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# Role of central corneal thickness on baseline parameters and progression of visual fields in open angle glaucoma

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PURPOSE. *To evaluate the relationship of central corneal thickness (CCT) to baseline visual field parameters and visual field progression in patients with primary open-angle glaucoma (POAG).*
METHODS. *Charts of consecutive patients with POAG were reviewed to obtain visual field data. Visual field was measured by standard threshold static perimetry. Variables analyzed included mean deviation (MD) and pattern standard deviation (PSD).*
RESULTS. *A total of 121 eyes examined over 4 years were evaluated. A significant negative relationship between CCT and PSD (correlation coefficient: -0.02, p<0.05) was found. Analyses comparing CCT to change in PSD and MD (visual field progression) were statistically not significant.*
CONCLUSIONS. *Patients with thinner corneas initially present with a greater visual field defect, indicating that thin corneas may contribute to advanced glaucomatous damage at the time of diagnosis. However, CCT does not seem to be a significant risk factor for progression of the disease. (Eur J Ophthalmol 2007; 17: 545-9)*

KEY WORDS. *Central corneal thickness, Primary open angle glaucoma, Perimetry, Visual field defect, Disease progression*

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## INTRODUCTION

Intraocular pressure (IOP) strongly influences the diagnosis, management, and follow-up of patients with ocular hypertension (OHT), glaucoma, or suspected glaucoma. Therefore, caution must be taken to assure that such measurements are accurate. Several studies have described a positive correlation between central corneal thickness (CCT) and IOP readings using Goldmann applanation tonometry (GAT) (1-8). Previously, Whitacre and colleagues determined that thick corneas produce overestimations by as much as 6.8 mmHg (9). It is now known that patients diagnosed with OHT have higher CCT values than patients with glaucoma and normal subjects, suggesting that thicker corneas may have led to an overestimation of IOP (10, 11). Patients whose IOP is overestimated may be considered at risk for glaucoma, resulting in unnecessary tests and examinations, or even unwarranted treatment. On the other hand, patients who have underestimated IOP are at risk for missed diagnosis and delay in treatment, possibly leading to irreparable damage to the optic nerve and finally to functional vision loss. Therefore, precise IOP measurement is imperative for accurate screening, diagnosis, and management of glaucoma and CCT measurement appears essential for the correct interpretation of GAT.

The purpose of this study was to observe if a thin CCT measurement correlated with more advanced optic nerve

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damage as indicated by visual field loss at the time of diagnosis, and if a thin CCT is a significant variable associated with visual field progression.

## MATERIALS AND METHODS

After institutional review board approval, charts of 121 eyes of 70 consecutive patients with primary open angle glaucoma (POAG) examined over 4 years in two glaucoma subspecialty practices (SL, RLS) at the Department of Ophthalmology, University of California San Francisco (UCSF), were reviewed and pertinent demographic and medical data were obtained. Patients with POAG were recruited from a search of the computerized database based on diagnostic coding. Information recorded included age, gender, race, mean CCT, IOP (by Goldmann applanation tonometry), and visual field data. CCT was measured by ultrasonic pachymetry (DGH-500; DGH Technology Inc., Exton, PA). The pachymetry measurement recorded for each eye was the average of five measurements taken per eye. Measurements were taken during the workday between 8 AM and 6 PM. Static, automated perimetry was performed by the Humphrey Visual Field Analyzer (Model II-i, Dublin, CA) with standard Swedish Interactive Threshold Algorithm (SITA). Data utilized in this study included mean deviation (MD), pattern standard deviation (PD), false positives, false negatives, and fixation losses. Inclusion criteria included diagnosis of open angle glaucoma and a follow-up greater than or equal to 1 year. Exclusion criteria included corneal or retinal disease, refraction errors (> +6.0 and < –6.0 diopters) and fixation losses, false positives, or false negatives greater than 25%.

### *Statistical analysis*

All analyses are based on mixed effects regression models. These models have fixed effects such as CCT or race or age and a random patient effect. The random patient effect allows the observations from multiple occasions for a given patient to be correlated. This property also applies to data from two eyes from the same patient on one occasion or on multiple occasions. For overall estimates of CCT, MD, and PSD, the fixed effects consist of an intercept only. For associations of CCT with MD, PSD, or the slopes of these measures over time, the fixed effects include an intercept and CCT. Normal probability plots were used to examine normality of residuals. All analyses were done using SAS version 8.2.

## RESULTS

A total of 121 eyes diagnosed with POAG were included in this study. The mean age of the study population was 70.1 years (95% CI 68–75). Fifty-six percent of the patients were female and 44% were male; 79% were Caucasian (Tab. I). Mean CCT was 546 µm (95% CI 536–556), with 30% of the group having a CCT between 526 and 550 µm (Tab. II). Figure 1 shows the distribution of CCT in the study group. Average IOP (on treatment) was 16.9 mmHg (±0.4, 95% CI 15.1–16.6) and mean MD and PSD were –6.3 (±0.7, 95% CI –7.7 to –4.9) and 5.1 (±0.4, 95% CI 4.3–5.8) respectively, determined by static perimetry (SITA standard).

A statistically significant relationship was discovered between CCT and presenting PSD. A negative relationship between CCT and PSD (mixed effects regression model estimate: –0.020, 95% CI –0.037 to –0.002, p = 0.028) re-

**TABLE I -** DEMOGRAPHIC DATA OF STUDY POPULATION

| Characteristics | Values |
|---|---|
| Age, yr, mean (95% CI) | 70 (68–75) |
| **Gender, %** | |
| Male | 44 |
| Female | 56 |
| **Race, %** | |
| Asian | 9 |
| African American | 7 |
| Caucasian | 79 |
| Hispanic | 6 |

**TABLE II -** OPHTHALMOLOGIC FINDINGS OF STUDY GROUP

| Characteristics | Mean (SD) |
|---|---|
| Intraocular pressure, mmHg | 15.9 (0.4) |
| Central corneal thickness, | m 546 (4.9) |
| Initial mean deviation | –6.24 (0.7) |
| Initial pattern standard deviation | 5.04 (0.4) |

*Parameter of visual field test

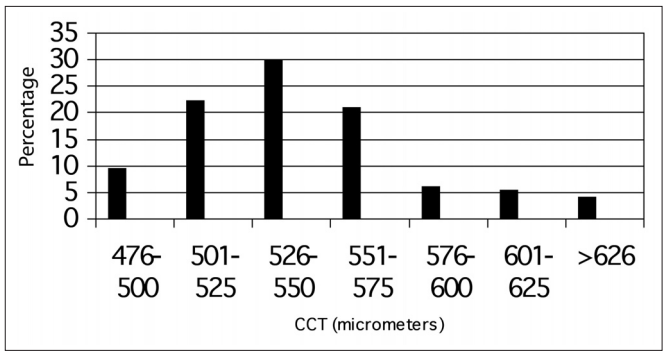


**Fig. 1 -** *Distribution of central corneal thickness (CCT) among the study population. Thirty percent of the patients have a CCT between 525 and 550 µm.*

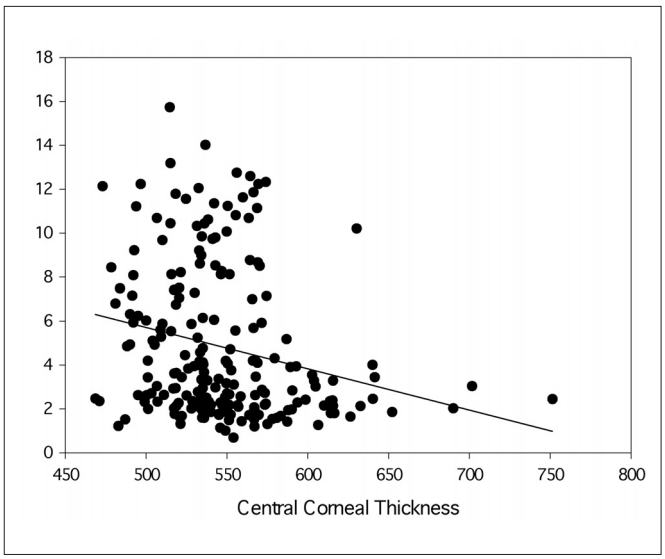


**Fig. 2 -** *Distribution of pattern standard deviation (PSD) values among different central corneal thickness. There was a correlation between thinner corneas and greater PSD.*

vealed that patients with thinner corneas presented with a greater standard deviation, signifying a more localized visual field defect, consistent with glaucomatous damage (Fig. 2). Adding a quadratic CCT term to the model did not improve predictability (p = 0.62).

Two independent relationships investigating the effect of CCT on visual field progression were analyzed. Slopes of MD and PSD over time were computed separately for each eye in the study. The relationships of these slopes to CCT were analyzed using mixed effects regression models with a fixed predictor of CCT and a random patient effect. The estimates for the effects CCT on slope of MD (in MD units per year) and slope of PSD (in PSD units per year) were not statistically different from zero. For slope of MD, the estimate was –0.0093, 95% CI –0.023 to 0.0044, p = 0.18, and for slope of PSD the estimate was 0.0029, 95% CI –0.0031 to 0.0089, p = 0.34.

The subgroup of patients without a surgical history was independently analyzed. In concurrence with the total group, analyses comparing CCT to initial PSD was significant with similar regression estimates (CCT vs initial PSD: regression estimate –0.177; p = 0.05).

## DISCUSSION

In this study, we found a statistically significant negative relationship between CCT and presenting PSD, indicating that patients with thinner corneas presented with a glaucomatous visual field defect. It is assumed that one factor in the development of a visual field defect in this group is the inaccurately low IOP measurements, as a result of their thinner corneas. After being referred to a tertiary care center, progression of visual field damage slowed significantly with medical management. As demonstrated by this study and the following literature, the significance of accurate IOP measurements is essential in the prevention and treatment of glaucoma.

Recent large-scale prospective studies have reinforced the importance of IOP and IOP lowering in preventing glaucoma development and progression (12-14). Therefore, accurate IOP measurements are important in the diagnosis and management of glaucoma. To prevent delay in the detection and treatment of glaucoma, factors that can cause inaccurate IOP measurements should be determined and taken into account. Physical properties such as CCT, corneal curvature, area of applanation, and hydration state can all affect IOP measurement (8, 10, 15-18).

Applanation tonometry was designed at a time when it was thought that corneal thickness fluctuations were rare and only occurred in cases of scarred corneas, keratoconus, and other corneal diseases. It was assumed that normal corneas were approximately 540 µm thick and varied minimally among individuals. However, as pachymeters became widely available, CCT variation in the normal population and between races was observed, leading to concerns that IOP measurement could be more seriously influenced than previously thought (10, 15, 16, 18).

A large body of evidence points to a positive correlation between IOP and CCT in normal patients and those with

ocular hypertension (1-8, 19, 20). This "error" in IOP measurement related to CCT can have significant clinical implications. For example, it has been reported that CCT is reduced in patients with low-tension glaucoma, suggesting that IOP is being underestimated because of thin corneas (21). Moreover, several studies have demonstrated that patients currently diagnosed with ocular hypertension have a significantly higher mean CCT than normal patients or patients with glaucoma (1, 2, 10, 22, 23). If CCT is such a significant factor in the determination of IOP, a corrected IOP will be better able to assess the risk relationship to glaucoma and ocular hypertension than uncorrected IOP.

Several equations have been proposed to "correct" IOP on the basis of CCT. Doughty and Zaman suggest a correction of 2.5 mmHg for each 50 micrometers difference from 525 micrometers in CCT in patients with chronic eye conditions, while Ehlers et al concluded a 5 mmHg correction for every 70 µm change in CCT (24, 25). Whitacre et al described a 2.0 mmHg change for each 100-µm difference in CCT (9). While it is suggested that measuring CCT is necessary to interpret properly the results of GAT, no consensus has been reached on an equation to appropriately achieve this goal (26).

We observed a significant correlation between CCT and visual field defect on initial presentation, suggesting that patients with thinner corneas initially present with a worse glaucomatous visual field than patients with normal or thick corneas. Recently, CCT has been recognized as a significant risk factor for the progression of OHT to POAG. Furthermore, Herndon et al recently reported that patients with POAG with visual field loss demonstrated more advanced loss, greater cup-to-disc ratios, and more glaucoma medication use at presentation to the clinic, if they had thinner CCTs (11).

Collectively, these results support CCT as a strong predictor of the degree of glaucomatous damage in ocular hypertensive patients and those with POAG at presentation. Whether this is due to delayed diagnosis because of underestimation of IOP or to some additional risk conveyed by a thin cornea is not known at this time.

Our study could not identify a relationship between CCT and visual field progression, as no correlation was seen between CCT and the slope of change of MD and PSD. Although patients with thinner corneas more often presented with worse glaucomatous functional damage – as indicated by more advanced PSD – their visual field did not deteriorate more rapidly over 4 years than patients with normal or thick corneas, while under medical care. However, many factors can affect visual field progression, the most important of which may be treatment differences.

Although not statistically significant, an analysis comparing IOP to CCT showed a trend toward lower IOPs in our patients with lower CCTs. It is likely that IOPs were targeted lower in eyes with thinner corneas due to more advanced field loss. This may have led to more aggressive treatment and prevention of greater visual field loss compared to those with thicker CCTs. Additionally, we were unable to compare our treated groups of patients to a comparable group who did not receive treatment. Therefore, the overall low extent of deterioration in visual field may be an outcome of treatment, regardless of lower targeted IOPs.

This study is limited by its retrospective nature and tertiary care setting in which patients with more advanced disease are more frequent. However, these data support the importance of assessing CCT in any patient with or suspicious for glaucoma. This study also strongly suggests the need for further prospective studies to elucidate the exact role of CCT in glaucoma management.

In conclusion, glaucoma patients with thin corneas in our study presented with more advanced visual field damage than those with normal or thick corneas. However, after referral to a tertiary care center, aggressive medical management prevented the progression of visual field damage. Therefore, thin corneas do not seem to be a risk factor for progression in our cohort of patients. While numerous factors are known to affect glaucoma and progression of the disease, treatment depends on accurate IOP measurements, into which CCT must be taken into consideration.

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