



The Role of Ocular Biomechanics In Glaucoma Management

Understanding the role of ocular biomechanical properties may be key in the future of glaucoma management. Here's why. **By Michael Sullivan-Mee, O.D.**

In the early 1800s, Sir William Bowman, an English ophthalmologist, recognized the relationship between “hardness” of the eye and the structural optic nerve changes that we now identify as glaucomatous optic neuropathy. Since that discovery, we place great emphasis on obtaining accurate measurements of intraocular pressure (IOP).

However, biomechanical properties of the anterior segment, such as hydration, elasticity, hysteresis and rigidity, have substantial and widely variable influence on IOP measurement. So, achieving accurate estimates of intraocular pressure remains difficult.

This article discusses these ocular biomechanical properties and how they relate to IOP measurement and glaucoma treatment.

History of IOP Measurement

Early efforts to monitor IOP primarily involved indentation techniques, which essentially measured how easily the globe was

compressed. These techniques were highly dependent on rigidity of the ocular tissue. Thus, they typically overestimated true IOP in eyes with more rigid corneas and underestimated true IOP in eyes with softer corneas.

Schiotz tonometry, the best-known form of indentation tonometry, was first used to estimate IOP in the early 1900s. In the late 1940s, Jonas Stein Friedenwald, M.D., who was building on the work of Hjalmar Schiotz, developed a method to improve Schiotz IOP estimates by accounting for corneal rigidity.¹ While Dr. Friedenwald's work significantly added to the existing knowledge of IOP and ocular rigidity, his methods (along with Schiotz tonometry) quickly fell out of favor with the advent of Goldmann applanation tonometry (GAT) in the mid-1950s.

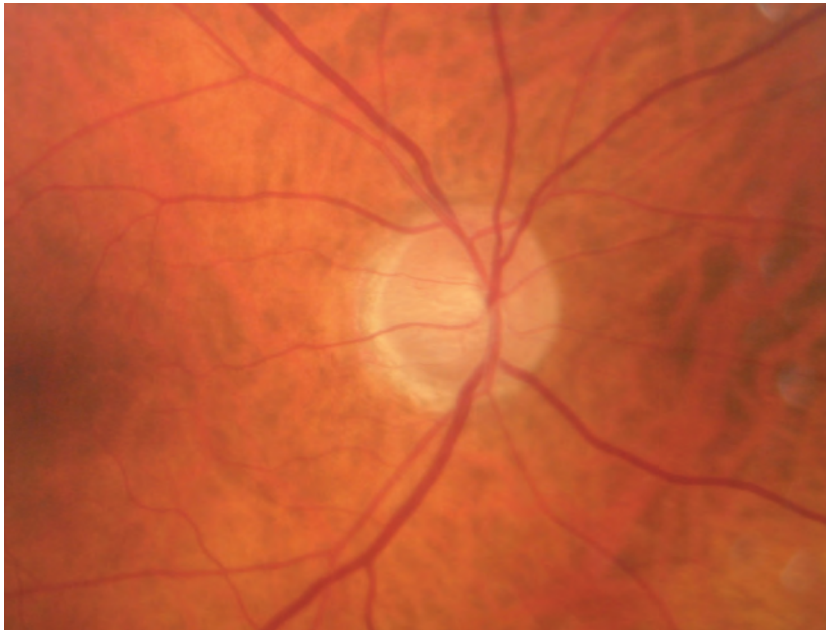
Goldmann applanation tonometry quickly became the preferred method to measure intraocular pressure, primarily because it is far less affected by ocular rigidity than

Schiotz tonometry. GAT is designed to minimize the effect of ocular rigidity on IOP measurement.

However, GAT assumed that there was minimal variation in corneal biomechanical properties, including central corneal thickness (CCT), between individual patients. Since then, research has shown that individuals demonstrate wide variations in corneal biomechanical properties.^{2,3} Although GAT may be less prone to biomechanical influence than Schiotz tonometry, it is clearly affected by ocular biomechanical influences as well.^{4,5}

DCT and ORA

Since awareness of corneal influence on GAT-IOP estimates has increased, researchers have renewed efforts to improve tonometry methods. Two particularly interesting techniques have emerged during the last few years: Pascal Dynamic Contour Tonometry (DCT) and Ocular Response Analyzer (ORA) tonometry. DCT is designed to measure IOP in a manner that is



Courtesy: James L. Fanelli, O.D.

Use of both Pascal Dynamic Contour Tonometry (DCT) and Ocular Response Analyzer (ORA) to monitor IOP can help you potentially reduce glaucomatous nerve damage, as seen here.

free from corneal biomechanical influence, while ORA uniquely measures, and then incorporates, corneal biomechanical data into its IOP estimates.

DCT uses a concave “contour-matching” surface that allows transcorneal measurement of IOP without significant applanation of the cornea. This helps overcome the influence of corneal biomechanical characteristics (including central corneal thickness) that typically complicate traditional IOP-measurement techniques.

To date, several studies have found that DCT measurements are relatively independent of central corneal thickness, while GAT measurements consistently demonstrate significant relationships with corneal thickness.⁶⁻⁸ Additionally, intracameral manometric studies using harvested human eyes have demonstrated a strong correlation between true IOP (per manometry) and DCT measurements of IOP.^{9,10}

Further, results from

intracameral, manometric *in vivo* studies using human eyes suggest that IOP measured by DCT closely approximates that measured by manometry.^{11,12}

Thus, the existing evidence suggests that DCT may indeed be capable of minimizing variations in corneal structure among individuals, resulting in more accurate measurements of IOP when compared to GAT.

Conversely, ORA is designed to improve the accuracy of IOP by using corneal biomechanical data to calculate a biomechanically-adjusted estimate of intraocular pressure. Using a precisely metered, progressively escalating pulse of air, the ORA acquires corneal biomechanical data by quantifying the differential inward and outward corneal response to an air pulse over a time span of approximately 20 milliseconds.

Once the air pulse induces the desired indentation/applanation, it symmetrically reverses, which

allows the cornea to resume its original shape.

Because a time lag is necessary to activate the reversal of the air pulse, the cornea actually indents mildly beyond the intended applanation point. This action permits the detection of a second applanation point, as the cornea returns from its over-applanated state. Using the first applanation pressure point (P1) and the second applanation pressure point (P2), the ORA generates two separate IOP output parameters.

- *Goldmann-correlated IOP (IOP_g)*, the average of the inward (P1) and outward (P2) applanation pressures. This parameter is closely correlated with GAT-IOP.¹³

- *Corneal-compensated IOP (IOP_{cc})* is derived from both IOP and corneal biomechanical data. Similar to DCT-IOP findings, several published clinical studies have reported that IOP_{cc} is unrelated to central corneal thickness.^{14,15}

Corneal Hysteresis and Corneal Resistance Factor

The ORA supplies two additional parameters that reflect biomechanical properties of the cornea and demonstrate inter-individual variation: corneal hysteresis (CH) and corneal resistance factor (CRF). During the ORA measurement process, the cornea absorbs some energy from the initial air pulse, which causes the second applanation pressure measurement to be lower than the initial measurement. The difference between the two pressures is CH. This ORA parameter is thought to represent the viscoelastic nature of the cornea, or its “viscous-damping” capacity.

The concept of viscous-damping capacity may be important clinically, as some researchers have proposed that increased damping capability may permit an eye to

more effectively buffer potentially harmful IOP fluctuations.¹⁶ Theoretically, this improved buffering might result in reduced stress/strain on both the optic nerve and peripapillary scleral tissues; this, in turn, reduces the risk for glaucomatous structural damage.

Because CCT and CH are moderately correlated, it is rather intriguing to consider that the protective effect associated with thicker central corneas in the Ocular Hypertension Treatment Study (OHTS) could be explained by generally higher CH in patients with thicker CCT.

CRF reflects the overall resistance of the cornea to deformation, and it is well correlated with CCT.¹⁷

Preliminary evidence suggests that DCT-IOP and IOPcc may provide unique value for predicting the course of glaucoma. In a recent study that analyzed the paired eyes of individuals with asymmetric open-angle glaucoma, DCT-IOP was significantly higher in the more diseased eye than in the less diseased eye, while GAT-IOP was not significantly different between individual pairs.¹⁸ Furthermore, the study found a congruent increase between inter-method IOP differences and the severity of glaucomatous visual field loss.¹⁸

These findings suggest that not only is DCT-IOP more closely associated with glaucomatous visual field loss than GAT-IOP, but also that GAT-IOP underestimation may increase the risk of sub-therapeutic clinical treatment of IOP. This underestimation could lead to a higher likelihood of progressive glaucoma damage.

Results from a separate study that compared ORA parameters, GAT, CCT, age and ethnicity between different diagnostic groups (normal patient, glaucoma suspect,

ocular hypertensive and treated open-angle glaucoma patient) suggest that IOPcc may be valuable for independently discriminating glaucoma patients from both glaucoma suspects and normal patients.¹⁹ Specifically, the researchers found that IOPcc was significantly higher in the glaucoma group compared to the other two groups, while GAT-IOP was not different between these groups.¹⁹

Thus, initial results suggest that both DCT-IOP and IOPcc hold significant promise as useful adjuncts when making decisions about treatment. However, neither parameter is currently validated for that purpose. Prospective, longitudinal studies are required to definitively qualify and quantify the predictive ability of DCT-IOP and IOPcc. Also, the clinical value and cost-effectiveness of these parameters need to be compared against GAT-IOP before their clinical roles can be ultimately determined.

Ocular Biomechanics and the Risk for Glaucoma

Thus far, this discussion has considered biomechanical properties as primarily negative factors; many experts generally consider such parameters as obstacles to accurate IOP measurement. Ironically, however, evidence from recent studies suggests that biomechanical properties may actually have intrinsic, independent value for assessing glaucoma risk.²⁰

In fact, biomechanical properties may be more predictive of glaucoma development and progression than IOP level. The best evidence for this hypothesis is the OHTS finding that suggested CCT is the strongest predictor for conversion from ocular hypertension to primary open-angle glaucoma.²⁰

Besides CCT, preliminary

investigations of CH and CRF suggest that these factors may also provide unique value in risk analysis.²¹

In a retrospective study of 230 subjects from the Wilmer Eye Institute in Baltimore, CH was related to progressive glaucomatous visual field loss, while CCT and GAT-IOP showed no relationship.²¹

Another study reported that subjects with congenital glaucoma demonstrated significantly lower CH compared to age-matched control subjects.²²

And, one other study demonstrated that patients with glaucoma-induced pits of the optic nerve had lower CH than glaucoma patients without such findings.²

Finally, in a study conducted in our facility, mean CH was significantly lower in subjects diagnosed with glaucoma when compared to glaucoma suspects, ocular hypertensives and normals.¹⁹ In the same study, CRF was useful for differentiating between subjects with ocular hypertension and glaucoma.¹⁹

When combined, the early evidence suggests that corneal biomechanical factors hold considerable promise as IOP-independent predictive variables for glaucoma development or progression.

Anterior and Posterior Biomechanical Properties

While the relationship between glaucoma susceptibility and corneal biomechanical variables (beyond their effects on IOP measurement) is being vigorously studied, substantial efforts are also being directed at answering questions about how biomechanical factors in the posterior segment might be related to those in the anterior segment.

In a recently published study in *Investigative Ophthalmology and Visual Science*, Anthony P. Wells, M.D., Ch.B., and colleagues

examined the relationship between optic nerve compliance and anterior segment biomechanical properties. Their study used the Heidelberg Retinal Tomograph-3 (HRT-3) to measure posterior deformation of the optic nerve in 100 eyes (38 with glaucoma and 62 without), both before and after IOP elevation was induced by a suction ring.²³

In their multivariate analysis that included CCT, axial length, refractive error and ORA variables, CH was the only variable that was associated with any degree of posterior lamellar deformation. This relationship was significant for subjects with glaucoma, but not normal subjects.²³ These results suggest that CH, an anterior segment biomechanical metric, may be related to distensibility of the posterior segment/optic nerve complex.

Dr. Claude F. Burgoyne, M.D., is currently pioneering research that looks at the optic nerve as a biomechanical structure with behavior that can be predicted based on the nerve's geometry, material properties, boundary conditions, and degree of mechanical loading.²⁴

In this model, if the clinician knows the values of the first three parameters, he or she can predict how much mechanical loading can be tolerated before optic nerve damage/mechanical failure occurs. By accounting for inter-individual differences in laminar nutrient supply/blood flow, material properties of lamina and peripapillary sclera, and cellular (ganglion, glial and astrocyte) response to IOP load, the model can also account for individual tolerances to mechanical load.²⁴

Other studies have also contributed to research in this field, primarily through the use of finite element modeling. Most notably, one study identified posterior segment structures that are highly

susceptible to biomechanical strain induced by IOP, and reported that peripapillary sclera may play a highly significant role in an individual's susceptibility to glaucoma.²⁵

Our understanding of ocular biomechanics has greatly improved in recent years, and it seems likely that additional research in this area will have a substantial impact on future glaucoma treatments.

While measurement of central corneal thickness has now become a routine part of practice, it seems highly likely that future diagnostic procedures in glaucoma will be directed toward the measurement of anterior segment properties beyond simple geometric thickness.

Additionally, the impending capability to clinically measure biomechanical properties of the optic nerve and adjacent tissues will greatly enhance our ability to determine an individual's susceptibility to glaucoma. It will also allow us to better target and specifically tailor our treatment options.

As primary eye care providers, we need to stay informed of the current research that will dictate how glaucoma may be managed in the near future. ■

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