

Measuring Intraocular Pressure: How Important is the Central Corneal Thickness?

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INTRODUCTION

Measurement of intraocular pressure (IOP) is fundamental to the management of glaucoma since it remains the only modifiable risk factor. Recent studies, especially on ocular hypertensives (OHT),¹⁻³ have stressed upon the influence of central corneal thickness (CCT) on IOP measurement. It is now quite well recognized that abnormally thick or thin corneas give rise to fallacious IOP measurement. Recent evidence suggests that it is not the central corneal thickness alone, but that other factors of corneal biomechanics also matter in influencing the IOP measurement.

This review will look at the importance of central corneal thickness in the management of glaucoma and glaucoma suspects. We will also discuss other corneal factors such as elasticity and corneal hysteresis, and how new technology promises to measure IOP taking these factors into consideration.

WHY IS IOP MEASUREMENT BY GAT NOT PERFECT?

The CCT affects the accuracy of IOP measurement by applanation tonometry, because the assumptions of the basic technique of tonometry are not met. Briefly, Goldmann applanation tonometry (GAT), which is the current gold standard for measuring IOP, is based on the Imbert-Fick's law. This states that the pressure within an infinitely thin, dry, smooth-walled, flexible sphere is equal to the external force required to flatten the surface of the sphere divided by the area flattened. However, these assumptions are made to the cornea, which is actually neither infinitely thin, nor its surface dry. In

1957, Goldmann and Schmidt⁴ deduced that for an average corneal thickness of 520 microns, the force of surface tension caused by the tear film was counteracted by the opposite force of corneal elasticity when the flattened area was 3.06 mm.

WHAT IS THE "NORMAL" CCT?

Professor Goldmann, at the time of designing the GAT assumed that in non-diseased corneas, the thickness would not vary much from 520 microns. However, it has since been shown that "normal CCT" varies between ethnic groups⁵⁻⁹ and, indeed varies considerably within any normal population. In a meta-analysis of CCT in eyes designated normal,¹⁰ the mean CCT was 536 ± 31 microns. Slit-lamp based pachymetry values were slightly less than ultrasonic measurements (530 ± 29 microns vs 544 ± 34 microns respectively).

CCT DISTRIBUTION IN OCULAR HYPERTENSIVES AND NORMALS

In a study in Indian eyes,¹¹ the authors found that the normal curve of CCT for normal patients was between 500 and 550 microns, while the normal distribution in ocular hypertensives was markedly skewed to the right (Table 1, Fig. 1). This also indicates the fallacious labeling of ocular hypertensives in individuals who are normal but for their uncorrected IOP measurement.

RELEVANCE OF CCT IN IOP MEASUREMENT

IOP is overestimated in thicker corneas and underestimated in thinner ones. However, the relationship has not been precisely

Table 1: Mean CCT values in normal and ocular hypertensive individuals

Diagnosis	CCT (μ)			Min	Max
	Mean \pm SD	Median	95% CI		
Normal	542.3 \pm 21.5#	548.0	534.9 and 549.7	475	575
OHT	565.2 \pm 41.4#	563.0	553.5 and 576.8	484	690

Courtesy: Kaushik et al. Am J Ophthalmol 2006

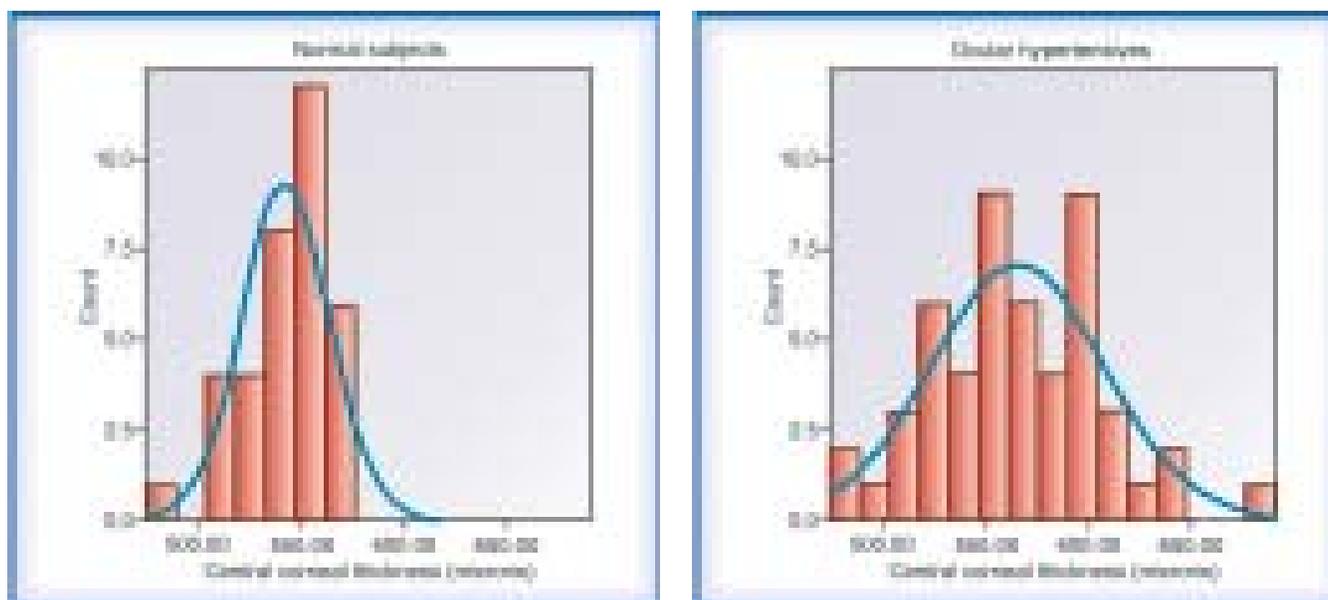


Fig. 1: Distribution of central corneal thickness in normal and ocular hypertensive individuals (Kaushik et al. Am J Ophthalmol 2006)

specified, and may or may not be linear. In 1975, Ehlers¹² reported a manometric study on 29 eyes compared to Perkin's tonometry. Applanation tonometry agreed with manometric readings only at a CCT of 520 microns. He noted the relation of central corneal thickness to IOP in glaucomatous eyes to be as much as 7 mm Hg per 100 microns. A more recent meta-analysis¹⁰ of 133 data sets estimated the mean relationship to be 3.4 ± 0.9 mm Hg for every 10 percent change in CCT.

However, it is not the CCT alone which would affect the IOP measurement. Corneal rigidity plays an important role. In clinical situations, corneal edema, with excessive hydration of the stroma, would give rise to falsely low IOP reading, even though the central corneal thickness would be increased. This is simply because it would be easier to applanate the softer edematous cornea, and consequently the end point would be reached earlier than usual. Similarly, a central corneal scar would result in a thinner cornea in the region of the scar tissue, but the greater tissue rigidity would give rise to falsely high IOP measurement.

Physiological Variability of the CCT

The CCT is a relatively stable measurement, but there are certain conditions which give rise to its variability, which must be kept in mind. Physiologically, the CCT may be increased immediately after waking up due to overnight corneal hydration. Peak circadian CCT values have been reported at 4 am.¹³ It is therefore advisable to measure the CCT at least 2 hours after waking. CCT may also be increased with chronic contact lens wear and dry eye.

Racial Variation

Several studies⁵⁻⁷ have found that African-Americans have thinner corneas on average than Caucasians, Hispanics and Asians. Though POAG is reported to be four times more prevalent among African-Americans than among Caucasians,^{8,9} it is unclear whether the thinner CCT is responsible for this increased risk of POAG.

Effect of Refractive Surgery

With the increasing incidence of refractive surgery procedures, it is important to be aware of pre-procedure corneal thickness measurements. It is inadvisable to use only the CCT to correct for IOP since the corneal biomechanics also changes after these procedures. The structural change is unpredictable, so there is no linear relationship of the post-procedure CCT to the IOP. After myopic LASIK or photorefractive keratectomy (PRK), the CCT decreases, and the measured IOP decreases by 1 to 2 mm Hg. After hyperopic LASIK or PRK, the measured IOP also drops by 1 to 2 mm Hg with negligible change in CCT. Therefore, it is more useful to carry a card with key pre-LASIK data including IOP and CCT. Since the IOP recording may be inaccurate in the setting of refractive surgery, it is very important to ensure careful disk examination in these patients, especially those with borderline IOP measurements.

PROGNOSTIC VALUE OF THE CCT

Both the Ocular Hypertensive Treatment Study and the European Glaucoma Prevention Study showed that thinner

corneas had an independent risk factor in predicting the progression of ocular hypertensives to primary open-angle glaucoma.

Recent studies also demonstrated that ocular hypertensives with abnormal Frequency Doubling Perimetry (FDP)¹⁴ or Short Wave Automated Perimetry (SWAP)¹⁵ results had thinner corneas, indicating that they may actually be individuals with “pre-perimetric” glaucoma which had not been detected by white-on-white standard automated perimetry.

CCT AS STRUCTURAL CORRELATE FOR GREATER SUSCEPTIBILITY TO GLAUCOMA

The CCT has also been thought to be a marker of the structural properties of the eye as a whole, including the retinal nerve fiber layer and lamina cribrosa. In a study¹¹ of RNFL thickness measurements by optical coherence tomography (OCT) in ocular hypertensives, the authors found that ocular hypertensives with thin corneas had thinner RNFL measurements compared to OHTs with thick corneas and normal subjects. Similar findings were reported by Henderson *et al*¹⁶ using the GDx for RNFL measurements.

In a study on patients with primary open-angle glaucoma (POAG) with 35 percent reduction in IOP, Lesk *et al*¹⁷ demonstrated that patients with thinner corneas showed significantly greater lamina cribrosa displacement on the HRT. Whether this indicates a more mobile lamina cribrosa in patients with thinner corneas, and what implications it has for glaucoma, remains unclear as yet.

BEYOND THE CCT: HYSTERESIS AND ELASTICITY

Other factors of corneal biomechanics apart from the CCT are now thought to affect IOP measurements. Whereas CCT has been widely studied, it is likely that other factors, including corneal hydration,¹⁸ and bioelasticity, all determine to some extent the response of the corneoscleral shell to the force applied during the measurement of IOP. When stress is applied and removed, elastic materials follow the same path during deformation and relaxation, ultimately recovering their original shape. Viscoelastic materials are also able to recover their original shape after stress is removed, but the relaxation path is different from the deformation path. This behavior is referred to as hysteresis and is due to the dissipation of energy as heat within the material.

Measurement of Hysteresis

The Reichert Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Depew, New York) is a relatively new NCT device that measures IOP using a bidirectional applanation method. It determines IOP and corneal hysteresis during rapid motion of the cornea in response to a short duration (20 ms) air

impulse. The air impulse causes the cornea to move inward, through applanation, and into slight concavity. Milliseconds after applanation, the air pump shuts off and the cornea moves through a second applanation while returning from concavity to its normal convex curvature. The difference of the two applanation event pressures is determined by viscoelastic properties of the corneoscleral shell.¹⁹ The rapid motion of the cornea during deformation creates velocity (rate)-dependent forces that oppose the forces (pressure) created by the air impulse. These opposition forces absorb energy from the air impulse, causing time delays (hence the term “hysteresis”) in the occurrence of the applanation events. These time delays cause the inward and outward applanation event pressures to increase and decrease, respectively. Thus the difference in the pressures reflects a viscoelastic biomechanical property of the cornea, which is termed hysteresis.

Recently, there has been interest in the possible association between corneal hysteresis and glaucoma risk. Luce and Taylor²⁰ found that patients with normal tension glaucoma and primary open angle glaucoma had lower corneal hysteresis. They have hypothesized that this may be related to corneal remodeling. In another study, Congdon *et al*²¹ found that low corneal hysteresis was predictive of visual field progression in patients with glaucoma.

THE CLINICAL UTILITY OF KNOWING THE CENTRAL CORNEAL THICKNESS

The CCT is undoubtedly of value in management of both glaucoma and glaucoma suspects, especially occur hypertension. However, in the absence of a well-established nomogram to “convert” IOP readings according to the CCT, it may be prudent to be able to classify the cornea into thin, average or thick category, and base management decisions accordingly. Some practical questions about the CCT which arise during clinical practice are summarized in Box 1 below.

Box 1: Practical questions about CCT

- 1. For which patient is pachymetry appropriate?**
 - Preferably all patients presenting to a glaucoma clinic
 - ALL glaucoma suspects.
- 2. Why?**
 - Significant deviation from population mean may change management strategy
 - OHT with thick corneas
 - Thin corneas with borderline IOP in disk or field suspects.
- 3. What is the optimal way to measure CCT?**
 - Ultrasonic pachymetry
 - Should be done early in examination
 - The probe should be centered on cornea

Contd...

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- Take care to measure at least 2 hours after awakening
- Consider repeating at least once on different visit
- Look out for confounders—contact lens wear, corneal edema, dry eye.

4. What correction factor should be applied?

- Though many different algorithms have been published, there is no uniformly accepted correction factor for IOP according to the CCT
- A meta-analysis of many different populations deduced 2.5 mm Hg for every 50 μ increase in CCT
- It may be therefore useful to just document the (uncorrected) IOP reading and note the CCT in brackets adjacent to it—IOP mm Hg (CCT μ)
- It is better not to record “corrected” IOP readings.

SUMMARY

Central corneal thickness is important to complete the overall picture of the individual patient. It helps tailor management decisions especially in borderline suspects and ocular hypertensives. Actual IOP correction appears unnecessary in each patient, since we would only be attempting to correct for an already imprecise measurement, given the many assumptions made about the cornea while measuring IOP by GAT. It may be clinically more useful to characterize cornea as “thin” “average” or “thick.” However, with the recognition of corneal biomechanical properties other than the structural corneal thickness alone, newer measurement tools such as the Ocular Response Analyzer, which measures corneal hysteresis, may provide answers hitherto missed by applanation tonometry alone.

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