The Role of the Modern Tonometer in Glaucoma

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Disclosures

- Aerie Pharmaceuticals
- Diopsys
- Ellex
- EyePromise
- iCare
- Ivantis
- Lumenis
- Maculogix
- Nidek
- Nova Oculus
- Novartis
- Optovue
- Quantel
- Reichert
- RevolutionEHR
- Sight Sciences
- Sun Pharma
- Triad Ophthalmics

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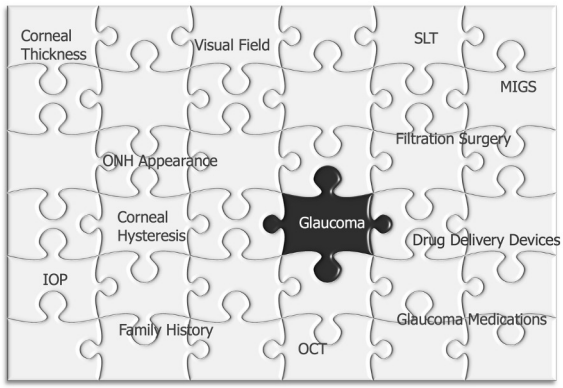

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Diagnosis

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Lowering IOP Reduces the Risk of Disease Progression

Study	IOP	Progression (Tx/No Tx)
OHTS[1]	20% reduction	4.4%/9.5% (5 years)
EMGT[2]	25% reduction	45%/62% (6 years)
CNTGS[3]	30% reduction	12%/35% (7 years)
CIGTS[4] (medicine)	≈35% reduction	No progression (5 years)
CIGTS[4] (surgery)	≈48% reduction	No progression (5 years)
AGIS[5]	< 18 mm Hg	No progression (6 years)
AGIS[5]	> 18 mm Hg	1.93 units (7 years)

1. Kass et al. *Arch Ophthalmol.* 2002; 2. Heijl et al. *Arch Ophthalmol.* 2002; 3. CNTG Study Group. *Am J Ophthalmol.* 1998; 4. Lichter et al. *Ophthalmology.* 2001; 5. AGIS Investigators. *Am J Ophthalmol.* 2000.

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Target pressure rules of thumb:

- Early POAG and ocular hypertension: Reduction of 25-30% from high IOP reading
  - OHTS, EMGT, CIGTS
- Moderate POAG: 35% or more reduction; no higher than 18 mmHg
  - AGIS, CIGTS
- Severe POAG: no higher than 15 mmHg and optimally 10-12 mmHg
  - AGIS
- Always exceptions! And the target is not set in stone

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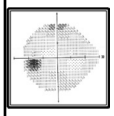
Recognizing Mild or Early Stage Glaucoma



Optic nerve abnormalities associated with glaucoma

But NO visual field abnormalities on any visual field test

OR abnormalities present only on short-wave- length automated perimetry or frequency doubling perimetry

- Current ICD-10 Glaucoma Reference Guide

Source: American Academy of Ophthalmology
American Glaucoma Society

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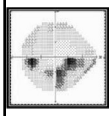
Moderate Stage Glaucoma



Optic nerve abnormalities consistent with glaucoma

AND glaucomatous visual field abnormalities in ONE hemifield and

NOT within 5 degrees of fixation

- Current ICD-10 Glaucoma Reference Guide

Source: American Academy of Ophthalmology
American Glaucoma Society

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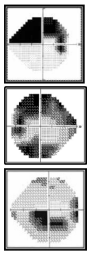
Advanced, Late, Severe Stage Glaucoma



~~0.~~ Optic nerve abnormalities consistent with glaucoma

~~02.~~ AND glaucomatous visual field abnormalities in BOTH hemifields

~~03.~~ AND/OR loss within 5 degrees of fixation in at least one hemifield

- Current ICD-10 Glaucoma Reference Guide

Source: American Academy of Ophthalmology
American Glaucoma Society

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Target pressure rules of thumb:

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- Moderate POAG: 35% or more reduction; no higher than 18 mmHg
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  - AGIS
- Always exceptions! And the target is not set in stone

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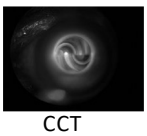
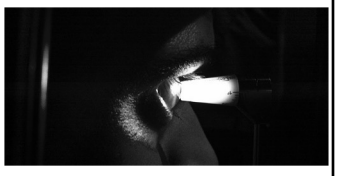
Influences on IOP Measurement



CCT



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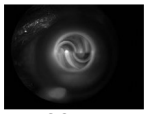
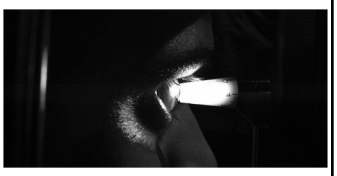
Influences on IOP Measurement



CCT
Post-Refractive
Time of Day
Medications



Physical Activity and Posture

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Reducing the Corneal effect on Measured IOP
ORA's Patented IOPcc

- Goldmann and other tonometers provide *one number*, but this number is comprised of *two* things:
  IOP and cornea

You can't measure two things with one number!

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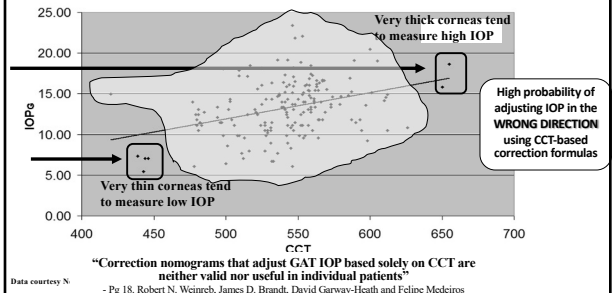
CCT-based IOP adjustment is not advisable
"Neither valid nor useful" – World Glaucoma association



Data courtesy N.

"Correction nomograms that adjust GAT IOP based solely on CCT are neither valid nor useful in individual patients"
- Pg 18. Robert N. Weinreb, James D. Brandt, David Garway-Heath and Felipe Medeiros
World Glaucoma Association on Intraocular Pressure; Consensus Series 4; May 5, 2007

50% chance of adjusting IOP in the WRONG DIRECTION

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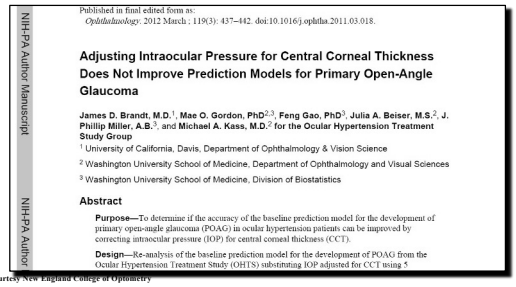
CCT-based IOP adjustment is not advisable
From the OHTS



NIH-PA Author Manuscript

NIH-PA Author

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Adjusting Intraocular Pressure for Central Corneal Thickness Does Not Improve Prediction Models for Primary Open-Angle Glaucoma

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[1] University of California, Davis, Department of Ophthalmology & Vision Science
[2] Washington University School of Medicine, Department of Ophthalmology and Visual Sciences
[3] Washington University School of Medicine, Division of Biostatistics

Abstract

Purpose—To determine if the accuracy of the baseline prediction model for the development of primary open-angle glaucoma (POAG) in ocular hypertension patients can be improved by correcting intraocular pressure (IOP) for central corneal thickness (CCT).

Design—Re-analysis of the baseline prediction model for the development of POAG from the Ocular Hypertension Treatment Study (OHTS) substituting IOP adjusted for CCT using 5

Data courtesy New England College of Optometry

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Reducing the Corneal effect on Measured IOP
ORA's Patented IOPcc

- Goldmann and other tonometers provide *one number*, but this number is comprised of *two* things:
  IOP and cornea

You can't measure two things with one number!

- ***How can we overcome the corneal influences?***
  - ***CATS***
  - ***ORA/IOPcc***

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The Correcting Applanation Tonometer Surface (CATS)

British Journal of Ophthalmology

Modified Goldmann prism intraocular pressure measurement accuracy and correlation to corneal biomechanical metrics: multicentre randomised clinical trial

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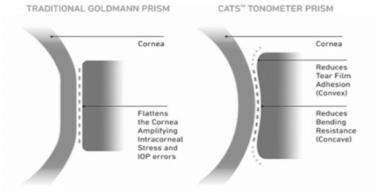
CATS: Correcting Applanation Tonometry Surface

"The New Shape" of Goldmann IOP"

Invented by Sean McCafferty (Ophthalmologist / mechanical and optical engineer). FDA Cleared in 2018.

CATS is simply a replacement prism for the Goldmann applanation tonometer. The CATS prism utilizes a dual-curved contact surface to minimize corneal bending resistance and tear-film adhesion error factors.



Sean McCafferty, MD

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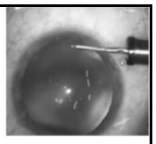
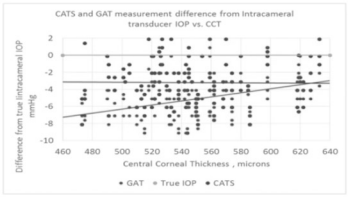
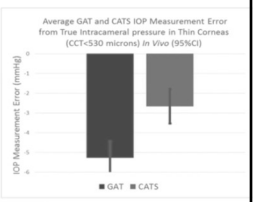
Goldmann vs CATS

IOP Error Relative to True Intercameral IOP



- IOP measured with a CATS and GAT prism on 58 eyes undergoing cataract surgery
- Pressure set to 10, 20, and 40 mmHg, monitored with intercameral transducer
- CATS and GAT difference from true IOP correlated to error parameters (CCT and CH)





- Significant underestimation in GAT IOP measurement (5.2 +/-1.6 mmHg)
- Significant GAT correlation to CCT *in vivo*, [5,6,7,8]
- No CATS correlation to CCT demonstrated

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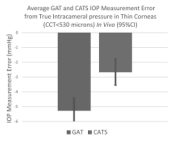
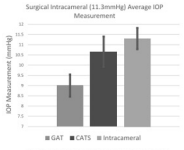
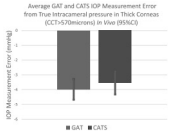
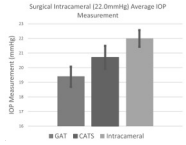
The Correcting Applanation Tonometer Surface (CATS)









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Reducing the Corneal effect on Measured IOP

ORA's Patented IOPcc

- Goldmann and other tonometers provide *one number*, but this number is comprised of *two* things:
  IOP and cornea

You can't measure two things with one number!

- ***How can we overcome the corneal influences?***
  - ***CATS***
  - ***ORA/IOPcc***
    - IOPcc is still a *Goldmann correlated* IOP measurement. That is; it is designed to agree with Goldmann on average, but is not influenced by the cornea in the same way as Goldmann and other tonometers are.
    - IOPcc has no correlation with CCT, changes minimally after refractive surgery, and is more associated with glaucoma status than actual GAT values.

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Ocular Response Analyzer

Generation 3 device

- **3rd Generation "ORA G3" introduced September 2015**
  Measures:
  - Corneal Hysteresis (CH)
  - Goldmann-correlated IOP (IOP_G)
  - Corneal compensated IOP (IOP_{CC})
  - Waveform Score (WS)

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3

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Ocular Response Analyzer Technology

Interpretation of measurement values

Corneal Compensated IOP: An IOP measurement that is less influenced by corneal properties than Goldmann or other tonometers. This value is closer to the "true pressure" and has been shown to be a better indicator of glaucoma than Goldmann. Matches GAT on average, so numerical "Scale" is the same

Corneal Hysteresis: An indication of corneal biomechanical properties that has been show to be *independently* predictive of future glaucoma progression. Reimbursable under CPT 92145. Typical average value is 10.5. Typical Range is 8-14. Low is a risk

IOPg: A Goldmann-correlated IOP measurement for reference purposes so that clinicians can appreciate what a Goldmann would read simultaneously with the IOPcc value above.

Waveform Score: A signal analysis algorithm that rates the "quality" of the measurement signal on a scale of 0-10. The higher the value, the more reliable the IOP and CH values are. 6-10 is excellent. 4-5 is not so good. 3 or below is poor.

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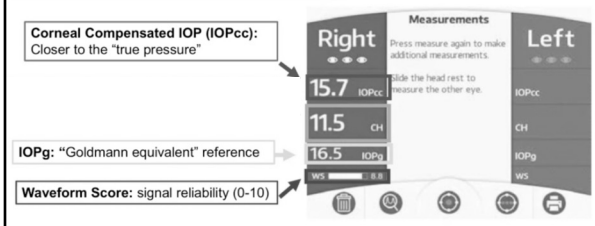
Ocular Response Analyzer G3
Measurement Values, range, and interpretation



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Corneal Compensated IOP (IOPcc):

Making a more accurate pressure measurement based on Corneal Hysteresis

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Reducing the Corneal effect on Measured IOP
ORA's Patented IOPcc

- Goldmann and other tonometers provide *one number*, but this number is comprised of *two* things:

  IOP and cornea

  You can't measure two things with one number!

- The ORA Bi-Directional Applanation process results in *two* applanation measurements in rapid succession. The derived Corneal biomechanical information, which gives us Corneal Hysteresis, can also be used to quantify (and reduce) the biomechanical impact of the cornea on the IOP measurement.

- ***IOPcc*** is a pressure measurement that is less affected by corneal properties than other methods of tonometery, such as Goldmann (GAT).
  - IOPcc is still a *Goldmann correlated* IOP measurement. That is; it is designed to agree with Goldmann on average, but is not influenced by the cornea in the same way as Goldmann and other tonometers are.
  - IOPcc has no correlation with CCT, changes minimally after refractive surgery, and is more associated with glaucoma status than actual GAT values.

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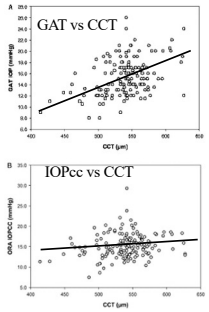
IOPcc – a superior indicator of IOP
Not correlated with CCT

TABLE 1. Clinical Characteristics of the 153 Eyes Included in the Study

Parameter	Mean ± Standard Deviation	Range
CCT (μm)	538 ± 35	414-627
Corneal curvature (mm)	7.74 ± 0.33	7.00-9.04
Axial length (mm)	23.82 ± 1.08	20.92-26.70
GAT IOP (mm Hg)	15.3 ± 3.3	8.0-26.0
ORA IOPCC (mm Hg)	15.2 ± 3.0	7.4-29.3
CRF (mm Hg)	9.47 ± 1.75	4.68-14.15

IOPg agrees with Goldmann. IOPcc provides an estimate of IOP that is less influenced by corneal properties than those provided by GAT



Evaluation of the Influence of Corneal Biomechanical Properties on Intraocular Pressure Measurements Using the Ocular Response Analyzer.
Felipe A. Medeiros, MD and Robert N. Weinreb, MD
J Glaucoma 2006;15:364–370.

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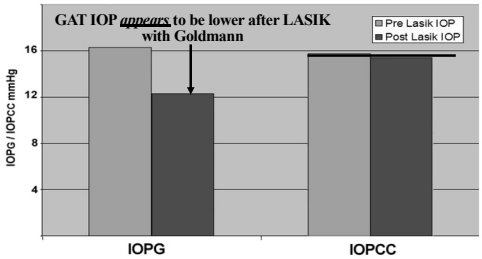
IOPcc – a superior indicator of IOP
Little influence from refractive surgery



28 eyes pre and post LASIK.
Data courtesy Dr. David Castellano, MD / Dr. Jay Pepose, MD

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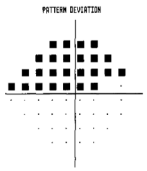
IOPcc – a superior indicator of IOP
Case 2: IOPcc agrees better with status of VF loss

53 yo black male with Glaucoma
- CCT 598/582
- GAT: 15mm Hg
- On IOP medication OU

IOPcc Measurements
- IOPg: 15.5 OD / 15.0 OS
- IOPcc: 19.2 OD / 18.9 OS



Note: IOPcc is the opposite direction from a CCT adjustment and is properly associated with the status of glaucoma

Data Courtesy of Nathan Radcliffe, MD
Assistant Professor of Ophthalmology
Weill Cornell Medical College, New York-Presbyterian Hospital

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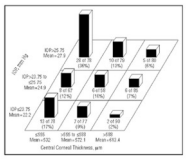
The cornea and glaucoma
Lessons from the OHTS



OHTS put the cornea on the map in glaucoma

- Corneal Thickness was found to be an independent risk factor for development of glaucoma
  - NOT an IOP correction factor
- But CCT is a simple geometrical attribute of the cornea / eye
  - Investigations into the "connection" between CCT and whole eye (scleral, ONH, lamina cribrosa) properties have come up empty
- Is there a corneal property that better explains back of the eye behavior?
- Corneal Hysteresis
  - **What is it?**
  - **How is it measured?**
  - **What is normal? What is abnormal?**
  - **The literature**

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Ocular Response Analyzer Technology
Interpretation of measurement values

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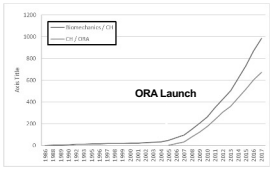
What is Corneal Hysteresis (CH)?

- **CH is a tissue property that reflects the ability of the cornea to *absorb and dissipate energy*** [1]
  - Measurement output specific to the Patented Reichert Ocular Response Analyzer
  - The only in-vivo measurement of ocular biomechanics
  - Indicative of visco-elastic damping[2]
  - **"How good of a shock absorber is the eye"?**
- **Commercial availability since 2005**
  - ORA G3 model 2015

Publications on Corneal Biomechanics / Hysteresis



1. Luce DA. *J Cataract Refract Surg.* 2005;31:156-162.
2. Duppe WJ Jr. *J Cataract Refract Surg.* 2007;33:1499-1501.
3. Pubmed search on terms "corneal biomechanics" & "corneal hysteresis", ORA peer reviewed bibliography provided by Reichert, with review of the sample size (N) in each publication

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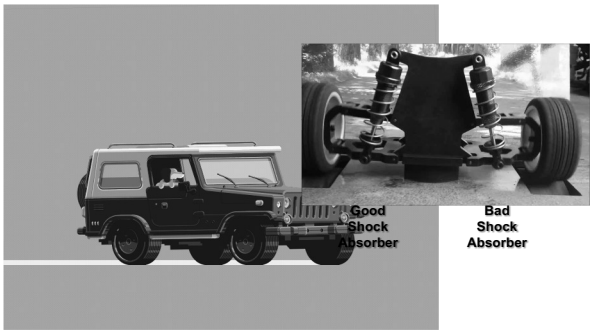
How is the eye like automotive suspension?
Energy and Damping



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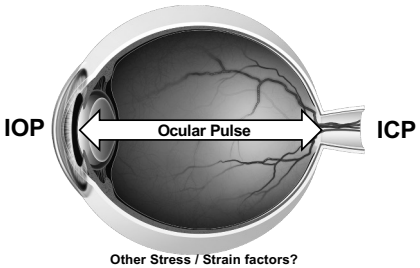
How good of a shock absorber is your eye?



Other Stress / Strain factors?

- What's happening to this energy?
- Can the eye absorb & dissipate all this shock?
- **Can we measure the shock-absorption capacity of the eye?**

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Hysteresis
What it is – What it is NOT

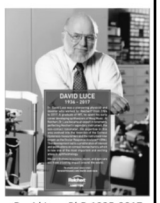
Hysteresis characterizes the response to application and removal of force in materials that ***dissipate a portion of applied energy*** [1]

- *Not a new concept (term defined in 1890)*
- *13,000+ medical publications on hysteresis in a variety of fields* [2]

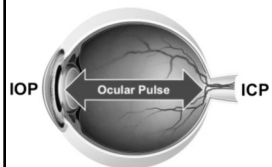
Corneal Hysteresis (CH)

Reflects cornea's ability to ***absorb and dissipate energy*** [3]

- An indication of "damping" capacity of the ocular tissue
  - **NOT an indication of "stiffness" or "rigidity"**



David Luce PhD 1935-2017
Pioneered Corneal Hysteresis



"The eye is under a constant assault"

Hysteresis tells us "How good of a shock absorber" the eye is.

1. Vincent J. Basic elasticity and viscoelasticity. In: Vincent J, ed. *Structural Biomaterials*. 3rd ed. Princeton, NJ: Princeton University Press; 2012:1-28.
2. PubMed Search for "hysteresis" on March 11, 2021 returned 13,766 results.
3. Luce DA. *J Cataract Refract Surg.* 2005;31:156-162.

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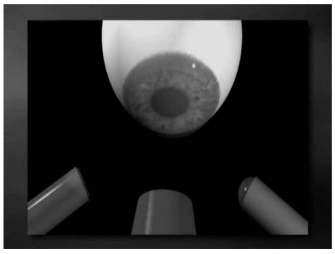
Ocular Response Analyzer Technology
Method of Operation

Measured by rapidly deforming the cornea under a gentle air pulse

- *This is not your father's NCT!*



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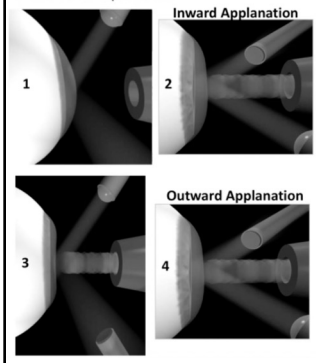
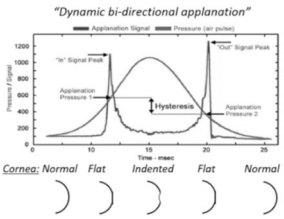
Ocular Response Analyzer G3
Method of Operation





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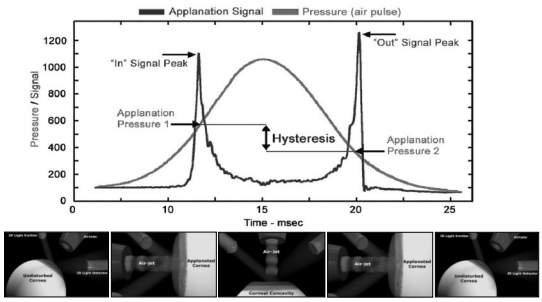
Ocular Response Analyzer Technology
Bi-directional Applanation Signal



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Corneal Hysteresis: Basic Evidence
CH Average Values in Normal Subjects

CH Values in Normals around the world	N	CH*
Brazil[1]	105	10.1 ± 1.8
UK[2]	272 pairs	10.2 ± 1.2
China[3]	125	10.9 ± 1.5
Japan[4]	204	10.2 ± 1.3
Spain[5]	88	10.8 ± 1.5
USA[6]	44	10.5 ± 1.2

*CH units are mmHg

1. Fontes BM J Refract Surg. 2008 Nov;24(9):941-5.
2. Carbonaro, The Heritability of Corneal Hysteresis and Ocular Pulse Amplitude A Twin Study doi:10.1016/j.ophtha.2008.02.011
3. Lam A. Et Al. Optom Vis Sci. 2007 Sep;84(9):909-14.
4. Kamiya Et Al. J Refract Surg. 2009 Oct;25(10):888-93
5. Ortiz Et Al. J Cataract Refract Surg. 2007 Aug;33(8):1371-5
6. John Et. Al. 2007 Spring;39(1):9-14

40

Ocular Response Analyzer G3
Measurement Values, range, and interpretation

- Average Normal CH is 10.5 mmHg
- Standard dev 1.5 mmHg
- Fairly stable diurnally and with age

Corneal Compensated IOP (IOPcc): Closer to the "true pressure"

Corneal Hysteresis: Normal average 10.5 Typical Range is 8-14 (low = risk)

IOPg: "Goldmann equivalent" reference

Waveform Score: signal reliability (0-10)

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The Evidence

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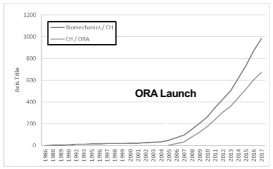
What is Corneal Hysteresis (CH)?

- **CH is a tissue property that reflects the ability of the cornea to *absorb and dissipate energy*** [1]
  - Measurement output specific to the Patented Reichert Ocular Response Analyzer
  - The only in-vivo measurement of ocular biomechanics
  - Indicative of visco-elastic damping[2]
  - **"How good of a shock absorber is the eye"?**
- **700 publications citing clinical evidence**
  - with data from 80,000+ patients[3]
- **Commercial availability since 2005**
  - ORA G3 model 2015

Publications on Corneal Biomechanics / Hysteresis



1. Luce DA. *J Cataract Refract Surg.* 2005;31:156-162.
2. Duppe WJ Jr. *J Cataract Refract Surg.* 2007;33:1499-1501.
3. Pubmed search on terms "corneal biomechanics" & "corneal hysteresis", ORA peer reviewed bibliography provided by Reichert, with review of the sample size (N) in each publication

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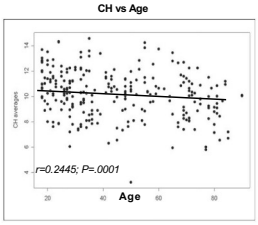
Corneal Hysteresis: Basic Evidence

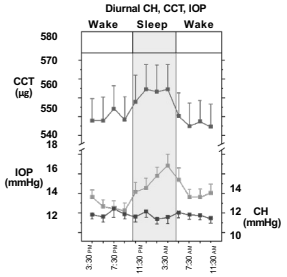
CH Diurnal Stability and changes over time

- CH does not display a 24-hour rhythm[1]
- CH has been shown to decrease slightly with age[2]

CH vs Age



Diurnal CH, CCT, IOP



1. Kida T et al. *Invest Ophthalmol Vis Sci.* 2008;47:4422-4426.
2. Fontes BM. J Refract Surg. 2008 Nov;24(9):941-5.

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Corneal Hysteresis in Glaucoma

Association with Progression in a Retrospective Study

	OR	LCL	UCL	*P*-value
Age per year <65	1.12	1.01	1.24	.03
Age per year >65	1.08	1.01	1.15	.02
GAT IOP per mmHg	1.22	0.95	1.58	.12
Treatment	1847.6	3.16	10^6	.02
IOP by treatment interaction	0.79	0.61	1.03	.08
CCT per 100 microns	1.65	0.66	0.98	.30
Years with glaucoma	1.00	0.96	1.04	.98
Baseline IOP	0.99	0.93	1.06	.79
CH per mmHg	0.81	0.66	0.98	**.03**

[illegible] upper confidence limit. CCT Central Corneal Thickness; CH Corneal Hysteresis

- 230 POAG or suspected POAG patients were included in the study
- 3 years or more FU
- Minimum 5 VF exams

Conclusions: Corneal Hysteresis was the parameter most associated with progressive field worsening

Congdon NG et al. *Am J Ophthalmol.* 2006;141:868-875.

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Corneal Hysteresis in Glaucoma

Association with Progression in Normal Tension Glaucoma (NTG)

- A retrospective study to investigate the clinical significance of CH in patients with progressing NTG.
- 82 eyes of 82 NTG patients receiving topical anti-glaucoma medications were included.
  - Subjects were included if they had an established diagnosis of NTG made by a glaucoma specialist based on glaucomatous optic disc damage and abnormal VF test results. Signs of glaucomatous optic disc damage were considered diffuse or localized neuroretinal rim loss, excavation, and RNFL defects.
  - An abnormal VF was defined as a pattern standard deviation outside of the 95% normal confidence limits or a Glaucoma Hemifield Test result outside normal limits.
  - At least two consecutive abnormal VF examinations were required, with the most recent test performed within 12 months of enrollment.
- NTG was defined by repeatable IOP ≤21 mm Hg, glaucomatous optic disc changes, and VF loss.
- Patients were allocated to two groups based on the mean value of corneal hysteresis
  - Mean CH was 10.08 mmHg.
  - Assessment of progression was based on the trend analysis using VF MD slope.
- Uni and multivariable analyses were constructed to identify factors associated with increased odds of progression, including CH, IOP, central corneal thickness (CCT), and RNFL thickness.

MV Multi-Variate; CCT Central Corneal Thickness; RNFL Retinal Nerve Fiber Layer; VF MD Visual Field Mean Deviation; CH Corneal Hysteresis, IOP Intraocular Pressure

Park Et. Al Br J Ophthalmol. 2015 Jan 2. pii: bjophthalmol-2014-305962. doi: 10.1136/bjophthalmol-2014-305962.

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Corneal Hysteresis in Glaucoma

Association with Progression in Normal Tension Glaucoma (NTG)

Logistic regression with VF progression as a binary outcome (stepwise MV)	β (95% CI)	*P-Value*
Baseline VF MD (dB)	1.18 (0.96 to –1.44)	0.12
CCT (µm)	0.99 (0.97 to 1.01)	0.35
Subfoveal choroidal thickness	0.99 (0.98 to 1.00)	0.08
RNFL thickness (average)	0.96 (0.92 to 0.99)	0.04
RNFL thickness (temporal)	0.97 (0.94 to 1.01)	0.09
RNFL thickness (inferior)	0.98 (0.96 to 1.01)	0.13
Corneal Hysteresis (mmHg)	0.32 (0.17 to 0.62)	<0.01

- Of the **39 eyes with low CH, 26 (66.7%) showed progression** of VF damage while 13 (33.3%) showed no progression.
- Of the **43 eyes with high CH, 15 (34.9%) showed progression** of VF damage, whereas 28 (65.1%) showed no progression.

These findings suggest that CH can be used as one of the prognostic factors for progression, independent of corneal thickness or IOP

MV Multi-Variate; CCT Central Corneal Thickness; RNFL Retinal Nerve Fiber Layer; VF MD Visual Field Mean Deviation; CH Corneal Hysteresis, IOP Intraocular Pressure

Park Et. Al Br J Ophthalmol. 2015 Jan 2. pii: bjophthalmol-2014-305962. doi: 10.1136/bjophthalmol-2014-305962.

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Corneal Hysteresis in Glaucoma

Predictive of Progression in Prospective, Longitudinal Study (DIGS)

- Adults ≥18 years of age[1]
- Only subjects with open angles on gonioscopy were included[1,2]
- Excluded subjects[1,2]
  - BCVA <20/40
  - Spherical refraction outside of ±5.0 diopters or cylinder correction outside 3.0 diopters
  - Any ocular or systemic disease that could affect the optic nerve or visual field

Evaluation[2]
- Follow-up at 6 month intervals with comprehensive ophthalmologic exam

• Review of medical history	• Dilated fundoscopic exam
• BCVA	• Steroscopic optic disc photography
• Slit lamp biomicroscopy	• Automated perimetry
• IOP measurement (GAT)	• CCT (ultrasound pachymetry)
• Gonioscopy	• Axial length (IOL Master)

Medeiros FA et al. *Ophthalmology.* 2013;120:1533-1540.

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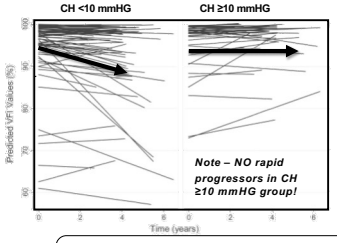
Corneal Hysteresis in Glaucoma

Predictive of Progression in Prospective, Longitudinal Study (DIGS)



- Univariate model: each 1 mmHg decrease in CH was associated with a 0.25%/year increase in rate of VFI decline (*P*<0.001)
  - By comparison, each 1 mmHg higher baseline GAT IOP was associated with a 0.11%/year faster rate of VFI loss (*P*<0.001)
- In the multivariate model, CH was >3X more associated with rate of VF progression than CCT (17.4% vs 5.2%)
- The relationship between CH and IOP is complex:
  - For eyes with lower CH, the impact of IOP was significantly larger than in eyes with higher CH levels.

The prospective longitudinal design of this study supports the role of CH as an important factor to be considered in the assessment of risk for glaucoma progression

Medeiros FA et al. *Ophthalmology.* 2013;120:1533-1540.

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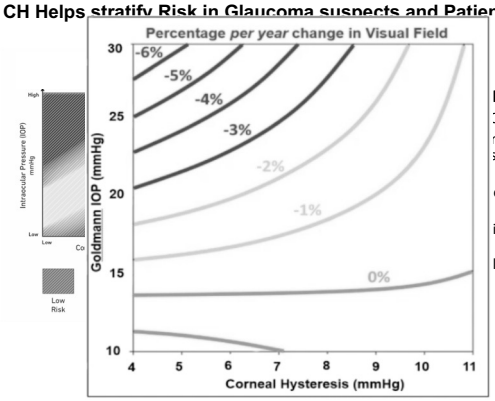
CH Helps stratify Risk in Glaucoma suspects and Patients



Risk
CT & IOP
risk
s
o to treat;
ith highest
low risk for

50

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Clinical Evidence

Why is CH relevant in Glaucoma?

(Low) CH has been consistently shown to be independently and strongly associated with or predictive of glaucoma progression

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Ophthalmology. 2013 Aug;120(8):1533-40. doi: 10.1016/j.ophtha.2013.01.032. Epub 2013 May 1.

Corneal hysteresis as a risk factor for glaucoma progression: a prospective longitudinal study.

Medeiros FA[1], Meira-Freitas D, Lisboa R, Kuang TM, Zangwill LM, Weinreb RN.

⊕ Author information

Abstract

PURPOSE: To evaluate the role of corneal hysteresis (CH) as a risk factor for the rate of visual field progression in a cohort of patients with glaucoma followed prospectively over time.

DESIGN: Prospective observational cohort study.

PARTICIPANTS: The study group included 114 eyes of 68 patients with glaucoma followed for an average of 4.0 ± 1.1 years. Visual fields were obtained with standard automated perimetry. Included eyes had a median number of 7 (range, 5-12) tests during follow-up.

METHODS: The CH measurements were acquired at baseline using the Ocular Response Analyzer (Reichert Instruments, Depew, NY). Evaluation of rates of visual field change during follow-up was performed using the visual field index (VFI). Linear mixed models were used to investigate the relationship between rates of visual field loss and baseline CH, baseline intraocular pressure (IOP), and central corneal thickness (CCT), while adjusting for potentially confounding factors. An interaction term between IOP and CH was included in the model to investigate whether the effect of IOP on rates of progression depended on the level of CH.

MAIN OUTCOME MEASURES: Effects of CH, IOP, and CCT on rates of VFI loss over time.

RESULTS: The CH had a significant effect on rates of visual field progression over time. In the univariable model including only CH as a predictive factor along with time and their interaction, each 1 mmHg lower CH was associated with a 0.25%/year faster rate of VFI decline over time (P<0.001). The multivariable model showed that the effect of IOP on rates of progression depended on CH. Eyes with high IOP and low CH were at increased risk for having fast rates of disease progression. The CH explained a larger proportion of the variation in slopes of VFI change than CCT (17.4% vs. 5.2%, respectively).

CONCLUSIONS: The CH measurements were significantly associated with risk of glaucoma progression. Eyes with lower CH had faster rates of visual field 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.

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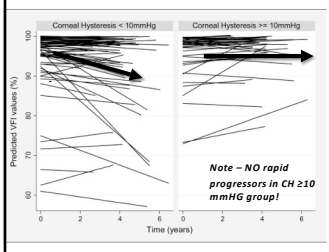
CH as a Predictor of Progression



114 POAG eyes followed at 6 month intervals for 4 years.

CH was 2x more predictive of VF progression than GAT and 3X more predictive than CCT

The prospective longitudinal design of this study supports the role of CH as an important factor to be considered in the assessment of risk for glaucoma progression

Medeiros FA et al. *Ophthalmology.* 2013;120:1533-1540.

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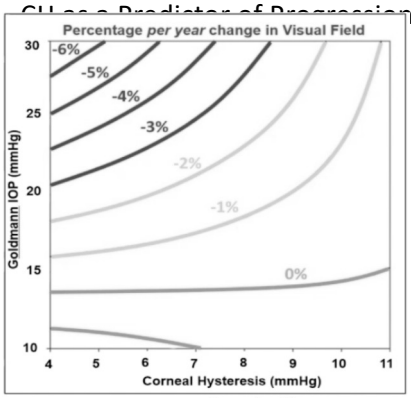
CH as a Predictor of Progression



Medeiros FA et al. *Ophthalmology.* 2013;120:1533-1540.

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CH is Predictive of Response to Glaucoma Therapy

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]

Baseline CH is independently associate with the magnitude of IOP reduction from PGA therapy.

The relationship between corneal hysteresis and the magnitude of intraocular pressure reduction with topical prostaglandin therapy. Br J Ophthalmol. 2012 Feb;96(2):254-7. Daniel R. Agarwal, Joshua R. Ehrlich, Mitsugu Shimmyo, Nathan M. Radcliffe

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- How about diagnostically?

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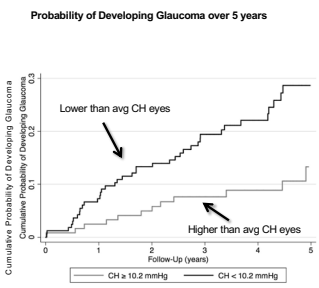
Corneal Hysteresis in Glaucoma

Predictive of conversion to Glaucoma in pre-perimetric Glaucoma Suspects

Purpose: To investigate the role of CH as a risk factor for **development** of glaucoma in a prospective longitudinal study.

Results: Fifty four (19%) of the 287 eyes developed repeatable visual field defects during a 4 year follow-up.

CH was *independently* predictive of conversion to glaucoma even when adjusted for age, IOP, and CCT.



A Prospective Longitudinal Study to Investigate Corneal Hysteresis as a Risk Factor for Predicting Development of Glaucoma Am J Ophthalmol. 2018 Mar; 187: 148–152. Feilin Zhu , Alberto DinizFilho, Linda M. Zangwill , Felipe A. Medeiros

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AMERICAN ACADEMY OF OPHTHALMOLOGY

Corneal Biomechanics and Visual Field Progression in Eyes with Seemingly Well-Controlled Intraocular Pressure

Bianca N. Susanna, MD,[1,2,3] Nara G. Ogata, MD,[1] Alessandro A. Jammal, MD,[1] Carolina N. Susanna, MD,[1,2,3] Samuel I. Berchuck, PhD,[1,4] Felipe A. Medeiros, MD, PhD[1]

460 eyes of 334 glaucoma patients
Follow-up – 4.3 years
Well controlled if IOP < 18 mm HG

CH (8.6 vs 9.4)
CCT (515 vs 531)

68% higher risk of progression

179 eyes well controlled
42 (23.5%) of those eyes had VF progression

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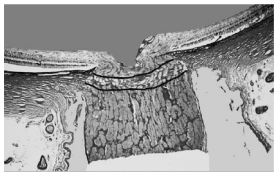
Relationship of Corneal Hysteresis and Anterior Lamina Cribrosa Displacement in Glaucoma

BRANDON J. WONG, SASAN MOGHIMI, LINDA M. ZANGWILL, MARK CHRISTOPHER, AKRAM BELGHITH, EREN EKICI, CHRISTOPHER BOWD, MASSIMO A. FAZIO, CHRISTOPHER A. GIRKIN, AND ROBERT N. WEINREB

147 eyes of 96 glaucoma patients
Follow-up – 3.5 years



Choroidal thickness = posterior ALCS displacement
Low Corneal hysteresis

Each 1 mmHg lower CH
=
0.66 microns of posterior ALCS displacement

Wong BJ, Moghimi S, Zangwill LM, et al. Relationship Of Corneal Hysteresis and Anterior Lamina Cribrosa Displacement in Glaucoma. Am J Opthalmol. 2019 Nov 23.

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Ocular Response Analyzer Corneal Hysteresis

92145

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Corneal Hysteresis and IOPcc: Glaucoma Vitals for the Modern Era

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