Glaucoma: Then and Now

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Financial Disclosure

- Allergan
- Bausch & Lomb
- Carl Zeiss Meditec
- M&S
- Santen

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Outline

- History of Glaucoma
- Landmark Clinical Trails
- Diagnostic Tools
  - ONH
  - Perimetry
  - Ocular Imaging
  - Other
- Management Decisions
  - Target IOP
  - Follow-Up Schedule
- Treatment Options
  - Meds
  - Lasers
  - Surgical Options
- Angle Closure Spectrum

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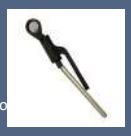
Evaluation of Structure: Then and Now

- Early 1900s through mid-1970s: DIRECT OPHTHALMOSCOPY
- Mid 1970s:
  - Direct Ophthalmoscopy
  - Rarely Hruby lens
  - Draw concentric circles
  - Occasional non-stereoscopic photo



- Early 1980s:
  - Appreciation of focal rim thinning as a hallmark ON finding of glaucoma
    - Not size of cup per se, but remaining rim that is important
  - Hruby lens and Goldmann contact lens became gold standard

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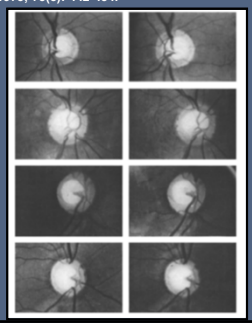
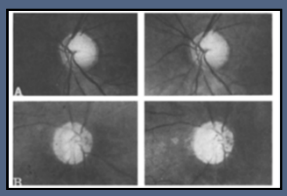
Kirsch RE, Anderson DR. Clinical Recognition of Glaucomatous Cupping. Am J Ophthalmol 1973; 75(3): 442-454.





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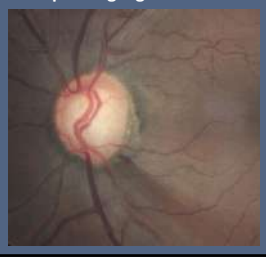
Importance of optic disc hemorrhage

- **Drance SM, Fairclough M, Butler DM, Kottler. The Importance of disc hemorrhage in the prognosis of chronic open angle glaucoma. Arch Ophthalmol 1977; 95(2): 226-228.**



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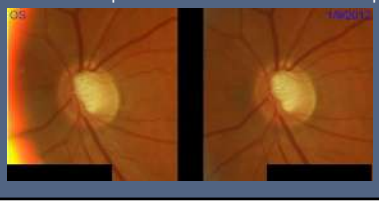
1980s until now

- Decreased use of Goldmann, Hruby lens
- Increased use of biconvex non-contact lens (+78D, etc)
- Documentation: sequential or simultaneous stereo optic disc photos



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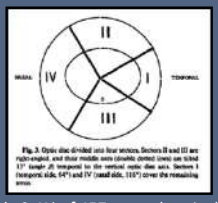
ISNT Rule



- Only 0.4% of 457 normal optic discs had NRR smallest outside of the temporal disc sector

Optic Disc, Cup and Neuroretinal Rim Size, Configuration and Correlations in Normal Eyes

Jonas JB, Gusek GC, Naumann OH. Optic disc, cup and neuroretinal rim size, configuration and correlations in normal eyes. Invest Ophthalmol Vis Sci 1988; 29(7): 1151-1158.

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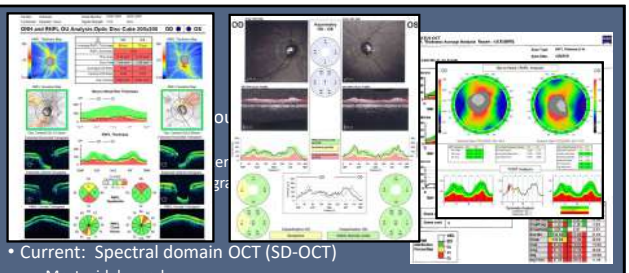

- Current: Spectral domain OCT (SD-OCT)
  - Most widely used
- What about OCT angiography?

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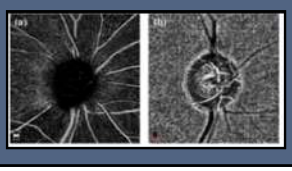
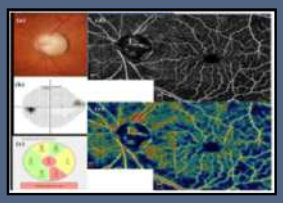
OCT Angiography

HHS Public Access

Optical coherence tomography angiography in glaucoma





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How do we **CLINICALLY** assess the ONH?

- Murray Fingeret: "It's become an OCT world"
- AAOphth PPP: "Examination of the ONH and RNFL provides valuable structural information about glaucomatous optic nerve damage and thinning of the RNFL"
  - Vertical elongation of cup/diffuse or focal thinning of NRR
  - Optic disc hemorrhage
  - Diffuse or focal thinning of RNFL
  - Beta zone peripapillary atrophy
  - Nasalization of central ONH vessels
  - Baring of circumlinear vessels
  - Absence of pallor

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Disc Damage Likelihood Scale

THE DISC DAMAGE LIKELIHOOD SCALE

	Narrowest width of rim (rim/disc ratio)					Examples	
DDLS Stage	For Small Disc <1.50 mm	For Average Size Disc 1.50-2.00 mm	For Large Disc >2.00 mm	DDLS Stage	1.25 mm optic nerve	1.75 mm optic nerve	2.25 mm optic nerve
1	.5 or more	.4 or more	.3 or more	0a			
2	.4 to .49	.3 to .39	.2 to .29	0b			
3	.3 to .39	.2 to .29	.1 to .19	1			
4	.2 to .29	.1 to .19	less than .1	2			
5	.1 to .19	less than .1	0 for less than 45°	3			
6	less than .1	0 for less than 45°	0 for 46° to 90°	4			
7	0 for less than 45°	0 for 46° to 90°	0 for 91° to 180°	5			
8	0 for 46° to 90°	0 for 91° to 180°	0 for 181° to 270°	6			
9	0 for 91° to 180°	0 for 181° to 270°	0 for more than 270°	7a			
10	0 for more than 180°	0 for more than 270°		7b			

Disc Damage Likelihood Scale reference Spaeth Trans Am Ophthalmol Soc 2002

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Five rules to evaluate the optic disc and retinal nerve fiber layer for glaucoma

Murray Fingeret, O.D.,[a,b] Felipe A. Medeiros, M.D.,[c] Remo Susanna, Jr, M.D.,[d] and Robert N. Weinreb, M.D.[c]

OPTOMETRY 2005;76:661-8.

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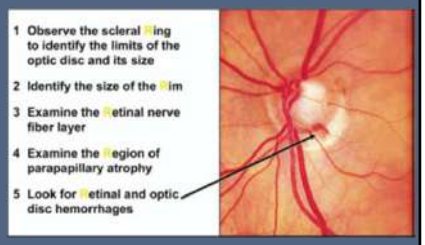
FORGE – what do we look at on ONH?

- Size of disc
- Rim configuration (ISNT)
- RNFL dropout (largely done by OCT)
- Beta zone peripapillary atrophy
- Disc hemorrhage



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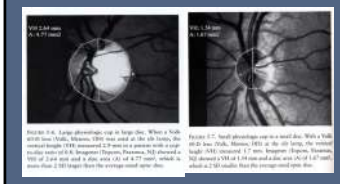
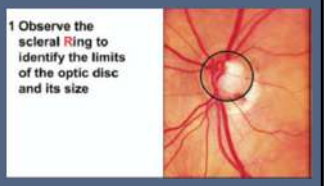
Size of Disc

- Size of disc
  - Mean vertical diameter 1.88mm (linear)
  - How do we judge?
    - Direct ophthalmoscope (small spot)
    - 78D lens with reticle
    - SD-OCT (area, not linear)



Litwak. Glaucoma Handbook



Fingeret, et al. Optometry 2005

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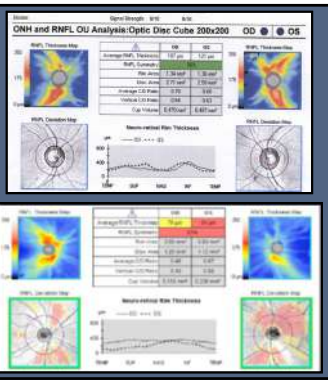
Size of Disc

- SD-OCT can measure disc (area mm^2):
  - Cirrus:
    - 1/3 <1.58 mm^2
    - 1/3 1.58-1.88 mm^2
    - 1/3 >1.88 mm^2
    - Gray tone = larger or smaller disc area than database, or Avg/Vert C/D <0.25



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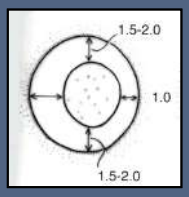
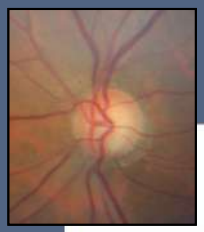
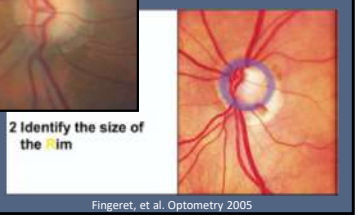
Rim (ISNT)



Litwak. Glaucoma Handbook





Fingeret, et al. Optometry 2005

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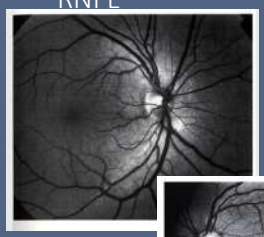
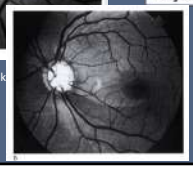
RNFL





Litwak. Glaucoma Handbook

1 Observe the scleral Ring to identify the limits of the optic disc and its size

2 Identify the size of the Rim

3 Examine the Retinal nerve fiber layer

Fingeret, et al. Optometry 2005

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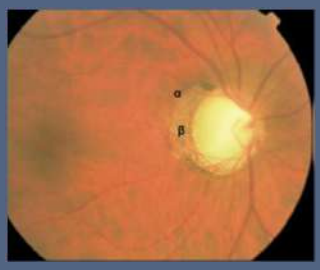
Beta zone PPA



1 Observe the scleral Ring to identify the limits of the optic disc and its size

2 Identify the size of the Rim

3 Examine the Retinal nerve fiber layer

4 Examine the Region of parapapillary atrophy

Fingeret, et al. Optometry 2005

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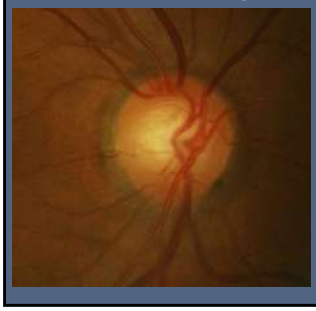
Disc Hemorrhage



1 Observe the scleral Ring to identify the limits of the optic disc and its size

2 Identify the size of the Rim

3 Examine the Retinal nerve fiber layer

4 Examine the Region of parapapillary atrophy

5 Look for Retinal and optic disc hemorrhages

Fingeret, et al. Optometry 2005

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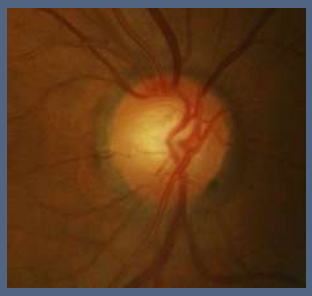

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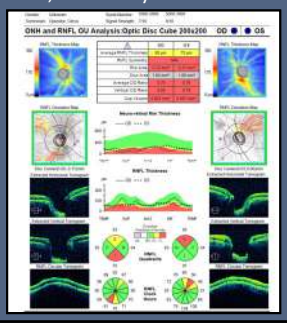
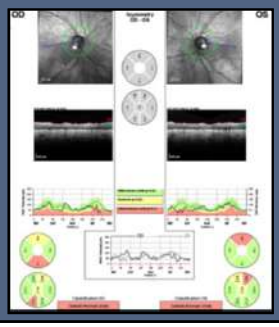
But, it really IS an OCT World…





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What Information Do the Instruments Give Us?

- Optic Nerve Parameters
  - Disc Size
  - Rim Area
  - Rim Volume
  - Cup Volume
- Retinal Nerve Fiber Layer Parameters
  - TSNIT curves
  - Average RNFL thickness
  - Sectoral RNFL thickness
- Macular Thickness
  - Ganglion Cell Complex
  - Inner Retina
  - Total Macular Thickness

Optic Disc/RNFL Scan

Macular Scan

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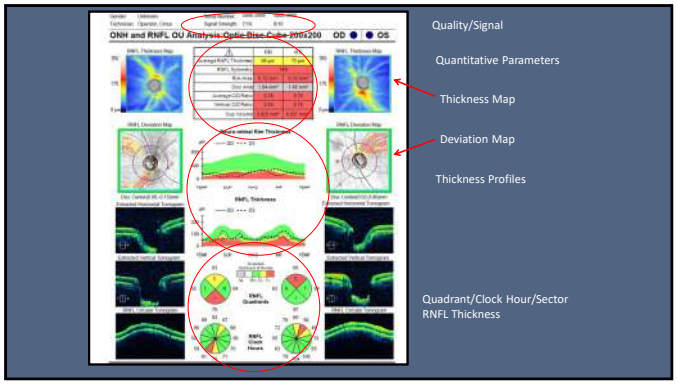

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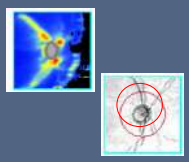
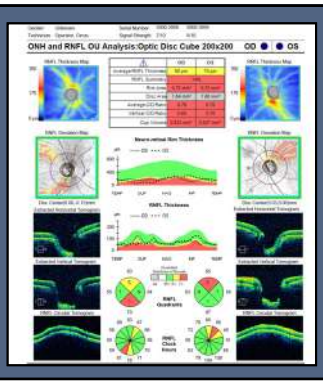
Systematic Strategy

- Quality
  - Signal Strength
  - Circle Placement
  - Movement?





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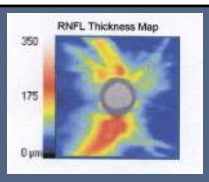
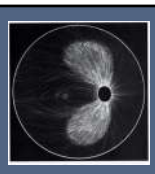
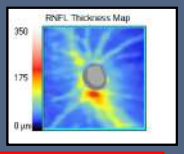
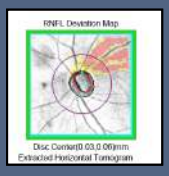
Systematic Strategy

- Thickness Map
- Deviation Map









IMPORTANCE OF BLOOD VESSELS!!!!

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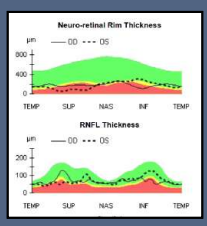
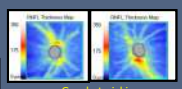
Systematic Strategy

- Thickness Profiles
  - Compared to normative data





Good at picking up notches in NRR

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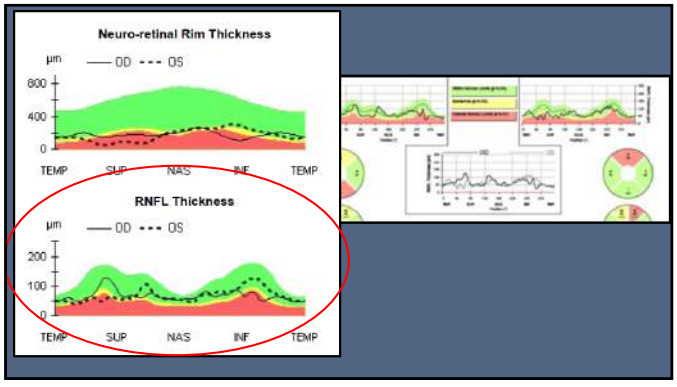

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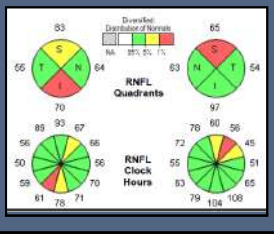
Systematic Strategy

- Quadrant and Clock Hour RNFL analysis



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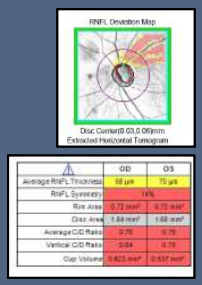
Systematic Strategy

- Quantitative Parameters
  - Average RNFL
    - Measures average thickness around calculation circle
    - Affected by blood vessels, astrocytes, glial cells
    - Global measure (will miss focal loss)
  - RNFL Symmetry



	OD	OS
Average RNFL Thickness	68 µm	70 µm
RNFL Symmetry	14%	
Rim Area	0.72 mm²	0.72 mm²
Disc Area	1.64 mm²	1.68 mm²
Average C/D Ratio	0.75	0.75
Vertical C/D Ratio	0.84	0.78
Cup Volume	0.623 mm³	0.537 mm³

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REVIEW

Glaucoma versus red disease: imaging and glaucoma diagnosis

Gabriel T. Chong and Richard K. Lee

Purpose of review
The use of ophthalmic imaging for documentation and diagnosis of ocular disease is rising dramatically. Optical coherence tomography (OCT), confocal scanning laser tomography (CSLT), scanning laser polarimetry (SLP) and photographic imaging of the optic nerve head (ONH) are currently used to document baseline characteristics of the ONH and for diagnosing glaucoma and glaucoma progression secondary to loss of retinal nerve fiber layer (RNFL). Imaging modalities typically provide information on ONH and RNFL characteristics which are outside of the normal (relative to normative database) in red lettering or boxes, whereas ONH and RNFL characteristics within the normal range are presented in green.

Recent findings
As imaging modalities have become more sophisticated and are validated in research studies, clinicians have come to rely upon data from these imaging devices to aid in differentiating between normal and glaucomatous states of the ONH and RNFL – typically by examining if the data are green or red suggesting normal or abnormal. However, normative databases can sometimes be flawed relative to atypical ONH or RNFL morphologies and imaging can provide artifacts which do not represent true ocular disease but secondary to limitations of imaging technology.

Summary
Ophthalmic imaging is an important adjunct to clinical diagnosis but the results from imaging devices need to be assessed critically relative to artifacts of imaging and the limitations of the technology and its normative databases.

Keywords
confocal scanning laser tomography, glaucoma, imaging, optical coherence tomography, peripapillary, scanning laser polarimetry

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KEY POINTS

- Glaucoma imaging is an integral part of the glaucoma management armamentarium for glaucoma screening, diagnosis, and follow-up, that is real disease.
- Glaucoma imaging results can be easily misunderstood without a good understanding of the underlying technology limitations and result in false-positive results and diagnosis, that is red disease.
- The normative databases for the different imaging technologies have limitations in defining what is a normal versus a glaucomatous optic nerve head.

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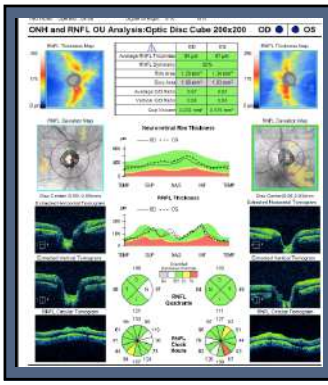

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REVIEW

Green disease in optical coherence tomography diagnosis of glaucoma

Mohamed S. Sayed[a], Michael Margolis[a,b], and Richard K. Lee[a]

Purpose of review
Optical coherence tomography (OCT) has become an integral component of modern glaucoma practice. Utilizing color codes, OCT analysis has rendered glaucoma diagnosis and follow-up simpler and faster for the busy clinician. However, green labeling of OCT parameters suggesting normal values may confer a false sense of security, potentially leading to missed diagnoses of glaucoma and/or glaucoma progression.

Recent findings
Conditions in which OCT color coding may be falsely negative (i.e., green disease) are identified. Early glaucoma in which retinal nerve fiber layer (RNFL) thickness and optic disc parameters, albeit labeled green, are asymmetric in both eyes may result in glaucoma being undetected. Progressively decreasing RNFL thickness may reveal the presence of progressive glaucoma that, because of green labeling, can be missed by the clinician. Other ocular conditions that can increase RNFL thickness can make the diagnosis of coexisting glaucoma difficult. Recently introduced progression analysis features of OCT may help detect green disease.

Summary
Recognition of green disease is of paramount importance in diagnosing and treating glaucoma. Understanding the limitations of imaging technologies coupled with evaluation of serial OCT analyses, prompt clinical examination, and structure–function correlation is important to avoid missing real glaucoma requiring treatment.

Keywords
glaucoma, green disease, optical coherence tomography

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KEY POINTS

- OCT is an integral part of modern glaucoma practice that is now considered standard of care in the diagnosis and follow-up of glaucoma patients and suspects.
- Careful evaluation of serial OCT analyses over extended follow-up periods with careful clinical examination and structure–function correlation is paramount in glaucoma practice.
- A single normal (i.e., green labeled) OCT analysis may confer false sense of security, leading to unrecognition of early-onset glaucoma or glaucoma progression.
- A number of conditions as well as limitations inherent to the imaging technology may lead to artifactual green labeling of OCT analysis in glaucoma, giving rise to 'green disease.'

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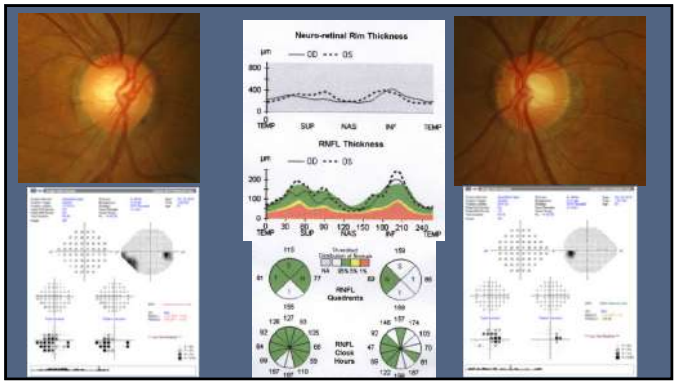

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Newest Addition to Glaucoma Diagnosis Arsenal: Macular Imaging

- 1998: Zeimer et al reported on macular thickness loss in patients with known glaucomatous damage
- 2003: Greenfield reported correlation between total macular thickness and MD on VF in glaucoma patients (time domain OCT)
- 2013: Hood et al – extensive investigation of segmented "RGC+" (RGC + IPL) layer and description of the "Macular Vulnerability Zone" (MVZ)

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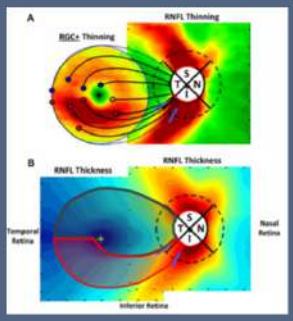

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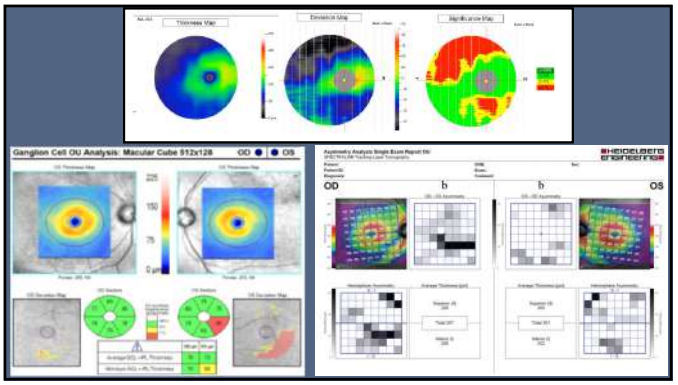

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Evaluation of Function: Then and Now

- Before 1970s:
  - Finger counting
  - Goldmann visual fields (highly reliant on technician)
- 1979: Octopus introduced static perimetry
- Mid 1980s:
  - Transition away from kinetic perimetry
  - Transition from Octopus to HFA
    - HFA to HFA-2 (1994), to HFA II-I (2000) to HFA3 (2015)

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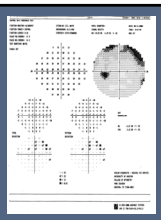
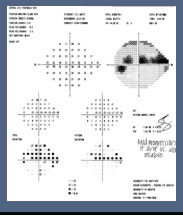
Visual Field "Moments"

- Full threshold 30-2 (1984) and 24-2 (1987)
- STATPAC database (1987)
- SITA Standard and Fast testing algorithm 1997
- SITA Faster 2018
- 24-2C

- Short wavelength (SWAP)
- FDT – screening





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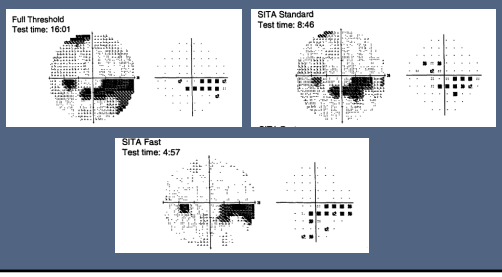
SITA Test Time Comparison



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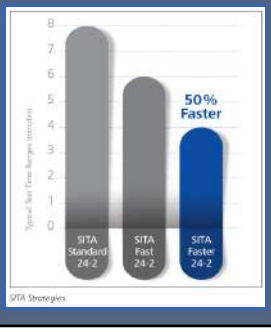
SITA Faster – tests in 2 minutes or less without compromise to test results

Two minute test for near normal patients

- ~50% faster than SITA Standard; ~30% faster than SITA Fast
- Clinically equivalent to SITA Fast and Standard
- Same SITA algorithm and normative data as Standard and Fast
- Removes unnecessary "dead time" during the test
- No Blind Spot or False Negatives
  - Uses Gaze Monitoring and False Positives for test quality monitoring

Mixed SITA GPA Reports

- Allows mixing all SITA test strategies for GPA reports
- Helps immediately adopt SITA Faster
- Clinical equivalence of tests allows intermixing



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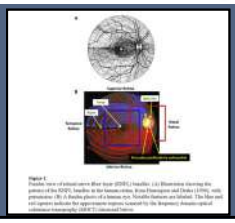
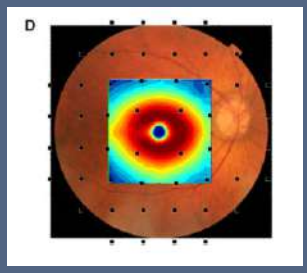
What about the 10-2 VF?

- Central 8 degrees from the center of the foveal contains more than 30% of retinal ganglion cells
- 24-2 and 30-2 test strategies use a 6 degree test grid pattern; these points fall outside of the densest region of ganglion cells
- 10-2 test strategy uses a 2 degree test grid
- Recent research has shown that in some patients with small regions of macular gangion cell loss, 10-2 testing may be better able to detect VF loss

45

Glaucomatous damage of the macula





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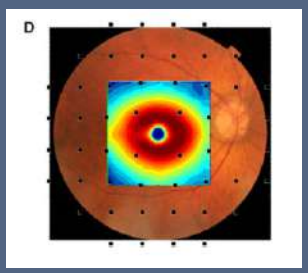

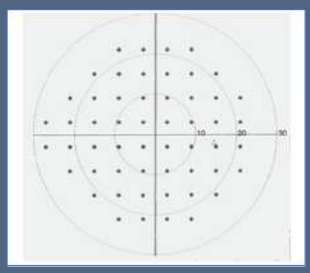

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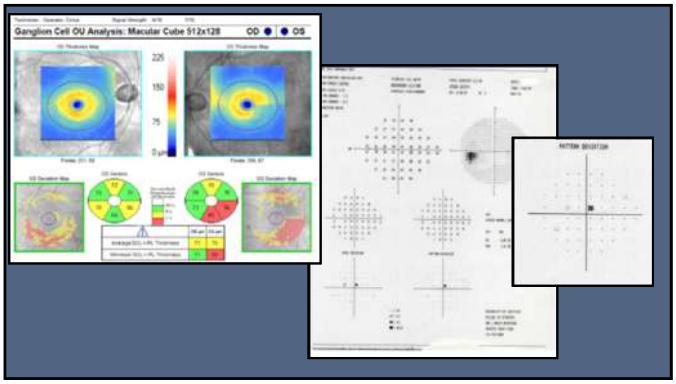

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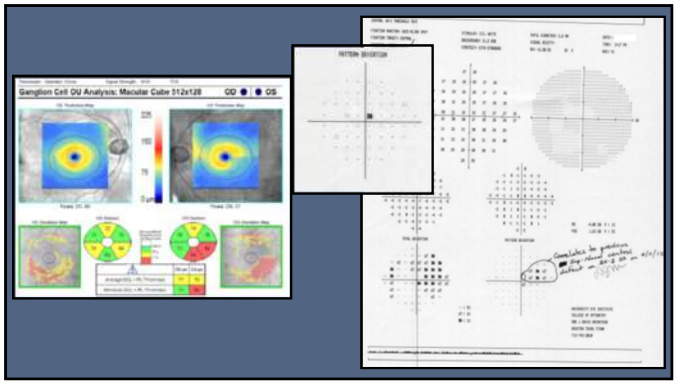

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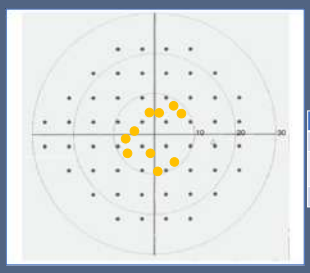
SITA Faster 24-2C Pattern on HFA3



The 24-2C test pattern combines all 24-2 points + ten selected 10-2 points (shown in OD orientation)

Large Gray	24-2 pattern
Large Orange	Ten additional 24-2C points
Small Gray	10-2 pattern

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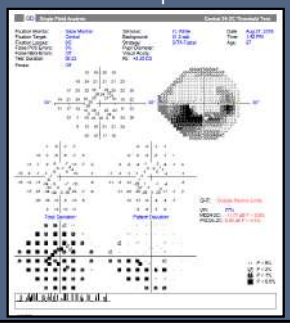
24-2C: The newest pattern on the HFA



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Newest addition: headset perimetry

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What Constitutes a "Glaucoma Exam"?

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Key Elements of POAG Suspect (Initial/Follow-up)

- Comprehensive exam:
  - CVF
  - ONH and RNFL evaluation (clinical)
- Diagnostic Testing:
  - Central Corneal Thickness
  - Visual Field
  - ONH, RNFL, and macular imaging
  - (Gonioscopy)

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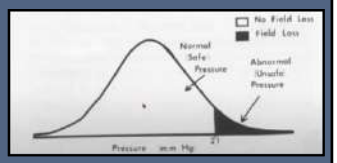
Management of Glaucoma – All About the IOP?

- Historically:
  - 1600s: glaucoma was a "hard" eye
  - 1800s: palpate the eye for firmness
  - 1900s: Tonometers (Schiotz 1905)
  - Mid 1950s: Glaucoma = IOP >21mmHg
    - TREATMENT: Lower the IOP to <21 ("Treat to Normal")
      - ? OHTN
      - ? NTG



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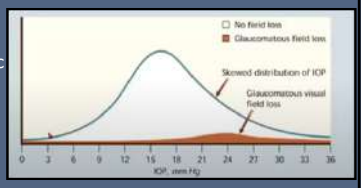
Management of Glaucoma – All About the IOP?

- We still know that elevated IOP is a MAJOR risk factor for disease
- Late 20th century: recognition of OH and NTG- move toward definition of "glaucomatous optic neuropathy"
  - 1996: AAOph PPP proposed that neither level of IOP nor VF defect were needed for diagnosis of glaucoma
  - At same time, RCTs confirmed the importance of IOP control



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"Safe IOP Theory" and "Ocular-Cranial Pressure Gradient Theory"

- Safe IOP Theory: The "safe" IOP is a range of IOP that will not cause optic neuropathy in individuals; safe IOP is individualized and can be different from statistically normal; Helps to explain NTG and OH
- Ocular-Cranial Pressure Gradient Theory: A pressure gradient (trans-laminar pressure difference or TLPD) exists along the optic nerve due to the difference between the intraocular pressure and the intracranial pressure; elevated TLPD causes impingement of ON (not elevated IOP); increased TLPD can be caused *either* by elevated IOP or by decreased ICP

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Management Decisions in Glaucoma

- Recommendation:
  - Clinical Decisions in Glaucoma, 2nd edition (Chang, et al.)
  - AKA "CDIG"
  - Free download: https://www.aao.org/Assets/afffaca5-37b2-4943-b67f-fde95c3089dd/636294273819400000/clinical-decisions-in-glaucoma-pdf?inline=1

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Precepts for Glaucoma Decision-Making (CDIG)

1. The higher the IOP, the greater the risk of acquiring glaucoma damage and the faster the rate of progression
2. Elevated IOP is not the only risk factor, but it's the only thing we can treat.
3. Lowering IOP helps, but we can't tell how low is ok prospectively
4. All methods of lowering IOP have costs, risks, and side effects
5. GOAL OF TREATMENT is to preserve good vision for life as inoffensively as possible

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Steps to Glaucoma Management (CDIG)

1. Treat the treatable cause of elevated IOP, if possible
2. Establish baseline
3. If treatment is needed, set a target
4. Treat to achieve target (re-evaluate if difficult)
5. Follow IOP and follow for progression
6. Modify treatment and target based on the clinical course of the dz

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Establish a Baseline – maybe over months

- Multiple IOP readings, preferably at different times of day
  - Patients benefit more from multiple IOP readings than they do from 2 extra weeks of drug therapy
- Gonioscopy
- Pachymetry
- Visual fields x2 (or x3 if first two are very different)
- RNFL and macular OCT
- ONH photography

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Minimum Criteria for Diagnosing Glaucoma (CDIG)

- Initial exam: "Trifecta"
  - Elevated IOP
  - Structural damage
  - Correlating functional deficit
- Over multiple visits:
  - Subsequent increase in IOP in presence of structural and functional damage
  - Progression of VF/OCT/ONH in presence or absence of elevated IOP

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Let's talk about Ocular Hypertension

- OHTS
  - Long-term, multicenter randomized controlled trial (RCT)
  - Subjects with OH randomized to observation or medical therapy to lower IOP
  - Followed for minimum of 5 years (OHTS 1); now have 20 year data

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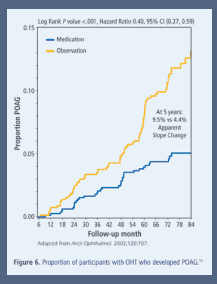

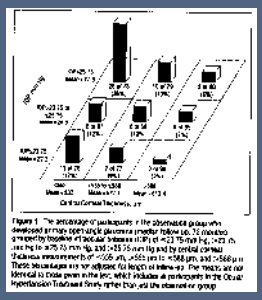

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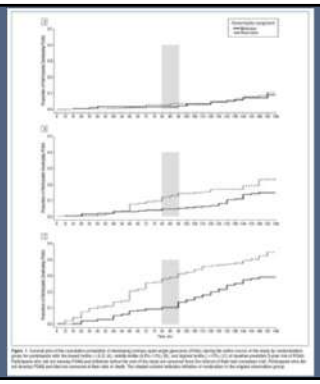
OHTS II



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OHTS III - RESULTS

JAMA Ophthalmology | Original Investigation

Assessment of Cumulative Incidence and Severity of Primary Open-Angle Glaucoma Among Participants in the Ocular Hypertension Treatment Study After 20 Years of Follow-up

- 20 year cumulative incidence of POAG:
  - Original observation group: 49.3%
  - Original treatment group: 41.9%
  - All subjects: 45.6%
- 20 year cumulative incidence of POAG
  - Lowest risk: 31.7%
  - Medium risk: 47.6%
  - Highest risk: 59.8%
- 20 year cumulative incidence of VF loss = 25.2%

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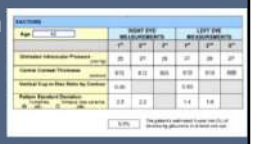
Clinical Decisions in Glaucoma – OHT



- High risk: ~20% risk of conversion within 5 years
  - IOP >32
  - CCT <555 with IOP >26
  - Treat unless patient is opposed; follow same as early glaucoma patient
- Moderate risk: 10-20% risk of conversion within 5 years
  - Does not fulfill high- or low- risk criteria
  - Don't treat unless patient has strong preference, OR if VF/OCT not reliable, OR if ONH is difficult to evaluate
- Low risk: 10% or lower risk of conversion within 5 years
  - Not high risk – AND -
  - CCT >588
  - Don't treat unless patient has strong preference
  - Follow semi-annually for 1 year, then yearly
- TREATMENT: Lower by 15% (CDIG) or 20% (OHTS); re-evaluate if difficult

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"The Baseline and Target IOP Approach"

- Quigley, 21st Century Glaucoma Care Eye 2019
  - Avoid beginning treatment on first visit; suggests at least 3 visits
    - Do we really want to base decades of therapy on one IOP reading?
  - The acceptable amount of IOP lowering needs to be set as a medium term goal (couple of years)
  - Suggests 20% reduction for OHT and for early POAG eyes
  - CIGTS showed that we can tailor the target to the degree of glaucoma, extending to 40% reduction for patients with severe loss at baseline

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Target IOP: What? How?

- Target IOP is IOP at which you *expect* to maintain functional vision or limit progression
- Target IOP should strike a balance between over- and under-treatment
- Target IOP is "arbitrary and imperfect" (Hodapp)
- Set target according to age, severity of disease, and other factors

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Target IOP – two "Rules of Thumb"

- Stage of Disease:
  - Mild: ~30% IOP drop from highest IOP
  - Moderate: 30-40% drop
  - Severe Loss: 40-50% drop
- Stage of Disease: (problems with this method)
  - Mild: high teens (17-19)
  - Moderate: mid teens (14-16)
  - Severe loss: low teens (<14)

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Simplified Target IOP (CDIG)

- OH: 15%
- Early glaucoma:
  - 25% reduction from Tmax
- Moderate-advanced disease:
  - If OLDER, and NO THREAT TO FIXATION: Target 17mmHg
  - If YOUNGER, and/or if there is THREAT TO FIXATION: Target 14mmHg
- Question: Who does this NOT work for?

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How do we achieve target IOP?

- Medications
- Laser
- Incisional surgery
  - MIGS
  - Conventional surgery (Trabeculectomy, Tube Shunt)

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Glaucoma Medications: Timeline

- ~~1876: Cholinergic agonists~~
  - Physostigmine, pilocarpine
- ~~1904: Osmotic agents~~
- 1954: Oral carbonic anhydrase inhibitor (acetazolamide)
- ~~1955: Adrenergic agonists (epinephrine)~~
- 1978: Beta-adrenergic antagonists (Timolol)
- ~~1987: alpha-adrenergic agonists (apraclonidine)~~
- 1995: topical CAI
- 1996: brimonidine
- 1996: prostaglandin analogs
- 2017: Rho kinase inhibitors

Fixed Dose Combination Medications
Various preservatives/non-preserved

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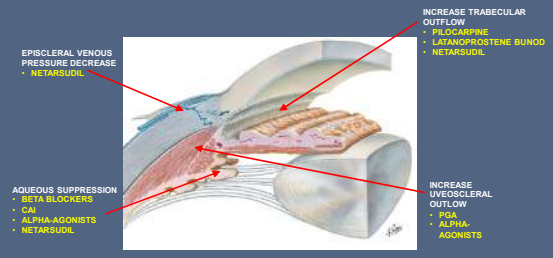
IOP-Lowering Drugs: Sites of Action



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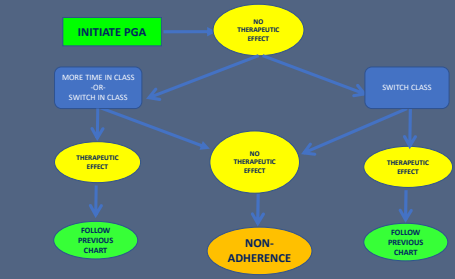

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Glaucoma Drugs: What's Next?

- "Interventional Glaucoma"
- Drug Delivery System (DDS)
  - Contact lens delivery
  - Punctal plug delivery
  - Insertable
  - Injectable
    - Sub-conjunctival
    - Anterior chamber

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Bimatoprost SR – Nate Lighthizer, OD

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Where Does Laser Fit In?

The Glaucoma Laser Trial (GLT). 2. Results of argon laser trabeculoplasty versus topical medicines. The Glaucoma Laser Trial Research Group

Abstract

The Glaucoma Laser Trial, a multicenter, randomized clinical trial involving 271 patients, was designed to assess the efficacy and safety of argon laser trabeculoplasty (ALT) as an alternative treatment with topical medication for controlling intraocular pressure (IOP) in patients with newly diagnosed, previously untreated primary open-angle glaucoma (POAG). Each patient had one eye randomly assigned to ALT (the laser-first [LF] eye) and the other eye assigned to timolol maleate 0.5% (the medication-first [MF] eye). Medication was initiated or changed for either eye according to the same stepped regimen if the IOP was not controlled. Throughout the 2-year follow-up, LF eyes had lower mean IOPs than MF eyes (1-2 mmHg), and fewer LF eyes than MF eyes required simultaneous

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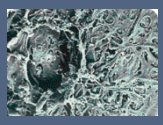
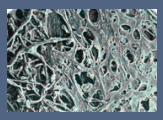
SELECTIVE LASER TRABECULOPLASTY

- Specially designed laser used to treat pigmented trabecular meshwork cells
- Application of laser is same technique as for Argon Laser Trabeculoplasty (ALT)
- Differences:
  - Very short pulse (3 nanoseconds)
  - Eliminates collateral "burn" damage
  - Mechanism appears to be cytokine-mediated macrophage recruitment
  - Can be repeated





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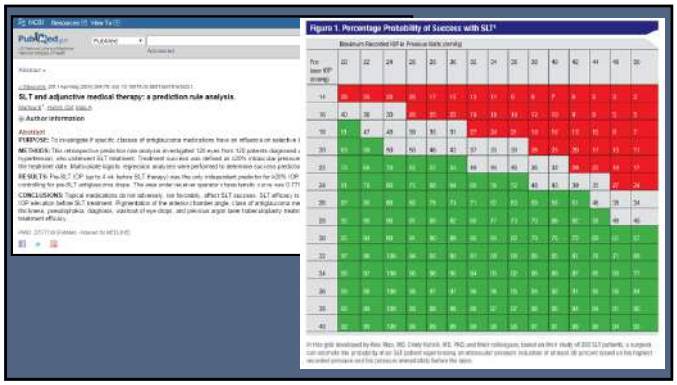

SLT and adjunctive medical therapy: a prediction rule analysis.

Figure 1. Percentage Probability of Success with SLT

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HEALTH TECHNOLOGY ASSESSMENT

National Institute for Health Research

- Newly diagnosed OAG and OHTN (treatment-naïve)
- Two groups:
  - Medicine 1st
  - Laser 1st
- Compared
  - HRQoL
  - Clinical Efficacy
  - Cost effectiveness
- Followed for 36 mo

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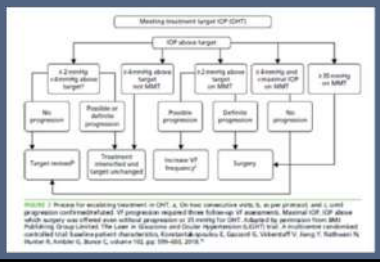
LiGHT Trial

- 356 SLT-1
- 362 Med-1



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LiGHT Trial Results

- 91% patients completed 36 months
  - No difference in HRQoL
  - Proportion of patients at target IOP:
    - SLT-1 93% (0 patients requiring surgery)
    - Med-1 91% (11 patients requiring surgery)
  - SLT-1 provided medicine-free treatment for at least 36 months in 74% of group

- ODs in TEN states can now perform laser procedures!

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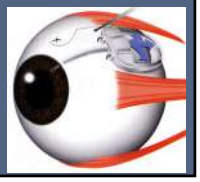
Surgical Intervention

- Exponential increase in surgical options in last 10-15 years
- Traditional incisional surgery:
  - Trabeculectomy 1960's
  - Tube shunt (glaucoma drainage device)
  - Best efficacy, most significant risks/complications





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Minimally Invasive Glaucoma Surgery (MIGS)

- Typical features:
  - Ab interno approach
  - Minimal trauma to tissue
  - Rapid recovery
  - Excellent safety profile
  - Modest efficacy
  - Frequently performed with cataract surgery (changing somewhat)

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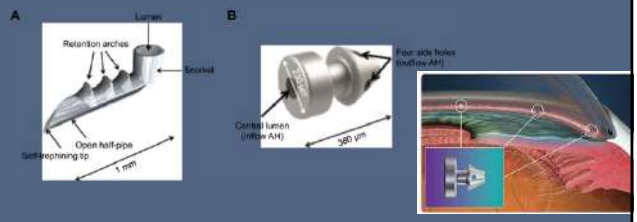
Trabecular Micro-Bypass Stent: iStent



Original iStent: greater IOP reduction compared to cataract surgery alone
iStent Inject: 2 stents placed 2-3 clock hours apart, with cataract surgery
iStent Infinite: 3 stents placed, approved as stand-alone surgery

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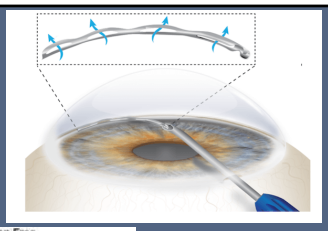
Hydrus Microstent

- 8mm nitinol scaffold placed in Schlemm's canal at time of cataract surgery
- HORIZON study:
  - 369 HMS + CS
  - 187 CS alone

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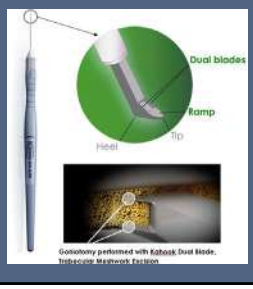
Trabectome, Kahook Dual Blade Goniotomy



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Other MIGS

- GATT/Trab 360
- ABiC / VISCO 360
- Xen gel
  - 1/3-1/2 need needling/revision

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MIGS/cataract versus cataract surgery alone

- Implantation of device: adds 2mm (10%) additional IOP reduction compared to cataract surgery alone
- About 2/3 of the IOP lowering comes from cataract surgery, 1/3 is due to device

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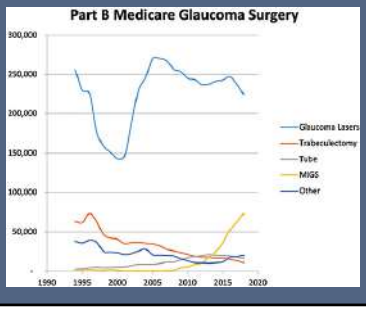
Trends in Glaucoma Procedures



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Back to Clinical Decision: When should you advance/escalate treatment?

- IOP at level previously shown to cause damage (not at target)
- IOP consistently above target and "next step" is not risky
- Presence of disc hemorrhage and "next step" is not risky
- Worsening of structure/function (CONFIRMED)
  - Our ability to manage glaucoma depends on our ability to recognize CHANGE

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Glaucoma Progression

"Once the diagnosis of glaucoma has been made, the **MOST IMPORTANT** remaining question is whether the disease is stable and the therapy/compliance are sufficient, or whether the disease is progressive and the therapy in relation to the life expectancy has to be intensified."

Progression of Glaucoma, World Glaucoma Association, 2011 Kugler Publications

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Progression of Glaucoma

"Although most glaucoma patients will show some evidence of progression if followed long enough, the rate of deterioration can be highly variable among them. While most patients progress slowly, others have aggressive disease with fast deterioration which can eventually result in blindness or substantial impairment unless appropriate interventions take place."

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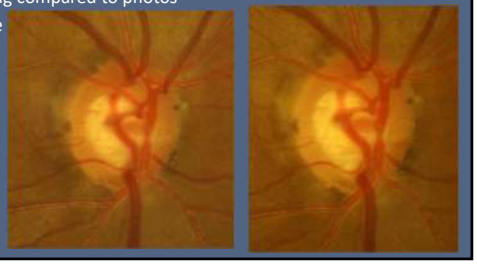
Optic Nerve Progression

- Increased cupping compared to photos
- Disc hemorrhage



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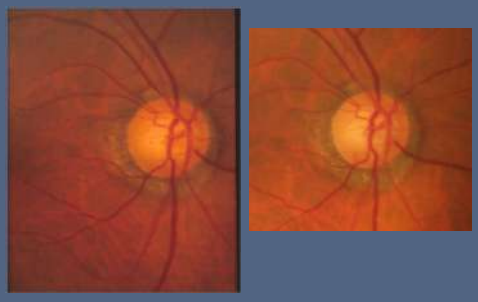

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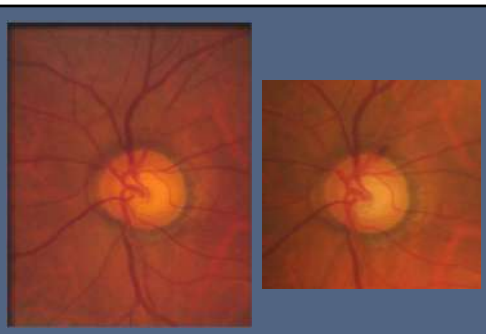

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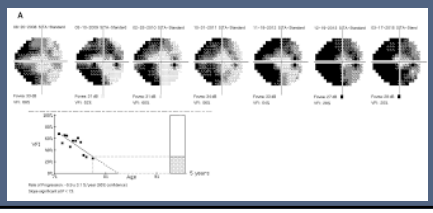
VISUAL FIELD PROGRESSION

- Deepening of existing defect
- Enlargement/expansion of existing defect
- Development of a new defect



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IDENTIFYING PROGRESSION in visual fields

- A **MUCH** harder task than recognizing an abnormal VF
- Long-term fluctuation (test-test variability)
  - The single biggest problem in determining progression
  - Deeper defects: more long term fluctuation
  - More advanced glaucoma: more long term fluctuation, more fatigue

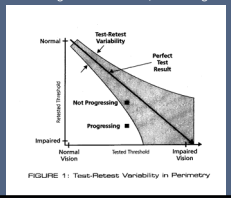

FIGURE 1: Test-Retest Variability in Perimetry

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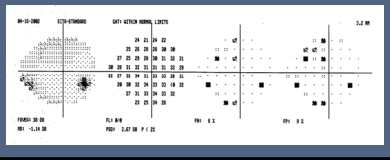
IDENTIFYING PROGRESSION: methods for detection

- Overview printout
  - Grayscale
  - Threshold values
  - Total and pattern deviation plots
  - GHT, global indices, reliability



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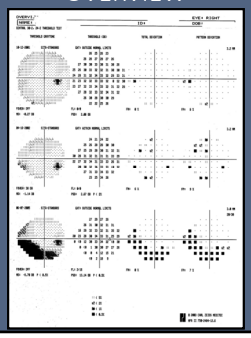
OVERVIEW



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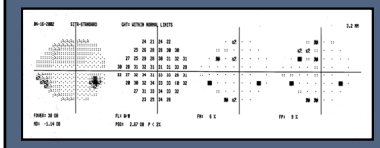
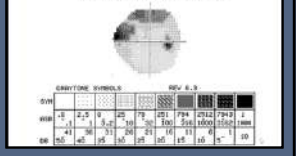
OVERVIEW PLOT: PITFALLS

- Total /Pattern Deviation Probability Plots
  - Once a black box…
- Grayscale
- Threshold values



Grayscale:
change can be 1-9 DB



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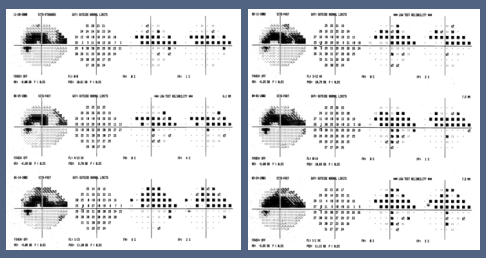
HAS THIS VF PROGRESSED?



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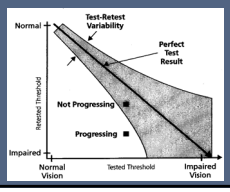
GUIDED PROGRESSION ANALYSIS (GPA)

- Humphrey Field Analyzer
  - Based on results of GLAUCOMA patients from mild to advanced disease
  - Patients took 12 different visual field tests within a 4 week period
  - Developed a model for what is "expected" test-test variation for patients with glaucoma



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GPA

- Uses 2 baseline exams
- **EVENT Analysis** (aka "Glaucoma change probability", aka triangle plot)
  - ***IDENTIFIES AREAS THAT HAVE CHANGED BY MORE THAN THE RANGE OF TESTING VARIABILITY TYPICALLY SEEN IN GLAUCOMA PATIENTS
    - (And…) is this a "repeat" point? 1st time? 2nd? 3rd?
  - GPA "ALERT" (Possible/Likely Progression)
  - Has TODAY's test changed more than the expected amount from the baseline?
- **TREND Analysis**
  - Once there are 5 reliable tests, a regression line of the VFI is performed
  - Provides a RATE OF CHANGE and helps to differentiate rapid progressors from more slow progressors

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GPA SYMBOLS

Points that have changed by more than the expected variability are identified with a simple and intuitive set of symbols:

- ● A **single, solid dot** indicates a point not changing by a significant amount.
- △ A **small open triangle** identifies a degree of deterioration expected less than 5% of the time at that location in stable glaucoma patients ($p < 0.05$).
- ◭ A **half-filled triangle** indicates significant deterioration at that point in two consecutive tests.
- ▲ A **solid triangle** indicates significant deterioration at that point in three consecutive tests.

An X signifies that the data at that point was out of range for analysis. For data that is out of range, GPA cannot determine whether or not the encountered deviation at that point is significant. This occurs mainly with field defects that were already quite deep at Baseline.

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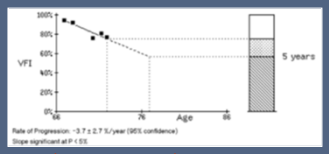
TREND ANALYSIS (rate of change)



The VFI Regression Plot
- VFI plotted against age
- Extrapolates rate of change up to 5 years

*In FORUM, this can be viewed as MD, MD/superior field, MD/inferior field

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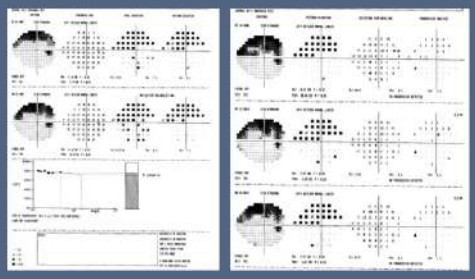
GPA - EXAMPLE



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How often should we run visual fields?

- Quigley (21st Century Glaucoma Care):
- Large database analysis shows that vast majority of OAG patients under treatment are stable or worsening very slowly
  - Small portion losing vision at catastrophic rates***
- Testing VF once per year – it can take 5-6 years to identify progression with confidence
  - Simple solution: 4-6 tests in first 18 months allows identification of rapid progressors
    - Escalate the therapy of rapid progressors
    - Back off to once yearly for others

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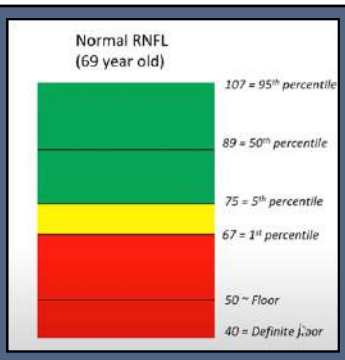
OCT progression

- Don't rely on COLORS!!!
- Example:
  - Start at average (89 microns)
  - From starting point to "floor" of 50 = 89-50 = 39 microns
  - To move from "green" to yellow" = 89-75 = 14 microns
  - 14/39 = 36% loss



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GPA – OCT (RNFL AND MAC)

- Event analysis: two baselines; each visit is compared to average of two baselines, change is based on instrument repeatability
  - Yellow symbols: first time change seen
  - Red symbols: change is repeatable
- Trend analysis: rate of change of various parameters

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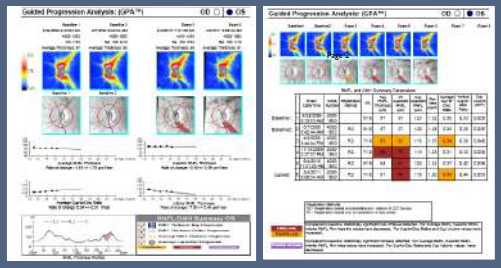

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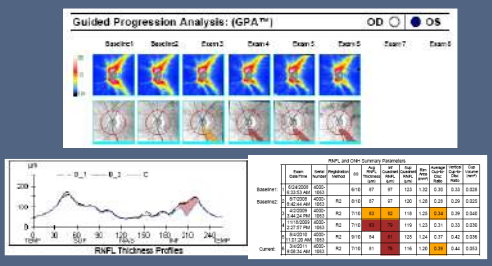
EVENT ANALYSIS



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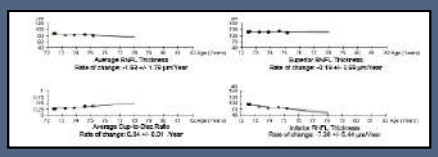
TREND ANALYSIS



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OCT Progression – Some guidelines

- CDIG: Things that should raise suspicion:
  - AVERAGE RNFL change >/= 10 microns, or >/= 5 microns if accompanied by CORRELATING change in VF or by presence of disc heme
  - GCIPL change >/= 4 micron
- Quigley: Average RNFL rate of loss (Spectralis):
  - Normals: 0.6 microns/year
  - Non-progressive glaucoma: 1.2 microns/year
  - Progressive glaucoma: >2.1 microns/year

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Modification of treatment: (CDIG)

- Do I **need** to modify?
  - How fast is patient progressing?
    - FAST and at target: What's going on???? Surgical referral
    - FAST and not at target: get to target, consider surgical referral
    - SLOW (target or not): What's going on? Do I need to amplify?
      - If yes: set new target to 25% below average IOP at which progression occurred
  - How bad is the disease to start with?
  - Was my IOP at target?
  - How long with patient live?

****If non-compliant: may not need to re-set target IOP*****

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Modification of treatment (CDIG):

- Modify sequence
  - Started with meds: add laser
  - Started with laser: add meds
  - Maximum topical therapy with tolerable side effects
    - *drug delivery device*
  - Non-bleb incisional surgery if appropriate
  - Oral medications
  - Bleb-forming surgery

****RE-SET BASELINE**
- 2 new VF
- New OCT
- New follow-up/testing schedule

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Conclusion:

- Glaucoma evaluation and management has changed dramatically in the past 100 years
- The careful clinical evaluation of the optic nerve remains a key element in diagnosis
- The ability to observe for change over time has improved the outcomes for glaucoma patients
- Treatment options have expanded and optometry is well-placed to care for the majority of glaucoma patients in the next century

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Thank you!

Questions? Email: dmarrelli@uh.edu

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