



## NEW TECHNOLOGIES IN GLAUCOMA MANAGEMENT: WHAT TO BUY, HOW TO MAKE IT WORK IN YOUR PRACTICE



J. James Thimons, O.D.,FAAO  
Chairman, National Glaucoma Society  
jimthimons@gmail.com

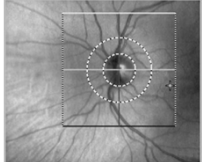


## Cirrus™ HD-OCT

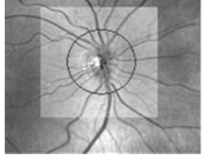
Certainty in Seconds. Certainty for Years.™

Cirrus software version 6.0  
Speaker Slide Set  
CIR.3992 Rev B  
01/2012

### Glaucoma – RNFL Thickness Analysis

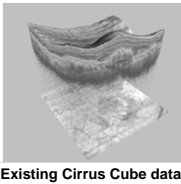


**OPTIC DISC CUBE SCAN**  
The 6mm x 6mm cube is captured with 200 A-scans per B-scan, 200 B-scans.




**CALCULATION CIRCLE**  
AutoCenter™ function automatically centers the 1.73mm radius peripapillary calculation circle around the disc for precise placement and repeatable registration. The placement of the circle is not operator dependent. Accuracy, registration and reproducibility are assured.

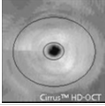
### Cirrus Software Version 6.0 New insights from the cube and more!



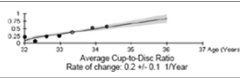
**Existing Cirrus Cube data**



**Advanced RPE Analysis**



**Ganglion Cell Analysis**

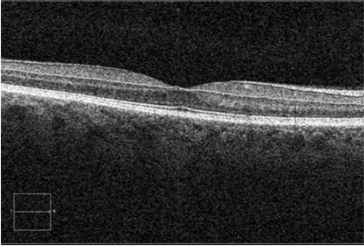


**GPA™ with Optic Nerve Head**

### Ganglion Cell Analysis

- Measures thickness for the sum of the ganglion cell layer and inner plexiform layer (GCL + IPL layers) using data from the Macular 200 x 200
- or 512 x 128 cube scan patterns.

RNFL distribution in the macula depends on individual anatomy, while the GCL+IPL appears regular and elliptical for most normals. Thus, deviations from normal are more easily appreciated in the thickness map by the practitioner, and arcuate defects seen in the deviation map may be less likely to be due to anatomical variations.

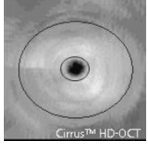


Carl Zeiss Medtec, Inc. Cirrus 6.0 Speaker Slide Set CIR.3992 Rev B 01/2012

### Ganglion Cell Analysis

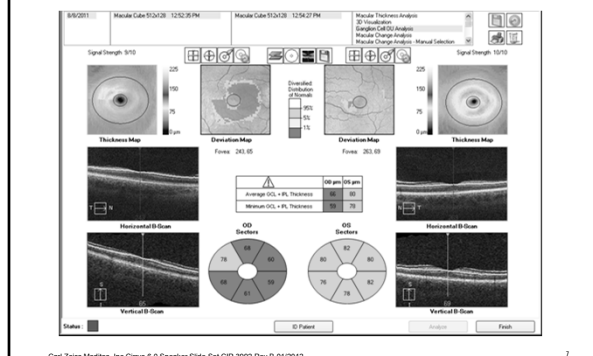
The analysis contains:

- Data for both eyes (OU)
- Thickness Map - shows thickness measurements of the GCL + IPL in the 6mm by 6mm cube and contains an elliptical annulus centered about the fovea.
- Deviation Maps - shows a comparison of GCL + IPL thickness to normative data.
- Thickness table - shows average and minimum thickness within the elliptical annulus.
- Sector maps - divides the elliptical annulus of the Thickness Map into 6 regions: 3 equally sized sectors in the superior region and 3 equally sized sectors in the inferior region. Values are compared to normative data.
- Horizontal and Vertical B-scans.



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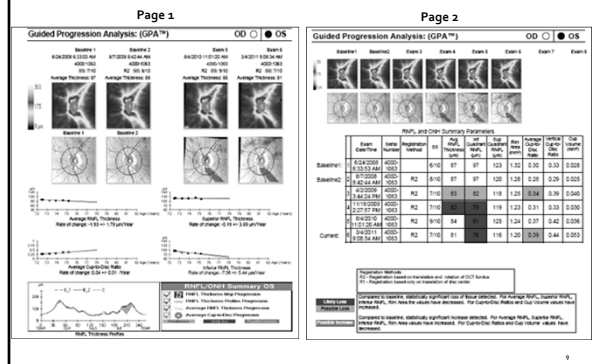
## Ganglion Cell Analysis



## Updated Guided Progression Analysis (GPA™) Optic Nerve Head information now included

- Average Cup-to-Disc Ratio plotted on graph with rate of change information.
- RNFL/ONH Summary includes item "Average Cup-to-Disc Progression".
- Printout includes an optional second page with table of values, including Rim Area, Disc Area, Average & Vertical Cup-to-Disc Ratio and Cup Volume. Each cell of the table can be color coded if change is detected.
- Miscellaneous updates to the report design.

## Updated Guided Progression Analysis (GPA™)



## RAPDX: UNDERSTANDING THE OPTIC NERVE IN GLAUCOMA

## RAPDX Expanded Pupil Diagnostics



- Relative
- Afferent
- Pupillary
- Defect

- Automated pupillometry
- Designed to detect a relative afferent pupillary defect (RAPD)
- Assessment of differential amplitudes and latencies
- Objective test of visual pathway function
- Test time is 1 to 5 minutes

## Relative Afferent Pupillary Defect

- Relative afferent pupillary defect (RAPD) is an **asymmetry** in the pupillary light response
- Detection of RAPD is performed by alternately illuminating each eye while comparing the velocity and amplitude of the pupillary responses
- Neutral density filters in 0.3 logarithmic unit steps aid in the detection and quantification of RAPD
- The size of the RAPD can be quantified by the density of the neutral density filter required to balance the response of each eye

Youtis AA, Eggenberger ER. Correlation of Relative Afferent Pupillary Defect and Retinal Nerve Fiber Layer Loss in Unilateral or Asymmetric Demyelinating Optic Neuropathy. *Investigative Ophthalmology and Visual Sciences*. August 2010, Vol. 51: 4013-4016.

### Eye Diseases that may lead to a RAPD

- **Glaucoma:** Even though glaucoma affects both eyes, if the disease is more severe in one eye, a RAPD may be detected
- **Retinal Disease:** Diabetic retinopathy, arterial occlusions, sickle-cell retinopathy, and retinal detachments may produce a RAPD
- **Optic Nerve Disease:** Disorders such as optic neuritis are a common cause of RAPD
- **Neurological Disease:** Lesions of the midbrain, compressive lesions

### Clinical Benefits of RAPDx Testing

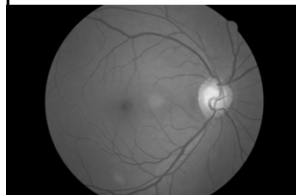
- RAPDx technology represents a paradigm shift in pupil testing
- Remarkable sensitivity for detecting glaucoma
  - Sensitivity = 81%
  - Specificity = 90%
- By comparison, IOP has a 65% sensitivity for detecting glaucoma
- RAPDx results correlate with VF and RNFL tests



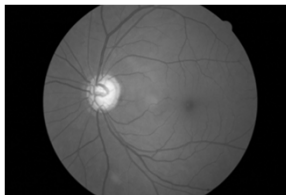
Chang OS. The Detection of Glaucoma Using Pupillography. Glaucoma Center of Excellence & Dana Center for Preventive Ophthalmology, Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland. 2012.

### Case Report

59-year-old black female with an eleven year history of glaucoma

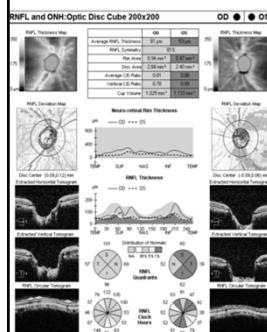


Cup-to-disc ratio = .65/.70



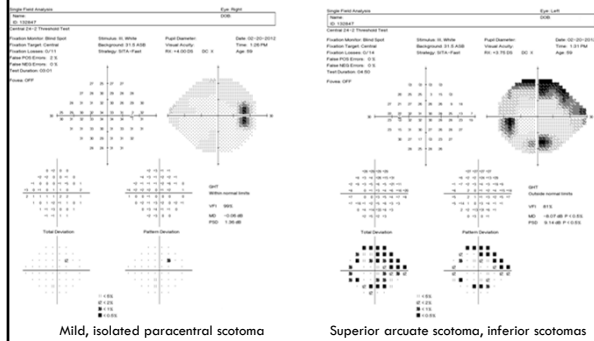
Cup-to-disc ratio = .75/.80

### Optical Coherence Tomography



- Severe fallout of the retinal nerve fiber layer in the left eye
- Abnormal TSNIT curve profile analysis
- Abnormal sector plot analysis
- Abnormal symmetry
- OCT test results are consistent with glaucoma

### Visual Field Examination



### RAPDx Pupillary Testing - Amplitude

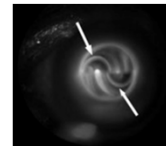


## RAPDx Pupillary Testing - Latency



## Goldmann Applanation

- The Gold standard in IOP measurement for 50 years
- Goldmann & Schmidt : when tonometer head is 3.06 mm in diameter and there is a normal central corneal thickness of 500 microns – surface tension = corneal rigidity
- **CCT is relatively constant in the absence of corneal disease**



Goldmann H, Schmidt T. Uber applanationstonometrie. Ophthalmologica 1957;134:221-42

## OHTN and CCT

- **Falsely elevated intraocular pressure due to increased central corneal thickness.** Graefes Arch Clin Exp Ophthalmol. 1999 Mar;237(3):220-4
- 48 OHTN subjects - 592 +/- 39
- 63 patients with POAG 536 +/- 34
- 106 normal subjects 545 +/- 33
- **Relationship between corneal thickness and measured intraocular pressure in a general ophthalmology clinic.** Ophthalmology. 1999 Nov;106(11):2154-60
- 232 OHTN subjects – 579.5
- 335 patients with POAG 550.1
- 235 normal subjects 545 +/- 33
- 52 Normal-tension glaucoma 514

## Central Corneal Thickness in the Ocular Hypertension Treatment Study (OHTS)

James D. Brandt, MD,<sup>1</sup> Julia A. Beiser, MS,<sup>2</sup> Michael A. Kass, MD,<sup>2</sup> Mae O. Gordon, PhD,<sup>2</sup> and the Ocular Hypertension Treatment Study (OHTS) Group

Mean CCT 573.0 +/- 39.0  $\mu$ m  
24% had a central corneal thickness > 600  $\mu$ m

CCT for African Americans subjects (555.7 +/- 40.0) was 23  $\mu$ m thinner than for white subjects (579.0 +/- 37.0) - P < 0.0001

Other factors associated with greater mean central corneal thickness were younger age, female gender, and diabetes.

## CCT as a risk factor in patients with glaucoma

- Analysis of 350 eyes of 190 patients with POAG during initial visit to specialist.
  - In **multivariate** analysis, lower CCT was significantly associated with worsened AGIS score, worsened mean deviation of visual field, and increased vertical and horizontal cup-disc ratios.
  - Herndon et al. Central corneal thickness as a risk factor for advanced glaucoma damage. Arch Ophthalmol. 2004 Jan;122(1):17-21



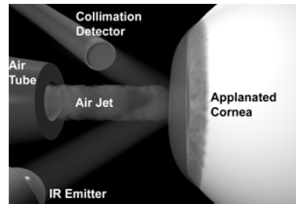
- **IOPcc**: IOP compensated for corneal effects, including corneal hysteresis, a measure of viscoelasticity of the cornea (elasticity)
- **IOPg**: Goldmann equivalent IOP

### ORA Signal Analysis

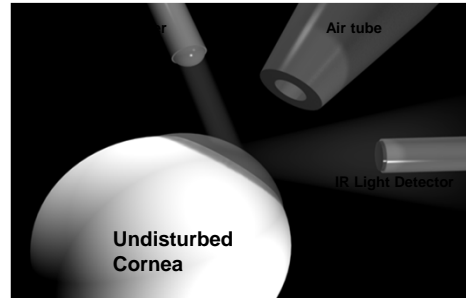
The ORA optical system records 400 data samples of reflected IR light intensity during the rapid (30 ms) in/out corneal deformation.

The optical signal (red curve) is a "dynamic map" of the cornea during the rapid in/out deformation.

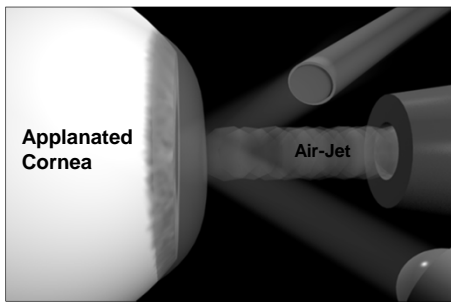
The signal provides additional information about corneal biomechanical properties, revealing "signature" characteristics of the eye being measured.



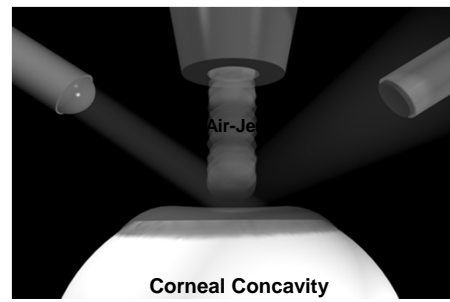
Applanation Detection I



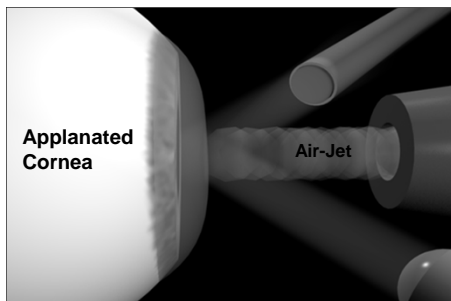
Applanation Detection II



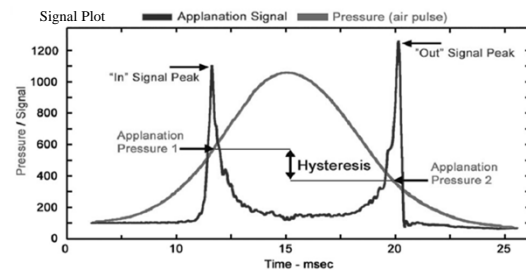
Applanation Detection III



Applanation Detection IV



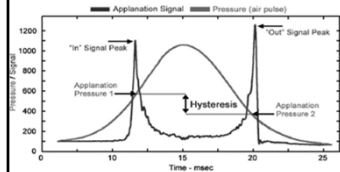
Applanation Signal Plot



## Corneal Hysteresis

### Corneal Hysteresis

Identified by David Luce, Ph.D., Corneal Hysteresis is the difference in the inward and outward pressure values obtained during the dynamic bi-directional applanation process employed in the Ocular Response Analyzer, as a result of viscous damping in the cornea.



## Corneal Resistance Factor

An indicator of the overall "resistance" of the cornea, including both the viscous and elastic properties. It is significantly correlated with Central Corneal Thickness (CCT) and GAT, as one might expect, but not with IOPCC.

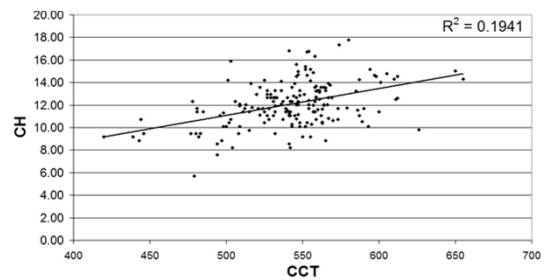
$$\bullet \text{CRF} = P1 - (0.7 * P2)$$

## Corneal-Compensated IOP (IOPcc)

- An Intraocular Pressure measurement that is less affected by corneal properties than other methods of tonometry, such as Goldmann (GAT). IOPcc has essentially zero correlation with CCT in normal eyes and stays relatively constant post-LASIK.

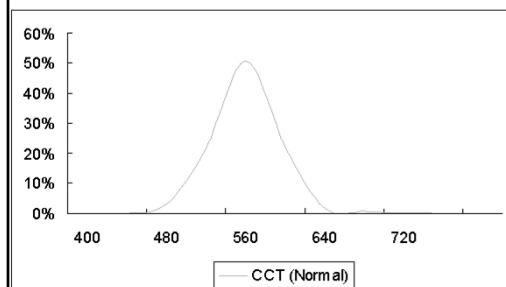
$$\bullet \text{IOPcc} = P2 - (0.43 * P1)$$

CCT vs. CH - 184 normal eyes



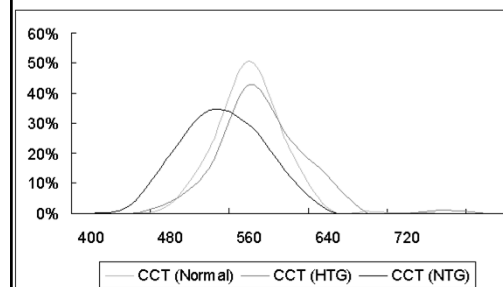
Data courtesy New England College of Optometry

## Frequency Distribution: CCT



C. E. Fraser, et al. ARVO, 2010.

## Frequency Distribution: CCT



C. E. Fraser, et al. ARVO, 2010.

**Lower Corneal Hysteresis is Associated With More Rapid Glaucomatous Visual Field Progression**

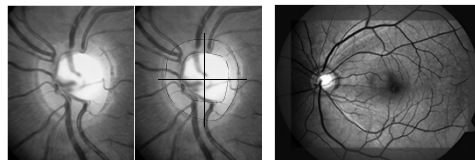
*Carlos Gustavo V. De Moraes, MD,\*† Victoria Hill, BS,\*‡ Celso Tello, MD,\*‡ Jeffrey M. Liebmann, MD,\*†§ and Robert Ritch, MD\*‡*

- 153 glaucomatous eyes, with >8 visual fields, followed for > 5 years
- Progressing eyes (n=25) had lower CCT (525 $\mu$  vs 542 $\mu$ , P=0.04) and lower CH (7.5 mmHg vs 9.0 mmHg), P<0.01) compared with nonprogressing eyes.
- By multivariate analysis, peak intraocular pressure (OR=1.13, P<0.01), age (OR=1.57, P=0.03), and CH (OR=1.55, P<0.01) were significant predictors of progression.

De Moraes, G. et al. J Glaucoma. 2011; ePub.

**Technologies in the Diagnosis and Management of Glaucoma**

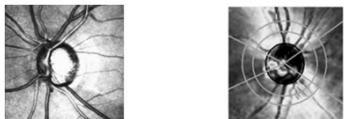
**Photograph**



<http://informahealthcare.com/doi/abs/10.3109/09286586.2012.691601>

**Technologies in the Diagnosis and Management of Glaucoma**

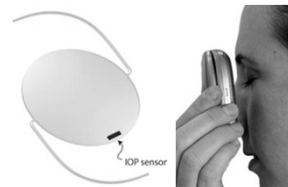
**Scanning Laser Ophthalmoscopy (SLO)  
Scanning Laser Polarimetry (SLP)**



Grewal DS, Sehi M, Cook RJ, Greenfield DS and Advanced Imaging in Glaucoma Study Group. The Impact of Retardance Pattern Variability on Nerve Fiber Layer Measurements over Time Using GDx with Variable and Enhanced Corneal Compensation. Invest Ophthalmol Vis Sci. 2011;52:4516-4524.

**Technologies in the Diagnosis and Management of Glaucoma**

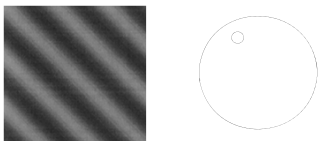
**IOL Tonometry**



<http://www.launchpnt.com/portfolio/biomedical/intraocular-pressure-sensor>

**Technologies in the Diagnosis and Management of Glaucoma**

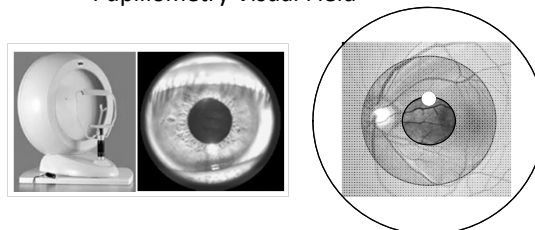
**FDT/SWAP**



Horn FK, Lämmer R, Mardin CY, Jünemann AG, Michelson G, Lausen B, Adler W. Combined evaluation of frequency doubling technology perimetry and scanning laser ophthalmoscopy for glaucoma detection using automated classification. J Glaucoma. 2012 Jan;21(1):27-34.

**Technologies in the Diagnosis and Management of Glaucoma**

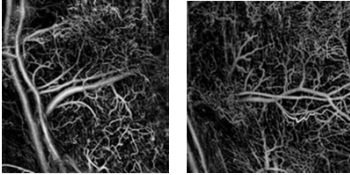
**Pupillometry Visual Field**



Yoshitomi T, Matsui T, Mukuno K, Ishikawa S. Objective visual field measurement using "pupil perimetry". Nihon Ganka Gakkai Zasshi. 1996 Oct;100(10):825-31.

**Technologies in the Diagnosis and Management of Glaucoma**

**Doppler Optical Coherence Tomography**

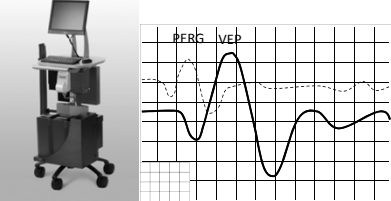


Schmoll, T. and Leitgeb, R. A. (2012), Heart-beat-phase-coherent Doppler optical coherence tomography for measuring pulsatile ocular blood flow. *J. Biophoton.*  
doi: 10.1002/jbio.201200029

**VEP in Glaucoma**

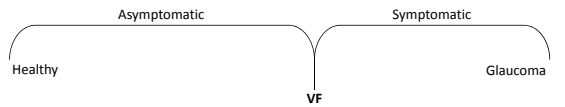
**Technologies in the Diagnosis and Management of Glaucoma**

**Pattern Electroretinogram / Visual Evoked Potential**



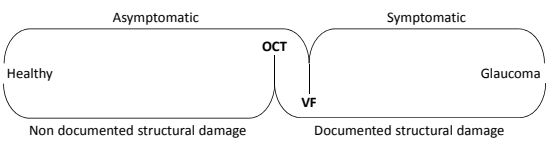
Prata TS, Lima VC, De Moraes GV, Trubnik V, Derr P, Liebmann JM, Ritch R, Tello C. Short Duration Transient Visual Evoked Potentials in Glaucomatous Eyes. *J Glaucoma* 2011.

**Technologies in the Diagnosis and Management of Glaucoma**



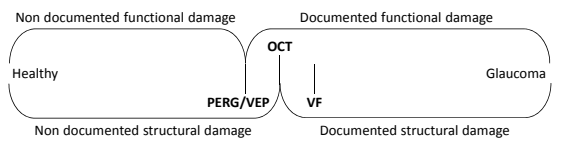
Ellish NJ, Higginbotham EJ. Evaluating a visual field screening test for glaucoma: how the choice of the gold standard affects the validity of the test. *Ophthalmic Epidemiol.* 2001 Dec;8(5):297-307.

**Technologies in the Diagnosis and Management of Glaucoma**



Schuman JS, Hee MR, Arya AV, Pedut-Kloizman T, Puliafito CA, Fujimoto JG, Swanson EA. Optical coherence tomography: a new tool for glaucoma diagnosis. *Curr Opin Ophthalmol.* 1995 Apr;6(2):89-95.

**Technologies in the Diagnosis and Management of Glaucoma**



Parisi V, Miglior S, Manni G, Centofanti M, Bucci MG. Clinical ability of pattern-electroretinograms and visual evoked potentials in detecting visual dysfunction in ocular hypertension and glaucoma. *Ophthalmology.* 2006 Feb;113(2):216-28.



**Technologies in the Diagnosis and Management of Glaucoma**

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**Normal IOP**

Bach M, Unsoeld AS, Philippin H, Staubach F, Maier P, Walter HS, Bomer TG, Funk J. Pattern ERG as an early glaucoma indicator in ocular hypertension: a long-term, prospective study. Invest Ophthalmol Vis Sci. 2006 Nov;47(11):4881-7.

**Technologies in the Diagnosis and Management of Glaucoma**

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**OHT**

Bach M, Unsoeld AS, Philippin H, Staubach F, Maier P, Walter HS, Bomer TG, Funk J. Pattern ERG as an early glaucoma indicator in ocular hypertension: a long-term, prospective study. Invest Ophthalmol Vis Sci. 2006 Nov;47(11):4881-7.

**Technologies in the Diagnosis and Management of Glaucoma**

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**Glaucoma**

Bach M, Unsoeld AS, Philippin H, Staubach F, Maier P, Walter HS, Bomer TG, Funk J. Pattern ERG as an early glaucoma indicator in ocular hypertension: a long-term, prospective study. Invest Ophthalmol Vis Sci. 2006 Nov;47(11):4881-7.

**Technologies in the Diagnosis and Management of Glaucoma**

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**EYE**

IOP

Ganglion Cell

**LGN**

**CORTEX**

Yücel YH, Zhang Q, Weinreb RN, Kaufman PL, Gupta N. Atrophy of relay neurons in magno- and parvocellular layers in the lateral geniculate nucleus in experimental glaucoma. Invest Ophthalmol Vis Sci. 2001 Dec;42(13):3216-22.

**QUANTEL MEDICAL**

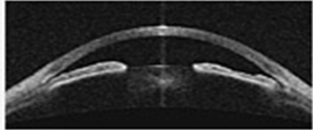
**Linear UBM**

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ClearScan™  
and Clinical Applications

**Ultrasound Biomicroscopy (UBM) of the eye**

### Visante™ OCT Anterior Segment Imaging and Biometry



### Problems with traditional Gel & Shell examination method

- Worry about probe tip hitting the cornea
- Probe sterility issues
- Methodology concerns
  - Patient must recline
  - Gel often required
  - Shell must be inserted under the lids and (uncomfortable)
  - Likelihood of corneal abrasions from shell as posterior structures are examined



### Methodology

- Fill bag ¾ with tap water
- Add water slowly to minimize air bubbles
- LIN50 - USE DISTILLED WATER



### Methodology (Preferred)

Patient can be examined sitting (ocular structures & dynamics same when viewed with slit lamp)



## Clinical Applications

## Glaucoma

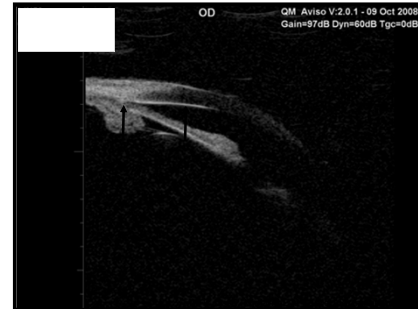
### Glaucoma (lights off exam)



Phakomorphic



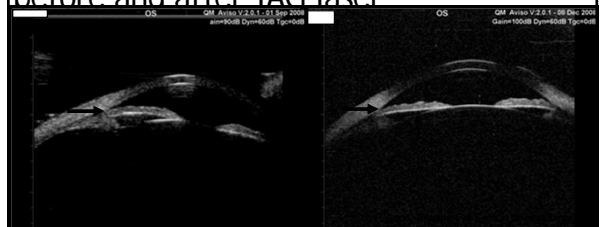
Phakomorphic  
Bulky ciliary body in phakomorphic angle closure



Convex iris  
in pupil block



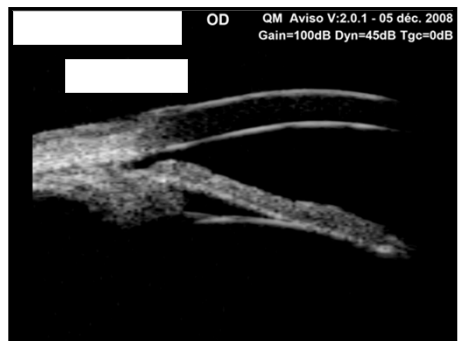
Pupil Block  
before and after YAG laser



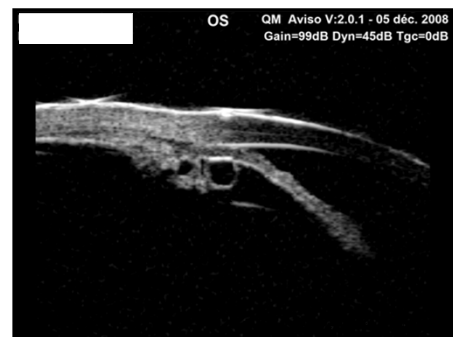
Before

After

Plateau iris



Cyst



## Drug Eluting Contacts

- Harvard Medical Center Researchers
- Recipients of MIT innovators in Life Sciences competition
- Daniel Kohane, MD, PhD (anesthesiology)
- Coating Polylactic co-glycolic acid (PLGA) is coated with films containing Polyhydroxy-methacrylate by UV polymerization
- Research is being funded by:
  - National Institute of Medical Studies
  - National Eye Institute
  - Boston KPro foundation
- Duration can be as long as 100 days
- Limitation will be the duration of CL wear

## Punctal Plugs with Latanoprost Core

- QLT, Inc
- 44-g Latanoprost Punctal Plug Delivery System
- Phase II
- Data:
  - Mean change from baseline -3.5 mmHg
  - 36% showed reduction of  $\geq 5$ mmHg
  - Overall goal of 90% retention/ Initial 75%
  - Second generation plug 90%
  - Goal of therapy 90 days of Tx

## Tracking the Elusive Diurnal!

- Sensimed: Swiss medical device company. Jean Marc Wismer CEO
- Device is called Triggerefish
- Tracks fluid pressure in the eye and beams data to palm size recorder.
- Uses a circular antenna taped around the eye and connected to a battery powered portable recorder.
- This transmits radio frequency energy to an ultra thin gold ring in the CL. This powers a chip embedded in the lens.
- Additionally on the lens in an ultra thin platinum ring that stretches in response in variation in eye shape secondary to pressure.
- Available in Europe. Primary trial at University Hospitals of Geneva