Topographical Thickness of the Epithelium and Total Cornea after Hydrogel and PMMA Contact Lens Wear with Eye Closure

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PURPOSE. To determine changes in topographical thickness of the epithelium and total cornea after hydrogel (2-hydroxyethyl methacrylate; HEMA or soft lens) and PMMA rigid contact lens wear with eyes closed, as measured by optical coherence tomography (OCT).

METHODS. Epithelial and total corneal thickness in 18 neophyte eyes was measured with OCT at intervals of 10° across a 10-mm zone of the horizontal meridian of the cornea, before and after 3 hours of soft and rigid contact lens wear with the eye closed. These measurements were repeated 20 minutes after removal of the lenses.

RESULTS. Lens type, time, and location were found to be significant main influences (P < 0.0001) on corneal swelling in patched eyes, by three-way ANOVA, and there was a significant three-way interaction among lens type, time, and location (F(16,272) = 1.78, P = 0.053). However, there was no significant main effect and interaction of epithelial thickness (F(16, 272) = 0.33, P = 0.99). Immediately after removal of the lenses, total corneal thickness in the horizontal meridian was significantly greater with both soft and PMMA lenses (P < 0.001) at each location with each lens, compared with the baseline measurements. With both lenses, the increase in actual thickness and percentage of corneal swelling at the center was greater than at each peripheral point (excluding the first 10° points; P < 0.005). HEMA lenses caused greater corneal swelling than the PMMA lenses at each location immediately after removal of the lenses (P < 0.005).

CONCLUSIONS. This study shows that corneal swelling is dependent on lens type and corneal location when eyes are closed, but epithelial thickness across the horizontal corneal meridian does not change during lens wear with eyes closed. OCT is an efficient method of measuring topographical corneal and epithelial thickness in response to contact lens wear. (Invest Ophthalmol Vis Sci. 2003;44:1070–1074) DOI:10.1167/iovs.02-0343

Previous studies have reported that the corneal thickness profile can be measured by optical pachymetry with a fixation device or an ultrasonic scanner,1–4 as well as a recently developed system (Orbscan; Bausch & Lomb, Tampa, FL).5 Using a modified optical pachometer, Holden et al.6 demonstrated that the periphery of the cornea swells significantly less than the central cornea during soft lens wear with eyes closed. However, there is no literature on the effects of topographical epithelial thickness after contact lens wear except for the studies that show there is no increase in central epithelial thickness under hypoxia induced by lens wear in vitro7,8 or in vivo.9,10

Optical coherence tomography (OCT) is a noninvasive imaging technique that can recreate a high-resolution, cross-sectional image of the cornea from many sagittal scans of backscattered light, using the low-coherence interferometric method. OCT offers the possibility of showing objective structural changes and provides exact and rapid biometric in vivo analysis of structures and dimensions in the eye without direct contact or immersion techniques. OCT has been widely studied for qualitative and quantitative analysis of the posterior segment of the eye, such as measurements of retinal thickness and nerve fiber layer thickness.11–14

In addition, OCT has been reported to be used to measure the anterior eye (i.e., epithelial and total corneal thickness, iris thickness, anterior chamber angle, lens thickness, and secondary cataract thickness).10,15–18 Using OCT, Izatt et al.17 made measurements of the thickness of the corneal epithelium, a layer that exhibits lower reflectivity. We have found that OCT is capable of measuring epithelial and total corneal thickness with high repeatability (approximate 2.5 and 3 μm for corneal epithelial thickness and total corneal thickness, respectively) as well as topographical thickness, if a fixation device is used.16,17 In this study, topographical thicknesses of the epithelium and total cornea were measured after 3 hours of hypoxia induced by hydrogel (2-hydroxyethyl methacrylate; HEMA or soft lens) and PMMA rigid contact lens wear with the eyes closed. We also compared the topographical corneal swelling induced by hydrogel and PMMA lenses.

METHODS

Subjects

Eighteen healthy subjects (8 men and 10 women; mean age, 25.9 ± 5.8 years) with no history of contact lens wear or any current ocular or systemic disease were recruited for the study. Informed consent was obtained from each subject after ethics approval was obtained from the Office of Research Ethics, University of Waterloo. All subjects were treated in accordance with the tenets of the Declaration of Helsinki.

Instrumentation and Lenses

An OCT system (Humphrey Systems, Zeiss-Humphrey, Dublin, CA) was used to measure topographical corneal and epithelial thicknesses. To measure the thickness across the horizontal meridian, a fixation device was mounted on the probe of the OCT, as shown in Figure 1. The fixation device was a compact disc on which several fixation dots were marked at angles from 0° to 40° (approximately 5.0 mm in half-chord distances) temporally and nasally. The distance (chord distance) between measuring locations and the corneal apex was calculated from...
the measuring angle and the corneal radius by simple triangle geometry, as suggested by Hitzenberger et al.20 In the current study, the corneal radius of 7.70 mm from Gullstrand’s schematic eye was used, and all results were plotted by calculated chord distances.

A fundamental concern about corneal thickness measurements is that the measurement be orthogonal to the surface. When a partially coherent beam is projected onto the cornea, its reflection is observed on the monitor. This can occur only when the incident light is perpendicular to the corneal surface. By using all two-dimensional images of the cornea, a corneal profile image can be reconstructed as shown in Figure 2.

Corneal and epithelial thicknesses were measured at each location, with the width of a horizontal scan being 1.13 mm. The principles of OCT and measurement of the cornea have been described previously.12,15,19 In this study, we measured corneal thickness as the distance between the first and last peaks and epithelial thickness as the distance between the first and second peaks, as described in other studies.10,15,18 The parameters of the lenses used to induce corneal swelling in this study are listed in Table 1.

**Procedures**

Three study visits were scheduled after 10 AM, to ensure that corneal edema induced by overnight eye closure had dissipated. All participants were asked to wake no later than 7 AM. At the initial visit, participants were asked to remain in the building. Normal blinking was encouraged in the open (control) eye, but participants were asked not to close the control eye for longer than 2 minutes.

OCT measurements were taken in the experimental eye immediately after removal of the lenses and 20 minutes later. The control eye was measured 20 minutes after removal of the lenses. The measurements and procedure were repeated with the other lens (soft or PMMA lens according to randomization) at the third visit.

**Data Analysis**

Custom software was used to process raw data, and multiple sagittal scan points were analyzed to yield precise measurement of epithelial and total corneal thickness. Data analysis was conducted on computer (Statistica; StatSoft, Inc., Tulsa, OK). Two-way or three-way repeated-measurement analysis of variance (Re-ANOVA) was used for overall effects and post hoc paired t-tests with Bonferroni correction were used to determine whether there were pair-wise differences (P < 0.05).

**Results**

Baseline measurements of 18 eyes showed corneal thickness increased gradually from the central point (visual axis) to 40° at the periphery, as shown in Figures 3 and 4. Baseline epithelial thickness remained constant across the cornea (F(16,272) = 0.83; P = 0.65). Immediately after 3 hours of contact lens wear with eye closure, the mean (±SD) central corneal thickness increased 13.4% ± 3.1% with soft contact lenses and 12.1% ± 2.5% with PMMA lenses compared with 3.8% ± 2.6% with soft lenses and 3.0% ± 2.2% with PMMA lenses at the most peripheral points (the mean of nasal and temporal 40° points corresponding to 5 mm from the central point), as shown in Figure 5.

Lens type, time (before and after lens wear and 20 minutes after removal of the lenses) and location were found to have significant main effects (P < 0.0001) on corneal swelling in patched eyes, by three-way ANOVA. There was also a significant three-way interaction among lens type, time, and location (F(16,272) = 1.78, P = 0.055), which indicates that corneal swelling in patched eyes was significantly increased compared to baseline measurements. Additionally, there was a significant interaction between lens type and time, indicating that PMMA lenses caused significantly more swelling than soft lenses.

**Table 1. Study Lens Parameters**

<table>
<thead>
<tr>
<th>Lens Type</th>
<th>Base Curve</th>
<th>Lens Diameter</th>
<th>Central Thickness</th>
<th>Water Content</th>
<th>Dk/t</th>
<th>Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEMA</td>
<td>8.3–8.9</td>
<td>14.0–14.3mm</td>
<td>0.20–0.40mm</td>
<td>38%</td>
<td>2.2</td>
<td>0.7+2.0</td>
</tr>
<tr>
<td>PMMA</td>
<td>7.50–8.44</td>
<td>9.20–9.80mm</td>
<td>0.14 mm</td>
<td>0.0</td>
<td>0</td>
<td>Plano</td>
</tr>
</tbody>
</table>

**Figure 1.** The OCT system (left) with a fixation device (right) mounted on the probe, indicating different fixation targets with different angles.

**Figure 2.** An entire corneal image constructed from different scans, showing corneal thickness gradually increasing from the center to the periphery.
swelling was dependent on lens type, time, and corneal location. However, there was no significant main effect and interaction for epithelial thickness among lens type, time, and location (F(16,272) = 0.33, P = 0.99) in patched eyes.

Immediately after 3 hours of lens wear with eye closure, total corneal thickness in the horizontal meridian was significantly greater with both soft and PMMA lenses (at each location with each lens: P < 0.001, compared with the baseline measurements). With both lenses, the increase in actual thickness at the center was greater than at each peripheral point (locations ≥ 20°; P < 0.005) and the percentage of corneal swelling was greater at the center than at each peripheral point (P < 0.005), as shown in Table 2.

The soft HEMA (2-hydroxyethyl methacrylate) lenses caused greater corneal swelling at each location immediately after removal of the lenses (P < 0.005), except for the temporal 40° position (P = 0.017). The greatest difference was found at the midperipheral points (20°) as shown in Figure 5.

The epithelial and corneal thickness over the 10 mm chord of the control eyes did not alter during the period of the experiment (F(1,17) = 0.01, P = 0.92 and F(1,17) = 1.09, P = 0.38 for corneal and epithelial thicknesses, respectively).

DISCUSSION

After 3 hours of contact lens wear with eye closure, OCT showed that epithelial thickness did not change (increase or decrease) across the cornea in response to hypoxia induced by either the low-Dk/t soft or PMMA lenses. This is consistent with previous findings for the central area of the cornea.7-9,10,21,22 This outcome was anticipated in response to the soft lenses, which transmit nearly no oxygen and are unlikely to have a mechanical or localized pressure effect on the epithelium. However, the rigid PMMA lenses could have exerted a mechanical effect on the epithelium20—orthokeratologic lens designs in particular have produced central epithelial thinning.24 Ladage et al.23 also found a decrease of central corneal epithelial thickness with daily wear of hyper-oxygen-transmissible rigid lenses after 4 weeks. Our study did not demonstrate epithelial thickening or thinning in either the central or peripheral areas of the cornea. Although the localized bearing of the secondary zone of the PMMA lens may induce pressure and hence compression of the cornea (localized thinning), this did not occur, as evidenced by the OCT measurements.

In contrast, significant corneal swelling occurred across the cornea with greater central than peripheral swelling after both soft and PMMA lens wear. The central corneal swelling with soft lenses is in agreement with our previous study10 in which we used the same set of HEMA lenses to indicate that the results are repeatable in different groups. Immediately after removal of the lenses, total central corneal thickness had increased by 13.4% with soft lenses, which was significantly greater and the 12.1% with PMMA lenses.

Holden et al.6 found that extended-wear soft lenses induce significantly greater central than peripheral corneal swelling, which they hypothesized was due to structural restraint of the limbal region. They found similar swelling profiles with three different types of soft lenses and concluded that the topographical swelling profiles were not lens-type related. Our study showed there were significant differences in corneal swelling between soft and PMMA lenses. The greatest difference was in the midperiphery. We hypothesize that the midperipheral cornea may swell less with PMMA, because it receives some oxygen from the tarsal conjunctiva, in that the peripheral cornea is exposed to the conjunctiva because of the small lens diameter. The closed-eye oxygen supply to the midperipheral cornea is also the most plausible explanation for the lower central swelling response with PMMA compared with the soft-
lens-induced swelling. We assume that the PMMA lenses did not move during eye closure and therefore tear exchange would be negligible and that there was no oxygen transmission through the PMMA lens, and thus the peripheral oxygen supply to the cornea must be sufficient for the relatively depressed central-swelling response.

The greatest difference in corneal swelling between soft and hard lenses was measured at the midperipheral area corresponding to approximately 2.5 mm from the center (Fig. 5). Although short-term pressure-related effects (compression) on corneal topographical thickness with rigid lenses, especially orthokeratologic lenses have been demonstrated,24,25, this was probably not the case in our study. Because the lenses were fitted more steeply than the flattest corneal meridian and were designed with an 8.00-mm optical zone diameter, the junction between base curve and secondary curve, and hence the pressure zone, should correspond to 4 mm from the center on the graph in Figure 5. This is why we think the swelling difference is more likely to be a hypoxic effect than localized pressure from the PMMA lens.

Using the Orbscan system (Bausch & Lomb), investigators in a recent study26 showed a fairly homogenous increase in central and midperipheral corneal thickness. If that were true, corneal curvature of the anterior and posterior surfaces would not change during corneal swelling. However, Moezzi et al.27 found posterior flattening of the corneal surface and no change to the anterior surface during corneal swelling, using the Orbscan, which indicates that corneal swelling is not uniform but is greater centrally than peripherally, as we found in this study.

We have demonstrated that OCT has a precision of 2.5 μm in measurements of epithelial thickness.10 Epithelial thickness can increase by 5 μm after overnight sleep19 or decrease by 5 to 7 μm after rigid lens wear,23,24 and for detecting a 5-μm group difference with 90% statistical power, the sample size should be five, according to a software program developed by Erdfelder et al.28 (Gpower, ver. 2). For detecting a 2.5-μm difference, total sample size should be 13. Therefore, an inadequate sample size cannot be the reason for the negative findings in the epithelium but rather that epithelial thickness does not alter, even though hypoxia is induced by the lenses and eye closure.9,10,22

In conclusion, In the current study, corneal swelling was dependent on lens type and corneal location after 3 hours of lens wear in a closed eye but epithelial thickness across the horizontal corneal meridian did not alter after lens wear with eye closure. Corneal swelling was greater centrally than peripherally with both HEMA and PMMA lenses, and the HEMA lens induced significantly more swelling than the PMMA lens. OCT is an efficient method for measuring topographical thickness of the cornea and epithelium in response to lens wear.

References
19. Fonn D, Wang JH, Simpson T. Topographical thickness of the


