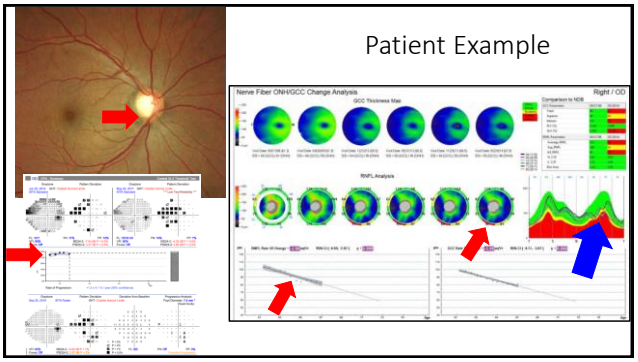


61

Patient Example



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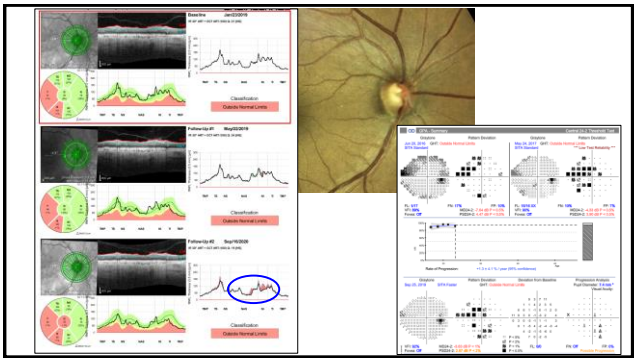

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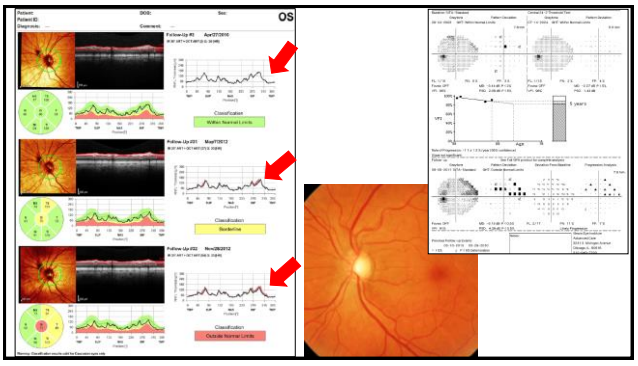

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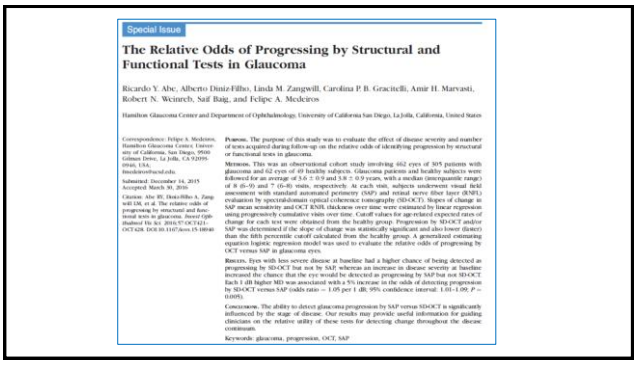


65

Summary Conclusions: Must Use Both

Disease Stage Matters:

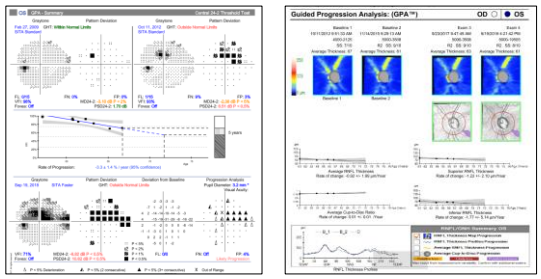
- More ***severe*** disease at baseline: **VF has edge**
- ***Early disease*** at baseline: **OCT has edge**

- Also noted, patients with:
  - More follow up visits (#12+): **VF performed better**
  - Fewer follow up visits (#8): **OCT was better**

66

Optimal Progression Review:

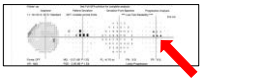
Visual Field, OCT, Photo. Examined Together.

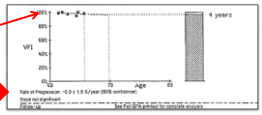


67

3 Tools to Identify Progression:

- Event Analysis
  - Comparison to baseline
  - Is there statistically significant change?
- Trend Analysis
  - Quantifies change over time →rate of change
  - Predict future change
- Mental analysis
  - (most important)



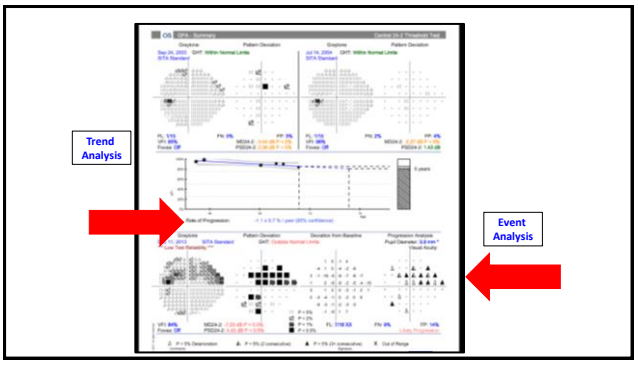


68

Measures of Progression: Trend Analysis

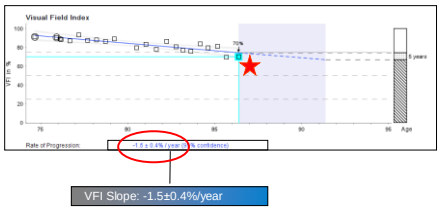
- **Trend Analysis**
  - *"Measures the rate of change"*
  - A regression line is drawn to determine rate of change for all the data that has been collected over time.
  - Using **VFI** (Visual Field Index) **or RNFL thickness** a percentage rate of change (slope is calculated
  - Most valuable when multiple VF tests have been completed
  - ***Good for identifying fast progressors and generalized, large defects***

69



70

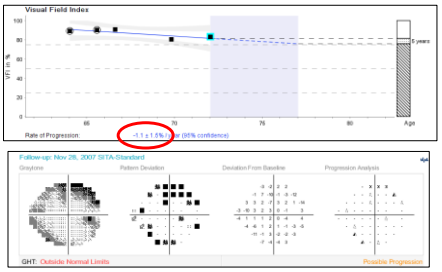
Looking at the Trend using VFI
Trend is plotted in % / year



The graph gives a prediction of future progression, if the current trend is maintained

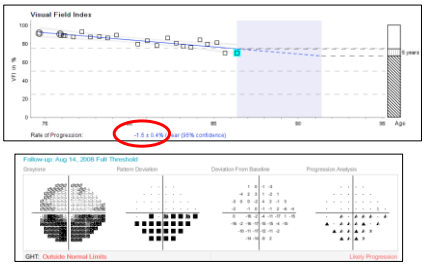
71

Possible Progression= ≥1.0% VFI/yr



72

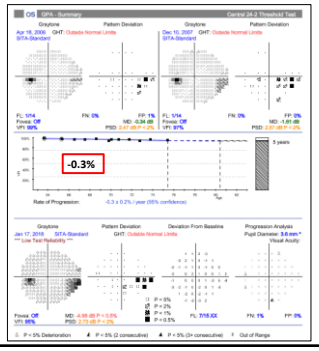
Likely Progression= ≥1.5% VFI/yr



73

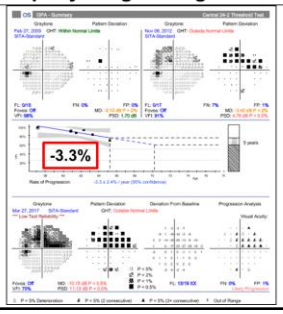
Trend Analysis

Stable with Local Defect



74

Rapidly Progressing



75

Significant rate of Progression?

EXPERT REVIEW OF OPHTHALMOLOGY, 2016
VOL. 11, NO. 3, 227–234
http://dx.doi.org/10.1080/17469899.2016.1180246

Taylor & Francis

REVIEW

What rates of glaucoma progression are clinically significant?

Luke J. Saunders, Felipe A. Medeiros, Robert N. Weinreb and Linda M. Zangwill

Hamilton Glaucoma Center, Shiley Eye Institute, Department of Ophthalmology, University of California, San Diego, CA, USA

ABSTRACT

Introduction: Clinically important rates of glaucoma progression (worsening) are ones that put a patient at risk of future functional impairment or reduction of vision-related quality of life (VRQoL). Most treated eyes do not progress at rates that will lead to future visual impairment, but there are a significant proportion (3–17%) of eyes, that are at risk of impairment even under clinical care. While very fast rates of progression (e.g. MD progression of –1.5 dB/year) are generally problematic, much slower rates also may be deleterious for young patients, particularly those diagnosed with late disease.
Areas covered: This review provides an overview of what we know about rates of glaucomatous visual field and structural loss. It also summarizes the literature on what stage of vision loss affects vision related quality of life, and the value of predicting functional impairment based on life expectancy and severity of the disease.
Expert commentary: It is important to consider life expectancy, disease severity and vision-related quality of life based treatment targets to estimate future prognosis when evaluating whether a rate of glaucoma progression can be clinically relevant.

ARTICLE HISTORY
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13 May 2016

KEYWORDS
Glaucoma; quality of life; progression rates; standard automated perimetry; spectral domain optical coherence tomography; confocal scanning laser ophthalmoscopy; life expectancy

76

Key Points:

- **Visual Field Rates of Progression**=
  - Slow = < 0.5 dB/yr
  - Fast = 0.5-1.0 dB/yr
  - Very Fast =
    - **-1.0-1.5 dB** per year or higher

Note:
This is in dB, not VFI. dB≠VFI

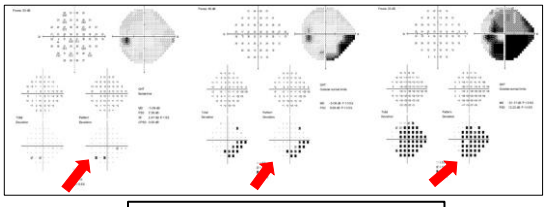
- However, slower rates in younger patients are still at risk due to longer life with disease

Luke J. Saunders, Felipe A. Medeiros, Robert N. Weinreb & Linda M. Zangwill (2016) What rates of glaucoma progression are clinically significant?, Expert Review of Ophthalmology, 11:3, 227-234, DOI: 10.1080/17469899.2016.1180246

77

Rapid Progression Example

(untreated, with multiple risk factors)

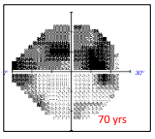


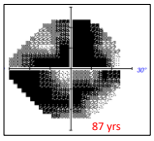
MD values:
-1 dB **-5 dB** **-25 dB**
5 Years IOP = 38 mmHg
~ -5 dB/yr (off the chart fast!)

78

Example: Glaucoma diagnosed at 50 yrs

- Average 50 yo pt. Progressing @ **-0.6 dB/year**
- 20 years to -12dB
  - defined as severe VF
- 17 more yrs to -22dB
  - defined as "legal blindness"
- Take Home:
  Identify Rate of Change ASAP





79

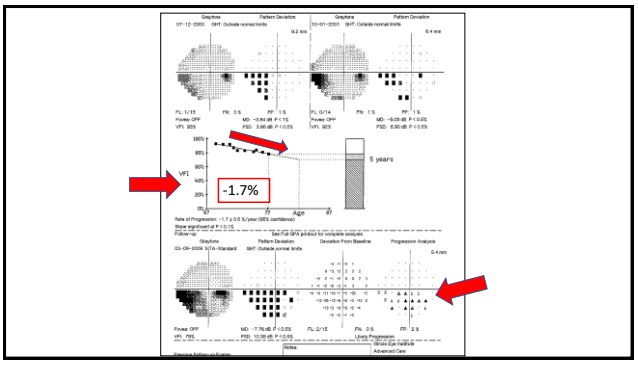
CASE WS

- 65 yo Patient
- POAG:
  - OD worse than OS
- Pre Tx IOP : 32 OD; 24 OS
- Currently: 19 OD; 17 OS
  - On PGA, FC, s/p SLT OD
- ONHs and VFs =>

80

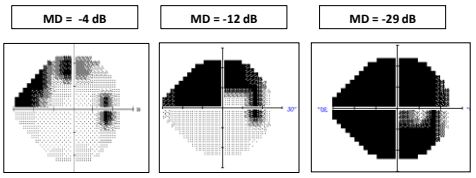
Right Eye 7 Year Difference

81



82

Review: Range of Grayscale MD



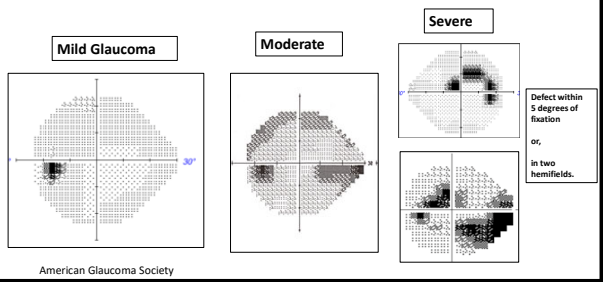
Staging Severity
- **Early = < -6 dB**
- **Moderate = < -12 dB**
- **Severe = > 12 dB**

(Hoddap –Parrish –Anderson criteria)

Mean Deviation

83

AGS and ICD10 Staging of Severity



American Glaucoma Society

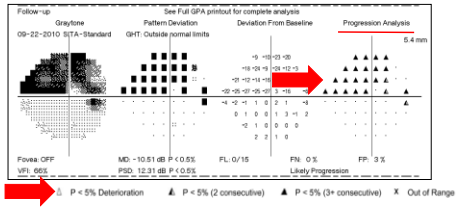
84

Measures of Progression: Event Analysis

- **Event Analysis**
  - Asks "Has this changed", compared to baseline an appearance on consecutive tests
    - Point by Point basis
  - Mostly used in early follow up time period
    - But also helpful in middle and late stages
  - Good for slow progressors and **focal** defects
  - ***Look for shaded triangles indicating a single point that is worsening over consecutive tests***

85

Event Progression Analysis

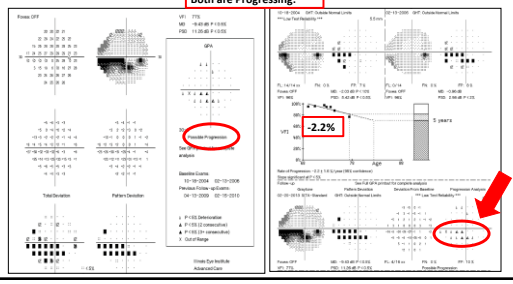


Point By Point Progression Analysis
- Shows which point have progressed from baseline

86

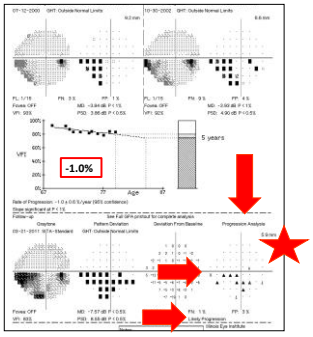
Event VF GPA Analysis Trend

Both are Progressing:



87

GPA Summary Report:



Trend Line looks +/- okay, Event Analysis is NOT!

88

Slow Progression May Still Be Vision Threatening:

89

How is possible to have patients perform all of this visual field testing?

Faster Testing Strategies

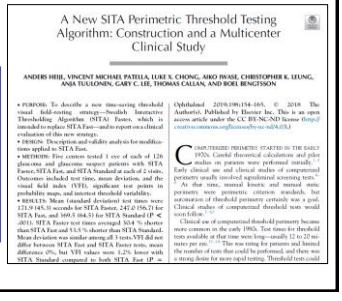
90

SITA-FASTER™:

- SITA Faster testing takes about two-thirds of the time required by SITA Fast and about ***half the time*** required by SITA Standard.
  - Test time reductions are largest in eyes with severe field loss.
  - and by about one-third compared to SITA Fast
- Many patients are able to complete SITA Faster 24-2 testing in ***about 2 minutes***
  - (SITA Faster is only available for 24-2).
- Clinical testing has shown that SITA Faster produces results that are clinically equivalent to SITA Fast with no loss of repeatability.

91

SITA Faster: Comparison and Validation

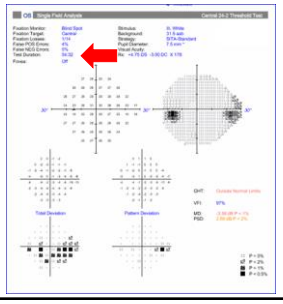


A New SITA Perimetric Threshold Testing Algorithm: Construction and a Multicenter Clinical Study

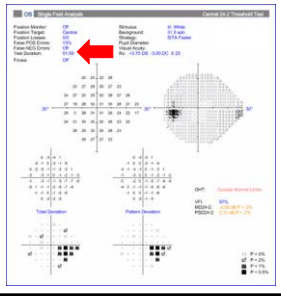
ANDERS HEIJL, VINCENT MICHAEL PATELLA, LUKE S. CHONG, AIKO IWASE, CHRISTOPHER K. LEUNG, ANJA TUULONEN, GARY C. LEE, THOMAS CALLAN, AND BOEL BENGTSSON

92

SITA Standard: 4:32



SITA Faster:



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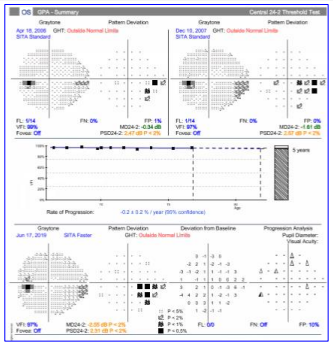


- SITA Faster is included in GPA Summary Progression Reports, with other strategies

94

Detecting *Structural* Progression of Glaucoma

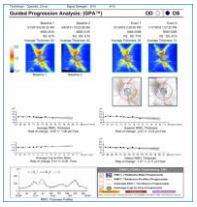
What tools do we have currently?

How are they used?

What is the evidence to support the use?

How can changes resulting from aging be differentiated from true progression?

Better than Visual Fields?

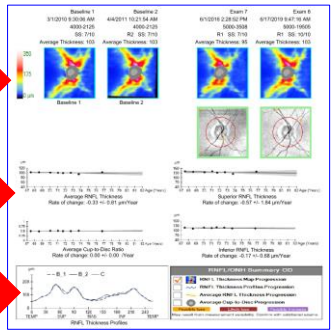


95

Event Based

OCT Progression Report

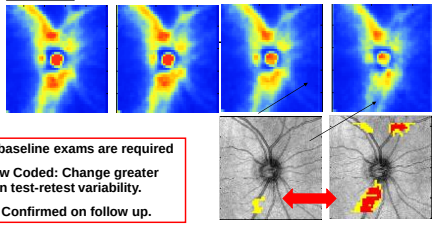
Trend Based



96

RNFL "Event" Analysis

Color Map



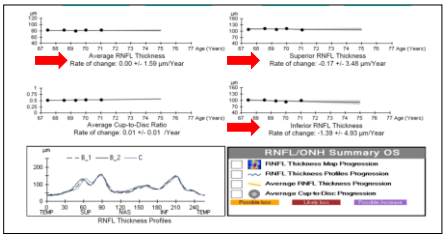
- **Two baseline exams are required**
- **Yellow Coded: Change greater than test-retest variability.**
- **Red: Confirmed on follow up.**

Deviation Map

97

OCT "Trend" Analysis

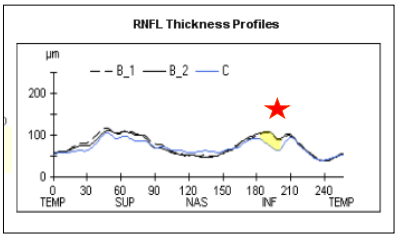
Four Parameters: Average, Superior, Inferior RNFL; Average C/D Ratio



98

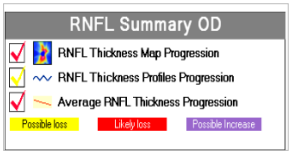
TSNIT Analysis

- **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.**



99

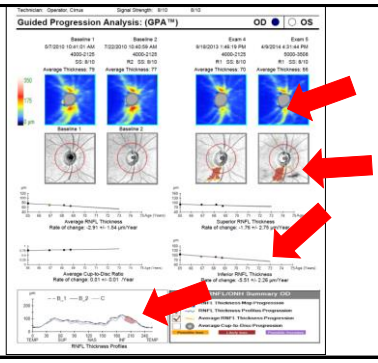
GPA Analysis
RNFL Summary Descriptor



Legend summarizes GPA analyses and indicates with a check mark if there is possible or likely loss of RNFL :

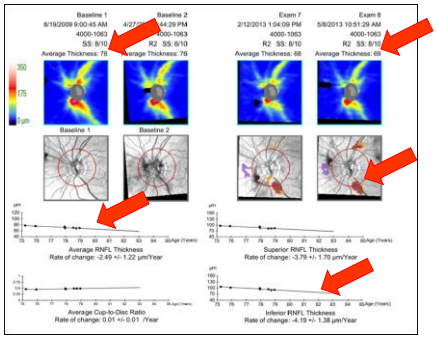
- RNFL Thickness Map Progression (best for focal change)
- RNFL Thickness Profiles Progression (best for broader focal change)
- Average RNFL Thickness Progression (best for diffuse change)

100



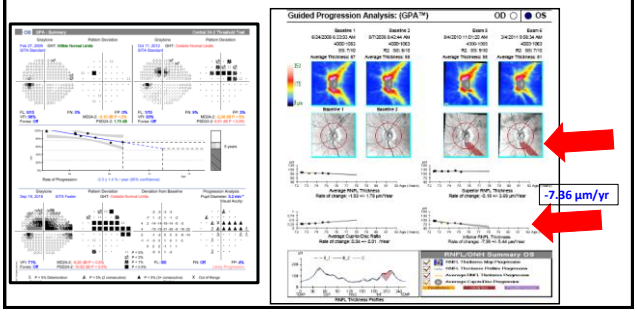
101

Progression



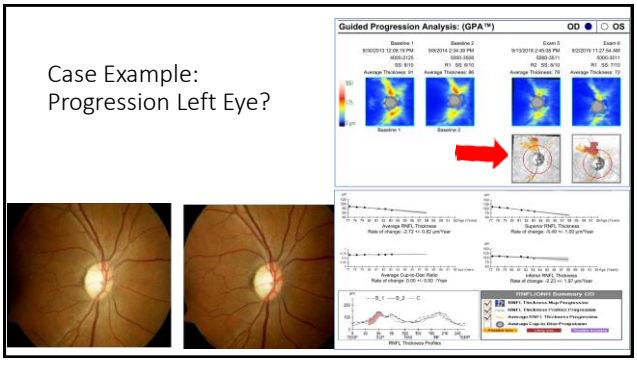
102

Progression Report



103

Case Example:
Progression Left Eye?



104

CASE AA

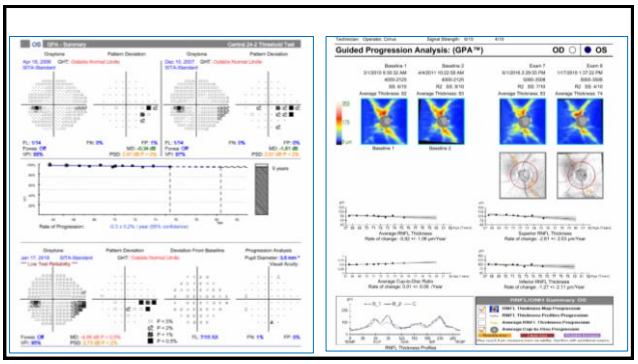
66 yo, AAM
HTN, Cholesterol, Anxiety Disorder,
IOP = 27, 26 mmHg OD and OS
CCT= 550

105

CASE BB

12 year history of OAG
Left eye with visual field defect

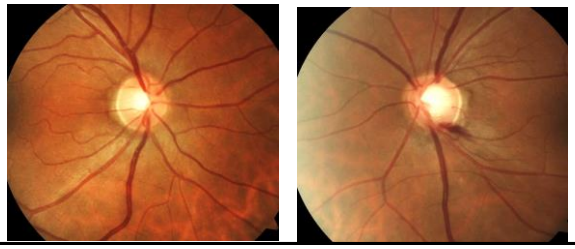
106



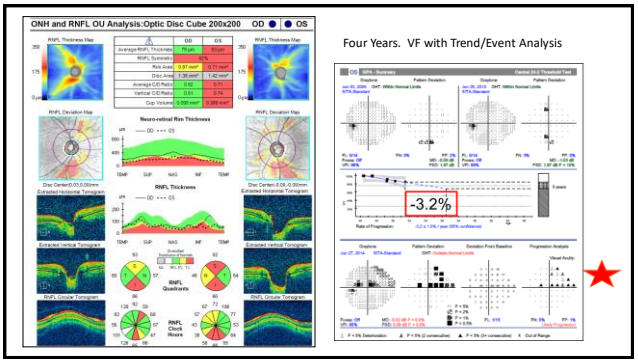
107

POAG, Normal IOPs (NTG)

- 47 yrs old
- GAT = ~ 21-23 mmHg OD and OS
- Asymmetric Cupping
- CCT= 520 OD/OS

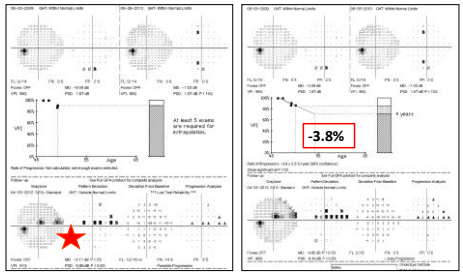


108



109

GPA at Two and Three Years Follow Up.



110