Topographical Thickness of the Epithelium and Total Cornea after Overnight Wear of Reverse-Geometry Rigid Contact Lenses for Myopia Reduction

Jianhua Wang, Desmond Fonn, Trefford L. Simpson, Luigina Sorbara, Richard Kort, and Lyndon Jones

PURPOSE. To investigate topographical thickness changes of the epithelium and total cornea measured with optical coherence tomography (OCT) after overnight wear of rigid gas-permeable lenses.

METHODS. Reverse geometry design CRT (Dk = 100) rigid (test) lenses (Paragon Vision Sciences, Mesa, AZ) were randomly fitted on one eye of each of 20 neophyte subjects (mean age, 24.6 ± 2.7 years) and the other eye was fitted with an alignment tricurve rigid lens of the same material (control). Epithelial and total corneal thickness was measured at intervals of 10° across a 10-mm zone of the horizontal meridian of the cornea, before and after overnight wear. Refractive error was measured with an autorefractor. These measurements were repeated 20 and 60 minutes and 3, 6, and 12 hours after lens removal.

RESULTS. After one night of lens wear, myopia decreased in the test eye by 1.18 ± 0.81 D, which was significantly different from baseline (P < 0.001). No significant change was found in the control eye. Twelve hours after removal, two thirds of the myopic reduction was still present. Different topographical swelling patterns were induced by the two lens designs, with greatest swelling occurring in the center with the control lens and in the midperiphery with the test lenses (polynomial regression: P < 0.005). Significantly greater central corneal swelling was found with the control lens than the test lens (6.9% ± 3.1% vs. 4.9% ± 2.0%, respectively, P = 0.006). The effect on epithelial thickness differed between lenses and depended on both position and time (F(2,312) = 2.5; P = 0.000). Immediately after removal of the test lens, the central epithelium was 5.1% ± 4.5% thinner than baseline, and all other locations (P < 0.005 post hoc tests) and the epithelium in the midperiphery showed significant thickening (1.9% on the temporal side and 2.4% on the nasal side, both P < 0.006 compared with the baseline). There were no significant changes in epithelial thickness with the control lens during the study period (post hoc tests: P > 0.05).

CONCLUSIONS. The optical coherence tomograph is a sensitive instrument that can detect small changes in epithelial and corneal thickness across the entire cornea. Topographical thickness changes of the epithelium and total cornea induced by one night of reverse-geometry lens wear appear to be associated with the decrease of myopia. (Invest Ophthalmol Vis Sci. 2003;44:4742–4746) DOI:10.1167/iovs.03-0239

Orthokeratology is defined as the temporary reduction of myopia by the programmed application of rigid contact lenses. Recently, reverse-geometry rigid gas-permeable lens designs have been successfully used to reduce myopia, which has led to renewed interest in this field.2–6 Recent studies2,5,7,8 suggest that modern designs can provide temporary reductions in myopia of 1.75 to 2.50 D for up to 8 hours after lens wear. The use of an overnight lens-wearing modality, with lens removal occurring during the day, has recently been approved by the U.S. Food and Drug Administration and has resulted in greater acceptance by patients. Although rapid growth in this specialty contact lens area has been predicted, relatively little is known about the effects on the cornea after the use of reverse-geometry lenses.3 In one of the few studies published to date, Swarbrick et al.3 measured corneal and epithelial thickness after the use of reverse-geometry lenses with a modified optical pachymeter and found central epithelial thinning and mid peripheral corneal thickening. However, the effect on the cornea of overnight wear of orthokeratology lenses (immediately on awaking) remains unknown. This study attempted to address whether lenses induce corneal swelling, and if so, what the difference is between that induced by CRT lens (Paragon Vision Sciences, Mesa, AZ) compared with the control.

Optical coherence tomography (OCT) has been used by our group to measure topographical corneal and epithelial thickness in normal and edematous corneas3 (Fonn D, et al. IOVS 2000;41:ARVO Abstract 3591). This is a noninvasive and non-contact technique that uses a low coherence light and complex image-processing technology.10–12 The purposes of this study were to compare topographical corneal thickness changes in the epithelium and total cornea after overnight wear of reverse geometry (CRT) and alignment-fitted rigid contact lenses and to determine the relationship between refractive error and changes in corneal thickness.

METHODS

Subjects

Twenty healthy subjects (4 men and 16 women; mean age, 24.7 ± 2.7 years; range, 21–31) with no history of contact lens wear or any current ocular or systemic disease were recruited for this study. Informed consent was obtained from each subject after 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. The refractive error distribution and corneal curvatures are listed in Table 1. There were no significant differences between the experimental and control eyes (P > 0.05).

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Table 1. Ocular Parameters

<table>
<thead>
<tr>
<th></th>
<th>Experimental Eyes</th>
<th>Control Eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractive Error (D)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sphere</td>
<td>-3.11 ± 1.24</td>
<td>-3.09 ± 1.12</td>
</tr>
<tr>
<td>Cylinder</td>
<td>-0.46 ± 0.22</td>
<td>-0.49 ± 0.31</td>
</tr>
<tr>
<td>Auto-keratometry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flat K</td>
<td>43.87 ± 1.83</td>
<td>43.73 ± 1.72</td>
</tr>
<tr>
<td>Cyl</td>
<td>-0.71 ± 0.45</td>
<td>-0.77 ± 0.51</td>
</tr>
</tbody>
</table>

Instrumentation and Lenses

A Humphrey OCT system (Carl Zeiss Meditec, Dublin, CA) was used in this study to measure topographical corneal and epithelial thickness. A detailed description of this instrument has been published previously (Fonn, et al. IOVS 2000;41:ARVO Abstract 3591). A fixation device was mounted on the probe of the OCT to measure the thickness across the horizontal meridian. On the device, several fixation dots were marked at angles from 0° to 40° (approximately 5.0 mm in half chord distance) temporally and nasally at intervals of 10°. A monitor was used to observe the specular reflex when the partially coherent beam was projected onto the cornea (indicating the incident light was perpendicular to the corneal surface).

The test contact lens consisted of a reverse-geometry rigid lens design (CRT; Paragon). Control lenses consisted of a tetracurve design and of the same total lens diameter, central thickness, and back optic zone diameter (BOZD) as the test lens, as detailed in Table 2. The RGP material used for both lens designs was the fluorosilicone acrylate material, HDS 100 (Dk=100; Paragon). The back optic zone radius (BOZR) of the test lens that was chosen was calculated based on the amount of projected correction of the myopia in the experimental eyes, which resulted in a radius approximately 0.8 mm flatter than flattest keratometry (K) readings. The BOZR of the control lens was fitted in alignment with the flattest keratometry reading of the control eye. A multipurpose solution (Simplicity; Bausch & Lomb, Rochester, NY) for rigid lenses was used to condition the lenses before insertion. Manifest refraction was measured with an autorefractor (NRK-8000; Nikon, Tokyo, Japan).

Procedures

Participant eligibility was determined at a screening appointment. Informed consent was obtained from all participants before enrollment in the study. Paragon CRT (Dk=100) rigid lenses were randomly fitted on one of the eyes, and the other eye was fitted with an alignment tetracurve rigid lens of the same material. The CRT lens was fitted according to the manufacturer’s recommendations, to achieve optimal centration and potentially maximal correction of myopia.

In the evening before the study day (day 0), baseline thickness of the epithelium and total cornea were measured at intervals of 10° across the central 10 mm of the horizontal corneal meridian, followed by auto refraction. The lenses were then inserted and assessed for appropriate fit (centration, movement, and fluorescein pattern) and subjects went to sleep in the laboratories of the Centre for Contact Lens Research from 10 PM, until they were awakened at 7 AM the next morning. Immediately after lens removal, epithelial and total corneal thickness measurements and auto refraction were repeated in the same manner as the baseline visit and again at 20 and 60 minutes, 3, 6, and 12 hours after lens removal.

Data Analysis

Custom software was used to process raw data and multiple sagittal scans were analyzed to yield measurements of epithelial and corneal thickness. Data analysis was conducted using Statistica (StatSoft, Inc., Tulsa, OK). Two- 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). Two-tailed paired t-tests were used to compare the changes in refraction. Polynomial regression was used to quantify each function relating to the percentage corneal swelling versus position (chord distance), to analyze topographical corneal swelling patterns.

Results

After 1 night of lens wear, myopia decreased significantly in the eyes wearing CRT (test) lenses (1.18 ± 0.81 D; paired t-test: P < 0.0001). There was no significant change in the eyes wearing the control lenses (P > 0.05), as shown in Figure 1. During the recovery period after lens removal, myopia continued to be reduced by 0.84 D (71%) and 0.74 D (63%) after 3 hours and 12 hours, respectively.

After lens removal, the experimental and control corneas were thicker than baseline, as shown in Figures 2 and 3. The cornea exhibited maximum swelling on eye opening and steady deswelling throughout the day (F(6,114) = 86.9; P = 0.000). Figure 4 shows that the amount of central corneal swelling differed between eyes (F(1,19) = 8.5; P = 0.0089), with greater central swelling induced by the control lens than by the CRT lens (6.9% ± 3.1% vs. 4.9% ± 2.0%, respectively, post hoc: P < 0.005). Immediately after lens removal, clear differences in the distribution of the corneal swelling between the two lens designs were apparent (F(1,13.6) = 2.10; P = 0.039), as shown in Figure 4. A polynomial regression approach was used to quantify the percentage swelling by corneal position. To assist in the fitting of the polynomial, the intercepts were set to be 4.9% and 6.9% (mean central corneal swelling values for the CRT and control lens, respectively). Preliminary analysis showed that the linear components of the polynomials were not different from zero, and they were therefore not included in subsequent curve fitting. The results, with coefficients of determination, are also shown in Figure 4 and the respective fits are the smoothed lines in each panel. As is apparent from the r² values, the fits describe the data very well. The analysis showed that for both the CRT and control data, a parabolic component (x²) was present (P < 0.001 and P < 0.007 for CRT and control lenses, respectively). There were no significant cubic (x³) factors, but for the CRT lens data there was a quartic (x⁴) component that was highly significant (P = 0.000). The CRT lens design had significant effects on the epithelial thickness distribution, which depended on both corneal position and time (F(13,912) = 2.3; P = 0.000), as demonstrated in Figure 5. Immediately after removal of the CRT lenses, the central epithelium was 5.1% ± 4.5% thinner than baseline (post hoc tests: P < 0.005), as shown in Figure 6. Compared with baseline, the epithelium in the midperiphery of the test lens wearing eye showed significant thickening (1.9% on the

Table 2. Study Lens Parameters

<table>
<thead>
<tr>
<th>Lens</th>
<th>Fitting</th>
<th>Design</th>
<th>Dk</th>
<th>Central Thickness (mm)</th>
<th>BOZD (mm)</th>
<th>Diameter (mm)</th>
<th>BOZR (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRT</td>
<td>Flat</td>
<td>Tetracurve</td>
<td>100</td>
<td>0.15</td>
<td>8.4</td>
<td>10.0</td>
<td>8.46 ± 0.53</td>
</tr>
<tr>
<td>Control</td>
<td>On-K</td>
<td>Tetracurve</td>
<td>100</td>
<td>0.15</td>
<td>8.4</td>
<td>10.0</td>
<td>7.69 ± 0.26</td>
</tr>
</tbody>
</table>
temporal side and 2.4% on the nasal side, both $P < 0.006$). The changes in epithelial thickness in the central and paracentral areas recovered to baseline approximately 3 hours after lens removal (Fig. 5). There was no significant change in epithelial thickness with the control lens during the study period (post hoc tests: $P > 0.05$).

**DISCUSSION**

This study demonstrated that a significant amount of corneal swelling occurs after overnight wear of rigid gas-permeable lenses with a Dk of 100, with both reverse-geometry and conventional-alignment lens designs. Corneal swelling induced by overnight lens wear has been well documented in the literature, which suggests that corneal edema and the amount of swelling are directly related to the oxygen supply underneath the lens during eye closure. The oxygen permeability of the lens materials plays a major role in the corneal response, and recent work has shown that the amount of corneal swelling after overnight wear of silicon-based hydrogel lens materials is similar to that achieved with no lens in place. In this study, after 1 night of wearing rigid lenses with a Dk/t of 67, both lenses induced approximately 6% corneal swelling, which is greater than the degree of corneal swelling seen on waking after no lens wear. According to the Holden-Mertz criterion, for 4% overnight corneal swelling, the Dk/t of a lens would have to be 87. However, these data were measured 2 to 4 hours after lens removal and eye opening. In our study, corneal thickness was measured immediately on lens removal and eye opening and up to 12 hours thereafter, and corneal swelling had fully recovered within 3 hours. The similar results may have been found in previous studies if the subjects in their studies would be examined immediately after awakening. This clearly indicates that any future studies examining the effects of overnight lens wear on corneal swelling must be undertaken very soon after eye opening.

Overnight wear of new-generation orthokeratology lenses results in a rapid reduction in myopia, as evidenced by this study and work by other groups. Reverse-geometry lenses have a flattening effect on the corneal anterior curvature, and...
which has been hypothesized to be responsible for the reduction of myopia.\textsuperscript{2,3} In this study we have shown that approximately two thirds of the myopia reduction achieved after one overnight session remained 3 hours after lens removal, and that during a 12-hour period, the refractive error did not return to baseline levels (Fig. 1). Examination of the epithelial and total corneal thickness results (Figs. 2, 5, 6) indicate that these return to baseline levels within approximately 3 hours of lens removal. This indicates that myopia reduction after orthokeratology lens wear is due not only to changes in thickness of the epithelium and total cornea but also to changes in the corneal curvature. The equation used to predict the reduction in myopia based on the change in thickness may not be applied in orthokeratology. The long-lasting corneal remodeling effect (surface flattening) with these novel lens designs makes it possible for patients to wear orthokeratology lenses only during sleeping hours, with the treatment effect still evident at the end of the day.

Figures 2 and 3 show that reverse-geometry lenses induced significantly less central and greater midperipheral swelling than the control lenses. Both lens designs produced less peripheral than midperipheral and central swelling, as shown in Figure 4. The most important difference is related to the additional quartic component from the polynomial regression, showing that for the CRT lens there were additional peaks corresponding to midperipheral corneal thickening. This finding suggests that a different swelling pattern induced by CRT lenses may serve as a contributing factor in the reduction of myopia through the alteration of corneal curvature. After 28 days of wearing orthokeratology lenses, central corneal thinning and midperipheral corneal thickening were found by Swarbrick et al.,\textsuperscript{3} and our study revealed the same relative difference between the center and periphery. Both studies support the theory of the redistribution of corneal thickness (fluid and corneal tissue), resulting in a temporary alteration in refractive error.

The epithelial thinning in the center and thickening in the midperiphery of the cornea found in this study are also in agreement with another study.\textsuperscript{16} Using a histologic method to investigate the change in corneal morphology induced by orthokeratology lenses in rabbit eyes, Matsubara et al.\textsuperscript{16} reported similar findings, in which the epithelial layer was slightly thinner in the central area of the cornea and thicker in the midperiphery. Using tandem scanning confocal microscopy, Ladage et al.\textsuperscript{16} demonstrated significant corneal epithelial thinning after 1 month of rigid gas-permeable lens wear. Investigators in these studies have suggested that there may be a redistribution of epithelial cells,\textsuperscript{3,16,17} in which the centrally positioned epithelial cells shift to a paracentral area, after the wearing of orthokeratology lenses. Further studies are warranted to confirm this theory.

There are a number of ways to measure corneal and epithelial thickness, including optical pachymetry,\textsuperscript{13,15} ultrasound pachymetry,\textsuperscript{18} and confocal microscopy.\textsuperscript{17,19} We have demonstrated that OCT is a highly repeatable, noncontact technique for measuring corneal and epithelial thickness across the cornea\textsuperscript{9} (Fonn D, et al. IOVS 2000;41:ARVO Abstract 3591), and subtle changes in epithelial thickness can be detected by such a technique.\textsuperscript{14,20} In addition, in this study, the differences of topographical corneal swelling between different lens designs and central epithelial thinning with reverse geometry lenses were found. Maldonado et al.\textsuperscript{21} used OCT to measure the thickness of the corneal cap and stromal bed after laser in situ keratomileusis (LASIK). These data collectively show that the OCT seems to be a useful tool to measure the corneal structure and could be widely used in research on the physiology and pathology of the cornea.

In summary, overnight wearing of CRT lenses induces corneal swelling and epithelial alterations after 1 night of lens wear that appear to contribute to the decrease in myopia. These changes appear to be due to the redistribution of corneal tissues and fluid.

\section*{Acknowledgments}

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\section*{References}