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ORIGINAL ARTICLE

A Novel Analytical Method Using OCT to Describe the Corneoscleral Junction

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ABSTRACT

Purpose. To develop and test a novel quantitative method of describing the corneoscleral junction, including metrics that reflect both the angle and the topography in this region of the ocular surface.

Methods. Forty-eight neophyte subjects were recruited (16 Asian, 16 white, and 16 Latino). Optical coherence tomography images of the nasal, temporal, superior, and inferior quadrants in both eyes were taken. Custom image analysis software was written in Matlab to allow the observer to select a point defining the center of the junction, from which 20 concentric circles were automatically drawn. The surface of the junction in the image was automatically located by edge-detection routines, and the circles intersecting this edge defined a series of points in the Cartesian plane. A linear regression was fit to these points, and a set of metrics based on the regression residuals was calculated.

Results. The sum of the squared orthogonalized residuals (SSRo) was the most repeatable metric and had the advantage of being unaffected by the orientation of the image. The SSRo was significantly greater in the nasal quadrant ($p < 0.001$), reflecting a more pronounced angle and/or rougher surface. The flattest and smoothest topography was found in the temporal quadrant. Whites had significantly higher SSRo than Asians and Latinos ($p < 0.001$).

Conclusions. This study presents a novel metric for characterizing the angle and topography of the corneoscleral junction using optical coherence tomography and establishes differences among quadrants and between ethnic groups. (Optom Vis Sci 2014;91:650-657)

Key Words: corneosclera, optical coherence tomography, image analysis, race, ethnicity, corneal curvature, scleral curvature, contact lenses

Characteristics of the corneoscleral junction (CSJ), the transitional region between the cornea and the sclera, have the potential to influence soft contact lens (SCL) fit, performance of the lens on the eye, and subjective comfort. To date, attempts to quantify the topographical characteristics of the CSJ have been limited, and few studies have attempted to address how such characteristics could impact contact lens wear.¹ Most SCLs have diameters ranging from 13.8 to 14.2 mm and corneoscleral gas-permeable (GP) lenses have diameters ranging from 12.9 to 13.5 mm. Because the typical human corneal diameter is approximately 11.7 mm,² the edge of a contact lens can be expected to overlap the limbus by approximately 0.6 to 1.3 mm, thus interacting with the CSJ. Therefore, the CSJ could have as important an influence on the fit and performance of a contact lens and on subjective comfort

during lens wear as do the central and midperipheral cornea, because of its interaction with the lens edge, which is the part of the lens that needs to make the greatest flexural change to fit the ocular surface.³ To date, however, detailed quantitative information on the topography of the CSJ has been limited.⁴⁻⁶

Among the limited work that has been done in quantifying properties of the CSJ, some researchers have attempted to estimate the angle formed by the intersection of the cornea and sclera, which have different curvatures.^{1,7} Angle measurement of the CSJ is actually an attempt to quantify the directional change along the anterior ocular surface in the transitional region connecting corneal and scleral tissues. Considering the geometrical characteristics of the CSJ, however, angle estimation is subject to some limitations. Two lines that are tangential to the corneal and scleral surfaces are required to define a CSJ angle. Because the CSJ is a transitional region of two types of tissues, it is generally not possible to locate a single junction “point” where one unique set of two tangential lines can be drawn for angle estimation. It is possible to draw several sets of tangential lines to form hypothetical CSJ angles, as shown in Fig. 1. A small change in the tilt and the location of the tangential lines can result in more than 5 degrees of variation in the estimated CSJ

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FIGURE 1.

Nonunique selection of tangential lines to define an angle in a CSJ image. A color version of this figure is available online at www.optvissci.com.

angle, leading to nonunique estimates with poor repeatability. A second limitation of angle estimation is that it does not take into account other characteristics of CSJ topography. A relatively flat CSJ with an angle between the cornea and sclera that would be estimated at close to 180 degrees can still have a rough surface topography. In terms of contact lens fit, performance, and comfort, the overall topography of the CSJ surface could be as important as the CSJ angle.

To elucidate the relationships among contact lens design parameters, lens performance on the eye, CSJ topography, and subjective comfort, the surface characteristics of the CSJ must be quantified by a more comprehensive metric than a simple angle estimate. Such a metric should reflect both the lateral density and the transverse magnitude (elevation) of concave or convex structures along the CSJ surface. In the present study, we introduce the calculation of a novel CSJ metric based on semiautomated image analysis of optical coherence tomography (OCT) images of the CSJ, assess its repeatability and reproducibility, and demonstrate its capability to quantify the CSJ profile and differentiate among varying CSJ topographies.

METHODS

Subjects

Because contact lens wear can have an influence on the CSJ profile,⁸ we recruited only healthy neophyte subjects with no contact lens wear for at least the prior 12 months. In addition, because there are known ethnic differences in corneal curvature and asphericity,⁹ and in the ocular surface response and subjective

symptoms with contact lens wear,^{10–12} we recruited subjects from three ethnic groups (Asian, white, and Latino) to assess the potential for a CSJ metric to identify corneoscleral profile differences among different eye types. A total of 48 subjects with a mean ($\pm$ SD) age of 21.6 ($\pm$ 2.8) years (range, 18 to 30 years) were recruited, with 16 subjects in each of the three ethnic groups. Table 1 provides a more detailed summary of the demographic characteristics of our subject sample. Informed consent was obtained from all study participants after a full description of the goals, potential risks and benefits, and procedures of the studies. This research project adhered to the tenets of the Declaration of Helsinki; it was approved by institutional review board (Committee for Protection of Human Subjects, University of California, Berkeley) and was compliant with the Health Insurance Portability and Accountability Act.

Instrumentation and Procedures

A CSJ image was taken by commercial spectral domain OCT (ENVISU 2300; BiopTigen Inc, Durham, NC) on each of the four quadrants (nasal, temporal, superior, and inferior) of both eyes on all 48 subjects, for a total of 384 images. To image the CSJ region in four quadrants, subjects were instructed to fixate on external targets with the test eye. The OCT has 12- μ m lateral and 3.3- μ m axial resolutions with 3.4 mm depth (in air). Linear scans were performed with a 4-mm scan length. First, the interface between the air and the ocular surface in the OCT image was located automatically by a custom edge-detection program written in Matlab. The next step was the selection of a point at the center of the CSJ region on this interface by a trained observer. Once the center point was specified, 20 points along the interface were

TABLE 1.

Subjects' ages, stratified on sex and ethnicity

	Asian (n = 16)		White (n = 16)		Latino (n = 16)	
	Female	Male	Female	Male	Female	Male
n	7	9	9	7	6	10
Age, mean (SD) (yrs)	20.71 (1.25)	21.00 (1.87)	22.33 (3.35)	23.43 (3.15)	19.50 (1.64)	22.00 (3.33)

FIGURE 2.

Corneoscleral junction topography described by 21 points along the air/ocular surface interface.

determined by 10 automatically generated concentric circles spanning a 2-mm region (Fig. 2). A linear regression was then performed based on the Cartesian coordinates of the 21 points (the center point and the 20 evenly distributed points).

Five metrics were derived from the regression output: the R^2 of the regression, the sum of the squared residuals (SSR), the sum of the squared orthogonalized residuals (SSRo), and the standard deviations of the residuals (SDR) and orthogonalized residuals (SDRo). The regression R^2 , also called the coefficient of determination, is generally used to evaluate the goodness of fit of the regression or the proportion of the total variability accounted for by the model. In this case, a relatively flat and smooth CSJ would result in the 21 points marking the surface of the CSJ clustering closely about the regression line, giving a relatively high R^2 value; alternatively, a very pronounced angle between cornea and sclera,

or a very rough CSJ surface, would result in a greater spread of the 21 points about the regression line and a relatively low R^2 . The SSR is the sum of the squared deviations of each coordinate point from the regression line. A relatively flat and smooth CSJ should give a relatively low SSR as all the residuals are small (Fig. 3); alternatively, a pronounced angle or rough surface would result in larger residuals and thus a relatively high SSR (Fig. 4). Similarly, the SDR represents the dispersion of the 21 surface-marking points about the regression line. Because the orientation of a CSJ image could be affected by the alignment of the OCT probe reference to the ocular surface, the SSR and SDR could vary with the orientation of the image. We therefore calculated the SSRo and SDRo using orthogonalized residuals to eliminate the effect of image orientation. In the simple linear regression used in this study, the orthogonalized residuals can be drawn perpendicular to the regression line, rather than vertically, and are therefore independent of the tilt of the line.

An additional final metric was computed for diagnostic purposes. Generally, a pronounced angle between cornea and sclera will result in a relatively high value of the SSRo; however, it is possible that an image of a flat CSJ with an extremely rough surface or poor image quality/artifacts could result in a high value of the metric. We therefore calculated the number of sign changes in the ordered residuals, because a pronounced angle should result in the regression line crossing the CSJ surface in the image only twice, as in Fig. 4, whereas a rougher, more “up-and-down” surface would result in the regression line crossing multiple times. We examined all images with SSRo values above the median, found 19 images with more than two residual sign changes, and manually inspected those image files and regression results. Of those, two had poor image quality and seven had high SSRo values owing to high surface roughness rather than a pronounced CSJ angle. After completing the analysis with all images included, we also recomputed descriptive statistics and multivariate models without those images and found only very minor quantitative and no qualitative differences in the overall results.

FIGURE 3.

Linear fit to a flat, smooth CSJ gives small residual values.

FIGURE 4.

Linear fit to a CSJ with a pronounced angle gives greater residual values.

Statistical Methods

A pilot repeatability and reproducibility study was conducted to evaluate the reliability of this technique. The study was performed on 10 eyes from five subjects, including one neophyte, one GP lens wearer, and three SCL wearers. All contact lens wearers discontinued CL wear at least 24 hours before the examination. Two visits were scheduled for each subject on 2 days within a 5-day period. The measurement on each quadrant of each eye was repeated by two OCT operators at each visit, resulting in a total of 160 CSJ images. The two operators also served as the study observers who inspected the CSJ images and defined the CSJ center points, which was done in random order after all images had been collected. Identifying information was masked to the observers during image processing. After the five metrics were generated by the automated process described above, we examined limits of agreement and difference-versus-means plots¹³ and conducted a variance component analysis to help identify the best metric. The metric with the best repeatability and greatest capability of differentiating the CSJ across quadrants was the SSRo, which also has the advantage of being unaffected by the orientation of the image. Following the repeatability study, using the full data set of 48 subjects, multivariate linear mixed-effects models were fit to assess differences in the SSRo among quadrants and to estimate the effects of age, sex, ethnicity, and time awake before measurement, while accounting for the potential internal correlations engendered by the repeat measurements on each subject. The Tukey honestly significant difference (HSD) statistic was used for *post hoc* multiple comparison testing of pairwise differences among the quadrants and among ethnicities.

RESULTS

In this section, we will first report the results of the pilot repeatability and reproducibility study that was conducted to establish the baseline performance of this novel technique, followed by the results

for our primary outcome metric and comparisons of the metric among quadrants and between ethnic groups.

Repeatability and Reproducibility

The repeatability of an instrument or measurement technique refers to the degree to which repeated measurements on the same subject, by the same observer, under the same conditions agree. Reproducibility refers to the degree to which two different observers can conduct measurements on the same subject, under the same conditions, and get the same result. In the present study, the variation among repeated measurements arises solely from observer criteria for identifying the center location of the set of regression points, because after the observer initiates the measurement process by choosing the center of the regression, the image analysis and calculation of metrics are entirely automated. There can be, however, differences between observers or within one observer on different occasions, in the criteria for selecting the center point, thus potentially introducing some error into the calculated metrics.

For observer 1, the limits of agreement between repeated measurements of the SSRo were centered very closely on zero (mean difference, -9.4×10^{-5}) with a 95% confidence interval for the difference of $[-0.0014, 0.0012]$. For observer 2, the SSRo also had very good repeatability, with a mean difference of -8.5×10^{-6} and a 95% confidence interval of $[-0.0009, 0.0008]$. Difference-versus-means plots revealed no obvious patterns of repeated measurement differences depending on the magnitude of the SSRo, for either observer.

In terms of reproducibility, observer 2 tended to obtain slightly higher values of the SSRo than did observer 1. This is a potential pitfall of any clinical assessment in which human judgment comes into play and highlights the need for training and periodic calibration of observers for such quasi-subjective outcomes. Variance component analysis confirms that the magnitude of the variability in the SSRo due to different observers is on the same order as, for example, the difference between superior and inferior quadrants, which suggests that using multiple observers in a given study could confound any analysis of interquadrant differences in the SSRo. The

FIGURE 5.

Factor plot of the SSRo shows clear interquadrant differences, good repeatability, and some need for improvement in interobserver reproducibility. I, inferior; N, nasal; S, superior; T, temporal.

factor plot in Fig. 5 shows very good within-observer repeatability, with the variability attributed to repeated measures being a small fraction of the true variability among quadrants. This suggests that a single trained observer can obtain good consistency in measuring the SSRo but that only a single observer should be employed in a given study until standardized training improves interobserver reproducibility. Therefore, to eliminate this potential bias, in the remainder of the analyses in this article, all images were processed by observer 1 only.

Primary Outcome: SSRo

Table 2 presents descriptive statistics for the SSRo stratified on eye and quadrant. The SSRo was highest in the nasal quadrant, indicating a more pronounced corneoscleral angle and/or rougher CSJ surface, followed by the inferior quadrant and then by the superior and temporal quadrants, which had the flattest, smoothest corneoscleral topographies on average. Examples highlighting the differences in corneoscleral angle between the nasal and temporal quadrants, along with their differences in SSRo, are shown in Figs. 6 and 7.

TABLE 2.

Sum of squared orthogonalized residuals (in square millimeters), shown $\times 10^3$ for readability, stratified on eye and quadrant

Quadrant	OD			OS		
	Median	Mean	SD	Median	Mean	SD
Nasal	4.6796	5.7847	3.9186	4.7662	5.5176	3.7993
Temporal	0.6735	0.8807	0.7449	0.6238	0.8666	0.7550
Superior	0.7008	1.0163	0.8905	0.6999	1.0111	0.9482
Inferior	1.2764	1.6365	1.4349	1.3754	1.8258	1.4809

Fig. 8 depicts the SSRo stratified on quadrant and ethnicity. It is clear from the figure that not only does the nasal quadrant have a much more pronounced corneoscleral angle and/or rougher CSJ profile (as reflected in the SSRo), there appear to be differences among ethnic groups, and these ethnic differences may not be the same for all quadrants. This is confirmed by multivariable mixed-effects modeling (Table 3), which revealed significant effects of ethnicity ($p < 0.001$) and quadrant ($p < 0.001$) and a significant ethnicity-quadrant interaction ($p < 0.001$). Whites had the highest estimated mean value of SSRo in the nasal, inferior, and temporal quadrants. In the nasal and inferior quadrants, Latinos had the second-highest mean SSRo, followed by Asians. Asians had the highest mean SSRo in the superior quadrant; however, values for the SSRo in the superior and temporal quadrants were generally very low, reflecting flat, smooth CSJ profiles, and differences between ethnicities in the superior and temporal quadrants were minimal. *Post hoc* multiple comparison testing using the Tukey HSD statistic showed that whites had significantly higher values of the SSRo overall than Asians and Latinos

FIGURE 6.

Corneoscleral junction profile in the nasal quadrant of one white subject. SSRo = 0.0186.

and that the SSRo values in the nasal quadrant were significantly greater than those in the other three quadrants. It was also found that the SSRo in the inferior quadrant was significantly higher than that in the temporal quadrant.

Diagnostic examination of the first model revealed some heteroscedasticity, with a plot of standardized residuals against the fitted values from the model revealing a megaphone pattern, which suggests that the model assumption of normality of errors may not have been met. We therefore transformed the SSRo by natural logarithm, refit the model, and back-transformed to obtain estimated SSRo values stratified on ethnicity and quadrant. Modeling the log-transformed SSRo resulted in significant effects for ethnicity ($p < 0.001$) and quadrant ($p < 0.001$) and an ethnicity-quadrant interaction ($p = 0.001$), similar to the untransformed model. Diagnostic plots revealed much improved homoscedasticity, and the Tukey HSD statistic confirmed that whites had significantly higher values of the SSRo overall than Asians and Latinos, that the SSRo values in the nasal quadrant were significantly greater than those in the other three quadrants, and that the SSRo in the inferior quadrant was significantly greater than that in the superior and temporal quadrants.

The SSRo was found not to be significantly related to age ($p = 0.839$), sex ($p = 0.115$), or time awake before measurement ($p = 0.468$). We also examined whether the SSRo could be systematically dependent on the number of attempts needed to acquire a clearly focused OCT image in the target quadrant and found no significant relationship ($p = 0.289$).

DISCUSSION

The SSRo metric proposed in the present study assesses the topography of the ocular surface in the transitional region between cornea and sclera. It has the advantage that both a steep angle and greater surface irregularity—the features of the CSJ that are most likely to provide a suboptimal interaction with a contact lens edge—are reflected in this metric. In this study, we have shown that this metric does quantitatively distinguish differences in CSJ

topography among quadrants and between different ethnic groups. In addition, because the procedure of CSJ assessment is largely automated, it is a more repeatable and less subjective measure than attempting to draw two tangential lines to the air/ocular surface interface to define an angle.

The geometric properties of the central and midperipheral corneal surface, including corneal curvature and shape factor, are widely measured in the clinic because of their influence on contact lens fit and performance. In contrast, there is no standard quantitative clinical assessment of the CSJ, in spite of the fact that the edges of SCL and corneoscleral GP lenses interact significantly with this region of the ocular surface. There is some evidence that contact lens wearers feel more comfortable with an SCL decentering temporally and less comfortable with the lens moving inferiorly.⁸ Our findings that the smoothest and flattest area of the CSJ is in the temporal quadrant, whereas the second highest values of our metrics are found in the inferior quadrant, may partly explain differences in comfort levels when the lens decenters in the different quadrants. Differing characteristics of the CSJ in different patients could also be one of the reasons that lenses of identical material and design show differing fitting characteristics and performance on the eye for different patients.¹⁰ We believe that the metrics proposed in this study, especially the SSRo, could be a valuable tool, both for clinicians in achieving optimum contact lens fit and comfort for patients and for researchers investigating the interaction of contact lenses with the ocular surface and improving contact lens design to reduce the risk of adverse ocular surface response and improve subjective comfort.

Although the metric developed in this study shows good repeatability and less subjectivity than angle measurement and reflects important features of the CSJ surface topography, it does have certain limitations. First, the SSRo lacks the capability of differentiating a pronounced CSJ angle from a flat but very irregular (rough) surface. Examining the number of sign changes in the ordered residuals has shown some promise in this area. However, further research is needed for improved accuracy and

FIGURE 7.

Corneoscleral junction profile in the temporal quadrant of one Asian subject. SSRo = 0.0001.

FIGURE 8.

Sum of squared orthogonalized residuals stratified on quadrant and ethnicity.

consistency in making this distinction and/or in characterizing the degree to which angle and surface roughness each contribute to the SSRo metric for a given image. The second limitation of this method is the subjective selection of the CSJ center by the observer before image analysis. Although we have shown that a single experienced observer can maintain his or her selection criteria and achieve good repeatability, our preliminary data suggest that good interobserver reproducibility may be more challenging to achieve. This is especially true for images with a very flat profile or with multiple concave/convex irregularities,

TABLE 3.

Fixed-effects parameter estimates and p values for the final multivariate model of SSRo, shown $\times 10^3$ for readability

Variable	Coefficient	p
Intercept (Asian, inferior quadrant)	1.312	0.0004
White	1.120	0.0287
Latino	0.152	0.7694
Nasal quadrant	2.459	<0.0001
Superior quadrant	0.014	0.9787
Temporal quadrant	-0.378	0.4626
White, nasal quadrant	2.569	0.0004
Latino, nasal quadrant	1.736	0.0170
White, superior quadrant	-1.367	0.0598
Latino, superior quadrant	0.831	0.2557
White, temporal quadrant	0.854	0.2372
Latino, temporal quadrant	0.560	0.4401

Asian ethnicity and the inferior quadrant serve arbitrarily as baseline categories.

making the “center” of the CSJ more difficult to identify with certainty. Development of some type of standard reference set, observer training and testing, and periodic calibration among observers will all contribute to improved reproducibility. We are also investigating a bootstrapping technique in which the distribution of the metric across a range of possible simulated CSJ “center points” is analyzed to derive a better estimate of the true value of the metric. Research is ongoing in this area.

In conclusion, quantitatively describing the CSJ in terms of angle can give highly variable estimates owing to the arbitrary selection of tangential lines. In addition, the important characteristics (e.g., for contact lens wear) of the regional topography of the CSJ cannot be described by angle alone. The method in the present study provides a metric (SSRo) that quantifies the characteristics of the CSJ region more comprehensively and with good repeatability for a trained observer. We have shown that the SSRo in the nasal quadrant is significantly greater than that in the other three quadrants, and we have presented quantitative evidence that suggests that different ethnic groups may have significantly different CSJ topographies. The SSRo will be particularly applicable for future studies assessing the relationships among ocular characteristics, contact lens fitting parameters, and subjective comfort.

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