Fluid Reservoir Thickness and Corneal Edema during Open-eye Scleral Lens Wear

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SIGNIFICANCE: There is debate concerning corneal oxygenation during scleral lens wear due to the potential additive hypoxic effect of a lens plus a fluid reservoir. This study investigated the agreement between theoretical models and empirical measurements of scleral lens–induced corneal edema with respect to central fluid reservoir thickness.

PURPOSE: The purpose of this study was to examine the effect of altering the fluid reservoir thickness on central corneal edema during short-term open-eye scleral lens wear and to compare these empirical measurements with predictive theoretical models.

METHODS: Ten participants (age, 30 ± 4 years) with normal corneas wore highly oxygen-permeable scleral lenses (141 Dk × 10⁻¹¹ cm² O₂/(cm²)(s)(mmHg)) on separate days with either a low (mean, 144; 95% confidence interval [CI], 127 to 160 μm), medium (mean, 487; 95% CI, 443 to 532 μm), or high (mean, 726; 95% CI, 687 to 766 μm) initial fluid reservoir thickness. Epithelial, stromal, and total corneal edema were measured using high-resolution optical coherence tomography after 90 minutes of wear, before lens removal. Data were calculated from published theoretical models of scleral lens–induced corneal edema for comparison.

RESULTS: Scleral lens–induced central corneal edema was stromal in nature and increased with increasing fluid reservoir thickness; mean total corneal edema was 0.69% (95% CI, 0.34 to 1.04%), 1.81% (95% CI, 1.22 to 2.40%), and 2.11% (95% CI, 1.58 to 2.65%) for the low, medium, and high thickness groups, respectively. No significant difference in corneal edema was observed between the medium and high fluid reservoir thickness groups (P = .37). “Resistance in series” oxygen modeling overestimated the corneal edema observed for fluid reservoir thickness values greater than 400 μm.

CONCLUSIONS: Scleral lens–induced central corneal edema increases with increasing reservoir thickness, but plateaus at a thickness of around 600 μm, in agreement with recent theoretical modeling that incorporates factors related to corneal metabolism.

Several studies have modeled the influence of the fluid reservoir thickness on corneal oxygen delivery or edema during scleral lens wear, some of which use a “resistance in series” approach, in which the fluid reservoir acts as a further barrier to the transmission of atmospheric oxygen. Data from various predictive models suggest that to minimize corneal hypoxia, the central apical fluid reservoir thickness should be limited to 50 to 200 μm, but in clinical practice, patients are often fitted with central fluid reservoir thickness values ranging from 200 to 1000 μm. Short-term laboratory-based experiments, typically using young healthy participants with normal corneas, have also reported minimal variation in corneal edema with increasing fluid reservoir thickness from 200 to 600 μm. Therefore, the aims of this study were to examine the influence of the thickness of the post-lens fluid reservoir upon corneal edema during open-eye, highly oxygen-permeable scleral lens wear in young healthy eyes over a wide range of fluid reservoir thickness values and to compare these empirical data with recent theoretical models of scleral lens–induced corneal edema.

METHODS

Participants: Ten young healthy adults, aged 30 ± 4 years (mean ± standard deviation), four female and six male, with visual acuity of 0.00 logMAR

Scleral lenses provide optical rehabilitation of the irregular cornea, particularly in cases of advanced ectasia, and therapeutic rehabilitation of the ocular surface. Corneal transplantation can also be delayed or avoided with appropriate scleral lens correction, unless the lens is fenestrated or channeled, or can be manufactured in a material of higher oxygen permeability, or can be manufactured in a material of higher oxygen permeability, as these materials are generally considered safe to use for therapeutic purposes.
or better in both eyes were recruited from the staff and students of the Queensland University of Technology. Participants underwent an initial ophthalmic screening to exclude those with any ocular or vision abnormalities, contraindications to contact lens wear, previous ocular injury or surgery, or current use of topical medications. Soft contact lens wearers ceased lens wear for 24 hours before any experimental session, and none of the participants were rigid contact lens wearers. This study was approved by the Queensland University of Technology human ethics research committee and conducted in accordance with the tenets of the Declaration of Helsinki. Participants provided informed consent after an explanation of the nature of the experiment.

Scleral Lens Fitting

In an initial lens fitting session, participants were fitted with various Irregular Corneal Design (ICD, Capricornia, Australia) scleral lenses of varying sagittal depth to determine the lenses required to achieve a fit with low (50 to 150 μm), medium (300 to 500 μm), and high (600 to 800 μm) central fluid reservoir thickness (the axial distance between the posterior scleral lens surface and the anterior corneal epithelium). These target central fluid reservoir thicknesses were selected to extend the thickness range of the post-lens fluid reservoir compared with previous studies, which have ranged from approximately 200 to 600 μm. All lenses used in this experiment were manufactured in hexafocon B material (Dk 141 × 10^-11 cm² O₂ (cm)/(s) (cm²) (mmHg)), with a nominal central thickness of 300 μm, back vertex power of −1.00 D, total diameter of 16.5 mm, back optic zone radius of 7.46 mm, and back surface optic zone eccentricity of 0.5. A spherical landing zone was used for all lenses, and the overall sagittal height of each lens was varied through modifications in the limbal tangent angles, with no modifications to the landing zone. This minimized any potential variation in the landing zone alignment with the underlying conjunctiva (and therefore potential tear exchange) across the different fluid reservoir thickness conditions. To calculate the average oxygen transmissibility of each scleral lens used in the experiment, the lens thickness profiles were assessed using an optical coherence tomography imaging technique described previously.

The initial scleral lens trialed was selected based on the average corneal sagittal height measured over a 10-mm chord using a videokeratoscope (E300; Medmont, Melbourne, Australia). In accordance with the manufacturer’s instruction, an additional 2000 μm was added to this height to extrapolate the corneal sagittal height to a 15-mm chord (the approximate inner edge of the landing zone), then an additional value was added to achieve the target fluid reservoir thickness. The lens was filled with preservative-free saline and inserted into the participant’s left eye, and the central fluid reservoir thickness was measured at the normal to the tangent of the corneal apex using the in-built calipers of an optical coherence tomographer (Spectralis, Heidelberg, Germany) using the central horizontal line scan within a volumetric scanning protocol centered on the pupil. If the initial central fluid reservoir thickness fell outside the target range, then alternate lenses with different sagittal depths were trialed until the target fluid reservoir thickness was achieved.

Measurement Sessions

After the screening and initial scleral lens fitting session, participants attended the laboratory for three measurement sessions conducted on different days and separated by at least 24 hours. The order of lens wear (low, medium, or high central fluid reservoir thickness) was randomized across the study visits, and the three measurement sessions were conducted at the same time of day for each participant to minimize the potential confounding influence of natural diurnal variations in corneal thickness. After applying the appropriate scleral lens (as determined previously in the lens fitting session) with preservative-free saline, corneal thickness (and central and limbal fluid reservoir thickness) was measured using the optical coherence tomographer and again after 90 minutes of lens wear before removal. This period of lens wear was selected because corneal edema peaks after 90 minutes of lens wear in young healthy eyes and then gradually decreases. A volumetric scanning protocol of three horizontal line scans centered on the pupil was used, with each line scan consisting of 20 B scans separated vertically by 139 μm.

Comparison with Theoretical Models of Corneal Edema

Whereas several theoretical models have been proposed concerning oxygen delivery to the cornea in terms of oxygen tension or flux, the proposed relationship between central fluid reservoir thickness and predicted corneal edema can be readily calculated or extrapolated from two published models for comparison with the measured empirical data. Michaud et al. used a resistance in series approach to calculate the theoretical oxygen transmissibility of a scleral lens system based on the lens thickness and oxygen permeability and the thickness of the post-lens tear layer, assuming an oxygen permeability of 80 Dk for the fluid reservoir. The authors then compared these calculated oxygen transmissibility values to the threshold value determined by Holden and Metz. From empirical measures of corneal edema (24.1 Dk/t) to determine which combinations of fluid reservoir thickness, lens thickness, and lens oxygen permeability would yield zero corneal edema.
swelling during open-eye conditions. To compare the data from the current study with the modeling approach used by Michaud et al.,

results

RESULTS

Scleral Lens Thickness Profiles

The mean scleral lens thickness for each target fluid reservoir thickness (averaged across the central 12.5 mm of each lens used to achieve the target fluid reservoir thickness for each participant) was 308 μm (95% confidence interval, 300 to 316 μm) for the low fluid reservoir thickness group, 313 μm (95% confidence interval, 309 to 316 μm) for the medium fluid reservoir thickness group, and 303 μm (95% confidence interval, 299 to 307 μm) for the high fluid reservoir thickness group (Table 1). A small but statistically significant difference was observed between the average lens thickness profiles for the medium and high target fluid reservoir thicknesses (10 μm greater for the high fluid reservoir thickness group; 95% confidence interval, 1 to 19 μm) (P ≤ .03). However, these small variations in lens thickness had minimal impact on the average scleral lens oxygen transmissibility for each target fluid reservoir thickness: low, 46 (95% confidence interval, 45 to 47); medium, 45 (95% confidence interval, 45 to 46); and high, 47 (95% confidence interval, 46 to 47).

Fluid Reservoir Thickness Values

Fluid reservoir thickness values for the different target groups immediately after lens application and after 90 minutes of lens wear are summarized in Table 1. The initial central fluid reservoir thickness values immediately after lens application were as follows: 144 μm for the low fluid reservoir thickness target condition (95% confidence interval, 127 to 160 μm), 487 μm for the medium fluid reservoir thickness target condition (one-way repeated-measures ANOVA, F10,2 = 506.11, P < .001). The initial limbal fluid reservoir thickness values (averaged across the nasal and temporal locations) were as follows: 64 μm (95% confidence interval, 40 to 89 μm) for the low fluid reservoir thickness target condition, 157 μm (95% confidence interval, 110 to 205 μm) for the medium fluid reservoir thickness target condition (one-way repeated-measures ANOVA, F10,2 = 26.89, P < .001). Unlike for the central fluid reservoir thickness values, no significant difference was observed between the medium and high fluid reservoir thickness target groups for limbal fluid reservoir thicknesses.

Table 2. Mean corneal edema (percentage swelling and 95% confidence interval) for the different fluid reservoir thickness conditions

| Layer    | Low            | Medium         | High           | ANOVA (main effect) F, P |
|----------|----------------|----------------|----------------|-------------------------|
| Epithelium | 0.27 (−1.21 to 1.75) | 0.61 (−0.78 to 2.01) | 0.70 (−1.33 to 2.73) | 0.15, .87 |
| Stroma    | 0.74 (0.34−1.13) | 1.92 (1.32−2.52)* | 2.27 (1.65−2.88)* | 30.37, <.001 |
| Total cornea | 0.69 (0.34−1.04) | 1.81 (1.22−2.40)* | 2.12 (1.58−2.65)* | 39.24, <.001 |

*Statistically significant Bonferroni corrected post hoc comparison with the low fluid reservoir thickness condition.
thickness ($P = .92$). The same trends were observed for both central and limbal fluid reservoir thickness after 90 minutes of lens wear, indicating that the variation in fluid reservoir thickness between the three conditions observed at lens application was maintained throughout the 90-minute period of lens wear for both central and limbal fluid reservoir thickness, despite lens settling.

**Central Corneal Edema**

The effect of the fluid reservoir thickness upon central corneal edema is summarized in Table 2. Epithelial edema did not vary significantly with increasing fluid reservoir thickness (repeated-measures ANOVA, $F_{10,2} = 0.15$, $P = .87$). However, a significant effect was observed for stromal edema, with greater swelling observed for medium and high fluid reservoir thickness conditions compared with the low fluid reservoir thickness condition (medium, 1.19% more stromal edema [95% confidence interval, 0.47 to 1.90%; $P = .003$]; high, 1.53% more stromal edema [95% confidence interval, 1.11 to 1.95%; $P < .001$]). No significant difference in stromal edema was observed between the medium and high fluid reservoir thickness conditions (0.34% increase in stromal edema; 95% confidence interval, $-0.30$ to $0.98$; $P = .45$), indicating a plateau in stromal edema between the medium and high fluid reservoir thickness conditions (Fig. 1).

As anticipated, based on the stability of the epithelial thickness across the different fluid reservoir thickness conditions, total corneal edema exhibited the same trends as the stroma (Table 2, Fig. 1). On average, for both the stromal and total corneal thickness data, compared with the low fluid reservoir thickness group, the medium and high fluid reservoir thickness groups had $3.4\times$ and $5\times$ thicker initial fluid reservoir, which resulted in $2.6\times$ and $3.1\times$ more central corneal edema after 90 minutes of lens wear.

**Comparison with Theoretical Models of Corneal Edema**

The corneal edema predicted by two theoretical models$^{16,17}$ for the oxygen transmissibility of the scleral lens used in the current study across a range of central fluid reservoir thickness values is displayed in Fig. 2. The theoretical data from each model were fitted with a third-order polynomial function, which yielded an $R^2$ value of 0.99. The predicted corneal edema data from the modeling of Kim et al.$^{17}$ closely follow the relationship observed between total corneal edema and fluid reservoir thickness observed in the current study (an increase, but a plateau in edema with increasing fluid reservoir thickness within the 95% confidence interval of the empirical data) but consistently underestimated the magnitude of edema by approximately 28% (for fluid reservoir thicknesses of 100 to 700 μm). The resistance in series approach modeled by Michaud et al.$^{16}$ was consistent with the empirical data for central fluid reservoir thickness values up to approximately 400 μm, but beyond this, the modeling substantially overestimated the effect of increasing central fluid reservoir thickness upon corneal edema. For example, increasing the fluid reservoir thickness from 300 to 700 μm in the current study resulted in a 1.72× increase in corneal edema, compared with the resistance in series modeling, which predicts a 3.18× increase (an overestimation of ~54%).

**DISCUSSION**

The main finding from the current study was that the fluid reservoir thickness does have a small but statistically significant influence on central corneal edema in the short term, which appears to plateau as the central fluid reservoir thickness increases to approximately 600 μm. However, on average, the magnitude of edema observed across a wide range of central fluid reservoir thicknesses was not significantly different from the low fluid reservoir thickness condition.
thickness values was relatively low, ranging from 0.7 to 2.1%, which would not be detectable during routine slit lamp examination because visible changes associated with corneal edema such as striae and changes in corneal transparency typically only manifest when edema reaches approximately 4 to 6%. The relatively small amount of edema observed in the medium and high corneal fluid reservoir thickness conditions (mean of 487 and 726 \(\mu m\), respectively) may partially explain why Sonsino and Mathe observed that patients can successfully wear scleral lenses fitted with large amounts of apical fluid reservoir thickness (e.g., up to \(~650\ \mu m\)) in the short term. However, given that increased central fluid reservoir thickness has been linked with greater lens decentration, reduced optical performance, and increased midday fogging, aiming for a thinner fluid reservoir thickness is likely to benefit the patient in terms of the lens fit, optical performance, and, to a lesser extent, corneal physiology. Although reducing the initial central fluid reservoir thickness from approximately 500 \(\mu m\) to 150 \(\mu m\) will reduce corneal edema, this may not be practical for longer-term lens wear because the central fluid reservoir thickness reduced to 95 \(\mu m\) after 90 minutes of lens wear and 10 \(\mu m\) at the limbus. Consequently, longer-term lens wear with an initial fluid reservoir thickness of approximately 150 \(\mu m\) may result in limbal and peripheral corneal bearing toward the end of the day and central touch in cases of advancing keratoconus. For example, Macedo-de-Araujo et al. observed that, after 12 months of lens wear, the central fluid reservoir thickness decreased by a further 50 \(\mu m\) in patients with corneal ectasia. Therefore, based on the current study, a fluid reservoir thickness of 150 \(\mu m\) after lens settling (rather than after initial application) may be a reasonable target to minimize edema and avoid mechanical contact.

The corneal edema observed in this study was primarily stromal in nature (89% of the total change in the cornea), consistent with a previous study of short-term scleral lens wear. Although epithelial edema did increase slightly with increasing central fluid reservoir thickness, this trend did not reach statistical significance. This finding suggests that epithelial edema observed during scleral lens wear may more likely be of a mechanical rather than hypoxic nature.

Previous repeated-measures studies using optical coherence tomography imaging have investigated the influence of the fluid reservoir thickness on corneal edema during short-term scleral lens wear. Arlt reported a small increase in edema from 1.59 to 1.76% when the mean central fluid reservoir thickness was tripled from 209 to 630 \(\mu m\) in young healthy adults. Tan et al. observed almost no change in corneal edema with increasing apical fluid reservoir thickness (0.1% increase in edema when increasing fluid reservoir thickness from 100 to 350 \(\mu m\)), most likely because of the relatively low fluid reservoir thickness values assessed. The current study extends the understanding of the influence of central fluid reservoir thickness on edema by examining a wider range of fluid reservoir thicknesses across three experimental conditions (Fig. 1). The results indicate a plateau effect with larger fluid reservoir thickness values, perhaps because of altered post-lens fluid dynamics, such as potential tear mixing related to convection currents within a thicker fluid reservoir; however, further research is still required to confirm this theory. Previous studies of corneal rigid corneal lenses have also shown that increasing the volume of the fluid reservoir through increased apical clearance decreased corneal hypoxia, even in the presence of tear exchange. Understanding the clinical effects of a thicker fluid reservoir is important because the fluid reservoir thickness can vary substantially.
across the cornea, particularly when fitting a highly irregular cornea (e.g., advanced keratoconus).

The modeling of Kim et al. was in general agreement with the empirical data obtained in the current study, likely because this modeling was previously confirmed using similar experimental corneal edema data obtained from clinical studies varying scleral lens material oxygen permeability over a smaller range of fluid reservoir thickness values (up to ~400 μm). Although this particular model stipulates settled fluid reservoir thickness values (after 5 hours of lens wear), it still followed the trend observed in the current study based on initial fluid reservoir thickness values (and also on the settled lens data from the current study not presented), and despite underestimating edema by approximately 28% on average, it still fell within the lower 95% confidence limit, even when extrapolating the model to a fluid reservoir thickness of 800 μm. Resistance in series modeling in conjunction with the well-established corneal edema data of Holden and Mertz was consistent with the data from the current experiment for fluid reservoir thickness values of ≤400 μm. For thicker post-lens fluid reservoirs, this modeling substantially underestimated the level of edema and therefore the potential benefits in minimizing corneal edema by reducing the apical fluid reservoir thickness. For example, this modeling overestimates the reduction in edema by reducing the fluid reservoir thickness from 700 to 800 μm to 300 to 400 μm by approximately 50%.

Previous work examining the other modifiable scleral lens parameters of lens thickness and oxygen permeability suggests that once the oxygen permeability of the lens material is ≥100 Dk, changes to these parameters have minimal effect upon corneal edema during short-term daily wear. Pullum et al. observed that, for a sealed scleral lens of 115 Dk, reducing the central thickness from 300 μm to 150 μm resulted in virtually no change in corneal edema; a 300-μm center thickness yielded 1.10% central edema on average compared with 1.34% for a 150-μm center thickness in healthy adults. Similarly, Dhallu et al. reported that doubling the scleral lens material oxygen permeability from 100 to 180 Dk did not significantly alter corneal edema when fixing 8 hours of lens wear (0.55% edema with 100 Dk compared with 0.48% for 180 Dk). While Kim et al. suggest that “emphasis for preventing hypoxia should be focused on Dk/t rather than on the thickness of the post-lens tear film,” data from the current study in addition to the above experiments indicate that, when fitting a highly oxygen-permeable scleral lens, corneal edema is minimal but can only be further reduced by minimizing central fluid reservoir thickness, likely because of the lower oxygen permeability of the tear reservoir (e.g., in the current study, reducing the initial fluid reservoir thickness from ~500 to ~700 μm to ~150 μm resulted in a 62 and 67% reduction in edema, respectively).

This study used a repeated-measures design to isolate the effect of the fluid reservoir thickness upon corneal edema while controlling for lens thickness and oxygen permeability. We assumed that tear exchange was minimal for this particular sealed lens design and similar between the experimental conditions, because the same spherical haptic design was used for all lenses. A wider range of central fluid reservoir thickness values (150 to 700 μm) were examined compared with previous studies (200 to 600 μm), across three experimental conditions, which revealed a plateau in edema, previously not observed from other studies using two conditions (e.g., high and low fluid reservoir thickness). Thickness profiling of the scleral lenses used in the study also allowed reliable calculation of the scleral lens oxygen transmissibility for comparison with theoretical models of corneal edema during open-eye scleral lens wear. The short-term nature of the current study and the inclusion of young healthy eyes only do not rule out the possibility that minimizing central corneal fluid reservoir thickness may be beneficial for long-term scleral lens wearers with compromised endothelial function who rely heavily on the lenses to restore visual function during all waking hours (e.g., post-penetrating keratoplasty).

In conclusion, when controlling for variables that influence corneal hypoxia, such as scleral lens thickness, oxygen permeability, and tear exchange, the fluid reservoir thickness does influence corneal edema. However, a plateau effect was observed at a thickness of around 600 μm, and for central fluid reservoir thickness values up to 700 μm, the magnitude of corneal edema remained relatively low at approximately 2%. Patients with normal healthy corneas may wear scleral lenses with minimal clinically observable physiological changes in the short term (i.e., low magnitude corneal edema) with initial central fluid reservoir thickness values of up to 700 to 800 μm if the oxygen permeability of the lens material is high (likely ≥100 Dk). Lowering the central fluid reservoir thickness will reduce central corneal edema (although somewhat less than predicted by resistance in series modeling) and potentially minimize lens decentration and adverse optical effects associated with high fluid reservoir thickness values.

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