A New Glaucoma “VITAL SIGN”

How Corneal Hysteresis is Improving Glaucoma Patient Management
Dear Colleagues,

Until recently, glaucoma diagnosis and management have been limited by tools that depend a great deal upon practitioner competence and due diligence. Some of these approaches—gonioscopy, optic nerve head (ONH) evaluation, visual fields (VFs), and IOP measurement—have various drawbacks. For example, poor ONH evaluations could lead to inaccurate assessments, and VFs are subjective tests that don’t catch all early damage, depending on what is being viewed.

In the last two decades, advancing imaging modalities to depict structural and functional issues in glaucoma have furthered disease management. Optical coherence tomography (OCT) has helped to visualize the retinal nerve fiber layer (RNFL) to reveal damage, while swept-source OCT has improved glaucoma assessment of the lamina cribrosa. As well, OCT angiography has made way for insights into capillary dropoff in the peripapillary region for better treatment decisions.

One increasingly important parameter that has shown itself to be an invaluable biomarker for determining risk of glaucoma development and progression is corneal hysteresis (CH). CH measures the capacity of the corneal tissue to dissipate energy (i.e., the eye’s ability to absorb shock). Studies such as the Ocular Hypertension Treatment Study (OHTS) have demonstrated the cornea’s involvement in glaucoma.1-6 More recent studies on CH have confirmed the importance of the cornea in glaucoma decision making and have shed light on the role of corneal biomechanics, as opposed to simply central corneal thickness (CCT).

The only device FDA approved to measure CH is the Reichert Ocular Response Analyzer (ORA). Since the ORA was approved in 2004 and described a year later by David Luce, PhD, nearly 700 publications have established the usefulness of CH.7 CH now has a reimbursement code, with coverage in several states.

Another useful measurement provided by the ORA to help guide glaucoma decision making is corneal compensated IOP (“IOPcc”). This IOP measurement is relatively cornea-independent, providing an assessment of IOP that has been shown to be less influenced by variables known to affect the accuracy of other tonometers, and is more associated with glaucoma progression than Goldmann applanation tonometry (GAT) measurements. IOPcc agrees with GAT on average, which means clinicians can interpret the value as they would a Goldmann measurement. But since IOPcc has essentially no correlation to CCT, and is minimally affected by corneal biomechanics, clinicians can place a great deal of confidence in the accuracy of this IOP measurement.

CH and IOPcc are rapidly changing the landscape of glaucoma management. The measurements are becoming essential tools for clinicians seeking to determine patient progression risk, and those looking to make the most informed decisions about treatments that will have the greatest chance for positive visual outcomes. — The Panel

How good of a shock absorber is your eye?

The Eye as a Shock Absorber
Corneal hysteresis measures the capacity of the corneal tissue to dissipate energy (i.e., the eye’s ability to absorb shock) by quantifying the cornea’s visco-elastic damping.

Ocular Response Analyzer Technology
Method of Operation
Measured by rapidly deforming the cornea under a gentle air pulse

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Corneal Hysteresis & Risk Factors for Glaucoma

By Felipe Medeiros, MD

Numerous studies have provided us with insights into why CH is associated with glaucoma. They have demonstrated how corneal biomechanics are related to optic nerve deformation and structural changes consistent with glaucoma development and progression. The problem with some of these studies has been that they have been retrospective. So, if a scientist measures CH today and looks back to see whether the patient has progressed, it isn’t clear if the result was a cause or an effect: Was CH a true risk factor for progressing, or did progression lead to a lower CH? As a result, prospective studies looking at whether CH is a risk factor for progression are necessary to draw any real conclusions.

Congdon, et al. gave us the first observational study to investigate the impact of CH and CCT on various indicators of glaucoma damage. In the study, patients had their CH measured by the Reichert ORA and CCT determined by ultrasonic pachymetry. Two glaucoma specialists reviewed the charts to determine the highest known IOP, target IOP, diagnosis, years with glaucoma, cup-to-disk ratio (CDR), mean defect (MD), pattern standard deviation (PSD), glaucoma hemifield test (GHT), and presence or absence of VF progression. The study revealed that thinner CCT was associated with glaucoma.

Strategies to Complete the Glaucoma Puzzle in Patients

By John Berdahl, MD

Glaucoma, like many pathologies, is not a straightforward disease; it requires a nuanced approach to understand each individual’s unique situation and arrest future progression. On one side of the glaucoma management puzzle are diagnostic pieces to identify evidence of disease and determine likelihood of progression in a given patient; on the other side are therapeutic pieces to help slow disease advancement. Lately, the field and research have offered us groundbreaking new information to fill in crucial parts of the glaucoma puzzle.

Clinicians must leave no stone unturned when it comes to glaucoma evaluation. Everything from patient history, to gonioscopy, ONH evaluation, VFs, OCT, IOP, CCT and CH can guide decisions on which type of intervention (e.g., medication, minimally invasive glaucoma surgery [MIGS], selective laser trabeculoplasty [SLT], invasive surgery) will be necessary to get a patient’s glaucoma under control. Yet, these tools are shifting in order of importance.

While gonioscopy has had a renaissance because of its utility with the rapidly growing adoption of MIGS, ONH evaluation is less important to my evaluation than it used to be. VFs are still where the rubber meets the road, as patients don’t necessarily know their RNFL loss or whether their IOP is high, but they know if they can see. However, VFs are subjective and variable and may take years to show progression.

OCT has changed how we look at glaucoma in a robust way, and I believe that all of the machines do a reasonably good job of looking at the nerve fiber layer. SS-OCT is playing a greater role, with its higher resolution and faster acquisition to image the lamina cribrosa—an important factor in determining high-risk glaucoma suspects. And OCTA’s potential is unfolding with its ability to illuminate changes in retinal and choroidal blood vessel flow.

IOP is still the only modifiable risk factor for glaucoma. From the wealth of studies available in the medical literature, we know that lowering IOP helps slow progression of glaucoma. However, measuring IOP isn’t easy, as many factors influence IOP. These can include time of day, CCT, CH, post-refractive status, etc. And IOP variability matters. It’s widely understood that the greater the eye pressure variability over time, the higher the risk of disease progression. We also know from the OHTS Study that lowering eye pressure reduces the chance of developing glaucoma from ocular hypertension. I have found that lowering IOP can reduce risk of progression by about 50 percent, depending on glaucoma stage.

Also consider that measuring IOP is actually measuring the pressure inside the eyeball or, more specifically, the pressure differential across the cornea. This is the amount of force being used to flatten the cornea so the pressure inside is equal to that outside. Since glaucoma doesn’t occur at the cornea, but rather at the ONH, IOP is really a surrogate for what’s happening at the ONH. So corneal hysteresis is giving us information that may be more directly related to ONH status than IOP or other measurements.

One of my favorite questions to ask patients is: Do you have someone in your family who has gone blind from glaucoma? For those who don’t think glaucoma is serious or don’t take medication compliance to heart, they hear the word “blind,” and the implications of this disease become real. For patients who have a parent who went blind, I am reminded how serious it is.

IOP MEASUREMENT VARIABILITY

Many factors influence IOP. These can include time of the day, corneal thickness, corneal hysteresis, post-refractive status, and others.

Images: John Berdahl, MD
damage, and CH and axial length were correlated with progressive VF worsening.

De Moraes, et al. prospectively assessed glaucoma patients who underwent evaluations including IOP by GAT and CH by the ORA. They looked at the relationships between CH and CCT, and rates of VF change. Researchers found that corneal biomechanical and physical properties such as CH and CCT were highly associated with each other and VF progression. The mean global rate of VF change was $-0.34 \pm 0.07$ dB/yr, and 25 eyes (16%) reached a progression endpoint. Progressing eyes had lower CH and CCT measurements compared with nonprogressing eyes, and CH and CCT corresponded significantly ($r=0.33, p<0.01$). By multivariate analysis, peak IOP (OR=1.13 per mmHg higher; $p<0.01$), age (OR=1.57 per decade older; $p=0.03$) and CH (OR=1.55 per mmHg lower; $p<0.01$) remained statistically significant. As such, researchers wrote that CH might more thoroughly describe corneal properties than CCT alone and be more closely associated with progression.

My team prospectively analyzed baseline CH and rates of glaucoma progression over time, and found that lower CH values yielded faster progression rates. A total of 68 glaucoma subjects (114 eyes) were evaluated at six-month intervals over four years. We assessed CH via the ORA, IOP by GAT, CCT using ultrasound pachymetry, and VF with the VF index. And we compared VF loss in eyes with CH less than 10 mmHg (average) and mean slopes of eyes with greater-than-average CH. The result: Eyes with lower CH had statistically significantly faster progression.

In addition, we compared CH's vs. CCT's predictive abilities, and found CH had greater prognostic ability than CCT; each 1 mmHg lower CH was associated with a 0.25%-per-year faster rate of VFI decline ($p<0.001$). Furthermore, baseline CH was associated with RNFL loss rates over time.

The OHTS first outlined risk factors that we use to determine whether a patient is a glaucoma suspect or at high risk for developing damage. When the OHTS was conducted, the ORA did not exist, so CH was not included. However, I am part of the follow-up OHTS 3 study in which we are assessing CH's role in development of glaucoma.

Given that CH can be affected by the viscoelastic properties of the cornea, some researchers have speculated that similar properties of posterior structures such as the lamina cribrosa and peripapillary sclera might also influence CH. Wells, et al. investigated the relationships between acute IOP-induced ONH surface deformation and CH and CCT in glaucomatous and normal eyes. The prospective, experimental study of 100 subjects (38 with glaucoma, 62 without glaucoma) investigated artificially induced IOP elevation using a LASIK suction ring. Researchers collected spherical equivalent, optic disc diameter, CCT, axial length, cylinder, GAT IOP, Pascal IOP, ocular pulse amplitude and ORA CH measurements. In glaucoma subjects, CH was associated with greater optic nerve surface deformation during transient elevations of IOP as well as cup depth changes.

Science has clearly demonstrated that CH is tied to glaucoma progression risk. Some researchers hypothesize that this association relates to biomechanical properties of tissues in the posterior eye. One group of investigators found a relationship between lamina cribrosa displacement and CH measurements before and after glaucoma medical therapies on spectral domain (SD)-OCT scans. Other investigators showed that biomechanical alteration of the sclera by cross-linking increased risk of RGC damage in a mouse model, though they didn’t specifically look at CH.

Turning to the IOPcc measurement, this parameter is also showing promise for predicting glaucoma patient outcomes. My team designed a study to see how the ORA’s IOPcc measurements vs. various tonometer pressure readings were associated with VF loss rates over time. Linear mixed models helped evaluate the relationship between each tonometer’s mean IOP and VF loss rate over time (while adjusting for age, race, CCT and CH). It turned out that mean ORA IOPcc was more predictive of VF loss than mean GAT or RBT IOP, after correcting for corneal-induced artifacts.

CH consistently has been identified as a risk factor for development and progression of glaucoma. Research continues to show that CH might provide an indirect clue about the ONH’s biomechanical susceptibility to damage. Further study would be needed to confirm whether IOPcc could be more valuable than RBT and GAT in predicting patient outcomes in glaucoma.
Using CH to Help Your Patients

By Nathan Radcliffe, MD

I use CH in clinical practice in a variety of ways: to estimate risk of glaucoma development and progression, stay abreast of IOP and the cornea’s impact on pressure; and gauge IOP response to eye drops, selective laser trabeculoplasty (SLT) and more invasive surgeries. My office has six pre-examining lanes, four with GAT and two with the ORA. I use Goldmann pressure findings from the ORA interchangeably with GAT.

My own research has found GAT and ORA measurements to be consistent. I published a paper showing that there’s as much variability between two Goldmann pressures taken five minutes apart as there is between GAT and ORA in that time. Some of my findings have revealed that the Goldmann-correlated measurements taken with the ORA can be cleaner than the GAT readings my techs take. The ORA is more objective; it’s never in a rush to get out of clinic, never mad at its boss, and when an eye is in front of it, it’s simply going to provide eye pressure measurements as accurately as possible.

The ORA also offers a very sterile and efficient way to measure pressure that doesn’t require topical anesthetics. Using fluorescein or tetracaine with fluorescein for GAT makes my patients wince in pain for a minute after instillation.

For surgical procedures, CH measurements help me predict SLT efficacy. I have performed surgery on many patients because of measurements achieved with the ORA. CH’s predictive ability for SLT was demonstrated in one particular study. Researchers evaluated clinical parameters for predicting SLT outcomes in medically uncontrolled open-angle glaucoma (OAG). They concluded that biomechanical properties (CH and corneal resistance factor [CRF]), in addition to baseline IOP, were significant predictors of SLT-induced IOP-lowering.

CORNEAL HYSTERESIS IN PRACTICE

Several cases demonstrate how I use corneal hysteresis in clinical practice:

CASE 1
A 53-year-old black male with glaucoma presented to me with the following evaluation: CCT: 598/582; GAT: 15mmHg; IOP medication OU; CH: 6.8 OD / 7.1 OS; IOPg: 15.6 OD / 15 OS; IOPcc: 19.2 OD / 18.9 OS. His GAT pressure was 15 mmHg. He had low CH, his IOPcc was higher (19 mmHg) than his GAT pressure, which meant that, despite a thick cornea, true pressure was higher than GAT measurements were revealing. There’s a correlation between CCT and CH, but they can go in different directions, and CCT is not a great way to correct IOP.

CASE 2
A 70-year-old man presented with GAT IOPs of 28 mmHg OU; CCT: 545 microns; VF: full (PSD 1.4); OCT: borderline, some thinning; VCDR: 0.7; and CH wasn’t available. The OHTS Glaucoma Risk Calculator yielded 30%. Five years later in 2012, the patient had been on three topical agents (PGA, beta-blocker and CAI), and GAT IOP was 24 mmHg. VFs revealed no progression. The old plan had been to consider surgery. CH was then available and recorded: CH: 13 mmHg; IOPcc: 13 mmHg; IOPg: 23 mmHg. Given the CH information, the new treatment plan was to continue medical therapy with ongoing monitoring of HVF and OCT. CH at baseline could have predicted low risk of VF loss. This is a case in which it became clear that the patient didn’t need multiple or possibly any topical agents.

CASE 3
The patient presented with OS CH 72; IOPcc: 21.7; OD CH 9.8; IOPcc 20.4; CH asymmetry was troublesome despite reasonably normal IOPs. OCT was “green,” but asymmetry was present. The nerves weren’t perfect; the left nerve inferiorly had a weak RNFL thickness and average. VFs revealed a possible early superior arc to scotoma. Because CH was significantly lower in the left than the right eye, we treated for early glaucoma.
CH is also an important factor in assessing glaucoma progression risk. Medeiros, et al. evaluated CH as a risk factor for the rate of VF progression in prospectively followed glaucoma subjects. A total of 114 glaucoma eyes were tracked for the rate of VF progression in prospectively followed glaucoma subjects. Medeiros, et al. evaluated CH as a risk factor for IOP, it’s essential to take the cornea into account. Rather than risk, low-CH patients. In addition, when it comes to targeting overtreating low-risk, high-CH patients but undertreating high-risk, low-CH patients. In addition, when it comes to targeting IOP, it’s essential to take the cornea into account. Rather than aggressively aiming for a low IOP number in someone with a high hysteresis, it might be more prudent to focus on IOP reduction in the low-CH patient due to the individual’s additional risk.

Other studies have revealed that CH and CCT are weakly correlated, and that CH varies between eyes. I keep that in mind when determining which eye has the highest risk. CH tends to vary more than CCT between fellow eyes, and is, on average, lower in the eye with worse glaucoma. CH, unlike CCT, is dynamic and may fluctuate a little with IOP shifts.

CH helps stratify risk in glaucoma suspects and patients. I believe it better explains VF loss than CCT and IOP, increasing confidence for clinical decisions on which patients to treat and monitor. There is some fluctuation in hysteresis. It’s a messy clinical parameter like everything else we measure, but when you add it to the rest of the glaucoma picture, it fits in a meaningful way that empowers you to take better care of your patients.

**CH Will Rock Your Clinical World**

*By Davinder Grover, MD*

CH measurements are revolutionizing glaucoma management in a new and exciting way, but they also are challenging dogma in the glaucoma world; if you don’t feel uncomfortable, you might not be paying attention. We spent decades thinking GAT was the gospel, and though we still use Goldmann because it encompasses the volume of evidence in our world, that is starting to change.

In Texas, CH is covered by Medicare. Since the test is reimbursable, patients don’t put up a fight. For my commercial payer patients, it’s not covered by major carriers, so I charge $50 to have it done. For many of my patients, $50 saves them hours of their lives because rather than seeing me every six months, they see me once a year to every 18 months.

As a glaucoma specialist, I fundamentally understand that pressure is high or low; and that’s how I think about hysteresis. The average CH measurement is 10 mmHg, so I consider above 10 mmHg to be great, and below 10 mmHg to be bad and associated with an increased risk of developing glaucoma and progressing from glaucoma, which has been evidenced by Dr. Medeiros and his team.

I truly feel that CH is a glaucoma vital sign. I do not make clinical decisions about my patients without knowing their CH because if their hysteresis is 8 mmHg, I treat them very differently than if it’s 13 mmHg. CH is an independent risk factor for glaucoma development and progression, which has been demonstrated in prospective and retrospective studies. It also provides invaluable information about the biomechanical structures of the eye. At the same time, IOPcc offers unique insights into IOP although the relationship between GAT IOP and IOPcc needs to be further evaluated.

What does this mean for me in practice? CH has changed my approach dramatically when it comes to making decisions about patient risk. I tell my patients, “I’m relying on the shock absorbing abilities of your eyes to give me important information about your disease. If your eyes are great shock absorbers, I’m reassured; if they’re bad shock absorbers, then I’m more concerned.” Everything starts from there.

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**CORNEAL HYSTERESIS IN PRACTICE**

Several cases demonstrate how CH has changed my clinical practice:

**CASE 1**

This was my partner’s patient whom I saw once. A 78-year-old female with POAG and no significant PHMs, the patient exhibited progression despite low IOP (between 10 and 14 mmHg OU since 2014). Our evaluation also revealed: CCT: 530 OU; C/D: 0.9 OU; timolol/dexamethasone combination BID OU; S/P Phaco/ECP OU in 2006 and 2008; VF progression; and no significant medical history. This was a patient in whom progression was difficult to explain. The left eye remained fairly stable, but the right eye progressed over five years. Pressure on both medications was 12 mmHg; CH was around 8 mmHg; IOPcc was much higher—revealing a discrepancy. I initiated Latanoprost in both eyes and had the patient come back a month later. IOPcc went down, but GAT didn’t change. I didn’t know why Goldmann missed this. This is a patient whom I would flag. When there is a stark discrepancy between GAT and IOPcc (with IOPcc being higher), I refer to the CH and, if low, I treat almost every time.
CASE 2

A 59-year-old Hispanic male was referred by an optometrist for a disc hemorrhage. He presented with the following evaluation: no family history of glaucoma or trauma; VA cc: 20/20; Rx: -3.25 and -3.75; CCT: 536 and 538; IOPs in the upper teens/low 20 mmHg; no medication, family history of glaucoma, and “normal” CCT and VFs. I followed him for two years. Two years later, CH was 13.5 and 13.8 mmHg. Those CH measurements gave me the confidence to follow the patient annually. The OHTS calculator put her five-year risk of progression at 10%. I've been following her every six months because she is scared. She has a strong family history of glaucoma, with family members who have lost vision. At the most recent visit, CH came back at 13 mmHg. So I don’t have to worry that this patient likely will go blind in her lifetime, based on what we know about hysteresis.

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Imaging: Davinder Grover, MD

CASE 3

A 46-year-old woman presented with suspicious nerves and the following evaluation: 0.75 OD and 0.8 OS; CCT: 565 and 570; IOPs in the upper teens/low 20 mmHg; no medication; family history of glaucoma; and “normal” OCT and VFs. I followed her for two years. Two years later, CH was 13.5 and 13.8 mmHg. Those CH measurements gave me the confidence to follow the patient annually. The OHTS calculator put her five-year risk of progression at 10%. I've been following her every six months because she is scared. She has a strong family history of glaucoma, with family members who have lost vision. At the most recent visit, CH came back at 13 mmHg. So I don’t have to worry that this patient likely will go blind in her lifetime, based on what we know about hysteresis.
References:

Only Ocular Response Analyzer® G3 measures Corneal Hysteresis, which is more predictive of glaucoma progression than CCT or IOP1-3, giving you a more personalized glaucoma risk assessment. CPT® Code 92145.

We share your passion for improving glaucoma care.