

Corneal Thickness Measurement in the Management of Primary Open-angle Glaucoma

A Report by the American Academy of Ophthalmology

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Objective: To evaluate published literature to assess whether central corneal thickness (CCT) is a risk factor for the presence, development, or progression of glaucomatous optic nerve damage related to primary open-angle glaucoma (POAG).

Methods: A PubMed literature search limited to English language articles conducted on November 15, 2004 retrieved 195 articles. The authors reviewed these abstracts and selected 57 to review in full text to determine relevance to the assessment questions. A further 24 studies of interest were identified from periodic updates to the literature search, surveillance of the literature, and reference lists of reviewed articles. From the 81 published reports identified, the first author applied specified selection criteria that yielded 37 articles for methodological review because of relevance to the assessment questions. The articles were rated according to the strength of evidence by the panel methodologist. A level I rating was assigned to well-designed properly conducted randomized clinical trials or similar quality-validated cohort studies with appropriate reference standards. A level II rating was assigned to well-designed case-control studies, exploratory cohort studies, and other nonrandomized clinical studies lacking consistently applied reference standards. A level III rating was reserved for poorly designed case-control studies, case series, and papers consisting only of expert opinion without supporting evidence. In addition, each study was graded as positive if it supported a statistical association of CCT with the risk of having or developing glaucomatous optic nerve damage or as negative if no such association was found.

Results: There is strong and consistent level I and level II evidence that CCT is a risk factor for progression from ocular hypertension to POAG. Studies that were rated as providing the highest quality of evidence revealed mixed results with respect to glaucoma prevalence. One population-based study (level II) showed a positive association, another larger study (level I) revealed an association of marginal significance, and 3 studies (all level I) found no association of CCT with POAG prevalence.

Conclusions: There is strong evidence that measuring CCT is an important component of a complete ocular examination, particularly for patients being evaluated for the risk of developing POAG. Therefore, CCT measurement should be included in the examination of all patients with ocular hypertension. Although the evidence supporting the necessity of measuring CCT as part of screening for POAG or as a risk factor for glaucoma progression is not as strong, intraocular pressure (IOP) is the only modifiable risk factor in the treatment of glaucoma, and CCT has the potential to significantly impact IOP measurement by applanation tonometry in all patients. *Ophthalmology* 2007;114:1779–1787 © 2007 by the American Academy of Ophthalmology.

Introduction

The American Academy of Ophthalmology prepares Ophthalmic Technology Assessments (OTAs) to evaluate new and existing procedures, drugs, and diagnostic and screening tests. The goal of an OTA is to evaluate the peer-

reviewed published scientific literature to help refine the important questions to be answered by future investigations and define what is well established. After appropriate review by all contributors, including legal counsel, assessments are submitted to the Academy's Board of Trustees for consideration as official Academy statements.

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Background

The Ocular Hypertension Treatment Study (OHTS)¹ revealed that central corneal thickness (CCT) was an impor-

tant risk factor for progression from ocular hypertension to primary open-angle glaucoma (POAG). Multivariate analysis showed that its effect in the OHTS was independent of intraocular pressure (IOP), also a risk factor for progression. Despite this result, it is still debated whether the effect of CCT is exerted through its influence on IOP measurement or through a truly independent expression of risk possibly based on biomechanical characteristics of ocular tissues, or both.

For several decades, Goldmann applanation tonometry (GAT) has been the most accepted method of measuring IOP. Even though it is less disruptive to ocular geometry than earlier indentation methods, flattening (applanation) of the cornea is influenced by its physical properties. This was well known to the developers of GAT,² who calculated that the innate resistance of the cornea to flattening at the chosen applanation area (a circle 3.06 mm in diameter) would be counterbalanced by the force of capillary attraction drawing the tonometer to the wet corneal surface. Thus, by carefully choosing the area of applanation, the small force needed to flatten the cornea would not register in the measurement unless it was outside the range that would be nullified by capillary attraction. With the 2 forces—innate corneal resistance to flattening and capillary attraction—canceling each other, the measured force of applanation would directly reflect IOP in accordance with the Imbert-Fick principle.

In making their calculations, Goldmann and Schmidt assumed an average corneal thickness of 550 μm ; they also assumed that corneal thickness would not vary greatly in the population. However, they were certainly aware that large variations, when they occurred, could affect the accuracy of the instrument. Specifically, a cornea that was thicker than normal would require greater flattening force, yielding a higher estimate of IOP, whereas a cornea that was thinner than normal would be more easily flattened, leading to an underestimate of IOP. (Other potential sources for error with GAT, beyond the scope of this article, are reviewed elsewhere.³)

Large variations in corneal thickness have been documented with the expected result. One noteworthy case⁴ involved a patient who had a corneal thickness of 900 μm , almost twice the value assumed in the calculations of Goldmann and Schmidt. In this case, direct simultaneous measurement of the IOP by cannulation of the anterior chamber (AC) showed a low normal value (11 mmHg), whereas the simultaneous IOP reading using GAT was 35 mmHg. Clearly, a large variation in corneal thickness can produce a clinically significant discrepancy between the IOP reading using GAT and true IOP.

Although extreme variations in corneal thickness may be rare, the normal range of CCT is probably greater than Goldmann and Schmidt envisioned, and there has been extensive interest in characterizing the impact of CCT on GAT more generally. In 2000, Doughty and Zaman⁵ presented an extensive review, including a meta-analysis, on the subject of human corneal thickness and its impact on tonometry. They found a significant association between CCT and IOP readings using GAT; thicker corneas yielded higher values and thinner corneas yielded lower readings, as

predicted by Goldmann and Schmidt. Combining the results from 52 reports on normal corneas, they calculated that each 10- μm change in corneal thickness induced a 0.2-mmHg change in IOP reading.

More recent reports have provided additional observations and updated information. Kniestedt et al⁶ stated that the reported impact of CCT on GAT covers a wide span, with changes in IOP reading ranging from 0.11 to 0.71 mmHg for each 10 μm of change in CCT. Their own data, from a glaucoma specialty clinic, estimated the inverse relationship to be 0.25 mmHg per every 10- μm measurement of CCT. Furthermore, stepwise analysis of the data suggested that the relationship was nonlinear, a possibility also suggested by others⁷ and supported by mathematical models.⁸

A review and report by Tonnu et al⁹ showed that the relationship between CCT and GAT, though similar, is smaller in population-based studies (range, 0–0.21 mmHg per 10 μm of CCT)^{10–14} than in studies based in ophthalmology clinics (range, 0.16–0.37 mmHg per 10 μm of CCT).^{15–18} Their own clinic-based study found an effect of 0.28 mmHg per 10 μm of CCT, similar to findings from studies (mostly clinic based) of normal corneas in the Doughty-Zaman⁵ meta-analysis and Kniestedt et al.⁶ Furthermore, Tonnu et al found that CCT affected not only GAT but also 3 other methods of tonometry in current use: pneumatonometry, Tonopen (Medtronic Xomed, Inc., Jacksonville, FL), and noncontact. Of these 4, GAT was the least affected, whereas noncontact tonometry was the most affected. A related article¹⁹ compared GAT with a new form of tonometry called dynamic contour tonometry (Swiss Microtechnology AG, Port, Switzerland) that claims to be unaffected by corneal thickness. Although the dynamic contour tonometer showed good independence from CCT compared with GAT, the measurement reproducibility of the dynamic contour tonometer instrument was inferior to GAT.

The predominant method of assessing the effect of CCT on GAT has been indirect, by comparing large numbers of paired readings and analyzing them for a statistical association. Although statistically significant associations can be identified in this manner, and the nature of the interaction can be characterized further by regression analysis, plots of this type of data typically show a wide scatter in the results, suggesting that factors other than CCT introduce substantial individual variability.^{7,12}

An alternative approach for exploring the relationship between CCT and GAT is through studies that use cannulation of the AC. By establishing a direct fluid connection to the AC, true IOP can be measured and compared with simultaneous measurements by tonometry. The relationship of CCT to any difference found between true IOP and measured IOP can then be analyzed. By providing a clear measure of induced inaccuracies, cannulation experiments can make a unique contribution to determining the impact of CCT on IOP measurement. The results have varied, however, ranging from high impact in some studies^{20,21} to no discernible effect in others.^{22,23}

In a recent study of the largest series (125 eyes) that used cannulation to measure IOP, Kohlhaas et al found that GAT readings rose or fell 0.4 mmHg for each 10 μm of CCT

above or below the null point—that is, the CCT at which the GAT reading matched true IOP.²⁴ Although cannulation studies like this are difficult to perform, the direct reliable IOP measurement provides valuable evidence about the impact of CCT on IOP readings. However, it should also be noted that the findings are most reliable when they are applied to the population studied; in this case, the population was elderly predominantly female Europeans who were undergoing cataract surgery. Interpretation of the results from this study deserves further consideration in the effort to formulate a universal correction method for the effect of CCT on GAT.

The patients in the Kohlhaas et al study had an average CCT greater than the determined null point, and their mean CCT was also greater than that expected for the general population of white Europeans. Mills²⁵ has pointed out that, in correcting IOP for CCT, it is necessary to know not only the slope of the correction but also at what point the correction switches from negative to positive (i.e., the null point). Simple linear regression analyses will place this transition at the population mean, but direct measurements may reveal a different value. Furthermore, mean CCT varies among racial groups,^{11,13,17,26,27} which further complicates the selection of a null point for any universal correction method. An additional factor, corneal curvature, was found to be unimportant in this study, but it had an impact in other studies²⁰ and in theoretical analyses.⁸ Finally and most importantly, biomechanical properties of the cornea that are not normally measured may have a greater potential to alter IOP readings than CCT, the parameter of most current attention.²⁸

Concern over the impact of CCT on GAT logically rests with the degree of inaccuracy of IOP measurement potentially introduced. Tonnu et al⁹ point out that Doughty–Zaman’s⁵ correction for normal corneas (0.2 mmHg per 10 μ m) used over a range of CCT that includes 95% of the

population produces a small range of inaccuracy: 2.7 mmHg from the thickest to the thinnest cornea. This is in the same range as the measurement error for GAT. Even if the impact of CCT is higher (e.g., 0.4 mmHg per 10 μ m, as found by Kohlhaas et al²⁴), there may still be limits on the amount of correction that is appropriate. As Brubaker²⁹ has pointed out, Goldmann and Schmidt predicted that an infinitely thin and flexible cornea would require a correction of 2.5 mmHg. Therefore, he concludes, “it seems improbable that the error of Goldmann tonometry induced by an abnormally thin cornea would ever exceed 2 or 3 mmHg.” It has been noted that some correction formulas would produce unreasonable (negative) estimates of true IOP based on certain combinations of CCT and IOP readings.^{7,30}

Clearly, the attention to tonometric accuracy in relation to corneal thickness has stimulated much interest and study, but as yet, there is no generally accepted correction formula,³¹ and the possibility of creating a simple formula applicable to all populations remains uncertain and of questionable clinical relevance. Brandt et al noted that “the implication that IOP can be ‘corrected’ with an arithmetic, linear ‘correction’ factor of some mmHg/ μ m clearly represents an oversimplification of what is undoubtedly a complex and nonlinear relationship between corneal thickness and ‘true’ IOP.”⁷

In contrast to the continuing uncertainty about the effect of CCT on tonometry, the reliability of CCT measurement has been much less controversial. The measurement of corneal thickness has evolved from optical methods to methods based on ultrasound that are far easier to administer. Ultrasonic pachymetry is now broadly accepted as the method of choice. Doughty and Zaman⁵ found that the average CCT measured by optical methods was 530 μ m and that the average normal CCT measured using ultrasound was 544 μ m.

The reproducibility of ultrasound pachymetry has been found to be good in large studies.^{7,13} Although some authors

Table 1. Summary of Results for Central Corneal Thickness as a Risk Factor for Progression of Ocular Hypertension to Glaucoma

Study	N (Patient)	Level of Evidence	Risk	Comments
Ocular Hypertension Treatment Study ¹	1636	I	+	Thin central corneas are a powerful risk factor for progression to glaucoma
Medeiros*	117	II	+	Thin central corneas are associated with more frequency-doubling technology perimetry field defects
Medeiros [†]	98	II	+	Thin central corneas are a risk factor for preperimetric glaucoma progressing to field loss
Medeiros [‡]	131	II	+	Thin central corneas are a risk factor for developing SWAP test defects in ocular hypertension
Zeppieri [§]	78	II	+	Thin central corneas are associated with development of visual field loss

SWAP = short-wavelength automated perimetry.

*Medeiros FA, Sample PA, Weinreb RN. Corneal thickness measurements and frequency doubling technology perimetry abnormalities in ocular hypertensive eyes. *Ophthalmology* 2003;110:1903–8.

[†]Medeiros FA, Sample PA, Zangwill LM, et al. Corneal thickness as a risk factor for visual field loss in patients with preperimetric glaucomatous optic neuropathy. *Am J Ophthalmol* 2003;136:805–13.

[‡]Medeiros FA, Sample PA, Weinreb RN. Corneal thickness measurements and visual function abnormalities in ocular hypertensive patients. *Am J Ophthalmol* 2003;135:131–7.

[§]Zeppieri M, Brusini P, Miglior S. Corneal thickness and functional damage in patients with ocular hypertension. *Eur J Ophthalmol* 2005;15:196–201.

Table 2. Summary of Results for Central Corneal Thickness (CCT) as a Risk Factor for the Presence of Glaucoma

Study	N (Patient)	Level of Evidence	Risk	Comments
Barbados Eye Study ¹³	1142	I	+/-	Population-based study: association of CCT with glaucoma ($P = 0.07$)
Tanjong Pagar Study ¹²	1232	I	-	Population-based study: IOP is influenced by CCT, but CCT is not associated with glaucomatous optic neuropathy
Vijaya*	3924	I	-	Population-based study: no association of CCT with glaucoma
Tajimi Study [†]	3021	I	-	Population-based study: no association of CCT with glaucoma
Argus [‡]	96	II	-	Thicker central corneas are associated with ocular hypertension; there is no difference between normal controls and glaucoma
Rotterdam Study ¹⁴	395	II	+	Population-based study: central corneas are significantly thinner in POAG than in normal subjects
Herndon [§]	109	II	-	Thicker central corneas are associated with ocular hypertension, but there is no difference between normal subjects and glaucoma cases
Copt	133	II	+/-	Thinner central corneas are associated with normal-tension glaucoma; there is no significant difference between normal controls and POAG
Shah ⁴²	908 eyes	II	+/-	Thinner central corneas are associated with normal-tension glaucoma and glaucoma suspect but not with POAG, chronic angle-closure glaucoma, or pseudoexfoliative glaucoma
Bron [¶]	273	II	-	Central corneas are thicker in OHT subjects, but there is no difference between glaucoma cases and normal subjects
Thomas [#]	98	II	-	Thicker central corneas are associated with OHT; there is no difference between normal controls and glaucoma cases
Bechmann**	167	II	+	Central corneas are thinner than controls in low-tension glaucoma ($P < 0.0001$), pseudoexfoliative glaucoma ($P < 0.0001$), and POAG ($P < 0.05$)
Ventura ^{††}	100	II	-	Thicker central corneas are associated with OHT; there is no difference between normal controls and POAG or pseudoexfoliative glaucoma
Hahn ²⁶	1699	II	-	Thicker central corneas are associated with OHT; there is no association with glaucoma
Herndon ^{‡‡}	190	II	+	Thin central corneas are associated with multiple indicators of glaucoma damage at the time of referral to a glaucoma specialist
Sullivan-Mee ^{§§}	344	II	+	Thin central corneas are associated with glaucomatous visual field loss
Jonas	454	II	+	Thin central corneas are associated with more glaucomatous optic nerve damage; see Table 3 also
Sullivan-Mee ³⁵	204	II	+	Thin central corneas are associated with the presence of visual field loss but not with severity of loss
Kniestedt ^{¶¶}	406	II	+	There is significant correlation between larger cup-to-disc ratio and thinner central corneas
Congdon ^{###}	230	II	+	Thinner central corneas are associated with higher cup-to-disc ratio; see Table 3 also
Sullivan-Mee ^{***}	52	II	+	When asymmetry of CCT exists, thinner central corneas are associated with greater severity of field loss

IOP = intraocular pressure; POAG = primary open-angle glaucoma.

*Vijaya L, George R, Paul PG, et al. Prevalence of open-angle glaucoma in a rural south Indian population. *Invest Ophthalmol Vis Sci* 2005;46:4461-7.

†Iwase A, Suzuki Y, Araie M, et al. The prevalence of primary open-angle glaucoma in Japanese. The Tajimi Study. *Ophthalmology* 2004;111:1641-8.

‡Argus WA. Ocular hypertension and central corneal thickness. *Ophthalmology* 1995;102:1810-2.

§Herndon LW, Choudhri SA, Cox T, et al. Central corneal thickness in normal, glaucomatous, and ocular hypertensive eyes. *Arch Ophthalmol* 1997;115:1137-41.

||Copt RP, Thomas R, Mermoud A. Corneal thickness in ocular hypertension, primary open-angle glaucoma, and normal tension glaucoma. *Arch Ophthalmol* 1999;117:14-6.

¶Bron AM, Creuzot-Garcher C, Goudeau-Boutillon S, d'Athis P. Falsely elevated intraocular pressure due to increased central corneal thickness. *Graefes Arch Clin Exp Ophthalmol* 1999;237:220-4.

#Thomas R, Korah S, Muliylil J. The role of central corneal thickness in the diagnosis of glaucoma. *Indian J Ophthalmol* 2000;48:107-11.

**Bechmann M, Thiel MJ, Roesen B, et al. Central corneal thickness determined with optical coherence tomography in various types of glaucoma. *Br J Ophthalmol* 2000;84:1233-7.

††Ventura AC, Bohnke M, Mojon DS. Central corneal thickness measurements in patients with normal tension glaucoma, primary open angle glaucoma, pseudoexfoliation glaucoma, or ocular hypertension. *Br J Ophthalmol* 2001;85:792-5.

‡‡Herndon LW, Weizer JS, Stinnett SS. Central corneal thickness as a risk factor for advanced glaucoma damage. *Arch Ophthalmol* 2004;122:17-21.

§§Sullivan-Mee M, Halverson KD, Saxon GB, et al. The relationship between central corneal thickness-adjusted intraocular pressure and glaucomatous visual-field loss. *Optometry* 2005;76:228-38.

|||Jonas JB, Stroux A, Velten I, et al. Central corneal thickness correlated with glaucoma damage and rate of progression. *Invest Ophthalmol Vis Sci* 2005;46:1269-74.

¶¶Kniestedt C, Lin S, Choe J, et al. Correlation between intraocular pressure, central corneal thickness, stage of glaucoma, and demographic patient data: prospective analysis of biophysical parameters in tertiary glaucoma practice populations. *J Glaucoma* 2006;15:91-7.

###Congdon NG, Broman AT, Bandeen-Roche K, et al. Central corneal thickness and corneal hysteresis associated with glaucoma damage. *Am J Ophthalmol* 2006;141:868-75.

***Sullivan-Mee M, Gentry JM, Qualls C. Relationship between asymmetric central corneal thickness and glaucomatous visual field loss within the same patient. *Optom Vis Sci* 2006;83:516-9.

have questioned whether a single reading might be insufficient,^{32,33} reported changes over time are not large. In a recent study, Weizer et al³⁴ found that CCT decreased approximately 20 μm in 8 years. The OHTS investigators reported the results of repeat testing (Invest Ophthalmol Vis Sci 47:e-abstract 4422, 2006). They found a slow decline in CCT over time of $0.7 \pm 3.6 \mu\text{m}$ per year, which was slightly greater among patients using prostaglandin analog therapy. They concluded that the magnitude of change was small enough that it would not impact tonometry or clinical decision making.

Because CCT can be simply and reliably measured and it was an independent risk factor for the development of glaucoma among subjects with ocular hypertension in the OHTS, there has been growing interest in determining whether CCT may be useful for determining the risk of glaucoma progression. The Glaucoma Panel of the OTA Committee therefore determined that a review of reports relating CCT with glaucoma risk would be useful at this time.

Questions for Assessment

The focus of this assessment is to address the following questions:

- Is CCT a risk factor for progression of ocular hypertension to glaucomatous optic neuropathy?
- Is CCT a risk factor for the presence of glaucomatous optic neuropathy?
- Is CCT a risk factor for progression of damage in POAG?

Description of Evidence

A PubMed literature search conducted on November 15, 2004 using the search terms *corneal thickness*, *CCT*, or *pachymetry and glaucoma* retrieved 195 articles. The search was limited to English language articles. The panel reviewed the abstracts and chose 57 articles to obtain in full text to determine relevance to the assessment questions. During preparation of the manuscript, an additional 24 studies of interest were identified from periodic updates to the literature search, surveillance of the literature, and the reference lists of reviewed articles. From the 81 published reports identified in this way, the first author chose 37 articles for methodological review based primarily on the relevance to the assessment questions but also on the quality of study design.

The methodologist rated the articles according to the strength of evidence. A level I rating was assigned to well-designed properly conducted randomized clinical trials or similar-quality validated cohort studies with appropriate reference standards. A level II rating was assigned to well-designed case-control studies, exploratory cohort studies, and other nonrandomized clinical studies lacking consistently applied reference standards. A level III rating was reserved for poorly designed case-control studies, case

series, and papers consisting only of expert opinion without supporting evidence. In addition, each study was graded as positive if it found a statistically significant association of CCT with the risk of having or developing glaucomatous optic nerve damage. It was graded as negative if no such association was found.

Published Results

The methodological review of literature was conducted based on how each article related to 3 risk categories: CCT as a risk factor for progression of ocular hypertension to glaucoma, CCT as a risk factor for the presence of glaucoma, and CCT as a risk factor for progression of glaucoma. Results for each risk category are presented in Tables 1 to 3. Some papers presented findings relating to 2 categories (e.g., CCT as a risk factor for the presence of glaucoma and CCT as a risk factor for progression of glaucoma). In such cases, the findings are presented in both tables, and this is noted in the comments.

As shown in Table 1, there is strong and consistent evidence that CCT is a reliable indicator of risk for progression of ocular hypertension to glaucoma, as was clearly evident in the OHTS results. The decision to treat a patient with ocular hypertension depends on an assessment of risk, and CCT is an important and necessary part of that determination.

Table 2 shows that CCT is frequently associated with the initial diagnosis of glaucoma or with the presence of glaucoma when patients already under care are reviewed. This may be a natural result of the high risk for progression from ocular hypertension noted in Table 1. However, the value of CCT in screening for glaucoma must be questioned, because the population-based studies show only 1 study with a positive result, 1 that found an association of marginal significance, and 3 that found no association of CCT with glaucoma.

Table 3 shows that there is little evidence that CCT is useful in predicting progression of glaucoma. This may appear inconsistent with the positive risk found for CCT for progression from ocular hypertension to glaucoma. On the other hand, if thin central corneas are associated with more advanced glaucoma damage at presentation, clinicians may treat such cases more aggressively and, therefore, compensate for any added risk from thin central corneas at that stage in the disease.³⁵ However, this rationale would not explain the lack of association of glaucoma progression with thin central corneas found in the Early Manifest Glaucoma Trial. In that study, approximately half of the patients initially received no treatment; the other half, who were selected regardless of the degree of glaucoma damage, received pressure-lowering treatment.³⁶

The results listed in Table 1 support the use of CCT measurement to help assess risk in cases of ocular hypertension, as recommended by the OHTS investigators.¹ The value of CCT measurement for assessing the other aspects of glaucoma risk is not supported by the same level of evidence. Nonetheless, CCT measurement is important, given that it is universally acknowledged that CCT influ-

Table 3. Summary of Results for Central Corneal Thickness (CCT) as a Risk Factor for Progression of Glaucoma

Study	N (Patient)	Level of Evidence	Risk	Comments
Early Manifest Glaucoma Trial*	255	I	–	CCT is not a risk factor for progression of glaucoma
Kim [†]	88	II	+	Thin central corneas are associated with visual field progression in glaucoma
Chauhan [‡]	54	II	–	CCT did not predict visual field or optic disc progression
Jonas [§]	454	II	–	CCT is not associated with progression of visual field damage; see Table 2 also
Jonas	390	II	–	CCT is not associated with optic disc hemorrhages
Congdon [¶]	230	II	–	CCT is not associated with glaucoma progression (though corneal hysteresis was); see Table 2 also
Stewart [#]	310	III	+/-	CCT is associated with progression on univariate analysis but is not associated on multivariate analysis

*Leske MC, Heijl A, Hussein M, et al. Factors for glaucoma progression and the effect of treatment: the Early Manifest Glaucoma Trial. *Arch Ophthalmol* 2003;121:48–56.

[†]Kim JW, Chen PP. Central corneal pachymetry and visual field progression in patients with open-angle glaucoma. *Ophthalmology* 2004;111:2126–32.

[‡]Chauhan BC, Hutchison DM, LeBlanc RP, et al. Central corneal thickness and progression of the visual field and optic disc in glaucoma. *Br J Ophthalmol* 2005;89:1008–12.

[§]Jonas JB, Stroux A, Velten I, et al. Central corneal thickness correlated with glaucoma damage and rate of progression. *Invest Ophthalmol Vis Sci* 2005;46:1269–74.

^{||}Jonas JB, Stroux A, Oberacher-Velten IM, et al. Central corneal thickness and development of glaucomatous optic disk hemorrhages. *Am J Ophthalmol* 2005;140:1139–41.

[¶]Congdon NG, Broman AT, Bandeen-Roche K, et al. Central corneal thickness and corneal hysteresis associated with glaucoma damage. *Am J Ophthalmol* 2006;141:868–75.

[#]Stewart WC, Day DG, Jenkins JN, et al. Mean intraocular pressure and progression based on corneal thickness in primary open-angle glaucoma. *J Ocul Pharmacol Ther* 2006;22:26–33.

ences IOP measurement and that IOP is not only an important parameter in glaucoma diagnosis but also the sole modifiable risk factor in the treatment of the disease. Available evidence suggests that thin central corneas are frequently associated with glaucoma in patients under clinical care and may help to indicate more advanced disease, though not in all studies. Given the mixed results from population-based studies, it is not clear whether CCT measurement would be helpful as a primary screening tool for new cases. The value of CCT as a risk factor for progression of glaucoma is still uncertain. The bulk of the studies do not show an association of CCT with progression of glaucomatous damage. Such a relationship may exist and may become evident through further investigation, but at this time, there is little evidence that determining CCT helps to ascertain risk of disease progression in an established case of glaucoma. The apparent absence of association of CCT with progression in the Early Manifest Glaucoma Trial is notable, because the design of that study was well suited to reveal such a risk.

It is difficult to separate CCT as a risk factor for glaucoma and preglaucoma without considering its possible influence on the measurement of IOP, another important risk factor. Many of the studies that recommend CCT for screening or for managing established cases do so on the basis of improving the accuracy of tonometry or, at least, identifying cases where CCT is so abnormal that it might substantially affect IOP determination. As noted earlier, improving the accuracy of GAT readings requires a correction formula for CCT. In the absence of a universally verified and accepted formula, and considering the wide range in magnitude of published correction methods, selecting a correction method is an arbitrary choice that carries

the risk of introducing errors rather than simply removing them.

Furthermore, accuracy in measuring true IOP is not absolutely necessary in every stage of glaucoma management. As Anderson³⁷ has noted, “There is only a slight difference between lowering the IOP by 25% or lowering the tonometer reading by 25%, even when CCT is abnormal.” With respect to glaucoma screening, it is widely accepted that measuring IOP is not particularly useful by itself and must be supplemented with morphologic and/or functional assessments of the optic nerve. Although greater accuracy in the IOP measurement might add incrementally to its value in glaucoma screening, it is unlikely that even a very accurate pressure test would establish a simple numeric boundary between normal and glaucoma.³⁸

Although sources for inaccuracy exist for GAT, it remains a reliable, robust, simple instrument that gives results with excellent repeatability.³⁹ Indeed, even the extensive knowledge about its inaccuracies is useful, because it provides the informed user with a clear understanding of the circumstances likely to compromise results. That thicker corneas yield artifactually higher GAT readings and thinner corneas yield artifactually lower GAT readings is generally accepted, soundly based on physical principles, and consistent with most clinical studies. For the majority of patients, the induced error will be small and of little clinical relevance.²⁹ Although the exact magnitude of a given CCT’s impact on the GAT reading may not be readily calculated from a broadly accepted formula, the error induced in an individual case is likely to be consistent over time and to allow valid tracking of IOP changes.³⁷ Nevertheless, knowing whether the CCT value is high, medium, or low is potentially useful for all patients, particularly when target

IOP ranges are used. In the absence of CCT measurements, the potential exists for practitioners to be misled into believing that patients with IOP readings in the low teens are well controlled, whereas some patients with very thin corneas may require even lower readings.

Other methods of tonometry in current use are not independent of CCT.^{15,16,40,41} One recent study found GAT to be the least affected by CCT of 4 tonometry methods in current use.⁹ The influence of CCT on IOP measurements with newer modalities such as dynamic contour tonometry has not been adequately studied at this time. Furthermore, thickness may not be the most important element of the cornea's physical characteristics influencing standard tonometry.²⁸ Although the development of new methods of tonometry that are potentially less influenced by corneal thickness are to be encouraged,⁶ especially in an age of increasing refractive surgery, any method to replace GAT should undergo careful testing in multiple diverse settings and demonstrate both accuracy and precision over prolonged periods.

Although some authors have argued for the measurement of CCT in all glaucoma-related circumstances,^{31,42} Mills,²⁵ before the use of the OHTS results, had suggested that the value of measuring CCT could be maximized by focusing on clinical situations where it is most likely to contribute to patient care. This includes situations in which a clinical decision rests solely on IOP level, when disc and field status cannot be reliably monitored, after corneal ablation, and in cases of normal-tension glaucoma and ocular hypertension (i.e., cases in which disc and field status are inconsistent with IOP). Given the limitations in the structural and functional assessment of the optic nerve and the simplicity of CCT measurement, however, a strong case can be made for obtaining CCT measurements for all patients when glaucoma is present or suspected.

Conclusions

There is level I evidence that measuring CCT is an important component of proper management of ocular hypertension. The decision to treat a patient with ocular hypertension is based on an assessment of risk, and there is clear and consistent evidence that CCT is a risk factor for progression to glaucoma (Table 1). Indeed, it was the strongest risk factor identified in the OHTS. Therefore, CCT measurement should be included in the examination of all patients with ocular hypertension.⁴³

There is mixed evidence about the association of CCT with the presence of glaucoma (Table 2). There are multiple studies showing that CCT is associated with glaucoma on initial presentation to a glaucoma clinic or among patients already enrolled in specialty clinics. However, the value of CCT measurement as an important screening parameter for glaucoma appears negligible, because it was not associated with glaucoma in 2 large population-based studies and only marginally associated in a third study.

The bulk of available evidence suggests that CCT is not helpful in predicting risk for progression of existing glaucoma (Table 3). Although some clinical studies have sug-

gested an association of CCT with glaucoma progression, the majority of clinic-based studies have not reached that conclusion. In addition, in the Early Manifest Glaucoma Trial, a randomized controlled trial, CCT was not found to be a predictor of progression of glaucoma. Thus, it is unclear from available evidence whether CCT is a risk factor for glaucoma progression. Despite the lack of evidence supporting CCT as an independent risk factor for glaucoma progression, CCT does influence IOP measurement by applanation tonometry. Because IOP is arguably the most important and only modifiable risk factor for glaucoma progression, knowledge of CCT is potentially important in managing patients either suspected of having open-angle glaucoma or diagnosed with it.^{43,44}

Future Research

There are numerous issues about corneal thickness that remain to be resolved. Thickness measurements in a variety of ethnic populations will lend themselves to comparative analysis and be of clinical interest in the future. Whether corneal thickness changes over time, in the presence of various medications, is a fertile area for further investigation. The issue of corneal compliance and its relationship to thickness was only beginning to be studied at the time of the writing of this OTA. Speculation that the collagens or other structural constituents found in the corneal stroma are similar in some way to those found in the lamina cribrosa may be worth investigating. As new corneal measurement devices come on the market, it will be important to compare them with existing devices in terms of accuracy and clinical utility.

Clinical Relevance

The results of the OHTS emphasized the importance of CCT in guiding therapeutic decisions in glaucoma prevention. To calculate the risk of a person with ocular hypertension progressing to glaucoma accurately, CCT measurement must be considered. Although this review has not found similar strong evidence that CCT will help predict progression of established disease, caution in applying this observation is in order. First, these conclusions are based on available evidence and are always subject to modification as additional research findings become available. Second, even if CCT never becomes as useful in predicting glaucoma progression as it is in predicting glaucoma development in ocular hypertension, it provides valuable information about the accuracy of IOP measurement by GAT, the most widely accepted method. Even though a universally accepted algorithm for correcting the reading does not exist, separating CCT into broad categories of thin, normal, and thick can provide valuable understanding of an individual patient's clinical course. This is supported by the current American Academy of Ophthalmology preferred practice pattern for POAG, which notes, "A thin central cornea (e.g., 490 μm) may explain loss of visual field in an eye despite normal applanation measurements of IOP, because the measure-

ments do not reflect a higher true IOP. Conversely, a thick central cornea (e.g., 610 μm) may explain high measured IOP associated with longstanding normal visual field and optic disc due to a lower true IOP.”⁴⁴

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Category	Abbreviation	Specific Financial Relationship
Consultant/Advisor	C	Consultant fee, paid advisory boards, or fees for attending a meeting.
Employee	E	Employed by a commercial entity.
Lecture Fees	L	Lecture fees (honoraria), travel fees, or reimbursements when speaking at the invitation of a commercial entity.
Equity Owner	O	Equity ownership/stock options of publicly or privately traded firms (excluding mutual funds) with manufacturers of commercial ophthalmic products or commercial ophthalmic services.
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