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Defocus Incorporated Multiple Segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial

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ABSTRACT

Aim To determine if 'Defocus Incorporated Multiple Segments' (DIMS) spectacle lenses slow childhood myopia progression.

Methods A 2-year double-masked randomised controlled trial was carried out in 183 Chinese children aged 8–13 years, with myopia between −1.00 and −5.00 D and astigmatism ≤1.50 D. Children were randomly assigned to wear DIMS (n=93) or single vision (SV) spectacle lenses (n=90). DIMS lens incorporated multiple segments with myopic defocus of +3.50 D. Refractive error (cycloplegic autorefraction) and axial length were measured at 6month intervals.

Results 160 children completed the study, n=79 in the DIMS group and n=81 in the SV group. Average (SE) myopic progressions over 2 years were −0.41±0.06 D in the DIMS group and −0.85±0.08 D in the SV group. Mean (SE) axial elongation was 0.21±0.02 mm and 0.55±0.02 mm in the DIMS and SV groups, respectively. Myopia progressed 52% more slowly for children in the DIMS group compared with those in the SV group (mean difference −0.44±0.09 D, 95% CI −0.73 to −0.37, p<0.0001). Likewise, children in the DIMS group had less axial elongation by 62% than those in the SV group (mean difference 0.34±0.04 mm, 95% CI 0.22 to 0.37, p<0.0001). 21.5% children who wore DIMS lenses had no myopia progression over 2 years, but only 7.4% for those who wore SV lenses.

Conclusions Daily wear of the DIMS lens significantly retarded myopia progression and axial elongation in myopic children. Our results demonstrated simultaneous clear vision with constant myopic defocus can slow myopia progression.

Trial registration number NCT02206217.

INTRODUCTION

The increasing prevalence of myopia is reaching an alarmingly high level globally.[1 2] In many parts of East and Southeast Asia, as many as 70%–80% of young adults are myopic,[1–3] and as many as 20% of children are highly myopic, with refractions worse than −6 D.[2] Highly myopic eyes have higher risk of developing blinding complications such as retinal degenerations[4 5] and glaucoma.[6] It is no doubt that epidemic of myopia debilitates both at individual level and public health level.[7 8] In fact, myopia is now identified as one of immediate concerns by the WHO's Global Initiative for the Elimination of Avoidable Blindness.[8]

Several clinical interventions are currently used for slowing the progression of myopia.[9 10] A meta-analysis in efficacy comparison of different interventions for myopia control reported that pharmacological treatment is relatively more effective than optical methods using contact lenses or spectacles.[9 10] High-dose (1%) atropine[11] eye-drops are highly effective, but the associated side effects, such as photophobia and blurry vision, are not well tolerated. Lower dose (0.01%–0.1%)[12–14] atropine yields similar treatment effects with less side effects. Ideally, an intervention for myopia control should be as minimally invasive as possible, making spectacle lenses the ideal alternative option.

Animal studies have provided solid evidence that imposed myopic defocus (MD) inhibits eye growth whereas hyperopic defocus promotes eye growth.[15] Studies using chicks,[16 17] guinea pigs,[18] marmoset[19] and rhesus monkey[20] have demonstrated that myopic eye growth could be inhibited or reversed by applying MD using dual-power or multifocal lenses. Indeed, MD is likely be the key mechanism that underlies a number of current myopia control strategies, such as orthokeratology[21] and multifocal soft contact lenses.[22–24]

Several years ago, we designed a concentric dual-power soft contact lens called 'Defocus Incorporated Soft Contact' (DISC) lens for myopia control which imposes MD on both the central and peripheral retinas.[23] The clinical trial has shown the DISC lens wear significantly slowed myopia progression in schoolchildren by 25% over 2 years compared with the single vision (SV) contact lenses and 60% for a subgroup of children who have worn the lenses for more than 8 hours/day.[23] We have now designed a spectacle lens based on the MD mechanism for myopia control, and named it as Defocus Incorporated Multiple Segments (DIMS) spectacle lens. This lens provides the same optical stimulus as the DISC lens without the disadvantages inherent with contact lens wear. This study aims to investigate if the DIMS lenses can slow myopia progression in schoolchildren.

MATERIALS AND METHODS

Study design

This study was a prospective, randomised and double-masked clinical trial conducted between August 2014 and July 2017. The subjects were randomly allocated to wear either DIMS spectacle lenses (treatment group) or SV spectacle lenses (control group). Spherical equivalent refraction (SER) and axial length (AL) were measured at baseline and every 6 months over 2 years. The changes in SER and AL between two groups were compared over the study period. Data collection and eye examinations were carried out in the Centre for Myopia Research at the Hong Kong Polytechnic University. Written assent and informed consent were obtained from the children and their parents before participation.

Subjects

Phone screening and visual screening were performed to determine whether the child met the study criteria. One hundred and eighty-three schoolchildren were recruited between August 2014 and July 2015. Inclusion criteria were:

- Hong Kong Chinese.
- 8–13 years old.
- SER: −1.00 to −5.00 dioptres (D).
- Astigmatism and anisometropia of 1.50 D or less.
- Monocular best corrected visual acuity (VA) of 0.00 logMAR (6/6) or better.
- Acceptance of random group allocation and the masked study design.

Exclusion criteria were:

- Strabismus and binocular vision abnormalities.
- Ocular and systemic abnormalities.
- Prior experience of myopia control.

Randomisation

Simple randomisation was implemented by the unmasked investigator (UI) by putting subject file numbers (1–200) in a spreadsheet of Excel (Microsoft Office) and creating a column of random numbers for the group allocation. Eligible subjects were then assigned to either group by following a random software sequence generated from Excel.

Sample size calculation

To achieve a 90% power to detect a 0.50D difference (0.70D of SD)[23] in myopia progression between two groups with an alpha level of 0.01 (2-tailed); the minimum subject number required in each group was 59. Assuming a dropout rate of about 15%, at least 70 subjects were required in each group.

Intervention and control

The children in the treatment group wore the DIMS spectacle lenses while those in the control group wore ordinary SV spectacle lenses.

The DIMS lens is a custom-made plastic spectacle lens. It comprises a central optical zone (9 mm in diameter) for correcting distance refractive errors, and an annular multiple focal zone with multiple segments (33 mm in diameter) having a relative positive power (+3.50 D) (figure 1). The diameter of each segment is 1.03 mm. This design simultaneously introduces MD and provides clear vision for the wearer at all viewing distances. There are multiple foci from MD at a plane in front of the retina, which would be received as blur images on the retina.

The final distance prescription was determined by the UI using cycloplegic subjective refraction measured by the masked investigator (MI). The lenses were replaced with an updated prescription when the change of SER was more than 0.50 D.

Masking and wear compliance

We adopted the same study protocol in our previous randomised controlled trials using progressive addition lenses[25] and the DISC lenses.[23] The UI was responsible for group allocation, spectacle-dispensing work, measuring visual performance of lenses, record keeping, data entry and compliance checking. The MI was responsible for refraction and related eye data measurement. Both the children and their parents were masked to group allocation until data analysis was completed. The masking procedures fulfilled the Consolidated Standards of Reporting Trials requirements.[26] Prior to the data measurement by MI, the spectacles were removed from the children by the UI.

At spectacles delivery, the children were instructed to wear the spectacles in full-time mode, except during sleeping and taking shower. Wear compliance was monitored and checked by phone calls and questionnaires.

Outcome variables

Refraction and AL under cycloplegia were measured at baseline and at 6-month intervals for 2 years. The primary outcome was myopia progression, which was the difference between the mean cycloplegic SER at the baseline and subsequent 6-month visits for 24 months. The secondary outcome was the change of AL,

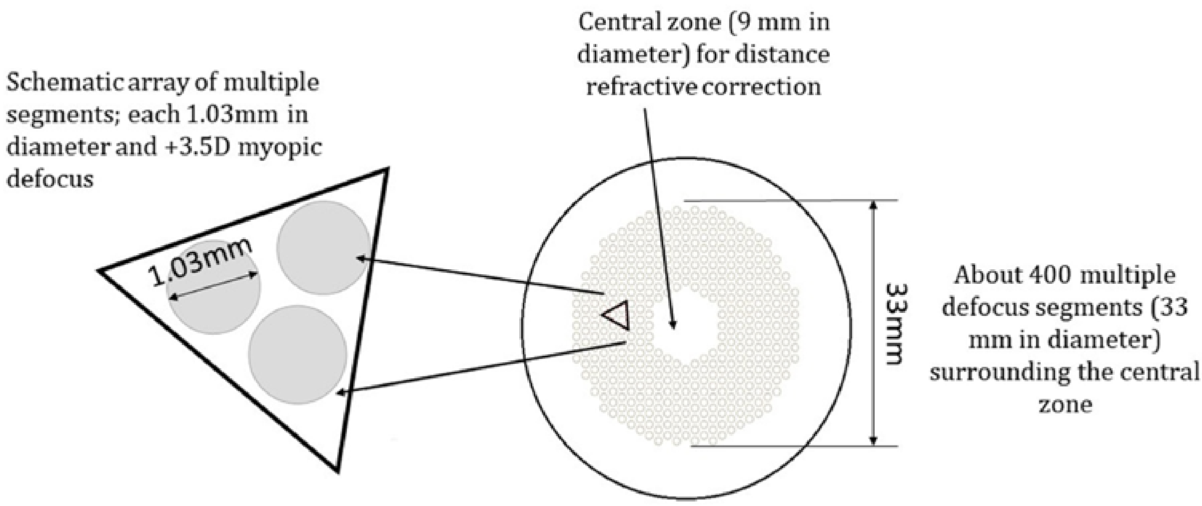

Figure 1 The design of the Defocus Incorporated Multiple Segments (DIMS) spectacle lens.

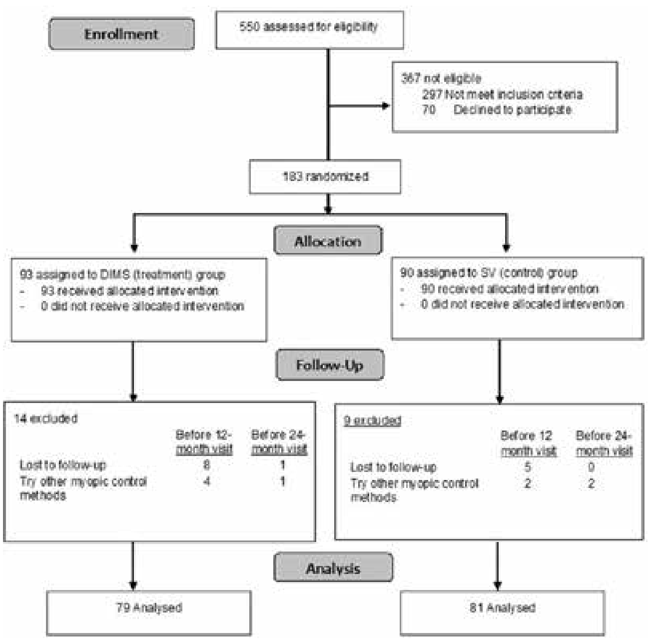

Figure 2 A flow diagram of the study design. DIMS, Defocus Incorporated Multiple Segments spectacle lens; SV, single vision spectacle lens.

which was the difference between the mean AL at the baseline and subsequent 6-month visits for 24 months.

One drop of Alcaine 0.5% followed by one to two drops of cyclopentolate HCL 1% were instilled to induce cycloplegia. Cycloplegia was confirmed by measuring the amplitude of accommodation using push-up method when accommodation was 2 D or less. Cycloplegic refraction was measured with an open-field autorefractor (Shin-Nippon NVision-K5001). AL was measured by partial coherence interferometry IOL Master (Carl Zeiss). Average of five measurements of autorefraction and AL for each eye were obtained for analysis.

Other measurements at each follow-up

Other outcomes such as distance and near VA, near phoria and accommodation lag were measured when the children were wearing full correction of distance at each 6-month follow-up.

Visual performance with the experimental lenses was also assessed. Distance and near VA, accommodation, phoria and stereopsis were measured when the subjects collected their spectacles. Vision quality, comfort and frequency of visual symptoms with lens wear were graded by the subjects themselves through questionnaires (online supplementary methods). Data between the two groups were compared.

Statistical analysis

There were no statistically significant differences between data from two eyes, only data of right eyes were used for analyses. Unpaired t-tests were used to compare baseline characteristics between groups when normality assumptions were preserved. Otherwise, Mann-Whitney U test for continuous data and the χ^2 test for categorical data were used.

Myopia progression over 2 years was calculated as the difference between SER at the baseline and the 2-year visits. For the subjects completed the study, the changes in SER and AL between two groups were compared using unpaired t-tests. The efficacy of myopia control of DIMS lens (%) was determined by dividing the difference in myopia progression (or axial elongation) between two groups with the myopia progression (or axial elongation) in the SV group, then multiplied by 100%.

Data analysis also followed the intention-to-treated approach for the subjects lost to follow-up. Generalised estimating equations (GEE) were adopted for handling missing data. GEE, with one within-subject factor (time), one between-subject factor (group: DIMS or SV) and their interactions, was used to determine the treatment effect on two main outcomes adjusted for some covariates. These covariates included age, gender, baseline refractive error, near phoria, lag of accommodation, number of myopic parents, time spent on near works and outdoor activities. The significant covariates ($p<0.05$) were tested for their correlation with the changes of SER and AL independently using Pearson correlation analysis.

RESULTS

Subject profile

Figure 2 is a flow diagram illustrating the number of subjects recruited, enrolled and dropped out. One hundred and eighty-three eligible schoolchildren participated and were randomly allocated to the DIMS group (n=93) and the SV group (n=90). One hundred and sixty subjects successfully completed the study: 79 (85%) children in the treatment group and 81 (90%) in the control group. The dropout rate was slightly higher in the treatment group (15%) than the control group (10%) (online supplementary eTables 1 and 2). Fourteen out of 23 children dropped out early soon after the baseline data collection.

Both groups showed an overall good compliance and could wear the spectacles full time. The mean daily lens-wearing time in the DIMS group and SV group was 15.5±2.6 and 15.3±2.1 hours, respectively, and was not significantly different.

Baseline characteristics

There were no statistically significant differences between the DIMS and SV groups in the baseline characteristics ($p>0.05$) (table 1). The mean initial myopia in the DIMS and SV groups was −2.93±1.04 D and −2.70±0.98 D, respectively. The mean initial AL was 24.85±1.59 mm and 24.72±1.30 mm in the DIMS and SV groups, respectively.

Changes in the refraction and AL

Completed subjects

For subjects who completed the 2-year trial (table 2), the mean myopia progression (SE) over 2 years in the DIMS group (n=79) and the SV group (n=81) was −0.38±0.06 D and −0.93±0.06 D, respectively. The total increase in AL was 0.21±0.02 mm and 0.53±0.03 mm, respectively. Schoolchildren wearing DIMS lenses had myopia progression significantly reduced by 59% (mean difference −0.55±0.09 D, $p<0.0001$) and axial elongation decreased by 60% (mean difference 0.32±0.04 mm, $p<0.0001$) compared with those wearing SV lenses.

All enrolled subjects

Changes in SER

The mean myopia progression over 2 years in the DIMS group (n=93) and the SV group (n=90) was −0.38±0.06 D and −0.85±0.08 D, respectively. Children wearing DIMS lenses had significantly less myopia progression by 55% (mean difference −0.47±0.09 D, $p<0.0001$).

The tests of model effect (online supplementary eTable 3) indicated that group, time and age ($p<0.05$) had significant association with the magnitude of myopia progression. After model

Table 1 Baseline demographics data of all and the completed subjects

Baseline demographic data, mean (SD)	Mean (SD) All DIMS (n=93)	SV (n=90)	Completed DIMS (n=79)	SV (n=81)
Age at enrolment (years)	10.19±1.46	10.01±1.44	10.20±1.47	10.00±1.45
Gender				
Male, % (n)	59.1 (55)	55.6 (50)	58.2 (46)	54.3 (44)
Female, % (n)	40.9 (38)	44.4 (40)	41.8 (33)	45.7 (37)
Cycloplegic autorefraction in SER (D)	−2.93±1.04	−2.70±0.98	−2.97±0.97	−2.76±0.96
Axial length (mm)	24.85±1.59	24.72±1.30	24.70±0.82	24.60±0.83
Corneal power at steep meridian (D)	44.46±1.67	44.39±1.69	44.5±1.61	44.5±1.65
Corneal power at flat meridian (D)	43.14±1.41	43.09±1.45	43.2±1.41	43.2±1.44
Near phoria, Δ	−1.96±3.93	−0.98±3.53	−2.16±4.07	−0.15±3.28
Accommodation lag (D)	0.97±0.49	1.06±0.40	0.98±0.42	1.04±0.35
Myopics parents, n				
0	3	6	2	5
1	22	23	18	20
2	68	61	59	56

Δ, prism dioptres; AL, axial length; D, dioptres;DIMS, Defocus Incorporated Multiple Segments spectacle lens; SER, spherical equivalent refraction; SV, single vision spectacle lens.

adjustment, the mean myopia progressions were −0.41±0.06 D in the DIMS group and −0.85±0.08 D in the SV group (online supplementary eTable 4). Children wearing DIMS lenses had significantly less myopia progression by 52% (mean difference −0.44±0.09 D, $p<0.0001$). Controlling for covariates did not greatly change the treatment effect compared with the unadjusted means. The DIMS lens had the greatest effect on slowing myopia progression in the first 6 months, after that, the magnitude slightly decreased at 12-month visit and was sustained to the 24-month visits (figure 3).

For Pearson correlation analysis, the changes in SER significantly correlated ($r^2=0.22$, $p<0.001$) with subject's age in the DIMS group (online supplementary eFigure 1). Myopia progression was slightly slower in older children who wore DIMS lenses. In SV group, no significant correlation was found ($r^2=0.04$, $p>0.05$).

Table 2 Changes in the cycloplegic spherical equivalent refraction and axial length (from baseline) in the DIMS and the SV groups

	DIMS (n=79)	SV (n=81)	Mean difference (SE)
Time/visit	SER changes in dioptres, mean (SE)		
6 months	−0.13±0.03	−0.37±0.04	−0.24±0.05*
12 months	−0.17±0.05	−0.55±0.04	−0.38±0.07*
18 months	−0.31±0.06	−0.72±0.05	−0.42±0.08*
24 months	−0.38±0.06	−0.93±0.06	−0.55±0.09*
Time/visit	Changes in AL (mm), mean (SE)		
6 months	0.03±0.01	0.20±0.01	0.16±0.02*
12 months	0.11±0.02	0.32±0.02	0.21±0.02*
18 months	0.15±0.02	0.43±0.02	0.27±0.03*
24 months	0.21±0.02	0.53±0.03	0.32±0.04*

*Statistically significant difference between two experimental groups (unpaired t-tests, p<0.0001).
Δ, prism dioptres;D, dioptres;DIMS, Defocus Incorporated Multiple Segments spectacle lens; SER, spherical equivalent refraction; SV, single vision spectacle lens.

Changes in AL

The total increase in AL over 2 years was 0.21±0.02 mm and 0.56±0.02 mm in the DIMS and SV groups, respectively. The DIMS lenses significantly slowed axial elongation by 63% (mean difference 0.35 (0.04) mm, $p<0.0001$) as compared with the SV lenses. Group, time and age were found to be associated with AL changes. Model-adjusted mean changes in AL±SE were 0.21±0.02 mm and 0.55±0.02 mm in the DIMS and SV groups, respectively. The DIMS lens showed a significant effect on slowing axial elongation by 62% (mean difference 0.34±0.03 mm, $p<0.0001$).

For individual subjects

Seventeen (21.5%) out of 79 children wearing DIMS lenses had no myopia progression over 2 years (online supplementary eFigure 2), which was higher than the SV group (6 of 81, 7%). Likewise, 14% of the children wearing DIMS lenses had no axial elongation whereas all children in the SV group had axial elongation (online supplementary eFigure 3).

Visual performance with lens wear

There were no statistically significant differences between the two lens types in influencing VA and accommodation (unpaired t-test, $p>0.05$) (online supplementary eTable 5), except stereoacuity ($p=0.04$). However, the mean difference was only 5 s of arc, which is not clinically significant.

DISCUSSION

Children wearing the DIMS spectacle lenses had myopia progression significantly reduced by 52% and axial elongation by 62%

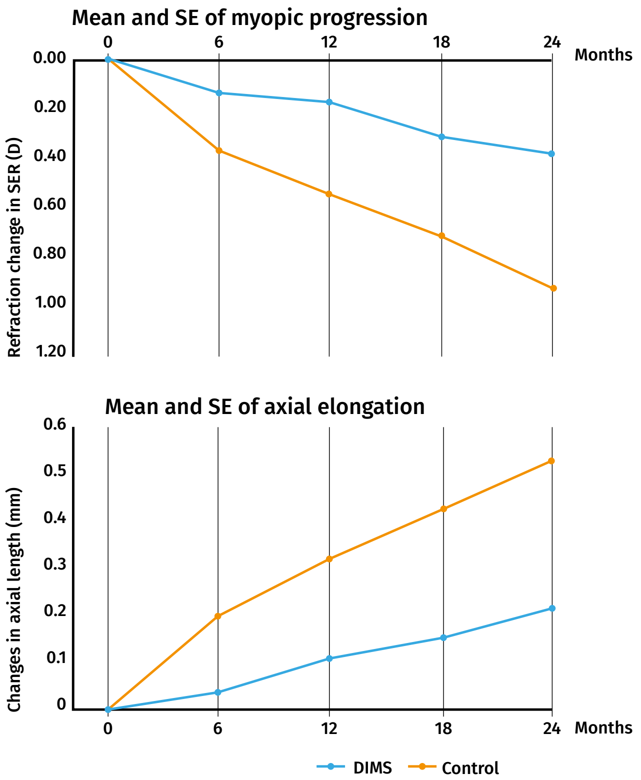

Figure 3 Model-adjusted mean and SE of myopia progression and axial length from baseline to 24 months. DIMS, Defocus Incorporated Multiple Segments; SER, spherical equivalent refraction.

over 2 years when compared with those wearing SV lenses. The greatest treatment effect was observed during the first 6 months of lens wear. It was due to the higher myopia progression in the SV group during this time, otherwise the treatment effect was quite consistent over the 2 years (figure 3, online supplementary eTable 4). The treatment effect with the DIMS lens was similar to that achieved with 6–8 hours daily wear of DISC lens, at around 50%–60%.[23] These findings are consistent with our previous animal studies[17 18] and the clinical trial of the DISC lens,[22] that the principle of employing MD does retard eye growth and myopia progression.

The DIMS lens design showed much better effect on slowing childhood myopia progression than existing progressive addition lenses (10%–35%),[25 27–31] spectacle lens with peripheral defocus[32] and contact lens[33] (34%) designed for reducing relative peripheral hyperopia (online supplementary eTable 6). The efficacy of myopia control is comparable to those of orthokeratology (60%),[10 21] prismatic bifocal spectacle lenses (about 50%)[34] and bifocal soft contact lenses (50%–60%)[10 23 35] and relatively less when compared with high and low-dose atropine (70+%).[11–14]

The DIMS lenses have slowed myopia progression, and have stopped myopia progression in some children (online supplementary eFigures 2 and 3). 21.5% of children in the DIMS group had no myopia progression over 2 years whereas only 7.4% in the control group. About 13% of children in the DIMS group still showed considerable progression in terms of refraction (>1 D). Such variations in retardation effect have been observed with prismatic bifocal spectacles, Cheng *et al*[34] showed that prismatic bifocals were more effective in the children with low accommodative lag. Also, they found that age, initial myopia and parental myopia were associated with the treatment effect. In contrast, in our study the magnitude of treatment effect was not dependent on lag of accommodation, initial myopia nor parental myopia.

Analysis of model effects indicated that age was the only associated factor that exhibited significant effect on myopia progression, and the effect of myopia control with DIMS lenses was greater in older children (aged 10–13) (online supplementary eFigure 1). About 80% of the DIMS wearers who had considerable myopia progression were younger children aged 8–9 years. We speculate that variations in treatment effect of the DIMS lenses may be due to different retinal profile or peripheral refraction among the children.[36] If there is a high amount of peripheral hyperopia, the amount of effective MD at the peripheral retina will be less, and thereby minimising the treatment effect.

In our previous study, wearing time was found to be a significant factor in determining the treatment effect of DISC lenses.[23] No such correlation was found in the present study. This is probably a result of the overall higher compliance, that the subjects were able to wear their assigned spectacle lenses constantly, with over 15 hours/day. The dropout rate in this study was much lower (13%) than that in our previous study using the DISC lenses (42%).[23]

The findings of visual performance (online supplementary eTable 5 and eFigure 4) showed that the DIMS lens could provide good vision at distance and near comparable to conventional SV spectacle lenses. Although some subjects initially noticed the slight blurriness at the mid-peripheral field, they fully adapted to the lenses in a few days. The symptoms (score below 2) such as ghost image, dizziness and headache seldom occurred during DIMS lens wear (online supplementary eFigure 5). No treatment-related adverse event was reported.

The current report includes only the first 2-year result, when the third year of the study is ongoing. Also, the current study is limited to Chinese children, further study will be needed to determine the treatment effect of the DIMS lenses in other ethnic populations. DIMS and SV lens could hardly be differentiated by their appearance unless the lens was tilted and the multiple segments may be observed from the reflection of a light source. Most children were not aware of the multiple segments features. A few children in the treatment group might recognise the multiple segments but they had no particular difficulties in using the lens as their previous spectacle lenses. Nevertheless, the study could not be totally masked for some subjects. Our study did not include children with over −5 D of myopia. The retardation effect on myopia progression in high myopes was yet to be determined. Further investigation is also required, in particular, to determine its optimal effectiveness in preventing myopia progression and incidence.

CONCLUSIONS

Daily wear of the DIMS lens significantly slowed myopia progression and axial elongation in myopic schoolchildren as compared with wearing SV spectacle lenses. They provided good vision while presenting simultaneous MD to the eyes. This intervention is simple to use and is the least invasive method compared with pharmacological or contact lens treatments. The DIMS spectacle lens offers an alternative treatment modality for myopia control.

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Contributors All the authors listed have been involved in the undertaking of the clinical trial with emphasis on various aspects, from the conception of the lens design, fabrication of the lens and registration of the clinical trial and preparation of clinical protocol to data collection and analysis, interpretation and conclusions. A few manuscripts are now in preparation by the author team.

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Competing interests None. Patents titled 'Spectacle Lens' in China (CN104678572 B) and in USA (US10268050 B2) were issued on 27 April 2018 and 23 April 2019 respectively.

Patient consent for publication Not required.

Ethics approval All aspects of the study met the tenets of the Declaration of Helsinki and were approved by the Human Subjects Ethics Subcommittee of the Hong Kong Polytechnic University.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Data are available upon request.

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Les verres ophtalmiques DIMS (Defocus Incorporated Multiple Segments) ralentissent l'évolution de la myopie : essai clinique randomisé sur 2 ans

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RÉSUMÉ

Objectif : déterminer si les verres ophtalmiques DIMS (Defocus Incorporated Multiple Segments) ralentissent l'évolution de la myopie infantile.

Méthodologie : Un essai mené à double insu, randomisé et contrôlé sur 2 ans a été réalisé sur un panel de 183 enfants chinois âgés de 8 à 13 ans, atteints d'une myopie comprise entre -1,00 et -5,00 D et d'un astigmatisme de ≤1.50 D. Des verres correcteurs DIMS (n=93) ou unifocaux (U) (n=90) ont été assignés de manière arbitraire aux enfants. Les verres DIMS comportaient des segments multiples avec une défocalisation myopique de +3,50 D. L'erreur de réfraction (auto-réfraction cycloplégique) et la longueur axiale ont été mesurées à des intervalles de six mois.

Résultats : 160 enfants, dont n=79 du groupe DIMS et n=81 du groupe témoin, ont suivi l'étude jusqu'à son terme. L'évolution moyenne de la myopie (± l'erreur-type) sur 2 ans a été de −0,41±0,06 D pour le groupe DIMS et de −0,85±0,08 D pour le groupe témoin.
L'allongement axial moyen (± l'erreur-type) a été respectivement de 0,21±0,02 mm et de 0.55±0.02 mm dans les groupes DIMS et unifocaux. La myopie a évolué 52 % moins vite chez les enfants dans le groupe DIMS comparés à ceux du groupe témoin (différence moyenne −0,44±0,09 D, 95 % CI −0,73 à −0.37, p<0.0001). De même, l'allongement axial constaté chez les enfants du groupe DIMS a été de 62 % inférieur à ceux du groupe témoin (différence moyenne 0,34±0,04 mm, 95 % ,22 à 0,37, p<0,0001). 21,5 % des enfants porteurs de verres DIMS n'ont montré aucune évolution de la myopie sur 2 ans, contre seulement 7,4 % chez les porteurs de verres unifocaux.

Conclusions : Le port quotidien de verres DIMS a sensiblement retardé l'évolution de la myopie et l'allongement axial chez les enfants myopes. Nos résultats ont démontré que l'association d'une vision claire à une défocalisation myopique constante peut ralentir l'évolution de la myopie.

Numéro universel de l'essai : NCT02206217.

INTRODUCTION

La prévalence de plus en plus forte de la myopie atteint des niveaux de plus en plus alarmants à l'échelle planétaire.[1 2] Dans de nombreuses régions de l'Asie orientale et du sud-est asiatique, le taux de myopie chez les jeunes adultes atteint 70 % à 80 %,[1–3] et chez les enfants le taux de forte myopie atteint 20 %, avec une réfraction dépassant −6 D.[2] Chez un sujet atteint d'une forte myopie, le risque de complications conduisant à la cécité, telles que des dégénérescences rétiniennes[4 5] et des glaucomes est plus élevé.[6] Cette prévalence de la myopie a des répercussions sanitaires aussi bien au niveau individuel que sur le plan de la santé publique.[7 8] A tel point que la myopie a été priorisée par l'OMS dans son Initiative mondiale pour l'élimination de la cécité évitable.[8]

Plusieurs interventions cliniques permettent aujourd'hui de ralentir l'évolution de la myopie.[9 10] Une méta-analyse comparant l'efficacité de ces différentes interventions a conclu que le traitement pharmacologique est relativement plus efficace que les méthodes optiques à base de lentilles de contact ou de lunettes.[9 10] L'application de gouttes d'atropine (1 %) à forte dose[11] est très efficace, mais les effets secondaires associés, tels que la photophobie et la vision floue, sont mal tolérés. A plus faible dose (0,01%–0,1%)[12–14] un traitement à l'atropine produit des effets similaires avec moins d'effets secondaires. Les traitements de la myopie devant être les moins invasifs possibles, l'utilisation de verres de lunettes constitue la solution alternative optimale.

Les études sur des animaux ont amplement démontré qu'une défocalisation myopique (DM) imposée inhibe la croissance de l'œil, alors qu'une défocalisation hypéropique favorise cette croissance.[15] Des études réalisées sur des poussins,[16 17] des cochons d'Inde,[18] des ouistitis [19] et des macaques rhésus[20] ont démontré qu'il était possible d'inhiber ou d'inverser l'allongement myopique de l'œil par la mise en œuvre de la défocalisation myopique via des verres bifocaux ou multifocaux. En effet, plusieurs stratégies actuelles pour le contrôle de la myopie telles que l'orthokératologie[21,] et le port de lentilles de contact multifocales[22–24], s'appuieront sans doute sur le mécanisme de la défocalisation myopique.

Il y a quelques années, nous avons conçu des lentilles DISC (Defocus Incorporated Soft Contact), des lentilles souples bifocales concentriques, pour contrôler l'évolution de la myopie. Ces lentilles imposent une défocalisation myopique sur les rétines centrales et périphériques.[23] L'essai clinique a démontré que le port des lentilles DISC a sensiblement ralenti (par 25 %) l'évolution de la myopie chez les enfants de plus de 2 ans comparé aux verres de contact unifocaux , et par 60 % dans un sous-ensemble d'enfants ayant porté les lentilles pendant plus de 8 heures par jour.[23] Nous présentons aujourd'hui un verre de lunettes mettant en œuvre le mécanisme de la défocalisation myopique, et nous l'appelons DIMS (Defocus Incorporated Multiple Segments). Ce verre apporte la même stimulation optique que la lentille DISC sans les inconvénients inhérents au port des lentilles de contact. Cette étude a pour objectif de démontrer que les verres DIMS peuvent ralentir l'évolution de la myopie chez les enfants.

MATÉRIELS ET MÉTHODOLOGIES

Conception de l'étude

L'étude, sous forme d'essai clinique prospectif randomisé et à double insu, a été réalisée entre les mois d'août 2014 et juillet 2017. Des verres de lunettes DIMS et des verres unifocaux ont été distribués selon une répartition arbitraire à deux groupes de sujets, respectivement un groupe expérimental (groupe traité) et un groupe témoin. Les données de référence -- équivalent sphérique (ES) et longueur axiale de l'œil (LA) – ont été mesurées au début de l'essai, puis ces valeurs ont été contrôlées à des intervalles de 6 mois sur une période de 2 ans. L'évolution des deux paramètres dans les deux groupes a été comparée pendant la période étudiée. La collecte des données et les examens ophtalmiques ont été réalisés au Centre de recherche en myopie de l'Université polytechnique de Hong Kong. L'accord par écrit et le consentement éclairé ont été obtenus auprès des enfants et leurs parents préalablement à la participation.

Sujets
L'aptitude des enfants à répondre aux critères de l'étude a été évaluée par une procédure d'entrevue téléphonique de présélection et de dépistage visuel. Un panel de 183 enfants scolarisés a été recruté entre les mois d'août 2014 et juillet 2015. Les critères d'inclusion étaient :
- nationalité chinoise de Hong Kong ;
- 8 à 13 ans ;
- ES de –1,00 à –5,00 dioptries (D) ;
- astigmatisme et anisométropie de ≤1,50 D ;
- acuité visuelle monoculaire optimale d'au moins 0,00 logMAR (6/6) ;
- acceptation des principes de répartition arbitraire aux deux groupes d'enfants et d'étude à double insu ;

Les critères d'exclusion étaient :
- le strabisme et des anomalies de vision binoculaire ;
- des anomalies oculaires et systémiques ;
- une expérience antérieure de contrôle de la myopie.

Randomisation
Une randomisation simple a été effectuée par un chercheur non masqué qui a consigné les numéros de dossier des sujets (1–200) dans une feuille de calculs Excel (Microsoft Office) comprenant une colonne de nombres arbitraires pour l'attribution aux groupes. Les sujets éligibles ont été alors affectés à l'un ou l'autre des deux groupes suivant une séquence arbitraire générée par logiciel à partir d'Excel.

Calcul de la taille des échelons
Pour atteindre une puissance de 90 % en mesure de détecter une différence de 0,50D (0,70D de SD) [23] dans l'évolution de la myopie entre les deux groupes avec un niveau alpha de 0,01 (test t bilatéral), le nombre minimum de sujets requis dans chaque groupe était de 59. Supposant un taux d'abandon possible d'environ 15 %, il fallait au moins 70 sujets par groupe.

Intervention et contrôle
Les enfants dans le groupe expérimental ont porté les verres DIMS alors que ceux du groupe témoin portaient des verres unifocaux ordinaires.
Le verre DIMS est un verre plastique personnalisé. Il comprend une zone optique centrale (ø 9 mm) pour la correction des erreurs de réfraction et une zone annulaire à segments de focalisation multiples (ø 33 mm) ayant une puissance positive relative (+3,50 D) *(figure 1)*. Le diamètre de chaque segment est de 1,03 mm. Cette conception induit la défocalisation myopique, tout en assurant une vision claire au porteur à toutes les distances. Plusieurs foyers créés par la défocalisation myopique sont situés dans un plan devant la rétine, et atteindraient la rétine sous la forme d'images floues. La prescription de la puissance de loin a été déterminée par autoréfraction cycloplégique mesurée par le chercheur à insu. Les verres ont été remplacés par une prescription dès que l'évolution de l'ES dépassait 0,50 D.

Insu et respect des conditions de port
Nous avons adopté le même protocole d'étude que lors de nos précédents essais randomisés sur des verres à addition progressive et[25] sur des verres DISC.[23] Le chercheur non masqué a été chargé des tâches suivantes : affectation des sujets aux groupes, distribution des lunettes, mesurage des performances visuelles des verres, tenue des enregistrements, saisie des données et vérification de la conformité. Le chercheur à insu a été chargé des tâches suivantes : mesure de la réfraction et des données oculaires liées. Les enfants et les parents ont été affectés aux groupes à leur insu jusqu'à l'achèvement de l'analyse des données. Les procédures d'insu étaient conformes à la norme Consolidated Standards of Reporting Trials requirements (Standards fusionnés dans la rédaction d'essais thérapeutiques).[26] Avant la prise des mesures par le chercheur à insu, le chercheur non masqué a enlevé les lunettes portées par les enfants.
Lorsque les lunettes ont été confiées aux enfants, ces derniers ont reçu la consigne de les porter à tout moment sauf pour dormir et pour la prise de douches. Le respect de cette consigne a fait l'objet d'un suivi et d'une vérification téléphonique et par des questionnaires.
Variables impactant les résultats

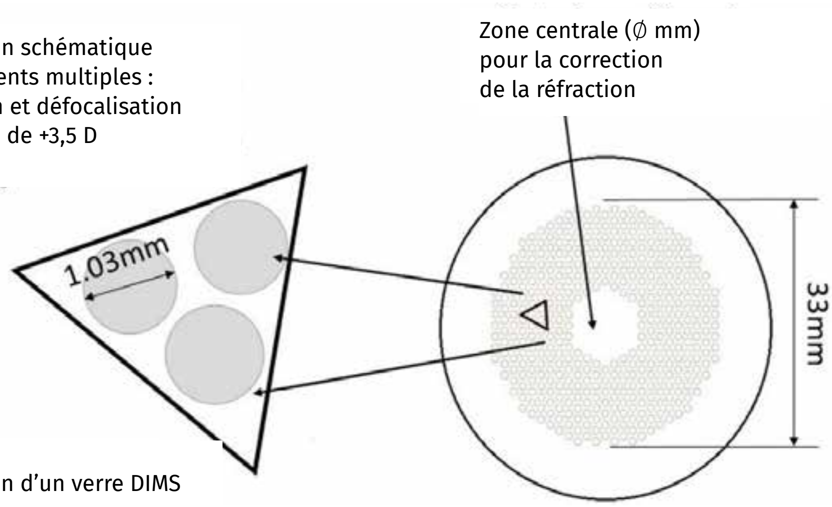
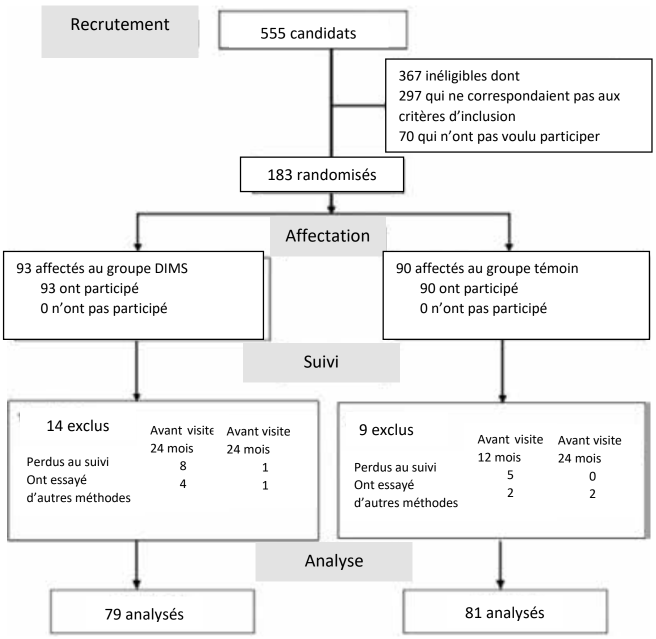


Fig. 1
Conception d'un verre DIMS

La réfraction et la longueur axiale de l'œil ont été mesurées au départ de l'essai pour constituer des données de référence, puis à des intervalles de 6 mois sur une période de 2 ans. Le principal paramètre mesuré a été l'évolution de la myopie, soit la différence entre l'ES cycloplégique moyen de référence et les valeurs relevées lors des visites semestrielles pendant 24 mois. Le paramètre secondaire mesuré a été l'évolution de la longueur axiale, soit la différence entre la longueur axiale moyenne de référence et les valeurs relevées lors des visites semestrielles pendant 24 mois.

La cycloplégie a été induite par l'administration d'une goutte d'Alcaine 0,5 % suivie d'une ou deux gouttes de cyclopentolate HCL 1 %. La cycloplégie a été confirmée en mesurant l'ampleur de l'accommodation par la méthode de Donders dès que l'accommodation mesurée était de ≤2 D. La réfraction cycloplégique a été mesurée avec un kératomètre/réfractomètre automatique/pupillomètre vidéo (Shin-Nippon NVision-K5001). La longueur axiale a été mesurée par interférométrie à cohérence partielle à l'aide d'un biomètre optique IOL Master (Carl Zeiss). La moyenne des cinq relevés de l'autoréfraction et de la longueur axiale pour chaque œil a été retenue pour les besoins de l'analyse.



Autres mesures à chaque étape de suivi

D'autres résultats tels que l'acuité visuelle en vision de loin (VL) et vision de près (VP, phorie en VP et retard accommodatif ont été enregistrés à chaque contrôle semestriel sur des enfants munis de verres assurant une correction complète de la distance.
Les performances visuelles avec les verres expérimentaux ont également été évaluées. L'acuité visuelle en VL et VP, l'accommodation, la phorie et la stéréopsie ont été mesurées quand les sujets ont pris possession de leurs lunettes. La qualité de vision, le confort et la fréquence de symptômes visuels associés au port des verres ont été évalués par les sujets eux-mêmes via des questionnaires (méthodes complémentaires en ligne). Les données des deux groupes ont été comparées.

Analyse statistique

Aucune différence statistique significative n'a été constatée entre les données des deux yeux, et seules les données de l'œil droit ont été retenues pour les analyses. Des tests t non appariés ont été utilisés pour comparer les caractéristiques de référence entre groupes quand des présomptions de normalité ont été conservées. Dans les autres cas, le test Mann-Whitney U pour les données continues et le test $\chi2$ pour les données catégorielles ont été utilisés.

L'évolution de la myopie sur 2 ans a été calculée en tant que différence entre l'ES de référence et les contrôles au terme des 2 ans. Pour les sujets ayant suivi l'étude jusqu'à son terme, l'évolution ES et LA des deux groupes a été comparée à l'aide de tests t non appariés. L'efficacité du contrôle de la myopie par les verres DIMS (en %) a été déterminée en divisant la différence dans l'évolution de la myopie (ou l'allongement axial) entre les deux groupes par l'évolution de la myopie (ou l'allongement axial) dans le groupe témoin, puis en multipliant par 100 %.

Une approche de type « intention de traiter » a également été adoptée pour les sujets perdus en cours de suivi. Des équations d'estimation généralisées (EEG) ont été utilisées pour la gestion des données manquantes. Ces équations, faisant intervenir un facteur intra-sujet (le temps), et un facteur inter-sujets (groupe : DIMS ou unifocaux) et les interactions entre facteurs ont été utilisées pour déterminer l'effet du traitement sur deux principaux résultats ajustés pour tenir compte de plusieurs covariables. Au nombre de ces covariables étaient l'âge, le sexe, l'erreur réfractive de référence, la phorie en VP, le retard accommodatif, le nombre de parents myopes, le temps passé sur des travaux en VP et des activités de plein air. L'analyse Pearson a été utilisée pour tester indépendamment la corrélation entre les covariables significatifs ($p<0,05$) et l'évolution des valeurs ES et LA.

RÉSULTATS

Profil des sujets

La Fig. 2 est un schéma illustrant le nombre de sujets recrutés, inscrits et ayant abandonné. 183 enfants scolarisés éligibles ont participés et ont été affectés arbitrairement au groupe DIMS (n=93) et au groupe témoin (n=90). 160 sujets ont suivi l'étude jusqu'à son terme : 79 (85 %) des enfants du groupe expérimental et 81 (90 %) dans le groupe témoin. Le taux d'abandon a été légèrement plus élevé dans le groupe expérimental (15 %) que dans le groupe témoin (10 %) *(cf. tableaux complémentaires en ligne 1 et 2)*. 14 des 23 enfants ont abandonné précocement après la collecte des données de référence.
Les deux groupes ont montré un bon respect global des consignes et ont pu porter des lunettes à plein temps. Le temps de port moyen quotidien des verres dans les groupes DIMS et unifocaux a été de 15,5±2,6 et de 15,3±2,1 heures respectivement, et ne présentait pas de différence significative.

Caractéristiques de référence

Aucune différence statistiquement significative n'a été constatée entre les groupes DIMS et unifocaux dans les caractéristiques de référence (p>0.05) (tableau 1). La myopie initiale moyenne dans les groupes DIMS et unifocaux a été de -2,93±1,04 D et de -2,70±0,98 D, respectivement. La longueur axiale initiale moyenne était de 24,85±1,59 mm et de 24,72±1, 0 mm dans les groupes DIMS et unifocaux respectivement.

Evolution de la réfraction et de la longueur axiale

Sujets ayant terminé l'étude

Pour les sujets ayant suivi jusqu'au terme les essais sur deux ans (tableau 2), l'évolution moyenne de la myopie (SE) sur deux ans dans le groupe DIMS (n=79) et le groupe témoin (n=81) a été de −0,38±0,06 D et de −0,93±0,06 D, respectivement. L'augmentation de la longueur axiale a été de 0,21±0,02 mm et de 0,53±0,03 mm, respectivement. Chez les enfants portant les verres DIMS une réduction significative de 59 % de l'évolution de la myopie a été constatée (différence moyenne −0,55±0,09 D, p<0,0001) et l'allongement axial a diminué de 60 % (différence moyenne 0,32±0,04 mm, p<0,0001) comparé aux porteurs de verres unifocaux.

Tous les sujets inscrits

Evolution de l'ES

L'évolution moyenne de la myopie sur 2 ans dans le groupe DIMS (n=93) et le groupe témoin (n=90) a été de −0,38±0,06 D et de −0,85±0,08 D, respectivement. Chez les enfants porteurs de verres DIMS une réduction significative de 55 % de l'évolution de la myopie a été constatée (différence moyenne −0,47±0,09 D, p<0,0001.

Tableau 1 Données démographiques de référence de tous les sujets et des sujets ayant suivi l'étude jusqu'à son terme

Données démographiques de référence, moyenne (± l'erreur-type)	Moyenne (± l'erreur-type)			
	Tous	Suivis jusqu'au terme		
	DIMS (n=93)	Unifocaux (n=90)	DIMS (n=79)	Unifocaux (n=81)
Age au recrutement (ans)	10,19±1,46	10,01±1,44	10,20±1,47	10,00±1,45
Sexe				
Masculin, % (n)	59,1 (55)	55,6 (50)	58,2 (46)	54,3 (44)
Féminin % (n)	40,9 (38)	44,4 (40)	41,8 (33)	45,7 (37)
Autoréfraction cycloplégique en ES (D)	−2,93±1,04	−2,70±0,98	−2,97±0,97	−2,76±0,96
Longueur axiale (mm)	24,85±1,59	24,72±1,30	24,70±0,82	24,60±0,83
Puissance cornéenne au méridien vertical (D)	44,46±1,67	44,39±1,69	44,5±1,61	44,5±1,65
Puissance cornéenne au méridien horizontal (D)	43,14±1,41	43,09±1,45	43,2±1,41	43,2±1,44
Phorie en VP, Δ	−1,96±3,93	−0,98±3,53	−2,16±4,07	−0,15±3,28
Retard accommodatif (D)	0,97±0,49	1,06±0,40	0,98±0,42	1,04±0,35
Parents myopes, n				
0	3	6	2	5
1	22	23	18	20
2	68	61	59	56

Δ = dioptrie prismatique ; D = dioptries

Les tests de l'incidence du modèle sur les résultats *(cf. Tableau complémentaire en ligne 3)* ont indiqué un lien significatif entre les paramètres groupe, temps et âge (p<0,05) et l'ampleur de l'évolution de la myopie. Après ajustement du modèle, l'évolution moyenne de la myopie était de −0,41±0,06 D dans le groupe DIMS et de −0,85±0,08 D dans le groupe témoin *(cf. Tableaux complémentaires en ligne 4 & 3)*. Chez les enfants porteurs de verres DIMS une réduction significative de 52 % de l'évolution de la myopie a été constatée (différence moyenne −0,44±0,09 D, p<0,0001). La prise en compte des covariables n'a pas eu d'incidence sensible sur l'effet du traitement, comparé aux moyennes non ajustées. Le verre DIMS avait l'impact le plus significatif sur le ralentissement de l'évolution de la myopie pendant les 6 premiers mois. L'ampleur du ralentissement a été moindre lors du contrôle à 12 mois, puis s'est maintenue jusqu'au contrôle à 24 mois *(Fig. 3)*.

Selon l'analyse Pearson, la corrélation significative a été constatée entre l'évolution de l'ES (r^2=0,22, p<0,001) et l'âge du sujet dans le groupe DIMS *(cf. Tableau complémentaire en ligne 1)*. L'évolution de la myopie a été un peu plus lente chez les enfants plus âgés portant des verres DIMS. Dans le groupe témoin, aucune corrélation significative n'a été constatée (r2=0,04, p>0,05).

Tableau 2 : Evolution de l'équivalent sphérique (ES) et de la longueur axiale de l'œil (LA)

	DIMS (n=79)	Unifocaux (n=81)	Différence moyenne (± l'erreur-type)
Etape de contrôle	Evolution de l'ES en dioptries, moyenne (± l'erreur-type)		
6 mois	0,13±0,03	0,37±0,04	0,24±0,05*
12 mois	0,17±0,05	0,55±0,04	0,38±0,07*
18 mois	0,31±0,06	0,72±0,05	0,42±0,08*
24 mois	0,38±0,06	0,93±0,06	0,55±0,09*
Etape de contrôle	Evolution de la longueur axiale (mm), moyenne ()		
6 mois	0,03±0,01	0,20±0,01	0,16±0,02*
12 mois	0,11±0,02	0,32±0,02	0,21±0,02*
18 mois	0,15±0,02	0,43±0,02	0,27±0,03*
24 mois	0,21±0,02	0,53±0,03	0,32±0,04*

* Différence statistiquement significative entre deux groupes expérimentaux (tests t non appariés, p<0,0001)

Evolution de la longueur axiale

L'augmentation totale de la longueur axiale sur 2 ans a été de 0,21±0,02 mm et de 0,56±0,02 mm dans les groupes DIMS et unifocaux respectivement. Les verres DIMS ont sensiblement ralenti l'allongement axial de 63 % (différence moyenne 0,35 (0,04) mm, p<0.0001), comparé aux verres unifocaux. Un lien a été constaté entre les paramètres groupe, temps et âge et l'évolution de la longueur axiale. Après ajustement du modèle, l'évolution moyenne de la longueur axiale AL±erreur-type était de 0,21±0,02 mm et de 0,55±0,02 mm dans les groupes DIMS et unifocaux, respectivement. L'étude a montré que le verre DIMS avait un impact significatif de 62 % sur le ralentissement de l'allongement axial (différence moyenne de 0,34±0,03 mm, p<0,0001).

Pour les sujets individuels

Chez dix-sept (21,5 %) des 79 enfants porteurs de verres DIMS aucune évolution de la myopie n'a été constatée sur 2 ans *(cf. Figure complémentaire en ligne 2)*, un chiffre supérieur à celui enregistré sur le groupe témoin (6 sur 81, soit 7 %). De même, aucun allongement axial n'a été constaté chez 14 % des 79 enfants porteurs de verres DIMS, alors que l'allongement axial a été constaté chez tous les enfants du groupe témoin *(cf. Figure complémentaire en ligne 3)*.

Performances visuelles

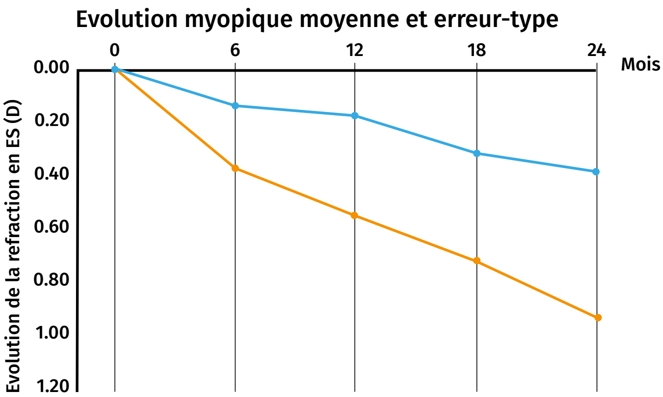
Aucune différence statistiquement significative n'a été relevée entre les deux types de verres en termes d'impact sur l'acuité visuelle et l'accommodation (tests t non appariés, p>0,05) *(cf. Tableau complémentaire en ligne 5)*, sauf pour la stéréoacuité (p=0,04), la différence moyenne constatée n'étant que de 5 s d'arc, un écart sans signification clinique.

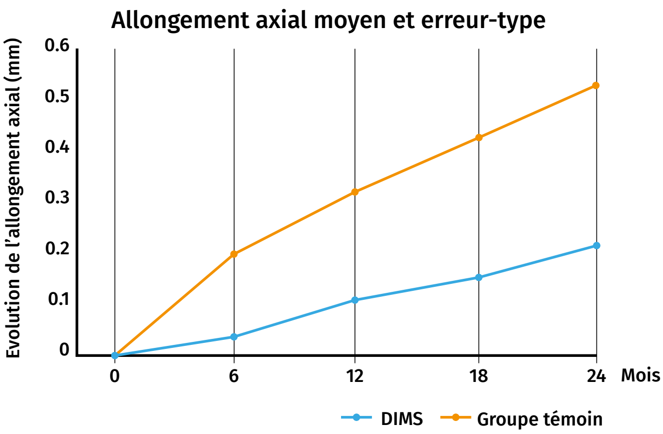
DISCUSSION

Une réduction significative de l'évolution de la myopie et de l'allongement axial, de 52 % et 62 % respectivement ,a été constatée chez les enfants porteurs de verres DIMS sur une période de 2 ans. Cette réduction se compare favorablement aux résultats constatés avec les verres unifocaux. L'impact le plus important du traitement a été constaté pendant les 6 premiers mois de l'étude. Ceci s'explique par l'évolution relativement plus forte de la myopie constatée dans le groupe témoin pendant cette période. Sinon, l'impact du traitement a été plutôt cohérent sur les 2 ans *(cf. Figure 3 et Tableau complémentaire en ligne 4)*. L'impact du traitement avec le verre DIMS a été proche de celui obtenu sur un temps de port quotidien de lentilles DISC de 6 à 8 heures, soit environ 50 % – 60 %.[23] Ces résultats concordent avec nos précédentes études sur les animaux[17 18] et sur l'essai clinique des verres DISC,[22] à savoir que le principe de la mise en œuvre de la défocalisation myopique retarde la croissance de l'œil et l'évolution de la myopie.

Un impact très supérieur des verres DIMS a été constaté sur le ralentissement de l'évolution de la myopie infantile comparé aux verres progressifs existants (10 % – 35 %),[25 27–31] les verres de lunettes avec défocalisation périphérique[32] et les verres de contact[33] (34 %) conçus pour réduire l'hypéropie périphérique relative *(cf. tableau complémentaire en ligne 6)*. L'efficacité du contrôle de la myopie est comparable à celle obtenue avec l'orthokératologie (60%),[10 21] les verres de lunettes bifocaux prismatiques (environ 50 %)[34] et les verres de contact bifocaux souples (50 % – 60 %)[10 23 35] et relativement moins comparé aux résultats obtenus avec l'atropine à forte ou faible dose (70+ %).[11–14]

Les verres DIMS ont ralenti, voire chez certains enfants arrêté l'évolution de la myopie *(cf. Figures complémentaires en ligne 2 et 3)*. Chez 21,5 % des enfants du groupe DIMS il n'y a eu aucune évolution de la myopie sur 2 ans contre seulement 7,4 % dans le groupe témoin. Une évolution considérable de la réfraction (>1D) a néanmoins été constatée chez environ 13 % des enfants du groupe DIMS. Ces variations dans l'effet de retardement ont été constatées avec des lunettes bifocales prismatiques. Cheng et al[34] ont montré que les verres bifocaux prismatiques étaient plus efficaces chez les enfants ayant un retard accommodatif faible. De même, ils ont constaté que l'âge, la myopie initiale et la myopie parentale avaient une incidence sur l'impact du traitement. En revanche, dans notre étude, l'ampleur de l'impact du traitement ne dépendait pas du retard accommodatif, de la myopie initiale ou de la myopie parentale.





L'analyse de l'incidence du modèle du test sur les résultats a montré que l'âge était le seul facteur associé pour lequel un impact significatif sur l'évolution de la myopie a été constaté, et l'impact du traitement de la myopie par les verres DIMS a été plus marqué chez les enfants plus âgés (10 – 13 ans) *(cf. Figure complémentaire en ligne 1)*. Environ 80 % des porteurs de verres DIMS exhibant une évolution considérable de la myopie étaient plus jeunes (8–9 ans). Nous émettons l'hypothèse que les variations dans l'impact du traitement au moyen des verres DIMS peut s'expliquer par des différences de profil rétinien ou de réfraction périphériques chez les enfants.[36] En cas d'hypéropie périphérique importante, le niveau de défocalisation myopique à la rétine périphérique sera réduite, minimisant l'impact du traitement.

Notre étude précédente a montré que le temps de port était un facteur significatif dans la détermination de l'impact du traitement au moyen des lentille DISC.[23]
Aucune corrélation de ce type n'est apparue dans la présente étude. Ce constat s'explique probablement par une forte conformité globale aux exigences de l'étude, les sujets ayant pu porter constamment les verres qui leur avaient été affectés, avec un port moyen de plus de 15 heures/jour. Le taux d'abandon pour cette étude était beaucoup plus faible (13 %) que pour l'étude précédente utilisant des lentilles DISC (42 %).[23]
Les observations en termes de performances visuelles *(cf. Tableau complémentaire en ligne 5 et Figure en ligne 4)* ont montré que les verres DIMS pouvaient fournir une bonne vision en VL et VP comparable à celle offerte par des verres de lunettes unifocaux classiques. Même si quelques sujets ont d'abord remarqué un léger flou dans la zone mi-périphérique, ils se sont pleinement adaptés aux verres en quelques jours. Les symptômes (score < 2) de type image fantôme, étourdissement ou maux de tête se sont très peu produits pendant le port des verres DIMS *(cf. Tableau complémentaire en ligne 5).* Aucun événement adverse lié au traitement n'a été signalé.

Dans les cas où une troisième année d'étude est en cours, le présent rapport ne porte que sur les résultats au terme des deux premières années. Par ailleurs, il ne concerne que l'étude d'enfants chinois. Une étude complémentaire sera nécessaire pour déterminer l'impact du traitement au moyen de verres DIMS sue d'autres populations ethniques. Les verres DIMS et unifocaux sont à peine différenciables par leur aspect. Il faut pour cela les incliner de manière à observer les segments multiples par les reflets d'une source lumineuse. Majoritairement les enfants n'ont pas été conscients des segments multiples. Quelques enfants dans le groupe expérimental ont pu reconnaître les segments multiples mais n'ont pas eu particulièrement plus de difficultés à utiliser les verres qu'avec leurs verres de lunettes précédents. Il a été néanmoins impossible d'assurer l'insu total pour certains sujets. Notre étude n'a pas inclus d'enfants présentant une myopie supérieure à –5 D. Le retardement de l'évolution de la myopie sur les sujets les plus myopes n'a pas encore été déterminé. Des recherches supplémentaires devront porter, particulièrement, sur la détermination de l'efficacité optimale de la méthode dans la prévention de l'évolution et de l'incidence de la myopie.

CONCLUSIONS

Le port quotidien de verres DIMS a sensiblement ralenti l'évolution de la myopie et l'allongement axial chez des enfants scolarisés myopes, comparé au port des verres de lunettes unifocaux. Les verres ont assuré une vision de qualité tout en présentant aux yeux une défocalisation myopique. Cette intervention est simple à mettre en œuvre et constitue la méthode la moins invasive, comparée aux traitements pharmacologiques ou par lentilles de contact. Les verres de lunettes DIMS offrent un mode de traitement alternatif pour contrôler la myopie.

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Contributeurs Tous les auteurs cités ci-dessus ont participé à la mise en œuvre de l'essai clinique notamment aux phases de conception du verre, à la fabrication du verre, à l'inscription de l'essai clinique et à la préparation du protocole clinique pour la collecte des données et l'analyse, l'interprétation et les conclusions. L'équipe des auteurs est en train de préparer une documentation afférente.

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Conflit d'intérêts Aucun. Les brevets intitulés « Spectacle Lens » (verres de lunettes) ont été publiés en Chine (CN104678572 B) et aux Etats-Unis (US10268050 B2) le 27 avril 2018 et le 23 avril 2019 respectivement.

Consentement du patient à la publication Non requis.

Validation éthique Tous les aspects de l'étude ont été conformes aux conditions de la Déclaration d'Helsinki et ont été validés par le Sous-comité responsable des questions d'éthique humaine de la Hong Kong Polytechnic University.

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Déclaration de partage de données Les données sont disponibles à la demande.

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Clinical Trials

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

Investigative Ophthalmology & Visual Science

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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 leds 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

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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 project[23] 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
Baseline						
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)
$P^{\dagger}$	0.16	0.86	0.14	0.21	0.55	0.49
6-Month						
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)
$P^{\dagger}$	0.98	0.32	0.40	0.96	0.08	0.02
12-Month						
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)
$P^{\dagger}$	0.26	0.85	0.32	0.74	0.12	0.003*
18-Month						
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)
$P^{\dagger}$	0.05	0.08	0.45	0.94	0.05	0.003*
24-Month						
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)
$P^{\dagger}$	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.

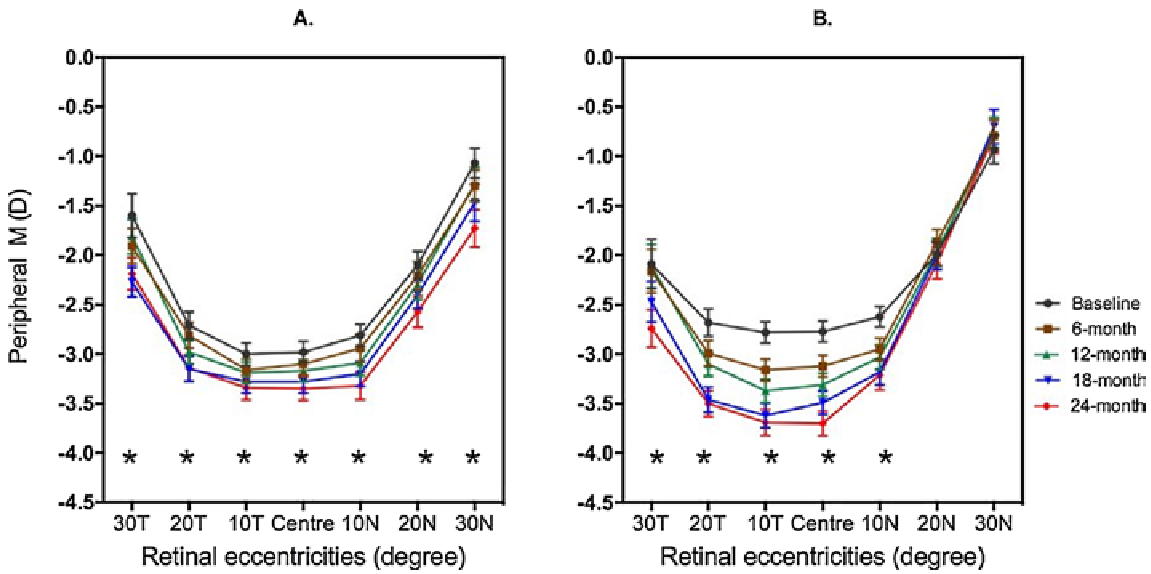

Figure 1. (**A**) Peripheral refraction changes across the horizontal retina over 2 years in the DIMS group. (**B**) Peripheral refraction changes across the horizontal retina over 2 years in the SV group. *Error bars* denote the SEM. The significance of the *P* value was considered as <0.008 after Bonferroni 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
Baseline						
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
6-Month						
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*
12-Month						
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*
18-Month						
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*
24-Month						
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 peripheral 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.

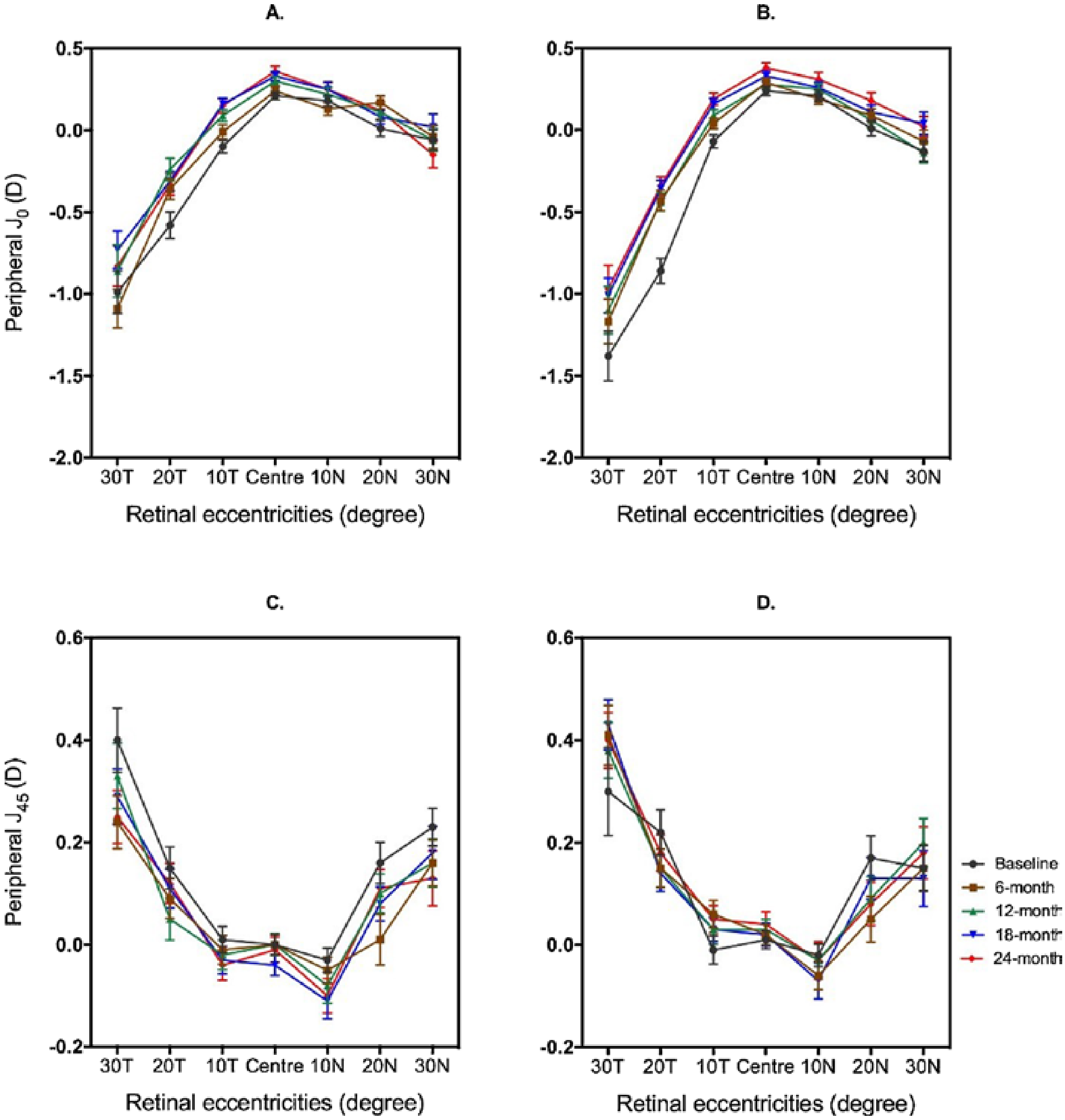

Figure 2. (**A**) Peripheral J_0 changes across the horizontal retina over 2 years in the DIMS group. (**B**) Peripheral J_0 changes across the horizontal retina over 2 years in the SV group. (**C**) Peripheral J_{45} changes across the horizontal retina over 2 years in the DIMS group. (**D**) Peripheral 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)

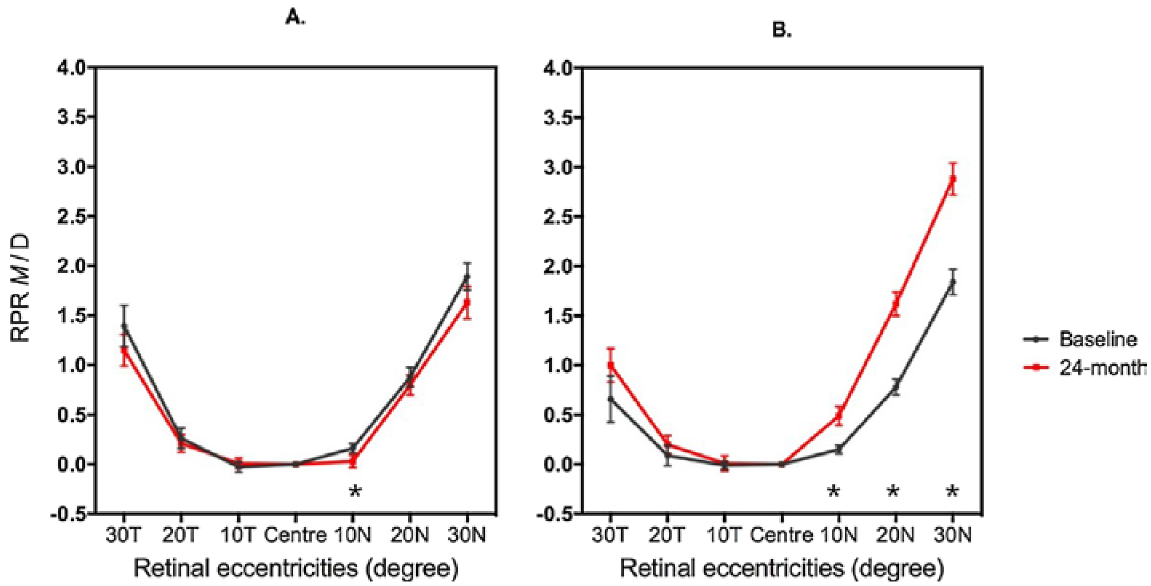

Figure 3. (**A**) RPR changes across horizontal retina over 2 years in the DIMS group. (**B**) RPR changes across horizontal retina over 2 years in the SV group. *Error bars* denote SEM. The significance of the *P* value was considered as <0.008 after Bonferroni adjustment. *P <0.008 indicates the significant 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 study[38]; 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 mechanisms 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, Pan[43] 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 knowlegde 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.

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Essais cliniques

Les verres ophtalmiques DIMS (Defocus Incorporated Multiple Segments) modifient la réfraction périphérique relative : essai clinique randomisé sur 2 ans

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Objectif : comparer les changements de la réfraction périphérique relative (RPR) associés à la progression de la myopie chez des enfants myopes équipés de verres ophtalmiques DIMS (Defocus Incorporated Multiple Segments) ou unifocaux sur une période de deux ans.

Methodologie : un essai mené à double insu, randomisé et contrôlé sur deux ans a été réalisé sur un panel de 183 enfants atteints de myopie. Des verres correcteurs DIMS (n=93) ou unifocaux (n=90) ont été assignés de manière arbitraire aux enfants. La réfraction périphérique à 10°, 20°, et 30° des excentricités rétiniennes nasales (10N, 20N, 30N) et temporales (10T, 20T, 30T), la réfraction centrale, et la longueur axiale après la cycloplégie ont été mesurées à des intervalles de six mois.

Resultats : sur le groupe DIMS nous avons constaté des LAG myopiques périphériques symétriques entre les rétines nasale et temporale (une comparaison des LAG myopiques entre rétines nasale et temporale n'a fait apparaître aucun écart significatif sur le plan clinique entre les excentricités correspondantes). Le groupe unifocal (U) a présenté des LAG myopiques périphériques asymétriques entre rétines nasale et temporale, avec davantage de LAG myopiques (tous $P \leq 0,001$) à 10T (0,32 ± 0,62 dioptries [D]), à 20T (-0,69 ± 0,95 D), et 30T (- 0,85 ± 1,52 D). Aucun changement significatif de l'équivalent sphérique RPR (*M*) n'a été constaté dans le groupe DIMS, tandis que des augmentations sensibles (tous $P < 0,0001$) de la RPR hypermétrope pour *M* ont été constatées à 10N (0,27 ± 0,45 D), 20N (0,75 ± 0,72 D), et 30N (0,98 ± 0,76 D) dans le groupe U.

Conclusions : le port des verres DIMS a produit un profil de réfraction périphérique et des changements de RPR sensiblement différents, ainsi que des effets de contrôle de la myopie significatifs, comparé au port des verres unifocaux. Le contrôle de la myopie adoptant la défocalisation myopique en mi-périphérique a eu une incidence sur la réfraction périphérique et a ralenti la progression de la myopie, probablement en raison du changement de la forme rétinienne globale.

Mots clefs : contrôle de la myopie, défocalisation myopique, réfraction périphérique relative, forme de la rétine

Habituellement les sujets myopes présentent une réfraction périphérique relative (RPR) hypermétrope, tandis que les emmétropes et les hypermétropes présentent une RPR myopique.[1,2] Les précédentes études de la relation entre RPR et apparition de la myopie, et entre RPR et progression de la myopie ne font pas encore l'objet de consensus.[3–8] Hoogerheide et al.[3] ont mesuré la réfraction le long de 120° du champ visuel horizontal chez de jeunes adultes (hypermétropes et emmétropes) entreprenant une formation de pilote d'avions. Ils ont constaté que 65 % des emmétropes et hypermétropes ayant développé ensuite une myopie présentaient une RPR hypermétrope. Or, il n'était pas certain que la mesure de la RPR ait été réalisée au début ou à l'issue de l'étude.[9] Il s'agissait de la première étude longitudinale à faire le point sur la relation entre RPR et développement de la myopie.

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Mutti et al.[8] ont constaté que la présence d'une RPR hypermétrope accentuée dans les 2 à 4 ans avant l'apparition de la myopie pouvait être un facteur permettant d'anticiper cette dernière ; or, la RPR était stable pendant les 5 ans suivant l'apparition de la myopie. Dans un rapport ultérieur, Mutti et al.[4] ont étudié des enfants issus de différents groupes ethniques, notamment, asiatiques, afro-américains et caucasiens, et ont conclu que la RPR présentait une incidence faible mais récurrente sur le risque d'apparition et de développement de la myopie ou de l'allongement axial. Sng et al.[5] ont suivi les changements de réfraction centrale et périphérique chez des enfants chinois de Singapour pendant plus d'un an et ont constaté que la réfraction périphérique ne permettait pas de prédire l'apparition d'une myopie et n'avait pas d'incidence sur la progression de celle-ci.

Il a été largement documenté parmi les études d'espèces animales que l'augmentation de la défocalisation hypermétrope entraîne une plus grande progression de la myopie,[10,11] tout en induisant une progression de la myopie ralentie par la défocalisation myopique[10,12–14]. Les résultats d'observations sur de jeunes singes[12,13] et des poussins[10,14] ont suggéré que la résolution spatiale au niveau anatomique du chemin optique pouvait moduler la croissance globale de l'œil.[15] Les études sur des animaux utilisant des lentilles de contact munies d'une défocalisation myopique intégrée ont conclu à un ralentissement possible de 20 % à 60 % de la progression myopique.[16–19]

Lors de notre précédent essai clinique, utilisant des lentilles de contact souples avec défocalisation intégrée (DISC), munie d'une défocalisation myopique de +2,50 dioptries (D) pour enfants myopes, un ralentissement significatif de la progression myopique d'environ 60 % sur 2 ans a été constaté chez les enfants portant ces verres pendant plus de 7 heures par jour.[17] Dans le cadre d'une autre étude utilisant les lentilles souples MiSight (Cooper Vision, Inc., Pleasanton, CA, USA) ou des lentilles unifocales dans un essai clinique randomisé, le niveau de progression de la myopie et l'allongement axial chez des enfants portant des lentilles MiSight pendant 3 ans a été sensiblement inférieur, de 59 % et 52 % respectivement, que chez des enfants équipés de lentilles unifocales.[19] Ces résultats impliquaient que la défocalisation myopique pouvait freiner la progression de la myopie chez les enfants myopes.[17,19]

Lors de la correction de la myopie à l'aide de verres à lunettes classiques, la lumière axiale est focalisée sur la fovéa, tandis que la lumière hors-axe entraîne une défocalisation hypermétrope périphérique[20,21]; d'où l'hypothèse qu'il s'agissait là d'un facteur possible de déclenchement de la progression de la myopie. Sankaridurg et al.[22] ont constaté qu'il n'y avait aucune incidence statistiquement significative sur le ralentissement de la myopie après le port de verres à lunettes comportant une défocalisation myopique intégrée dans la zone périphérique pendant un an, comparé aux sujets portant des verres unifocaux.[16] Ces résultats n'ont pas été corroborés par notre récent essai clinique sur des lunettes DIMS. Le verre DIMS comporte une zone de correction centrale entourée de segments multiples de défocalisation myopique constante (+3,50 D) dans la mi-périphérie, offrant en même temps une vision centrale claire et une défocalisation myopique périphérique.[23] Nous avons déjà publié des résultats d'une étude qui indiquaient que le port de verres DIMS pendant une période de 2 ans pouvait ralentir la progression de la myopie et l'allongement axial à hauteur de 59 % et 60 % respectivement, comparé au port de verres à lunettes unifocaux.[23]

La majorité des études précédentes portant sur la défocalisation myopique a rendu compte des effets du contrôle de la myopie en termes de changement de la réfraction oculaire et de la longueur axiale, et plus rarement sur le changement de la forme de la rétine. Certaines études ont postulé que cette forme puisse être déterminante pour le développement de la myopie via des facteurs biomécaniques, tels que l'amaigrissement de la sclère et l'ectasie localisée de la sclère postérieure pendant le développement de la myopie.[24,25] Des corrélations significatives entre la longueur de l'œil en périphérie et la réfraction périphérique ont été notées.[26–28] D'où l'utilisation de la réfraction périphérique ou RPR, aisément surveillée et mesurée par les cliniciens, pour décrire indirectement la forme de la rétine.[15,29] A ce jour, peu d'études ont fait état de changements de la RPR à la suite d'un contrôle de la myopie à l'aide de la défocalisation myopique chez l'humain. Dans le projet DIMS,[23] les effets du port de verres à lunettes DIMS sur la RPR ont été étudiés. Les changements de la RPR et de la forme rétinienne chez les groupes DIMS et U sont détaillés dans le présent article. Les données du projet DIMS[23] ont été utilisées dans cet article pour examiner l'incidence du port de verres à lunettes DIMS ou unifocaux sur la RPR.

Methodologie

Un essai clinique randomisé et à double insu a été réalisé au Centre for Myopia Research, School of Optometry, du Hong Kong Polytechnic University entre le mois d'août 2014 et le mois de juillet 2017.[23] Les verres DIMS (groupe traité) ou unifocaux (groupe témoin) ont été assignés de manière arbitraire aux enfants. Les critères de recrutement sont énumérés ci-après :

Les critères d'inclusion étaient :

1. nationalité chinoise de Hong Kong, âgés de 8 à 13 ans ;
2. ES de −1,00 à −5,00 dioptries (D) ;
3. astigmatisme et anisométropie de ≤1,50 D ;
4. acuité visuelle monoculaire optimale d'au moins 0,00 logMAR (6/6) ;
5. acceptation des principes de répartition arbitraire aux deux groupes d'enfants et d'étude à double insu

Les critères d'exclusion étaient :

1. le strabisme et des anomalies de vision binoculaire ;
2. des anomalies oculaires et systémiques
3. une expérience antérieure de contrôle de la myopie

L'étude a été validée par le Sous-comité responsable des questions d'éthique humaine de la Hong Kong Polytechnic University et est conforme aux conditions de la Déclaration d'Helsinki. Le consentement éclairé a été obtenu auprès des parents ou tuteurs de tous les participants. La procédure de randomisation a été décrite ci-dessus.[23] Les enfants et les parents ont été affectés aux groupes à leur insu. Les procédures d'insu étaient conformes à la norme *Consolidated Standards of Reporting Trials requirements* (Standards fusionnés dans la rédaction d'essais thérapeutiques).

Un examen normalisé des yeux a été réalisé tous les 6 mois pendant la période de 2 ans. La puissance cornéenne a été mesurée à l'aide d'un réfractomètre automatique Shin-Nippon NVision-K 5001 (Ajinomoto Trading Inc., Tokyo, Japon), sans cycloplégie. Une goutte de proparacaïne 0,4 % suivie de 1 à 2 gouttes de cyclopentolate HCL 1 % ont été utilisées pour induire une cycloplégie. La réfraction centrale et périphérique à travers les excentricités rétiniennes horizontales a été mesurée cinq fois à l'aide d'un réfractomètre automatique Shin-Nippon NVision-K 5001 avec centrage de la croix de fixation, puis avec excentricité rétinienne à 10°, 20°, et 30° nasale (10N, 20N, 30N) et temporale (10T, 20T, 30T). La consigne a été donnée aux sujets de garder la tête immobile et de tourner les yeux pour fixer les différentes cibles.[30] La réfraction périphérique a été mesurée dans l'œil droit, la biométrie oculaire entre les deux yeux étant fortement corrélée.[23,31] Dans ce groupe d'enfants, le coefficient de corrélation entre l'OD et l'OG était de 0,1 pour le *M* central, 0,97 pour la longueur axiale, 0,94 pour le rayon serré cornéen verticale, et 0,97 pour le rayon plat cornéen.[23] La longueur axiale a été mesurée cinq fois à l'aide d'un biomètre optique IOL Master (Carl Zeiss, Oberkochen, Allemagne), avec calcul de la moyenne. Les mesures de réfraction sphérocylindrique pour la puissance sphérique (S), la puissance cylindrique (C), et l'axe (θ) ont été converties en un vecteur de puissance par une formule conventionnelle à des fins d'analyse.[32]

$$M = S + C/2$$

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

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

La valeur J_0 positive représente l'astigmatisme selon la règle (direct), alors que les résultats négatifs représentent l'astigmatisme contre la règle (inverse). La valeur J_{45} représente l'astigmatisme oblique. La valeur RPR est calculée par soustraction de la réfraction centrale de la réfraction périphérique. Les valeurs RPR positives et négatives sont considérées respectivement comme des RPR hypermétrope, et myope. Dans notre précédent article nous avons conclu qu'il n'y avait aucune différence statistiquement significative en termes d'âge, de proportion de sexe, de *M* central ou de longueur axiale entre les groupes DIMS et U ($P > 0,05$) moyenne de référence.[23]

Analyses des données

Toutes les analyses statistiques ont été réalisées à l'aide du logiciel IBM SPSS v.16.0 (IBM Corporation, Armonk, NY, Etats-Unis). L'œil droit a été utilisé pour les analyses de données, et toutes les données ont fait l'objet d'une répartition normale. La méthode ANOVA a été répétée pour mesurer et estimer l'impact du port des verres DIMS et unifocaux sur la modification de la réfraction périphérique et de la RPR dans la durée. Des tests *t* indépendants ont été réalisés pour comparer les différences de valeur RPR relevées sur les deux groupes. L'écart entre les erreurs réfractives relevées sur les rétines nasale et temporale a été comparé au moyen d'un test *t* apparié. Prenant les changements de la valeur *M* centrale et les changements de la longueur axiale comme variable dépendante, des régressions linéaires ont été réalisées pour analyser la relation entre (1) la moyenne de référence RPR et les LAG myopiques, (2) la moyenne de référence RPR *M* et l'allongement axial, (3) les changements de RPR *M* et les LAG myopiques, et (4) les changements de RPR *M* et l'allongement axial, avec des ajustements pour tenir compte du sexe et de l'âge dans le groupe U. Une valeur *P* de <0,05 a été retenue comme étant statistiquement significative ; un ajustement Bonferroni a été appliqué le cas échéant. La valeur 0,008 a été adoptée comme référence pour juger de la pertinence des mesures puisque la réfraction a été mesurée dans six excentricités rétiniennes dans l'œil droit de chaque sujet.

RESULTATS

Réfraction périphérique (*M*, J_0, J_{45})

Le Tableau 1 et la Figure 1 ci-après montrent les résultats de la valeur *M* périphérique dans les groupes DIMS et U à des intervalles de 6 mois. Aucune différence significative de réfraction périphérique *M* n'a été constatée à travers la rétine horizontale entre les deux groupes à la moyenne de référence (test *t* indépendant, $P > 0,05$). Après 2 ans, les deux groupes ont présenté une augmentation régulière du LAG myopique au centre et en périphérie, mais suivant des schémas différents.

Toutes les excentricités rétiniennes horizontales dans le groupe DIMS ont présenté des LAG myopiques dans la valeur *M* périphérique dans une fourchette de −0,34 à −0,60 D (test *t* apparié, $P = < 0.0001$), et présentant un schéma symétrique de LAG myopiques entre les rétines nasale et temporale. (Fig. 1). La comparaison entre rétines nasale et temporale n'a retenu aucune différence cliniquement significative entre les excentricités correspondantes, l'écart moyen à 10° étant de 0,17 ± 0.49 D ($P = 0,003$), à 20° de 0,04 ± 0,71 D ($P = 0,65$), et à 30° de 0,23 ± 1,71 D (*P* 0,37).

Le groupe U a présenté des LAG myopiques significatives à certaines excentricités, dans une fourchette plus large de 0,59 à 0,91 D ($P < 0,0001$) sur 2 ans, et un schéma asymétrique de LAG myopiques entre les rétines nasale et temporale (Fig. 1). Sur les 2 ans les LAG myopiques à la rétine temporale étaient plus importants que sur la rétine nasale ; l'écart moyen à 10° était de 0,32 ± 0,62 D ($P < 0.0001$), à 20° de 0,69 ± 0,95 D ($P < 0.0001$), et à 30° de 0,85 ± 1,52 D ($P < 0,001$).

Tableau 1. Moyenne (écart type) de la réfraction périphérique *M* dans les groupes DIMS et unifocal (U) sur 2 ans

Groupe	10T	20T	30T	10N	20N	30N
Référence moyenne						
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)
U	−2,78 (0,98)	−2,68 (1,23)	−2,09 (1,74)	−2,62 (0,93)	−1,99 (1,06)	−0,93 (1,28)
P†	0,16	0,86	0,14	0,21	0,55	0,49
6 mois						
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)
U	−3,16 (1,01)	−2,99 (1,16)	−2,16 (1,56)	−2,95 (1,01)	−1,87 (1,19)	−0,79 (1,38)
P†	0,98	0,32	0,40	0,96	0,08	0,02
12 mois						
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)
U	−3,37 (1,07)	−3,10 (1,09)	−2,11 (1,66)	−3,03 (1,12)	−1,97 (1,27)	−0,76 (1,39)
P†	0,26	0,85	0,32	0,74	0,12	0,003*
18 mois						
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)
U	−3,62 (1,11)	−3,46 (1,16)	−2,47 (1,63)	−3,18 (1,16)	−2,00 (1,28)	−0,70 (1,53)
P†	0,05	0,08	0,45	0,94	0,05	0,003*
24 mois						
U	−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)
P†	0,06	0,06	0,03	0,59	0,03	<0,0001*

† La valeur *P* a été jugée significative si <0,008 après ajustement Bonferroni.

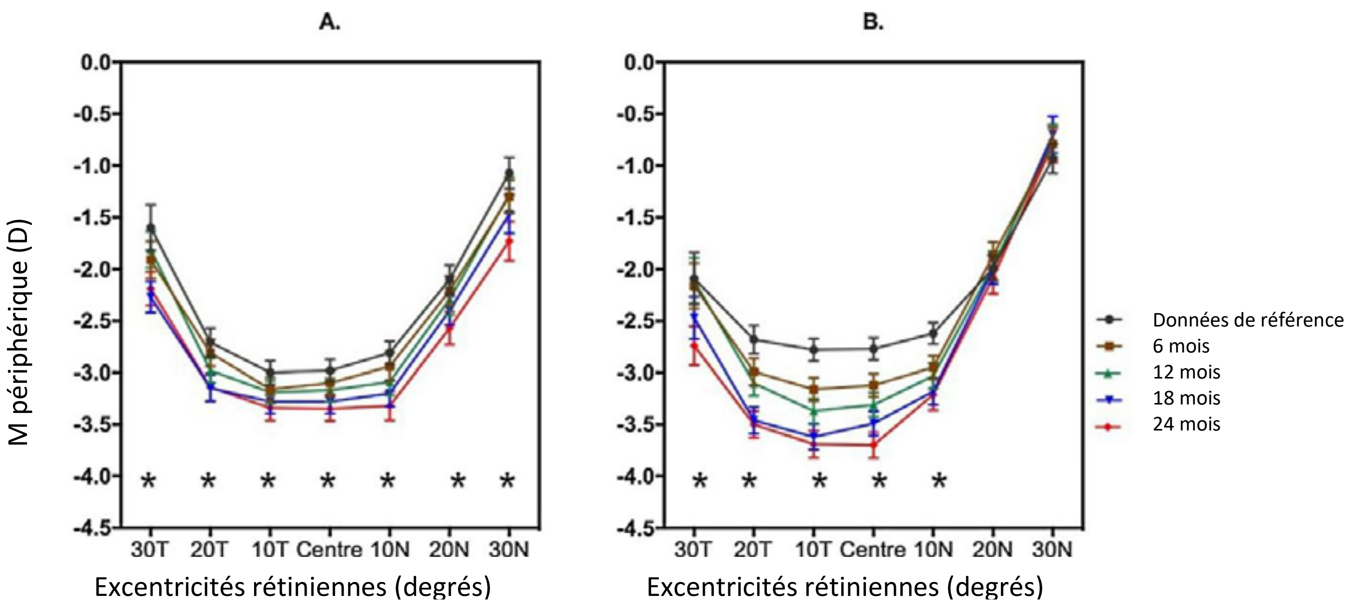

Figure 1. (A) Evolution de la réfraction périphérique à travers la rétine horizontale sur 2 ans dans le groupe DIMS. (B) Evolution de la réfraction périphérique à travers la rétine horizontale sur 2 ans dans le groupe U. Les barres d'erreur représentent l'erreur-type. La valeur *P* a été jugée significative si <0,008 après ajustement Bonferroni. *P <0,008 indique une différence significative entre la référence moyenne et 24 mois dans le groupe (test *t* apparié).

En fait, le groupe DIMS a présenté un LAG myopique plus uniforme à toutes les excentricités, tandis que le groupe U a présenté un LAG myopique asymétrique. La comparaison des deux groupes a révélé que le groupe DIMS présentait sensiblement plus de LAG myopiques dans *M* périphérique à 30N (écart moyen -0,70 ± 0,18 D, $P < 0,0001$) et 20N (écart moyen -0,38 ± 0,14 D, $P = 0,0006$), mais sensiblement moins de LAG myopiques à 10T (écart moyen 0,57 ± 0,12 D, $P < 0,0001$) comparé au groupe U sur la période d'observation de 2 ans.

Aucune différence statistiquement significative n'a été relevée sur les deux groupes entre les valeurs périphériques J_0 et J_{45} à la référence moyenne (à toutes les excentricités, $P > 0,05$). Après 2 ans, la valeur périphérique J_0 a présenté des LAG positifs significatifs à 10T et 20T, avec des changements de 0,25 ± 0,33 D ($P < 0,0001$) et 0,25 ± 0,47 D ($P < 0,0001$), respectivement dans le groupe DIMS. Dans le groupe U, des LAG positifs significatifs ont été constatés à 10T (écart moyen : 0,29 ± 0,28 D, $P < 0,0001$), 20T (écart moyen : 0,54 ± 0,50 D, $P < 0,0001$), 20N (écart moyen : 0,17 ± 0,38, $P < 0,0001$), et 30N (écart moyen : 0,16 ± 0,47, $P = 0,004$). Il n'y avait aucun changement de la valeur périphérique J_{45} dans les groupes DIMS ou U (à toutes les excentricités, $P > 0,05$). Il n'y avait aucune différence significative de la valeur périphérique J_0

entre les deux groupes après 2 ans ni de la valeur périphérique J_{45} sur 2 ans après correction Bonferroni ($P > 0{,}008$; Fig. 2).

Réfraction périphérique relative *M*

Le Tableau 2 et la Figure 3 décrivent la RPR *M* dans les groupes DIMS et U sur 2 ans. Il n'y avait aucune différence significative de la valeur RPR *M* entre les groupes DIMS et U à la référence moyenne après correction Bonferroni (à toutes les excentricités, toutes $P > 0{,}008$).

Après 2 ans, les LAG myopiques dans toutes les réfractions périphériques ont augmenté proportionnellement avec la réfraction centrale, et ont donc maintenu une RPR *M* plutôt constante dans le groupe DIMS. Malgré une réduction significative de la RPR hypermétrope *M* à 10N (écart moyen 0,13 ± 0,43 D, $P < 0{,}0001$) dans le groupe DIMS, tous les changements étaient jugés négligeables sur le plan clinique.

Dans le groupe U, des LAG hypermétropes significatifs de la RPR ont été observés sur la rétine nasale, avec des changements moyens de 0,27 ± 0,45 D, 0,75 ± 0,72 D, et 0,98 ± 0,76 D à 10N, 20N, et 30N ($P < 0.0001$) mais aucun changement significatif n'est apparu coté rétine temporale. La RPR a présenté un profil oblique.

La comparaison des deux groupes a révélé que le groupe U avait une valeur RPR M hypermétrope sensiblement supérieur à 10N (écart moyen 0,46 ± 0,11 D, P < 0,0001), 20N (écart moyen 0,82 ±0,16 D, P < 0.0001), et 30N (écart moyen 1,25 ±0,23 D, P < 0,0001) mais non pas de la rétine temporale, comparé au groupe DIMS

Corrélation de RPR *M* et d'autres facteurs

Dans le groupe U, il n'y avait aucune association significative entre la référence moyenne RPR pour *M* et la progression myopique, ni entre la référence moyenne pour RPR *M* et l'allongement axial, et ce à toutes les excentricités (régression linéaire, $P > 0{,}05$). Or, les changements de RPR *M* à 10N ont montré une association significative avec la progression myopique (coefficient normalisé : 0,84, $P = 0{,}003$), et l'allongement axial (coefficient normalisé : -0,79, $P = 0{,}004$) après ajustement pour tenir compte du sexe et de l'âge.

DISCUSSION

La présente étude avait pour objectif d'approfondir la connaissance des changements de la forme de la rétine à la suite de l'utilisation de la défocalisation myopique dans le cadre du contrôle de la myopie. Nous avons mesuré la réfraction périphérique et les changements de la RPR comparant des enfants équipés de lunettes à verres unifocaux et DIMS dans le cadre d'un essai clinique randomisé sur une période de 2 ans.

Sur cette période, il a été note que les sujets du groupe U présentaient des changements plus importants pour le *M* périphérique temporal de la rétine (champ visuel nasal) que pour la rétine nasale (champ visuel temporal), présentant un changement asymétrique, et que cette asymétrie avait augmenté pendant l'évolution de la myopie, un phénomène qui recoupait les résultats d'études précédentes.[6,33] Certaines études ont suggéré que cette asymétrie pouvait s'expliquer par une combinaison de plusieurs facteurs, dont la différence d'angle entre l'axe optique et l'axe visuel (angle alpha),[34,35] des asymétries dans la profondeur du corps vitré,[36] et la courbure de la cornée.[37] Il a été postulé que l'augmentation du profil périphérique asymétrique est due à différents niveaux d'expansion oculaire le long de la région axiale et équatoriale pendant la progression de la myopie, et tout particulièrement dans des yeux présentant une progression plus rapide de la myopie.[6] En revanche, après le traitement de la myopie à l'aide de verres DIMS, les enfants ont présenté des changements significatifs de la valeur *M* périphérique à toutes les excentricités rétiniennes, indiquant un LAG myopique uniforme le long de la rétine horizontale. On pourrait poser comme hypothèse que des enfants du groupe DIMS ont connu une croissance relativement lente et uniforme de l'œil, alors que dans le groupe U, l'expansion axiale a été relativement plus rapide que dans la région équatoriale.

Les changements de la RPR différaient aussi entre les deux groupes. Dans le groupe U, une augmentation sensible de la RPR *M* hypermétrope à la rétine nasale (dans la fourchette approximative de 0,27 à 0,98 D) a été constatée sur deux ans alors que la valeur RPR *M* a présenté un léger changement statistique dans le groupe DIMS, sans toutefois que cela ait une importance clinique. A notre connaissance, la présente étude est la seule sur l'humain à faire état de ce résultat. Parmi les études réalisées sur des animaux une étude sur des cochons d'inde a livré des résultats contradictoires [38]; une augmentation significative de la RPR *M* hypermétrope a été constatée après une superposition de la défocalisation myopique dans la zone périphérique. On peut supposer qu'il existe une zone de la rétine capable de décoder des signes de défocalisation, produisant ainsi des changements locaux de zones de la rétine.[37] Une telle capacité de décoder dépend de la zone ou du seuil de défocalisation, potentiellement différents chez l'humain, comparé à d'autres espèces animales.[38]

Si les changements de la RPR *M* à 10N ont montré une association significative avec le LAG myopique central et l'allongement axial sur les 2 ans dans le groupe U, la référence moyenne RPR *M* ne pouvait prédire la progression myopique ou l'allongement axial, un constat qui corrobore les études antérieures.[4–7] Mutti et al.[4] ont observé les changements de la réfraction périphérique à 30° dans le champ visuel nasal et ont constaté que la réfraction périphérique exerçait une faible influence sur la prédiction de l'apparition ou de la progression de la myopie. La RPR hypermétrope serait plus probablement une conséquence de l'allongement axial qu'une cause de la progression de la myopie.[39] Ceci s'explique par le fait que l'augmentation de la longueur axiale a été supérieure à celle du diamètre équatorial lors de l'allongement du globe oculaire, d'où une forme oculaire relativement prolate,[1,40] se traduisant par une myopie moindre dans la rétine périphérique que dans la fovéa centrale.

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TABLEAU 2. Moyenne (écart type) de la valeur RPR *M* dans les groupes DIMS et unifocal (U) sur 2 ans

Groupe	10T	20T	30T	10N	20N	30N
Référence moyenne						
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
6 mois						
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)
U	–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*
12 mois						
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)
U	–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*
18 mois						
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)
U	–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*
24 mois						
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*

† La valeur *P* a été jugée significative si <0,008 après ajustement Bonferroni

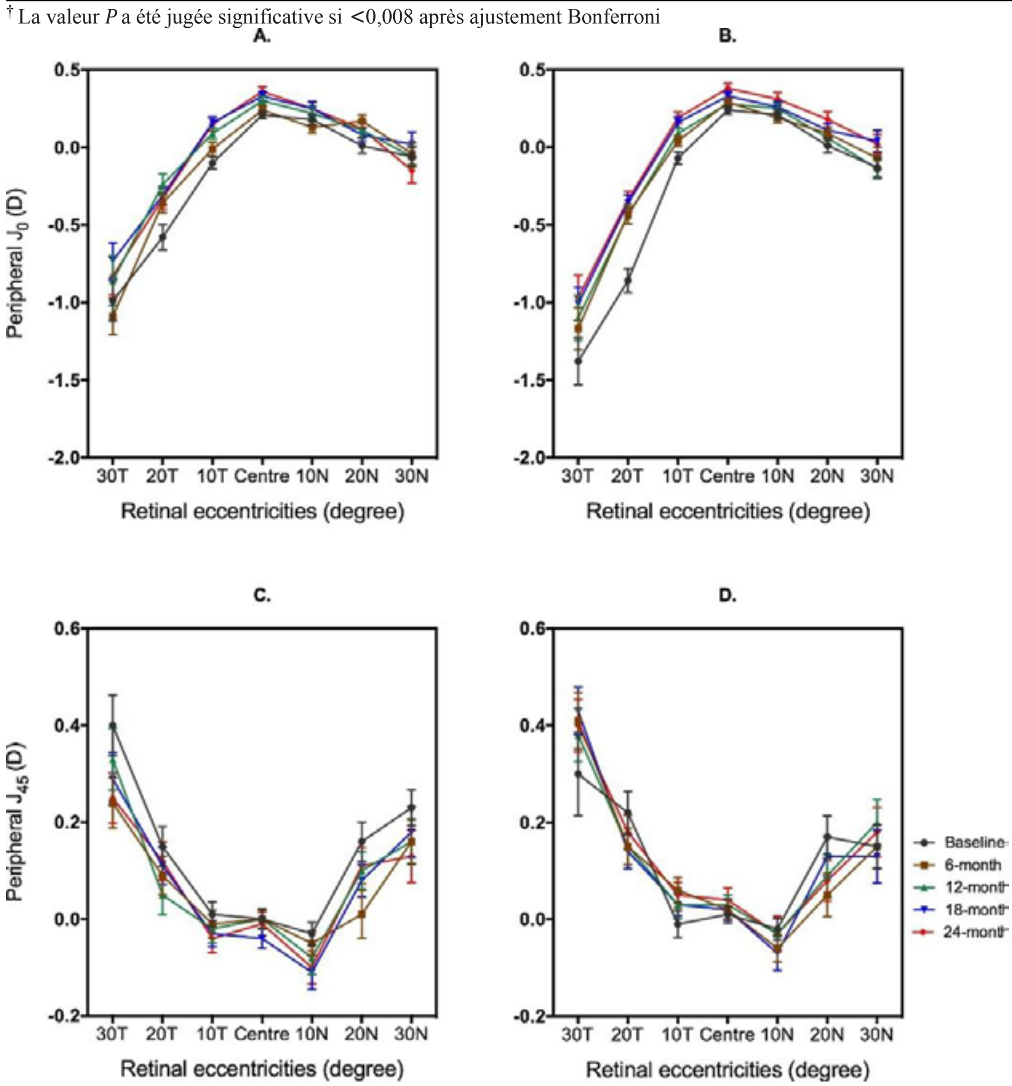

FIGURE 2. (**A**) Changements périphériques J_0 à travers la rétine horizontale sur 2 ans dans le groupe DIMS. (**B**) Changements périphériques J_0 à travers la rétine horizontale sur 2 ans dans le groupe U. (**C**) Changements périphériques J_{45} à travers la rétine horizontale sur 2 ans dans le groupe DIMS. (**D**) Changements périphériques J_{45} à travers la rétine horizontale sur 2 ans dans le groupe U. Les barres d'erreur représentent l'erreur-type.

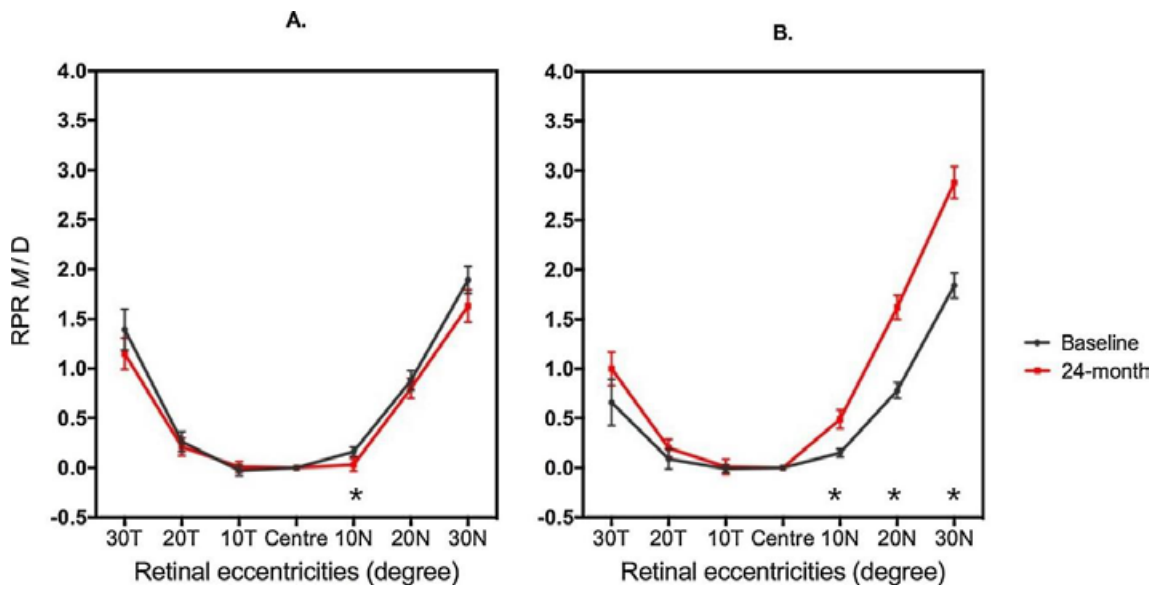

FIGURE 3. (A) Changements de RPR à travers la rétine horizontale sur 2 ans dans le groupe DIMS. (B) Changements de RPR à travers la rétine horizontale sur 2 ans dans le groupe U. Les barres d'erreur représentent l'erreur-type. La valeur *P* a été jugée significative si <0,008 après ajustement Bonferroni. **P* <0,008 indique une différence significative entre la référence moyenne et 24 mois dans le groupe (test *t* apparié).

Il a été suggéré que la RPR puisse servir à décrire indirectement la forme de la rétine.[15,29] Une valeur RPR hypermétrope supérieure a suggéré une image shell moins courbe comparé à la forme de la rétine,[41] et à courbure cornéenne et longueur axiale constantes, une RPR hypermétrope plus élevée a indiqué une inclinaison plus prononcée de la forme de la rétine.[29] Ceci laissait entendre que l'image shell avec une courbe réduite, comparé à la forme de la rétine constatée dans le groupe U indiquait une forme de la rétine plus inclinée, alors que la forme de la rétine était plus horizontale dans le groupe DIMS.

Pour ce qui concerne le profil asymétrique du groupe U, le mécanisme de l'expansion périphérique inhibée dans ce groupe n'a pas été élucidé, et, dans une étude précédente, Mutti et al ont considéré plusieurs mécanismes[8], indiquant qu'une insuffisance de matière dans le verre pourrait empêcher un étirement équatorial de l'œil au fur et à mesure de sa croissance.[1,8]

Nous avons proposé que le schéma uniforme de la croissance de l'œil stimulant davantage de la croissance périphérique de l'œil soit un mécanisme de la croissance normale de l'œil ou processus d'emmétropisation. Dans la présente étude, le ralentissement de la progression de la myopie et de l'allongement axial dans le groupe DIMS peut être interprété comme un retour à une croissance coordonnée de l'œil. Dans le groupe U l'allongement axial a progressé plus vite dans la zone équatoriale et indique peut-être une croissance non coordonnée de l'œil. Il est possible qu'une restriction équatoriale de l'œil en phase de croissance puisse accentuer l'allongement axial.[42]

Récemment, Pan[43] a noté chez une souris qu'une image défocalisée pouvait modifier le signalement ON-OFF des cellules ganglionnaires rétiniennes cellules (CGR), et a montré des réponses différentes à des variations de puissance de l'image défocalisée.[44] Nous avons supposé que le signalement de ces cellules puissant être modifié par la puissance de défocalisation dans les verres DIMS, entraînant un schéma uniforme et symétrique de changement dans la réfraction périphérique. Il faudra toutefois que cette théorie soit étayée par des études complémentaires sur des animaux.

Cette étude a été incomplète dans la mesure où la longueur de l'œil en périphérie n'a pas été mesurée ; or, prendre ces mesures pourrait permettre de déterminer la croissance réelle de la périphérie de l'œil. On notera aussi que la large fourchette de valeurs de l'écart type relatives aux valeurs RPR moyennes pourrait indiquer une variabilité de la forme réelle de la rétine.[2,15]

Les changements de la réfraction périphérique ou RPR durant le contrôle de la myopie ont été peu étudiés, et, à notre connaissance, notre étude est la première à démontrer que le contrôle de la myopie grâce à la défocalisation myopique, tout en assurant une vision claire, a une incidence sur les changements de la réfraction en mi-périphérique et sur la RPR, comparé aux verres unifocaux. Notre description de la forme de la rétine dans les deux groupes n'est peut-être encore qu'une partie d'un champ d'exploration encore plus large ; il conviendra de réaliser des études approfondies de la forme de la rétine ou de l'œil à l'aide de l'imagerie médicale : IRM ou échographie en mode B, par exemple. Un effort complémentaire pour comprendre l'action du mécanisme sur le schéma des changements de la réfraction périphérique dans le contrôle de la myopie à l'aide de la défocalisation myopique sera nécessaire.

CONCLUSIONS

A notre connaissance, la présente étude est la première à démontrer que l'utilisation de la défocalisation myopique pour le contrôle de la myopie permet d'intervenir sur la réfraction périphérique, tout en assurant une vision claire. Le contrôle de la myopie à l'aide de la défocalisation myopique dans la zone mi-périphérique a eu une incidence sur les changements de la réfraction périphérique et a ralenti la progression de la myopie centrale, probablement par le changement de la forme générale de la rétine. De nouvelles études permettant d'élucider les mécanismes intervenant dans ce processus seraient alors bienvenues.

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Article

Effect of Defocus Incorporated Multiple Segments Spectacle LensWear on Visual Function in Myopic Chinese Children

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Purpose: To compare visual function of myopic children who had worn either defocus incorporated multiple segment (DIMS) spectacle lenses or single vision (SV) spectacle lenses over two years.

Methods: We included 160 Chinese myopic (−1 diopter [D] to −5 D) children aged 8 to 13 years in a randomized clinical trial; they wore either DIMS lenses (DIMS; $n = 79$) or regular SV spectacles lenses ($n = 81$) full time for 2 years. Visual function, including high-contrast visual acuity (VA) and low-contrast VA at distance and near, binocular functions, and accommodation, before, during, and after 2 years of spectacle wear were assessed when both groups wore SV corrections. Changes of visual function between the two groups and within groups were compared.

Results: There were no statistically significant differences in the 2-year visual function changes between DIMS and SV groups (repeated measures analysis of variance with group as factor; $P > 0.05$). Statistically significant improvement in the best-corrected distance high-contrast VA ($P < 0.001$) and stereoacuity score ($P < 0.001$) were found after DIMS lens wear over 2 years. Similar findings were observed after SV spectacle lens wear. For both the DIMS and SV groups, there were statistically significant decreases in accommodative lag, monocular and binocular amplitude of accommodation after two years ($P < 0.01$), but not in the changes in distance low-contrast VA, near high-contrast VA, near low-contrast VA, or phoria.

Conclusions: Although changes in some visual function were shown during 2 years of DIMS lens wear, similar changes were found with SV lens wear. Wear of DIMS spectacle lenses for 2 years does not adversely affect major visual function when children return to SV corrections.

Translational Relevance: DIMS spectacle lenses did not cause any adverse effects on visual function.

Introduction

Myopia prevalence is increasing around the world at an alarming rate. If present trends continue, 50% of the world's population is predicted to be myopic by 2050 and nearly 1 billion people will probably become high myopes.[1,2] In Asian countries, the prevalence is reaching epidemic proportions with 70% to 80% of teenagers being myopic.[1,3,4] The risk of developing ocular pathologies, such as myopic macular degeneration, retinal detachment, glaucoma, and cataract, increases significantly with an increasing magnitude of myopia.[4–7] It is crucial, therefore, to control the level of myopia progression early in life to decrease the risk of developing myopia-related ocular complications. Myopia has emerged as a worldwide public health issue and is identified as one of the immediate priorities by the World Health Organization's Global Initiative for the Elimination of Avoidable Blindness.[8,9]

Several clinical methods are currently used for myopia control in children. These include atropine,[10–13]

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bifocal or multifocal soft contact lenses,[14–18] orthokeratology,[19–22] progressive addition spectacles (PALs),[23–27] and bifocal and prismatic bifocal spectacles.[28] Each treatment has its advantages and disadvantages, with varying levels of efficacy in slowing myopia progression.[29,30] None of the treatments has as yet been successful in completely stopping myopia progression or development.

The use of atropine eye drops in high concentration (1%) has been shown to be highly successful in decreasing the rate of progression, but the associated side effects, such as cycloplegia and pupil dilation, influence visual function.[10,29,30] Such side effects are minimized with lower concentrations of atropine (0.01%), but this amount does not slow axial elongation significantly.[11,12] Although overnight orthokeratology improves unaided visual acuity (VA) in the daytime, it increases higher order aberration and decreases low contrast VA.[31–33] Changes in accommodative responses have been reported when using varifocal spectacles or contact lenses. One study reported that children with high accommodative lag showed decreased accommodative lag by about 25% when wearing PAL spectacles of 2 diopters (D) addition.[34] Other authors found that both emmetropic and myopic children showed a lead in accommodation during wear of bifocal soft contact lenses, but myopes tended to accommodate less.[35] It has also been reported that children wearing multifocal contact lenses with a +2.5 D center distance addition exhibited reduced accommodative responses and more exophoria at increasingly higher accommodative demands than those children wearing single vision (SV) contact lenses.[36] These studies have demonstrated the existence of changes in visual function during the wear of myopia control lenses, but have rarely reported whether any changes occurred after lens wear. It is unclear whether any of these myopia control methods may have caused long-term or sustained changes in visual function, although the visual system has been shown to adapt to changes in the optics of the eye over time.[37–40]

Defocus incorporated multiple segments (DIMS) spectacle lenses are designed for childhood myopia control. DIMS lenses are now commercially available and under the name MiYOSMART. They are already being used by clinicians to manage myopia progression in young children in Asian countries, such as Hong Kong, China, and Singapore. Each DIMS spectacle lens comprises a hexagonal central zone of distance refractive correction surrounded by an annular zone with dense microlens segments of 3.5 D addition, so that it simultaneously provides myopic defocus and clear vision for the wearers (Figure).

Our double-blind, randomized clinical trial has reported that daily wear of DIMS spectacle lenses slows myopia progression and axial elongation in myopic children by 52% and 62%, respectively, over 2 years compared with wear of regular SV spectacle lenses.[41] Visual performance of myopic children wearing DIMS lenses has been reported and compared with that for similar children wearing SV lenses.[41] The results indicated that, when wearing the lenses, there were no significant differences between two lens types in influencing vision and accommodation. However, whether long-term wear of DIMS lenses affects the visual function of these children after discontinuation of the treatment is not known. In principle, such an effect is possible. If DIMS wear decreases changes with age in axial length, it may also influence other biometric parameters affecting the optical characteristics of the retinal image in a way that decreased visual performance when correction returns to SV lenses. Additionally some form of neuroadaptation may occur during DIMS wear, which compensates for optical deficiencies in the retinal image.[37–40] Although advantageous during DIMS wear, this adaptation might degrade visual performance. The current study therefore aimed to compare the 2-year changes in visual function in myopic children who normally wore either DIMS lenses or regular SV spectacle lenses to determine whether wearing DIMS lenses results in a change in visual function.

Methods

Study Design

This was a 2-year randomized controlled clinical trial of DIMS lenses conducted at the Centre for Myopia Research, The Hong Kong Polytechnic University, Hong Kong (Clinicaltrials.gov ref no.: NCT02206217). The recruited children were randomly assigned to wear either DIMS spectacle lenses or regular SV spectacle lenses for 2 years. All children had comprehensive eye examinations in which their refractive error and axial length were measured and monitored at baseline and every 6 months for 2 years. In addition, their visual function was assessed in the same follow-up visits over 2 years. In the present article, visual function at baseline and 6-month intervals over 2 years in both groups of the children were compared while both groups of children wore SV distance prescription to determine whether wearing DIMS lenses results in a change in visual function. The clinical trial was approved by the Human Subjects Ethics Subcommittee of The Hong Kong Polytechnic

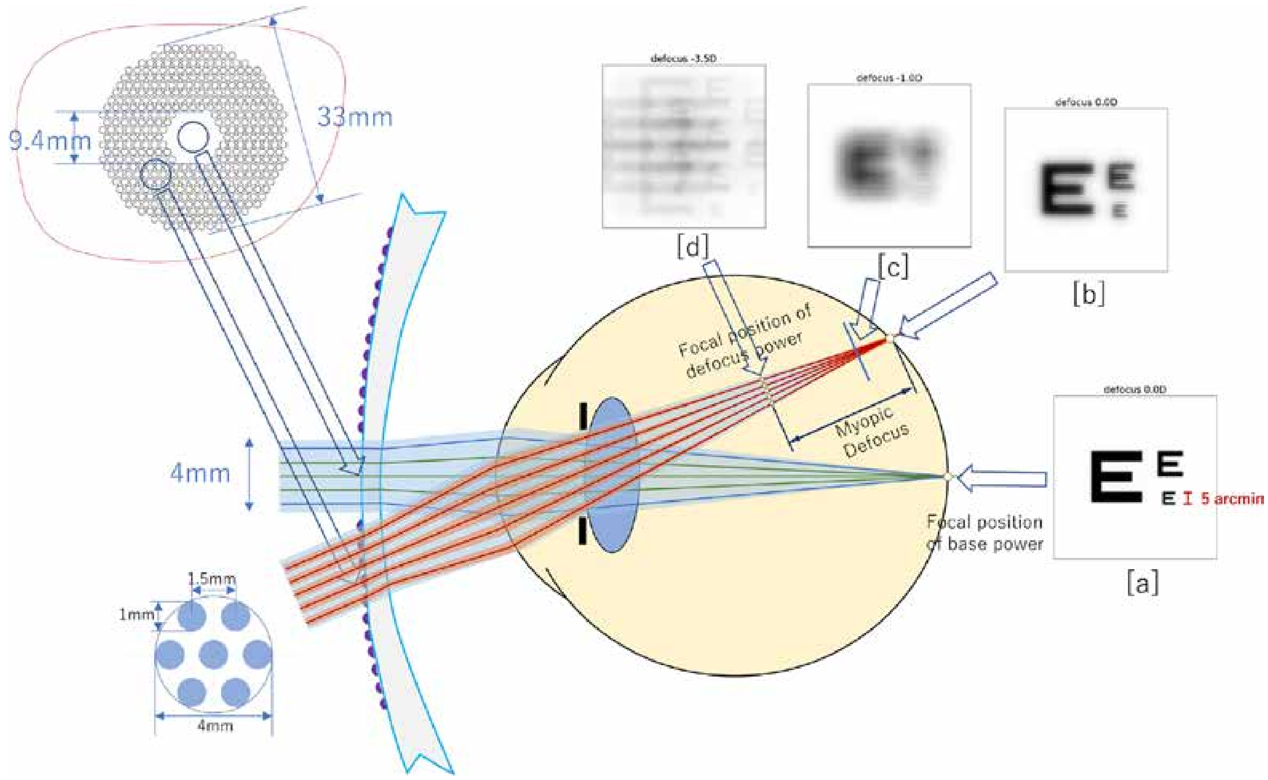

Figure. Basic structure and design of the DIMS lens. Blue rays represent ray traces from the central (carrier) part of the lens and forming a clear image on retina [a] and the red rays show ray traces from the peripheral part of the lens, which contains the lenslets, forming an image that is simultaneously refracted by both the base part and lenslets [b]. If the target is at near and the eye does not accommodate, the image [c] or [d] will be formed on retina. The smallest Snellen chart in each image in the figure has the size of 5 arcmin which indicates VA 0.0 logMAR (20/20). Other two charts indicate VA +0.30 logMAR (20/40) and +0.50 logMAR (20/80), respectively. All images were generated using real ray tracing and wave optics calculations. Viewing an object through the central part of the lens produces a clear image with no ghosting. Viewing a target through the peripheral part of the lens leads to ghosting depending on the relative refractive error at the retina as described in [c] or [d].

University and all procedures of the study met the tenets of the Declaration of Helsinki. Written assent and informed consent were obtained from the children and their parents before joining the study. The children, their parents, and the investigator who performed the measurements did not know the group allocation of spectacle lenses. Masking procedures are described elsewhere in the literature.

Participants

One hundred eighty Chinese myopic children participated in the randomized controlled clinical trial of DIMS lenses.[41] In the present article, only results for the children (n = 160) who completed the full 2-year trial are included. The participant inclusion criteria at enrolment were between 8 and 13 years of age, with myopia (spherical equivalent refraction from −1.00 to −5.00 D, astigmatism and anisometropia up to 1.5 D, and monocular best-corrected VA of 6/6 or better. The participating children did not have any ocular or systemic abnormalities, binocular vision problems, or any prior history of myopia control inventions. They were required to accept masking from the types of the lenses that they wore in the clinical trial. The children were randomly assigned to wear either the DIMS lenses or SV spectacle lenses full time for at least 10 hours per day throughout the trial. Their spectacle prescription was updated if more than 0.5 D of change in spherical equivalent refraction was found in any of the follow-up visits. The final distance prescription was based on the cycloplegic subjective refraction determined by the masked optometrist.

Participants' best-corrected VA at distance and near, binocular visual function, and accommodation were measured at baseline before prescribing the experimental spectacles. Two-year changes in visual function were compared between DIMS lens wearers and SV controls, and comparisons between groups were conducted every 6 months.

Visual Function Measurements

Each participant (for both the treatment and control groups) wore a full distance correction in a trial frame using full aperture trial lenses for all following measurements: distance and near VA, horizontal phoria, amplitude of accommodation (AA), lag of accommodation, and stereopsis. The distance correction was based on noncycloplegic subjective refraction determined by the masked optometrist. For monocular measurements, a full aperture occluder was inserted in front of the nonviewing eye. Participants wore SV correction for these tests because we wanted to determine whether long-term wear of DIMS lenses affected visual function, not whether current wear of the DIMS lenses altered visual function. Thus, all participants wore SV correction to eliminate the influence of DIMS lenses on the current measurements.

Visual Acuities

Both distance and near best-corrected VA were measured monocularly under photopic conditions (85 cd/m^2). The right eye was tested first and then the left eye. High-contrast VA (HCVA; 100%) and low-contrast (LCVA; 10%) at distance were assessed using Logarithmic 2000 series Early Treatment Diabetic Retinopathy Charts and Low Contrast Early Treatment Diabetic Retinopathy Charts at 4 m (Precision Vision Inc., Woodstock IL, USA) with an illuminator cabinet. The children were asked to read to the smallest row that they could read. The testing was stopped when three or more of the five letters per row were read incorrectly. VA was recorded in letter-by-letter logarithm of the minimum angle of resolution (logMAR) notation, each letter in the chart representing 0.02 score. HCVA and LCVA at near were measured at 40 cm using Mixed Contrast European-Wide Near Vision Card (Precision Vision Inc.). The near VA chart also had five letters per line. Therefore, the starting and stopping rules and recording of near VA test were same as those of distance VA test.

Binocularity and Accommodation

Distance and near phoria were measured in real space using Howell Phoria Distance and Near cards placed at 3 m and 33 cm. The magnitude (to the nearest 0.5 Δ) and the direction of phoria were recorded. Esophoria and exophoria are represented by positive and negative values, respectively. Monocular and binocular AA were measured by the push-up method using a Royal Air Force rule. The examiner slowly moved the chart toward the participant, who was instructed to try to keep the words being viewed clear and report when blur was first seen. The average values of the three measurements (in diopters) were used for data analysis. Accommodation responses were evaluated using an open-field autorefractor (Shin-Nippon NVision-K5001, Ajinomoto Trading Inc., Tokyo, Japan) while the children were viewing a letter target at 33 cm with a print size of 20/30 binocularly. Lag of accommodation was calculated as the difference between the measured accommodative response and the actual accommodative demand (3 D). Stereoacuity (seconds of arc) was assessed at 40 cm using Randot Stereotest with Polaroid goggles and the test was stopped after the first miss in the row.

Statistical Analysis

All statistical analyses were conducted using SPSS version 20 (SPSS Inc, Chicago, IL). Data are presented as mean and standard deviation for each experimental group. Monocular data for the two eyes showed no statistically significant differences ($P > 0.05$) and the data were highly correlated ($P > 0.85$); therefore, data from only the right eyes were used for statistical analysis. Unpaired *t*-tests were used to compare visual function between DIMS and SV groups. The Mann–Whitney *U* test was used if the data were not normally distributed.

The changes in visual function at different visits (6, 12, 18, and 24 months) between two lens groups were compared using repeated measures analysis of variance (ANOVA) with treatment group (DIMS vs SV) as the independent factor (multivariate tests). For significant outcomes, post hoc comparisons for each pair of visits were conducted subsequently. Analyses were also performed separately for the two groups. Repeated measures ANOVA was conducted to compare visual function at different visits within a group. A *P* value of less than 0.05 was considered to be statistically significant.

Results

Baseline Demographic Data

A total of 160 children completed the study ($n = 79$ in the DIMS group and $n = 81$ in the SV group). There was no significant difference between the two groups in the baseline demographic data, including age, gender, refractions, axial length, and corneal parameters (Table 1). Both groups showed overall good compliance and could wear the spectacles full time. The mean daily lens-wearing times in the DIMS and SV groups were 15.5 ± 2.6 and 15.3 ± 2.1 hours, respectively, and were not significantly different. There were no

Table 1. Baseline Demographics Data of the Children Who Completed the 2-Year Trial of DIMS Lenses

	DIMS ($n = 79$)	SV ($n = 81$)	t-Test or χ^2 Test, P Value
Age at enrolment, years	10.20 ± 1.47	10.00 ± 1.45	0.508
Gender, % (number)			
Male	58.2% (46)	54.3% (44)	0.118
Female	41.8% (33)	45.7% (37)	
Cycloplegic autorefraction in SER, D	−2.97 ± 0.97	−2.76 ± 0.96	0.174
Axial length, mm	24.70 ± 0.82	24.60 ± 0.83	0.515
Corneal power at steep meridian, D	44.5 ± 1.6	44.5 ± 1.7	0.855
Corneal power at flat meridian, D	43.2 ± 1.4	43.2 ± 1.4	0.955

SER, spherical equivalent refraction; Δ, prism diopters.
Parameters are given as means ± standard deviations.

statistically significant differences in baseline visual function between two lens groups ($P > 0.05$).

Visual Function

Table 2 shows the mean and standard deviation of visual function before (baseline) and after DIMS and SV lens wear (6-, 12-, 18-, and 24-month visits), respectively. In the comparison of the changes in visual function from baseline across 6-month visits between groups (Table 2), no statistically significant differences were found between the DIMS and SV groups (repeated measures ANOVA, time and treatment group as factors; $P > 0.05$). However, there were statistically significant effects of time on some visual function changes (time; $P < 0.05$), namely, distance HCVA, AA, accommodative lag, and stereoacuity. Significant changes in those visual function over time were found within individual groups.

Visual Acuities

For visual acuities, there were statistically significant time effects for distance HCVA in both the DIMS (repeat measures ANOVA; $P < 0.001$) and SV ($P < 0.001$) groups. For the DIMS group, significant differences were observed at all 6-month visits as compared with the baseline visit (post hoc Bonferroni adjustment; $P < 0.001$). Improvement in distance HCVA was shown in the first 6 months (−0.04 ± 0.06 LogMAR). This gradually increased over 24 months (−0.09 ± 0.07 logMAR). Similar findings were obtained in the SV group for whom equivalent improvements in distance HCVA occurred over the 2 years (from −0.03 ± 0.06 to −0.07 ± 0.06 logMAR).

Binocularity and Accommodation

The results revealed statistically significant differences over time for monocular and binocular AA, accommodative lag (for a 3D stimulus), and stereoacuity in both the DIMS and SV groups (repeated measures ANOVA; $P < 0.01$) (Table 2). For both lens groups, there were no statistically significant changes in distance and near phoria over 2 years as compared with the baseline values.

For both lens groups, statistically significant changes in monocular and binocular AA were observed at all 6-month visits over 2 years (post hoc Bonferroni adjustment; $P < 0.001$). Decreases in AA were observed in the first 6 months and within 18 to 24 months. The decreases in binocular AA (DIMS vs SV: −1.90 D vs −2.06 D) were greater than those in monocular AA (−1.68 D vs −1.56 D) after 2 years of lens wear. After DIMS lens wear, the accommodative lag was significantly reduced ($P = 0.001$) throughout the clinical trial. The significant reduction in accommodative lag (3 D stimulus) was found in the first 6 months, and the amount of reduction slightly increased over 2 years. Similar findings were noted in the SV group ($P = 0.002$).

Improvements in stereoacuity were shown in both groups after 2 years. Statistically significant changes mainly occurred after 12 months and these changes were maintained in the second year. However, the changes in stereoacuity (DIMS vs SV, −5.9 sec of arc vs −7.4 sec of arc) over 2 years were not clinically significant.

Discussion

The current study aimed to determine whether, after a period of continuous wear of DIMS lenses, the visual

Table 2. Visual Function at Baseline and 6-Month Intervals Over 2 Years of Spectacle Wear in the DIMS Group ($n = 79$) and SV Group ($n = 81$) and Their Comparison

Group	Baseline	6 Months	12 Months	18 Months	24 Months	Multivariate Tests, *P* Value		Repeat measures ANOVA, *P* Value
						Time	Time × Group	Within Group
Monocular VA, OD (logMAR)								
Distance HCVA								
DIMS	−0.02 ± 0.05	−0.06 ± 0.06	−0.09 ± 0.05	−0.09 ± 0.07	−0.11 ± 0.06	<0.001*	0.540	<0.001*
SV	−0.02 ± 0.06	−0.05 ± 0.05	−0.07 ± 0.06	−0.08 ± 0.07	−0.09 ± 0.07			<0.001*
Distance LCVA								
DIMS	0.14 ± 0.07	0.14 ± 0.06	0.14 ± 0.06	0.13 ± 0.05	0.12 ± 0.04	0.285	0.657	0.237
SV	0.14 ± 0.07	0.14 ± 0.05	0.14 ± 0.04	0.14 ± 0.04	0.13 ± 0.05			0.433
Near HCVA								
DIMS	0.02 ± 0.03	0.01 ± 0.03	0.01 ± 0.02	0.01 ± 0.03	0.01 ± 0.03	0.058	0.573	0.070
SV	0.02 ± 0.05	0.01 ± 0.03	0.00 ± 0.02	0.00 ± 0.02	0.01 ± 0.03			0.246
Near LCVA								
DIMS	0.13 ± 0.08	0.12 ± 0.06	0.12 ± 0.05	0.11 ± 0.05	0.11 ± 0.05	0.222	0.253	0.051
SV	0.12 ± 0.08	0.11 ± 0.06	0.11 ± 0.06	0.11 ± 0.06	0.11 ± 0.06			0.054
Binocularity and accommodative response								
Distance phoria (Δ)								
DIMS	−1.0 ± 1.9	−1.1 ± 1.9	−0.9 ± 1.6	−1.0 ± 1.7	−1.0 ± 1.8	0.440	0.063	0.072
SV	−0.6 ± 1.3	−0.6 ± 1.6	−0.4 ± 1.6	−0.4 ± 1.3	−0.4 ± 1.4			0.069
Near phoria (Δ)								
DIMS	−2.0 ± 3.8	−2.5 ± 4.1	−2.2 ± 3.7	−2.5 ± 4.1	−2.7 ± 3.9	0.062	0.759	0.058
SV	−0.8 ± 3.3	−1.0 ± 3.2	−0.7 ± 3.6	−0.9 ± 3.8	−1.3 ± 3.3			0.057
Monocular AA, OD (D)								
DIMS	12.6 ± 2.4	11.6 ± 2.7	12.1 ± 2.2	12.0 ± 2.5	11.0 ± 2.6	<0.001*	0.090	<0.001*
SV	13.2 ± 2.2	12.1 ± 2.5	11.9 ± 2.7	12.8 ± 2.7	11.6 ± 2.7			<0.001*
Binocular AA (D)								
DIMS	15.6 ± 2.9	15.0 ± 3.4	15.1 ± 3.0	14.3 ± 3.3	13.7 ± 3.5	<0.001*	0.232	<0.001*
SV	16.5 ± 3.1	15.4 ± 3.4	15.2 ± 3.3	15.3 ± 3.3	14.4 ± 3.3			<0.001*
Accommodative lag at 3D stimulus, OD (D)								
DIMS	1.0 ± 0.4	0.9 ± 0.4	0.8 ± 0.5	0.7 ± 0.5	0.8 ± 0.4	0.005*	0.543	0.001*
SV	1.0 ± 0.4	0.9 ± 0.4	0.9 ± 0.4	0.8 ± 0.4	0.9 ± 0.4			0.002*
Stereoacuity (sec of arc)								
DIMS	35.1 ± 17.0	35.1 ± 12.6	−33.5 ± 16.1	28.6 ± 12.4	29.2 ± 13.1	<0.001*	0.320	<0.001*
SV	35.3 ± 14.7	3.3 ± 14.7	34.7 ± 15.3	30.2 ± 13.1	27.9 ± 13.0			0.005*

Δ, prism diopter; OD, right eye.
*$P < 0.05$ (repeated measures ANOVA).

function of myopic children who were then corrected with SV lenses differed from those of similar children who had been continuously corrected by SV lenses. Our results showed that there were no significant differences in the visual function changes after 2 years between the DIMS and SV groups (Table 2). Any adaptation to DIMS lens wear did not lead to adverse effects on visual function when compared with SV spectacle lenses. Changes in some visual function over time were found only within individual lens groups.

Children in both lens groups showed statistically significant improvements in best-corrected distance HCVA and stereoacuity after 2 years. The changes in stereopsis performance were not clinically significant. Surprisingly, distance HCVA was improved by nearly one line of letters (mean differences of -0.09 ± 0.06 LogMAR) after 2 years of DIMS lens wear; such a change is clinically meaningful. The mean distance HCVA after DIMS wear was better than logMAR 0.00 (Table 2). For the SV group (Table 2), similar findings were obtained. The improvement in distance VA in both lens groups might occur because the children became older and more experienced with the data collection process. Such VA improvement also might be due to a practice or learning effect. However, no significant improvements were observed in distance LCVA, near HCVA, or LCVA in either group of children. Each participant had the distance HCVA test first and then underwent the other VA tests. It is possible that some children may have become bored or tired when they were repeatedly tested with similar procedures. This factor might limit the possible improvements in the forms of VA that were tested later in each measurement session. Differences in the difficulties presented by HCVA and LCVA tests might also influence the amount of VA improvement observed.

Children in the DIMS group have experienced decrease in monocular and binocular AA and accommodative lag with time over the study period. The children in the SV group exhibited a similar trend of AA decreases. Such changes in accommodation might simply be due to increases in age. Most studies in the literature have found that AA decreased significantly with age in young children,[42–46] although some authors have indicated that the effects of age on AA in children aged less than 10 years could be uncertain.[43–46] AA was found to decrease by 0.35 D to 0.5 D annually among schoolchildren using the push-up method,[46] whereas our study showed a greater decrease in AA in the range of 0.75 D annually. It could be related to the ethnicity or age of the study samples.

Our results showed that differences in accommodative lag over time did not depend on the child's treatment group (time by group interaction; $P = 0.543$). Children in both groups exhibited decreases in mean lag by about 0.15 D over 2 years. Therefore, the decrease in mean lag in the DIMS group was unlikely to be accounted for by the influence of the myopic defocus. Anderson et al.[47] reported that accommodative lag exhibited a significant linear decrease with age from 3 to 20 years at a rate of about 0.034D per year with a 3D stimulus. This rate was much less when compared with 0.15D over two years in our study. The study design, refractive status and ethnicity of the participants might be possible factors contributing to such differences. First, this study was not a cross-sectional study: we followed the longitudinal changes in lag. Second, the study by Anderson et al.[47] included both myopes and emmetropes, but our study only included myopic children. Myopes have been generally found to have greater accommodative lag than nonmyopes.[48–50] In the present study, the children in both DIMS (lag at baseline of 0.97 D) and SV groups (1.03 D) had a larger mean lag. A recent investigation also reported similar values in Chinese myopic children (mean, 0.97D), but it included a wider range of age groups (5–13 years).[50] These findings indicate that Chinese myopic children tend to have larger accommodative lag than Caucasians (0.43 D).[51,52] However, whether Chinese myopic children exhibit greater annual reduction rate in lag is not known: further investigation is needed.

For other myopic control spectacles, such as bifocals and PALs, most studies only reported the findings of visual performance when wearing the lenses or the initial visual data at the start of lens wear. The near additions in bifocal spectacles and PALs were supposed to correct or decrease accommodative lag at near, with the intended result of slowing myopia progression. Berntsen et al.[34] found that the children with high accommodative lag had a moderate reduction in accommodative lag when wearing PAL spectacles of 2 D addition. They suggested that a 2.00-D bifocal addition did not get rid of accommodative lag and reduced lag by less than 25% of the bifocal power, indicating that children mainly responded to a bifocal by decreasing accommodation. It was proposed that bifocals might not benefit exophoric myopic children because positive add induces extra exophoria and creates a greater demand on positive fusional vergence.[53] Cheng et al.[28] found that incorporating near base-in prism when prescribing bifocal lenses for progressing myopes with exophoria could decrease the positive lens-induced excess exophoria and slow myopia progression over 3 years. However, the effects on binocularity and accommodative functions after the treatment were not reported, and we could not make comparison with our findings in the current study.

Overall, no evidence was found for the existence of any adaptive process, which might have occurred during long-term DIMS lens wear and affected visual performance after DIMS lens removal. In the DIMS-treated children, removal of the DIMS corrections and their replacement by SV lenses gave visual performance results that were the same as those for the control group who had been continuously wearing SV corrections. Adaptation effects may be absent because foveal vision was usually through the clear center of the DIMS lens, which gave the same retinal image as the corresponding SV lens. Additionally, although imagery through the periphery of a DIMS lens included both lenslet and carrier contributions, the lenslet image was continuously changing with small changes in pupil diameter and fixation direction, making neuroadaptation to its characteristics impossible.

One limitation of this study is that we only determine accommodative lag using a target of a 3-D stimulus. Measurement with different accommodative stimuli (e.g., 2 D to 4 D target stimuli) could provide more information for the accommodation response in different viewing distances during reading.

Conclusions

There were no significant differences between the visual function of the DIMS and SV groups over 2 years. Although some changes in visual function, such as distance VA and accommodation, were observed in myopic children after 2 years of DIMS lens wear, similar changes occurred in those who wore regular SV spectacles. Children in both lens groups showed better distance HCVA, but decreased AA and accommodative lag after 2 years. In conclusion, DIMS lens wear had no adverse effect on the measured visual function. Further studies are needed to determine any effects occurring over longer periods of time.

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Optical and imaging properties of a novel multi-segment spectacle lens designed to slow myopia progression

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Abstract

Purpose: High sampling density optical metrology combined with pupil- and image-plane numerical analyses were applied to evaluate a novel spectacle lens containing multiple small zones designed to slow myopia progression.
Methods: High-resolution aberrometry (ClearWave, www.lumetrics.com) was used to sample wavefront slopes of a novel spectacle lens, Defocus Incorporated Multiple Segments (DIMS) (www.hoya.com), incorporating many small, positive-powered lenslets in its periphery. Using wavefront slope and error maps, custom MATLAB software ('Indiana Wavefront Analyzer') was used to compute image-plane point-spread functions (PSF), modulation transfer functions (MTF), simulated images and power distributions created by the dual-focus optic for different pupil sizes and target vergences.
Results: Outside of a central 10 mm zone containing single distance optical power, a hexagonal array of small 1 mm lenslets with nearest-neighbour separations of 0.5 mm were distributed over the lens periphery. Sagittal and curvature-based measures of optical power imperfectly captured the consistent +3.50 D add produced by the lenslets. Image plane simulations revealed multiple PSFs and poor image quality at the lenslet focal plane. Blur at the distance optic focal plane was consistent with a combination of diffraction blur from the distance optic and the approximately +3.50 D of defocus from the 1 mm diameter near optic zones.
Conclusion: Converging the defocused beams generated by the multiple small (1 mm diameter) lenslets to a blurred image at the distance focal plane produced a blur magnitude determined by the small lenslet diameter and not the overall pupil diameter. The distance optic located in between the near-add lenslets determines the limits of the optical quality achievable by the lens. When compared to the optics of a traditional concentric-zone dual-focus contact lens, the optics of the DIMS lens generates higher-contrast images at low spatial frequencies (<7 cycles per degree), but lower-contrast at high spatial frequencies.

1. Introduction

Prevalence of myopia has been increasing globally,[1] and in select East-Asian populations can exceed 95%.[2,3] High levels of myopia are associated with significantly elevated risk of developing retinal complications, potentially leading to severe visual impairments in later life.[4] Therapeutic interventions have been developed that include environmental control,[5] pharmaceutical drops,[6] optical manipulations that introduce multifocal optics[7-9] or contrast-attenuation filters.[10]

A novel dual-focus (bifocal) spectacle lens, which includes discrete, positive-power lenslets on its surface[11] has been employed as a myopia control device,[12] showing a certain degree of success. We have examined the imaging properties of this Defocus Incorporated Multiple Segments

(DIMS) lens (www.hoya.com), the design of which is unique in the field of ophthalmic dual-focus lenses, which are generally included in contact lenses[13,14] or intraocular lenses.[15,16] Precursor dual-focus lenses designed for presbyopes and pseudophakic eyes distribute distance and near optical corrections into different geographic zones across the lens and hence across the eye's pupil,[17] and work by creating a high-quality image when either the distance or near optic is focused on the retina.[14-18] To create a near image, the optics of each near zone must create a single focused image (*Figure 1a*). The new DIMS spectacle lens employs a zonal structure containing small, circular (≅1 mm diameter) lenslets, each containing add power, but images from each individual lenslet do not converge to create a single image in the focal plane corresponding to the add power (*Figure 1b*), but rather multiple separate images.[11] The present investigation examined the optical and imaging ramifications of this novel lens design.

2. Methods

A high-resolution single-pass Shack-Hartmann aberrometer with a 540 nm light source (ClearWave, www.lumetrics.com) was used to sample wavefront slopes every 104 microns[19] across a 10 mm aperture. Local integration methods were used to compute wavefront error maps of the pupil,[20] which were exported for analysis with custom imaging software (Indiana Wavefront Analyzer, IWA) running in MATLAB™ (https://www.mathworks.com/products/matlab.html). Wavefront slopes across a 9.3 mm measurement aperture were measured in one central, and two peripheral regions of a sample DIMS lens with distance correction of −0.50 D (*Figure 2*).

Wavefront error maps were corrected for astigmatism and prism, and local horizontal and vertical wavefront slopes were obtained from the wavefront by means of numerical differentiation. Sagittal power at each point in the pupil was computed by dividing radial wavefront slopes by radial distance from the pupil centre $(dW/dr)/r$.[21] Power was additionally calculated using the local curvature of the wavefront $(d^2W_x/dx^2 + d^2W_y/dy^2)/2$.[22] Fourier Transforms of the pupil functions were used to compute point-spread functions (PSFs) and modulation transfer functions (MTFs) in the image plane. Simulated images were computed by convolution.[23]

3. Results

Both visual inspection and wavefront metrology reveal a central lenslet-free region of approximately 10 mm, surrounded by an annular region containing lenslets 1 mm in diameter arranged in a triangular array with nearest neighbour centre-to-centre distance of approximately 1.5 mm giving a coverage factor of approximately 40% (*Figure 2*).

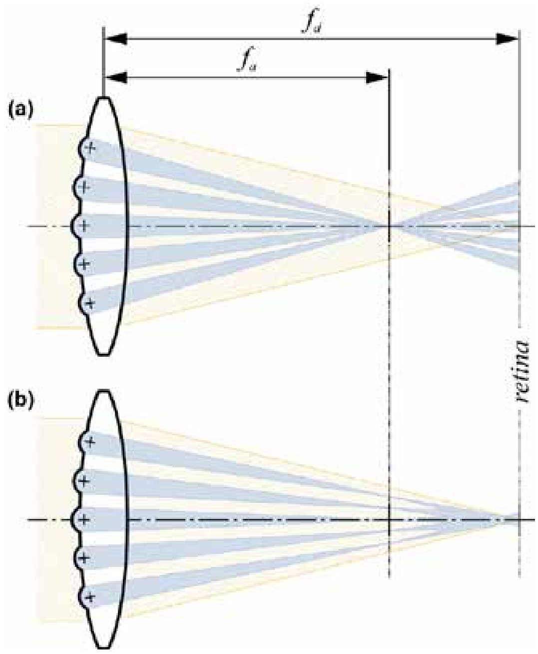

Figure 1. Schematic ray tracing of zonal bifocal lenses showing destinies of individual ray bundles passing through the near add zones (blue rays) and the distance base optic (yellow rays) being focused, respectively, at f_a (add) and f_d (distance). Lens design (a) shows a traditional zonal bifocal design, with a single focus at each focal plane, and (b) shows the novel focusing pattern of add zones that converge to a single blur pattern at the distance focal plane, but create multiple individual foci at the near focal plane.

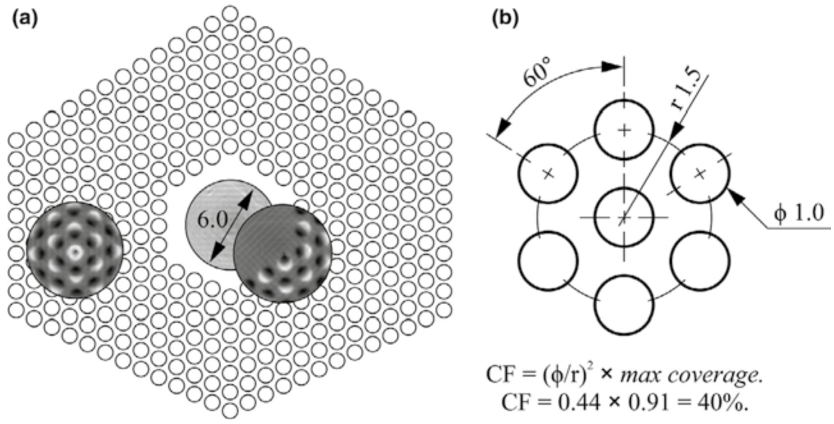

Figure 2. Geometry of the DIMS spectacle lens. (a) 1 mm diameter circular lenslets are arranged in a hexagonal pattern spaced along the primary meridian by centre-centre distances of 1.5 mm resulting in nearest neighbour separations of 0.50 mm (b). Three large circles in *Figure 2a* represent three 6.0 mm diameter locations on the DIMS lens that were sampled for optical analyses. Each 6.0 mm sample includes the corresponding radial wavefront slope maps sampled using a single-pass Shack-Hartmann aberrometer. CF stands for coverage factor, which is equal to the square of the ratio between the lenslet diameter and lenslet separation, multiplied by the maximum coverage factor (0.91) when said ratio is equal to 1.

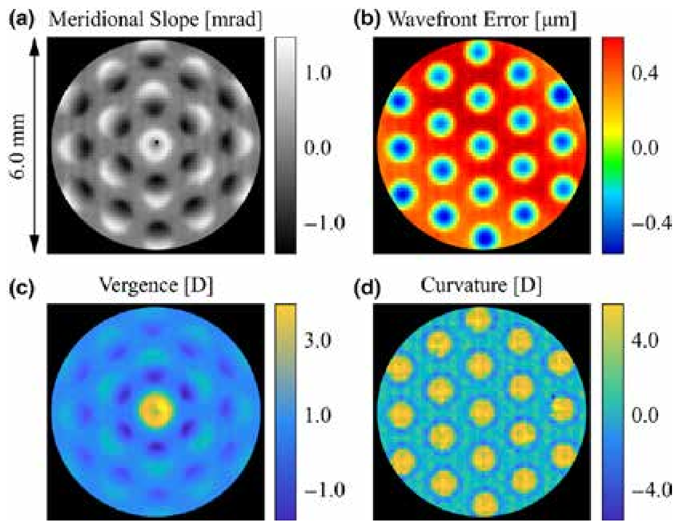

Figure 3. Wavefront slope (a), Wavefront error (b), Sagittal Power (c) and Curvature Power (d) maps from the 6.0 mm sample located in the DIMS lens peripheral region.

Example radial wavefront slope (mrad), wavefront error (microns), sagittal power (dioptres) and local curvature power (dioptres) are shown over a 6.0 mm analysis pupil centred in a region fully populated with the 1 mm diameter lenslets from a DIMS lens with a distance power of −0.50 D and power in the add zones of +3.00 D (*Figure 3a-d*). The wavefront slope changes across each 1 mm diameter lenslet are quite uniform (*Figure 3a*) with an edge-to-edge slope difference of 1.5 mrad, consistent with the expected +3.00 D of positive power in each lenslet.

When utilising the aforementioned radial 'slope/r' calculation to obtain sagittal power, only the central lenslet power is correctly reported (+3.00 D, *Figure 3c*), while the base power of −0.50 D is observed across the full measurement aperture. At the same time, powers of lenslets not centred on the measurement pupil are all underreported, which is anticipated because whereas the radial wavefront slopes within each lenslet are almost identical (*Figure 3a*), the distance from centre r increases, resulting in the decrease in calculated power. When power is calculated by the local curvature of the wavefront (obtained by calculating the second derivative of the wavefront), each lenslet power is correctly reported (*Figure 3d*). However, this method evaluates differences in local slopes, and reports

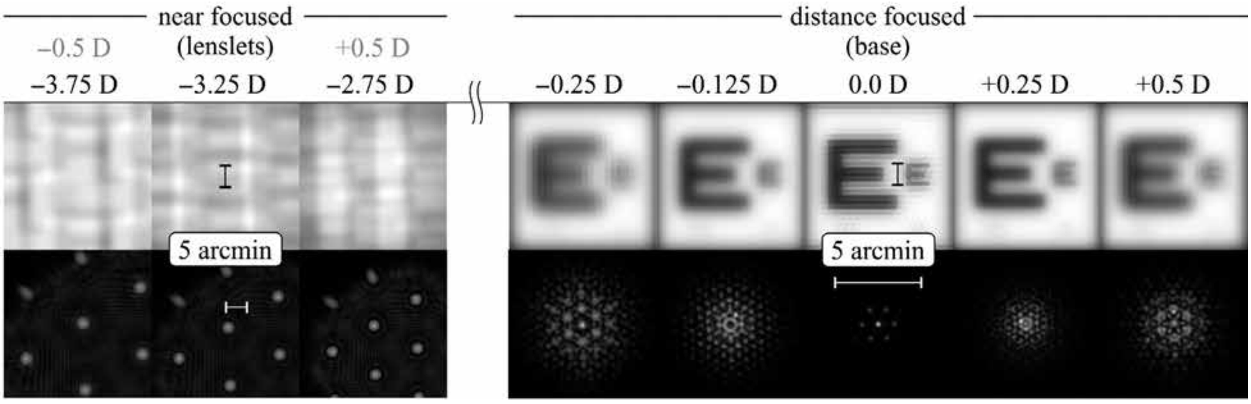

Figure 4. Point Spread Functions (PSFs) and simulated images of high contrast letter E targets (20/60 and 20/20) computed for a range of target vergences (values indicated above each panel) centred on the TVs required to focus the near (left) and distance (right) optics. Pupil diameter = 6.0 mm, sampled aperture fully within the peripheral lenslet region of the DIMS spectacle lens (see *Figure 2a*).

anomalous powers at the margins of each zone (note the dark blue ring indicating highly negative powers at the borders of the lenslets). The −6.00 D ring observed in the curvature power maps is not present in the optical design, and is an artifact created because sampled rays just inside and just outside of each lenslet will diverge relative to each other. The above analysis reveals the challenges of accurately reporting power of lenslets in the DIMS lens.

Image plane calculations do not require a power determination, but instead employ a Fourier Transform of the pupil function (wavefront error map across the pupil,[24] *Figure 3b*). *Figure 4* shows sample PSFs and simulated images of 20/20 and 20/60 high contrast letter E's for a 6.0 mm pupil sampled from within the area of the DIMS lens completely covered by lenslets, while *Figure 5* shows the same for a pupil that is approximately 50% covered by lenslets.

PSFs at and near to the distance focus (*Figures 4 and 5*, right panels) are small with sufficient image quality at the focal plane to image a 20/20 character. By contrast, the multiple individual PSFs superimposed on the large blur from the distance optic seen at and near the near lenslet focal plane (*Figures 4 and 5*, left panels) lead to low contrast and multiple repeated images. As the image plane moves farther from the distance optical focal plane, the image quality generated by the large aperture distance optic decreases rapidly, and the distance optic blur pattern expands in diameter becoming large at the near optic focal plane (*Figures 4 and 5*, left panels).

Blur associated with the 1 mm diameter lenslets remains dominated by diffraction over the 1.00 D range of defocus (*Figures 4 and 5*, left panels), and the array of lenslets within the measurement aperture generate an array of spatially separated PSFs as predicted from the schematic in *Figure 1b*. The simulated retinal images around the near focal plane of the lenslets reveal multiple repeated images, each with reduced contrast because each lenslet contributes

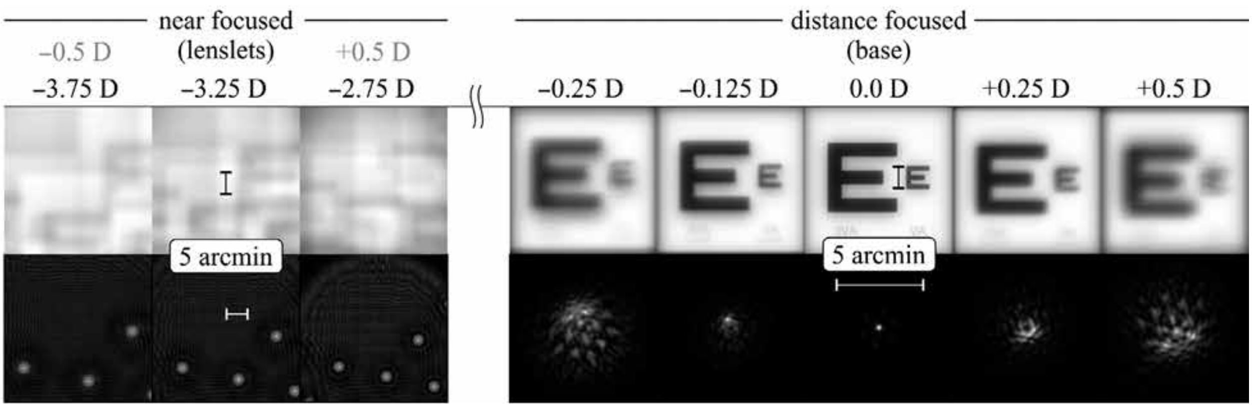

Figure 5. Point Spread Functions (PSFs) and simulated images of high contrast letter E targets (20/20 and 20/60) computed for a range of target vergences (values inset in each panel) with zero being the target vergence that focused either the distance optic (right). Pupil diameter = 6.0 mm for an aperture that was partially (~50%) covered by the lenslet region of the DIMS spectacle lens (see *Figure 2a*).

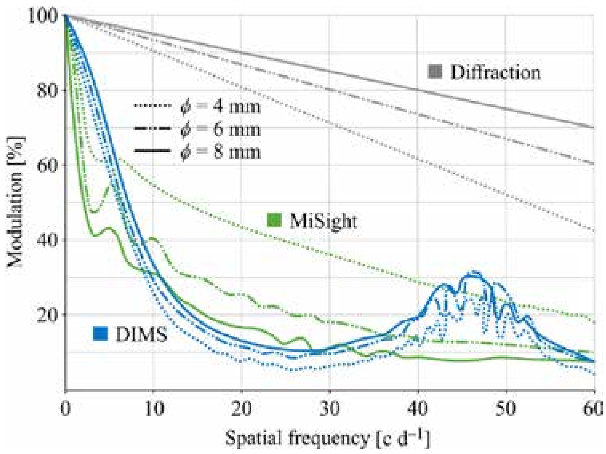

Figure 6. MTFs computed when the distance optic is focused for both the DIMS multi-zone spectacle lens (blue lines) and the MiSight multi-zone contact lens (green lines). For each lens, MTFs were computed for pupil diameters of 4.0 mm, 6.0 mm and 8.0 mm. Full aperture diffraction limited MTFs are shown for comparison (grey lines). The comparison MiSight lens has a 'centre-distance' optic surrounded by annular zones containing +2.00 D add power (zones 2 and 4), and a second distance optic (zone 3), with outer diameters of approximately 3.3 mm, 4.9 mm, 7.1 mm and 8.9 mm, respectively.[25]

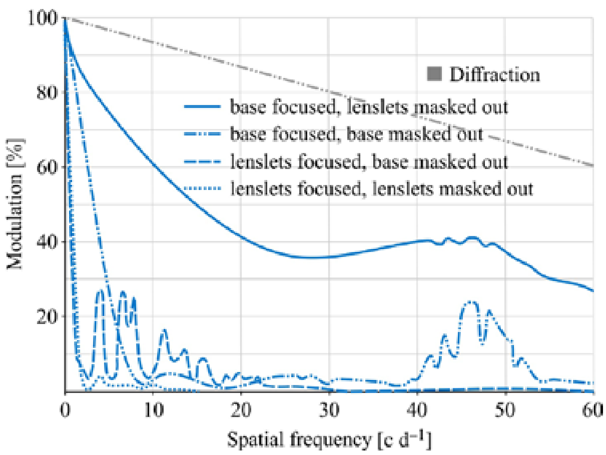

Figure 7. MTFs for the isolated distance and near components of a DIMS lens. The focused isolated distance (base) and near (lenslet) optics are represented by solid and dashed blue lines, respectively and the corresponding defocused optics by dotted and dot-dash lines, respectively.

only $(1/6)^2$ of the light in the image. Image quality at the distance optic focal plane is approximately diffraction limited for an analysis pupil centred on the DIMS centre lacking any lenslets (data not shown), and when the lenslets populate about 50% of the measurement pupil (*Figure 5*) the distance focal plane image quality is superior to that achieved when the full pupil is populated with lenslets (*Figure 4*).

Quantitative analysis of the image quality generated at the distance optic focal plane of the DIMS lens region fully populated by lenslets was performed using MTFs (*Figure 6*). Diffraction blur for a single focal power optic (grey lines) changed significantly over the 4-8 mm pupil diameters. However, the real MTFs (blue lines) remained similar for each pupil size, revealing a significant drop in image modulation between zero and 20 cycles per degree ($c\,d^{-1}$) and an increase in image modulation around 45 $c\,d^{-1}$. This pupil size independence is quite different from that seen with more traditional zonal bifocal designs (e.g. *Figure 6* green lines).

Image contrast at each of the focal planes of a traditional zonal bifocal lens is determined jointly by the significant diffraction blur created by the segmented and potentially narrow annular apertures, and the amount of defocused light contributed by the out-of-focus optics.[14] In the case where the apertures creating the focused image are small (e.g. narrow annular apertures in a concentric zonal bifocal lens), the focused MTF includes a drop at low spatial frequencies due to diffraction at the small sub-aperture size (width), but the total bandwidth is determined by the sum of local sub apertures (e.g. total diameter of the annular zone).[14] Since in the DIMS design the gaps between nearest-neighbour lenslets containing the distance optic are only 0.5 mm (*Figure 2b*), a drop in the MTF paralleling that created by a 0.5 mm diameter pupil (dropping to zero at about 15 $c\,d^{-1}$) contributes to the reduced modulation at low spatial frequencies at the distance optic focal plane (*Figure 6*). The increase in image modulation seen at higher spatial frequencies mirrors the effect seen in the diffraction-limited MTFs of a thin, annular-aperture lenses.[14] Also, the approximately +3.50 D defocus created by the multiple lenslets generates a localised defocused image at the distance focal plane (*Figure 1b*). Using Smith's equation to predict blur circle size (B = PD) a blur of 0.2 degrees is predicted, which will create an MTF that drops to zero at about 6 $c\,d^{-1}$.[26] Therefore, diffraction from the focused distance optic and defocus of the near optic are both contributing to the drop in the MTFs over the range of approximately 0-15 $c\,d^{-1}$.

MTFs reveal higher contrast generated with small pupils when imaging through the centre of a traditional, zonal, dual-focus lens (*Figure 6*, green lines, this model contains a 3.3 mm diameter distance optic centre zone). With pupil sizes large enough to include both the distance and near optics of the traditional zonal bifocal lens, the distance optic's focal-plane MTFs are attenuated by the amount of defocused light created by the near optic. When comparing these two lens designs, one can see that the DIMS design produces higher modulation below 5-8 $c\,d^{-1}$, but lower image modulation above 10 $c\,d^{-1}$. In terms of image formation, this result would translate to images with higher

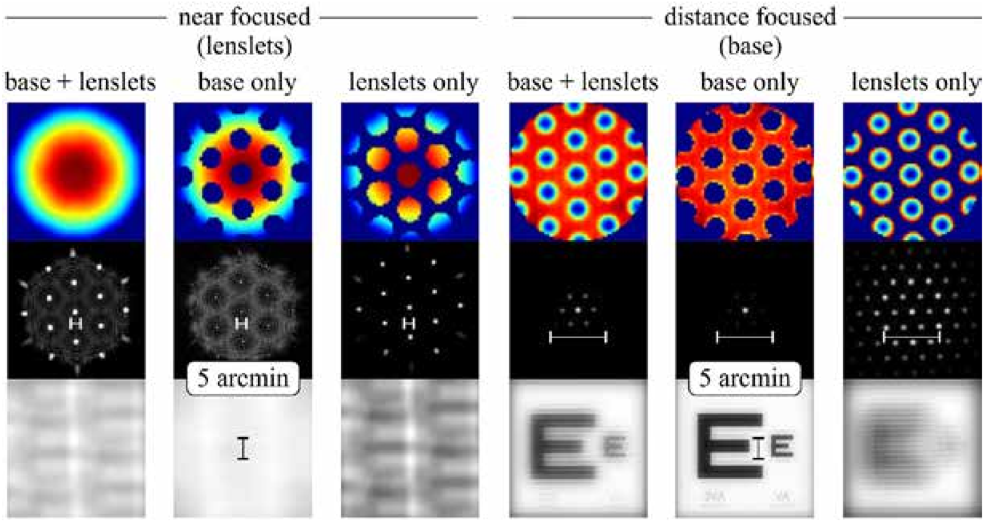

Figure 8. Wavefronts and images generated by the combined distance and near optics, and each optic isolated, were computed at the near optic focal plane (left three panels) and distance optic focal plane (right three panels). The top panels show the wavefront error maps, and middle and bottom panels show images of PSFs and 20/20 together with 20/60 letter E's, respectively. At the near focal plane, the PSFs generated by the near optic are a series of spatially-separated diffraction-limited points, whereas the out-of-focus distance optic generates a familiar large blur circle, but with areas absent due to the masking out of the lenslets. The out-of-focus but converged near optic lenslets create a series of localised diffraction limited PSFs in their focal plane (see schematic in *Figure 1b*).

contrast, but more blur generated by the DIMS lens compared to the traditional zonal bifocal design, which has much greater blur created by the near add zone, but a higher quality focused image generated by the distance optic.

The image quality at both distance- and near-image planes results from the combined impact of an array of near add power lenslets and a distance optic that exists at all locations other than the lenslets. Therefore, we examined the optical quality provided by each contributing optic (*Figure 7*). For example, the MTFs generated by the focused distance optic aperture drop below 40% at 25 $c\,d^{-1}$, but increase to >40% at 45 $c\ d^{-1}$. The defocused lenslet images (which approximately superimpose at the distance focal plane, *Figure 1b*) produce an MTF which drops to zero at about 9 $c\,d^{-1}$, as predicted from simple geometrical optics. The resulting MTF (*Figure 6*) is therefore a 60/40 weighted combination of the two-component optical MTFs seen in *Figure 7*. At the near focal plane, the resultant image is a combination of that produced by the 3.50 D defocused distance optic and the focused near optic generating multiple images. Both component MTFs are shown in *Figure 7*, neither yielding high image quality.

The wavefronts used to generate the images for each component optic are shown in the upper panels of *Figure 8*, and the resulting images of a point source and small letter E's are shown in the middle and bottom panels, respectively. The three left panels in *Figure 8*, labelled 'near focused', were computed for the near optic (lenslets) focal plane, whereas the three right panels, labelled 'distance focused', were computed for the distance (base optic) focal plane. The wavefront error map of the distance optic at its own focal plane is quite flat and dominated by spherical aberration ('distance focused, base only' panel in *Figure 8*), whereas the wavefronts of each small lenslet optic are highly curved due to the 3.5 D of defocus ('distance focused, lenslets only' panel in *Figure 8*). On the other hand, at the near optic focal plane there is no local curvature in the wavefronts of each lenslet (compare the 'lenslets only' panels for both 'near focused' and 'distance focused' conditions). The significant negative curvature in the base optic wavefront is observed at the near optic focal plane in the wavefronts of both the distance and near optics (see the 'near focused, base only' and 'near focused, lenslets only' panels). If the DIMS was a traditional bifocal lens, the wavefront error maps within each lenslet region would be flat at their focal plane, but the unique design of the DIMS lens retains the wavefront slopes expected from the out-of-focus distance optic across the pupil. Each lenslet introduces wavefront curvature but retains the overall wavefront slope of the distance optic, and thus the global wavefront error map ('near focused, base + lenslets' panel) in *Figure 8* is retained in both the distance and near optic sub-apertures.

4. Discussion

Traditional dual-focus or bifocal lenses designed to be worn by presbyopic and pseudophakic eyes must be able to generate high-quality images at both the distance- and near-optic focal planes. However, because of the poor image quality generated by the multiple separate PSFs associated with each lenslet of the DIMS lens design at the near add power focal plane (*Figures 4b and 5b*), the extra plus power of the lenslets cannot be used to focus near targets. Since dual-focus optics are now being used to successfully control myopic eye growth in children[7,12] who have large amounts of accommodation[27-29] which can be used to focus near targets, high image quality at the add focal plane is unnecessary. The MTF analysis reveals that the DIMS lens design can generate higher contrast images at low spatial frequencies compared to the traditional bifocal design (*Figure 6*), but because of the fragmented aperture of the distance optic, diffraction limits its ability to generate high contrast high spatial frequency images (*Figures 6 and 7*).

Earlier attempts to control myopic eye growth in children with spectacle lenses were generally unsuccessful.[30,31] However, a study of the DIMS lens by its inventors,[12] revealed a 40% slowing of myopia progression over two years. An ideal myopia control lens should not only control the rate of progression of myopia, but also provide high quality visual performance when looking through the distance optic. Our comparative analysis of the MTF's generated by the DIMS and a zonal bifocal design (Figure 6) reveal higher contrast generated by the DIMS design, but better spatial detail imaged by the concentric zonal design. The main advantage of the DIMS lens, therefore, other than it being a spectacle design, is that the image demodulation generated by the array of multiple 1 mm diameter lenslets (Figures 4-8) will be absent for a child viewing through the 10 mm central region of the spectacle lens, which lacks the lenslets. The image demodulation introduced by the multiple lenslets in the DIMS design (Figure 6) will, therefore, likely be manifest primarily in the peripheral retina. Recent studies in monkeys have shown that the optical characteristics of the peripheral retinal image can control myopic eye growth.[32] The optical results of the DIMS lens in the present study align with this myopia control theory, with the lens providing clear central vision while inducing optical defocus peripherally. Other spectacle lenses designed for myopia control also restrict the image manipulation to the lens periphery[33] as do zonal dual-focus contact lenses where the central zone (e.g. approximately 3.3 mm in the MiSight lens, see Figure 6) is surrounded by an annular add zone, which contributes significantly to peripheral image generation.[34,35]

Conflict of interest

The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

Author contributions

Mateusz Jaskulski: Data curation-Lead, Formal analysis-Equal, Software-Lead, Visualization-Lead, Writing-review & editing-Equal. **Neeraj Kumar Singh:** Data curation-Equal, Investigation-Equal, Methodology-Equal, Validation-Equal, Writing-original draft-Equal. **Arthur Bradley:** Conceptualization-Equal, Formal analysis-Equal, Investigation-Equal, Methodology-Lead, Project administration-Lead, Software-Equal, Writing-original draft-Lead, Writing-review & editing-Equal. **P Kollbaum:** Conceptualization-Equal, Funding acquisition-Equal, Investigation-Lead, Methodology-Lead, Project administration-Lead, Resources-Equal, Software-Equal, Writing-review & editing-Equal.

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