# Effects of Scleral-lens Tear Clearance on Corneal Edema and Post-lens Tear Dynamics: A Pilot Study

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**SIGNIFICANCE:** The present study with small-diameter scleral lenses (SLs) revealed that post-lens tear thickness (PoLTT) was significantly associated with post-lens tear mixing, but not with central corneal edema, after short-term SL wear.

**PURPOSE:** The aim of this study was to investigate the influence of SL tear clearance (PoLTT) on central corneal thickness and post-lens tear dynamics during 5-hour lens wear.

**METHODS:** Neophytes with no active ocular disease were fitted bilaterally with SLs (hofocon A; 15.6-mm diameter; ~438-μm thickness; 97 Dk; 1.44 refractive index) with various initial PoLTT values ranging from 74 to 543 μm. Central corneal thickness and PoLTT were measured using optical coherence tomography during lens wear. Tear mixing was assessed using fluorogram and "out-in" method.

**RESULTS:** The mean central corneal edema after 5-hour lens wear was 1.51% (95% confidence interval, 1.26 to 1.76%; $P < .001$), reached its peak at 2-hour post-lens insertion (1.65% [95% confidence interval, 1.45 to 1.85%]), and was independent of PoLTT. The fastest fluorescence decay of the post-lens tear film was observed superiorly. The fluorescence decay rate increased from center to periphery in all quadrants except superiorly. An inverse relationship was found between PoLTT and fluorescence decay rate at both 20-minute and 5-hour wear after lens insertion ($P < .05$). Excluding observations with out-in time exceeding 5 minutes, we found a direct relationship between PoLTT at 20 minutes after lens insertion and out-in time ($P = .047$). The % change in the PoLTT after 5-hour wear was greater with a thinner initial tear clearance than those with a thicker one ($P = .034$).

**CONCLUSIONS:** Within our study parameters, a thinner PoLTT under a small-diameter SL was associated with faster PoLTT mixing. However, there was no relationship between PoLTT and central corneal thickness during 5-hour SL wear.

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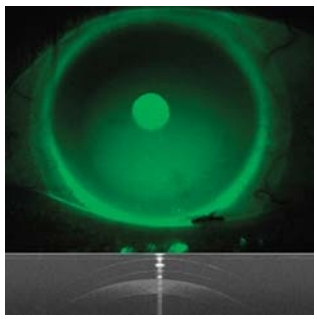

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A scleral lens is a large-diameter contact lens that rests on the sclera and creates a tear-filled vault over the cornea. Scleral lenses have been conventionally prescribed in the treatment of various ocular surface diseases.[1] In recent years, the use of scleral lenses has increasingly become the preferred choice for correcting refractive error and/or irregular astigmatism.[2] However, the thick post-lens tear film with scleral lenses can potentially create hypoxic effects, which may compromise ocular health (e.g., introducing corneal edema). There have been three main theoretical models presented in the literature. These models estimated oxygen tension at the corneal surface under a scleral lens and gave suggested values for material Dk, lens thickness, and corneal vault to avoid corneal hypoxia during daily wear. Compan et al.[3] suggested that post-lens tear film should be below 150 μm, scleral lens material should at least comprise 125 barrers of oxygen permeability, and the central lens thickness should be less than 200 μm[3]. Michaud and colleagues'[4] and Weissman and Ye's[5] groups suggested that the Dk of post-lens tear film (close to that of water, 80 barrers) should be considered while calculating the Dk/t of lens/tear system.[4] Michaud et al.[4] suggested that a lens material with Dk greater than 150 barrers, central lens thickness less than 250 μm, and a central post-lens tear thickness less than 200 μm were needed to avoid hypoxia-induced swelling. Using a different theoretical model, Jaynes et al.[6] also drew similar conclusions that only scleral lenses made from the highest Dk material and fitted without an excessive tear reservoir depth might avoid hypoxia. However, there are a limited number of case reports describing clinically significant hypoxic effects from modern high-Dk scleral lenses during daily wear. Besides oxygen tension, corneal edema should also be influenced by corneal metabolic reactions to the variation of oxygen availability. The discrepancy between theory and *in vivo* measurements may be partially due to limitations with slit-lamp biomicroscopy in observing the small levels of corneal swelling (e.g., 1.6 to 3.9%) after scleral lens wear.[3] It could also be a consequence of not accounting for corneal oxygen metabolism in the prediction models. Thus, *in vivo* studies with high-resolution measurements of corneal edema, which is a direct assessment of corneal metabolism, in healthy subjects are necessary.

Previous studies have provided indirect evidence that efficient post-lens tear mixing can help preserve ocular surface integrity.[7–9] Post-lens tear exchange has been most often evaluated with scanning fluorometry. However, this technique provides only a spot measurement of fluorescence from a small area without spatial resolution. In the present study, post-lens tear mixing beneath scleral lenses was evaluated with fluorogram and "out-in" methods. The

fluorogram is unique in that it provides a 2-D fluorescence intensity map of the post-lens tear film (approximately 2- to 6-mm region from the center of the cornea) and measures the relative change in fluorescein intensity over time. The fluorogram method requires a modified slit-lamp biomicroscope with an attached camera to capture fluorescein patterns of the post-lens tear film and the application of a novel image-processing technique.[10] The out-in method evaluates tear exchange near the lens periphery with fluorescein and slit-lamp biomicroscope.[9]

In the present study, we sought to understand how various initial central clearances impact post-lens tear dynamics and anterior ocular health of young healthy eyes during short-term scleral lens wear. Specifically, high-resolution spectral domain–optical coherence tomography was utilized to assess *in vivo* changes of central corneal thickness and post-lens tear thickness. The fluorogram and the out-in method were used to gain a better understanding of the tear-film dynamics under scleral lenses.

## METHODS

### Study Design

This was a prospective, double-masked, randomized, bilateral, crossover, single-center (University of California, Berkeley, Clinical Research Center) study. 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.

### Subjects

Neophytes (no prior history of contact lens wear or no contact lens wear for at least 1 year prior to enrollment) were recruited from the University of California, Berkeley, campus and the surrounding community. Eligibility criteria included age older than 18 years, a self-report eye examination in the last 2 years, spectacle spherical prescription between –0.25 and –8.00 D, corrected visual acuity of 20/30 or better (in each eye) with habitual spectacles, and healthy ocular surface (i.e., free of ocular pathology including moderate to severe dry eyes).

### Materials and Procedures

This study involved four visits on separate days. At the first visit, subjects read and signed an informed consent, followed by a screening examination of the ocular surface and scleral lens fitting. Baseline visual acuity was measured, and corneal topography was taken (Medmont E300; Medmont International Pty Ltd, Vermont, Australia). Based on corneal sagittal height, keratometry readings, and elevation maps generated by Medmont, subjects were fitted bilaterally with trial lenses provided by Essilor USA, to determine lens parameters for achieving three different fits (e.g., an ideal fit of ~200- to 250-μm tear clearance, a steep fit of ~400- to 500-μm tear clearance, and a flat fit of ~100- to 150-μm tear clearance), necessary to cover a spectrum of post-lens tear thickness. After 20 to 30 minutes of lens settling, overrefraction was performed, and post-lens tear thickness was measured using high-resolution spectral domain–optical coherence tomography (ENVSISU 2300; Bioptigen Inc, Durham, NC). The Bioptigen optical coherence tomography has an axial resolution of 3 μm.

For Visits 2 to 4, appointment times were kept the same (±30 minutes), with each subject arriving at least 2 hours after awakening and with discontinuation of eye drops or allergy medications 1 full day before the visit. Baseline visual acuity was measured, and anterior ocular health was assessed with slit-lamp biomicroscopy. The investigator then inserted one of three pairs of scleral lenses of hofocon A material (97 Dk), according to a predetermined randomization scheme. After the scleral lenses were inserted and allowed to settle for approximately 20 minutes, the investigator evaluated the lens surface, lens fit, and comfort. If poor wettability of the lens surface was observed, the lens was removed, rubbed with extra strength cleaner (Walgreens Co., Deerfield, IL), rinsed with sterile saline (Unisol 4 nonpreserved saline; Alcon Laboratories, Inc., Fort Worth, TX), and reinserted. It was also important to ensure that each pair of lenses had acceptable fit with appropriate peripheral curves to prevent lens seal. After lens fit and comfort were assessed, central corneal thickness and post-lens tear thickness were measured periodically using optical coherence tomography, whereas post-lens tear mixing was assessed using the out-in method and fluorogram for up to 5 hours of lens wear.

The out-in method was used to evaluate tear exchange near the lens periphery. 5 μL of 2% wt/vol fluorescein isothiocyanate–dextran solution (molecular weight = 10,000 Da) was placed on the superior bulbar conjunctiva using a micropipette. A slit-lamp biomicroscope was set at a 16 to 20× magnification with an optic section, and the post-lens tear film was monitored for the first sign of fluorescence. The subject was instructed to look straight ahead and blink normally throughout the entire measurement. Out-in time was measured with a stopwatch, with time beginning immediately after high-molecular-weight fluorescein instillation and ending at the first sign of fluorescence in the post-lens tear film. Because of dilution of fluorescein over time, out-in time was measured up to a cutoff time of 5 minutes. Out-in time was measured only at 20 to 30 minutes after lens insertion and was not repeated on the same visit day to avoid potential confounding effects on fluorogram. Lenses were then removed, and the subject's eyes were irrigated with sterile saline.

After out-in measurements, the investigator filled the bowl of the scleral lens with 0.01% wt/vol fluorescein isothiocyanate–dextran solution (molecular weight = 10,000 Da) and then inserted it into one eye first, based on the predetermined randomization. Then the fluorogram of the eye was collected immediately after lens insertion. The same procedure was then repeated in the other eye. High-molecular-weight fluorescein isothiocyanate–dextran solution used for fluorogram and out-in method typically has minimal or no corneal penetration. Fluorograms were obtained at time = 0 to 1 (immediately), 10, 20, 30, 60, 90, 120, 180, 240, and 300 minutes after lens reinsertion.

The detailed procedure of our unique technique of fluorogram can be found in our previous study.[10] To summarize, the fluorogram consists of two parts. First, hardware was modified on a Nikon FS-2 slit lamp (Nikon Corporation, Ophthalmic Instruments Section, Tokyo, Japan). A digital camera was attached to the slit lamp to save the images directly to a PC; the original excitation and emission filter set was replaced with a new set of filters designed for epifluorescence to remove any "hot spots," and the working distance was enlarged to expand the illumination area. Second, to compensate for nonuniform illumination, we also used a novel image-processing method by adjusting pixel fluorescence intensity

based on the illumination intensity at each pixel. Steps of a typical fluorogram are as follows:

(1) baseline imaging to confirm no residual fluorescein in the eye from previous examination,
(2) filling the bowl of a scleral lens with 0.01% wt/vol fluorescein isothiocyanate–dextran and then inserting the lens,
(3) focusing the camera,
(4) illuminating the unexamined eye with a transilluminator to shrink the pupil diameter (pupil area cannot be analyzed because of autofluorescence from the retina), and
(5) capturing the image.

To quantify a typical fluorogram, the whole cornea was first divided into four quadrants. Then the average intensities were calculated along each concentric arc as a function of radius. The average intensity at any given radius, *r*, was calculated by summing all pixel values along the concentric arc centered on the cornea and then dividing the sum by the number of pixels along the arc of interest. The variation in fluorescence intensity at different radial locations, times, and quadrants was studied. At each radius, 10 intensity data points were available from the aforementioned 10 measurements during the 5-hour lens wear period. These 10 points were fitted with the exponential model, as shown in Equation 1, and the fluorescence decay rate was calculated.

Fluorescence decay rate at a given radius:

$$I_t = I_0 e^{C - kt} \quad \text{(Eq. 1)}$$

where $I_0$ is the initial fluorescence at the very first measurement (normally within 1 minute after lens insertion); $I_t$ is intensity at time $t$ measured in minutes; $k$ is the decay rate.

Repeatability analysis was conducted on fluorogram image analysis using Bland and Altman 95% confidence interval limits of agreement (Fig. 1). Mean difference in fluorescein intensity ranged from 0.0005 to 0.0007 for all quadrants. The data points for paired-analysis difference in fluorescein intensity were clustered in the 95% confidence interval band with no exception, indicating acceptable repeatability. As suggested in the repeatability test, the same observer captured and analyzed all fluorogram images.

Immediately following each fluorogram snapshot, post-lens tear thickness and central corneal thickness were measured with optical coherence tomography. All the measurements were also performed by the same observer to minimize interobserver variability. To control for potential artifacts before and after lens insertion, the very first optical coherence tomography measurement of corneal thickness at 0 to 1 minute after lens insertion was used as a baseline to calculate central corneal thickness changes during 5-hour lens wear. To ensure that the same region of the cornea was examined while a radial scan was conducted at each time point, the subject was instructed to always look straight ahead at the fixed light source so that the operator could center the subject's corneal apex at both horizontal and vertical preview windows (when corneal apex was centered, a completely modulated white band would appear at the center presenting full saturation of brightness). The observer used a caliper tool provided by Bioptigen software to measure central corneal thickness and post-lens tear thickness at corneal apex located by the white band.

The repeatability of optical coherence tomography in thickness measurement has been inspected and published in our previous publication.[11] To summarize, a pilot study was conducted to assess the repeatability and reproducibility of the Bioptigen

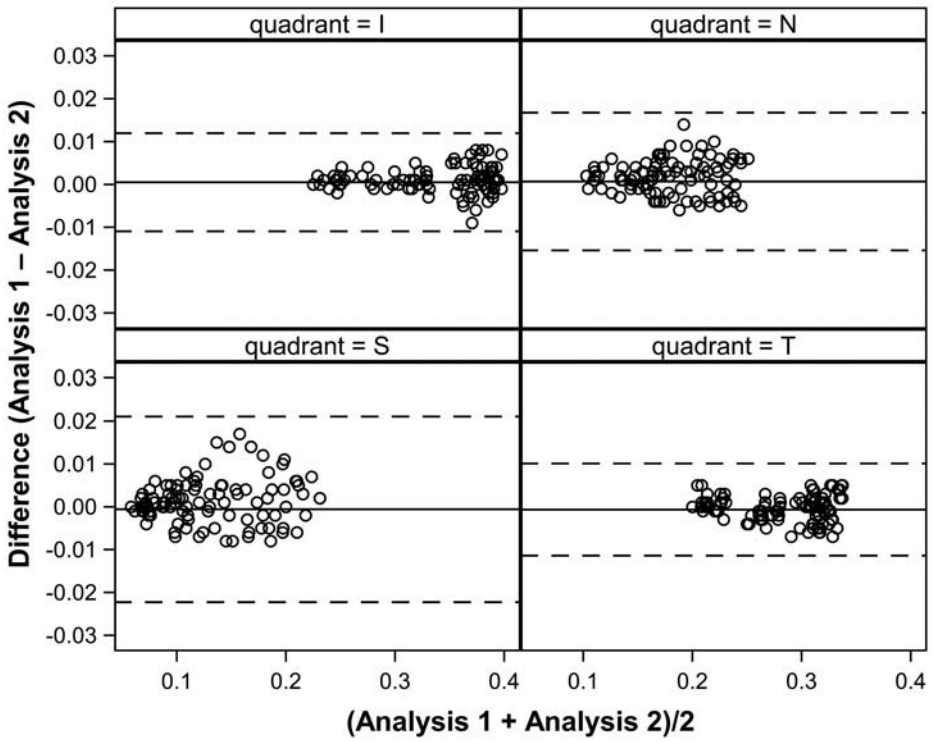


**FIGURE 1.** Bland and Altman 95% confidence interval limits of agreement.

**TABLE 1.** Descriptive statistics of ocular and lens parameters

| Variable | Mean (95% confidence interval) |
|---|---|
| Lens base curve (mm) | 7.53 (7.43 to 7.63) |
| Lens power (D) | –5.71 (–6.25 to –5.17) |
| Lens thickness (μm) | 442.43 (433.20 to 451.65) |
| Ocular sagittal height at a chord of 10 mm (μm) Degree 0 | 1.69 (1.67 to 1.70) |
| Ocular sagittal height at a chord of 10 mm (μm) Degree 180 | 1.69 (1.67 to 1.70) |
| Horizontal visible iris diameter (mm) | 12.15 (11.95 to 12.34) |

SD-OCT thickness measurement. Optical coherence tomography images were repeatedly captured by two operators and analyzed by two independent readers on 2 separate days. Data were obtained to assess the interoperator, interreader, and interday variability. The coefficient of repeatability was found to be 0.0121. The mean difference between the two optical coherence tomography operators (interoperator variability) was 0.63 μm, with 95% limits of agreement being [–5.75, 4.49 μm], and the mean difference between two optical coherence tomography readers (interreader variability) was 3.58 μm, with 95% limits of agreement being [–3.64, 10.79 μm]. Compared with the limits of agreement for interoperator and interday variance, the mean difference and the SD of the differences between readers were larger, implying that image readers were crucial in obtaining precise and consistent central corneal thickness. Therefore, only one investigator analyzed all central corneal thickness images in the present study.

After 5 hours of lens wear, the subject was asked to rate comfort, visual quality, fogging/haziness, and dryness in each eye. These parameters were evaluated using a visual analog scale questionnaire. Comfort was rated on a scale from 0 to 100, where 0 was defined as "can't be worn, causes pain" and 100 as "cannot be felt." Dryness was rated on a scale from 0 to 100, where 0 was defined as "no dryness felt" and 100 as "extremely dry." Visual quality was rated on a scale from 0 to 100, where 0 was defined as "extremely poor vision" and 100 as "excellent vision." Fogging/haziness was rated on a scale from 0 to 100, where 0 was defined as "no fogging/haziness ever" and 100 as "extreme fogging." Lens fit and assessment were evaluated by the investigator, and then the lenses were removed. Ocular surface health was assessed with a slit-lamp biomicroscope (with fluorescein), and exit visual acuity was measured.

### Statistical Analysis

The study was a bilateral crossover design. Multiple layers of correlation occurred from fellow eyes, repeated measurements, and sequences of lens fitting. In any case, the usual model assumption of independent errors would be violated. To account for the correlation when evaluating the time trend, mixed-effects models were implemented using Windows version SAS 9.2 (SAS Institute, Cary, NC). Effects of between and within subjects for each lens fitting sequence were considered as random effects. The standard error estimates in group comparison and time variation analysis were adjusted accordingly. Slope and intercepts were subject-specific estimates. Tukey adjustments were made to the degree of freedom. Paired-eye correlation was accounted for by specifying a variance-covariance matrix structure between the two eyes for each subject. Missing data, data validity, and distribution of input variables have been examined using SAS procedure.

## RESULTS

### Subject Demographics and Lens Parameters

Twenty eyes of 10 neophytes (two females; four Asians, four Caucasians, two Hispanics) with a mean age of 21.0 (SD, 2.0) years completed the study. Table 1 reports average lens parameters and ocular features. All the lenses were ordered with standard peripheral curves.

### Central Corneal Thickness

Central corneal thickness increased during the first 2 hours, reaching a plateau thereafter. The mean (95% confidence interval) central corneal thickness immediately upon lens insertion (baseline) was 531 μm (95% confidence interval, 528.4 to 533.5 μm). At the end of 5 hours, central corneal thickness increased to 539.1 μm (95% confidence interval, 536.6 to 541.5 μm), with an overall 1.51% (95% confidence interval, 1.26 to 1.76%) swelling. The edema showed a statistically significant difference from

**TABLE 2.** Descriptive statistics of central corneal thickness and percentage change of central corneal thickness

| | Central corneal thickness (μm) | | | Central corneal thickness % change |
|---|---|---|---|---|
| Time (min) | Mean (95% confidence interval) | Min | Max | Mean (95% confidence interval) |
| 0 | 531.0 (528.4–533.5) | 515.0 | 549.0 | — |
| 10 | 532.9 (530.5–535.3) | 519.0 | 550.0 | 0.39 (0.26–0.51) |
| 20 | 535.1 (532.6–537.6) | 520.0 | 553.0 | 0.80 (0.67–0.92) |
| 30 | 535.8 (533.4–538.2) | 521.0 | 554.0 | 0.93 (0.81–1.05) |
| 60 | 537.8 (535.5–540.1) | 524.0 | 554.0 | 1.31 (1.16–1.47) |
| 90 | 539.6 (537.2–542.1) | 525.0 | 559.0 | 1.64 (1.45–1.82) |
| 120 | 539.6 (537.2–542.1) | 523.0 | 559.0 | 1.65 (1.45–1.85) |
| 180 | 539.6 (537.2–542.0) | 524.0 | 558.0 | 1.63 (1.39–1.87) |
| 240 | 539.1 (536.7–541.5) | 524.0 | 558.0 | 1.52 (1.28–1.76) |
| 300 | 539.1 (536.6–541.5) | 521.0 | 560.0 | 1.51 (1.26–1.76) |

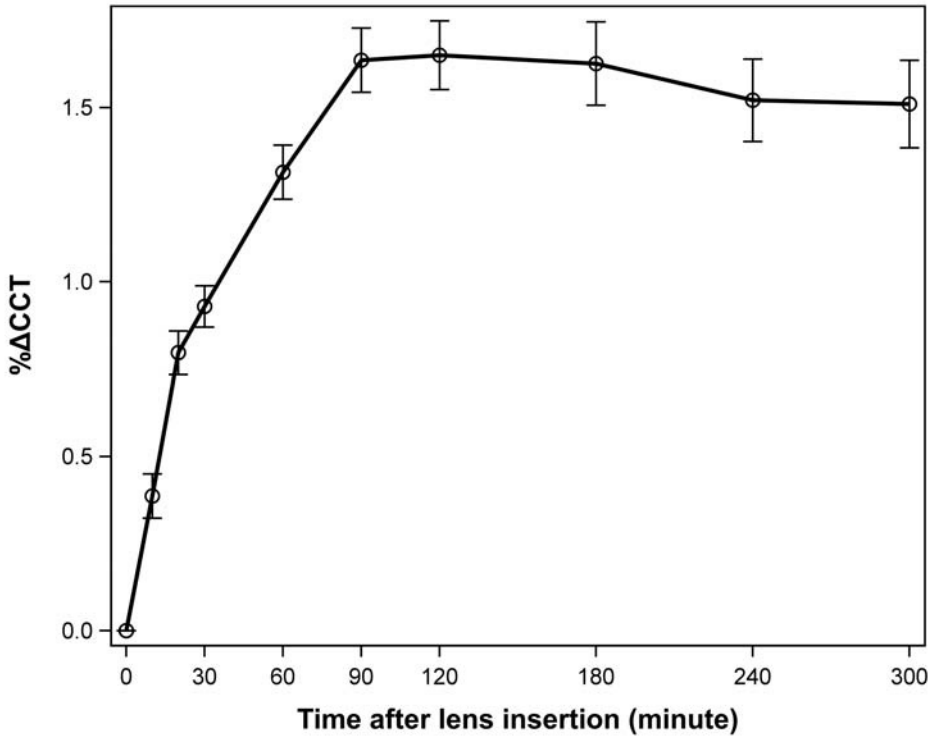


**FIGURE 2.** Percentage change of central corneal thickness (%ΔCCT) at 5-hour lens wear.

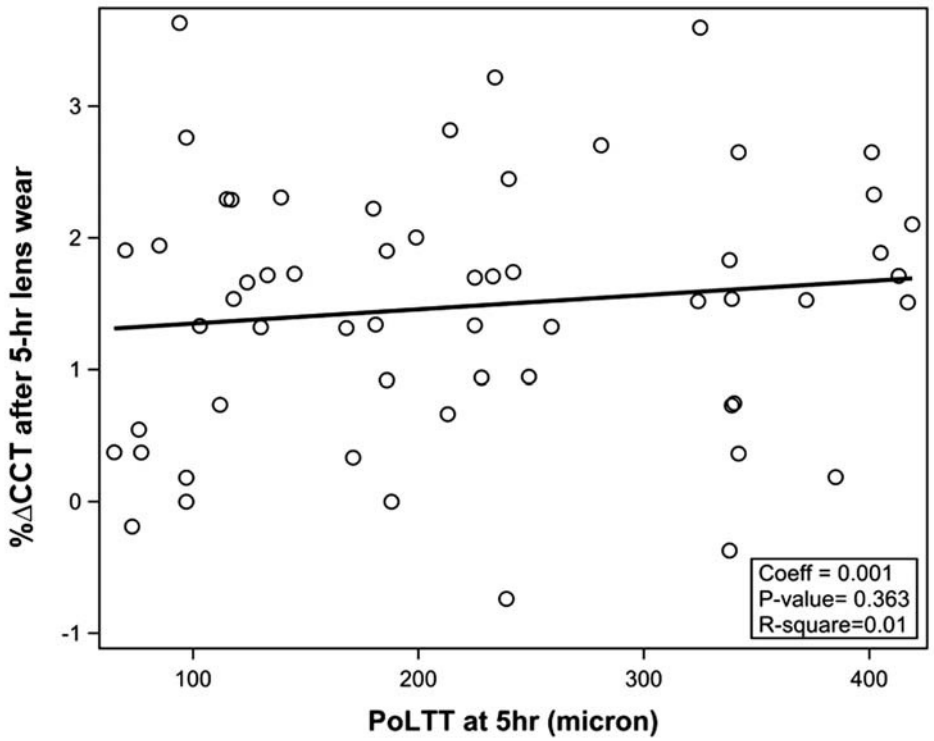


**FIGURE 3.** Scatter plot with regression line on percentage change of central corneal thickness (%ΔCCT) with respect to post-lens tear thickness (PoLTT) at 5 hours of lens wear.

**TABLE 3.** Descriptive statistics of out-in time

| Out-in time (s) | Frequency | Percent |
|---|---|---|
| <30 | 15 | 25.0 |
| 30–59 | 11 | 18.3 |
| 60–89 | 4 | 6.7 |
| 90–119 | 7 | 11.7 |
| 120–179 | 1 | 1.7 |
| 180–299 | 2 | 3.4 |
| ≥300 | 20 | 33.3 |

Median = 90.

baseline after 20 minutes ($P < .001$). Table 2 lists the overall percentage change of central corneal thickness from baseline at each measurement. A maximum of 1.65% (95% confidence interval, 1.45 to 1.85%) central corneal thickness edema was observed at 2 hours. Fig. 2 presents the central corneal thickness percentage change from baseline within 5 hours. No significant relationship was found between percentage change of central corneal thickness and post-lens tear thickness after 5 hours of lens wear (Fig. 3). Central corneal edema after 5 hours of lens wear was not significantly related to out-in time ($P = .919$).

## Out-in Time

As shown in Table 3, the majority (61.7%) of the out-in time measurements were less than 2 minutes, with 25.0% less than 30 seconds, and 18.3% equal to or greater than 30 seconds, but less than 60 seconds; 6.7% equal or greater than 60 seconds, but less than 90 seconds; and 11.7% equal or greater than 90 seconds, but less than 120 seconds. One third of out-in time measurements were equal to or greater than 5 minutes, which is the upper limit set for time counting. The overall median out-in time was 90 seconds. Excluding the observations with out-in time > 5 minutes, a positive relationship was found between post-lens tear thickness at 20 minutes after lens insertion and out-in time ($P = .047$), as shown in Fig. 4 (the observations with out-in time exceeding 5 minutes were excluded. Otherwise, there was no relationship found between post-lens tear thickness and out-in time).

## Fluorescein Intensity Variation

A series of regressions were performed on fluorescein intensity to estimate the exponential decay. Estimated fluorescence decay rate with statistical significance level of 0.05 or less was used for hypothesis testing. Descriptive statistics of decay rate is shown in Table 4. Overall decay rate was 0.0017 (95% confidence interval, 0.0016 to 0.0018). Superior had the fastest decay among all four quadrants ($P < .01$). By contrast, inferior exhibited the slowest decay rate ($P < .01$). No significant difference of decay rate was detected between nasal and temporal. Decay rate increased from center to periphery in all quadrants except for superior ($P < .01$), where there was a maximum decay rate at ~3.5 mm from central cornea. Fig. 5 depicted mean decay rate with standard error along the radial location in each quadrant. Decay rate was found to be inversely related to post-lens tear thickness at 20 minutes ($P = .001$) and 5 hours ($P = .001$), indicating a faster decay rate with thinner post-lens tear film. However, the effect size was small (coefficient

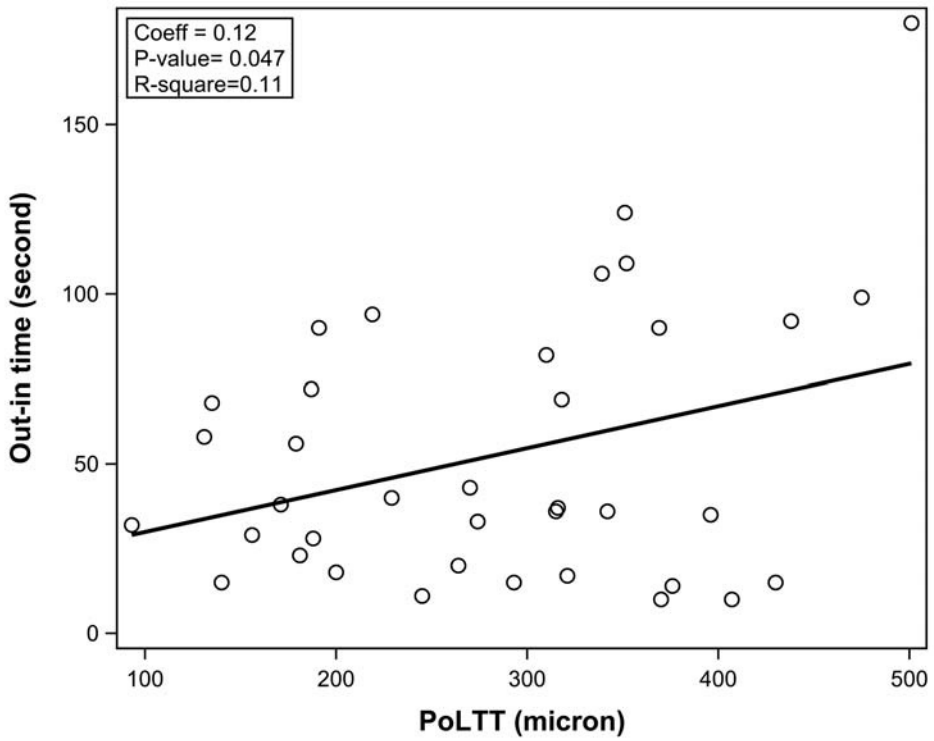


**FIGURE 4.** Scatter plot with regression line on out-in time with respect to post-lens tear thickness (PoLTT) at 20 minutes after lens insertion. Note: The observations with out-in time exceeding 5 minutes were excluded.

**TABLE 4.** Descriptive statistics of decay rate

| Quadrant | Mean (95% confidence interval) |
|---|---|
| Inferior | 0.0014 (0.0012–0.0015) |
| Nasal | 0.0016 (0.0015–0.0018) |
| Superior | 0.0021 (0.0020–0.0022) |
| Temporal | 0.0016 (0.0015–0.0018) |
| Overall | 0.0017 (0.0016–0.0018) |

$n_{missing\ at\ 300\ min} = 2$.

<–0.001). Decay rate was also found to be inversely related to corneal edema at both 20 minutes and 5 hours at significant level of 0.01, but effect sizes were small (–0.0002 and –0.0004) as well.

## Post-lens Tear Thickness (Central)

Overall, the post-lens tear thickness continued to thin after lens insertion, from 299 µm (95% confidence interval, 268 to 329 µm) upon lens insertion to 222 µm (95% confidence interval, 193 to 250 µm) at 5 hours, thinning by 26%, as shown in Table 5. The lenses with less initial clearance were also found to settle significantly more in percentage through the 5-hour lens wear period ($P = .034$), as shown in Fig. 6.

## Subjective Ratings

As shown in Table 6, the mean comfort and vision scores reported by subjects at the end 5-hour lens wear were both 81 (range, 45 to 100 for comfort; 36 to 99 for vision). Dryness was 24 (range, 0 to 72), and fogging/haziness was reported as 20 (range, 0 to 87). No abnormality was observed in lens surface assessment.

## Anterior Ocular Surface Health

After 5-hour lens wear, bulbar redness increased by an overall mean of 0.75 compared with baseline, with superior showing the highest increase of 0.80 (95% confidence interval, 0.68 to 0.92). Limbal redness worsened by 0.7 (95% confidence interval, 0.56 to 0.82) in nasal, 0.80 (95% confidence interval, 0.69 to 0.91) in temporal, 0.85 (95% confidence interval, 0.74 to 0.97) in superior, and 0.81 (95% confidence interval, 0.69 to 0.94) in inferior, as shown in Table 7. Corneal staining increased in all quadrants except center, but the average change was less than 0.5 of all three staining grading metrics.

# DISCUSSION

We investigated central corneal edema and post-lens tear exchange, lens-settling patterns, and subjective rating of comfort and dryness in a group of 10 young and healthy subjects who wore scleral lenses with various tear clearances for 5 hours.

Oxygen availability to the cornea was related to oxygen transmissibility of scleral lens and post-lens tear film as a system. A recent study using equivalent oxygen percentage evaluation showed that an 18-mm scleral lens fitted with a 400-µm clearance reduces the oxygen tension available to the cornea by 30% compared with a similar lens fitted with a 200-µm clearance after 5 minutes of wear.[12] However, this finding did not imply that corneal edema should have the same impact caused by different tear clearances because corneal edema is a result of corneal metabolic reactions to oxygen availability. The percentage change of central corneal thickness based on *in vivo* measurement is an excellent indicator of corneal metabolism. There has been discrepancy between theory

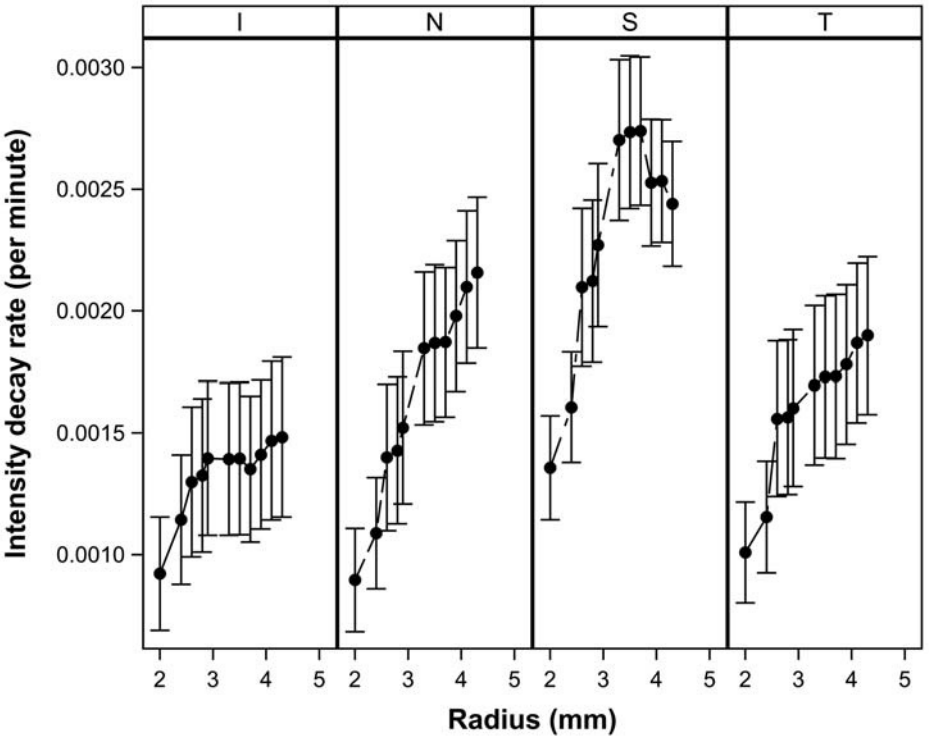


**FIGURE 5.** Mean decay rate with respect to radial location from the center of the cornea in each quadrant, with whisker representing standard error.

**TABLE 5.** Descriptive statistics of post-lens tear thickness (PoLTT)

| | PoLTT (μm) | | | PoLTT % change |
|---|---|---|---|---|
| Time (min) | Mean (95% confidence interval) | Min | Max | Mean (95% confidence interval) |
| 0 | 299 (268–329) | 74 | 543 | — |
| 10 | 282 (252–312) | 75 | 531 | –6% (–8% to –5%) |
| 20 | 272 (242–302) | 85 | 512 | –9% (–11% to –7%) |
| 30 | 267 (236–297) | 71 | 507 | –12% (–14% to –10%) |
| 60 | 255 (225–285) | 80 | 480 | –15% (–19% to –12%) |
| 90 | 246 (217–275) | 70 | 457 | –19% (–22% to –16%) |
| 120 | 243 (214–273) | 80 | 454 | –19% (–23% to –16%) |
| 180 | 236 (207–266) | 82 | 448 | –22% (–26% to –18%) |
| 240 | 230 (201–259) | 80 | 433 | –24% (–28% to –20%) |
| 300 | 222 (193–250) | 65 | 419 | –26% (–30% to –22%) |

$n_{missing\ at\ 300\ min} = 2$.

and clinical practice in terms of corneal hypoxic effects from scleral lens wear.[13] Because of lack of *in vivo* data about corneal edema caused by scleral lens wear, especially for the uncompromised healthy eye, attempts to explain this discrepancy have not been very successful.

In the present study, we found that scleral lens worn by normal and healthy subjects did induce corneal edema, which was at most 1.65%, that is, smaller than physiological corneal swelling after overnight eye closure (~3.6%).[10] The time course of corneal edema induced by scleral lens wear in the present study was similar to the findings reported by Collins et al. (Collins et al., ARVO ASIA 2017). However, the corneal thickness can restore within 2 hours of eye opening from sleeping, after being exposed to atmospheric oxygen, whereas the thickness restoration after 8-hour scleral lens wear could take up to 3 hours after lens removal.[14] There are no data available to estimate the potential impact of such chronic hypoxic stress over time, despite its low level, which is similar to many market-available hydrogel lenses. We found no statistically significant correlation between central corneal edema and post-lens tear thickness ranging from 200 to 400 μm, suggesting that achieving a scleral lens fit with a low clearance (e.g., 200 μm) will not necessarily provide additional benefit to a corneal metabolic system

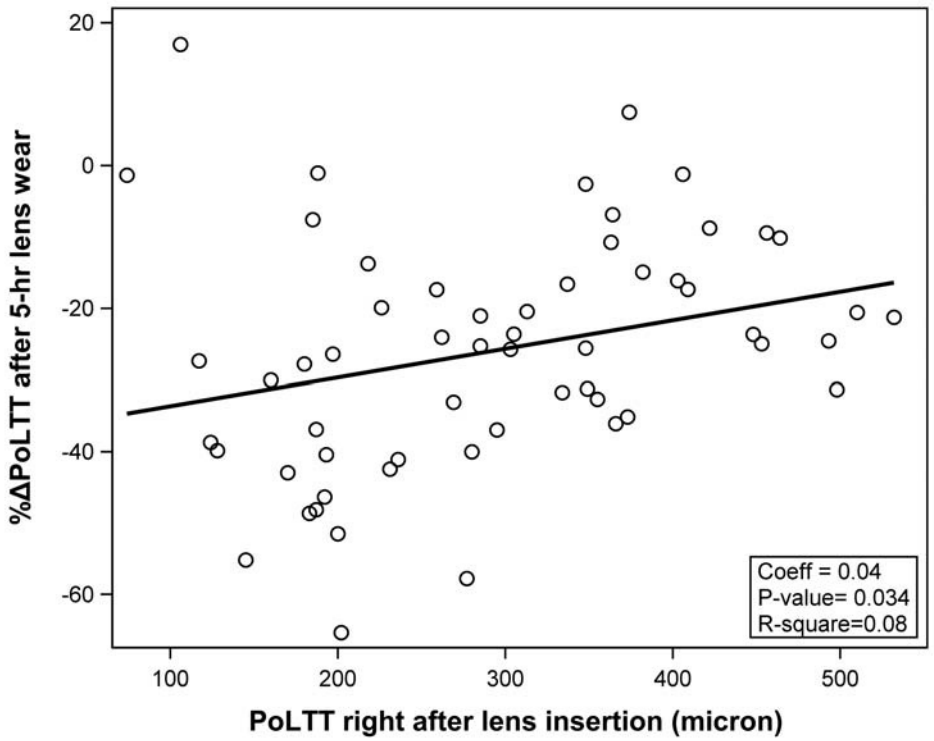


**FIGURE 6.** Scatter plot with regression line on percentage change of post-lens tear thickness (%ΔPoLTT) after 5-hour lens wear and initial post-lens tear thickness.

**TABLE 6.** Descriptive statistics of comfort, dryness, vision, and haziness

| Variable | Mean (95% confidence interval) | Min | Max |
|---|---|---|---|
| Comfort | 81 (77–85) | 45 | 100 |
| Vision | 81 (77–85) | 36 | 99 |
| Fogging/haziness | 20 (14–26) | 0 | 87 |
| Dryness | 24 (18–29) | 0 | 72 |

during lens wear. These findings are consistent with other published *in vivo* data from study cohorts of normal and diseased corneas.[14–16]

In this study, we used two different methods for assessing post-lens tear dynamics during scleral lens wear: the out-in method is a useful and quick tool in a clinical setting to assess post-lens tear mixing, whereas the fluorogram method provides a more comprehensive assessment of post-lens tear dynamics of scleral lens. When a clinician observes out-in mixing with fluorescein dye within 5 minutes of dye instillation, it is likely that the clinician is working with a fit that provides adequate post-lens tear mixing. Of interest, 33.3% of out-in observations did not have measurable tear mixing within 5 minutes from fluorescein dye instillation; however, none of these subjects reported discomfort or presented significant conjunctival staining.

Fluorogram is a good method to describe quantitative and qualitative post-lens tear dynamics. With the fluorogram method, we found that the superior quadrant appeared to have the fastest decay compared with the other three quadrants, whereas inferior exhibited the slowest decay rate. The decay rate at periphery was always faster than center except in superior quadrant. These decay patterns may be limited to the study lens design. Further investigation is needed for other scleral lens designs to confirm these observations. Alonso-Caneiro et al.[17] have shown that additional pressure from superior eyelid on scleral lenses could contribute to significant tissue compression on the ocular surface. We speculate that our observations could indicate some tissue compression in addition to lens settling and gravity.

It has been well established that intracorneal rigid gas-permeable lenses have much more efficient post-lens tear mixing than soft contact lenses. When comparing soft contact lens with scleral lens, overall fluorescence decay rate of scleral lens (~$10^{-3}$/min) was approximately 1 to 10% of soft contact lens (~$10^{-2}$ to $10^{-1}$/min) (Tan et al., IOVS 2014;55; ARVO E-Abstract 4667), suggesting that post-lens tear mixing with scleral lens may be even slower than that with a soft contact lens. However, this direct comparison must be interpreted with caution, as the initial tear reservoirs (scleral lens post-lens tear thickness >70 μm vs. soft contact lens post-lens tear thickness <10 μm) are vastly different between the two lens types. Therefore, decay rates from fluorogram cannot be used to compare lens types with vastly different on-eye lens-tear dynamics. Nevertheless, fluorogram remains a very useful methodology to compare relative difference of post-lens tear dynamics of similar lens types with different lens fit parameters, as these lenses share similar on-eye lens-tear dynamics.

Another way to answer the question "Does scleral lens tear mixing exist?" is to assess subjects' ocular surface health and subjective rating of dryness/comfort during lens wear. Given that every subject in this study could wear scleral lens comfortably during the 5-hour lens wear, we suspect that these scleral lenses are not causing a seal between the lens and the sclera, as ocular staining was minimum. In addition, every subject in the cohort reported good comfort and dryness with SLs, and their subjective ratings were comparable with ratings of soft contact lens wear.[18,19] Therefore, we conclude that post-lens tear mixing is slow during scleral lens wear, as the changes of bulbar and limbal redness, and corneal staining and average comfort score after 5-hour scleral lens wear, were comparable with published data for soft contact lens wear.[20,21] This finding may be different with other lens designs and especially in the light of the emergent trend of customizing the scleral lens fit with toric peripheries.

Another aspect of lens dynamics that differs between soft contact lens and scleral lens is on-eye lens settling. Lens settling is much more significant and long lasting with scleral lens wear compared with soft contact lens. In general, scleral lens settling could continue throughout the entire 5 hours of lens wear, although the progress appeared to slow down after 4 hours, which was consistent with other published studies.[15,22,23] It has been reported that a faster settling as defined by more reduction of post-lens tear thickness in a given time is associated with a thicker post-lens tear thickness.[15,22] We found an average of 77 μm of lens settling for 5 hours as shown in Table 5. This is comparable to what was reported by Kauffman et al.[22] However, examining the absolute

**TABLE 7.** Redness and corneal staining change after lens insertion

| Bulbar redness change | Mean (95% confidence interval) |
|---|---|
| Nasal | 0.71 (0.58–0.84) |
| Temporal | 0.80 (0.68–0.92) |
| Superior | 0.77 (0.63–0.90) |
| Inferior | 0.72 (0.58–0.86) |
| **Limbal redness change** | **Mean (95% confidence interval)** |
| Nasal | 0.69 (0.56–0.82) |
| Temporal | 0.80 (0.69–0.91) |
| Superior | 0.85 (0.74–0.97) |
| Inferior | 0.81 (0.69–0.94) |
| **Corneal staining change** | **Mean (95% confidence interval)** |
| Type-central | –0.03 (–0.12 to 0.05) |
| Type-nasal | 0.44 (0.23 to 0.65) |
| Type-temporal | 0.43 (0.21 to 0.64) |
| Type-superior | 0.34 (0.19 to 0.49) |
| Type-inferior | 0.18 (–0.03 to 0.38) |
| Depth-central | –0.02 (–0.07 to 0.04) |
| Depth-nasal | 0.30 (0.17 to 0.43) |
| Depth-temporal | 0.32 (0.18 to 0.46) |
| Depth-superior | 0.28 (0.17 to 0.40) |
| Depth-inferior | 0.15 (0.02 to 0.28) |
| Extent-central | –0.03 (–0.09 to 0.04) |
| Extent-nasal | 0.41 (0.22 to 0.59) |
| Extent-temporal | 0.41 (0.22 to 0.60) |
| Extent-superior | 0.30 (0.16 to 0.44) |
| Extent-inferior | 0.28 (0.11 to 0.46) |

$n_{missing\ for\ bulbar\ redness\ change} = 2$; $n_{missing\ for\ limbal\ redness\ change} = 2$.

change of post-lens tear thickness can be misleading, as the initial post-lens tear thickness may differ. Therefore, we assessed the percentage change of post-lens tear thickness (Fig. 6) and found that the lenses with shallow fitting settled significantly faster than did the steep-fitting ones with thicker post-lens tear film. Our results also suggest that if clinicians want to maintain a minimum of 100 μm central tear clearance after 5-hour lens settling they would need a greater than 30% buffer at lens insertion by having the initial central tear clearance be no less than 145 μm.

In conclusion, a modern scleral lens used in the present pilot study during short-term wear induces limited corneal edema, which is less than physiological edema caused by overnight eye closure. The small amount of corneal edema was not dependent on tear clearance. The long-term effect of this hypoxic stress on the cornea during lens wear remains unknown. Scleral lens settled quickly during the first 2 hours after lens insertion and continued settling through the 5-hour lens wear period. At the end of 5 hours, the lens fit with thinner initial post-lens tear thickness appeared to settle more in percentage, although the absolute changes were not significantly different from those with thicker initial post-lens tear thickness. This long process of lens settling required that we interpret the fluorogram results with caution, as we needed to consider both fluorescein dilution caused by both tear mixing and lens settling. Although we found that SLs exhibited slow tear mixing, it remains unclear what the critical threshold of tear mixing is to maintain good lens-wearing comfort and good ocular surface health. If such a threshold exists, would healthy and diseased corneas require different critical levels? To answer these questions, further studies on both healthy and compromised eyes wearing scleral lens of different designs with various Dk/t are warranted.

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