Analytical Model of Scanning Laser Polarimetry for Retinal Nerve Fiber Layer Assessment

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PURPOSE. To develop a quantitative understanding of scanning laser polarimetry (SLP) for retinal nerve fiber layer (RNFL) assessment in glaucoma diagnosis and management.

METHODS. The Mueller calculus was used to model the polarization optics of SLP. A birefringent retinal structure (RNFL or macula) was represented as a circularly symmetric linear retarder with a radial slow axis. The birefringent cornea and a corneal compensator within the SLP instrument were represented as fixed linear retarders. The model provided images of the radial retarder that were compared with retardance images obtained by SLP of the macula in eight normal subjects. Theoretical and experimental images were quantified with circular profiles around the center of the radial retarder or macula. Experimental retardance profiles were varied by tilting the subject's head to rotate the corneal axis. The SLP model was fit to the experimental profiles by nonlinear least-squares curve fitting.

RESULTS. The combined retarder formed by the cornea and corneal compensator induced bow-tie patterns in images of the radial retarder. Macular SLP images exhibited similar patterns. Retardance profiles could be characterized by three parameters: modulation, mean, and axis. The SLP model fit the experimental profiles very well ($r^2 = 0.8–0.9$).

CONCLUSIONS. The SLP model provided a quantitative framework within which to interpret SLP studies. Modulation-based parameters were generally more sensitive to retinal birefringence than mean-based parameters. Corneal birefringence is an important source of variance in SLP, especially for mean-based parameters. The theory developed for this study may guide improvements in clinical SLP. (Invest Ophthalmol Vis Sci. 2002;43:385–392)

The diagnosis and management of glaucoma require sensitive methods for detecting and measuring damage to retinal ganglion cells. The potential value of retinal nerve fiber layer (RNFL) assessment in glaucoma has long been known, and recognizable loss of the RNFL often precedes measurable loss of vision. Scanning laser polarimetry (SLP), a technology that incorporates ellipsometry into a confocal scanning laser ophthalmoscope, detects the birefringence of the peripapillary RNFL. SLP is attractive, because it provides rapid assessment, a visual image of the RNFL, and the potential for reproducible, objective measures of RNFL loss.

The RNFL exhibits substantial linear birefringence with the slow axis parallel to the direction of nerve fiber bundles (approximately radial around the optic disc) and retardance that correlates well with RNFL thickness. This birefringence probably results from form birefringence of closely spaced cylindrical structures. The normal RNFL thickness in humans at the location of typical SLP scans may range from 130 to 250 μm. Two current estimates of RNFL birefringence are 0.1 nm/μm in fixed macaque retina (calculated from Fig. 5 of Reference 10) and 0.23 nm/μm in ex vivo rat retina. Estimating with these two values results in double-pass RNFL retardances of 25 to 50 nm and 60 to 120 nm, respectively. Because fixation decreases the RNFL birefringence, the actual values in normal human subjects are likely to be closer to the higher estimate.

A potential confounding variable for SLP is corneal birefringence. Commercial SLP instruments have incorporated a corneal compensator (CC) intended to neutralize it but no analysis of the cornea-SLP system has been published. Although a general model describes the cornea as a curved biaxial crystal, for perpendicularly incident light the cornea is well-represented as a linear retarder. The mode of the distribution of corneal slow axes falls between 10° and 20° nasally downward (ND), and double-pass retardance ranges from near 0 to 250 nm. Early concepts for a CC used a variable retarder but the current instrument uses a fixed 60-nm linear retarder with its fast axis oriented 15° ND (information courtesy of Qienyuan Zhou, Laser Diagnostic Technologies, Inc., San Diego, CA). Although the CC fast axis lies at the mode of the corneal slow axis distribution and is thus oriented to oppose the birefringence of many corneas, the CC is not aligned with the axes of many other corneas. Furthermore, CC retardance (120 nm in double-pass) is greater than approximately 80% of corneal retardance. Thus, in spite of corneal compensation, corneal birefringence can contribute significant population variance to SLP measurements. For example, several SLP output parameters are strongly correlated with the slow axis of corneal birefringence. SLP measurements, however, are reproducible at least in part because within individuals the corneal axis has good long-term stability.

Additional evidence that corneal birefringence complicates SLP measurements comes from SLP images of the macula. Henle’s fiber layer, long parallel photoreceptor axons extending radially from the fovea, imparts substantial radial birefringence to the macula with an estimated double-pass retardance of approximately 50 nm (measured at 1.25° and 2.9° from the fovea at a wavelength of 568 nm). This birefringence is distinct from the dichroism at short wavelengths associated with Haidinger’s brush. Henle’s fiber layer is more circularly symmetric than the RNFL, yet SLP images of the macula show distinct “bow-tie” or “double-hump” patterns that do not correspond to the underlying anatomy. This study was designed to gain a quantitative understanding of the role of corneal birefringence in SLP measurements, first by analyzing the interaction of corneal compensation and the cornea over a wide range of corneal birefringence, next by incorporating corneal compensation into a theoretical model of SLP of a radial retarder, and finally by experimentally testing the model with SLP measurements of the birefringent macula.
in normal subjects. The model produced bow-tie patterns similar to those in macular images. The theoretical and experimental patterns were quantified with circular profiles around their centers. The variation of theoretical profiles with corneal axis was then compared with the variation of experimental profiles obtained while tilting the subject’s head to rotate the corneal axis. This study found that the SLP model fit the experimental profiles very well and that it could explain many results from other, previously published studies of SLP.

**METHODS**

**Matrix Methods**

The interaction of the optical components in the SLP model was determined by means of the Mueller calculus, in which the polarization properties of a component X are completely specified by a $4 \times 4$ matrix, the Mueller matrix $M_X$. The properties of multiple components in series are then given by the Mueller matrix formed by successively multiplying the Mueller matrices of all components in the order in which a light beam encounters them. Similar calculations have been used previously in the eye, to determine the interaction of corneal and macular birefringence in retinal birefringence scanning. All calculations were performed on computer (Matlab; The MathWorks, Inc., Natick, MA) using well-established Mueller matrices. The Mueller matrix of a linear retarder with fast axis ($\rho$) and retardance ($\delta$) is

$$
\mathbf{M} = \begin{pmatrix}
1 & 0 & 0 & 0 \\
0 & C_2 \sin^2(\delta/2) + C_1 \cos^2(\delta/2) & -S_2 \sin(\delta) & S_1 \cos(\delta) \\
0 & S_2 \sin(\delta) & C_1 \sin^2(\delta/2) + C_2 \cos^2(\delta/2) & -S_1 \sin(\delta) \\
0 & S_1 \cos(\delta) & -S_2 \cos(\delta) & C_1 \sin^2(\delta/2) + C_2 \cos^2(\delta/2)
\end{pmatrix}
$$

where $C_2 = \cos(2\rho)$, $C_1 = \cos(4\rho)$, $S_2 = \sin(2\delta)$, and $S_1 = \sin(4\delta)$.

In this article, retardance is expressed as a difference in optical path length (units of $\delta$ are in nanometers). It is understood that before a value for $\delta$ was used in equation 1, it was converted to a phase difference at $780$ nm. Subscripts on $\rho$ and $\delta$ identify the optical component to which they refer. It was frequently necessary, both for convenience and for consistency with the existing literature, to describe the slow axis of a retarder. These cases are denoted with a superscript $s$; thus, for example, $\rho_s$ denotes the slow axis of the cornea, and a $\rho_{S_2}$ of $\rho_{S_2} + 90^\circ$ was used in equation 1. All axis orientations are relative to the horizontal nasal meridian, as viewed by an observer facing the eye, with ND taken as negative.

**Model of SLP**

The analysis of SLP used the model in Figure 1. In SLP, images of the ocular fundus are formed by scanning the beam of a near-infrared laser ($780$ nm) in a raster pattern. The ellipsometer (E) measures at each image point the total retardance in the optical path, by detecting the ellipticity induced in a linearly polarized input beam. In the model, the measuring beam passed through three linear retarders: the corneal compensator (CC), the cornea (C), and a uniform radial retarder (R) that represented birefringent regions in the retina (e.g., peripapillary RNFL or macula). The slow axis of R was oriented radially, and distance around R was measured from the horizontal nasal meridian by angle $\beta$. At each point, therefore, the fast axis of R was $\rho_R = \beta + 90^\circ$. Retinal variations in retardance were not analyzed. The measuring beam was reflected at a deeper layer and traveled back through the three retarders to the ellipsometer. Reflection from the ocular fundus exhibits a high degree of polarization preservation, and the reflector in the model (polarization-preserving reflector [PPR]) was assumed to preserve completely the polarization state of the incident beam, except for a $180^\circ$ phase change due to the reversal in direction. This phase change reversed the sign of the azimuth and the handedness of the reflected polarization. Each optical component in the model experienced a double pass of the measuring beam. A component that had axis $\rho$ in the incident beam had axis $-\rho$ in the reflected beam and the relative orientation of the component axis to the polarization azimuth was maintained. Because the ellipsometer was insensitive to handedness, a double pass with reflection was equivalent to a single pass through the components of the model followed by the components in reverse order. Thus, an image of R was described by a profile around its center derived from

$$
\mathbf{M}(\beta) = \mathbf{M}_R \mathbf{M}_s (\beta) \mathbf{M}_s (\beta) \mathbf{M}_R \mathbf{C},
$$

where $\mathbf{M}_R$ is the total retardance in the image was, from equation 1,

$$
\delta_R (\beta) = \frac{\lambda}{360^\circ} \cos^{-1}(m_{S_2}),
$$

where $\lambda$ is $780$ nm.

**Experimental Methods**

Eight subjects (four women, four men, ages 25-58), who on clinical examination had normal anterior segments and maculas, were studied after providing written informed consent. The research followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of the University of Miami. One eye was tested in each subject.

Macular birefringence was imaged with a commercially available SLP nerve fiber analyzer (GDX; Laser Diagnostic Technologies, Inc., San Diego, CA). The GDX imaged the fundus with a $256 \times 256$-pixel raster scan that covered an area of $15^\circ \times 15^\circ$ in visual angle. To obtain macular images, the instrument was aligned on the cornea and pupil as usual, and the subject was instructed to fixate the center of the red rectangle formed by the $780$-nm scanning laser. To achieve stable but tilted head position, the usual head-and-chin rest was replaced with one that pivoted in the plane of the subject’s face and gave support to the side of the subject’s head.

For each scan, the GDX provided two images of the fundus, a reflectance image (intended as a means to judge scan quality) that showed retinal blood vessels at high contrast and a retardance image that provided the data from which perifoveal profiles were extracted. Reflectance images were cropped from the GDX screen display. Retardance images were written to a file by a software routine provided with the instrument. Subsequent image and data processing was performed on computer (Matlab software; The MathWorks, Natick, MA).

The amount of head tilt was difficult to control and, because of compensatory torsional eye movements, did not necessarily correspond to the rotation of the corneal axis. Fortunately, the reflectance images provided a means to determine the rotation of the eye. Using one image as a reference, the rotation and translation of all other images were determined by registration with triple invariant image.
descriptors, followed by manual adjustment. Images were registered to within 1 pixel of translation and 0.5° of rotation. The average rotation of images obtained with the usual instrument headrest was used to define the vertical head position. The corneal rotation was assumed to be equal to the fundus rotation and was added to the corneal axis at vertical to provide a value of $\rho_C$ for the particular image.

For each retardance image, a perifoveal profile was extracted from an annular region with an inner radius of 1.8° and an outer radius of 2.2° (1.3 mm in diameter in an emmetropic eye), a region that corresponded approximately to the peak of macular birefringence, as observed in GDx images. The center of the annulus was determined from several retardance images with pronounced macular bow-tie patterns by manually placing a cursor in the middle of the saddle-shaped center of the bow tie. Contour lines superimposed on the image aided this placement. When corrected for translation and rotation and superimposed on the reference image, the selected points clustered close to the region in the reflectance image judged to be the anatomic fovea. The centroid of the cluster was used as the annulus center in all images. At each of 128 angular steps around the annulus, the pixel values across its width were averaged to produce a profile value.

In each subject, the SLP model was fit to the perifoveal profiles by nonlinear least-squares curve fitting (routine LSQCURVEFIT of the Matlab Optimization Toolbox, ver. 2.0; MathWorks)—that is, the set of measured profiles was fit by a set of calculated profiles that minimized the square of the difference between the two sets. Standard errors of the parameters were calculated from the Jacobian of the curve fit.

To provide a comparison to values obtained by fitting the SLP model, in six subjects corneal birefringence was also measured with a corneal polarimeter described elsewhere. Briefly, the polarimeter provided a view of the fourth Purkinje image of a 585-nm light through crossed polarizers and a variable retarder. The Purkinje image was extinguished by adjusting the fast axis and retardance of the retarder to match the slow axis and retardance of the cornea, and the corneal parameters were read from calibrated dials. The other two subjects were not available for corneal polarimetry, but their corneal axes, measured in an earlier study, were included.

**RESULTS**

**Analysis of Corneal Compensation**

It was useful to consider the combined retarder (CR) formed by a double pass through CC and C, namely,

$$M_{CR} = M_{CC}M_CM_{CR}$$

The slow axis ($\rho_{CR}^s$) and retardance ($\delta_{CR}$) of CR were used to characterize the effects of corneal compensation. (Although shown in Fig. 1 as $\frac{1}{2}\rho_{CR}$, the system formed by a single pass through CC and C is not strictly a retarder, but is equivalent to a retarder followed by a rotator.) The rotations cancel in the symmetric chain of linear retarders in equation 4, and $M_{CC}$ is the Mueller matrix of a linear retarder.) $M_{CC}$ was calculated from equation 1, where $\delta_{CC}$ is 60 nm and $\rho_{CC}$ is $-15^\circ$.

The behavior of CR as a function of $\rho_{CC}^s$ is shown in Figure 2. For all corneas, $\delta_{CR}$ declined to a minimum where the slow axis of C and the fast axis of CC were parallel ($\rho_{CC}^s = \rho_{CC}$). For $\delta_{CC}$ = 60 nm, this minimum was zero—that is, CC exactly canceled C, but for $\delta_{CC} \neq 60$ nm, the minimum occurred at the vernal equinox. The behavior of $\rho_{CR}$ was more complex (Fig. 2B). Near $\rho_{CC}^s = 15^\circ$, $\delta_{CR}$ could be produced by some combination of $\rho_{CC}$ and $\delta_{CC}$, although in actual corneas some values of $\rho_{CR}^s$ were more common than others (see the Discussion section).

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To compactly display the results in a wide range of corneas, each retardance profile was characterized by three measures: peak-to-peak modulation ($A_{pp}$), mean level (average around which the profile swings), and orientation (i.e., bright axis of the bow tie). Figure 4 shows the variation of $\rho_{CC}^s$ of these measures for five values of $\delta_{CC}$ and three values of $\delta_{CC}$. Modulation (Fig. 4, top row) varied nearly linearly with $\delta_{CC}$ except near $\rho_{CC}^s = 15^\circ$. Near $\rho_{CC}^s = 0$, especially for corneas with $\delta_{CC} = 120$ nm, the modulation exhibited a dip toward 0. On the slope of this dip, the modulation did not change with

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**SLP of a Radial Retarder**

The retardance pattern in SLP images of the radial retarder in Figure 1 was determined from $\delta_{CC}(\beta)$ in equation 3. Some results are displayed in Figure 3 as retardance images and profiles. The patterns can be understood as an interaction between R and CR. As $\rho_R$ varied with $\beta$, $\delta_{CR}$ alternated and added and subtracted with the double-pass radial retardance ($2\delta_{CC}$) to produce the bow-tie pattern seen in the images. The bright arms of the bow tie (i.e., the peaks of the profile) occurred where $\rho_R$ and $\rho_{CR}$ were aligned. The profile modulation depended on the relative values of $\delta_{CC}$ and $\delta_{CR}$. The peak-to-peak amplitude ($A_{pp}$) of the modulation was

$$\rho_{CC}^s = |\delta_{CC} + 2\delta_{CC} - |\delta_{CC} - 2\delta_{CC}|$$

In theory, profile modulation could be governed either by the retarder R undergoing measurement, by the combined retarder CR formed by CC and C, or by a combination of both. When R had no birefringence ($2\delta_{CC} = 0$) there was no modulation of the profile; it was constant at a value equal to $\delta_{CC}$ (flat dashed lines in Fig. 3).

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In the region of the minimum, the mean varied with a wide range of corneal parameters, but for the retardance, the mean was approximately constant for 2

The bow-tie axis was approximately vertical over a middle row. The variation of total retardance (axis of highest brightness in the images). Images of a uniform radial retarder displayed a bow-tie pattern that varied in orientation and magnitude with the parameters of C and R. The bow-tie axis was specified by the angle of maximum brightness (axis of highest brightness in the images).

δR, except at very low values (e.g., Fig. 3B and the corresponding points labeled b in Fig. 4). The mean retardance (Fig. 4, middle row) increased with the difference between ρC and ρCC, resulting in a minimum at ρC = −15°. The height of the minimum increased with the difference between 2δR and 2δCC. In the region of the minimum, the mean varied with δR, but away from the minimum the mean was much less sensitive than the modulation to changes in δR. The variation with ρC of the bow-tie bright axis (Fig. 4, bottom row) was the same as that of ρCC in Figure 2B, because maximum total retardance occurred when the slow axes of R and CR were aligned. The variation of bow-tie axis with ρC did not depend on δR. The bright axis of the bow tie was approximately vertical over a wide range of corneal parameters, but for 2δR > 120 nm and ρC > −15° the bow-tie axis lay closer to horizontal.

Experimental Test of the SLP Model

To test the theoretical concepts developed in the foregoing section, we reproduced experimentally the situation depicted in Figures 3 and 4 and then attempted to fit the data with the model expressed in equations 2 and 3. Henle’s fiber layer in the macula of the eye provided a circularly symmetric birefringent structure corresponding to R in Figure 1. It was assumed that corneal retardance (δR) remained constant; the corneal axis (ρC) was varied by tilting the subject’s head.

Three examples of macular retardance images and perifoveal profiles are shown in Figure 5. Pronounced bow-tie patterns, similar to those in Figure 3 but with retardance that varied with distance from the center, were apparent in this subject for head tilts to either side of vertical (images A and C). Near vertical, there was only weak modulation of the macular retardance (image B). The bow-tie patterns were quantitatively evaluated by means of perifoveal profiles (left column) obtained from the annular region of maximum modulation. Each profile was approximated by a simpler, smooth profile synthesized from terms 0, 2, and 4 of its Fourier series (i.e., the mean and first two even harmonics for a total of five independent coefficients per profile). To aid the comparison of data to theory, the three parameters used in Figure 4 to characterize the theoretical profiles—A_{PP}, mean level, and bow-tie orientation—were derived from the synthesized profile. In each subject the data fitted by the model consisted of 19 to 45 perifoveal profiles acquired with various amounts of fundus tilt.

To fit the corneal compensation model to the head tilt data, two additional properties of the GDx were taken into account. First, the output of the GDx was in arbitrary units, which we termed GDx units (GU), and we added as a parameter the scale factor s required to convert GU to retardance in nanometers. Second, the retardance values in GDx images never approached zero (as they can in theory). We hypothesized a “noise floor,” a minimum value determined by instrumental factors and by random variation in the raw images from which retardance was calculated. This concept was introduced into the model by means of the arbitrary transfer function shown in Figure 6A, which had the form (δR + F)n, where F was the noise floor and n controlled the sharpness of the transition between F and the line of equality. A value of n = 3 gave a good balance between an unrealistic presentation of the troughs of some fitted profiles and a rapid approach to equality. Thus, the SLP model fitted to the data was

\[ G(\beta) = s(\delta_R(\beta)^3 + F^3)^{1/n} \]

where G(β) is a set of profiles expressed in GU that depend on five parameters: s, F, and the three ocular properties that control δR(β) through equations 2 and 3: macular retardance (δR), corneal retardance (δs), and corneal axis at vertical head position.

Figures 6B and 7 show the result of fitting the SLP model to perifoveal profiles from three subjects. The fitted parameters of the model for all eight subjects are displayed in Table 1. Values for noise floor (sF) and the SD of the residuals (SD) are reported in GU to allow comparison with the output display of the GDx instrument. As seen in Figure 6B, in six examples (one high-modulation and one low-modulation profile from each subject) most model profiles followed closely the actual profiles, although exceptions occurred, usually near the modulation minimum (e.g., Fig. 6A). The fit across all head positions is shown in Figure 7, where the measures used to characterize both actual and fitted profiles are plotted in the same format as Figure 4. The solid curves in Figure 7 were calculated from theoretical profiles, i.e., profiles generated from the parameter values in Table 1 inserted into the SLP model (equations 2, 3, and 6). The circles show measures of the smooth Fourier description of each actual profile (as exemplified in Fig. 5); these measures were independent of the model parameters. Overall, the SLP model fit the data quite well, explaining 80% to 90% of the profile variance (r^2 = 0.81–0.91 in Table 1; P < 0.0001).

For Table 1 the SLP model was applied to the profiles from each subject individually to produce eight separate tests of the model. This also produced eight estimates of the scale factor s.
Figure 4. Retardance profiles were characterized by three measures: modulation, mean, and the orientation of the bright axis of the bow tie. The graphs show the variation of these measures as a function of corneal axis for five values of corneal retardance. The dots labeled a–c mark values from corresponding profiles in Figure 3A–C. Stars: an extreme value for corneal birefringence (see the Discussion section); vertical dashed lines: where $\rho_C$ is equal to $\rho_C$; horizontal dashed lines: horizontal (H) and vertical (V) orientations of the bow-tie axis.

and the noise floor $F$. In fact, these two parameters were properties of the instrument and should have been the same for each subject. For this reason, the entire set of 250 profiles was reanalyzed in a single curve-fitting procedure with 26 free parameters (3 × 8 subject parameters + 2 instrument parameters). The subject values obtained were similar to those in Table 1. The instrument values were $s = 0.58 ± 0.01$ GU/nm and $sF = 28 ± 0.6$ GU with SD = 3.6 GU and $r^2 = 0.86$.

DISCUSSION

In this study, we analyzed SLP, including the role of corneal compensation, and developed a model for SLP of a radial retarder. The SLP model was then tested with experiments in which the radial birefringence of the macula was imaged with the GDx instrument while the corneal axis was varied by tilting the subject’s head. The range of corneal parameter values used to test the model (Table 1), although not as wide as in Figure 4, included a majority of the normal population. The range of corneal retardance ($2\delta_C = 21–138$ nm, measured with the corneal polarimeter) spanned more than 85% of normal values, including one unusually low value. 18 Unfortunately, no subjects with corneas in the upper 10% of the normal retardance range were available to test the model. The range of corneal axes ($\rho_C = -8^\circ$ to $-40^\circ$) included more than 75% of normal eyes. 19 The range of radial retardance was limited ($2\delta_R = 30–42$ nm, as provided by the fit to macular retardance) and could not be measured independently. The corneal axes determined by the model were statistically identical with those determined by polarimetry ($P < 0.002$). In six subjects, the corneal retardance determined by the model did not correspond well to that measured with the corneal polarimeter. This is consistent with a report that corneal retardance measured with a modified GDx, although well-correlated with retardance measured with the corneal polarimeter, is not the same. 20

Wavelength (780 nm vs. 585 nm) and the area of cornea measured are both possible reasons for the difference, but require further investigation. It was encouraging that the SLP model fit the experimental profiles very well and elicited confidence that the model provided a framework for understanding clinical SLP.

An ideal imaging polarimeter should portray accurately the spatial distribution of specimen retardance. For example, the ideal image of R in Figure 1 should have uniform brightness and a profile that is flat and equal to the double-pass retardance. The model showed, however, that the birefringent C and the CC combined to produce bow-tie patterns in the images and double-hump patterns in the retardance profiles. Clearly, a clinical SLP retardance pattern does not necessarily (or even usually) match the retinal retardance pattern. Nevertheless, the model showed that SLP images encode clinically useful information about retinal retardance.

The SLP model assumes that the retinal structure imaged is a uniform radial retarder (Fig. 1, R). This assumption fits macular anatomy very well, but it does not apply quite as well to the RNFL. Two properties of the peripapillary RNFL clearly differ from R. First, $\rho_C \neq \beta$ for the RNFL. Nerve fiber bundles are only approximately radial as they emanate from the optic nerve head. They are crowded toward the temporal direction and spread apart nasally. 38–40 When introduced into the model, this should distort the symmetry of a vertical bow tie by broadening the temporal trough, narrowing the nasal trough, and moving the peaks to the nasal side of vertical. Exactly these features are present in actual RNFL profiles obtained clinically. 41–42 Second, the RNFL does not have uniform thickness; hence, $\delta_B$ is not a constant. The peripapillary RNFL is thinner temporally and nasally and thicker superiorly and inferiorly. 12 This RNFL anatomy elevates the retinal surface into a double-hump pattern that is apparent in scanning laser tomography 43 and optical coherence tomography (OCT). 44 and most observers expect to see a double hump in SLP profiles of the RNFL. Although these differences are important for a detailed inter-
pretation of RNFL retardance patterns, to develop a global picture of the information provided by SLP, it is useful to ignore the differences and maintain the concept of the RNFL as a uniform radial retarder.

Compensation of Normal Corneas

The practical consequences of corneal compensation were explored by calculating the properties of CR for the untilted corneas of a population of normal subjects. Birefringence values, measured at 585 nm in each of the two corneas of 73 normal subjects, were inserted into equation 4 for two situations, with corneal compensation as used in SLP and without corneal compensation (i.e., with the cornea alone). Although corneal retardance at 585 nm and at the SLP wavelength of 780 nm may not be the same, the two are well correlated, and the calculation provides useful insight. Recall that the bow-tie patterns in SLP images of R (Fig. 3) were induced by CR, with the bright arms of a bow tie lined up with the slow axis of CR and the mean and modulation determined by the retardations of CR and R. The results of the calculation are plotted in Figure 8, which shows the distribution of retardations CR and R in polar coordinates. In polar coordinates, a line connecting a point to the origin has the same orientation as and a length equal to the retardation. Thus, the clusters of points in Figure 8 provide a sense of the population variability that CR introduces into SLP images of a radial retarder.

From Figure 8A it is evident that if SLP were performed without corneal compensation, the bright arms of the bow tie pattern in most eyes would oppose the anatomic double hump of the RNFL. This could produce RNFL images that defy expectations and may suppress information from the important superior and inferior RNFL where the majority of nerve fiber bundles occur. The addition of CC rotated the distribution of bow-tie axes to near vertical (Fig. 8B). Some bow-tie patterns could fall at any orientation, but those far from vertical usually had weak modulation (usually, was low). Extreme cases, however, (e.g., the stars in Fig. 4 and in Fig. 8B) could induce a strong horizontal bow tie that could overwhelm the anatomic pattern of the RNFL. The addition of CC also decreased the median of in the 146 corneas from 86 (Fig. 8A) to 56 nm (Fig. 8B).

Relation of the SLP Model to Clinical Studies of the RNFL

The chief clinical application of SLP is the assessment of the peripapillary RNFL, a birefringent structure with retardance that varies directly with its thickness. In part because commercial SLP instruments have used “thickness” as the name for the displayed output variable, papers in the literature fre-
moderate correlation. The measurements that originally comparison of the two variables in a macaque showed only spatial distribution of RNFL thickness and, indeed, a direct retardance image produced by SLP cannot be the same as the (Fig. 6B). Thin horizontal- and vertical dashed lines: as in Figure 4. Thick vertical dashed lines: fitted values for ρ_c with no head tilt. The calibration bars in the central row of panels represent a double-pass retardance of 50 nm calculated from the scale factor s for each subject.

SLP instruments usually combine to produce a vertical bow tie (Fig. 8B), only two parameters, modulation and mean, are required to characterize most patterns. The behavior of these parameters in Figure 4 is complex but, with important exceptions, generally the modulation is more sensitive to δ_y (the variable of interest) and the mean is more sensitive to ρ_c. The predicted sensitivity to δ_y of profile modulation is borne out by a number of clinical studies that correlate SLP parameters to measures of visual field loss (mean deviation, corrected-pattern SD) that can serve as surrogates for decreases in thickness, or to the actual RNFL thickness as measured by OCT. Hoh et al. found that the modulation-based GDx parameters Maximum Modulation and Ellipse Modulation are better than the mean-based parameters Ellipse Average and Total Integral at discriminating between normal and glaucomatous eyes, are better correlated with visual field loss and are also better correlated with RNFL thickness obtained by OCT. Sinai et al. use sectors of SLP output to form two parameters,

\[
\begin{array}{ccccccccc}
\text{Subject} & n & \rho_c^* (\text{deg}) & 2\delta_c^* (\text{nm}) & s (\text{GU/nm}) & \mathcal{S}_F (\text{GU}) & \text{SD} (\text{GU}) & r^2 & \rho_c (\text{deg}) & 2\delta_c (\text{nm}) \\
1 & 19 & -11.0 & 95.2 & 53.4 & 0.64 & 0.03 & 24 & 1.5 & 3.3 & 0.88 & -8 & 71 \\
2 & 20 & -35.0 & 106.1 & 44.2 & 0.66 & 0.02 & 30 & 1.4 & 3.1 & 0.91 & -49 & 94 \\
3 & 34 & -18.2 & 148.2 & 45.1 & 0.57 & 0.01 & 27 & 1.0 & 2.7 & 0.91 & -22 & 120 \\
4 & 28 & -26.0 & 77.2 & 45.2 & 0.62 & 0.02 & 25 & 1.7 & 3.4 & 0.90 & -22† & — \\
5 & 26 & -37.2 & 119.5 & 42.3 & 0.51 & 0.04 & 32 & 2.4 & 3.0 & 0.87 & -31† & — \\
6 & 36 & -14.0 & 130.1 & 46.2 & 0.66 & 0.02 & 26 & 1.6 & 4.4 & 0.87 & -18 & 98 \\
7 & 42 & -45.2 & 83.2 & 53.3 & 0.46 & 0.02 & 30 & 1.6 & 2.8 & 0.87 & -37 & 138 \\
8 & 45 & -34.2 & 63.2 & 51.3 & 0.48 & 0.02 & 34 & 1.6 & 3.2 & 0.81 & -36 & 21 \\
\end{array}
\]

\(n\), number of profiles in fitted set.  
* Parameters of fit ± SE.  
† Ref. 18, except † from ref. 19; repeatability is ±2.2° in axis, ±10% in retardance.
peak-to-trough amplitude (modulation-based) and average thickness (mean-based). The modulation-based parameter discriminates between the normal and glaucomatous condition and is significantly correlated with mean deviation; the mean-based parameter has neither attribute. Chen et al. 48 form SLP measures from retinal differences in quadrants: sums (mean-based), ratios to the nasal valve, and modulation in the same sense as used herein. (Ratios are complex, containing modulation of SLP parameters based on the pro

FIGURE 8. Polar plots of $\delta_{\text{CR}}$ and $\rho_{\text{CR}}$ calculated for the corneas of 75 normal subjects. The calculation used values for $\rho_{\text{CR}}$ and $2\delta_{\text{CR}}$ measured at 585 nm in a previous study. Each cornea was plotted twice at $\rho_{\text{CR}}$ and $\rho_{\text{CR}} + 180^\circ$ to visually emphasize the bow-tie pattern that CR induces in R. (A) Cornea alone (i.e., $\delta_{\text{CC}} = 0$). (B) Compensated cornea. Coordinate systems for the right and left eyes are mirror symmetric to show axis orientations as they would appear when facing the subject. The stars mark CR for a hypothetical extreme (rare, but possible) value for corneal birefringence ($\rho_{\text{CR}} = -8^\circ$ and $2\delta_{\text{CR}} = 220$ nm). NU, nasally upward; ND, nasally downward.

The SLP model also explains most of the results of a study that is conceptually similar to the head-tilt experiment of Figures 5, 6, and 7, except that $\rho_{\text{CR}}$ varied across a population rather than within an individual. Greenfield et al. 49 report SLP of the RNFL and macula from normal subjects in whom they had also measured $\rho_{\text{CR}}$. For both RNFL and macula the GDx parameters related to the mean—Average Thickness, Ellipse Average, Superior Average, Inferior Average, Superior Integral, and Total Integral—show a strong linear correlation with $\rho_{\text{CR}}$ ($r^2 = 0.6 - 0.8$) from $+4^\circ$ to $-76^\circ$. (Note that Greenfield et al. express nasally downward angles as positive, the opposite to this study.) It is clear from their figures that the correlation is even stronger when the data are limited to axes more nasally downward than $-15^\circ$. The profile mean in Figure 4 (middle row) showed exactly this behavior for all values of $\delta_{\text{CC}}$: the mean increased as the difference between $\rho_{\text{CR}}$ and $\rho_{\text{CC}}$ increased. Unlike the model and the results for subjects 1 and 3 in Figure 7, the data of Greenfield et al., do not increase for $\rho_{\text{CR}}$ nasally upward from $-15^\circ$, but there are only five subjects covering a $20^\circ$ range. A coincidental combination of retinal changes and axes could have easily obscured the small increase expected. In contrast to parameters related to the mean, the correlation with $\rho_{\text{CR}}$ of GDx parameters related to modulation—Inferior Ratio, Superior/Nasal, Maximum Modulation, and Ellipse Modulation—is weak in the RNFL ($r^2 = 0.13 - 0.24$) and absent in the macula. 19 The difference between RNFL and macula follows directly from the modulation curves produced by the SLP model (Fig. 4, top row). Except for a narrow range of corneal parameters, the modulation curve for $2\delta_{\text{CR}}$ of 30 nm (similar to macula) did not vary with $\rho_{\text{CR}}$. The curve for a $2\delta_{\text{CR}}$ of 90 nm (similar to RNFL), however, showed a broader range of variation with its minimum at $-15^\circ$.

CONCLUSIONS

The CC used in SLP followed by a birefringent cornea forms a CR in the light path of the measurement, and in most corneas the slow axis of CR is approximately vertical. An SLP image of a radial retarder exhibits a bow-tie pattern with its bright arms aligned with the slow axis of CR. In clinical SLP, the bow tie due to CR usually exaggerates the anatomic double-hump pattern of the RNFL. In general, therefore, the peripapillary SLP profile is not the same as the RNFL thickness profile. The SLP model explains why corneal properties are a significant source of variance for SLP measurements within a population, especially for SLP parameters based on the profile mean.

The SLP model also reveals the strengths of SLP for assessing the RNFL. First, the model shows that SLP should be sensitive to RNFL birefringence, the variable it was designed to detect. The induction of a double-hump pattern requires the presence of RNFL birefringence, and loss of this birefringence produces a decline in SLP measurements, especially in parameters based on profile modulation. Second, SLP should be reproducible, because corneal birefringence is stable. 27 If the RNFL is always imaged through the same corneal location, the effects modeled in the current study are the same for every measurement. Observed changes can then be attributed to change in $\delta_{\text{CR}}$. Reproducibility, of course, is key to detecting progression of RNFL damage. Finally, the model shows that SLP measurements depend on the cornea in a predictable way. It may be possible to correct for this dependence with auxiliary information obtained by measuring the cornea, 53,54 or both. 55

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References


