VA TO VEP:

Update on structure and function testing in glaucoma

Pinakin Davey OD, PhD, FAAO Professor and Director of Research



Disclosure

- Research Grants VectorVision, ZeaVision, Topcon
- Consultant Bausch & Lomb, ZeaVision
- Speaker Optovue, Sanofi, Bausch & Lomb

If damage occurs throughout the retina, how does visual acuity remain stable?

What about other visual tasks?

Axonal facts



- 700,000 to 1.2 million
- Large variation
- Count of axons increase with increase in area.
- 50% of axons to the macula

Contrast sensitivity

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So many types of CS which one to use?

- To some extent it does not matter...
- The values from one can predict the values of other... in healthy population
- So use any CS testing
- In part specific testing at various cycles per degree
- 3, 6,12 and 18 cycles/degree testing

Association of Structural and Functional Measures With Contrast Sensitivity in Glaucoma

NIMA FATTHU, SARA NOWROOZIZADDH, SHARON HENRY, ANNE E, COLEMAN, JOSEPH CAPRIOLI, AND KOUROS NOURI-MANDANI

 CONCLUSIONS: Structural and functional measures showed a fair relationship with contrast sensitivity. This association was most prominent between full-thickness macular measures or central VF parameters and CS at 6CPD

AJO 2017;178;129-139.



Varying spatial frequencies and contrast levels Without and with glare •

•









- affected in patients with glaucoma.
- Mid spatial frequencies perhaps the most indicative of damage
- Visual acuity is affected when central 4 visual field points are affected

Risk Assessment technology

- Amount of nerve tissue remaining
- Level of damage
- Cellular damage- sub-clinical
 - Electrophysiology
 - Blood Flow

The Scoring Tool for Assessing Risk (S.T.A.R. II) calculator



Probability of conversion in 5- years <5% observe and monitor 5 to 15% consider treatment >15% treat

- OHTs and EGPS data
- Intended for use only in untreated OHT patients
- Age (30-80)

ultrasound

- IOP 20-32 mmHg
- CCT 475 to 650 microns
 PSD 0.50 to 3.00 dB
- C/D ratio vertical 0.00 to 0.8
- On average OCT corneal thickness lesser than

Anterior segment OCT







Difference between optical and ultrasound pachymetry measurments

Author	Difference in OCT and ultrasound values
Kim et al AJO 2008	26 microns
Wang et al J Refract Surg 2008	38 microns
Gunvant & Darner Medical Imaging 2011	13 microns

Kim, H.Y., Budenz, D.L., Lee P.S. et al., "Comparison of central corneal thickness using anterior segment optical coherence tonography vs ultrasonic pachymetry. Am J Ophthalmol.; 19;238-323 (2008).
Wang, J.C., Bunec, C., and Lee, H.M., "Intrasperative corneal thickness measurement using optical coherence pachymetry and corneo-gage plus ultrasound pachymetry J Refract Surg. 24(5):60-6 (2008)
P Gunavant, R. Damer: Evaluation of corneal thickness measurements toking optical coherence tomography and ultrasound technique and determination of specificity in keratoconus screening Medical Imaging: 7566i Br-B8

Corneal Thickness Maps





Glaucoma Symptom Scale

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Lee B et al. Arch Ophthalmol 1998

Evaluate the cornea and conjunctiva

- Look at Epithelium
- Pay attention to dry eye and glaucoma -particularly if multiple meds
- Even when patient does not complain they may have sub-clinical dry eyes.
- Extreme dryness changes in stromal thicknessErroneous estimates of risk ??







Stromal thickness



Gonioscopy

 $\begin{array}{l} \mathsf{A} = \mathsf{Above Schwalbe line, totally}\\ \mathsf{occluded angle.}\\ \mathsf{B} = \mathsf{Behind the Schwalbe line,}\\ \mathsf{peripheral iris is in contact with}\\ \mathsf{TM.}\\ \mathsf{C} = \mathsf{Scleral spur liris root at the}\\ \mathsf{level of scleral spur}\\ \mathsf{D} = \mathsf{Deep anterior ciliary body}\\ \mathsf{seen.}\\ \mathsf{E} = \mathsf{extremely deep} \end{array}$

Guidelines recommend once a year procedure



Curvature of periheral iris

Angle approach

Iris insertion

Angle Measurement with Quantification





Anterior segment Angle Analysis



Factors contributing pathophysiology in glaucoma



Changes in visual function after intraocular pressure reduction using antiglaucoma medications TS Rate, KIV Rave and LAS Ment P

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54 patients, timolol 0.5% or brimonidine 0.2% or travoprost 0.004%

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18 Gyzlet/Urgerei	0.07 (0.40	0.55 (0.46)	6/18 (0.42)	1.102



Summary

- Contrast sensitivity, glare and difficulty in seeing at night time is prevalent in patients due to glaucoma
- The contrast sensitivity when measured shows decline even with clinical tests.
- Changes post treatment in visual function is present independent of IOP levels decline.



Summary cont

- Evaluating contrast sensitivity can give a quality of life measure and perhaps additional information on treatment efficacy.
- Corneal evaluations with OCT may give insights that may be missed by ultrasound measurements
- Angle evaluations a must and OCT may be quick and comfortable method



Visual fields – don't like them; cant live without them.



1.00100.000.0000

4 Total deviation Devidation from average 5 Total deviation probability plot

6 Pattern

deviation Removes any generalized defects Cataract Pupil miosis

7 Pattern deviation probability plot











- Points spread evenly
- Data not representative of RNFL





Problems continued

• No real blind spot monitoring



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- No stimuli during fixation loss
- Automatic repetition of stimuli after blinking or darting
- Most accurate test possible



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HFA II versus HFA 3

- Larger touch screen
- Liquid crystal lens -8 to +8 only sph correction

Visual Field Index

- Percentage of normal age adjusted field
- Greater the number more normal
- Trend over time is given with a probability values as well



• Should work in theory; in reality does not!



Unique features of Octopus

 Octopus Features: Fixation Control
 Correct fixation
 No stimuli during fixation loss
 Automatic repetition of stimuli after blinking or darting

Most accurate test possible

Cluster analysis



Why cluster analysis?

Individual points may vary
Overall clusters are more stable
Also close representation to various bundles of RNFL
So in some respect better structure function relationship.

















Is this defect a sign of "early glaucoma"

Criteria for glaucomatous damage

1) GHT outside normal limits

2) PSD < 5% of normal individuals

3) A cluster of three or more **non-edge** points (pattern deviation plot) all of which are depressed at a p<5% and one of which is depressed at a p<1% on two occasions (respecting horizontal meridian)

- This criterion was written for 30-2, if 24-2 field is analyzed edge points are included.
- Criteria should be met on 2/3 issues mentioned above
- Confirmed on two occasions!

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Staging of disease



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Why is staging important?

- Treatment issues
- Management issues
- Prognosis
- Research

Glaucoma staging system-Brusini GSS -2









Outopus 600 too low / Patient too ligh Octopus 600 too high / Patient too low

Pulsar perimetry



Why does it help targeting specific ganglion cells?



Design of the PULSAR stimulus



Sensitivity thresholds with PULSAR perimetry



Example of SAP and functionspecific perimetry in the same eye



Principle of using stimulus V for low vision patients



Patient has cataract what do I do with Visual fields?

ORIGINAL ARTICLE

Effect of Cataract Opacity Type and Glaucoma Severity on Visual Field Index

Hyr Jin Chung*, Jeong Hoon Choi[†], Young-Chun Lee¹, and So-Young Kim[†]

- Visual field parameters improved after cataract surgery
- MD, PSD and VFI- less influenced in nuclear sclerosis
- MD, PSD and VFI greater effect in cortical cataract, particularly for early glaucoma

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Cataract in glaucoma patient

- Dilate as much as possible
- Depend on PSD plot more than total deviation
- Use imaging modalities more.

Sources of error

- Miosis: decreases threshold peripherally, increases variability centrally
- Lens opacities
- Uncorrected refractive error –decrease in contrast sensitivity
- Spectacles
- Ptosis

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Summary

- Time for change is here.
- Doing what we have always done is unlikely to yield progress.
- Great programs that make a lot of sense clinically
- New technology may identify glaucoma early and easier to follow

Electrophysiology



Electrophysiology has come a long way



Electrodes have come a long way









ERG sensors





Reference

Pattern Electroretinogram (PERG)



Retinal ganglion cell signal recorded at the lower lid in response to pattern stimuli



Steady sate- clinical state Pattern ERG Flicker ERG Steady state response (high frequency) Greater amount of information in shorter time:

300 responses

So where are the a, b, c waves?

- Transient ERG that are less in frequency produce them.
- Variable and very much laboratory dependent.
- Difficult to obtain clinically.



Sick versus dead ganglion cells- a debate











Interpretation of OCT



Eye and Brain

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ORIGINAL RESEARCH

Sensitivity and specificity of the iVue iWellnessExam™ in detecting retinal and optic nerve disorders

Catherine Awadi Samantha Slotnick^{3,3} Sanjeev Nath⁵ Jeroma Sheriman³⁴⁴

Non Southanson Colage of Optimizing Sc Dank role Store, 5. 3UHY Store Colage of Optimizing SUHY 5: Insolution "Optimized Super Conten-New York, NY USA Sensitivity and specificity were calculated for identifying normal and abnormal individuals

99 % Specificity 95.5% sensitivity in identifying retinal diseases 90% identifying optic nerve disease

Ganglion Cell Complex (GCC)





Other devices

- Zeiss Ganglion Cell analysis- GCL+ IPL
- Topcon Maestro gives both
 - NFL+ GCL+ IPL
 - GCL+IPL
- Spectralis gives individual layers.



How is GCC measured







Can GCC be used as an independent parameter to diagnose glaucoma?

The Applicability of Ganglion Cell Complex Parameters Determined From SD-OCT Images to Detect Glaucomatous Eyes

Paramastri Arimanast. MD.* Tahashi Sone, MD.* Tomoyaki Akira, PhD.9 Junko Tanaka, PhD.1 and Yoshiski Kinchi, MD. PhD*

(J Glaucoma 2013;22:713-718)

Methods: Two hundred sixty-one eyes, including 68 normal eyes and 32 preperimetric glaucoma, 81 early glaucoma, and 80 advanced glaucoma were analyzed in the present study. The thicknesses of the GCC and retinal nerve fiber layer were measured using RTV us spectral-domain optical coherence tomographic (SD-OCT) images. The area under the receiver operating characteristic (AUROC) curve and sensitivities at fixed specificities were calculated for each parameter. A logistic regression analysis was used to determine the risk factors for glaucoma.

cvaruation	for the OCT Patameter	s as briagnostic resis w	in the Abroc Care
	N vs. PG	N vs. EG	N vs. AG
GCCa	0.795 (0.667-0.882)	0.806 (0.727-0.866)	0.902 (0.838-0.942
GCCs	0.754 (0.617-0.853)	0.761 (0.678-0.828)	0.880 (0.809-0.928
GCCi	0.815 (0.690-0.897)	0.795 (0.714-0.858)	0.915 (0.851-0.953
FLV	0.745 (0.622-0.839)	0.789 (0.709-0.851)	0.948 (0.888-0.977
GLV	0.806 (0.679-0.891)	0.816 (0.740-0.874)	0.929 (0.871-0.961
RNFLa	0.740 (0.620-0.832)	0.734 (0.647-0.806)	0.910 (0.846-0.949
RNFLs	0.748 (0.626-0.840)	0.725 (0.636-0.798)	0.889 (0.817-0.935
RNFLi	0.723 (0.605-0.816)	0,700 (0,611-0,776)	0.912 (0.858-0.947

Arintawati et al / Glaucoma • Volume 22, Number 9, December 2013

Progression and glaucoma

- Progression
- Consensus is limited
- Visual fields tend to fluctuate in early glaucoma
- Reliable and repeatable structural measurements is very valuable
 - Fourier domain OCT 5 microns accuracy.



CASE MR.X

- DOB 1951
- Asian Male
- Medical unremarkable
- Family medical Brother Glaucoma
- Tmax 23 OU
- On PGA IOPs 15-18 OU
- Overall quite regular in care and compliance

During follow-up

- One year had changed to generics PGA
- Seen by 4 different doctors in practice....
- Charts And observations





Case # 1 Easy Case /OCT helps Management

- 61 year old male referred to UEC for high IOP readings (pt. asymptomatic)
- MH: Atrial fib. (2 yrs.), HTN (10yrs.), Pre-diabetic (3 yrs.)
- POH: Wears bifocals, no Ocular surgeries
- FOH: Glc (maternal), RD (paternal)
- Meds.: eliquis, metoprolol, Multi-V
- CC: Reports loss of side Vision/OD x 2 mon.

Courtesy David Sendrowski OD

Exam Data

- BCVA: R 20/20 L 20/20
- Pupils: Normal (-) APD
- IOP: R 34,35 mm Hg L 29,29 mm Hg
- Pachymetry R 525, L 523
- C/DR.90 L.80
- VF (see next slides)
- OCT (see next slides)





OCT results: what does it mean?

- Ave RNFL 65 microns, Ave GCC 58.27 microns
- Patient has advanced POAG
- Both RNFL and GCC near "floor effect" need to follow patient with VF
- Left:
 - Ave RNFL 76 microns, Ave GCC 75.15 microns
 - Patient has mod/advanced POAG
 - Can use OCT for GCC and RNFL for monitoring progression

Questions

- Would you treat?
- How did the OCT help with the decision for treatment for the right eye? Left eye?
- What VF would be best to do in the right?
- What would be your best management of the right eye?
- What might the best management be in the left eye?
- When would you do the next VF and OCT?



- We know the advantages of multivitamins and AMD
 - · Prevents oxidative damage
 - Quenches any free radical
 - Prevents photoreceptor death
 - Absorbs stray light
- Oxidative damage can also occur in glaucoma

Where is the evidence?

- Aqueous humor has lot of vitamin-C
- Macular pigment optical density is lower in glaucoma patients than individuals without glaucoma

Evidence of lower macular pigment optical density in chronic open angle glaucoma

Estera Igras,¹ James Loughman,^{2,3} Matthew Ratzlaff,⁷ Rönän O'Casimh,⁴ Colm O'Brien^{1,5} Jam L. et al. W / dothamer 2013/87/94-398. ac. N1005pgetweek 2013 (0115)

Charman Same

may 2010/2020/2020/2027 0 2070

Macular pigment is a modifiable risk factor and can be increased with vitamin intake

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Lower Macular Pigment Optical Density in Foveal-Involved Glaucoma

We Frag had, ABCTR, BETTAM, Jones Longboor, CHOL MAX "Code of Bons, 1993 (add. 1837

Summary

- Measure Macular pigment in glaucoma patients
- Measure Ganglion Cell Complex/ Analysis
- Recommend multivitamin intake with good amount of Lutein and Zeaxanthin- **Dosage matters**!
- Helps all age related diseases.

Whats new with OCT

OCT Angiography: A New Approach to Protecting Vision

- Non-invasive visualization of individual layers of retinal vasculature
- Pathology not obscured by fluorescein staining or pooling
- Image acquisition requires less time than a dye-based procedure
- Reduced patient burden allows more frequent imaging to better follow disease progression and treatment response



How Does AngioVue Work?

Principles of AngioVue OCTA

- Uses motion contrast to detect blood flow
- Rapidly acquire multiple crosssectional images from a single location on the retina
- Flow is the difference between two sequential scans
 - Flow = Frame #1 Frame #2



Structure + Function: Retina















Structure + Function: Optic Nerve







Structure: En Face

See The Vessels Like You've Never Seen Them Before!

- Segment retinal vasculature into individual layers
- Eliminate effects of dye-based blurring and pooling
- Isolate areas of interest
- View 3x3mm and 6x6mm scans



30 µm Below RPE Reference → 60 µm Below RPE Reference

Non-Invasive, Dye-Free & Fast

- No injection, no fluorescein
- Order test as needed to more closely monitor disease progression and treatment response
- Image acquisition in less than three seconds
- Total time in room approximately 10 minutes

Motion Correction Technology (MCT™): Minimizes Saccadic Motion to Enhance Image Intensity





Without MCT

Angle Measurement with Quantification







AngioMontage Provides a Wider Field of View



AngioVueHD High-Resolution Automatic Montage



Images courtesy of Adil El Maftouhi, O.D., Lyon, France

AngioVue Montage for imaging outside the macula.

10x6 mm FOV with outstanding resolution of retinal vasculature in the macula and optic disc.



OCT: Structure 800000



sly diagnosed patient. Images courtesy of Michel Puech, MD, FRCS







Moderate Glaucoma



Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego



Advanced Glaucoma



Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

Quantification of Optic Disc Vasculature

- OCT and OCTA analysis from the same scan: Automatic detection of BMO
 - Rim and Cup area measured within BMO plane
- Vessel density analysis based on RPC (ILM-NFL)
 Enables extensive analysis of disc structure and vasculature •



AngioDisc Trend Analysis



RNFL Thickness Trend Analysis



Overview Report Provides Disc Health at a Glance

One scan generates report showing:

- OCT Intensity
- RPC
- RPC Density
- RNFL Cup/Disc



Disc Overview Report Brings New Information to Glaucoma Management



Image Courtesy: Drs. Weinreb, Nudleman, Goldbaum, Zangwill, UCSD, San Diego, CA (USA)



Summary

- We live in exciting times
- Early detection is getting within reach.
- Functional measures and structural measures are improving rapidly.
- Next step....reverse glaucomatous damage