# Ocular Response Analyzer (ORA) and Glaucoma, Is it helpful?

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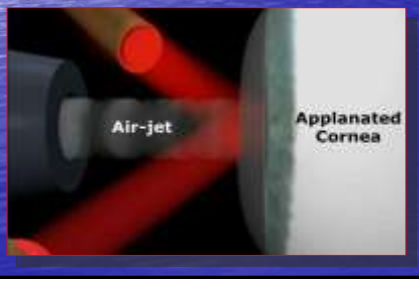
I haven't any financial interest

# One Device, Four Parameters

- **IOPCC** - Corneal Compensated IOP
- **IOPG** - Goldmann Correlated IOP
- **CH** - Corneal Hysteresis
- **CRF** - Corneal Resistance Factor

# Ocular Response Analyzer

ORA Provides a dynamic, precisely metered collimated air pulse and a quantitative electro-optical system that monitors the deformation of the cornea through the corneal reflex of an infrared light. (Luce, J Cataract Refract Surg, 2005).




# Ocular Response Analyzer

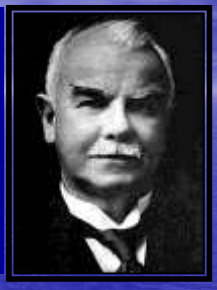
- **CH:** is a difference in the inward and outward pressure obtained during the dynamic applanation, as a result of viscous damping in the cornea.

- **CRF:** "Resistance" of the cornea, including viscous and elastic properties, ***Correlated with CCT.***

## Definitions

**Hysteresis** **Hys`te*re"sis\, n. [NL., fr. Gr. to be behind, to lag.]. coined by Sir James Alfred Ewing in 1890.**

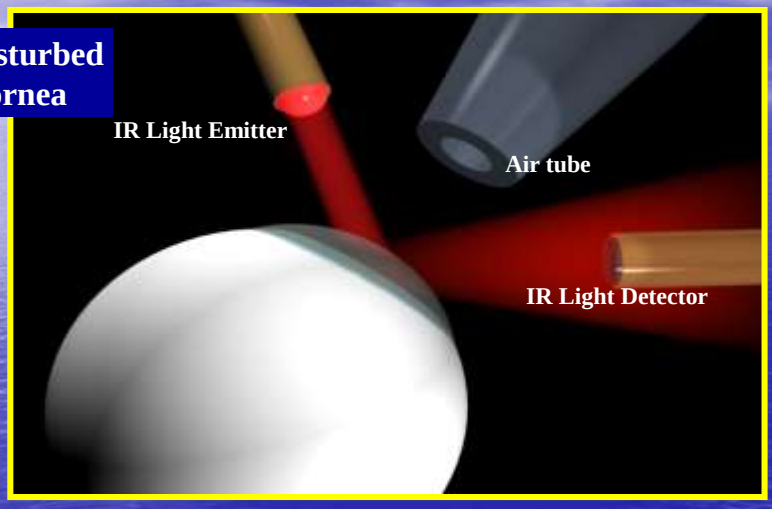
**It is a property of physical systems that do not instantly follow the forces applied to them, but react slowly, or do not return completely to their original state.**



Corneal Hysteresis Cor'ne·al \Hys`te*re"sis\. Identified by David Luce, Ph.D., in **2005.**

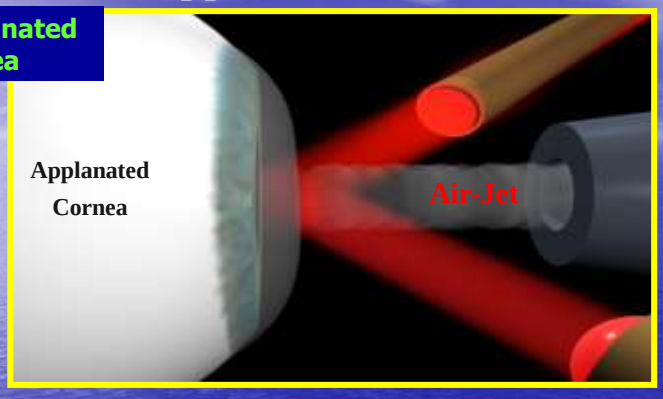
**It is the difference in the inward and outward pressure values obtained during the dynamic bi-directional applanation process employed in the ORA, as a result of viscous damping in the cornea.**

# Applanation Detection I



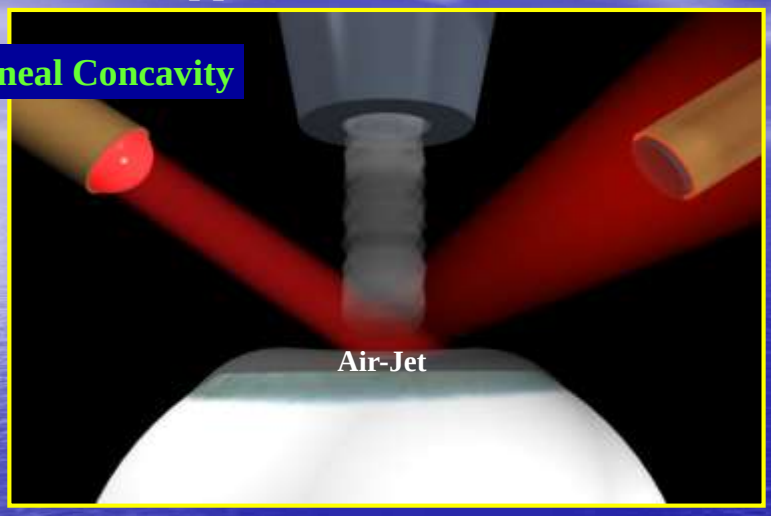

Once the instrument air tube is precisely aligned to the apex of the patient's cornea, the test is automatically initiated.

# Applanation Detection II



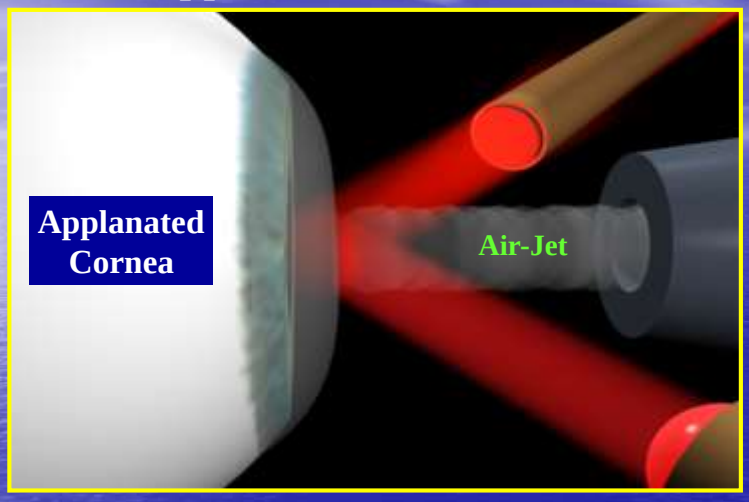

**The air pump now delivers a collimated stream of air directly onto the eye, causing the cornea to flatten under the force of impingement.**
**As the cornea moves inwards towards applanation, the reflected light beam becomes less convergent, directing an increasing amount of light onto the detector.**
**When applanation is achieved, the reflected light is close to being collimated and the detector records a signal peak.**
**This signal peak identifies the exact moment of applanation and triggers the ORA's sophisticated electronics to record the pressure value from a transducer located in a plenum chamber in the air delivery system. At the same time, the power being delivered to the air pump is removed in a controlled fashion so that the air pulse starts to subside.**

## Applanation Detection III



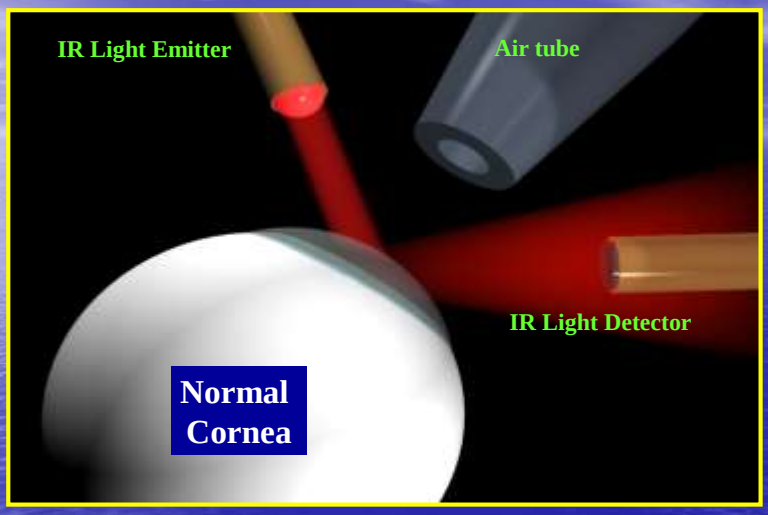

Following applanation, the air pulse continues to impinge upon the cornea causing it to deflect into a state of partial concavity. This causes the reflected light to become dispersed again and the detector signal reduces.

## Applanation Detection IV




As the air velocity of the jet declines towards zero, the cornea returns to its natural shape and once again passes through an applanation state. Once again, the reflected light reaches maximum intensity and causes a signal peak at the detector, triggering the ORA electronics to record the pressure in the plenum chamber a second time.

# Applanation Detection V



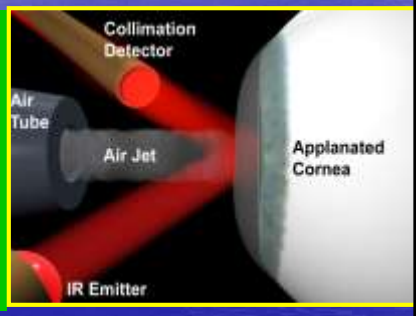

The cornea completes its return to its normal configuration and the sequence is concluded.

The entire measurement process takes approximately 20-30 milliseconds.

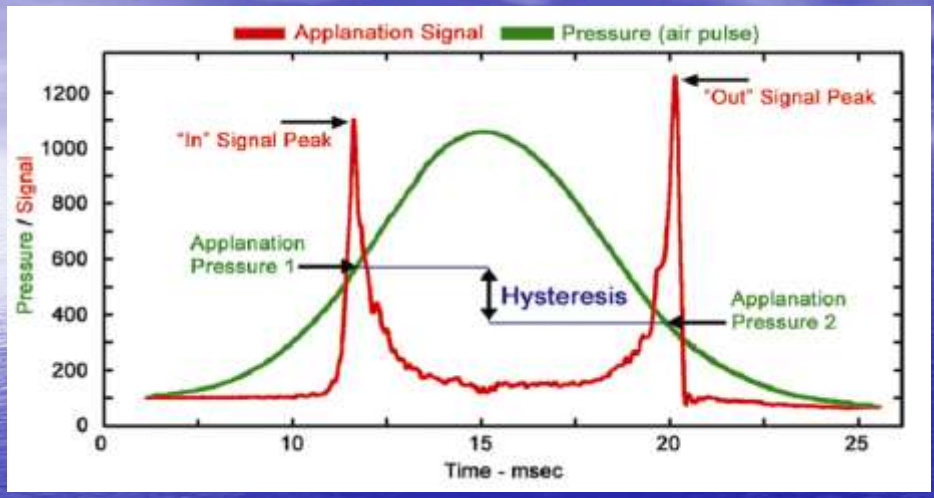
# ORA Signal Analysis

The ORA records 400 data samples of reflected IR light intensity during the rapid (20-30 ms) in/out corneal deformation.

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



## ORA Signal Plot

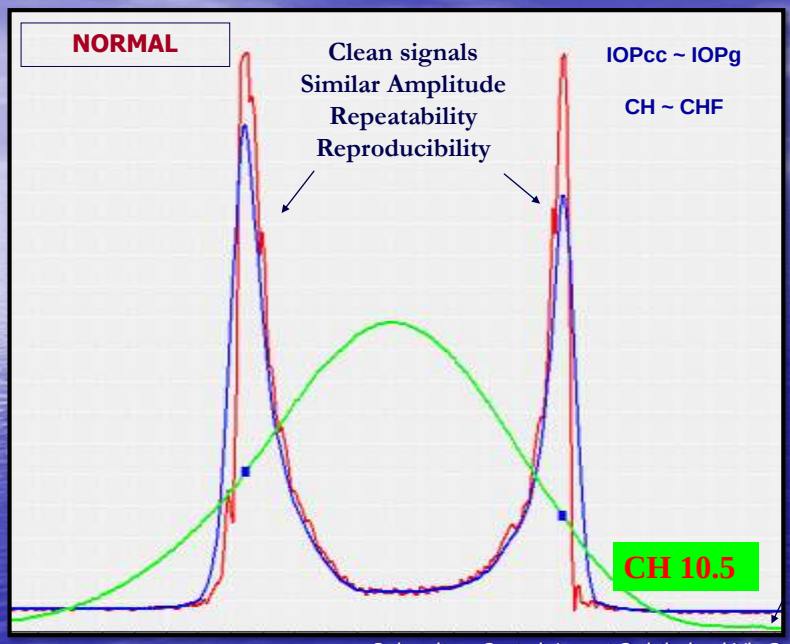



**NORMAL**

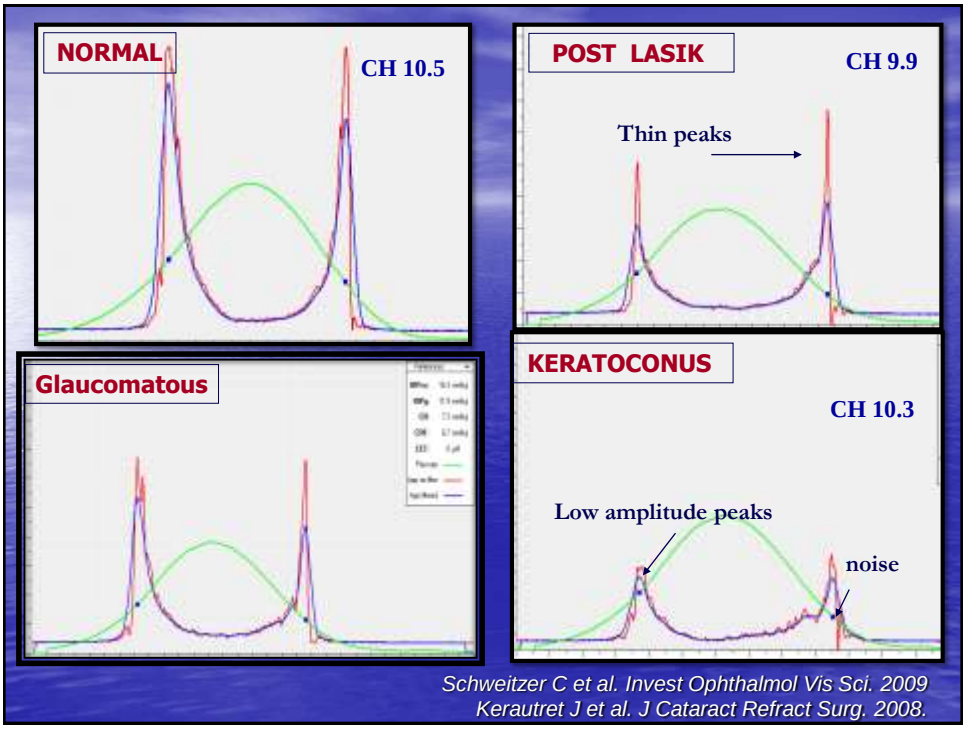
Clean signals
Similar Amplitude
Repeatability
Reproducibility

IOPcc ~ IOPg

CH ~ CHF




*Schweitzer C et al. Invest Ophthalmol Vis Sci. 2009*
*Kerautret J et al. J Cataract Refract Surg. 2008.*




*Schweitzer C et al. Invest Ophthalmol Vis Sci. 2009*
*Kerautret J et al. J Cataract Refract Surg. 2008.*

Ocular Response Analyzer

# The Cornea, IOP, and Glaucoma

## The cornea and IOP measurement

**Many studies have concluded that variation in CCT affects with the accuracy of measured IOP.**

**However, the over or under estimation of IOP caused by corneal interference is only valid ON AVERAGE and the relationship is not very significant.**

As such, glaucoma opinion leaders caution against using CCT based IOP correction algorithms:

## The cornea and IOP measurement

**"Adjusting IOP by means of a fixed CCT algorithm is almost certainly wrong in the majority of our patients.**
- James Brandt, Director of Glaucoma Services, UC Davis

**"Correction nomograms that adjust GAT IOP based solely on CCT are neither valid nor useful in individual patients"**
- Pg 18. Robert N. Weinreb, et al. World Glaucoma Association on IOP; Consensus Series 4; May 5, 2007

**"We should not assume that CCT is the parameter of greatest interest in monitoring glaucoma or in determining what features of the eye are important in ON damage. Physiology is more important than anatomy"**
- Harry Quigley, Director of Glaucoma Service, Wilmer Eye Institute

## The problem with CCT-based IOP adjustment

**Thickness is NOT resistance**

**In theory, thicker corneas overstate IOP values and thinner corneas understate IOP values.**

**Many attempts have been made to establish a CCT-based correction algorithm to adjust Goldmann-obtained IOP values.**

**However, the magnitude of the CCT/IOP relationship identified by the various studies is inconsistent.**

**This variation has resulted in numerous algorithms that differ significantly from one another.**

**Also, adjusted IOP based on CCT could lead not only to errors in the magnitude of the adjustment, but also in the *direction* of the adjustment.**

Concluded by (Harry Quigley, Jamie Brandt, Ted Garway-Heath, Cindy Roberts, etc)

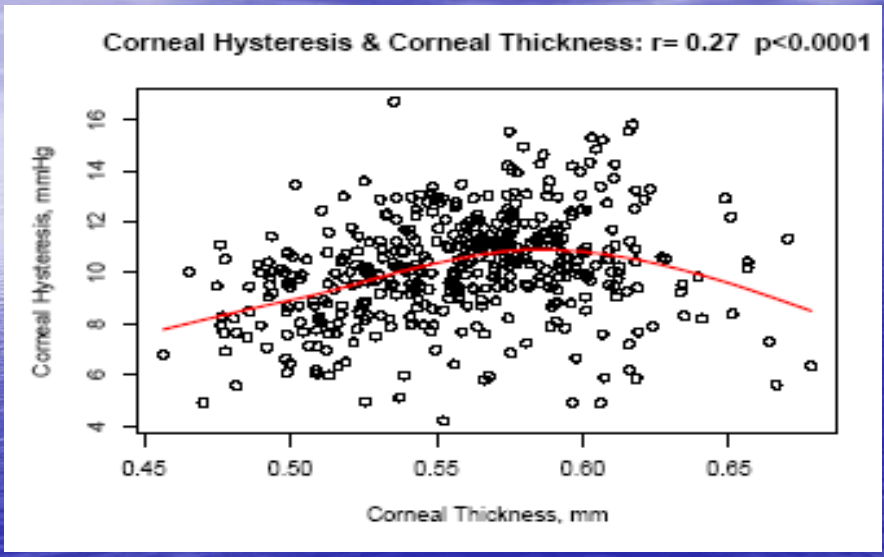
## The problem with CCT-based IOP adjustment

- Two corneas, both 0.65 mm
- One is clear
- The other is edematous
- The first reads high (compared to manometry), the second low
- **Thickness can't be the whole answer**

- Other corneal factors besides thickness determine response of corneo-scleral shell to force
  - Hydration
  - Connective tissue composition
  - Bio-elasticity

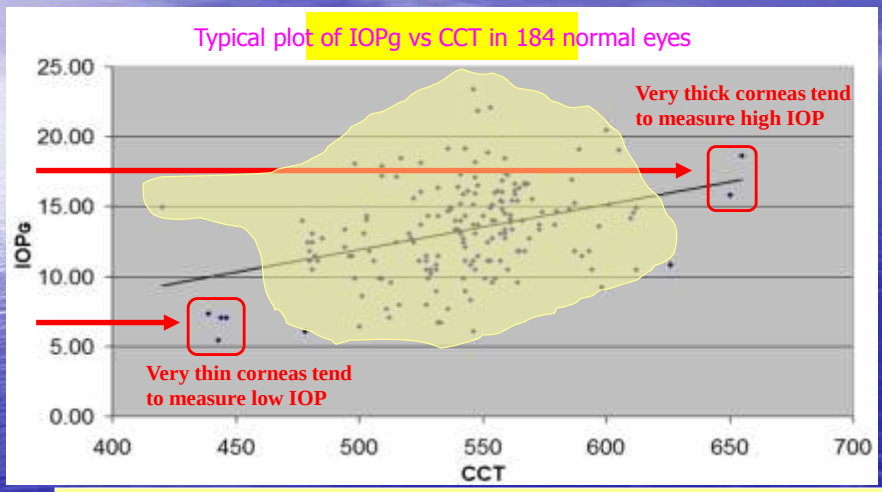
Data courtesy Harry Quigley, Wilmer Eye Institute

## The problem with CCT-based IOP adjustment




Data courtesy Harry Quigley, Wilmer Eye Institute

## Why CCT-based IOP correction is flawed



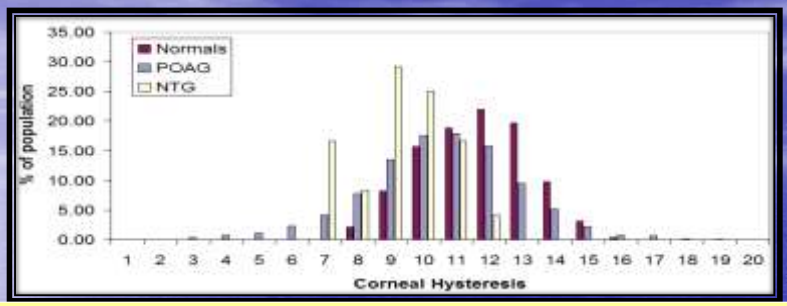

**But SCATTER in the data makes accurate mathematical "adjustment" of IOP impossible for individuals!**

## The cornea and Glaucoma

**Numerous studies, such as OHTS have found that corneal thickness is an independent indicator of glaucoma risk.**

**More recent research has indicated that the CH measurement appears to be even more powerful in this regard.**

## CH distribution - Normal & Glaucoma




**Glaucoma pts have lower CH than normal, especially those who are still progressing in the disease.**

- **Recently, the OHTS, and other studies, *have suggested that low CCT (thin cornea) may be an independent risk factor for the development and progression of glaucoma.***
- ***Evidence suggests that the cornea may reflect the condition of the lamina cribrosa. Clinical studies utilizing ORA support this hypothesis.***
- **As shown in this slide, compared to normals, glaucomatous subjects have a significantly lower than average CH and a much wider range.**
- **An interesting observation is that lower-than-average CH is also observed in patients who have been identified as NTG subjects. Currently individuals who unknowingly have NTG are missed during routine IOP screening.**

Data courtesy New England College of Optometry and Mitsugu Shimmyo, MD

## Key Clinical Benefits

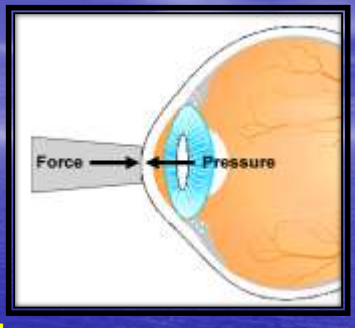
- There are over 300 peer-reviewed publications about this technology
- CH is *independently* predictive of glaucoma visual field progression rate
- CH is predictive of response to IOP reduction medication
- CH facilitates our "corneal compensated" IOP (IOPcc): an IOP measurement that is less influenced by corneal properties than other tonometers, including Goldmann. *This is superior to CCT-based adjustment formulas.*

**ORA provides CH and IOPcc.**

## Key Clinical Benefits

**What about the "gold standard"**

The Goldmann Tonometer has long been considered the gold standard for measuring pressure, but its accuracy is widely questioned today.



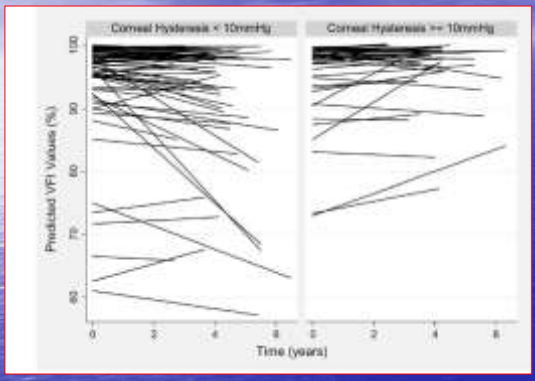

**Goldmann Design Assumptions:**
- Cornea is infinitely thin and perfectly flexible
- Tear-film and CCT effect cancel each other out

**Flaws:**
- Experimentation done on cadaver eyes (not representative of live eyes).
- Variations in CCT is significantly greater than assumed.
- Variations in corneal biomechanical properties was attempted.

Goldmann cannot compensate for differences in thickness, elasticity, and other biomechanical parameters that influence accuracy.

## Key Clinical Benefits

### CH predicts glaucoma progression




**"This study supports the role of CH as an important factor to be considered in the assessment of the risk of progression in patients with glaucoma"**

- **CH was more the 3X associated with rate of VF progression than CCT**
- **CH was over 2X more associated with rate of progression than IOP**

CH as a Risk Factor for Glaucoma Progression: A Prospective Longitudinal Study
Felipe A. Medeiros, et al, Ophthalmology, September 2013

## Key Clinical Benefits

### CH predicts IOP response to medical treatment

Eyes with lower CH achieve a greater magnitude of IOP reduction with PGs

Table 2. IOP response to therapy by baseline CH and CCT

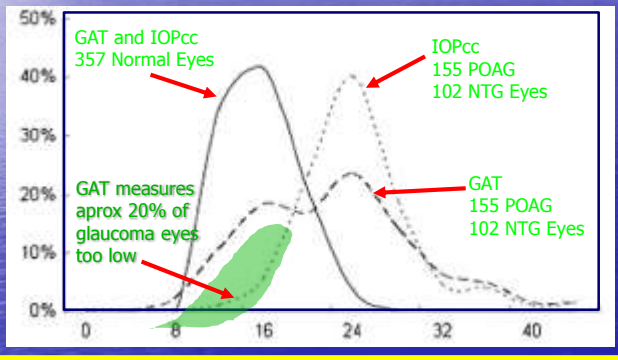
| | Baseline CH (mm Hg) | Baseline IOPg (mm Hg) | IOPg change (mm Hg) | p-value | IOPg percent change | p-value |
|---|---|---|---|---|---|---|
| | | | | ANOVA: | | ANOVA: |
| First quartile CH | 7.0 | 19.4 | -5.8 | p=0.002 | -29.0% | p=0.008 |
| Second quartile CH | 8.8 | 17.4 | -3.7 | 0.1[1] | -20.7% | 0.2[1] |
| Third quartile CH | 10.0 | 16.5 | -3.7 | 0.2[1] | -19.9% | 0.3[1] |
| Fourth quartile CH | 11.9 | 15.9 | -1.1 | 0.001[1] | -7.6% | 0.006[1] |
| | **Baseline CCT (µm)** | **Baseline IOPg (mm Hg)** | **IOPg change (mm Hg)** | **p-value** | **IOPg percent change** | **p-value** |
| | | | | ANOVA: | | ANOVA: |
| First quartile CCT | 497.3 | 16.4 | -3.9 | p=0.7 | -21.9% | p=0.4 |
| Second quartile CCT | 525.2 | 17.1 | -4.0 | 0.8[1] | -23.1% | 0.8[1] |
| Third quartile CCT | 549.1 | 16.9 | -3.1 | 1.0[1] | -15.9% | 0.8[1] |
| Fourth quartile CCT | 586.2 | 18.3 | -2.6 | 0.5[1] | -13.4% | 0.5[1] |

The relationship between CH and the magnitude of IOP reduction with topical PGs therapy.
Br J Ophthalmol. 2012 Feb;96(2):254-7.

## Key Clinical Benefits

IOPcc is a better than GAT for glaucoma

"The results of this study suggest that IOPcc may represent a superior test for the evaluation of glaucoma"




from this study:

- 39% of NTG eyes would be re-classified as POAG with IOPcc
- Average IOPcc was 5 mmHg higher than GAT in NTG eyes

GAT compared with IOPcc in the evaluation of POAG. Joshua R E, et al. Ophthalmology 2012, 12:52

# ORA, Some studies

**Lit. 1**

## CH and VF Asymmetry in OAG

**CONCLUSIONS:**

- **Asymmetric POAG was associated with asymmetry in ORA parameters but not in CCT and GAT.**
- **Lower CH was associated with worse eyes independently of its effect on IOP and had the best discriminability for the eye with the worse VF.**

Aashish Anand, et al., IOVS, 2010;51:6514 – 6518)

**Lit. 2**

## Lower CH is associated with more rapid glaucomatous VF progression

- **Conclusions:**
  - Corneal biomechanical and physical properties, such as CH and CCT, are highly correlated and associated with VF progression.
  - As CH may describe corneal properties more completely than thickness alone, it may be a parameter that is better associated with progression.

Carlos Gustavo V. et al., (J Glaucoma 2012;21:209–213)

**Lit. 3**

CH as a risk factor for glaucoma progression: A prospective longitudinal study

- Conclusions:
  - ❑The CH measurements were significantly associated with risk of glaucoma progression.
  - ❑Eyes with lower CH had faster rates of VF loss than those with higher CH.
  - ❑The prospective longitudinal design of this study supports the role of CH as an important factor to be considered in the assessment of the risk of progression in patients with glaucoma.

- Felipe A. M, et al., *Ophthalmology 2013;-:--- by the American Academy of Ophthalmology.*

**Lit. 4**

**Evaluation of the influence of corneal biomechanical properties on IOP measurements using the ORA**

- Conclusions:
  - ❖ORA IOPcc measurements seem to provide an estimate of IOP that is less influenced by corneal properties than those provided by GAT.

Felipe A. Medeiros, MD and Robert N. Weinreb, MD. J Glaucoma 2006;15:364–370.

## Lit. 5

**IOP measured by DCT and ORA in NTG**

- **Conclusions:**
  - **We investigated the values of IOP in NTG eyes as measured by the DCT and ORA. IOPcc was significantly greater than GAT-IOP, DCT-IOP and IOPg in NTG eyes, suggesting the possibility that IOP values may be underestimated.**

Tetsuya Morita et al Graefes Arch Clin Exp Ophthalmol. DOI 10.1007/s00417-009-1169-4

## Lit. 6

**GAT compared with IOPcc in the evaluation of POAG**

- **Conclusions:**
  - While IOP is unlikely to be an effective diagnostic test, the results of this study suggest that a IOPcc may represent a superior test for the evaluation of glaucoma, especially among patients with low to normal IOPs.

Joshua R Ehrlich, et al, Ehrlich et al. BMC Ophthalmology 2012, 12:52
http://www.biomedcentral.com/1471-2415/12/52

Lit. 7

# Evaluation of Corneal Bio-mechanics using Ocular Response Analyzer for Normal and POAG eyes.

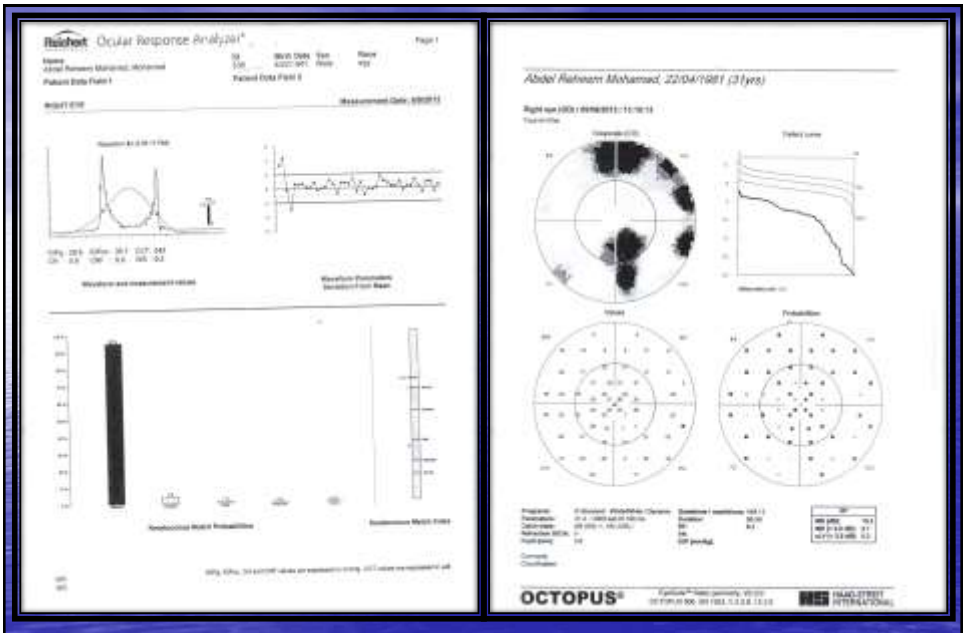
Mohamed A. El-Malah, MD, PhD.
.....
Assistant Prof. of ophthalmology
Al-Azhar Univ., Cairo, Egypt.
EOS, Mar. 2013

## Results:

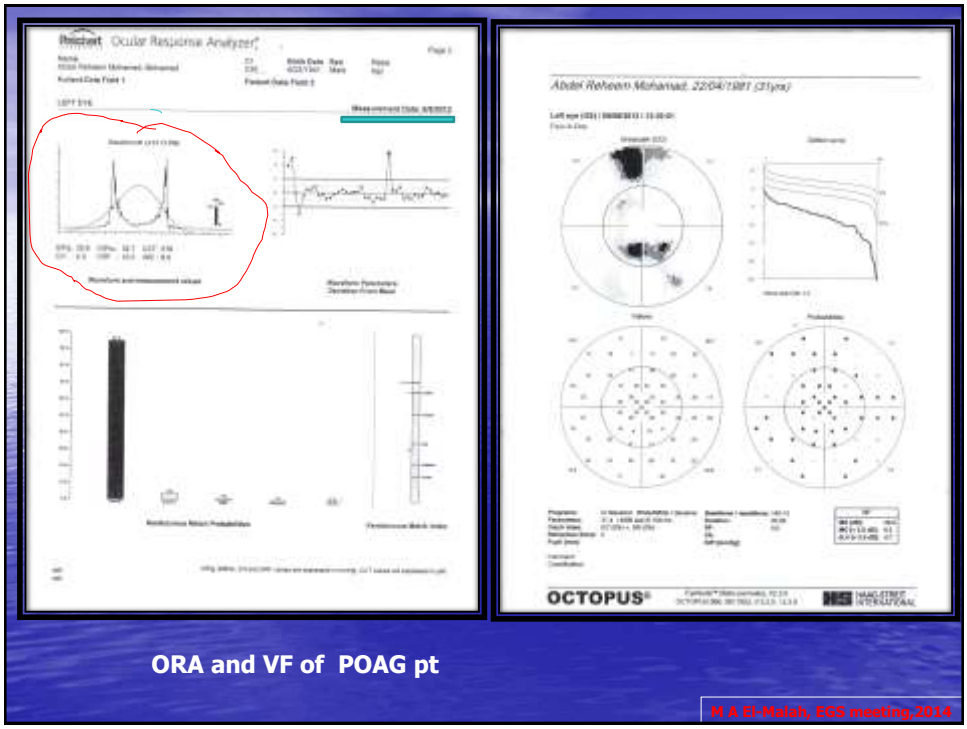
| | Control group | POAG group | P-value |
|---|---|---|---|
| No of eyes | 47 eyes | 47 eyes | |
| M/F | 20/25 | 23/26 | |
| Age | 55±7.8 years | 54±7.1 years | |
| IOPg | 15.8±1.3mmHg | 23.6±2.6mmHg | |
| IOPcc | 14.7±0.2mmHg | 26.8±2.4mmHg | |
| CH | 11.6±1.2mmHg | 8.4±2.3mmHg | |
| CRF | 12.4±1.8mmHg | 9.4±0.6mmHg | |

Table (1) the demographic data of all eyes control and POAG groups.

# SOME CASES FROM MY OWN WORK

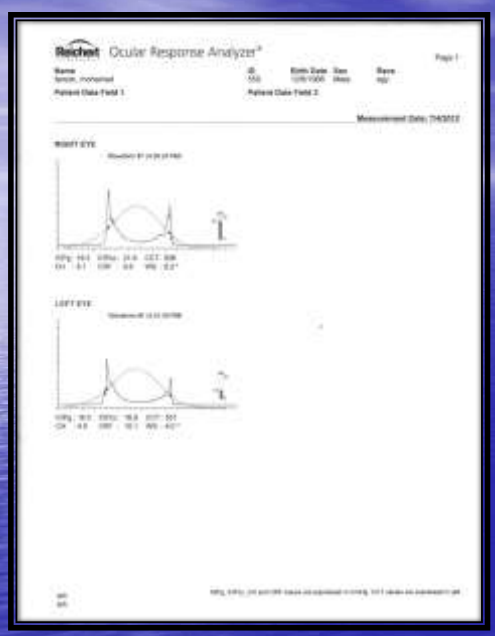



**ORA and VF of POAG pt**



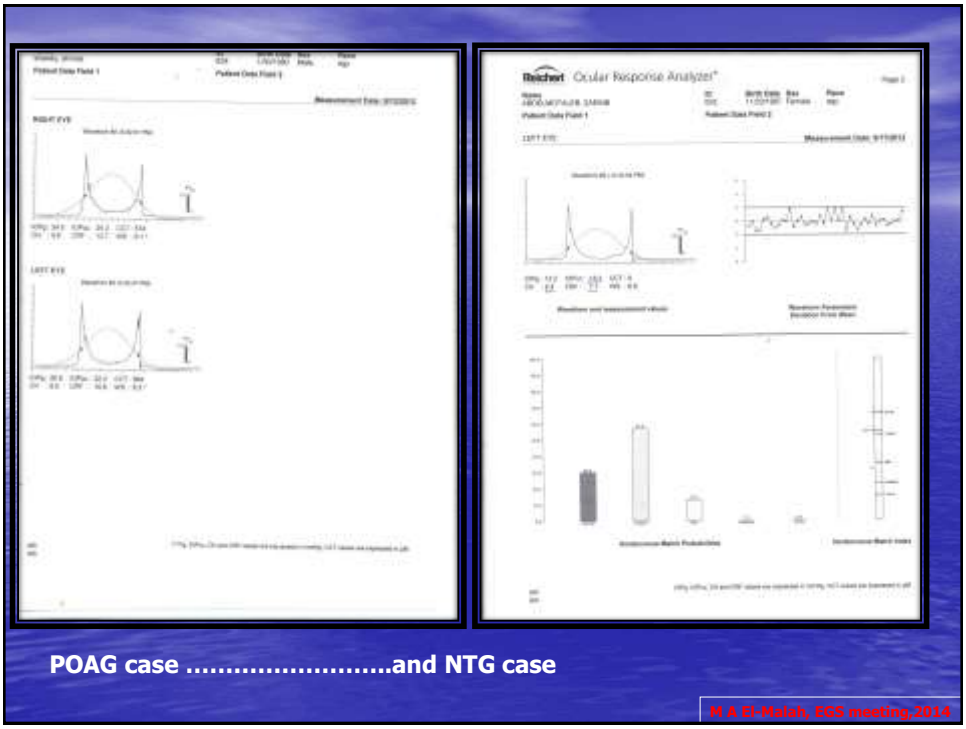

**ORA and VF of POAG pt**

M A El-Malah, EGS meeting 2014



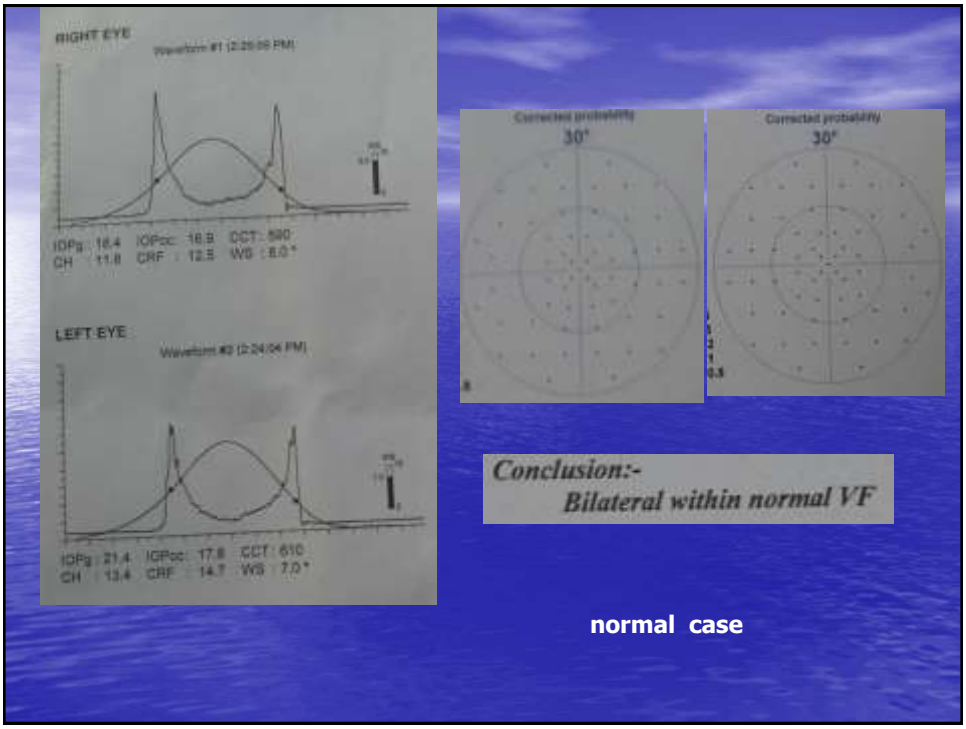

**ORA with bad Wave score, excluded**

M A El-Malah, EGS meeting 2014

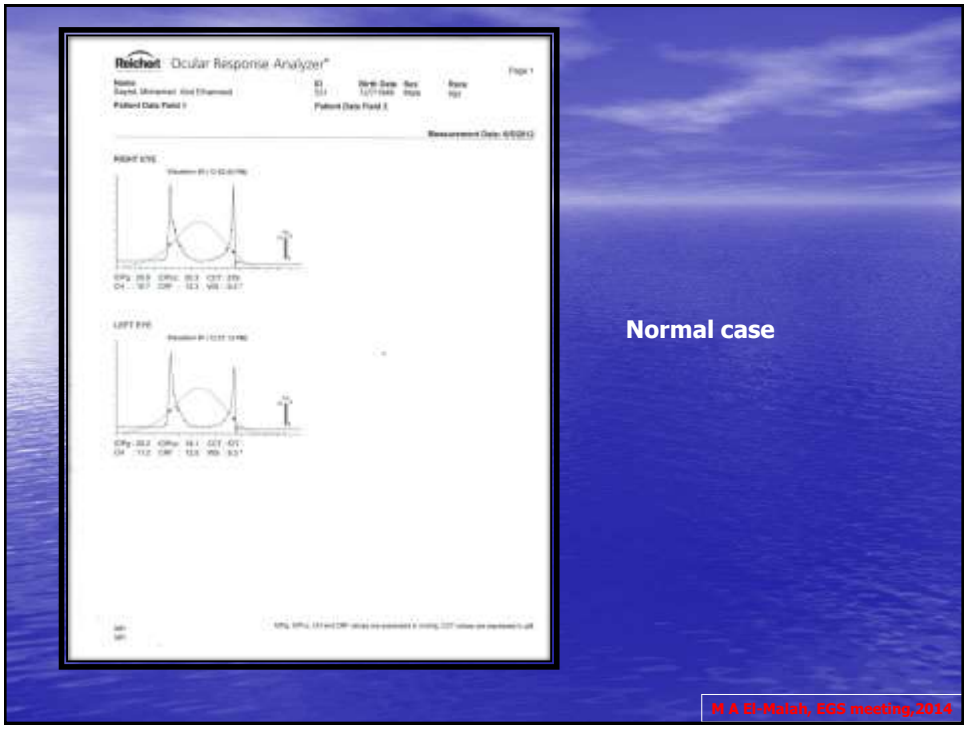


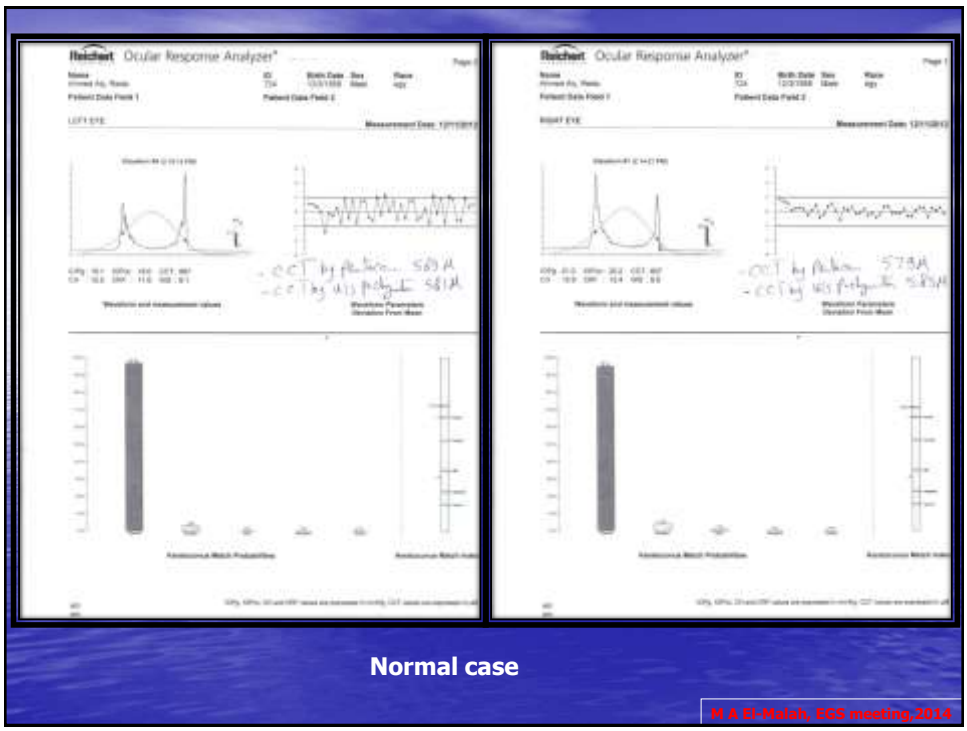

**POAG case .....and NTG case**

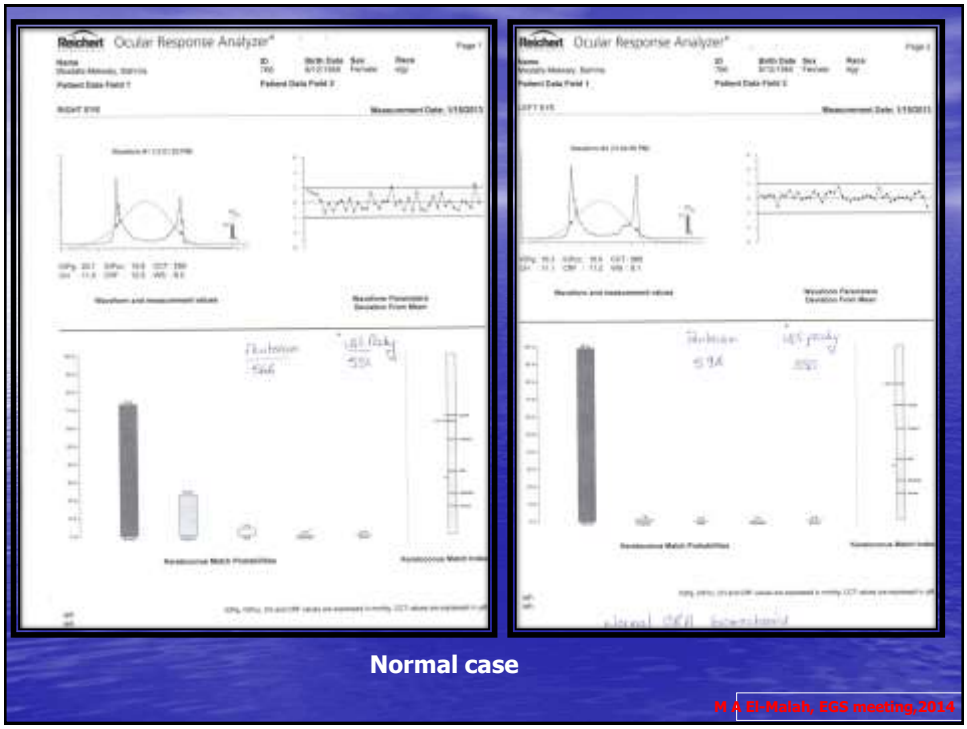
M A El-Maleh, EGS meeting 2014

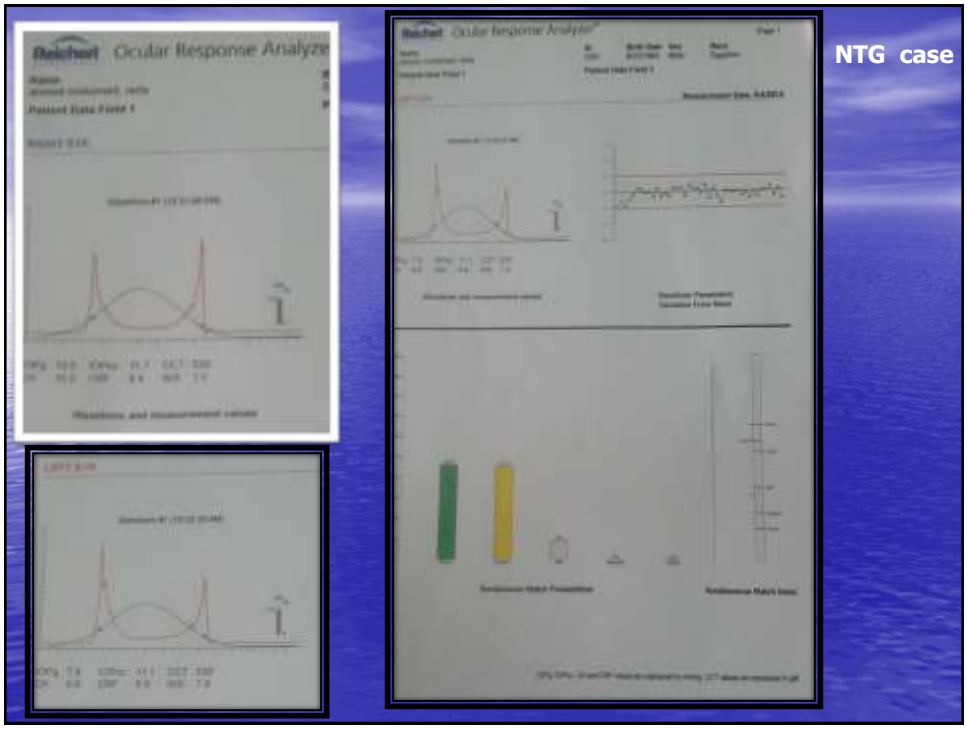


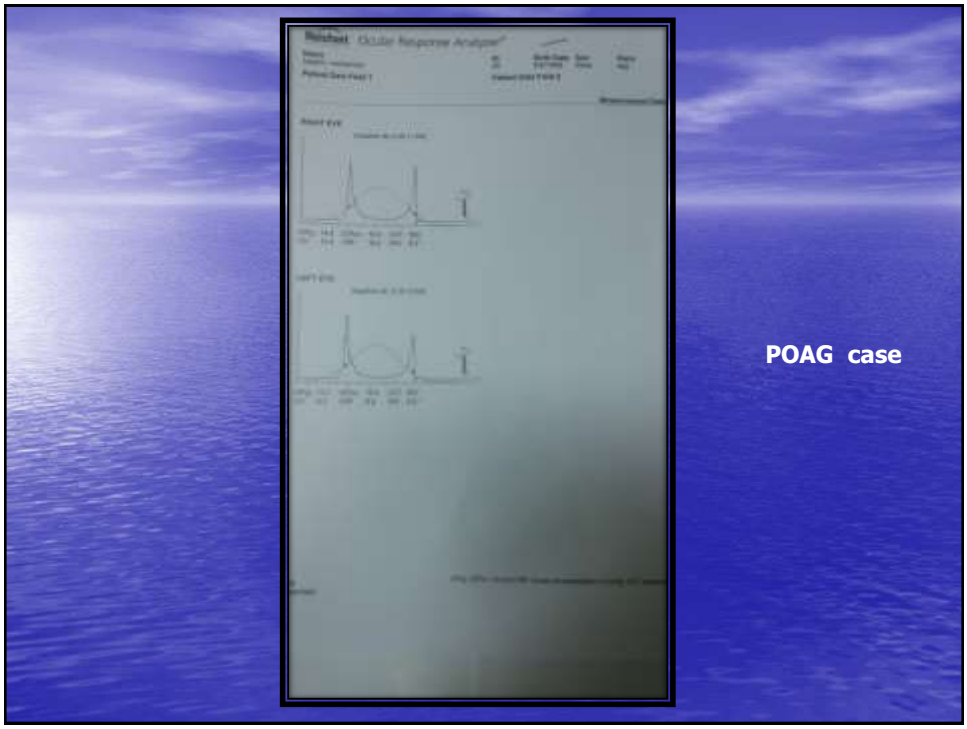

**normal case**

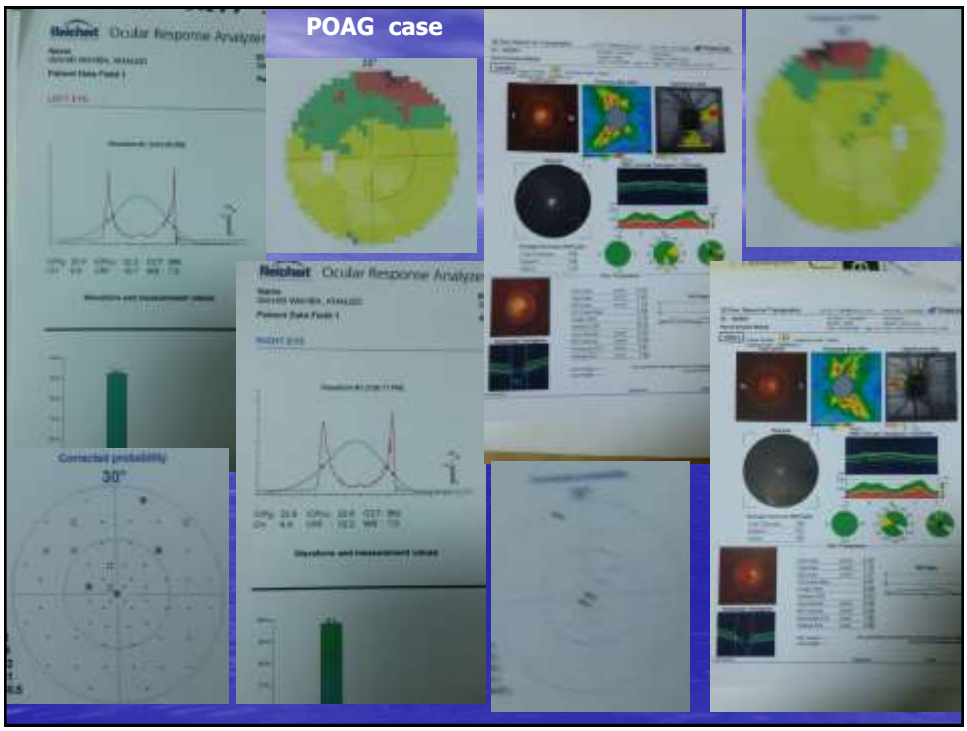

Reichert Ocular Response Analyzer*
Normal case
M A El-Malah, EGS meeting 2014

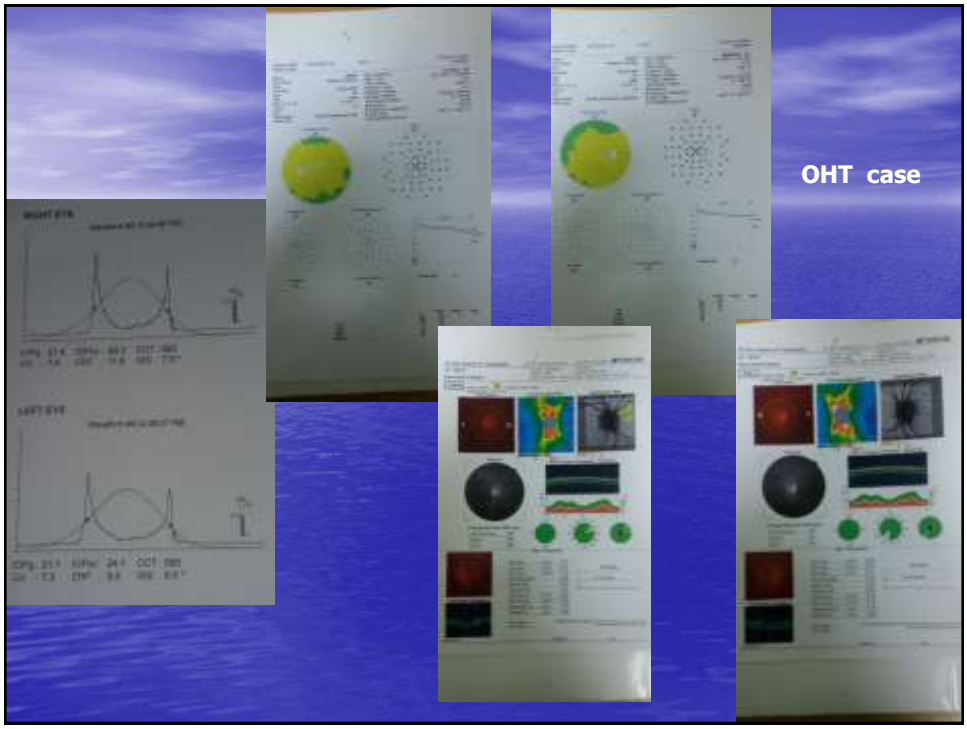

Reichert Ocular Response Analyzer*
Reichert Ocular Response Analyzer*
Normal case
M A El-Malah, EGS meeting 2014

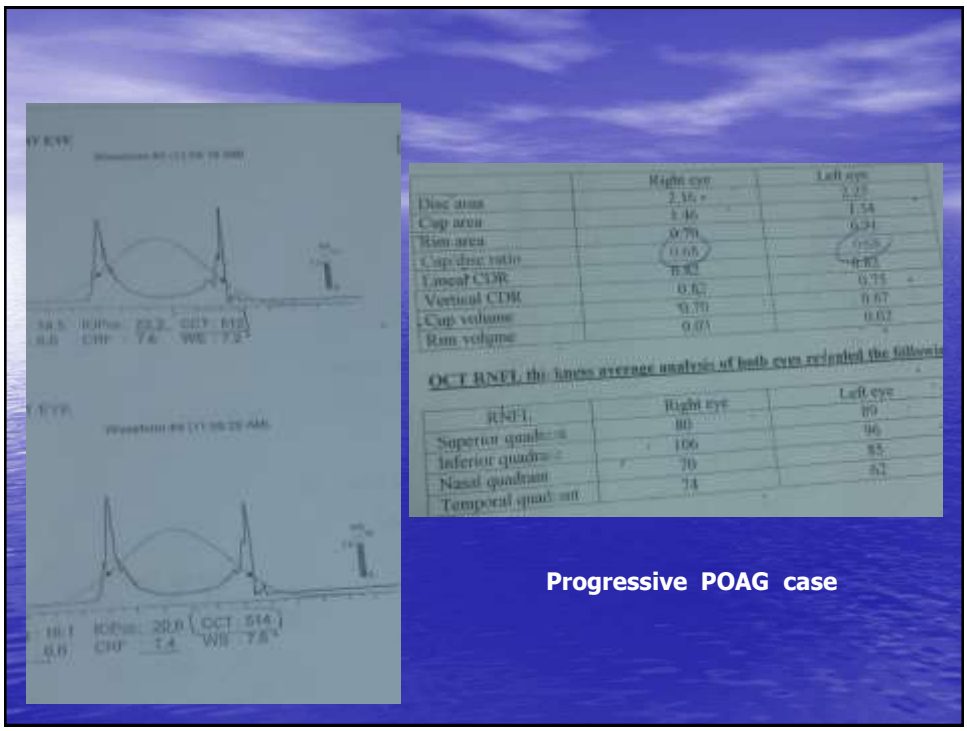

Reichert Ocular Response Analyzer
Reichert Ocular Response Analyzer
Normal case
M A El-Malah, EGS meeting,2014

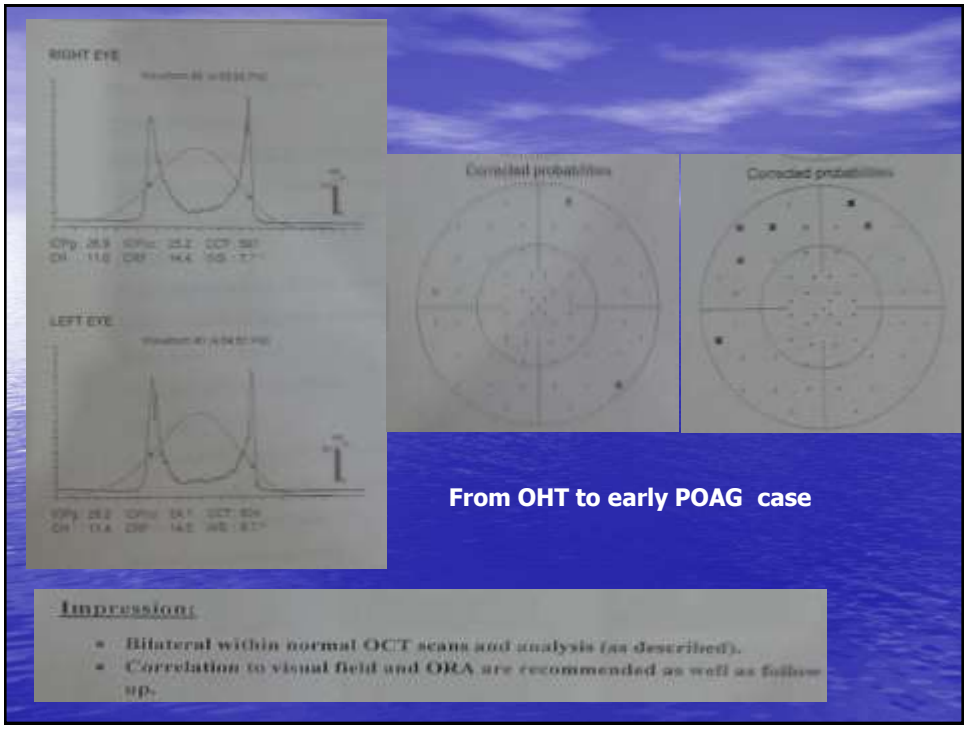

Reichert Ocular Response Analyzer
NTG case

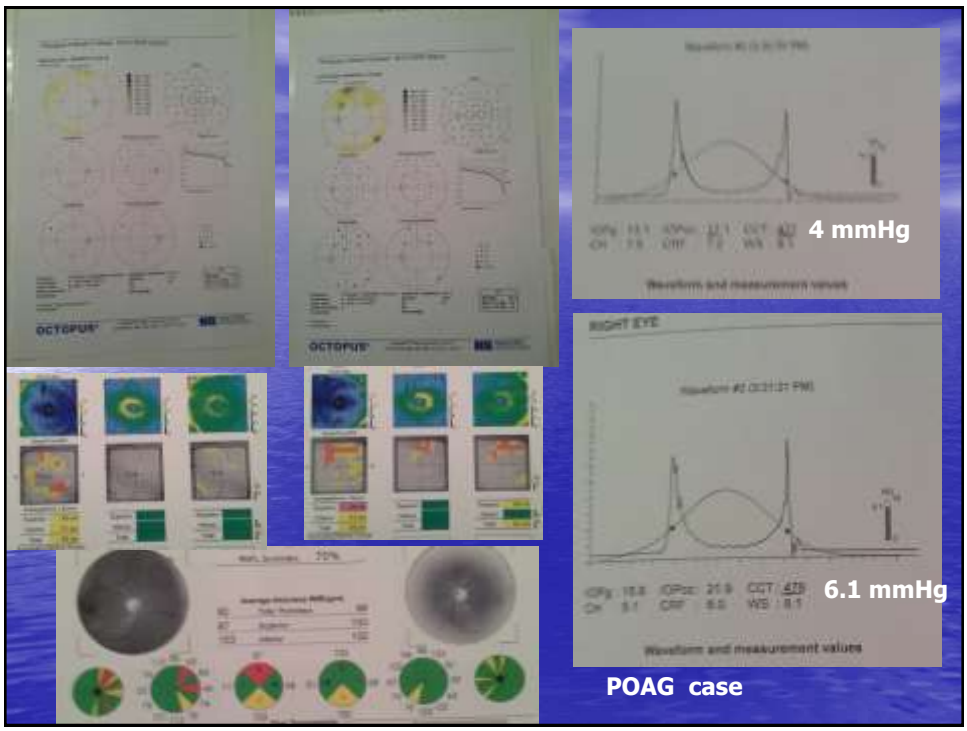

POAG case

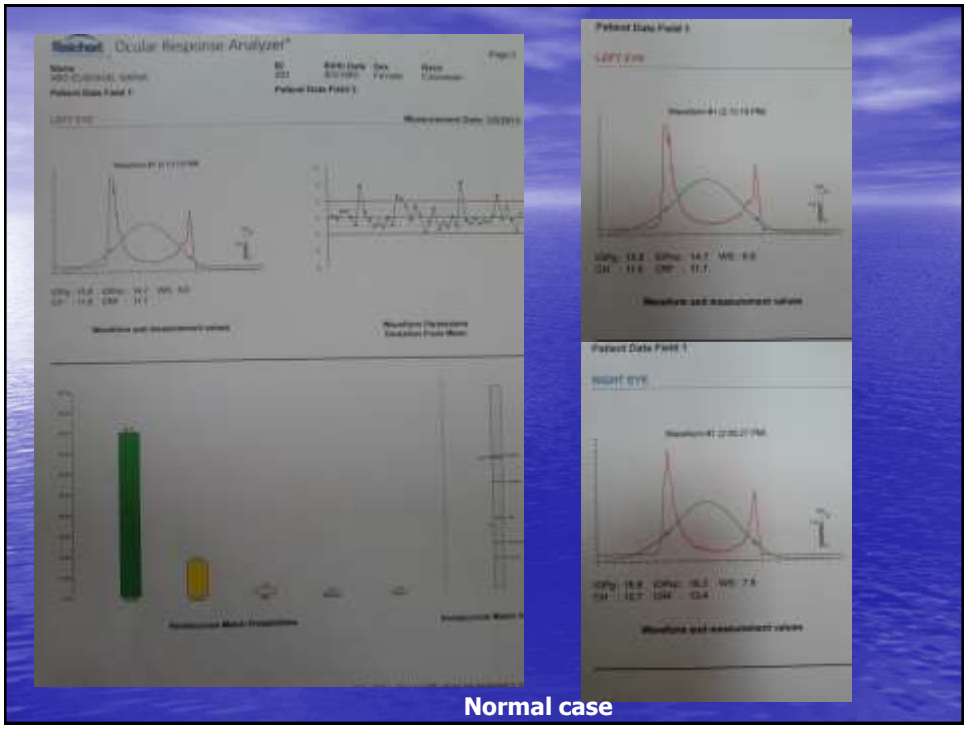

POAG case


OHT case


Right eye
Left eye
Disc area
Cup area
Rim area
Cup/disc ratio
Local CDR
Vertical CDR
Cup volume
Rim volume
Right eye
Left eye
Superior quadrant
Inferior quadrant
Nasal quadrant
Temporal quadrant
Progressive POAG case


RIGHT EYE
LEFT EYE
Corrected probabilities
Corrected probabilities
From OHT to early POAG case
Impression:
Bilateral within normal OCT scans and analysis (as described).
Correlation to visual field and ORA are recommended as well as follow up.


OCTOPUS
OCTOPUS
4 mmHg
RIGHT EYE
6.1 mmHg
POAG case




Normal case

# THANK YOU

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