

Corneal Hysteresis, Central Corneal Thickness, & Glaucoma

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How do we know patients are at risk for glaucoma progression?

Well-established risk factors

- IOP
- Age
- Ethnicity/Race
- Family history
- **Central Corneal Thickness (CCT)**

Possible novel risk factors

- **Corneal hysteresis**

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Central corneal thickness basics

- Average central thickness: 540 μ m
- Measured via pachymetry
- Every 10% increased thickness, add 1.1 mmHg (Doughty & Zaman 2000, Surv Ophth)



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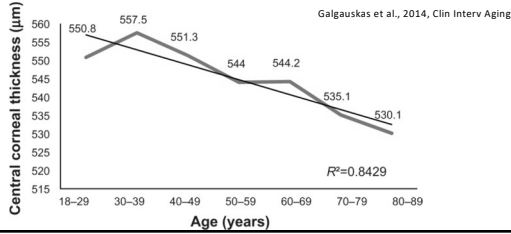
The Ocular Hypertension Treatment Study (Gorden et al., 2002)

- Prospective study: patients with ocular htn were randomized to treatment or no treatment, watched over 5 years. Double the risk of glaucoma in un-treated group.
- First to report CCT as a risk factor.
- "Participants with a corneal thickness of **555 μm or less** had a 3-fold greater risk of developing POAG compared with participants who had a corneal thickness of more than 588 μm."
- Likely related to direct correlation with IOP measurement: thinner cornea → artificially low reading → delayed intervention

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Effect of age on CCT?

- Most studies conclude that it thins with age



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Corneal thickness associated with race/ethnicity

TABLE 4. Mean Central Corneal Thickness: Total Population and by Ethnic Groups

	Total Population	African American	Asian	Caucasian	Hispanic
Number	1,855	116	170	1,466	203
Mean	551.16	535.46	549.79	552.59	551.10

Shimmyo et al., 2003, Am J Ophthalmology

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So is corneal hysteresis...

- Study of CH vs CCT in blacks, Hispanics, and whites
- Included 807 POAG or POAG suspect eyes (abnormal disc or fam hx)
- Multivariate analysis:
 - When CCT is the outcome, CH, but not race, matters
 - When CH is the outcome, both CCT and race matter

Haseltine et al., 2012, Acta Ophthalmologica

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Inheritance also important

- Another interpretation is that since CCT is highly heritable, it may be that genetic risk factors for glaucoma that are unrelated to CCT may nonetheless be co-inherited with CCT (Wang et al., 2014, J Glaucoma)
- Monozygotic vs dizygotic twin studies show monozygotic have stronger correlation for both CCT (Toh et al., 2005, IOVS) and corneal hysteresis (CH) (Carbonaro et al., 2008, Ophthalmology)

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Failure to understand this → delayed diagnosis → racial disparity

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What is hysteresis?

- The difference between the pressure at which the cornea bends inward during an airjet applanation and the pressure at which it bends out again
- Measured by "ocular response analyzer"
- Normal range: 10-11.

Ocular Response Analyzer® G3

The only Tonometer with a CPT code for Corneal Hysteresis

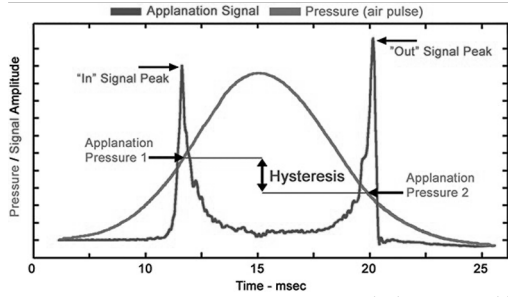


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- Determined by biochemical and biomechanical properties of the cornea relating to elasticity as well as the current pressure of the eye
- It is a behavior of the cornea, not a static property
- Implies the nature of the eye's elasticity in general (i.e. extracellular matrix)

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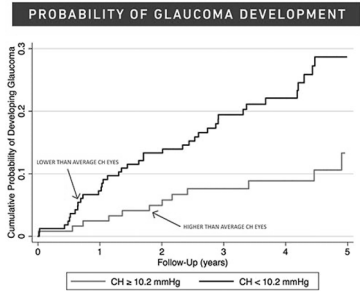


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So what?

- Predicts POAG onset and progression (Susanna et al., 2018, Am J Ophthalmology)
- Prospective cohort study of glaucoma suspects, at least 18 months (287 eyes)
- Glaucoma def: repeatable (at least 3 consecutive) abnormal visual field test results
- Every 1 mmHg lower CH, 21% more chance of developing POAG.
- Mean CH in healthy eyes, mean age 49: 10.97 ± 1.59 mmHg (Mangouritsas et al., 2009, Acta Ophthalmologica)
- Mean CH in POAG, mean age 62: 8.95 ± 1.27 mmHg

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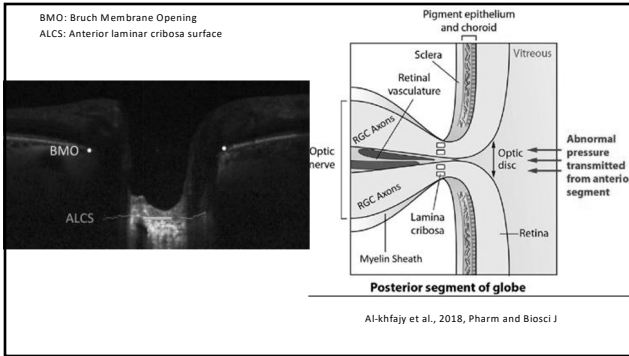


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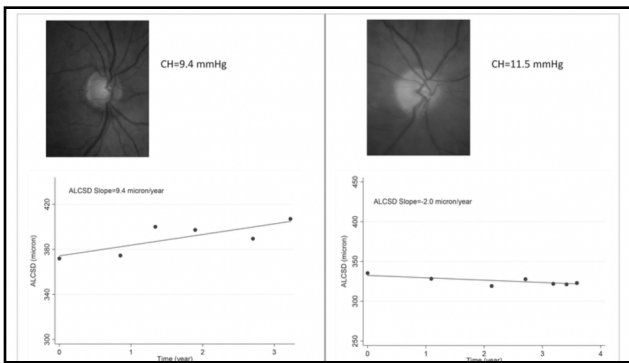
How does CH relate to risk of optic neuropathy?
Answer: Possibly a reporter for the optic nerve structures

- Prospective case series at UCSD (Wong et al., 2019)
- 147 eyes, minimum 3-year follow-up
- Every 1 mm Hg decrease in CH leads to a $0.66 \mu\text{m}/\text{year}$ posterior displacement of the anterior lamina cribosa surface

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Effect of age on CH?

Age groups (years)	10-20	21-30	31-40	41-50	>50
IOPg (mean ± SD, range, median) (mmHg)	15.6 ± 3.8 (7.8-25.7, 15.1)	14.1 ± 2.8 (7.8-22.8, 14.0)	14.1 ± 3.5 (5.7-26.6, 14.0)	14.9 ± 3.3 (7.4-23.8, 15.1)	15.4 ± 4.1 (7.5-25.4, 15.4)
OS	15.3 ± 3.5 (9.1-26.9, 14.7)	13.9 ± 3.2 (3.0-23.2, 14.2)	13.5 ± 3.0 (5.9-25.9, 13.8)	14.5 ± 3.7 (7.7-25.1, 14.5)	15.3 ± 4.0 (6.9-25.2, 14.8)
IOPec (mean ± SD, range, median) (mmHg)	15.3 ± 3.3 (8.2-24.1, 14.5)	15.3 ± 2.5 (8.4-20.3, 15.5)	15.1 ± 3.0 (8.6-24.6, 15.1)	16.0 ± 3.2 (8.6-23.4, 16.1)	16.6 ± 3.7 (8.5-27.4, 16.3)
OS	15.7 ± 3.3 (7.9-25.3, 15.6)	15.6 ± 2.9 (8.1-24.5, 16.0)	15.1 ± 2.7 (7.8-24.8, 15.2)	16.1 ± 3.3 (9.5-25.7, 15.8)	16.9 ± 3.8 (8.0-25.1, 16.2)
CH (mean ± SD, range, median) (mmHg)					
OD	11.2 ± 3.0 (6.0-15.8, 11.0)	10.0 ± 1.5 (5.9-14.2, 9.9)	10.1 ± 1.4 (7.2-13.8, 10.0)	9.8 ± 1.7 (6.8-14.1, 9.7)	9.7 ± 1.5 (6.3-13.2, 9.7)
OS	10.6 ± 2.2 (6.7-20.4, 10.7)	9.6 ± 1.5 (5.6-13.5, 9.5)	9.6 ± 1.4 (6.5-14.2, 9.4)	9.5 ± 1.6 (6.6-14.3, 9.4)	9.3 ± 1.6 (5.0-13.1, 9.2)

El Massry et al., 2020, International Ophthalmology

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What accounts for more glaucoma: CH or CCT?

- Prospective cohort study at UCSD (Medeiros et al, 2013, Ophthalmology)
- Multivariate analyses for visual field decline
- Both CH and CCT statistically significant
- CH explained a larger proportion of the variation in slopes of VFI change than CCT (17.4% versus 5.2%, respectively)

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- Prospective study at New York Eye & Ear Infirmary (Gustavo De Moraes et al, 2012, J Glaucoma)
- 153 eyes with mean follow-up 5 years
- Multivariate analysis for visual field decline
- Higher IOP, age, and CH, but not CCT, showed significance

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So what's more important: CCT vs CH

- Some evidence that CH is more important but more research is needed. Regardless, CCT is a great, readily accessible, simple measurement that should be included in all assessments of a glaucoma evaluation.

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Thank you!
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