Decrease in Rate of Myopia Progression with a Contact Lens Designed to Reduce Relative Peripheral Hyperopia: One-Year Results

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Purpose. To determine whether a novel optical treatment using contact lenses to reduce relative peripheral hyperopia can slow the rate of progression of myopia.

Methods. Chinese children, aged 7 to 14 years, with baseline myopia from sphere $-0.75$ to $-3.50$ D and cylinder $\leq 1.00$ D, were fitted with novel contact lenses ($n = 45$) and followed up for 12 months, and their progress was compared with that of a group ($n = 40$) matched for age, sex, refractive error, axial length, and parental myopia wearing normal, single-vision, spherocylindrical spectacles.

Results. On adjusting for parental myopia, sex, age, baseline spherical equivalent (SphE) values, and compliance, the estimated progression in SphE at 12 months was $34\%$ less, at $-0.57$ D, with the novel contact lenses ($95\%$ confidence interval [CI], $-0.45$ to $-0.69$ D) than at $-0.86$ D, with spectacle lenses ($95\%$ CI, $-0.74$ to $-0.99$ D). For an average baseline age of 11.2 years, baseline SphE of $-2.10$ D, a baseline axial length of 24.6 mm, and 320 days of compliant lens wear, the estimated increase in axial length (AL) was $33\%$ less at 0.27 mm ($95\%$ CI, 0.22–0.32 mm) than at 0.40 mm ($95\%$ CI, 0.35–0.45 mm) for the contact lens and spectacle lens groups, respectively.

Conclusions. The 12-month data support the hypothesis that reducing peripheral hyperopia can alter central refractive development and reduce the rate of progression of myopia.

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should not only correct central refractive error to obtain clear vision but also correct peripheral hyperopia to slow the progress of myopia.\textsuperscript{20,27} In a recent study, we found that though there was no significant difference in progression overall, 1 of 3 experimental spectacle lenses designed to reduce relative peripheral hyperopia produced a statistically significant 30\% reduction in myopia progression over a 12-month period in a subgroup of children 6 to 12 years of age whose parents had a history of myopia.\textsuperscript{28}

In the present study, we tested the peripheral hyperopia reduction hypothesis using novel contact lenses. In contrast to the experimental spectacle lenses used previously,\textsuperscript{29} these novel contact lenses were designed not only to correct central vision with a central zone that corrected for the central refractive error but also to produce a peripheral hyperopia-reducing effect by greater reduction in the degree of relative peripheral hyperopia, shifting in the effective peripheral treatment zone closer to the visual axis, and a more prevailing consistent stimulus because contact lenses largely remained aligned with the eyes when they moved.

\section*{Methods}

\subsection*{Study population}

The two study population groups were derived from two separate, randomized, prospective clinical studies conducted at Zhongshan Ophthalmic Centre, Guangzhou, China. The study group consisted of 60 Chinese children aged 7 to 14 years, with baseline spherical refractive corrections ranging from −0.75 to −3.50 D and −1.00 D or less of astigmatism based on cycloplegic autorefraction, who were fitted with the novel contact lenses. The group used for comparison consisted of 40 children who wore standard, single-vision, spherocylindrical spectacles. The children in both contact lens spectacle lens groups were from the same geographic and demographic locale; were examined by the same researchers using the same facilities, equipment, and methods; and had the same baseline ocular characteristics and age range. Eligible children from both studies had vision correctable to at least 6/9.5 in both eyes, exhibited normal ocular findings, and were willing to wear the lens type assigned to them and to adhere to the protocol schedule. Children with binocular vision conditions such as strabismus, any ocular or systemic condition associated with myopia (e.g., Marfan syndrome, retinopathy of prematurity), history of orthokeratology lens wear, bifocal or progressive addition spectacles in the past 12 months, atropine treatment for myopia control, or known allergy to tropicamide or proparacaine were excluded from participation in the trial. The study was approved by the Institutional Ethics Committee of Zhongshan Ophthalmic Centre and adhered to the Declaration of Helsinki for Experimentation on Humans. Both trials were registered with the China Clinical Trial Registry and adhered to ICH and WHO Good Clinical Practice guidelines.

\subsection*{Contact lens design}

Treatment contact lenses were made of a silicone hydrogel lens material (8.6-mm base curve, 14.2-mm diameter; Lotrafilcon B, CIBA Vision, Duluth, GA). The lenses had a clear central zone that corrected for the refractive error of the eye as measured centrally (1.5-mm semichord and 1.5 mm within a relative plus of +0.25 D). Outside the central zone, the refracting power of the lens increased progressively in relative positive power to reach a relative positive power of +1.00 D at 2 mm semichord and +2.00 D at the edge of the peripheral treatment zone (total treatment zone, 9 mm).

The contact lenses were worn for at least 8 hours a day, 5 days a week. A hydrogen peroxide disinfection system (Clear Care; CIBA Vision) was used for lens cleaning and disinfection, and the lenses were replaced on a monthly basis. Standard spectacle lenses were worn at other times.

\subsection*{Study procedures}

The contact lens–wearing subjects were examined after 1 month and then at 3-month intervals. The spectacle lens–wearing subjects were examined at 6-month intervals. The primary outcome measures were change in central refractive error and axial length as measured at the 6- and 12-month visits. Central spherical equivalent refractive error was determined using cycloplegic autorefraction and a modified open-field autorefractor (NVision K5001; Shin-Nippon, Tokyo, Japan). Cyclopia was induced with 2 drops of tropicamide 1\% preceded by 1 drop of a topical anesthetic (1\% proparacaine).\textsuperscript{29} At least 30 minutes passed between the instillation of the drops to measurements. Before examination, the pupils were checked to ensure that they were dilated and nonresponsive to light. Accommodative responses were not measured. Five autorefractor measurements were obtained for each eye and averaged. Axial length was measured by partial coherence interferometry (IOLMaster; Carl Zeiss, Oberkochen, Germany). Three axial length measurements were obtained and averaged before data analysis. Both cycloplegic autorefraction and axial length were measured at baseline and at 6-month intervals for both groups.

Peripheral refraction for each eye was measured using the Shin-Nippon autorefractor at baseline, both with and without optical correction in place. To limit potential translocation of the contact lenses associated with large eye turns, off-axis measurements were obtained by having the subject rotate his or her head to fixate on auxiliary fixation targets to maintain the eyes in the primary position. Measurements were made in the nasal and temporal horizontal hemifields at 20°, 30°, and 40°. Measurements at each fixation point were repeated five times.

At baseline, both spectacle and contact lenses were dispensed based on the spherical equivalent of cycloplegic manifest refraction and were refined using subjective refraction. At follow-up visits, children received new lenses if either their visual acuity had dropped by more than a full line of logMAR chart letters or if there had been a change in refractive error of −0.50 D or greater or at the clinician’s discretion if the child experienced visual symptoms.

To measure compliance, subjects were provided with a diary to record the number of hours the lenses were worn in a given day and the days on which the lenses were not worn. Data from this diary were used to compute compliance days with the following formula: Compliance Days = (Total Days in Study − Total Days Not Worn) × (Average Hours Worn Each Day/12).

\section*{Statistical analysis}

For the analysis, data for children who attended at least the 6-month visit were included in the analysis of progression of myopia. In the contact lens group, 15 children discontinued from baseline before 6 months primarily because of lens discomfort and loss to follow-up; therefore, information on the progression of myopia was not available for these children. Data for 45 children from the contact lens group and 40 children from the spectacle group were analyzed. Changes in spherical equivalent and axial length from baseline computed for each subject-eye were compared between the two groups at 6 and 12 months using a linear mixed model with fixed and subject random intercepts. The percentage of subject eyes that progressed by 0.75 D was analyzed using logistic regression with a robust estimate of variance. Both linear mixed model and logistic regression were adjusted for age at baseline, sex, parental myopia, compliance, and baseline values of the outcome variables, and both analyses accounted for the within-subject correlation of data. Based on the models, estimated means and odds ratios with their 95\% confidence intervals (CIs) were calculated. Peripheral refraction of the right eyes relative to central refraction was compared between the groups using repeated-measures ANOVA, with the degrees of eccentricity as the within-subject factor. The level of statistical significance was set at 5\%. Data analysis was performed in two programs (SPSS, version 17 [SPSS, Inc., Chicago, IL] and STATA, version 10 [StataCorp, College Station, TX]).
RESULTS

Figure 1 outlines the subject flow through the study, and Table 1 compares the biometric data of subjects in the contact lens and spectacle lens groups included in the analysis. The 15 children who discontinued before the 6-month visit did not differ significantly from those who continued in their baseline characteristics except for age (Table 2). At baseline, there were no significant differences between the contact lens and the spectacle lens groups in the relative numbers of boys and girls, the prevalence of parental myopia, axial length, and M and J45 refractive error components. The J0 component was slightly larger in the spectacle lens group. Although falling into the same overall age range, the spectacle lens group was slightly younger than the contact lens group. Adjustment was made for this age difference, as described.

Relative Peripheral Refractive Error Profile

The relative peripheral refractive error profiles for both subject groups at baseline are shown in Figure 2. Without the correcting lenses, the contact lens and spectacle lens groups exhibited similar amounts of relative hyperopia in the periphery, and there were no differences between the groups in the magnitude of relative hyperopia at any eccentricity (P = 0.157). For both subject groups, the rate of increase in relative hyperopia varied between the nasal and the temporal retinal hemifields. In the nasal field, there was little change in spherical-equivalent refractive error over the central 20°; thereafter, the relative hyperopia increased rapidly to +2.23 ± 1.51 D and +2.50 ± 1.09 D at the 40° nasal field eccentricity in the spectacle lens and contact lens groups, respectively. In the temporal field, the average degrees of relative hyperopia increased gradually to +1.46 ± 0.86 D and +1.77 ± 1.1 D at the 40° temporal field eccentricity for the spectacle lens and contact lens groups, respectively.

TABLE 1. Biometric Data of Subjects Enrolled in the Study

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Novel Contact Lens Group (n = 45)</th>
<th>Spectacle Group (n = 40)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.6 ± 1.5</td>
<td>10.8 ± 1.9</td>
<td>0.040</td>
<td></td>
</tr>
<tr>
<td>Girls/boys, %</td>
<td>51:49</td>
<td>43:57</td>
<td>0.515</td>
</tr>
<tr>
<td>Parental myopia, %</td>
<td>None</td>
<td>62.2</td>
<td>66.7</td>
</tr>
<tr>
<td>≥1 parent</td>
<td>37.8</td>
<td>32.5</td>
<td>0.858</td>
</tr>
<tr>
<td>Baseline M, D</td>
<td>−2.24 ± 0.79</td>
<td>−1.99 ± 0.62</td>
<td>0.193</td>
</tr>
<tr>
<td>Baseline J0, D</td>
<td>0.04 ± 0.19</td>
<td>0.18 ± 0.16</td>
<td>0.001</td>
</tr>
<tr>
<td>Baseline J45, D</td>
<td>−0.01 ± 0.14</td>
<td>−0.03 ± 0.13</td>
<td>0.691</td>
</tr>
<tr>
<td>Baseline axial length, mm</td>
<td>24.57 ± 0.77</td>
<td>24.57 ± 0.93</td>
<td>0.886</td>
</tr>
</tbody>
</table>

The standard design spectacle lenses increased the amount of relative peripheral hyperopia symmetrically in the nasal and temporal hemifields (P < 0.001 at 30° nasal and 40° temporal; P = 0.120 and P = 0.136 at 20° nasal and temporal). In contrast, and by design, the novel contact lenses reduced peripheral hyperopia. The reduction was most obvious in the nasal hemifield. Compared with spectacle lens–wearing eyes, the contact lens–wearing eyes had less hyperopic/myopic relative peripheral refractions (P < 0.001 at 20°, 30°, and 40° eccentricities in the nasal field and at the 30° and 40° eccentricities in the temporal field; P = 0.201 at 20° in the temporal field). Moreover, at the 20° and 30° nasal field eccentricities, average ametropias for the contact lens–wearing eyes were relatively more myopic than the central refractions.

Relative peripheral refractions in the nasal and temporal fields (each of the eccentricities) were assessed for association with progression of central myopia at 12 months (Table 3). After adjusting for age, sex, and parental myopia, relative peripheral refractions at the 30° and 40° nasal field eccentricities and the 40° temporal field eccentricity were negatively correlated with myopia progression (i.e., greater relative peripheral hyperopia at these field positions was associated with greater central progression at 12 months).

Spherical Equivalent: Changes at 6 and 12 Months

The spectacle lens group exhibited more change in SphE than the contact lens group at both 6 months (−0.57 ± 0.33 D vs. −0.28 ± 0.28 D; P < 0.001) and 12 months (−0.84 ± 0.47 D vs. −0.54 ± 0.37 D; P = 0.002) (Fig. 3). After adjusting for age, sex, parental myopia, baseline SphE, and compliance, the estimated progression mean at the 12-month visit was −0.86 D for the spectacle group (95% CI, −0.74 to −0.99 D) and −0.57 D for the contact lens group (95% CI, −0.45 to −0.69 D), a 34% reduction.

At 12 months, 59.4% of the spectacle lens–wearing eyes had progressed by at least −0.75 D in comparison to only 28.6% of the eyes in the contact lens group, with the odds of progressing by at least −0.75 D significantly higher in the spectacle lens group (odds ratio, 3.8; 95% CI, 1.5–9.5; P = 0.005).

Axial Length: Changes at 6 and 12 Months

Mean changes in axial length at 6 months were 0.26 ± 0.12 mm for the spectacle group versus 0.09 ± 0.11 mm for the contact lens group, and at 12 months they were 0.39 ± 0.19 mm versus 0.24 ± 0.17 mm, respectively (Fig. 3). Both sets of differences were significant (P < 0.001 and P = 0.001 at 6 and 12 months). After adjusting for age, sex, parental myopia, baseline axial length, and compliance, the estimated mean...
change in axial length at 12 months was 0.40 mm for the spectacle lens group (95% CI, 0.35–0.45 mm) and 0.27 mm for the contact lens group (95% CI, 0.22–0.32 mm), a 33% reduction.

Visual Acuity
Corrected high-contrast visual acuity measured in LogMAR units was not different between the spectacle lens– and the contact lens–wearing eyes at baseline (0.01 ± 0.04 for spectacle lens– vs. −0.02 ± 0.06 for contact lens–wearing eyes; \( P = 0.148 \)) or at the 6-month visit (0.05 ± 0.08 for spectacle lens– vs. 0.02 ± 0.06 for contact lens–wearing eyes; \( P = 0.125 \)). Moreover, presenting high-contrast visual acuities were not different between the spectacle lens– and the contact lens–wearing eyes at the 6-month (\( P = 0.761 \)) and 12-month (\( P = 0.577 \)) visits.

Corneal Radius of Curvature
There were no between-group differences in the radii of curvature of the cornea for the steep and flat meridians, as obtained with the IOL master at baseline and at 6 and 12 months (Table 4).

Compliance with Lens Wear
Children wearing spectacles reported that they wore spectacles for 350 ± 65 days compared with 296 ± 81 days for children wearing contact lenses. The difference between the groups was significant (\( P = 0.002 \)).

### Table 3. Relation between Relative Peripheral Hyperopia at Baseline (with Lenses) and Progression of Myopia at 12 Months

<table>
<thead>
<tr>
<th>Peripheral Field Position</th>
<th>Slope*</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20°</td>
<td>−0.04</td>
<td>0.528</td>
</tr>
<tr>
<td>30°</td>
<td>−0.09</td>
<td>0.016</td>
</tr>
<tr>
<td>40°</td>
<td>−0.06</td>
<td>0.012</td>
</tr>
<tr>
<td>Temporal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20°</td>
<td>−0.05</td>
<td>0.277</td>
</tr>
<tr>
<td>30°</td>
<td>−0.05</td>
<td>0.255</td>
</tr>
<tr>
<td>40°</td>
<td>−0.08</td>
<td>0.028</td>
</tr>
</tbody>
</table>

* Progression in myopia for every 1D increase in relative peripheral hyperopia.

**DISCUSSION**

After adjusting for factors that are known to influence myopia progression, such as age, sex, parental myopia, baseline refractive error, and compliance, the novel contact lenses that reduced relative peripheral hyperopia reduced myopia progression by approximately one-third in similar comparison with traditional spectacle lenses over the 12-month period. From a therapeutic perspective, it is important that this reduction in myopia progression was associated with a decrease in the axial elongation rate of the eye. It is important to note that, as reported previously,23 traditional single-vision spectacle lenses actually increased the degree of peripheral hyperopia from the uncorrected state.

The analysis included only data from subjects who attended at least the 6-month visit; data on change in or progression of myopia were not available for subjects who discontinued before the 6-month visit. Overall, the novel contact lenses used in this study produced a greater relative reduction in the rate of myopia progression than that observed in the previous study of spectacle lenses designed to reduce the degree of relative peripheral hyperopia.28 It is likely that the novel contact lenses were more widely effective in reducing myopia progression. At times, the peripheral treatment zones of the contact lenses were more consistent because they moved with the eyes and were located closer to the central retinas than were the peripheral treatment zones in the spectacle lenses. As illustrated in Figure 2, in comparison to the uncorrected state, the novel contact lenses reduced the amount of peripheral hyperopia, particularly in the nasal field, where the treated eyes showed absolute myopic peripheral refractions. In contrast, the treatment zones of the experimental spectacle lenses28 did not significantly reduce the degree of relative peripheral hyperopia at all within the 40° field.

Although the peripheral treatment zones of the novel contact lenses were concentric and radially symmetric, there were nasal-temporal asymmetries in the peripheral refractive error changes produced by the contact lenses, with a greater reduction of relative peripheral hyperopia in the nasal field than in the temporal field. A likely explanation for the asymmetry is that the lenses were systematically decentered from the visual axis, centering, as contact lenses usually do, on the geometric center of the cornea.

The present study used modified open-field autorefractor (NVision-K5001; Shin-Nippon) for central and peripheral re-
fractive error measurements. The small target (2.3 mm) has advantages when measuring eccentric angles because the small target diameter fits easily into the horizontal minor axis of the elliptical pupil. However, we have not determined whether the off-axis measurements taken through the novel, aspheric contact lenses are comparable to results obtained with an aberrometer.

Studies have indicated that reduction in the lag of accommodation\textsuperscript{14,15,18} and sustained and simultaneous myopic defocus may act to slow the progression of myopia.\textsuperscript{30,31} Bifocal contact lenses have also been found effective in controlling the progression of myopia in children with near esophoria.\textsuperscript{17} In the present study, it is possible that with lens decentration and with varying pupil sizes, portions of the treatment zone encroached on the pupil, resulting in some amount of simultaneous myopic defocus on the retina or a reduction in the lag or accommodation. It is a limitation of the study that effects such as accommodative lag, pupil size, and retinal image quality have not been specifically investigated; therefore, it is unclear whether the lenses played a role in the reduction of myopia by mechanisms other than the reduction of peripheral hyperopic defocus. In addition, as stated previously, the role of peripheral hyperopia as a risk factor for central myopia is uncertain.\textsuperscript{20} In a recent study, we found that overall there were no significant differences in the rates of progression of myopia for children wearing 1 of 3 experimental spectacle lenses designed to reduce relative peripheral hyperopia compared with a control single-vision lens. However, with one of the experimental designs, there was a statistically significant 30\% reduction in myopia progression over a 12-month period in a subgroup of children 6 to 12 years of age with a history of parental myopia.\textsuperscript{28} It is possible that the reduction in hyperopic defocus in children at higher risk for progression reduced the rate of progression of myopia.

Another limitation of the study was the lack of randomization (though each group had been randomly assigned to its respective treatment regimens in spectacles or contact lenses in separate studies). Although the contact and spectacle lens groups had similar entry criteria for age and other features, there was still a slight difference in age between the groups, with the spectacle group presenting at a slightly younger baseline age than the contact lens group. However, when we adjusted for age in the analyses, the percentage reduction in progression rates between the spectacle and contact lens groups was essentially unaffected by this difference. The percentage reduction based on observed means was 36\%, and it was 34\% based on estimated means. Another limitation was that information on the efficacy of the treatment was available only for a 1-year follow-up. Although some studies found optical treatment effects to continue beyond 12 months,\textsuperscript{12,18} the Correction of Myopia Evaluation trial found the effect to be limited to the first year of treatment.\textsuperscript{14} Clearly, further studies are required to determine the efficacy of these contact lenses in slowing the progression of myopia over several years.

Myopia control strategies based on manipulating peripheral vision might be more effective using contact lenses than spectacle lenses; however, many more children wear spectacle lenses than contact lenses. Moreover, factors such as convenience, ability to handle contact lenses, and potential adverse events are greater issues with contact lens wear. There is mounting

| TABLE 4. Corneal Radius of Curvature (mm) for the Spectacle Lens–and the Contact Lens–Wearing Eyes |
|---------------------------------|----------------|----------------|----------------|
|                                | Steeper meridian | Spectacle | Contact Lens |
|                                | n               | Novel Lens Group | n               | Contact Lens Group | n | Spectacle Group | n | Contact Lens Group | n | P   |
| Baseline                        | 45              | 7.67 ± 0.29 | 35              | 7.69 ± 0.27 | 0.730 |
| 6 months                        | 45              | 7.64 ± 0.31 | 35              | 7.67 ± 0.26 | 0.706 |
| 12 months                       | 43              | 7.64 ± 0.31 | 39              | 7.68 ± 0.27 | 0.558 |
| Flatter meridian                | 45              | 7.87 ± 0.29 | 35              | 7.87 ± 0.27 | 0.976 |
| 6 months                        | 45              | 7.86 ± 0.29 | 35              | 7.88 ± 0.26 | 0.820 |
| 12 months                       | 43              | 7.87 ± 0.29 | 39              | 7.90 ± 0.24 | 0.552 |

FIGURE 3. Change in spherical equivalent refractive error and axial length with spectacles and novel contact lenses.
Novel Contact Lens Reduces Relative Peripheral Hyperopia

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