

The Glaucoma Puzzle: When the Pieces Don't Always Fit

Every piece of information helps

Mark T. Dunbar, OD, FAAO
 Director of Optometry
 Bascom Palmer Eye Institute
 Miami, FL

1

Mark Dunbar OD: Financial Disclosure

- Optometry Consultant
 - Carl Zeiss
 - Allergan
 - Regeneration
- Advisory Board for:
 - Allergan
 - Carl Zeiss
 - Regeneration
 - Genentech

Mark Dunbar does not own stock in any of the above companies

2

Why does glaucoma matter?

3

Glaucoma: 2nd leading cause of blindness in developed nations¹

~40%

of patients have moderate-to-severe visual field loss by the time they are diagnosed²

~10%

of people with glaucoma lose vision over time, even if they are treated³

1. WHO/WHO-10 Things you should know about glaucoma. 2017. Available at <http://www.who.int/mediacentre/factsheets/fs104/en/>
2. Osborne MP, et al. Invest Ophthalmol Vis Sci. 2004;45(24):8269-8. doi: 10.1167/45.24.8269
3. <http://www.aao.org/eye-health/eye-conditions-and-diseases/glaucoma>

4

More People Will Need Help Lowering IOP Due to a Growing and Aging Population

- The US population is aging
 - 10,000 people will turn 65 every day through 2030¹

Patient populations who have higher risk of glaucoma will also be increasing²

African-American and Hispanic populations: Projected to increase from 17% of the US population in 2012 to 34% by 2050³

1. Office of Economic Policy and Research. US Census Bureau. 2015. Available at <http://www.census.gov/prod/2015/pub/c2k15br01-01a.pdf>
2. Park Research Center. 2016. Available at <http://www.parkresearchcenter.com/wp-content/uploads/2016/05/2016-05-10-Park-Research-Center-Report-on-Global-Prevalence-of-Glaucoma.pdf>
3. <http://www.pewresearch.org/fact-tank/2015/08/13/black-hispanic-population-growth/>

5

Glaucoma Is on the Rise, With 3x More Cases by 2050^{1,2}

2015¹
 2.2 million people in the US ≥40 yrs old had glaucoma

2030¹
 4.3 million

2050²
 6.3 million will have glaucoma

Glaucoma Population by Age Group³
 2014 - 2032 - 2050 (in millions)

Age Group	2014	2032	2050
40-59	~600,000	~700,000	~800,000
60-69	~700,000	~800,000	~900,000
70-79	~800,000	~900,000	~1,000,000
80-89	~900,000	~1,000,000	~1,100,000
90+	~100,000	~150,000	~200,000

1. CDC. Vision health initiative 2015. Available at <http://www.cdc.gov/visionhealth/>
2. <http://www.parkresearchcenter.com/wp-content/uploads/2016/05/2016-05-10-Park-Research-Center-Report-on-Global-Prevalence-of-Glaucoma.pdf>
3. M.I. Glaucoma Program. Available at <http://www.miglucoma.org/>

6

Underdiagnoses of Open-Angle Glaucoma

- Population studies suggest **over half** of all glaucoma cases in the US have not been diagnosed
 - Percentage of patients with undiagnosed glaucoma
 - Baltimore Eye Survey: 56%¹
 - Proyecto VER: 62%²
- Many suffer severe visual field (VF) loss before diagnosis³

1. Sommer et al. Arch Ophthalmol. 1991.
2. Quigley et al. Arch Ophthalmol. 2001.
3. Colquhoun et al. Invest Ophthalmol Vis Sci. 2003.

7

Primary Open-Angle Glaucoma: Definition

From the American Academy of **Ophthalmology's** (AAO's) Preferred Practice Pattern for Primary Open-Angle Glaucoma:


"Primary open-angle glaucoma (POAG) is a chronic, progressive optic neuropathy in adults in which there is a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons..."

Preferred Practice Guidelines: Primary Open-Angle Glaucoma
© American Academy of Ophthalmology, 2010.

8

What does that mean?

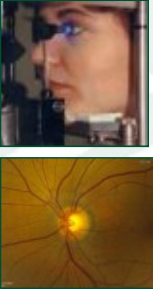
- Acquired disease that affects the optic nerve
- Loss of the ganglion cells and their axons
- Characteristic "cupping" of the optic nerve
- Results in visual field loss
 - Starts peripheral (nasal field)
 - But can be paracentral
 - Can result in blindness
- Traditionally – thought to be from IOP that is too high



9

How do we diagnose glaucoma?

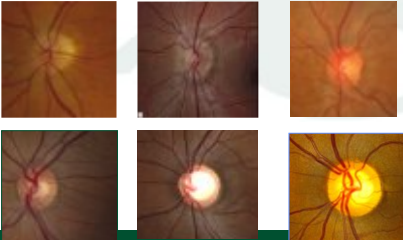
- Measure the IOP
 - Is it normal?
 - Traditionally 10-21 mmHg
 - Is it elevated?
- Look at the optic nerve
 - Does it look normal?
 - Is there "cupping"?
 - Is there asymmetry between the R and L eye?



10

Here are the difficulties?

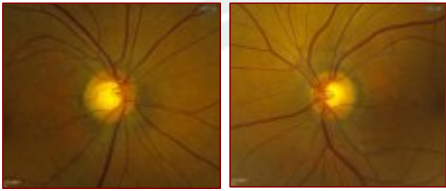
- Individual variability of the optic nerve



11

Difference in the Size Between Each Eye

Berta: 65 y/o Hispanic Female: Followed for OHTN



2005-2014: TA 20-24

12

Optic Nerve Cup

- Highly variable even in normal patients
- Most people are 0.3 to 0.4
 - Jonas .42 (0 - .79) V; .50 (0 - .84) H
- Racial differences in disc size
 - Baltimore .56 (blacks) .49 (whites)
- Larger discs larger cups

13

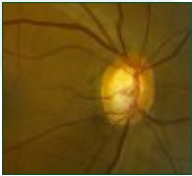
Physiologic vs. GL Damage

<p><u>Physiologic</u></p> <ul style="list-style-type: none"> • Smaller • Horizontally oval • Uniform rim • Similar to shape of nerve • R=L 	<p><u>GL Cupping</u></p> <ul style="list-style-type: none"> • Larger • Vertically oval • Non uniform rim • May be asymmetric
---	--

14

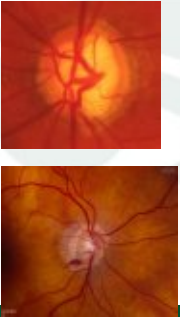
Classic Optic Nerve Findings Suggestive of Glaucoma

- Obvious large cup
- Vertical elongation of the cup
- Focal Notch
- Thinning of neuroretinal rim
- Superficial splinter hemorrhage
- Baring of vessels
- Cup/disc ratio asymmetry



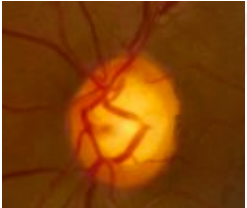
15

- Focal thinning of rim at superior and inferior poles
- Disc hemorrhage



16

Size of the disc




- Large Optic Disc
- Large C/D
- No focal thinning
- Superior and Inferior poles are thickest part of rim

17

Asymmetry

- Larger nerve and cup



18

How do we diagnose it?

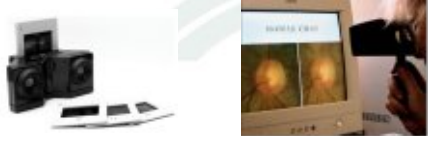
If we are suspicious or concerned...

- Fundus photograph
- Visual field
- OCT: RNFL and ganglion cell layer

19

Diagnosing Glaucoma Until Mid-1990's

- Stereoscopic evaluation of the optic nerve



- Goldmann visual field -> Automatic visual fields
 - Humphrey visual fields

20

Sounds simple

1 + 1 = 2

21

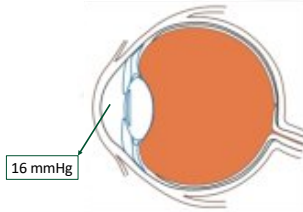
Here are the difficulties with IOP?

- Patients can have glaucoma when the pressure is **“normal”**
 - Beaver Dam Eye Study: 1/3 of glaucoma patients had IOP at a normal pressure¹
 - Baltimore Eye Study: ~ 50% of glaucoma patients had IOP < 21 mmHg
- Not every with “high” IOP develops glaucoma

1. Klein, B. E. et al. Ophthalmology 1992;99(10):1499-1504

22

What Does a Pressure of 16 really mean?

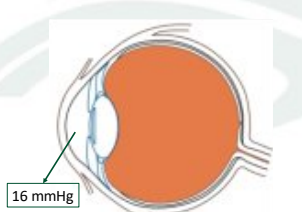


23

What are we measuring when we measure the IOP?

Conventional wisdom

- The intraocular pressure
- The pressure **INSIDE** the eye



24

What are we measuring when we measure the IOP?

Conventional wisdom

- The intraocular pressure
- The pressure **INSIDE** the eye

776 mmHg

25

IOP = 16

What Does That Really Mean?

Normal Atmospheric Pressure = 760 mmHg

Sea level

760 mmHg

776 mmHg

760 mmHg

26

IOP = 16

What Does That Really Mean?

Normal Atmospheric Pressure = 760 mmHg

Sea level

760 mmHg

776 mmHg

776 mmHg - 760 mmHg = 16 mmHg

Atmospheric pressure (inside) - normal atmospheric pressure = Intraocular pressure

27

What is IOP?

- When we measure the IOP, we are really measuring the **“trans-corneal”** pressure
- Pressure difference across the cornea
- The pressure inside the eye minus the atmospheric pressure that surrounds the eye.

28

High IOP = 26 Glaucoma

	Atmospheric	Intraocular
Absolute pressure	760 mmHg	784 mmHg
Trans-Corneal Pressure Difference	26 mmHg	

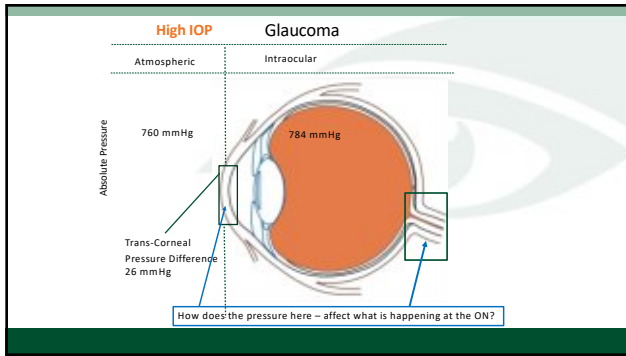
29

High IOP = 26 Glaucoma

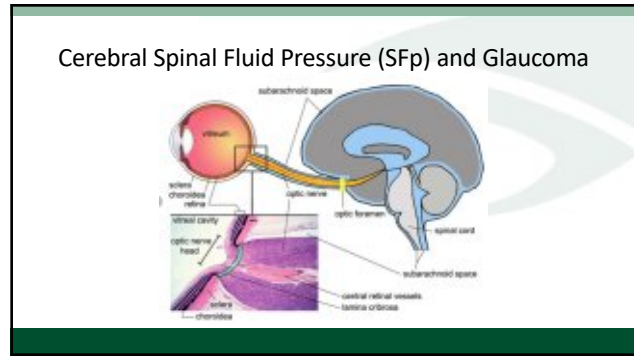
	Atmospheric	Intraocular
Absolute pressure	760 mmHg	774 mmHg
Trans-Corneal Pressure Difference	26 mmHg	

Lower intraocular pressure - reduces Trans-Cornea difference

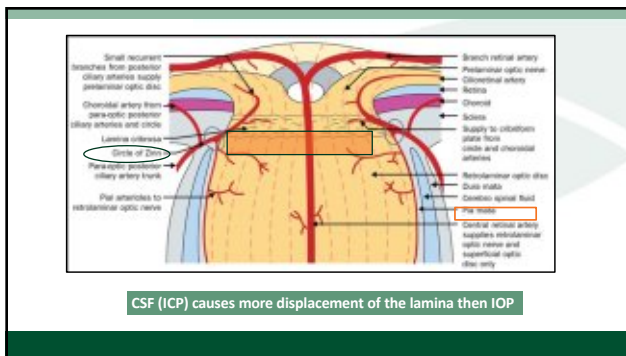
30



31



32



33

CSF and Glaucoma

45 Years ago: (1976) Volkov pointed out that cerebrospinal fluid pressure (CSF-P) could pathogenetically be associated with glaucomatous optic neuropathy

Volkov VV. Essential element of the glaucomatous process neglected in clinical practice [in Russian]. Ophthalmol Zh 1976;31: 500-4.

- 1979: Yablonsky et al postulated that an abnormally **low CSF-P around the optic nerve** may be the reason for a barotraumatocally induced optic nerve damage in normal-pressure glaucoma.

Yablonski M, Ritch R, Pokorny KS. Effect of decreased intracranial pressure on optic disc. Invest Ophthalmol Vis Sci 1979;18(Suppl):165.

34

2008

Cerebrospinal Fluid Pressure Is Decreased in Primary Open-angle Glaucoma

Min P, Berdahl MD,¹ R. Reed Allington, MD,¹ Douglas H. Johnson, MD^{2,3}

Purpose: To compare cerebrospinal fluid (CSF) pressure in patients with primary open-angle glaucoma (POAG) with that in nonglaucomatous patients.

Design: Case-control study.

Participants: Thirty-one thousand, seven hundred and eighty-six subjects underwent lumbar puncture (LP) between 1988 and 2007 at the Mayo Clinic, Rochester, Minnesota. CSF from 28 patients who had POAG and 28 patients who did not have POAG were analyzed.

Methods: Retrospective review of medical records. Comparison of the 2 groups and factors associated with CSF pressure were analyzed by univariate and multivariate analyses.

Main Outcome Measures: Demographic (age and gender), medical history, medication use, indication for LP, intraocular pressure (IOP), optic disc cup-to-disc ratio, visual field assessment, and CSF pressure.

Results: The mean CSF pressure ± standard deviation was 13.2 ± 4.0 mmHg in nonglaucoma patients and 9.2 ± 3.8 mmHg in POAG patients (P < 0.0005). The CSF pressure was lower in POAG patients regardless of indication for LP or age. Linear regression analysis showed that cup-to-disc ratio correlated independently with IOP (P < 0.0005), CSF pressure (P < 0.0001), and the transocular pressure difference (P < 0.0001). Multivariate analysis demonstrated that larger cup-to-disc ratio (P < 0.0001) was associated with lower CSF pressure.

Conclusions: Cerebrospinal fluid pressure is significantly lower in POAG patients compared with that in nonglaucomatous controls. These data support the notion that CSF pressure may play an important contributory role in the pathogenesis of POAG. Ophthalmology 2008;115:763-768 © 2008 by the American Academy of Ophthalmology.

35

Mayo Clinic Study: CSF and Glaucoma

- Retrospective review of 31,786 patients that had lumbar punctures over a 11-year period
- Determined # who had complete eye exams
- 28 met inclusion criteria of POAG, 49 controls
- ICP was significantly lower** in patients with POAG compared to the non-glaucoma control

Berdahl JP, et al. Ophthalmology. 2008;115(5):763-768.

36

Berdahl 2nd Mayo Clinic Study: CSF and Glaucoma POAG vs. NTG vs OHT

- Retrospective review of 62,468 patients that had lumbar punctures over a 20-year period
- 189 met inclusion criteria of complete eye exam
- ICP was significantly **lower** in patients with POAG and NTG and **significantly higher** in OHT

Berdahl JP, Fautsch MP, Stinnett SS, et al. Intracranial pressure in primary open angle glaucoma, normal tension glaucoma, and ocular hypertension: a case-control study. *Invest Ophthalmol Vis Sci.* 2008;49(12):5412-5418

37

Cerebrospinal Fluid Pressure in Glaucoma A Prospective Study

South Kim, MD^{1,2}, Joe B. Jonas, MD^{1,2}, Chonglin Tan, MD^{1,3}, Yi Zhu, MD^{1,3}, Mo, MD^{1,3}, Shuang Li, MD¹, Huiqun Wang, MD^{1,3}, Bo Li, MD¹, Susen Zhang, MD¹, Ning Wang, MD¹

Purpose: To assess whether a low cerebrospinal fluid pressure (CSF-P) is associated with open-angle glaucoma or with normal-tension glaucoma (NTG).

Design: Prospective, interventional study.

Participants: The study included 43 patients with open-angle glaucoma (14 with a normal IOP, and 29 with an elevated IOP) and 71 subjects without glaucoma.

Intervention: All patients underwent standardized ophthalmologic and neurologic examinations and measurement of lumbar CSF-P.

Main Outcome Measures: Cerebrospinal fluid pressure and IOP.

Results: Lumbar CSF-P was significantly ($P < 0.001$) lower in the normal IOP glaucoma group (8.8 ± 2.3 mmHg) than in the high IOP glaucoma group (11.7 ± 2.7 mmHg) or the control group (12.8 ± 1.9 mmHg). The mean trans-lamina-cribrosa pressure difference (LCP-P) was significantly ($P < 0.001$) higher in the normal IOP glaucoma group (8.0 ± 3.0 mmHg) and the high-IOP glaucoma group (7.3 ± 4.1 mmHg) than in the control group (4.4 ± 1.7 mmHg). The extent of glaucomatous visual field loss was negatively correlated with the height of the CSF-P and positively correlated with the trans-lamina-cribrosa pressure difference. In the control group, CSF-P was significantly correlated with both systolic blood pressure ($P = 0.004$) and IOP ($P = 0.005$). The trans-lamina-cribrosa pressure difference was not significantly associated with blood pressure ($P = 0.87$).

Conclusions: In open-angle glaucoma with normal IOP, CSF-P is abnormally low, leading to an abnormally high trans-lamina-cribrosa pressure difference. Paradoxically, a low CSF-P in normal-IOP glaucoma may be similar to a high IOP in high-IOP glaucoma. Consequently, the glaucomatous visual field defect is positively correlated with the trans-lamina-cribrosa pressure difference and inversely correlated with the CSF-P. In nonglaucomatous subjects, CSF-P, blood pressure, and IOP are significantly associated with each other.

Financial Disclosures: The authors have no potential or commercial interest in any of the materials discussed in this article. *Ophthalmology* 2010;117:2088-2095 © 2010 by the American Academy of Ophthalmology

38

Lumbar CSF Pressure in NTG, POAG and Non GL

Ophthalmology, Volume 117, Number 2, February 2010

Table 3. Measurements of Lumbar Cerebrospinal Fluid Pressure in Patients with Normal-Tension Glaucoma, High-Pressure Glaucoma, and Nonglaucomatous Subjects

	Normal-Tension Glaucoma Group	P-Value	High-Pressure Glaucoma Group	P-Value	Control Group
N	18		29		71
Cerebrospinal fluid pressure (mmHg)	8.5 ± 2.2	0.003	11.7 ± 2.7	<0.001	11.9 ± 1.9
Mean	12.1		12.2		12.9
Range	3.5-12.9		6.6-19.1		7.0-18.9

P value: Statistical significance of the difference between the group in the preceding column and the group in the next column (Mann-Whitney U test).
The difference in cerebrospinal fluid pressure was statistically significant ($P < 0.001$) also for the comparison between the normal-tension glaucoma group and the control group.

39

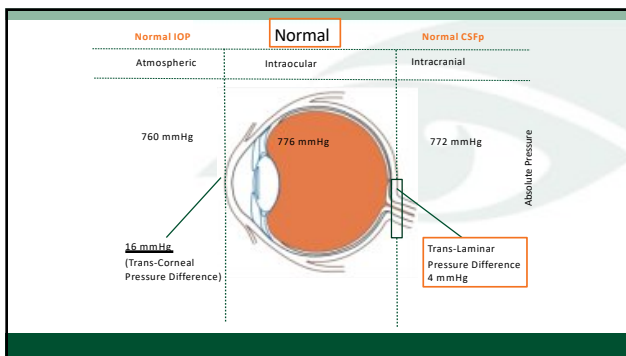
Trans-Lamina Cribrosa Pressure Difference

Table 4. Measurements of the Trans-Lamina Cribrosa Pressure Difference (Transoperative Pressure Minus Cerebrospinal Fluid Pressure) in Patients with Normal-Tension Glaucoma, High-Pressure Glaucoma and Nonglaucomatous Subjects

	Control Group	P-Value	Normal-Tension Glaucoma Group	P-Value	High-Pressure Glaucoma Group
N	71		18		29
Trans-lamina cribrosa pressure difference (mmHg)	4.4 ± 1.7	<0.001	8.0 ± 3.0	<0.001	11.7 ± 2.7
Mean	1.6		6.9		11.9
Range	-3.6 to 8.5		1.6-11.3		6.5-24.9
Trans-lamina cribrosa pressure difference (mmHg) (higher ocular volume)	5.2 ± 1.6	<0.001	9.2 ± 2.6	<0.001	18.8 ± 4.8
Mean	1.8		8.4		15.3
Range	-1.1 to 6.9		4.1-11.3		5.3-21.9

P value: Statistical significance of the difference between the group in the preceding column and the group in the next column (Mann-Whitney U test).
The difference in the trans-lamina-cribrosa pressure difference was statistically significant ($P < 0.001$) also for the comparison between the high-pressure glaucoma group and the control group.

40

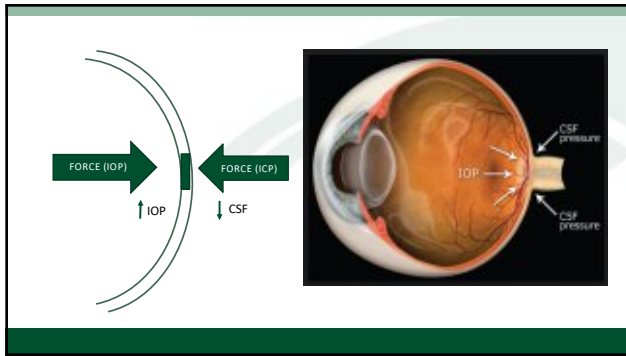


41

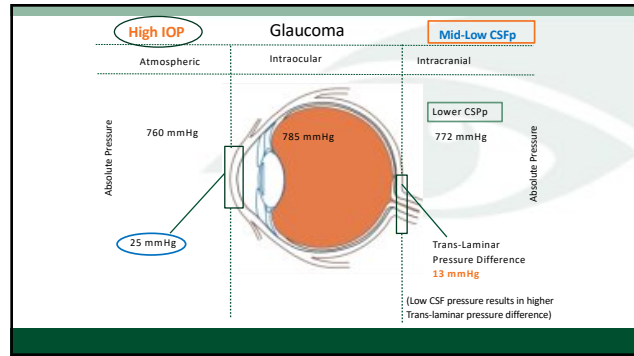
Relationship between IOP and CSF

- In the normal state IOP and CSF have **minimal trans-lamina pressure differences**
- Increasing the difference **alters the homeostatic balance** and results pressure gradient difference at the lamina

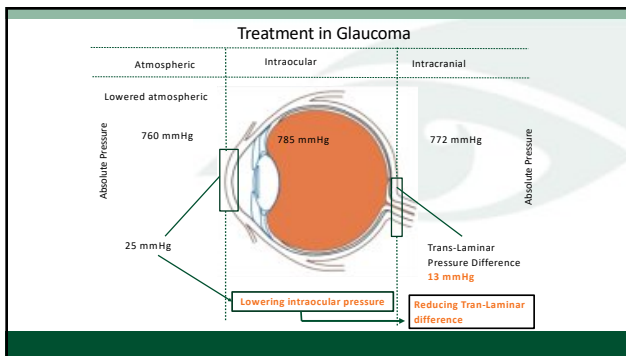
42



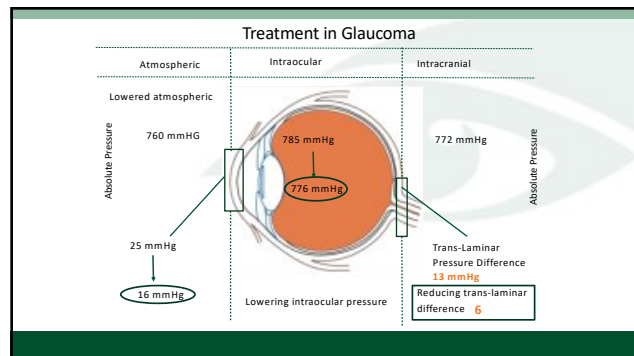
43



44



45



46

60% of astronauts suffer ocular problems related to prolonged space travel

- Globe flattening
- Hyperopic shift
- Choroidal folds
- Disc swelling

47

Spaceflight Associated Neuro-ocular Syndrome: (SANS)

npj Microgravity

REVIEW ARTICLE OPEN

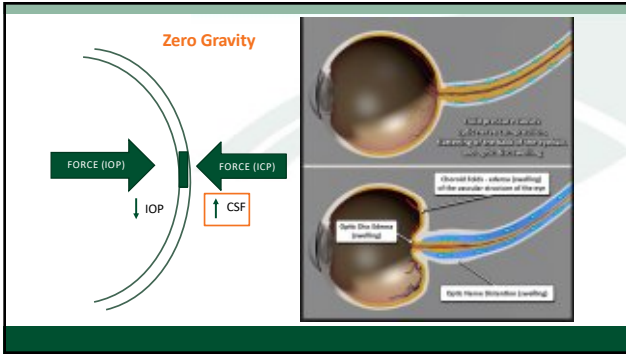
Spaceflight associated neuro-ocular syndrome (SANS) and the neuro-ophthalmologic effects of microgravity: a review and an update

Andrew S. Lee^{1,2,3,4,5,6,7,8}, Thomas R. Mader⁷, C. Robert Olson⁷, William Tso⁹, Peypen Nakas¹⁰, Ray E. Alvarez¹¹, Laura A. Goldstone¹² and Tyson Suckale¹³*

Extended microgravity exposure during long-duration spaceflight (LDF) produces unusual physiological and pathologic neuro-ophthalmologic findings in astronauts. These microgravity-associated findings collectively define the "Spaceflight Associated Neuro-ocular Syndrome" (SANS). We compare and contrast LDF-associated SANS with the historical neuro-ocular and optic chiasmatic abnormalities (NCA), known as the "Spaceflight Associated Neuro-ocular Syndrome" (SANS) and the "Spaceflight Associated Neuro-ocular Syndrome" (SANS). We also discuss the knowledge gaps for in-flight and terrestrial human research including potential countermeasures for SANS study. We encourage the NASA and its research partners continue to study SANS in preparation for future longer duration crewed space missions.

npj Microgravity (2020) 1:1 | https://doi.org/10.1038/s41550-020-0004-4

48



49

Glaucoma Today

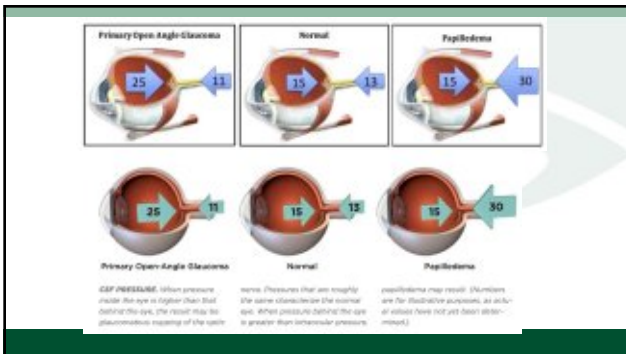
RESEARCH RESULTS

Cerebrospinal Fluid Pressure and Glaucoma

Intracranial pressure may hold the key to understanding why IOP plays a major role in the development of glaucoma.

BY JOHN BEEDARI, MD

50



51

THE SPLETTEN! HYPOTHEZIZED ROLE OF IOP vs. CSF PRESSURE ON OPTIC DISC

Hypotension Glaucoma	Normal Optic Nerve	Papilloedema
IOP: 25, CSF: 13	IOP: 15, CSF: 13	IOP: 15, CSF: 30

Acute Angle Closure Glaucoma and the Transocular Pressure Difference. Fuchsberg, David, Berlin, 1984. International Ophthalmology Clinics, 24(2):74-84, Winter 1984. DOI: 10.1007/978-1-4939-9134-9_10

52

What other factors besides IOP contribute to glaucomatous ON damage?

- Intracranial pressure (ICP)
- Blood pressure
 - High vs Low blood pressure (BP)
- Reduced ocular blood flow
 - Lower ocular perfusion pressure (OPPO)

53

Where Does Blood Pressure Fit In?

54

Where Does Blood Pressure Fit In?

- Not high blood pressure...but low blood pressure
- 1990's: Hayreh, Drance, and others 1st raised the important issues of **systemic hypotension** and **nocturnal blood pressure dips** in the progression of glaucoma
- The problem: difficult to measure systemic BP during sleeping hours

55

When is the highest IOP during the 24-hour cycle?

- IOP is a dynamic physiological parameter that doesn't remain constant over the course of 24 hours
- **Peak IOP is usually recorded at the end of the nocturnal sleep period**
- Trough IOP levels tend to occur at the end of the waking period

Liu, JH, Kripke, DJ, Twa, MD, et al. Twenty-four hour pattern of intraocular pressure in the aging population. Invest Ophthalmol Vis Sci. 1999;40:2912-2917.

56

Risk Factors For Progression

- **BP is lowest** at night
- **IOP is highest** during the night time
 - Highest prior to waking
- Combination of **↑ IOP** and **↓ BP** may result in a critical **↓ ocular perfusion pressure (OPP)** in susceptible people
 - Patients with faulty autoregulation

Mason S, Liu JH, Weinreb RN. Correlation between office and peak nocturnal intraocular pressure in healthy subjects and glaucoma patients. Am J Ophthalmol. 2005;139:230-4.

57

Ocular Perfusion Pressure (OPP)

- **OPP is the relative pressure at which blood enters the eye**
- Defined as the ocular arterial pressure minus the IOP
- OPP is a delicate balance between **IOP** and **blood pressure**
- Low ophthalmic perfusion pressure (OPP) is a risk factor for progression
 - Low BP and/or high IOP

$$MOPP = 2/3 \times [DBP + 1/3 \times (SBP - DBP)] - IOP$$

Simple: Diastolic BP - IOP = OPP

58

Low OPP and Glaucoma

Epidemiologic Studies Linking Diastolic Perfusion Pressure and Glaucoma

Study	Design	Participants	Glaucoma Risk From Low DPP vs Normal DPP
Baltimore Eye Survey ¹	Cross-sectional	Non-Hispanic Whites and African Americans	2-6-fold
Egna-Neumarkt Study ²	Cross-sectional	Non-Hispanic Whites	2.5-fold*
Projecto VER ³	Cross-sectional	Hispanics	4-fold
Los Angeles Latino Eye Study ⁴	Cross-sectional	Hispanics	1.9-fold
Barbados Eye Study ⁵	Longitudinal	Afro-Caribbeans	3.2-fold (4 years)

1. Devereux RB, et al. Arch Ophthalmol. 1988;106:1000-1005. 2. Borrmann M, et al. Ophthalmology. 2003;110:1000-1005. 3. Linn S, et al. Arch Ophthalmol. 2003;121:1000-1005. 4. Linn S, et al. Arch Ophthalmol. 2003;121:1000-1005. 5. Linn S, et al. Arch Ophthalmol. 2003;121:1000-1005.

59

Low OPP and Glaucoma

Table 1. Low diastolic ocular perfusion pressure and prevalence of open-angle glaucoma

Study	n	Diastolic OPP <50-55 mmHg
Baltimore Eye Survey	5308	Prevalence: 2-6-fold
Egna-Neumarkt Study	4297	Prevalence: 3-fold only in high-tension glaucoma*
Projecto VER	4774	Prevalence: 4-fold
Barbados Eye Study	4631	Prevalence: >3-fold
Rotterdam Eye Study	1329	Prevalence: >4-fold only in high-tension glaucoma (mainly probable glaucoma) receiving treatment for systemic hypertension

Adapted from [10-13,14]. *OPP, ocular perfusion pressure. *Low OPP was defined as <66 mmHg in this study.

60

Risk Factors for Visual Field Progression in the Low-pressure Glaucoma Treatment Study

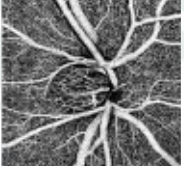
CARLOS GUSTAVO DE MORAES, EFFREY M. LIEHMANN, DAVID S. GREENFIELD, STUART K. GARDNER, ROBERT BITCH, AND THEODORE KRUPIN, ON BEHALF OF THE LOW-PRESSURE GLAUCOMA TREATMENT STUDY GROUP

We determined that a lower MOPP during follow-up was significantly associated with visual field progression in our model and this effect was not significantly affected by other covariates, such as use of systemic antihypertensives and randomization arm (Table 4). An imbalance between

61

OPP and Glaucoma – The Reality

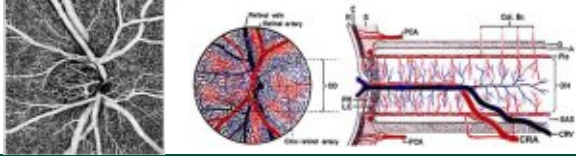
- Perfusion pressure is **difficult to accurately measure**
- There is currently **no widely accepted consensus** regarding **which techniques** should be used to evaluate blood flow or how the results should be interpreted
- **None of the methods** used to estimate blood flow **have been standardized** or externally validated for humans
- Ocular blood flow measurements are not currently used in the diagnosis or management of patients with glaucoma



62

Vascular Supply to the ON

- COMPLEX arterial supply and an even more complex venous drainage system
- Which vascular network is most critical for development of glaucoma?



63

Putting it all together...



64

Compromised Autoregulation in Glaucoma

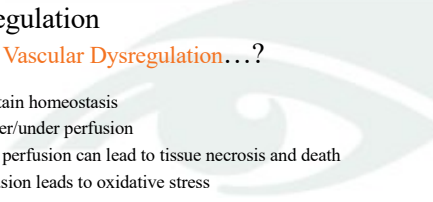
- **Autoregulation: The body's ability to regulate itself in the presence of change: The ability to maintain homeostasis**
 - Vascular factors
 - Cardiovascular disease
 - Vasospasm
 - Postural changes
 - Atmospheric pressure
 - Temperature
 - Fatigue can lead to **abnormal pressure-flow relationship**
- Periods of ischemia are then more likely to occur
 - Can result in reduced or fluctuating OPP

65

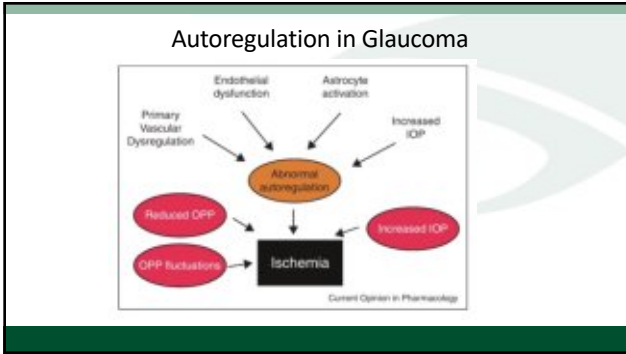
Autoregulation
Or **Vascular Dysregulation...?**

Inability to maintain homeostasis

- Can lead to over/under perfusion
- Chronic under perfusion can lead to tissue necrosis and death
- Unstable perfusion leads to oxidative stress



66



67



68

80 yo White Female

- Presented for "annual eye exam"

HPI
 80 yrs old, female New Patient here for annual check
 Feels vision at distance was not as good as it has been, especially the LE
 She uses glasses to see small prints, reports good vision at distance OU.
 Denies pain, floaters or flashes of light.
 S/p: CEIOL OU, YAG laser posterior capsulotomy OD (Baptist Hospital)
 LEE: 02/2017 by M.D. (w/DFE)
 Mom had glaucoma and used drops
 Generally does not wear glasses for driving

69

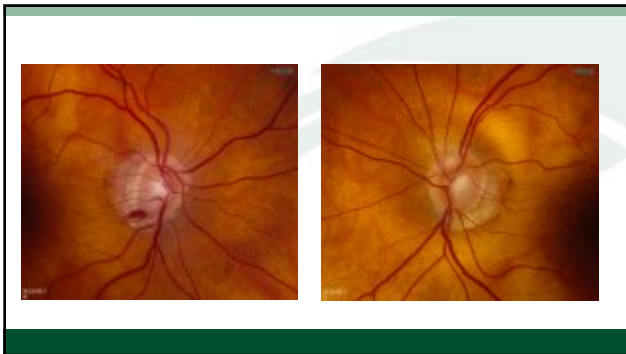
80 yo White Female

Oct 2017

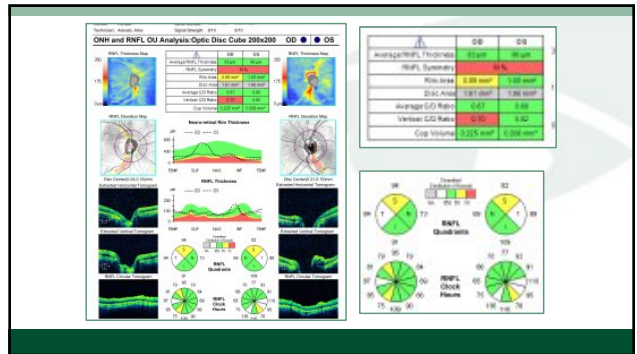
Visual Acuity (Conden - Linear)				Pupils	
Distance	Right	Left	Far	Right	Left
Distance	20/30-2	20/30-1	Far	Right	Left
Distance	20/30-2	Far	Visual Fields (Confronting Program)	Result	Full
Near	J1	J2	Result	Full	Full
Near	J1	J2	Result	Full	Full
Color Vision	20/20	20/20	Color Vision	20/20	20/20
Color Vision	20/20	20/20	Color Vision	20/20	20/20

Refraction				Cycloplegic Refraction				
Wearing Rx	Sphere	Cylinder	Axis	Sphere	Cylinder	Axis	Add	
Right	+1.50	Sphere		Right	-1.00	+0.75	184	+2.75
Left	+1.50	Sphere		Left	-1.00	+0.50	179	+2.75

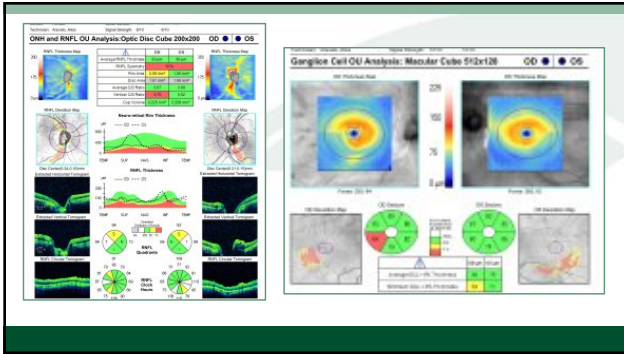
70



71



72



73

So now what?
 Is this low/normal tension glaucoma?
 Would you begin treatment today?

74

Would you begin treating on this visit?

1. Yes
2. No
3. I would refer to ophthalmologist

75

This is what I did...

Impression

- 1) Probable Normal Tension Glaucoma OU
 Inferior thinning OU
 Disc hemorrhage RE inferior
 OCT and GCC thin corresponding to clinical presentation
 TA ~ 15 OU
- 2) Pseudophakia OU
- 3) PVD OU

Plan

- 1) Ed and reassure
- 2) RTC 1-2 weeks for VF and IOP measurement
- 3) Will start Tx at next visit
- 4) Rx given for specs

76

1 week later: 10/25/17

Base Eye Exam

Visual Acuity (Snellen - Linear)			
	Right	Left	Both
Dist cc	20/20	20/20 -2	20/20
Dist ph		Ni	
CC			

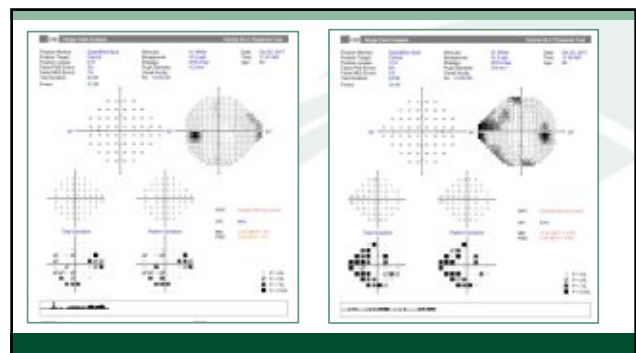
Tonometry (Tonopen, 12:06 PM)

	Right	Left
Pressure	15	14

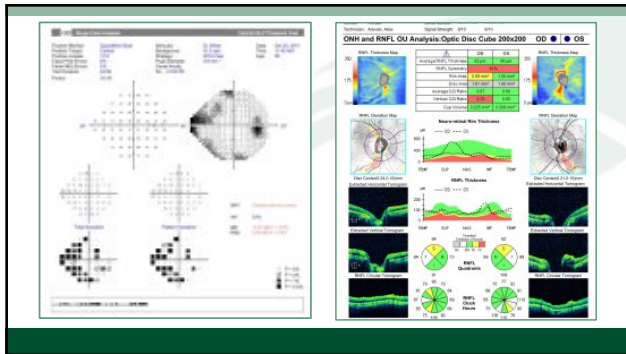
Pupils
 OU: 3/2 mm, round, reactive to light
 No APD seen

Neuro/Psych
 Oriented x3: Yes
 Mood/Affect: Normal

77



78



79

Putting the Pieces of the Puzzle Together...

- The IOP is normal
- Abnormal optic nerve
 - Disc hemorrhage
- OCT shows RNFL thinning
 - Ganglion cell complex also shows thinning
- Visual field defect in a location where we see ON damage

80

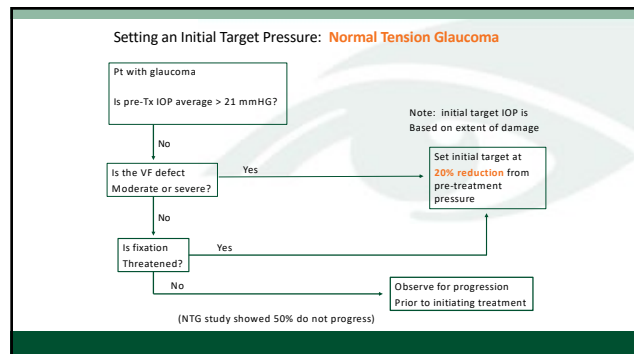
How do you manage this patient?

Normal Tension Glaucoma

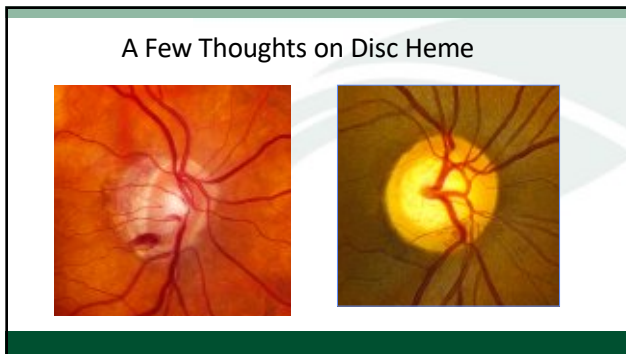
Treatment?

- This is what I did
 - Latanoprost qhs OU
 - RTC 3 months
 - Should I bring her back sooner to check IOP?

81



82



83

Detection and Prognostic Significance of Optic Disc Hemorrhages during the Ocular Hypertension Treatment Study

David L. Finkel, MD, MPH,¹ Douglas E. Anderson, MD,¹ William J. Feuer, MD,¹ Julie A. Sider, MD,² Lynn Schepens, MD,¹ Richard R. Farnish II, MD,¹ Judy E. Fitz-Simons, MD,¹ Mia O. Gordon, PhD,¹ Michael A. Kass, MD,¹ Ocular Hypertension Treatment Study Group

- Disc hemorrhages detected in 128 eyes of 123 participants
- 21 cases detected by both doctor and photos
- 107 cases (84%) were detected only by a review of photography

Ophthalmology Dec 2006

84

Of Note:

glaucoma, and retinal status. The occurrence of a disc hemorrhage increased the risk of developing POAG 6 fold in a univariate analysis (P<0.0001; 95% confidence interval: 3.8–10.7) and 3.7 fold in a multivariate analysis that included baseline factors predictive of POAG (P<0.001; 95% confidence interval: 2.1–6.6). The 96-month cumulative incidence of POAG in the eyes without optic disc hemorrhage was 5.2%, compared with 13.9% in the eyes with optic disc hemorrhage. In eyes with a disc hemorrhage in which a POAG and point developed, the median time between the 2 events was 13 months.

Incidence of Progressing to POAG

- No Disc Heme: 5.2%
- + Disc Heme: 13.6% -> at 10 years 25.6% vs. 13%
- Presence of a disc heme increase risk of developing POAG 6 fold

85

13 Year Follow Up of Disc Hemorrhages in the OHTS

- ODH 179 eyes of 169 participants
- Incidence of POAG in eyes with ODH was **25.6% vs. 12.9%** in eyes without ODH
- ODH increased the risk of developing POAG
- Risk Factors for ODH:
 - Older age, thinner central corneal thickness, larger vertical cup to disc ratio, higher intraocular pressure, and self-reported black race

86

Perhaps the Bigger Question?

- How is it that a patient can continue to “progress” or develop a disc hemorrhage with a pressure ~ 12?
- What are the factors that result in progression?

87

Compromised Autoregulation in Glaucoma

- Autoregulation:** The body's ability to regulate itself in the presence of change: **The ability to maintain homeostasis**
 - Vascular factors
 - Cardiovascular disease
 - Vasospasm
 - Postural changes
 - Atmospheric pressure
 - Temperature
 - Fatigue can lead to **abnormal pressure-flow relationship**
- Periods of ischemia are then more likely to occur
 - Can result in reduced or fluctuating OPP

88

Autoregulation
Or **Vascular Dysregulation...**?

Inability to maintain homeostasis

- Can lead to over/under perfusion
- Chronic under perfusion can lead to tissue necrosis and death
- Unstable perfusion leads to oxidative stress

89

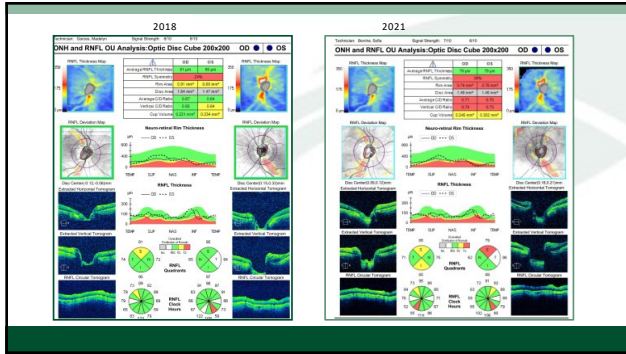
1/6/21 Latanoprost
Ta: 13/11 Alphagan P

ONH and RNFL OU Analysis: Optic Disc Cube 200x200

Macular Thickness

Single-Cell OU Analysis: Macular Cube 172x172

90



91



92

Jan 2021

- NTG: Stable
 - No Disc heme
 - Good IOP today at 13/11 on Latanoprost and Alphagan P
 - OCT done today is “stable” but poor quality scans
- Plan
 - Continue with Latanoprost and Alphagan P
 - Follow 6 mo
 - Repeat VF
 - No need to dilate at next visit

93

Visual Field

- Various testing methods
- Standard automated perimetry
 - SAP or White on White most commonly used
- It is a difficult test to perform
- It relies on the patient being able to provide subjective input on what they see
 - Many patients have extreme difficulties

94

Some Things to Keep in Mind

- GL visual field loss shows more variability than normal fields
- There tends to be **high variability and reductions in sensitivity preceding definite field loss**
- Local depressions of sensitivity frequently come and go before finally resolving into stable repeatable VF defects

95

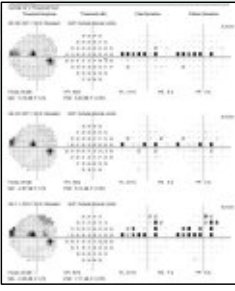
Visual Fields in OHTS

- 86% of retests had normal visual fields
- Abnormal confirmed in 14%

96


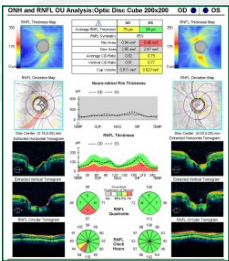
Visual Fields and Glaucoma

- Visual fields can be **difficult** to perform
- Visual fields can be **variable**
 - Some days better and some days worse
- Determining progression can be very difficult
 - Because of long term fluctuations



97

OCT: The missing piece of the puzzle?


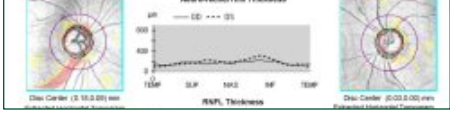



98

ONH and RNFL OU Analysis: Optic Disc Cube 200x200

OD OS

Average RNFL Thickness	76 µm	78 µm
RNFL Standard Deviation	0.54 µm	0.06 µm
Disc Area	2.88 mm²	2.47 mm²
Average C-Plane	0.92	0.75
Vertical C-Plane	0.97	0.77
Cap Volume	0.811 mm³	0.622 mm³

Disc Center (S: 16.0, 0.0) mm

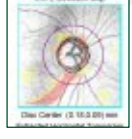
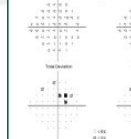
Disc Center (O: 0.0, 0.0) mm

99

ONH and RNFL OU Analysis: Optic Disc Cube 200x200

OD OS

Position Monitor: Flaps / Blind Spots
 Position Target: Central
 Position Location: 1/15
 Pulse PDR Strokes: 0/3
 Pulse WDR Strokes: 0/3
 Total Duration: 00:21
 Error: 00:40


Disc Center (S: 16.0, 0.0) mm

Disc Center (O: 0.0, 0.0) mm

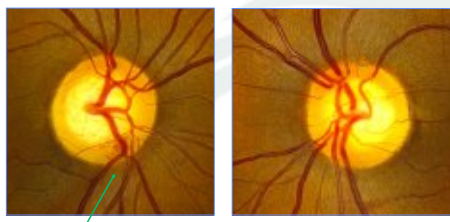
100

51 y/o Hispanic Female

- Reports shadow peripherally in her **L.E.**
- TA: 16-17 on 3 visits

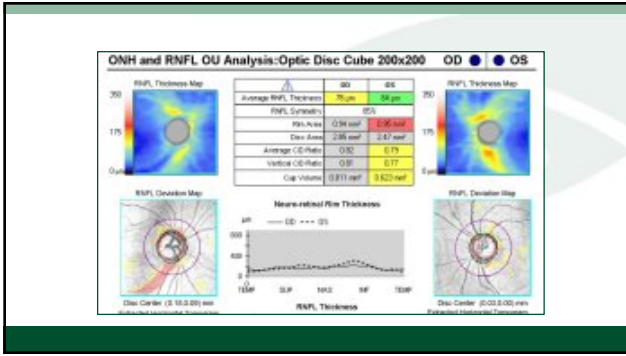


101

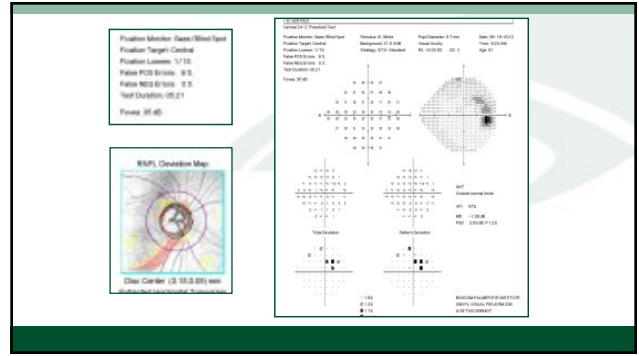


Disc Hemorrhage

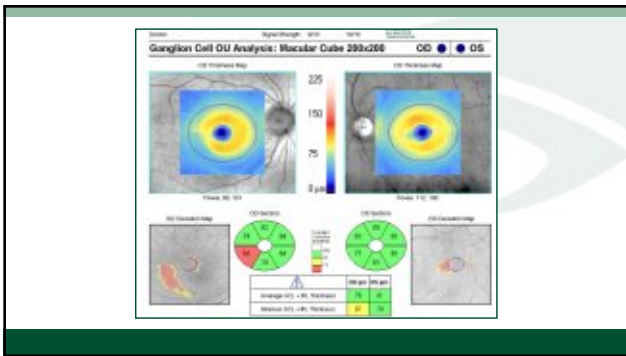
102



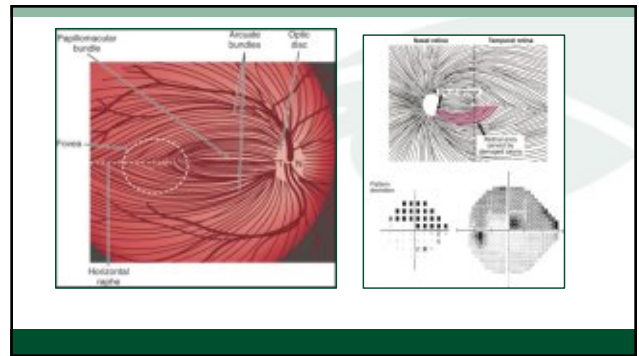
103



104



105



106

The RNFL thickness measurements are based on a "normative data base"

Can the optic nerve of this patients be compared to the normative data base?

107

Can the RNFL/optic nerve of your patient be applied to the normative data base?

- High myopia
- Tilted disc
- Extremely large cups (and small)
- Patients less than 18 yo

108

The OCT can show glaucomatous change
BEFORE it is seen on visual fields



109

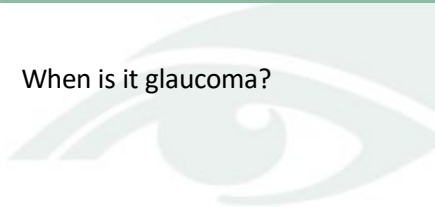
Estimating the Lead Time Gained by Optical Coherence Tomography in Detecting Glaucoma before Development of Visual Field Defects

Tammy M. Kang, MD,^{1,2,3} Chuan Zhang, MD,^{1,2} Linda M. Zangall, PhD,¹ Robert N. Weinreb, MD,¹
Folger A. Holden, MD, PhD¹

- At 95% specificity, up to **35% of eyes had abnormal average RNFL thickness** 4 years before development of visual field loss and **19% of eyes had abnormal results 8 years before field loss.**
- **Conclusions:** Assessment of RNFL thickness with OCT was able to detect glaucomatous damage before the appearance of VF defects on SAP. In many subjects, significantly large lead times were seen when applying OCT as an ancillary diagnostic tool.

110

When is it glaucoma?



111

Case MC

- 73 yo female presents for follow up: GL Suspect
- Past history single elevated IOP
- BCVA 20/25 and 20/20
- IOP 21 RE 19 LE;
– CCT 560u R 565u L
- Anterior segment normal
- Mild NS and cortical cataracts

112

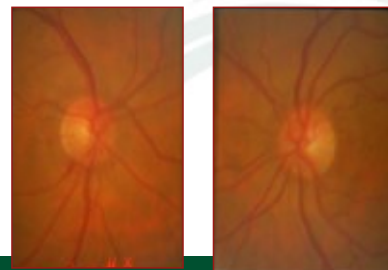
The ON

- Small optic discs OU
- RE c/d ~ 0.6 but
 - Appeared saucerized infero temporally
 - Broadening of a vein as it crossed edge disc
 - ? Small disc hemorrhage
- LE c/d .35

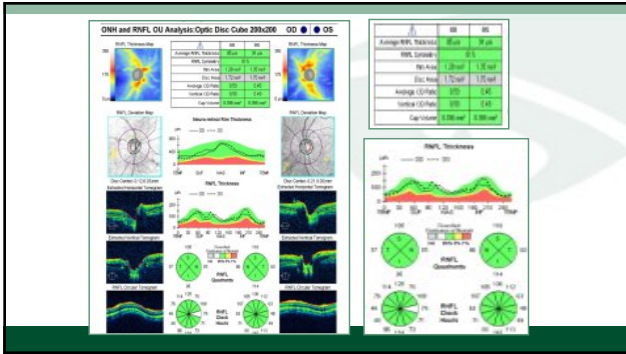


113

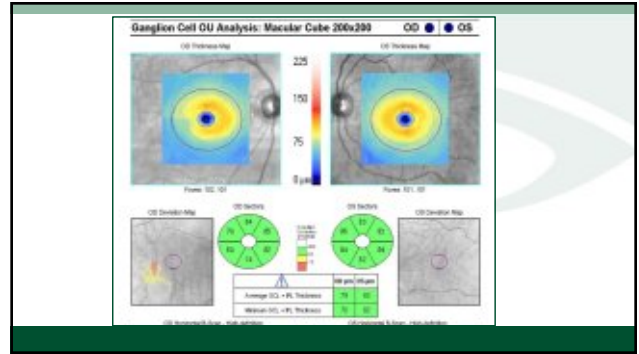
Photos



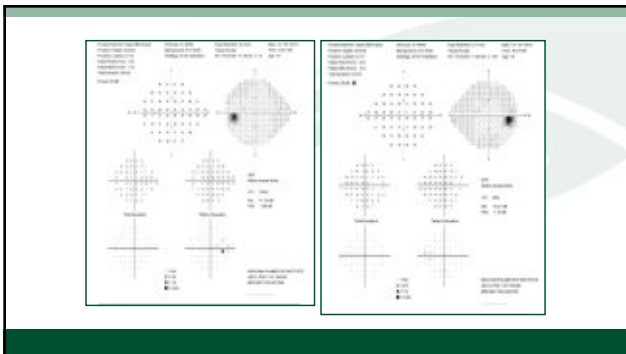
114



115



116

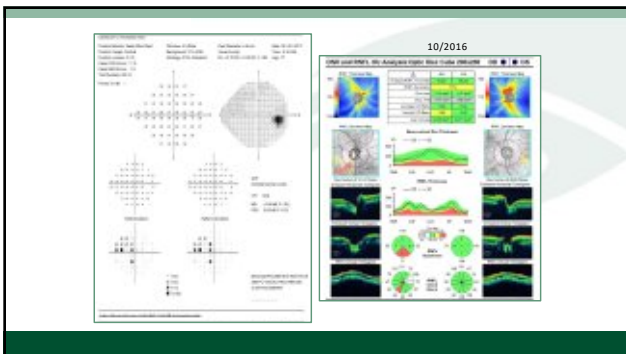


117

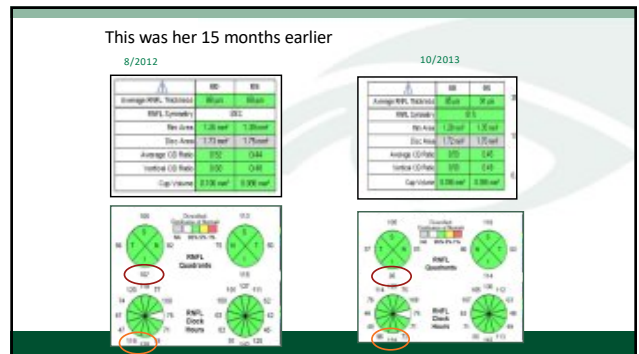
Summary

- Suspicious disc
- Borderline IOP
- Normal visual field
- Normal OCT *
- What did I do? Observed (but did discuss tx)
 - Patient education
 - Importance of follow up

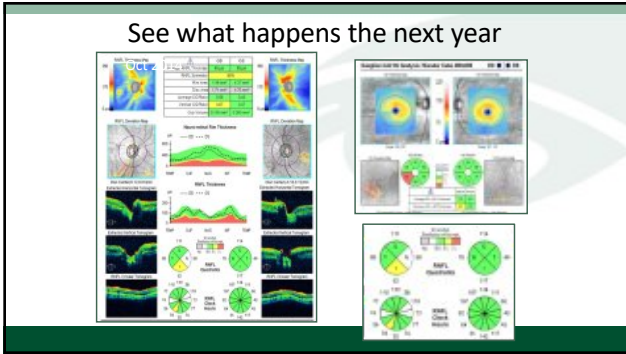
118



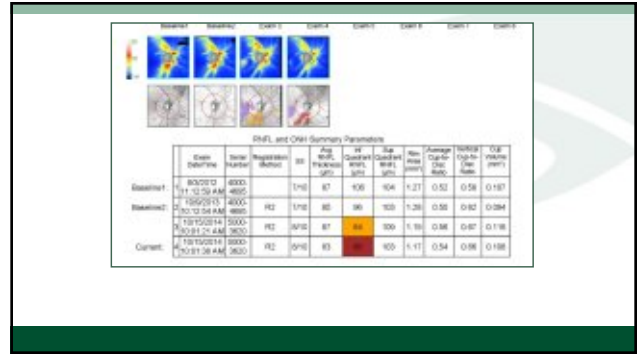
119



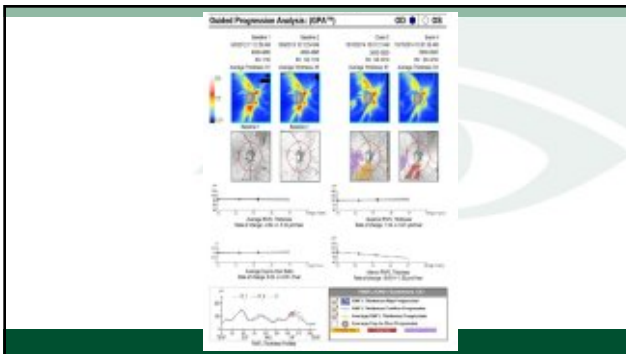
120



121



122

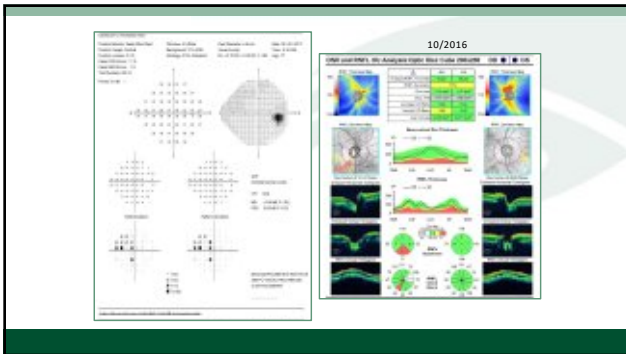


123

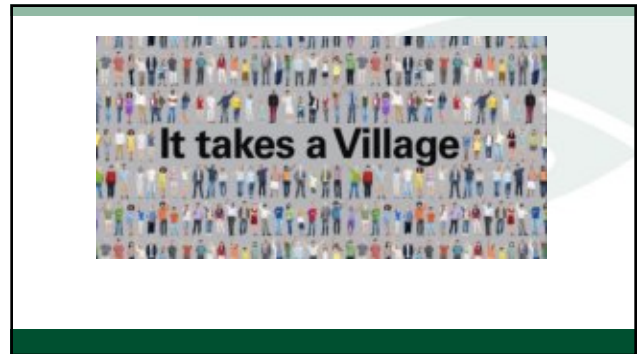
Case MC progression

- Clinical suspicion proved true
- Initial progression in normal range and continued
 - Rate is important consideration
- Treatment initiated
- Subtle corresponding VF defect evolved
- Currently stable in short term on well tolerated meds

124



125



126

It Takes a Village to Manage Glaucoma Patients

- All the data that is gathered is critical!
 - IOP measurement
 - Optic nerve evaluation
 - Visual fields
 - OCT
- The data needs to be accurate and reliable
- Even though the patient comes to see **“their doctor”** for glaucoma
- Everybody who sees these patients along the way plays a critical role in the care of a glaucoma patient

