

Defocus Incorporated Multiple Segments Spectacle Lenses Changed the Relative Peripheral Refraction: A 2-Year Randomized Clinical Trial

Han Yu Zhang,¹ Carly Siu Yin Lam,¹ Wing Chun Tang,¹ Myra Leung,^{1,2} and Chi Ho To¹

¹Centre for Myopia Research, School of Optometry, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong

²Discipline of Optometry and Vision Science, Faculty of Health, University of Canberra, Canberra, Australia

Correspondence: Carly Siu Yin Lam, Centre for Myopia Research, School of Optometry, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong; carly.lam@polyu.edu.hk

Received: November 6, 2019

Accepted: April 6, 2020

Published: May 27, 2020

Citation: Zhang HY, Lam CSY, Tang WC, Leung M, To CH. Defocus Incorporated Multiple Segments spectacle lenses changed the relative peripheral refraction: a 2-year randomized clinical trial. *Invest Ophthalmol Vis Sci.* 2020;61(5):53. <https://doi.org/10.1167/iovs.61.5.53>

PURPOSE. To compare changes in relative peripheral refraction (RPR) associated with myopia progression in myopic children wearing Defocus Incorporated Multiple Segments (DIMS) lenses and single vision (SV) spectacle lenses over 2 years.

METHODS. A 2-year double-blind, randomized controlled trial was conducted on 183 myopic children. Subjects were allocated to either wearing DIMS (n = 93) or SV spectacle lenses (n = 90). Peripheral refraction at 10°, 20°, and 30° of the nasal (10N, 20N, 30N) and temporal (10T, 20T, 30T) retinal eccentricities, central refraction, and axial length after cycloplegia were monitored every 6 months.

RESULTS. DIMS group showed symmetrical peripheral myopic shifts between the nasal and temporal retina (comparing myopic shifts between the nasal and temporal retina, the difference between the corresponding eccentricities were nonclinically significance). SV group showed asymmetrical peripheral myopic shifts between the nasal and temporal retina, with more myopic shifts (all $P \leq 0.001$) at 10T (-0.32 ± 0.62 diopters [D]), at 20T (-0.69 ± 0.95 D), and 30T (-0.85 ± 1.52 D). No significant changes in RPR spherical equivalent (M) were noted in the DIMS group, whereas significant increases (all $P < 0.0001$) in hyperopic RPR M were observed at 10N (0.27 ± 0.45 D), 20N (0.75 ± 0.72 D), and 30N (0.98 ± 0.76 D) in the SV group.

CONCLUSIONS. Wearing DIMS lenses resulted in a significantly different peripheral refraction profile and RPR changes, as well as significant myopia control effects when compared with SV lenses. Myopia control adopting myopic defocus in the midperiphery influenced peripheral refraction and slowed central myopia progression, most likely through alteration of overall retinal shape.

Keywords: myopia control, myopic defocus, relative peripheral refraction, retinal shape

Typically, myopes display hyperopic relative peripheral refraction (RPR), whereas emmetropes and hyperopes display myopic RPR.^{1,2} Previous studies on the relationship between RPR and myopia onset, and between RPR and myopia progression remains controversial.^{3–8} Hoogerheide et al.³ measured refraction along 120° of the horizontal visual field in young adults (hyperopes and emmetropes) who were undertaking pilot training. They found 65% of emmetropes and hyperopes who developed myopia afterward showed hyperopic RPR, however, it was not clear whether the RPR was measured at the beginning or at the end of the study.⁹ This was the first longitudinal study to report the relationship between RPR and myopia development.

Mutti et al.⁸ found that more hyperopic RPR within 2 to 4 years before myopia onset may be one of the factors predicting the onset of myopia; however, RPR was stable from the year of onset to 5 years following myopia onset. In a later report, Mutti et al.⁴ investigated children from different ethnicities, including Asians, African-Americans,

and Caucasians, and reported that RPR showed a weak consistent influence on the risk of myopia onset and development or axial elongation. Sng et al.⁵ monitored changes in central and peripheral refraction in Singapore Chinese children over 1 year and found that peripheral refraction did not predict myopia onset or influence myopia progression.

It has been well documented among animal studies that more hyperopic defocus leads to greater myopia progression,^{10,11} while inducing myopic defocus retarded myopia progression.^{10,12–14} Findings in infant monkeys^{12,13} and chicks^{10,14} suggested that spatial resolution at the anatomic level of the optical pathway could modulate overall eye growth.¹⁵ Animal studies using contact lenses with embedded myopic defocus found that myopia progression could be slowed by 20% to 60%.^{16–19}

In our previous clinical trial, using the Defocus Incorporated Soft Contact lenses, which incorporated a myopic defocus of +2.50 diopters (D) for myopic children, significant retardation of myopia progression of approximately 60% over 2 years was seen for those who wore these lenses



for more than 7 hours per day.¹⁷ In another study using the MiSight soft contact lenses (Cooper Vision, Inc., Pleasanton, CA, USA) or single vision (SV) contact lenses in a randomized clinical trial, there was significantly less myopia progression by 59% and less axial elongation by 52% in children who wore MiSight lenses for 3 years compared with children who wore SV contact lenses.¹⁹ This suggested that myopic defocus could slow myopia progression in myopic children.^{17,19}

When correcting myopia using traditional spectacle lenses, on-axis light will focus on the fovea, whereas off-axis light will lead to peripheral hyperopic defocus^{20,21}; this has been hypothesized to be a possible trigger for myopia progression. Sankaridurg et al.²² found there were no statistically significant effects in myopia retardation after wearing spectacle lenses with incorporated myopic defocus in the periphery over 1 year compared with SV lenses.¹⁶ This differed from the results of our recent Defocus Incorporated Multiple Segments (DIMS) spectacles clinical trial. The DIMS lens comprises a central correction zone surrounded by multiple segments of constant myopic defocus (+3.50 D) at the midperiphery, which can simultaneously provide clear central vision and peripheral myopic defocus.²³ We previously reported that wearing the DIMS lenses over 2 years resulted in significant retardation of myopia progression of up to 59% and slowing of axial elongation by up to 60% when compared with wearing SV spectacle lenses.²³

The majority of previous studies of investigating myopic defocus have reported myopia control effects as changes in ocular refraction and axial length (AL), with few reporting the changes in retinal shape. Some studies have reported that retinal shape might be a determinant for the development of myopia through biomechanical factors, such as the thinning of the sclera and localized ectasia of the posterior sclera during myopia development.^{24,25} Significant correlations between peripheral eye length and peripheral refraction have been found.^{26–28} Therefore peripheral refraction or RPR, which can be easily measured and monitored by clinicians, have been used to indirectly describe the retinal shape.^{15,29} To date, few studies have reported changes of RPR after myopia control using myopic defocus in humans. In the DIMS project,²³ the effects of DIMS spectacle lens wear on RPR was investigated. The changes in RPR and retinal shape between the DIMS and SV groups were reported in the current article. The data from the DIMS project²³ were used in the current article to investigate the influence of DIMS and SV spectacle lens wear on RPR.

METHODS

A randomized and double-blind clinical trial was conducted at the Centre for Myopia Research, School of Optometry, the Hong Kong Polytechnic University between August 2014 and July 2017.²³ The children were randomly assigned to wear either the DIMS lens (treatment group) or SV spectacle lens (control group). The recruitment criteria are listed as follows.

Inclusion criteria were:

1. Hong Kong Chinese children ages 8–13 years
2. Central spherical equivalent (M): -1.00 to -5.00 D
3. Astigmatism and anisometropia of 1.50 D or less
4. Monocular best-corrected visual acuity of 0.00 logMAR (6/6) or better
5. Acceptance of random group allocation and the masked study design

Exclusion criteria were:

1. Strabismus and binocular vision abnormalities
2. Ocular and systemic abnormalities
3. Prior experience of myopia control

The study was approved by the Human Subjects Ethics Subcommittee of The Hong Kong Polytechnic University and adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from the parents or guardians of all participants. The procedure of randomization has been described previously.²³ The children and their parents were masked to group allocation. The masking procedures fulfilled the Consolidated Standards of Reporting Trials Requirements for a double-blinded trial.

A standardized eye examination was performed every 6 months over the 2-year trial period. Corneal power was measured by Shin-Nippon NVision-K 5001 (Ajinomoto Trading Inc., Tokyo, Japan) autorefractor without cycloplegia. One drop of proparacaine 0.4% followed by 1 to 2 drops of cyclopentolate HCL 1% were used to induce cycloplegia. Central and peripheral refraction across the horizontal retinal eccentricities were measured five times by using a Shin-Nippon NVision-K 5001 autorefractor with the Maltese cross-target placed at the straight-ahead position (center) and 10° , 20° , and 30° at nasal (10N, 20N, 30N) and temporal (10T, 20T, 30T) retinal eccentricity. Subjects were asked to keep their head stationary and turn their eyes to fixate on the different targets.³⁰ Peripheral refraction was measured in the right eye because the ocular biometry between the two eyes was highly correlated.^{23,31} In this group of children, the correlation coefficient between right and left eye was 0.91 for the central M , 0.97 for AL, 0.94 for the steep corneal curvature, and 0.97 for flat corneal curvature.²³ AL was measured five times by using the IOL Master (Carl Zeiss, Oberkochen, Germany) and then averaged. Spherocylindrical refraction measurements regarding spherical power (S), cylindrical power (C), and axis (θ) were converted into a power vector by a conventional formula for analysis.³²

$$M = S + C/2$$

$$J_0 = -(C/2)\cos(2\theta)$$

$$J_{45} = -(C/2)\sin(2\theta)$$

Positive J_0 represents with-the-rule astigmatism, whereas negative results represent against-the-rule astigmatism. The J_{45} stands for oblique astigmatism. RPR is calculated as central refraction subtracted from peripheral refraction. A positive RPR is considered hyperopic RPR, whereas negative RPR is considered myopic RPR. Our previous article reported that there were no statistically significant differences in age, sex proportion, central M , or AL between the DIMS and SV groups ($P > 0.05$) at baseline.²³

Data Analyses

All statistical analyses were performed using IBM SPSS v.16.0 (IBM Corporation, Armonk, NY, USA). The right eye was used for data analyses, and all data were normally distributed. Repeated measures ANOVA was used to assess the impact of DIMS and SV lenses wear on the changes of peripheral refraction and RPR over time. Independent t -tests were used to compare differences in RPR between the two

TABLE 1. Mean (SD) of Peripheral Refraction *M* in the DIMS and SV Group Over 2 Years

| Group | 10T | 20T | 30T | 10N | 20N | 30N |
|-----------------------|--------------|--------------|--------------|--------------|--------------|--------------|
| <i>Baseline</i> | | | | | | |
| DIMS | -3.00 (1.02) | -2.71 (1.23) | -1.60 (1.58) | -2.81 (0.99) | -2.10 (1.22) | -1.07 (1.33) |
| SV | -2.78 (0.98) | -2.68 (1.23) | -2.09 (1.74) | -2.62 (0.93) | -1.99 (1.06) | -0.93 (1.28) |
| <i>P</i> [†] | 0.16 | 0.86 | 0.14 | 0.21 | 0.55 | 0.49 |
| <i>6-Month</i> | | | | | | |
| DIMS | -3.16 (0.99) | -2.81 (1.15) | -1.91 (1.24) | -2.94 (1.26) | -2.21 (1.29) | -1.30 (1.41) |
| SV | -3.16 (1.01) | -2.99 (1.16) | -2.16 (1.56) | -2.95 (1.01) | -1.87 (1.19) | -0.79 (1.38) |
| <i>P</i> [†] | 0.98 | 0.32 | 0.40 | 0.96 | 0.08 | 0.02 |
| <i>12-Month</i> | | | | | | |
| DIMS | -3.19 (0.98) | -2.98 (1.05) | -1.81 (1.15) | -3.09 (1.15) | -2.29 (1.38) | -1.28 (1.50) |
| SV | -3.37 (1.07) | -3.10 (1.09) | -2.11 (1.66) | -3.03 (1.12) | -1.97 (1.27) | -0.76 (1.39) |
| <i>P</i> [†] | 0.26 | 0.85 | 0.32 | 0.74 | 0.12 | 0.003* |
| <i>18-Month</i> | | | | | | |
| DIMS | -3.28 (1.02) | -3.15 (1.12) | -2.27 (1.16) | -3.20 (1.13) | -2.40 (1.24) | -1.47 (1.54) |
| SV | -3.62 (1.11) | -3.46 (1.16) | -2.47 (1.63) | -3.18 (1.16) | -2.00 (1.28) | -0.70 (1.53) |
| <i>P</i> [†] | 0.05 | 0.08 | 0.45 | 0.94 | 0.05 | 0.003* |
| <i>24-Month</i> | | | | | | |
| DIMS | -3.34 (1.10) | -3.14 (1.20) | -2.19 (1.35) | -3.32 (1.26) | -2.57 (1.41) | -1.73 (1.68) |
| SV | -3.69 (1.20) | -3.50 (1.16) | -2.74 (1.56) | -3.21 (1.37) | -2.08 (1.43) | -0.79 (1.60) |
| <i>P</i> [†] | 0.06 | 0.06 | 0.03 | 0.59 | 0.03 | <0.0001* |

[†] The *P* value was considered as significant if <0.008 after Bonferroni adjustment.

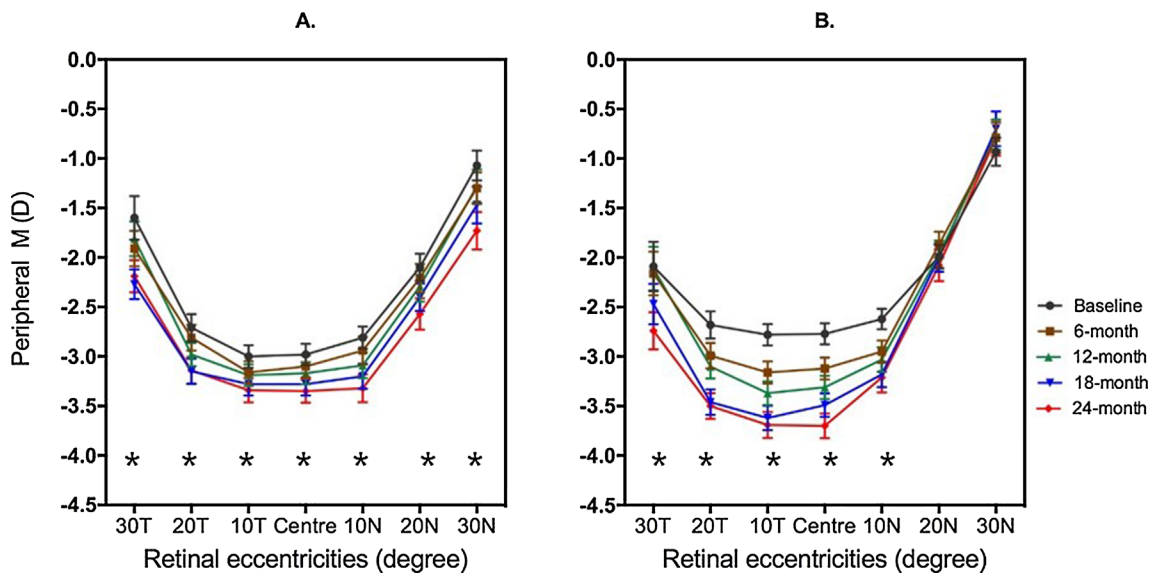


FIGURE 1. (A) Peripheral refraction changes across the horizontal retina over 2 years in the DIMS group. (B) Peripheral refraction changes across the horizontal retina over 2 years in the SV group. Error bars denote the SEM. The significance of the *P* value was considered as <0.008 after Bonferroni adjustment. **P* <0.008 indicates the significant difference between baseline and 24 months within the group (paired *t*-test).

groups. The difference in refractive error between the nasal retina and temporal retina was compared by a paired *t*-test. With changes in central *M* and changes in AL as the dependent variable, linear regressions were performed to analyze the relationship between (1) baseline RPR *M* and myopic shifts, (2) baseline RPR *M* and axial elongation, (3) changes in RPR *M* and myopic shifts, and (4) changes in RPR *M* and axial elongation, adjusting for sex and age in the SV group. A *P* value of <0.05 was considered statistically significant; Bonferroni adjustment was applied when applicable. The adjusted significance level was set to 0.008 as refraction was measured at six retinal eccentricities in the right eye of each subject.

RESULTS

Peripheral Refraction (*M*, *J*₀, *J*₄₅)

Table 1 and Figure 1 show the results of peripheral *M* in the DIMS and SV groups at 6-month intervals. There were no significant differences in peripheral refraction *M* across the horizontal retina between the two groups at the baseline (independent *t*-test, *P* > 0.05). After 2 years, both groups have shown a steady increase in myopic shift centrally and peripherally, but the patterns of the shift were different.

All the horizontal retinal eccentricities in the DIMS showed myopic shifts in peripheral *M* with a range from -0.34 to -0.60 D (paired *t*-test, *P* < 0.0001), and presenting

TABLE 2. Mean (SD) of RPR M in the DIMS and SV Group Over 2 Years

| Group | 10T | 20T | 30T | 10N | 20N | 30N |
|-----------------|--------------|-------------|-------------|-------------|-------------|-------------|
| <i>Baseline</i> | | | | | | |
| DIMS | -0.03 (0.47) | 0.26 (0.91) | 1.39 (1.49) | 0.16 (0.41) | 0.88 (0.89) | 1.89 (1.20) |
| SV | -0.01 (0.35) | 0.09 (0.93) | 0.66 (1.64) | 0.15 (0.38) | 0.78 (0.72) | 1.84 (1.15) |
| P^\dagger | 0.77 | 0.25 | 0.02 | 0.84 | 0.46 | 0.80 |
| <i>6-Month</i> | | | | | | |
| DIMS | -0.05 (0.41) | 0.29 (0.75) | 1.15 (0.97) | 0.16 (0.82) | 0.89 (0.94) | 1.80 (1.07) |
| SV | -0.04 (0.34) | 0.13 (0.72) | 0.97 (1.40) | 0.18 (0.44) | 1.25 (0.86) | 2.33 (1.19) |
| P^\dagger | 0.77 | 0.17 | 0.46 | 0.90 | 0.01 | 0.003* |
| <i>12-Month</i> | | | | | | |
| DIMS | -0.01 (0.42) | 0.19 (0.70) | 1.21 (1.05) | 0.08 (0.46) | 0.88 (0.87) | 1.90 (1.18) |
| SV | -0.06 (0.34) | 0.21 (0.67) | 1.15 (1.45) | 0.28 (0.60) | 1.35 (0.92) | 2.55 (1.26) |
| P^\dagger | 0.44 | 0.86 | 0.81 | 0.02 | 0.001* | 0.001* |
| <i>18-Month</i> | | | | | | |
| DIMS | 0.00 (0.45) | 0.14 (0.80) | 1.05 (0.99) | 0.09 (0.78) | 0.88 (1.00) | 1.84 (1.35) |
| SV | -0.13 (0.35) | 0.03 (0.70) | 0.96 (1.23) | 0.31 (0.55) | 1.48 (0.90) | 2.70 (1.31) |
| P^\dagger | 0.04 | 0.34 | 0.67 | 0.04 | <0.0001* | <0.0001* |
| <i>24-Month</i> | | | | | | |
| DIMS | 0.01 (0.47) | 0.21 (0.78) | 1.15 (1.31) | 0.03 (0.56) | 0.80 (0.89) | 1.63 (1.42) |
| SV | 0.01 (0.68) | 0.20 (0.80) | 1.00 (1.39) | 0.49 (0.86) | 1.62 (1.10) | 2.88 (1.42) |
| P^\dagger | 0.98 | 0.97 | 0.52 | <0.0001* | <0.0001* | <0.0001* |

[†] The P value was considered as significant if <0.008 after Bonferroni adjustment.

a symmetrical pattern of myopic shifts between the nasal and temporal retina (Fig. 1). When comparing between the nasal and temporal retina, the difference between the corresponding eccentricities were all clinically not significant, with the mean difference at 10° was 0.17 ± 0.49 D ($P = 0.003$), at 20° was 0.04 ± 0.71 D ($P = 0.65$), and at 30° was 0.23 ± 1.71 D ($P = 0.37$).

The SV group showed significant myopic shifts at certain eccentricities, with a larger range from -0.59 to -0.91 D ($P < 0.0001$) over 2 years, and presenting an asymmetrical pattern of myopic shifts between the nasal and temporal retina (Fig. 1). There were more myopic shifts at the temporal retina compared with the nasal retina over 2 years; mean difference at 10° was -0.32 ± 0.62 D ($P < 0.0001$), at 20° was -0.69 ± 0.95 D ($P < 0.0001$), and at 30° was -0.85 ± 1.52 D ($P = 0.001$).

In fact, the DIMS group showed a more uniform myopic shift at all eccentricities, whereas the SV group presented an asymmetrical myopic shift. Comparison of the two groups revealed that the DIMS group had significantly more myopic shifts in peripheral M at 30N (mean difference -0.70 ± 0.18 D, $P < 0.0001$) and 20N (mean difference -0.38 ± 0.14 D, $P = 0.006$) but significantly less myopic shifts at 10T (mean difference 0.57 ± 0.12 D, $P < 0.0001$) compared with the SV group over the 2-year observation period.

There were no statistically significant differences in peripheral J_0 and J_{45} between the two groups at baseline (at all eccentricities, $P > 0.05$). After 2 years, peripheral J_0 showed significant positive shifts at 10T and 20T, with the changes of 0.25 ± 0.33 D ($P < 0.0001$) and 0.25 ± 0.47 D ($P < 0.0001$), respectively, in the DIMS group. In the SV group, significant positive shifts were observed at 10T (mean difference: 0.29 ± 0.28 D, $P < 0.0001$), 20T (mean difference: 0.54 ± 0.50 D, $P < 0.0001$), 20N (mean difference: 0.17 ± 0.38 , $P < 0.0001$), and 30N (mean difference: 0.16 ± 0.47 , $P = 0.004$). There were no changes in peripheral J_{45} within the DIMS or SV groups (at all eccentricities, $P > 0.05$). There was no significant difference of peripheral J_0 between two groups after 2 years nor in periph-

eral J_{45} over 2 years after Bonferroni correction ($P > 0.008$; Fig. 2).

Relative Peripheral Refraction M

Table 2 and Figure 3 describe the RPR M in the DIMS and SV groups over 2 years. There was no significant difference in RPR M between the DIMS and SV groups at baseline after Bonferroni correction (at all eccentricities, all $P > 0.008$).

After 2 years, the myopic shifts in all the peripheral refractions increased proportionally with the central refraction, and therefore maintained a rather constant RPR M in the DIMS group. Despite a significant decrease of hyperopic RPR M at 10N (mean difference -0.13 ± 0.43 D, $P < 0.0001$) in the DIMS group, all the changes were regarded to be clinically negligible.

In the SV group, significant hyperopic shifts in RPR were seen at the nasal retina, with mean changes of 0.27 ± 0.45 D, 0.75 ± 0.72 D, and 0.98 ± 0.76 D at 10N, 20N, and 30N ($P < 0.0001$) but no significant changes were shown in the temporal retina. The RPR presented a skewed pattern.

Comparison of the two groups revealed that the SV group had significantly greater hyperopic RPR M at 10N (mean difference 0.46 ± 0.11 D, $P < 0.0001$), 20N (mean difference 0.82 ± 0.16 D, $P < 0.0001$), and 30N (mean difference 1.25 ± 0.23 D, $P < 0.0001$) but not in the temporal retina when compared with the DIMS group.

Correlation of RPR M and Other Factors

In the SV group, there was no significant association between either baseline RPR M and myopic progression nor baseline RPR M and axial elongation at all eccentricities (linear regression, $P > 0.05$). However, the changes in RPR M at 10N showed a significant association with myopia progression (standardized coefficient: 0.84 , $P = 0.003$), and axial elongation (standardized coefficient: -0.79 , $P = 0.004$) after adjusting for sex and age.

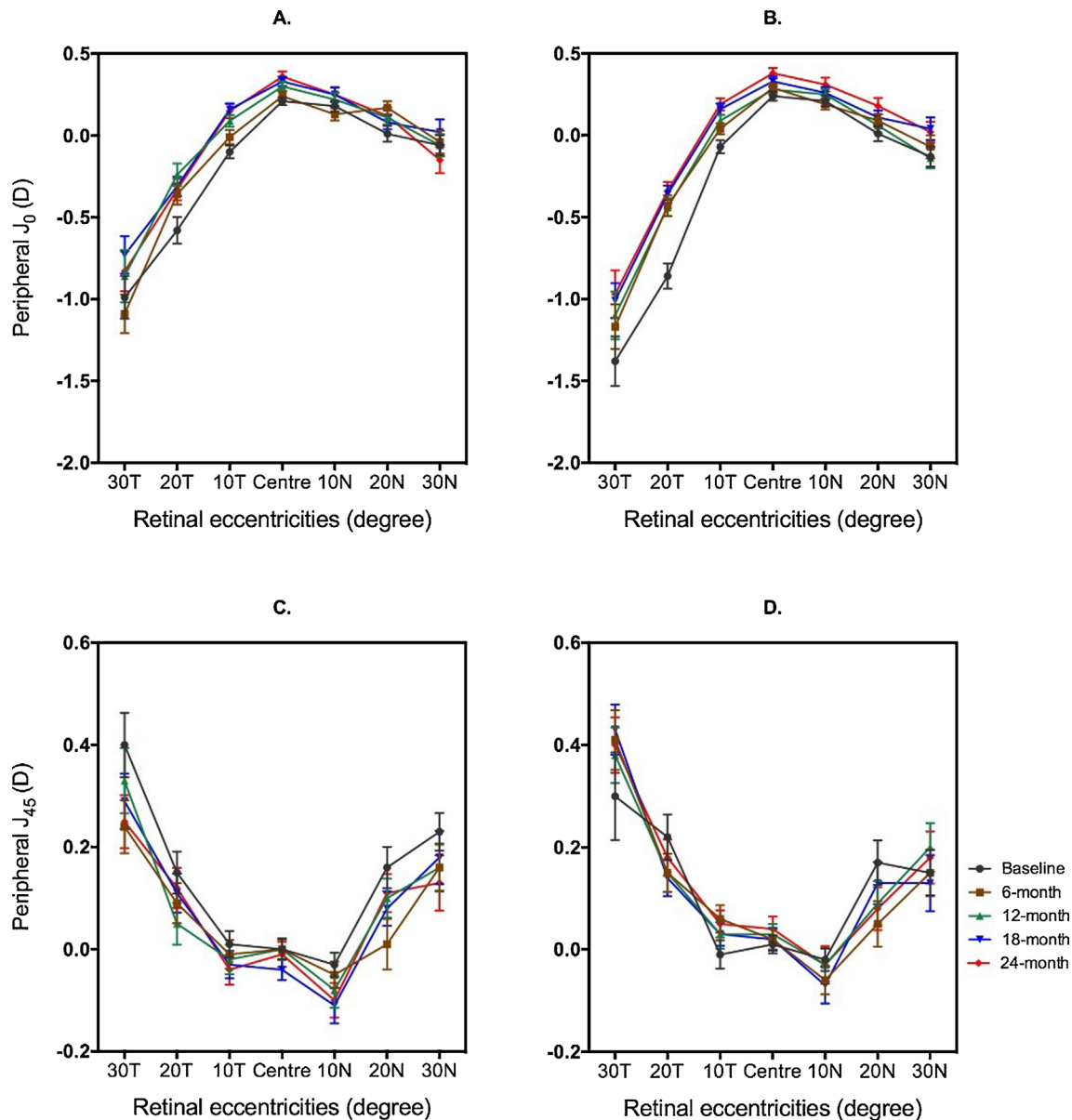


FIGURE 2. (A) Peripheral J_0 changes across the horizontal retina over 2 years in the DIMS group. (B) Peripheral J_0 changes across the horizontal retina over 2 years in the SV group. (C) Peripheral J_{45} changes across the horizontal retina over 2 years in the DIMS group. (D) Peripheral J_{45} changes across the horizontal retina over 2 years in the SV group. Error bars denote SEM.

DISCUSSION

The current study aimed to provide insight into the change of the retinal shape following the use of myopic defocus for myopia control. We measured the peripheral refraction and RPR changes between children wearing SV and DIMS spectacles in a randomized controlled trial over 2 years.

Over the 2 years, subjects in the SV group were found to have greater changes in peripheral M in the temporal retina (nasal visual field) compared with the nasal retina (temporal visual field), presenting as an asymmetric change, and this asymmetry increased during myopia progression, which is consistent with previous reports.^{6,33} Some studies suggested that this asymmetry can be explained by a combination of a few factors, including the difference in angle between the optical axis and visual axis (angle alpha),^{34,35} asymmetries

in vitreous chamber depth,³⁶ and corneal curvature.³⁷ The increased asymmetric peripheral profile has been suggested to be caused by the different rates of ocular expansion along the axial and equatorial region during myopia progression, and particularly in eyes with faster myopia progression.⁶ In contrast, after the myopia treatment of DIMS lenses, children showed significant changes in peripheral M at all retinal eccentricities, which indicated a uniform myopic shift along the horizontal retina. It could be speculated that children in the DIMS group experienced a relatively slower and uniform eye growth, whereas in the SV group, there was a relatively faster axial expansion than the equatorial region.

RPR changes were also different between the two groups. In the SV group, a significant increase in hyperopic RPR M at the nasal retina (ranging from approximately 0.27–0.98 D)

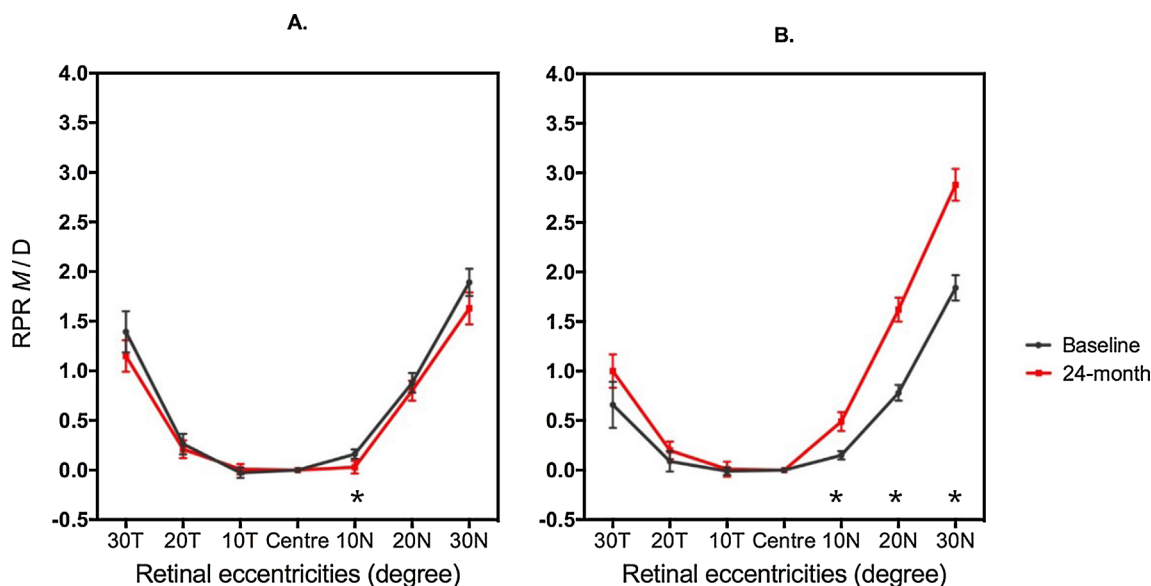


FIGURE 3. (A) RPR changes across horizontal retina over 2 years in the DIMS group. (B) RPR changes across horizontal retina over 2 years in the SV group. Error bars denote SEM. The significance of the P value was considered as <0.008 after Bonferroni adjustment. * $P < 0.008$ indicates the significant difference between baseline and 24 months within the group (paired t -test).

was found over 2 years, whereas PRP M showed a slightly statistical change in the DIMS group, but it was not clinically significant. To the best of our knowledge, this is the first human study to report this result. Among animal studies, contradictory findings have been reported from a guinea pig study³⁸; there was a significant increase in hyperopic RPR M after superimposing myopic defocus in the periphery. It is supposed that there may be an area of retina that can decode signs of defocus and result in local retinal area changes.³⁷ Such an ability to decode depends on the area or threshold of the defocus, which may be different in humans compared with other animals.³⁸

Although the changes in RPR M at 10N showed a significant association with central myopic shift and axial elongation over 2 years in the SV group, the baseline RPR M could not predict myopia progression or axial elongation, which is consistent with previous studies.⁴⁻⁷ Mutti et al.⁴ observed the changes in peripheral refraction at 30° nasal visual field and found peripheral refraction exerted a weak influence on predicting myopia onset or progression. Hyperopic RPR was more likely to be a consequence of axial elongation rather than a cause of the myopia progression.³⁹ This is because the AL increased to a larger extent than the equatorial diameter when eyeball elongation, resulting in a relatively more prolate ocular shape,^{1,40} which can be seen as less myopia in the peripheral retina than the central fovea.

It has been suggested that RPR could be used to indirectly describe the retinal shape.^{15,29} A higher hyperopic RPR suggested a less curved image shell compared with the retinal shape,⁴¹ and when corneal curvature and AL are constant, a higher hyperopic RPR indicated a steeper retinal shape.²⁹ This suggested the image shell with a reduced curve compared with the retinal shape of the SV group indicated a steeper retinal shape, whereas there was a flatter retinal shape in the DIMS group.

Regarding the asymmetrical profile in the SV group, the mechanism of the inhibited peripheral expansion in the SV group remained unclear, and various potential mecha-

nisms have been discussed in a previous study by Mutti et al.⁸ The authors indicated that insufficient lens material might prevent the eye from stretching equatorially as the eye grows.^{1,8}

We proposed that the uniform pattern of eye growth that stimulated more peripheral eye growth might be a mechanism of normal eye growth or emmetropization process. In this study, retardation of myopia progression and axial elongation in the DIMS group may be interpreted as switching back to a coordinated eye growth. In the SV group, the axial elongation increased faster than the equatorial region and may indicate a noncoordinated eye growth. A suggestion of equatorial restriction of the growing eye has the potential to accentuate axial elongation.⁴²

Recently, Pan⁴³ reported that the signaling of ON-OFF retinal ganglion cells (RGCs) in the mouse retina could be changed by a defocused image, and showed different responses to varied powers of defocus image.⁴⁴ We assumed the signaling of RGCs might be altered by the defocus power in the DIMS lens and resulting in a uniform and symmetrical pattern change in the peripheral refraction. Nevertheless, further animal studies will be needed.

One of the limitations of this study was that the peripheral eye length was not measured; measuring peripheral eye length could enable determination of the actual peripheral eye growth situation. It is worth noting that the wide range of the standard deviations relative to the mean RPR values could indicate that the actual retinal shape may be variable.^{2,15}

Few studies have investigated the changes of peripheral refraction or RPR during myopia control, and to our knowledge this is the first study that demonstrated myopia control using myopic defocus with simultaneous clear vision results in changes in the midperipheral refraction and RPR compared with SV lenses. Our current description of retinal shape in two groups may only be part of the wider picture; further study on investigating the retinal or eye shape need to be conducted by using imaging examination,

such as magnetic resonance imaging or B-ultrasonography. More work on the understanding of the mechanism on the pattern of peripheral refraction changes in myopia control utilizing myopic defocus are required.

CONCLUSIONS

To our knowledge, this is the first study to demonstrate myopia control using myopic defocus with simultaneous clear vision results in changes in the peripheral refraction. Myopia control using myopic defocus in the midperiphery influenced changes in peripheral refraction and slowed central myopia progression, most likely through alteration of overall retinal shape. Further studies to elucidate the mechanism of this intervention are warranted.

Acknowledgments

The authors thank Maureen Boost for proofreading, Roger Pak Kin Lee for data collection, and Yee Mui Kwok for liaison with the parents and data entry.

Supported by PolyU Grant 1-87LK and was partly supported by collaborative research by HOYA Corporation, Tokyo, Japan, and PolyU Grant no. H-ZG3B.

Disclosure: **H.Y. Zhang**, None; **C.S.Y. Lam**, HOYA Corporation (F), HOYA Corporation (P); **W.C. Tang**, None; **M. Leung**, None; **C.H. To**, HOYA Corporation (F), HOYA Corporation (P)

References

- Mutti DO, Sholtz RI, Friedman NE, Zadnik K. Peripheral refraction and ocular shape in children. *Invest Ophthalmol Vis Sci.* 2000;41:1022–1030.
- Sng CC, Lin XY, Gazzard G, et al. Peripheral refraction and refractive error in Singapore Chinese children. *Invest Ophthalmol Vis Sci.* 2011;52:1181–1190.
- Hoogerheide J, Rempt F, Hoogenboom W. Acquired myopia in young pilots. *Ophthalmologica.* 1971;163:209–215.
- Mutti DO, Sinnott LT, Mitchell GL, et al. Relative peripheral refractive error and the risk of onset and progression of myopia in children. *Invest Ophthalmol Vis Sci.* 2011;52:199–205.
- Sng CC, Lin XY, Gazzard G, et al. Change in peripheral refraction over time in Singapore Chinese children. *Invest Ophthalmol Vis Sci.* 2011;52:7880–7887.
- Lee TT, Cho P. Relative peripheral refraction in children: twelve-month changes in eyes with different ametropias. *Ophthalmic Physiol Opt.* 2013;33:283–293.
- Radhakrishnan H, Allen PM, Calver RI, et al. Peripheral refractive changes associated with myopia progression. *Invest Ophthalmol Vis Sci.* 2013;54:1573–1581.
- Mutti DO, Hayes JR, Mitchell GL, et al. Refractive error, axial length, and relative peripheral refractive error before and after the onset of myopia. *Invest Ophthalmol Vis Sci.* 2007;48:2510–2519.
- Rosén R, Lundström L, Unsbo P, Atchison DA. Have we misinterpreted the study of Hoogerheide et al. (1971)? *Optom Vis Sci.* 2012;89:1235–1237.
- Tse DY, Lam CS, Guggenheim JA, et al. Simultaneous defocus integration during refractive development. *Invest Ophthalmol Vis Sci.* 2007;48:5352–5359.
- Smith EL, 3rd, Hung LF, Huang J. Relative peripheral hyperopic defocus alters central refractive development in infant monkeys. *Vision Res.* 2009;49:2386–2392.
- Arumugam B, Hung LF, To CH, Holden B, Smith EL, 3rd. The effects of simultaneous dual focus lenses on refractive development in infant monkeys. *Invest Ophthalmol Vis Sci.* 2014;55:7423–7432.
- Arumugam B, Hung LF, To CH, Sankaridurg P, Iii EL. The effects of the relative strength of simultaneous competing defocus signals on emmetropization in infant rhesus monkeys. *Invest Ophthalmol Vis Sci.* 2016;57:3949–3960.
- Liu Y, Wildsoet C. The effect of two-zone concentric bifocal spectacle lenses on refractive error development and eye growth in young chicks. *Invest Ophthalmol Vis Sci.* 2011;52:1078–1086.
- Stone R, Flitcroft D. Ocular shape and myopia. *Ann Acad Med Singapore.* 2004;33:7–15.
- Sankaridurg P, Holden B, Smith E, 3rd, et al. Decrease in rate of myopia progression with a contact lens designed to reduce relative peripheral hyperopia: one-year results. *Invest Ophthalmol Vis Sci.* 2011;52:9362–9367.
- Lam CS, Tang WC, Tse DY, Tang YY, To CH. Defocus Incorporated Soft Contact (DISC) lens slows myopia progression in Hong Kong Chinese schoolchildren: a 2-year randomised clinical trial. *Br J Ophthalmol.* 2014;98:40–45.
- Anstice NS, Phillips JR. Effect of dual-focus soft contact lens wear on axial myopia progression in children. *Ophthalmology.* 2011;118:1152–1161.
- Chamberlain P, Peixoto-de-Matos SC, Logan NS, Ngo C, Jones D, Young G. A 3-year randomized clinical trial of MiSight lenses for myopia control. *Optom Vis Sci.* 2019;96:556–567.
- Lin Z, Martinez A, Chen X, et al. Peripheral defocus with single-vision spectacle lenses in myopic children. *Optom Vis Sci.* 2010;87:4–9.
- Taberner J, Vazquez D, Seidemann A, Uttenweiler D, Schaeffel F. Effects of myopic spectacle correction and radial refractive gradient spectacles on peripheral refraction. *Vision Res.* 2009;49:2176–2186.
- Sankaridurg P, Donovan L, Varnas S, et al. Spectacle lenses designed to reduce progression of myopia: 12-month results. *Optom Vis Sci.* 2010;87:631–641.
- Lam CSY, Tang WC, Tse DY, et al. Defocus Incorporated Multiple Segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. *Br J Ophthalmol.* 2020;104:363–368.
- McBrien NA, Gentle A. Role of the sclera in the development and pathological complications of myopia. *Prog Retin Eye Res.* 2003;22:307–338.
- Rada JAS, Shelton S, Norton TT. The sclera and myopia. *Exp Eye Res.* 2006;82:185–200.
- Schmid G. Retinal steepness vs. myopic shift in children. 2004;12:23.
- Verkicharla PK, Suheimat M, Schmid KL, Atchison DA. Peripheral refraction, peripheral eye length, and retinal shape in myopia. *Optom Vis Sci.* 2016;93:1072–1078.
- Mutti DO, Sinnott LT, Reuter KS, et al. Peripheral refraction and eye lengths in myopic children in the bifocal lenses in nearsighted kids (BLINK) study. *Transl Vis Sci Technol.* 2019;8(2):17.
- Verkicharla PK, Mathur A, Mallen EA, Pope JM, Atchison DA. Eye shape and retinal shape, and their relation to peripheral refraction. *Ophthalmic Physiol Opt.* 2012;32:184–199.
- Radhakrishnan H, Charman WN. Peripheral refraction measurement: does it matter if one turns the eye or the head? *Ophthalmic Physiol Opt.* 2008;28:73–82.
- Lam CS, Lam CH, Cheng SC, Chan LY. Prevalence of myopia among Hong Kong Chinese schoolchildren: changes over two decades. *Ophthalmic Physiol Opt.* 2012;32:17–24.
- Thibos LN, Wheeler W, Horner D. Power vectors: an application of Fourier analysis to the description and statistical analysis of refractive error. *Optom Vis Sci.* 1997;74:367–375.

33. Atchison DA, Pritchard N, White SD, Griffiths AM. Influence of age on peripheral refraction. *Vision Res.* 2005;45:715–720.
34. Calver R, Radhakrishnan H, Osuobeni E, O'Leary D. Peripheral refraction for distance and near vision in emmetropes and myopes. *Ophthalmic Physiol Opt.* 2007;27:584–593.
35. Charman WN, Atchison DA. Decentred optical axes and aberrations along principal visual field meridians. *Vision Res.* 2009;49:1869–1876.
36. Smith EL, 3rd, Hung LF, Huang J, Arumugam B. Effects of local myopic defocus on refractive development in monkeys. *Optom Vision Sci.* 2013;90:1176–1186.
37. Atchison DA, Pritchard N, Schmid KL. Peripheral refraction along the horizontal and vertical visual fields in myopia. *Vision Res.* 2006;46:1450–1458.
38. Bowrey HE, Zeng G, Tse DY, et al. The effect of spectacle lenses containing peripheral defocus on refractive error and horizontal eye shape in the guinea pig. *Invest Ophthalmol Vis Sci.* 2017;58:2705–2714.
39. Atchison DA, Jones CE, Schmid KL, et al. Eye shape in emmetropia and myopia. *Invest Ophthalmol Vis Sci.* 2004;45:3380–3386.
40. Atchison DA, Pritchard N, Schmid KL, Scott DH, Jones CE, Pope JM. Shape of the retinal surface in emmetropia and myopia. *Invest Ophthalmol Vis Sci.* 2005;46:2698–2707.
41. Shen J, Clark CA, Soni PS, Thibos LN. Peripheral refraction with and without contact lens correction. *Optom Vis Sci.* 2010;87:642–655.
42. Mutti DO, Zadnik K, Fusaro RE, Friedman NE, Sholtz RI, Adams AJ. Optical and structural development of the crystalline lens in childhood. *Invest Ophthalmol Vis Sci.* 1998;39:120–133.
43. Pan F. Defocused image changes signaling of ganglion cells in the mouse retina. *Cells.* 2019;8:640.
44. Banerjee S, Wang Q, So CH, Pan F. Defocused images change multineuronal firing patterns in the mouse retina. *Cells.* 2020;9:530.