Measurement of the Magnitude and Axis of Corneal Polarization With Scanning Laser Polarimetry

Robert N. Weinreb, MD; Christopher Bowd, PhD; David S. Greenfield, MD; Linda M. Zangwill, PhD

**Background:** Scanning laser polarimetry uses a polarization compensator to isolate corneal birefringence from the birefringence of the retinal nerve fiber layer. This compensator assumes a fixed corneal polarization magnitude (CPM) of 60 nm and a fixed corneal polarization axis (CPA) of 15° in all subjects.

**Objectives:** To measure the CPM and CPA with a scanning laser polarimeter and to determine if the assumed compensation values are representative of those observed in healthy and glaucomatous eyes.

**Methods:** The CPM and CPA were measured in 51 healthy eyes and 55 glaucomatous eyes using a modified scanning laser polarimeter (GDx Nerve Fiber Analyzer; Laser Diagnostic Technologies Inc, San Diego, Calif) with an experimental variable CPM and CPA compensator. The CPM and CPA distributions in healthy and glaucomatous eyes were compared, and the CPM and CPA relationships with age, corneal thickness, and corneal curvature were also investigated. Nasally upward CPA values (in degrees) were recorded as negative; nasally downward CPA values were recorded as positive.

**Results:** The CPM and CPA measurements were normally distributed with many eyes having values different from those assumed by the GDx corneal compensator. For healthy and glaucomatous eyes combined, CPM measurements ranged from 7 nm to 91 nm (mean±SD, 40.0±13.7 nm). The CPA measurements ranged from −13° to 73° (mean±SD, 24.5°±17.4°). A significant effect of age on CPA was observed when all eyes were combined (R²=0.10; P<.001). There were no differences in CPM or CPA between healthy and glaucomatous eyes after adjusting for age. No effects of corneal thickness on CPM (R²=0.04; P=.05) or CPA (R²=0.01; P=.24) or of corneal curvature on CPM (R²=0.002; P=.67) or CPA (R²=0.009; P=.34) were observed.

**Conclusions:** The range of CPM and CPA values observed in glaucomatous and healthy eyes suggests that the narrow-band corneal compensator used by the GDx scanning laser polarimeter is inappropriately compensating for anterior segment birefringence in many eyes.

Arch Ophthalmol. 2002;120:901-906
SUBJECTS AND METHODS

SUBJECTS

Patients with glaucoma and healthy subjects meeting entry criteria were enrolled in this prospective study. A total of 106 individuals were evaluated at the University of California, San Diego, Glaucoma Center, including 55 patients with glaucoma and 51 healthy subjects. Of these individuals, 47 were men and 59 were women: 81 subjects were white, 9 were Asian American, 6 were African American, 6 were Hispanic, and 3 were Indo-European. One eye per subject was included by random selection.

Prior to imaging, all subjects underwent a complete ophthalmologic examination including refraction and best-corrected visual acuity, slitlamp biomicroscopy, intraocular pressure measurement, a dilated stereoscopic fundus examination, stereoscopic photography of the optic disc, and Swedish Interactive Threshold Algorithm (SITA) or standard (achromatic) full-threshold visual field testing with program 24-2 (Humphrey Field Analyzer, Humphrey Instruments, Dublin, Calif). Only eyes with a visual acuity of 20/40 or better were included. The range of refractive error in the subject population was -9.0 diopters (D) to 2.88 D (mean±SD, -0.92±1.91 D). Eyes with coexisting retinal disease, uveitis, or nonglaucomatous optic neuropathy were excluded from this investigation. Informed consent was obtained from all participants. All methods were approved by the University of California, San Diego, Human Subjects Committee and adhered to the Declaration of Helsinki for research involving human subjects.

Healthy subjects had no history of ocular disease or increased intraocular pressure and normal ophthalmologic examination results, including an intraocular pressure of 22 mm Hg or less (Goldmann applanation tonometry), a healthy appearance of the optic disc and RNFL (no diffuse or focal rim thinning, cupping, or RNFL defects in-
terior), a healthy appearance of the macula (no diffuse or focal macular degeneration, neovascularization, or macular defects) and a normal finding on SITA or standard full-threshold Humphrey 24-2 visual field tests. Normal visual field indexes were defined as a mean defect (MD) and corrected pattern standard deviation within 95% confidence limits and a glaucoma hemifield test result outside of the 99% normal limits.

MEASUREMENTS

The experimental setup was a commercial GDx system, modified so that the original fixed corneal compensator was replaced with a variable corneal compensator, as described by Zhou and Weinreb.6 In brief, the GDx variable corneal compensator comprises a set of 4 linear retarders in the path of the measurement beam. The first 2 retarders are optical lenses that have equal retardance and form a variable cornea and lens compensator. The third retarder is composed of the cornea and lens, and the fourth retarder is the retinal birefringent structure (RNFL or macular Henle fibers).

The CPM and CPA were determined by aligning the fast axis of the first retarder with the slow axis of the second, identical retarder (essentially setting the compensating retarders to 0 nm) and imaging the macula. The resulting retardation profile represents the additive effects of cornea, lens, and macular Henle fiber birefringence. The compensating retarders were then adjusted to minimize the effects of anterior segment birefringence, resulting in a flat macular retardation profile. The CPM and CPA values that resulted in adequate compensation were then recorded. Nasally upward CPA values (in degrees) were recorded as negative; nasally downward CPA values were recorded as positive.

For each subject, 3 sets of CPM and CPA measurements were acquired, and a mean value was used for the analyses. We determined the within-subject variability for CPM and CPA for each individual by calculating the SD of the 3 measurements from which these means were obtained. Ultrasound pachymetry was used to measure corneal thickness (Pachette GDH 500; DGH Technology Inc, Philadelphia, Pa), and keratometry was used to measure corneal curvature (Keratometer 12990; Reichert Ophthalmic Instruments, Depew, NY).

We also determined the percentage of variance in the change of CPM and CPA measurements across time that was attributable to interpatient and intervisit factors; we used a cohort of 13 healthy eyes that were imaged 3 times during the course of 3 months or less using the criteria, instrument, and procedures described previously. The mean±SD age of these subjects was 46.3±12.8 years (range, 24.6-73.2 years) on their first imaging date. Seven subjects were men, and 6 were women. Nine subjects were white, 3 were African American, and 1 was Hispanic.

ANALYSIS

We compared CPM and CPA measurements between healthy and glaucomatous eyes using 2-tailed t tests. We also reported and compared the SDs of the CPM and CPA as indexes of measurement variability. The relationships of corneal thickness, corneal curvature, and subject age with CPM and CPA were assessed using linear regression. To determine sources of variability across time in CPM and CPA measurements, we employed a random-effects analysis of variance model using restricted maximum likelihood. The components of this model were subject (between-subject variability), visit (between-visit variability), and residuals.
the fourth Purkinje image (image formed by the reflection of illuminating light from the posterior surface of the crystalline lens), Greenfield et al\(^3\) established the distribution of the CPA in 112 healthy eyes and reported a range between 90° nasally downward and 54° nasally upward, in contrast to the 15° nasally downward assumed by the GDx fixed compensator (although the mode of distribution was between 10° and 20° nasally downward). Similarly, Knighton and Huang\(^4\) used a modified version of the corneal polarimeter used by Greenfield and colleagues to measure the central anterior segment birefringence of 146 healthy eyes and demonstrated that corneal polarization magnitude (CPM) ranged from 0 nm to 250 nm when double passing the cornea, in contrast to the 60 nm (120-nm double pass) assumed by the GDx fixed compensator. Because the wide range of these measurements deviates significantly from the assumed values of the fixed compensator, this could be a significant source of error in RNFL assessment with the current GDx.

Greenfield et al\(^3\) recently demonstrated the important effect of the CPA on the discriminating power of scanning laser polarimetry in mild to moderate glaucoma. To exclude the contribution of corneal birefringence, however, the compensator must account for the variation not only in the birefringence axis but also in the magnitude. The purpose of this study was to use a GDx scanning laser polarimeter with a variable corneal compensator to describe the variation in both CPM and CPA birefringence in healthy subjects and patients with glaucoma.

### RESULTS

The mean ±SD CPM in all eyes combined was 40.0 ± 15.7 nm (range, 7-91 nm). The distribution of CPM measurements was normal (Shapiro-Wilk W test; \(P = .40\)) with a mean ± SD of 40.0 ± 15.7 nm.

The mean ± SD CPA in all eyes combined was 24.5° ± 17.4° (range, −13° to 73°). The distribution of CPA measurements was normal (Shapiro-Wilk W test), with the largest percentage of eyes between 10° and 20° (20%) and between 30° and 40° (18%). The median CPA was 21.8° (Figure 2). Table 1 indicates the CPM, CPA, corneal thickness, corneal curvature, and refraction results for all eyes. The CPM and CPA were not linearly related (\(R^2 = 0.4; P = .54\)) (Figure 3).

### EFFECTS OF AGE

There was a negative, although likely not statistically significant, relationship (slope, −0.26) between age and CPM in healthy eyes (\(R^2 = 0.09; P < .04\)) but not in glaucomatous eyes (\(R^2 < 0.001; P = .90\)). For multiple comparisons, \(\alpha = .005\) based on regression analyses between CPM and age, corneal thickness, corneal curvature, and refraction in glaucomatous eyes, healthy eyes, and all eyes combined. There was also a negative relationship (slope, −0.34) between age and CPA in healthy eyes (\(R^2 = 0.13; P = .008\)) but not in glaucomatous eyes (\(R^2 = 0.004; P = .65\) (\(\alpha = .005\) as mentioned previously). However, the age of healthy subjects ranged from 21 to 82 years (61-year range), whereas that of patients with glaucoma ranged from 51 to 90 years (39-year range). Therefore, we evaluated whether the larger age range of healthy subjects was a possible reason for the difference in the age/CPM/CPA relationships between the diagnostic groups by completing additional univariate and multivariate analyses. When we included only healthy subjects older than 50 years (\(n = 17\)) in the linear regression of age with CPM and CPA, the relationships were no longer statistically significant (\(R^2 = 0.001\) and \(P = .64\), and \(R^2 = 0.007\) and \(P = .29\), respectively). For CPM, when both age and diagnosis were included in a linear regression model using all subjects, the effect of age was not significant (\(P = .12\)). When age and diagnosis were included in a linear regression model with CPA, the effect of age remained (\(P = .02\)). Table 2 and Table 3 indicate the relationships of CPM and CPA with age (as well as corneal thickness, corneal curvature, and refraction). Figure 4 and Figure 5 show the relationships between age and CPM and CPA, respectively.

### EFFECTS OF DIAGNOSIS

The mean ± SD CPM was similar in individuals with glaucoma (39.0 ± 16.5 nm; range, 7-91 nm) and healthy subjects (41.1 ± 14.3 nm; range, 11-75 nm) (\(P = .48\)). In uni-
Variate analysis, the mean ± SD CPA was marginally lower in patients with glaucoma (20.5° ± 18.3°; range, −13° to 73°) compared with healthy subjects (28.8° ± 15.4°; range, −6° to 57° (P < .01; α = .01 for multiple comparisons) (Table 1). On further investigation, however, the effect of diagnosis on CPA was influenced by the significant age difference between diagnostic groups (t test; P < .001). Multivariate linear regression indicated that after adjusting for age, the difference between healthy and glaucomatous eyes was no longer statistically significant (P = .66). Furthermore, when the healthy group was truncated to include only patients the same age as or older than the youngest patient with glaucoma (n = 17), the mean ± SD CPA in the healthy group (19.3° ± 15.9°; range, −5.7° to 50.7°) was similar to that in the glaucoma group (20.5° ± 18.3°) (P = .82).

**OTHER EFFECTS**

No significant correlations were found between corneal thickness, corneal curvature, or refraction and CPM or CPA in healthy or glaucomatous eyes (for all comparisons).

### Table 1. Corneal Polarization Magnitude, Corneal Polarization Axis, Corneal Thickness, Corneal Curvature, and Refraction Measurements From Glaucomatous Eyes, Healthy Eyes, and All Eyes Combined*

<table>
<thead>
<tr>
<th></th>
<th>Glaucomatous Eyes (n = 55)</th>
<th>Healthy Eyes (n = 51)</th>
<th>P Value (t Test)</th>
<th>All Eyes (N = 106)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPM, nm</td>
<td>39.0 ± 16.5 (7 to 91)</td>
<td>41.1 ± 14.3 (11 to 75)</td>
<td>.48</td>
<td>40.0 ± 15.7 (7 to 91)</td>
</tr>
<tr>
<td>CPA, degrees</td>
<td>20.5 ± 18.3 (−13 to 73)</td>
<td>28.8 ± 15.4 (−6 to 57)</td>
<td>.01</td>
<td>24.5 ± 17.4 (range: −13 to 73)</td>
</tr>
<tr>
<td>CPM (), nm</td>
<td>2.8 ± 2.3 (0.0 to 9.2)</td>
<td>3.7 ± 3.2 (0.0 to 15.5)</td>
<td>.14</td>
<td>3.2 ± 2.8 (range: 0.0 to 15.5)</td>
</tr>
<tr>
<td>CPA () degrees</td>
<td>3.8 ± 3.3 (0.6 to 17.6)</td>
<td>2.8 ± 2.0 (0.6 to 8.3)</td>
<td>.06</td>
<td>3.3 ± 2.8 (range: 0.6 to 17.6)</td>
</tr>
<tr>
<td>Corneal thickness, mm†</td>
<td>535.0 ± 34.7 (460.7 to 613.0)</td>
<td>552.6 ± 34.9 (483.3 to 630.3)</td>
<td>.02</td>
<td>544.5 ± 35.7 (range: 460.7 to 630.3)</td>
</tr>
<tr>
<td>Corneal curvature, units</td>
<td>7.8 ± 3.0 (7.0 to 8.7)</td>
<td>7.8 ± 0.30 (7.1 to 8.5)</td>
<td>.57</td>
<td>7.8 ± 0.3 (range: 7.0 to 8.7)</td>
</tr>
<tr>
<td>Refraction, D</td>
<td>−1.6 ± 2.3 (−9.0 to 2.5)</td>
<td>−0.1 ± 1.4 (−5.0 to 2.8)</td>
<td>.13</td>
<td>−1.29 ± 1.94 (range: −9.0 to 2.8)</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD (range). CPM indicates corneal polarization magnitude; CPA, corneal polarization axis; and D, diopters.
†Corneal thickness was measured in 42 glaucomatous eyes and 49 healthy eyes.

### Table 2. Linear Regression Relationships Between Corneal Polarization Magnitude and Age, Corneal Thickness, Corneal Curvature, Refraction, Race, and Sex*

<table>
<thead>
<tr>
<th></th>
<th>CPM, Glaucomatous Eyes (n = 55)</th>
<th>CPM, Healthy Eyes (n = 51)</th>
<th>CPM, All Eyes (N = 106)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.0003 (.90)</td>
<td>0.09 (.04)</td>
<td>0.03 (.70)</td>
</tr>
<tr>
<td>Corneal thickness†</td>
<td>0.07 (.08)</td>
<td>0.007 (.58)</td>
<td>0.04 (.05)</td>
</tr>
<tr>
<td>Corneal curvature</td>
<td>0.002 (.72)</td>
<td>0.001 (.89)</td>
<td>0.002 (.67)</td>
</tr>
<tr>
<td>Refraction</td>
<td>0.03 (.22)</td>
<td>0.001 (.86)</td>
<td>0.02 (.15)</td>
</tr>
</tbody>
</table>

*Data are presented as $R^2$ (P value). CPM indicates corneal polarization magnitude.
†Corneal thickness was measured for 42 glaucomatous eyes and 49 healthy eyes.

### Table 3. Linear Regression Relationships Between Corneal Polarization Axis and Age, Corneal Thickness, Corneal Curvature, and Refraction*

<table>
<thead>
<tr>
<th></th>
<th>CPA, Glaucomatous Eyes (n = 55)</th>
<th>CPA, Healthy Eyes (n = 51)</th>
<th>CPA, All Eyes (N = 106)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.004 (.65)</td>
<td>0.13 (.008)</td>
<td>0.10 (.001)</td>
</tr>
<tr>
<td>Corneal thickness†</td>
<td>0.008 (.58)</td>
<td>0.004 (.68)</td>
<td>0.02 (.24)</td>
</tr>
<tr>
<td>Corneal curvature</td>
<td>0.007 (.54)</td>
<td>0.006 (.58)</td>
<td>0.009 (.34)</td>
</tr>
<tr>
<td>Refraction</td>
<td>0.03 (.22)</td>
<td>0.005 (.62)</td>
<td>0.02 (.19)</td>
</tr>
</tbody>
</table>

*Data are presented as $R^2$ (P value). CPA indicates corneal polarization axis.
†Corneal thickness was measured for 42 glaucomatous eyes and 49 healthy eyes.

Figure 3. The linear regression relationship between corneal polarization magnitude and corneal polarization axis (CPA) for all eyes combined (n = 106). Nasally upward CPA values were recorded as negative; nasally downward CPA values were recorded as positive.
VARIABILITY OF CPM AND CPA MEASUREMENTS

For CPM and CPA, the mean standard deviation of the 3 measurements used to create the single average measurement analyzed for each subject was 8% and 13.5% of the mean CPM and CPA values (coefficient of variation), respectively, indicating minimal interimage variability. The mean ± SD variability (the SD of 3 images that comprised the mean image used for analysis) was 3.2 ± 2.8 nm and 3.3° ± 2.8° for CPM and CPA, respectively.

In the 13 healthy subjects with 3 sets of CPM and CPA measurements within 3 months, the variability of these measurements across time was overwhelmingly attributable to differences among subjects (93% of the variance for both CPM and CPA). Intervisit variability accounted for 0% and 1% of the variability in CPM and CPA, respectively.

COMMENT

In our study, the intersubject variability of both the measured CPM and CPA was large. The CPM in our subject population ranged from 7 nm to 91 nm in glaucomatous eyes and from 11 nm to 75 nm in healthy eyes. The CPA ranged from −13° to 74° in glaucomatous eyes and from −6° to 57° in healthy eyes. The mean CPM and CPA were different from the values assumed by the GDx. The mean CPM of 40 nm in our study is in contrast to the assumed CPM of 60 nm with the fixed GDx corneal compensator. Similarly, the mean CPA of 24.5° in our study is in contrast to the assumed CPA of 15° with the fixed compensator. These findings, coupled with large intersubject variability in the measurements, suggest that inaccurate GDx RNFL measurements exist in a subset of patients. The inaccuracies may increase with a greater disparity between actual values and compensated values, although this hypothesis was not tested. These results illustrate the need for a variable or wide-band compensator if RNFL birefringence is to be effectively isolated from anterior segment contributions.

Our reported results (healthy and glaucomatous eyes combined) for CPA (mean ± SD, 24.5° ± 17.4°) are similar to those of Greenfield and colleagues (healthy eyes only),3,7 who reported a mean ± SD CPA of 24.8° ± 21.4° using a different device. Our mean ± SD CPA for healthy eyes was also similar to their results (28.8° ± 15.4°). The mode of CPA distribution reported in the study by Greenfield et al3 was between 11° and 22° (34% of eyes), similar to that assumed by the GDx corneal compensator. In our study, the distribution for all eyes combined was normal, with 20% of eyes having a CPA between 10° and 20° and 18% of eyes with a CPA between 30° and 40°.

Our reported results (healthy and glaucomatous eyes combined) for CPM are also similar to those reported previously by Knighton and Huang.4 They reported a CPM ranging from 0 nm to 250 nm (double pass). The observed range in our population was slightly less broad (single pass: 7-91 nm; double pass: 14-182 nm). These authors reported a moderate relationship between CPM and CPA (Pearson r = approximately 0.50), whereas this relationship was not observed in our study ($R^2=0.004$; $P=.54$).

Along with the results of Greenfield et al3 and Knighton and Huang,4 our results provide insight into the relatively poor performance of the GDx scanning laser polarimeter for discriminating between glaucomatous and healthy eyes that has been reported in some studies (although other studies have reported good discrimination,6–11 sometimes using parameters with no equivalent in the commercially available GDx). Studies from our labo-

Figure 4. The linear regression relationship between age and corneal polarization magnitude for all eyes combined (n=106).

Figure 5. The linear regression relationship between age and corneal polarization magnitude (CPA) for all eyes combined (n=106). Nasally upward CPA values were recorded as negative; nasally downward CPA values were recorded as positive.
reported significantly lower sensitivities at fixed specificities for various GDx parameters compared with those obtained using other imaging and visual function techniques; however, receiver operating characteristic curve areas for the best parameter using each technique were similar. In some cases, GDx parameters performed no better than chance at discriminating between healthy and glaucomatous eyes. This finding might be due to an overall increase in the RNFL thickness profile in some glaucomatous eyes, caused by improperly compensated CPM or CPA,13 that results in their classification as normal.

Another likely effect of inappropriate CPM and/or CPA compensation is the inclusion of inaccurate normal data in the GDx normative database.13 Such inclusion would increase the reported variability in the measurement of RNFL birefringence, resulting in a range of normative values for GDx parameters that would provide artificially high specificity or artificially low sensitivity.

In our study, we reported a significant relationship between CPA and age (R²=.10; for all eyes, P<.001). Knighton and Huang found no such relationship in a larger number of eyes (n=146; R<.0.2; P=.09) spanning a similar age range (21-71 years). The difference between their results and ours might be due to variations in the tested populations. They did not report the distribution of ages for their subjects. Another possibility is that these results are due to methodological differences.4 The significant relationship observed in our study suggests that the CPA may change with time, although longitudinal studies are necessary for this conclusion. Greenfield and Knighton have shown a mean change in CPA of 4° in healthy eyes during the course of 1 year; however, the magnitude of this change was likely within the limits of measurement variability. Because the reported effect of age on CPA in healthy eyes was relatively small for the full range of ages examined (21-82 years), it is unlikely that this effect would meaningfully influence the longitudinal monitoring of GDx-measured RNFL thickness in patients with glaucoma during a 20- to 30-year course of the disease. This idea is reinforced by the lack of an age effect on CPA in our glaucoma group (age range, 51-90 years).

We also investigated the relationships between corneal thickness, corneal curvature, and refraction on CPM and CPA. Modest or weak relationships were observed between corneal thickness and CPM in glaucomatous eyes and all eyes combined (R²=0.07 and P=.08, and R²=0.04 and P=.05, respectively), but not in healthy eyes. No significant effects of these variables on CPA were observed. Although small, the effects of corneal thickness on CPA may have some relevance to GDx imaging prior to and after laser-assisted in situ keratomileusis (LASKI).

The effect of LASKI on GDx measurements has been investigated,1314 but its direct effects on CPM and CPA have not been reported. A weak cross-sectional relationship between corneal thickness and CPM and CPA does not imply that CPM and/or CPA will remain stable after a LASKI-induced change in corneal thickness.

We used macular imaging to determine the CPM and CPA. One limitation of this technique is that some macular abnormalities that disrupt the Henle layer and/or macular birefringence may affect the ability of this method to measure CPM and CPA. Because both glaucoma and macular degeneration are age-associated diseases, some patients may not provide stable macular images for correct CPM and CPA determination cross-sectionally and across time. This issue requires additional study.

In summary, our results indicate that the CPA and CPM vary widely in healthy and glaucomatous eyes. Although a substantial percentage of eyes show CPM and CPA values that are within the range compensated for by the commercially available GDx scanning laser polarimeter, the evaluation of many other patients results in data that are very different from these values. Furthermore, there is a small cross-sectional effect of age on CPA, indicating the possibility of change with time. For scanning laser polarimetry to best detect and monitor glaucoma, these findings must be addressed.