scientific reports

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New design peripheral defocus spectacle lens vs. single-vision for slowing myopia progression in children: randomized controlled trial

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This study reports the 1-year results of a 2-year multicenter prospective randomized, controlled, double-masked trial aimed to determine whether Myoslow lenses (Crystal Optic Industries Ltd., Acre, Israel) based on the peripheral defocus mechanism of action can slow myopia progression. Children aged 6–12 years with myopia between − 1.00 D and − 5.00 D and astigmatism ≤ 1.50 D (*N* = 121) received either Myoslow (treatment) or single vision (control) spectacle lenses. The mean change in spherical equivalent refractive error from baseline was − 0.46 D in the treatment group and − 0.65 D in the control group ($p = 0.015$), with myopia progression slowed by 0.19 D (29.5%). The mean change in axial length was 0.27 mm in the treatment group and 0.36 mm in the control group ($p = 0.002$), with myopia progression slowed by 0.09 mm (23.6%). Younger age was the only covariate significantly associated with the treatment effect across both outcome measures, with a significant correlation between the treatment effects in the two measures ($R = -0.71$, $p < 0.001$). Treatment was well tolerated, with only one ocular complication: myopia progression (0.08%). Myoslow lenses effectively and safely slow myopia progression in children, with greater benefit in younger ages compared to single vision lenses.

Keywords Myopia, Myopia control, Myopia progression, Children, Peripheral defocus

The prevalence of myopia exceeds 20% worldwide and is expected to reach 50% by 2050, including 39.8% of children and adolescents[1–4]. In many parts of East and Southeast Asia, up to 80% of young adults are myopic, with a risk of reaching 95% prevalence in certain communities[5,6], of them 10–20% children and adolescents with high myopia, exceeding than 6 diopters (D)[6,7]. Myopic eyes are at risk of the development of vision loss complications, including retinal degeneration, retinal detachment, and glaucoma, among others[2,7,8]. Each additional diopter of myopia is associated with 58%, 20%, 21%, and 30% higher risks of myopic maculopathy, open-angle glaucoma, posterior subcapsular cataract, and retinal detachment, respectively[8]. Myopia is now identified as one of the immediate concerns by the World Health Organization WHO[9].

According to a recent Cochrane meta-analysis of randomized controlled trials (RCTs), at 1 year the median change in spherical equivalent refractive error (SER) in control participants without treatment was − 0.65 D and the median change in axial length (AL) was 0.31 mm[10], substantially fluctuating with age[11]. Animal studies have provided solid evidence that myopic de-focus (MD) inhibits eyeball elongation, whereas hyperopic de-focus (HD) accelerates eyeball elongation, including studies performed on chicks, voles, marmosets and rhesus monkeys have shown that the elongation of the eyeball can be reduced by myopic de-focusing and by using multifocal lenses[12]. Because increased time outdoors can reduce the onset of myopia, but not prevent its progression[13], various therapeutic approaches (optical, pharmaceutical, environmental, or behavioral) have been proposed to decrease myopic progression, however, results are variable and lack standardization[5,12,14]. During the past decade, atropine and orthokeratology have been the most prevalent treatments, while lenses

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with novel designs are typically referred to as emerging treatments[14]. Other emerging therapies include violet light-transmitting eyeglasses[15] and repeated low-level red-light (RLRL) therapy[16].

High-dose (1%) atropine in eye drops is very effective, but induces several side effects, such as photophobia and blurred vision, which are not well tolerated, and rebound effect. A lower dose (0.01%) of atropine yields significant effects on the refractive error[13] with fewer side effects[17], with however a limited effect of slowing down the AL progression[5,18]. Moreover, a recent meta-analysis of 13 studies involving 2060 children, specifically focused on the rebound effect following atropine treatment discontinuation, with reported recurrence of myopia at 6 and 12 months post-cessation, measured in both SE and AL. Shorter treatment durations, younger age, and higher baseline SE levels are associated with more pronounced rebound effects[2]. Orthokeratology contact lenses, such as Abiliti Overnight (J&J)[19,20] are approved for myopia control, however present a risk of corneal infiltrative events, allergies, ocular pain or discomfort, and microbial keratitis and are not suitable for young children[8,13,21].

Myopic defocus is one of the main mechanisms in the focus of current myopia control studies[5,12]. For instance, the Defocusing Incorporated Soft Contact Lens (DISC) consists of a central correction zone and a series of alternating defocusing and corrective zones spreading to the perimeter in a 50:50 ratio. An RCT with DISC (Biofinity Multifocal, CooperVision) reported slowing of myopia and AL progression over 3 years[22]. An RCT of another myopic de-focus contact lens presented simultaneously with an additional optical power, termed dual-focus optics (MiSight, CooperVision) also reported slowing of myopia and AL progression over 3 years[12].

To address the growing need for an intervention that is simple to use and less invasive compared with pharmacological or contact lens treatments, spectacle lenses with myopic defocus designs offer an alternative safer treatment modality with a relatively low cost for myopia control in children[1,21,23]. Defocus Incorporated Multiple Segments (DIMS) dual-focus spectacle lenses (e.g., Miyosmart, Hoya)[24] have a zonal structure with miniature circular lenslets in the mid-periphery, each with add power, providing the same optical image as the DISC without the drawbacks inherent with contact lenses[2]. An RCT with DIMS reported slowing of myopia and AL progression of 50%-60% relative to control SV control over 2 years[24], with minimal adverse events, persistent at 3 years[25] and with no rebound effect 6 years after cessation[26]. Moreover, DIMS combined with atropine were effective in a study in European children, with increased effectiveness when used in combination[27]. Another spectacle lens based on diffusion optics technology (DOT, SightGlass Vision) modulates peripheral contrast with no impact on the on-axis vision was effective over 1 year[28]. A recent double-masked RCT with another spectacle lens incorporating highly aspherical lenslets (Stellest, Essilor) in Chinese children was effective over 1 and 2 years[29,30], with no rebound 1 year after cessation[31].

This RCT aims to assess the safety and effectiveness of a newly designed peripheral defocus spectacle lens (Myoslow, Crystal Optic) in slowing the progression of myopia in Caucasian school-aged children, compared to single-vision spectacle lenses. The lens design is based on the peripheral defocus mechanism of action, aimed to provide the same optical image as the Defocus Incorporated Soft Contact (DISC) lens, producing myopic defocus on both the central and peripheral retinas and thereby slowing down the axial elongation.

Results

Between January 3, 2023, and August 3, 2023, 125 eligible children were randomly allocated to the Myoslow spectacle lenses (MSL) treatment group ($n=84$) and the single vision spectacle lens (SV) control group ($n=41$) (Fig. 1). One hundred and twenty-three (123) subjects successfully completed the 6-month FU visit and 122 successfully completed the 1-year FU visit. The last subject reached the 1-year follow-up on August 12, 2024. The dropout rate at 12 months was 2.4% in both groups (2/84 MSL, 1/41 SV). Both groups showed overall high compliance (95.2% in MSL and 94.3% in SV) where compliance is defined as wearing the spectacles for an average of at least 10 h a day during the 12 months, with the mean daily spectacle lens-wearing time of 14.1 ± 2.8 and 13.7 ± 2.4 h in the MSL and SV groups, respectively, with no significant difference between the groups ($p=0.36$).

Baseline characteristics

All efficacy analyses are presented for the full analysis set (FAS). The FAS included all children that received the spectacles and had at least one post baseline measurement ($n=123$). The demographic and baseline characteristics for the FAS population are summarized in Table 1. The two treatment groups were well balanced for all characteristics except age at enrollment. About half the children enrolled were female and the average age of the children enrolled was 8.9 years (range: 6–12 years). Children in the SV group were slightly older than children in the MSL group ($p=0.01$). Most children had at least one myopic parent (92.7%) and at least one myopic sibling (61.0%).

At baseline, in the mean (±SD) SER in the right eye was -2.56 ± 1.06 D and -2.82 ± 1.12 in the MSL and SV groups, respectively, and the mean AL was 24.13 ± 0.82 mm and 24.23 ± 1.02 mm, respectively. There was no significant difference between right and left eye measurements ($p=0.24$ and $p=0.56$ for SER and AL, respectively).

Myopia progression

Children wearing MSL lenses had myopia progression (SER) significantly reduced by 66.8% and 29.5% at 6 months and 1 year follow-up visits, respectively, compared with those wearing SV lenses, with the mean group difference of 0.30 ± 0.08 D ($p=0.0002$) at 6 months and 0.19 ± 0.08 D ($p=0.015$) at 1 year (Table 2; Fig. 2). Children wearing MSL lenses had AL significantly reduced by 32.1% and 23.6% at 6 months and 1 year follow-up visits, respectively, compared with those wearing SV lenses, with the mean between-group difference of 0.07 ± 0.03 mm ($p=0.012$) at 6 months and 0.09 ± 0.03 mm ($p=0.002$) at 1 year. There was a significant correlation (R = -0.71, $p<0.001$) between the change from baseline in SER and change from baseline in AL.

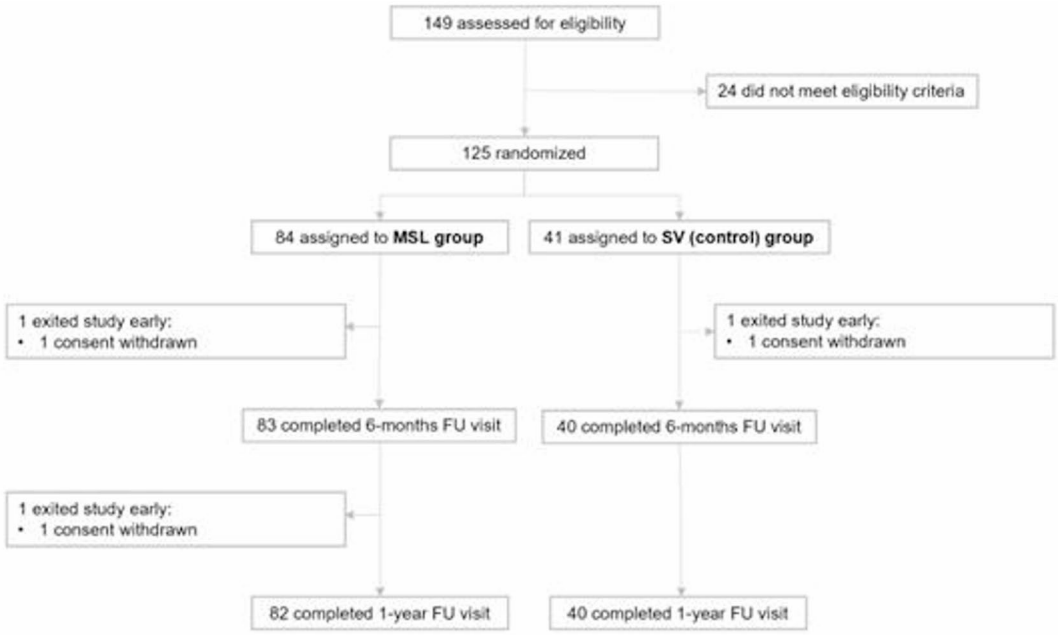


Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) diagram of the trial. Treatment allocation and participant number in different stages of the study. *MSL* Myoslow spectacle lenses (treatment), *SV* single-vision spectacle lenses (control); FU, follow-up.

In the younger age group (6–9 years), the LS means change from baseline in SER (mean, SE) were − 0.56 ± 0.05 D in the MSL group and − 0.87 ± 0.09 D in the SV group at 12 months ($p = 0.005$). Similarly, the LS means change from baseline in AL (mean, SE) were 0.33 ± 0.02 mm in the MSL group and 0.47 ± 0.03 mm in the SV group. In the older age subgroup (10–12 years), there was no significant difference between MSL and SV groups. Age at enrollment was significantly associated with change from baseline in SER and change from baseline in AL in both MMRM models. No other covariates were significantly associated with change from baseline in SER or change from baseline in AL in the MMRM models.

Using a cut-off of myopia progression of ≥ 1 D as clinically significant myopia progression, five (6.0%) out of 83 children wearing MSL lenses had clinically significant myopia progression at 6 months, which was advantageous compared to the SV group (6 of 40, 15%). At 1 year, 21 (25.6%) out of 83 children wearing MSL lenses had clinically significant myopia progression, again advantageous compared to the SV group (15 of 40, 38.5%).

A subgroup analysis based on parental myopia showed that for a single myopic parent ($n = 39$ in the MSL group (47.0%) and $n = 17$ in the SV group (42.5%), the children wearing MSL lenses had significantly reduced myopia progression compared with those wearing SV lenses at 6 months and 1 year follow-up visits (mean difference 0.35 ± 0.12 D ($p = 0.004$) at 6 months and 0.33 ± 0.12 D ($p = 0.006$) at 1 year). In the subgroup with 2 myopic parents, there was no significant difference between the MSL and SV lenses.

There was no significant difference between MSL and SV groups in the average number of daylight hours or phone, computer exposure, or television exposure during the 12 months of treatment (Table 3). There was no correlation between change from baseline in either SER nor AL with daily time of exposure to daylight, spent reading or using a tablet and watching television.

Quality of life and safety

There was no significant difference between MSL and SV groups in change from baseline to 12 months in vision quality of life for any of the seven PREP2 QOL summary scores (Table 4) ($p > 0.05$).

No serious adverse events were reported. Seldom symptoms reported during treatment included 3 (2.4%) cases of headaches, 2 of which were possibly related to treatment and resolved spontaneously, a single (0.8%) case of myopia progression that was judged by the investigators as possibly related to treatment and addressed by a daily dose of 0.01% atropine and single (0.8%) cases of redness, swelling and discharge from both eyes, morphea (skin condition), blepharospasm and diplopia that were judged by the investigators as not related to treatment.

Discussion

Schoolchildren wearing MSL lenses had myopia progression (SER) significantly reduced by 66.8% and 29.5% at 6 months and 1 year follow-up visits compared with those wearing SV lenses, and AL increase significantly reduced by 32.1% and 23.6% at 6 months and 1 year follow-up visits compared with those wearing SV lenses. The MSL lens had a comparable or advantageous effect of slowing myopia progression in children following 1 year

	Myoslow Lens	SV Lens	Total
	n = 83	*n* = 40	*n* = 123
Sex, n(%)			
Female	37 (44.6%)	26 (65.0%)	63 (51.2%)
Male	46 (55.4%)	14 (35.0%)	60 (48.8%)
Race, n(%)			
White	83 (100.0%)	40 (100.0%)	123 (100.0%)
Ethnicity, n (%)			
Not Hispanic or Latino	83 (100.0%)	40 (100.0%)	123 (100.0%)
Age at Enrolment (years)			
Mean (SD)	8.7 (1.7)	9.5 (1.7)	8.9 (1.7)
Age at Enrolment Categories			
6–9 Years	25 (30.1%)	22 (55.0%)	47 (38.2%)
10–12 Years	58 (69.9%)	18 (45.0%)	76 (61.8%)
Age at First Glasses (years)			
Mean (SD)	7.4 (1.7)	7.6 (1.8)	7.5 (1.8)
Age at First Glasses Categories			
< 6 Years	5 (6.0%)	2 (5.0%)	7 (5.7%)
6–10 Years	76 (91.6%)	37 (92.5%)	113 (91.9%)
> 10 Years	2 (2.4%)	1 (2.5%)	3 (2.4%)
Parental Myopia			
Both Parents	37 (44.6%)	21 (52.5%)	58 (47.2%)
One Parent	39 (47.0%)	17 (42.5%)	56 (45.5%)
Neither Parent	7 (8.4%)	2 (5.0%)	9 (7.3%)
Number of Siblings with Myopia			
0	32 (38.6%)	16 (40.0%)	48 (39.0%)
1	27 (32.5%)	7 (17.5%)	34 (27.6%)
2–9	24 (28.9%)	17 (42.5%)	41 (33.3%)
Number of Siblings with Myopia			
Mean (SD)	1.3 (1.7)	1.6 (1.8)	1.4 (1.7)
Cycloplegic autorefraction in SER (D)			
Mean (SD)	-2.56 (1.06)	-2.82 (1.12)	-2.65 (1.08)
Axial length			
Mean (SD)	24.13 (0.82)	24.23 (1.02)	24.16 (0.89)

Table 1. Baseline demographics data.

of treatment vs. single vision glasses compared to RCT reports with the available progressive addition spectacle lenses (15.2% – 30.2%) [32–34], spectacle lenses with peripheral defocus (15.4% – 25%)[35,36], annular refractive element spectacle lenses (21.1%)[37], soft contact lens designed for reducing relative peripheral hyperopia (25.0% – 34%)[38,39] and with a low-dose (0.01%) atropine treatment vs. placebo (27.2% – 34.2%)[18,40] (Table 5). Some RCTs, including highly aspherical lenslets (HALs), slightly aspherical lenslets (SALs), DIMS, DOT, MiSight and diversified segmental defocus optimization (DSDO) spectacle lenses reported higher effects of slowing myopia progression (40% – 74%) [24,28,30,41,42] (Table 5).

The MSL lens had a comparable or advantageous effect of reduction in AL increase vs. SVL to RCT reports with the available progressive addition lenses (PALs) (2.7% – 20%)[32,33], spectacle lens with peripheral defocus (16.0%)[35], DSDO spectacle lenses combined with placebo eye drops (8.9%)[42], annular refractive element spectacle lenses (27.8%)[37], contact lens designed for reducing relative peripheral hyperopia (33%)[38] and with a low-dose (0.01%) atropine treatment vs. placebo (12% – 22%)[18,40] (Table 5). Some RCTs, including highly aspherical lenslets (HALs), slightly aspherical lenslets (SALs), DIMS, DOT and MiSight lenses reported higher effects of reduction in AL increase (31% – 66%) [24,28,30,41] (Table 5).

The effect of slowing the myopia progression was most pronounced during the first six months, consistent with other studies and reviews reporting the greatest treatment effect within the first 6 months of defocus spectacles lenses as an intervention, resulting in a more pronounced rate of myopia progression reduction initially compared to later periods, including orthokeratology, 0.01% atropine combined with orthokeratology, PALs, positively aspherized PALs and DIMS lenses[10,20,24,33,36,43–46]. One of the possible explanations is the adaptation of subjects to the optical signal that slows myopic progression. The patient's age can also significantly influence the efficacy observed over time. For example, with DIMS lenses[45], older children (≥ 10 years) showed slower progression after 6 months, while younger patients progressed at a similar rate, leading to larger overall progression at 12 months for the younger age group. Shamir lenses demonstrated that the efficacy for older

		Myoslow Lens	SV Lens	Treatment Effect
		n = 83	*n* = 40	(Myoslow vs. SV)
Change from Baseline in SER				
Month 6	LS Means (SE)	-0.15 (0.04)	-0.45 (0.06)	0.30 (0.08) [66.8%]
	95% CI for LS Means	-0.24, -0.06	-0.58, -0.33	
	p-value			*0.0002*
Month 12	LS Means (SE)	-0.46 (0.04)	-0.65 (0.06)	0.19 (0.08) [29.5%]
	95% CI for LS Means	-0.55, -0.37	-0.78, -0.53	
	p-value			*0.015*
Change from Baseline in AL				
Month 6	LS Means (SE)	0.14 (0.01)	0.21 (0.02)	-0.07 (0.03) [32.1%]
	95% CI for LS Means	0.12, 0.17	0.17, 0.26	
	p-value			*0.012*
Month 12	LS Means (SE)	0.27 (0.01)	0.36 (0.02)	-0.09 (0.03) [23.6%]
	95% CI for LS Means	0.25, 0.30	0.32, 0.40	
	p-value			*0.002*

Table 2. Changes from baseline to 12 months in the cycloplegic spherical equivalent refraction and axial length in the myoslow and SV groups based on a mixed model repeated measures analysis. AL = axial length, CI = confidence interval, LS = Least Squares, MMRM = mixed model repeated measures, SER = spherical equivalent refraction, SV, single vision, SE, standard error. The analysis is performed using MMRM with baseline SER (or baseline AL), age at enrolment, gender, parental myopia, treatment group, visit, and treatment group by visit interaction as fixed effects. Eye is a random effect.

children (10–13 years) on SER significantly decreased from 24% at 6 months to 7% at 12 months, whereas for younger children (6–10 years), the efficacy remained stable or slightly increased during the same period[36].

In this study, the change in SER in control participants without treatment was – 0.65 ± 0.06 D at 1 year, similar to -0.65 D reported in a recent Cochrane meta-analysis of RCTs of myopia control interventions in 38 studies in a total of 6525 children[10]. Likewise, the change of 0.36 ± 0.02 mm in control participants without treatment at 1 year is consistent with the 0.31 mm reported in the meta-analysis. Importantly, there is a large variability in the rate of myopia progression reported in different studies for the period of 1 year with single vision control treatments in a similar age group, with differences exceeding 0.2 D [24,35]. Possible accounts include ethnicity (in many studies either 100% White Caucasian or 100% Asian), initial myopia levels (with differences of 1 D and above between studies), parental myopia distribution (with differences of about 20% in the frequency of two myopic parents), compliance and ethnic differences in the speed of myopia progression[47,48]. More RCTs with heterogenic demographics are thus warranted to facilitate comparison between the effects of different treatment approaches.

The effectiveness of the MSL lenses was positively affected by younger age, consistent with the notion that earlier treatment is more effective in myopia management. Out of all RCTs included in the recent Cochrane review and meta-analysis of interventions for myopia control[10], only 18 studies included findings in the younger subjects (aged 6 years), however only several inspected the effect of age sub-groups directly. Similarly to the current study, a more profound slowing of myopia progression following 18 months of treatment with PALs compared with SV control was reported in younger subjects up to 9 years old (difference of 0.46 D) than subjects 10 and above years old (difference of 0.26 D)[43]. Similarly, in a later study with positively aspherized PALs a more profound slowing of myopia progression following 2 years of treatment compared to SV control was reported in younger subjects aged 6 to 9 years (difference of 0.2 D or 0.38 D for additions of + 1.0 or + 1.5, respectively) than subjects aged 10 and above (difference of -0.06 D or 0.13 D for additions of + 1.0 or + 1.5, respectively)[44]. A similar trend was also reported after 1 year of treatment with PALs compared with SV control (difference of 0.27 D vs. 0.11 D in children aged 10 year or younger vs. older children)[49] and in a recent study with peripheral myopic defocus lenses compared with SV control[36]. Other treatments show an opposite effect of age, for instance the DIMS lens[23,24,45,50], although the 12-months dataset with DIMS in a recent retrospective real-world study demonstrated similar efficacy in slowing down myopia progression for both younger and older subjects[48]. Similar to this report, most studies indicate a higher likelihood of achieving efficacy that meets the minimal clinically important difference in younger children in this age group, compared to older children in the 9–12 year age group[28,36,44,48]. Furthermore, using a cut-off of myopia progression of ≥ 1 D as clinically significant myopia progression that is typically designated as "rapid" or "fast" progression[15,20,22], likely due to its strong association with significantly increased risks of severe ocular complications and irreversible vision loss[5,8,10], the proportion of children with no myopia progression, i.e. treatment responders, was higher in children wearing the MSL lenses, consistent with the current report with DIMS spectacle lenses using the same cut-off[48].

The observed differences in efficacy percentages can be attributed to several factors, such as ethnicity. This study included only the Caucasian population, whereas many studies reporting higher efficacies (e.g., HAL, DIMS, higher-dose atropine) were conducted in Asian populations[18,24,30]. For instance, children from Asian countries typically have more rapid myopia progression[6,10,23,34,40,51], and earlier onset of myopia[39,52]. A slower progressing control group (often seen in Caucasian populations) may result in a lower percentage efficacy for

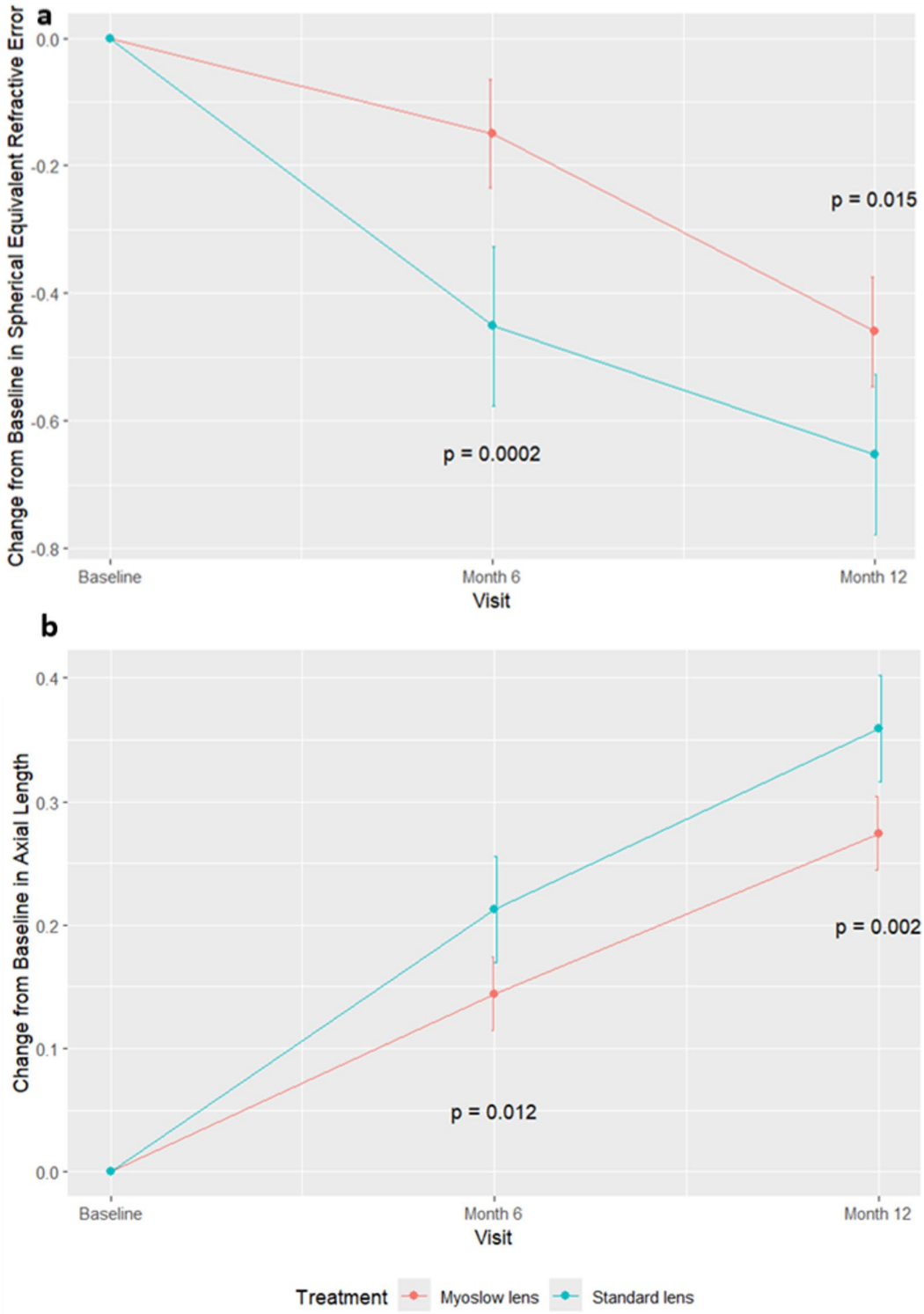


Fig. 2. Myopia progression. Myopia progression measured as change from baseline to 1 year in spherical equivalent refraction (LS Means and 95% CI) and axial length (LS Means and 95% CI).

a similar absolute treatment effect. The 1-year control group progression in our study (SER − 0.65 D, AL 0.36 mm) is indeed at the lower end compared to some Asian control groups, such as 1-year SER − 0.81 D[30] or 1-year SER − 1.07 D[47]. However, the finding that younger age was significantly associated with a better treatment effect contrasts with some DIMS studies in Chinese populations where efficacy was found to be greater in older children (e.g., 10–15 years vs. 6–9 years)[23]. Other studies in European populations also report that younger age is associated with faster progression and suboptimal outcomes with DIMS[45]. Such complex and sometimes

	Myoslow Lens	SV Lens	Total
	n = 83	*n* = 39	*n* = 122
Daylight Exposure (hours/day)			
Mean (SD)	2.2 (1.0)	2.4 (0.9)	2.3 (0.9)
p-value	*0.33*		
Phone / Computer Exposure, (hours/day)			
Mean (SD)	3.3 (1.6)	3.3 (1.5)	3.3 (1.6)
p-value	*0.86*		
TV Exposure, (hours/day)			
Mean (SD)	0.9 (1.1)	0.6 (0.9)	0.8 (1.1)
p-value	*0.17*		

Table 3. Average daily daylight exposure, phone / computer usage and television exposure in the myoslow and SV groups. P-values are based on independent t-test.

	Myoslow Lens	SV Lens
	n = 83	*n* = 40
Overall Score		
n	75	38
Mean (SD)	3.33 (20.09)	3.95 (19.72)
p-value	*0.88*	
Vision Score		
n	77	38
Mean (SD)	12.44 (21.81)	11.88 (23.42)
p-value	*0.91*	
Symptom Score		
n	77	38
Mean (SD)	6.12 (19.17)	7.22 (21.91)
p-value	*0.79*	
Appearance Score		
n	77	38
Mean (SD)	2.42 (18.69)	5.29 (21.34)
p-value	*0.48*	
Activities Score		
n	75	38
Mean (SD)	7.99 (22.45)	7.03 (25.44)
p-value	*0.84*	
Handling Score		
n	75	38
Mean (SD)	1.59 (14.45)	3.37 (17.26)
p-value	*0.59*	
Peer Perception Score		
n	75	38
Mean (SD)	1.24 (13.92)	4.22 (13.38)
p-value	*0.27*	

Table 4. Changes from baseline to 12 months in the PREP2 quality of life in the myoslow and SV groups. P-values are based on independent t-test.

conflicting interactions of age with treatment effect across different ethnicities further contributes to variability in efficacy of MD. Equally important are genetic factors, such as parental myopia. Whereas scarce studies report statistically higher parental myopia rate in the control group compared to the treatment group[36] or explicitly discuss that it is not clear if the spectacles would have a differential effect based on parental myopia, such is with DIMS[48], most publications do not provide direct comparisons of the percentage of participants with both parents myopic between their respective treatment and control groups with statistical significance[45]. Such an imbalance would imply the control group's progression could be inherently faster due to this demographic

Authors (years)	Age range (years), ethnicity	Criteria of Rx at baseline in D	Interventions and sample size (*n*)	Treatment effect in retarding myopia progression in D (%)	Treatment effect in retarding axial elongation in mm (%)
Present study	6–12, Caucasian	-1.00 to -5.00	Myoslow (83) SV (40)	0.19 (29.5%)	0.09 (23.6%)
COMET2 Study Group for PEDIG (2011)[34]	8–12, diverse ethnicity	-0.75 to -2.50	PAL (59) SV (59)	0.14 (30.9%)	Not reported
Edwards et al. (2002)[32]	7–10.5, Chinese	-1.25 to -4.50	PAL (121) SV (133)	0.11 (15.2%)	0.01 (2.7%)
Gwiazda et al. (2003)[33]	6–11, diverse ethnicity	-4.5 to -1.25	PAL (235) SV (234)	0.14 (30.9%)	0.06 (20.0%)
Lam et al. (2014)[39]	8–13 Chinese	-1.00 to -5.00	DISC (49) SV (47)	0.12 (25.0%)	0.08 (38.1%)
Liu X et al. (2023)[37]	8–12, Chinese	-1.50 to -4.50	CARE (52) SV (44)	0.15 (21.1%)	0.10 (27.8%)
Sankaridurg et al. (2010)[35]	6–12, Chinese	-0.75 to -3.50	Type III (50) SV (50)	0.12 (15.4%)	0.04 (16.0%)
Wei et al. (2020)[40]	6–12, Chinese	-0.50 to -6.00	Atropine 0.01% (220) Placebo (220)	0.28 (34.2%)	0.10 (22.0%)
Yam et al. (2019)[18]	4–12, Chinese	-1.00 to -10.00	Atropine 0.01% (110) Placebo eyedrops (111)	0.22 (27.2%)	0.05 (12.2%)
Bao et al. (2022) [30]	8–13, Chinese	−0.75 to −4.75	HAL (54) SAL (55) SV (52)	0.50 (63%) 0.32 (40%)	0.21 (61%) 0.11 (31%)
Lam et al. (2020)[24]	8–13, Chinese	−1.00 to −5.00	DIMS (79) SV (81)	0.38 (55%)	0.21 (66%)
Rappon et al. (2022)[28]	6–10, diverse ethnicity	−0.75 to − 4.50	DOT Test 1 (71) DOT Test 2 (71) SV (91)	0.40 (74%) 0.32 (59%)	0.15 (50%) 0.10 (33%)
Chamberlain et al. (2019)[41]	8–12, diverse ethnicity	−0.75 to − 4.00	MiSight CL (56) SV (52)	0.38 (69%)	0.13 (63%)
Lu et al. (2025)[42]	5–12, Chinese	0.00 to 1.00	DSDO and placebo eye drops (121) SV and placebo eye drops (124)	0.16 (53.3%)	0.024 (8.9%)

Table 5. Comparison with previous studies.

difference, potentially leading to an overestimation of the treatment group's percentage effectiveness if not adequately adjusted for.

The current report encompasses only the first year of the 2-year study, and results will need to be confirmed with more long-term data, including the effects of covariates. Also, the enrollment in the current study was limited to Caucasian White children with myopia not exceeding − 5 D, therefore the effectiveness of the MSL lenses in other ethnic populations and children with higher myopia remains to be investigated. Other study limitations include slight inter-group differences in mean age and gender distribution despite participants' initial randomization, unknown parental myopia severity that has been shown to affect the risk of myopia[53] and the unknown onset age of parental myopia[54]. The young age of the subjects is also a potential confound with the percentage reduction in AL, due to the normal physiological growth. Despite these limitations, the results of this interim analysis provide support for the hypothesis that peripheral defocus can slow axial growth and myopia progression.

The subjects fully adapted to the treatment within a few days. The Quality of life questionnaire indicated no significant inter-group difference despite the optical elements incorporated in the MSL design. During the 1-year study period, no serious adverse events were reported and only a single ocular adverse event possibly related to the treatment. Since parents frequently hesitate to adopt contact lenses or atropine treatments[21], slowing myopia progression using spectacles is an effective and safe option, especially since the child is already wearing glasses.

In summary, treatment with the novel lens incorporating peripheral defocus over 12 months significantly slowed myopia progression and axial elongation in myopic schoolchildren as compared with wearing single vision spectacle lenses. The effectiveness was higher in younger children. Given the increased risk of high myopia with a younger age of myopia onset[55], this noninvasive method represents a promising intervention for myopia management during early childhood to slow myopia progression and possibly reduce later myopia-related risks, in addition to pharmacological or contact lens treatments.

Methods

Study design

This study was designed as a multicenter 2-year prospective randomized, controlled, double-masked trial to evaluate the safety and effectiveness of a newly designed peripheral defocus myopia spectacle lens (Myoslow, Crystal Optic) in school-aged children, with follow-up visits every 6 months and a planned interim analysis after 12 months. Participants were randomly assigned in a 2:1 ratio to receive the Myoslow spectacle lenses (MSL, treatment) or single-vision spectacle lenses (SV, control).

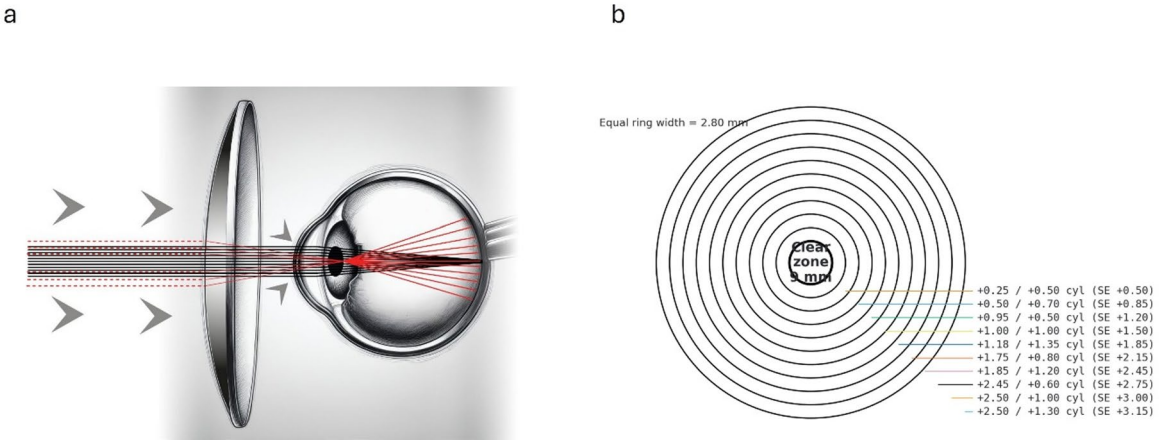


Fig. 3. Myoslow Lens. (**a**) Illustration of the peripheral defocus myopia spectacle lens (Myoslow, Crystal Optic). Solid lines, focused central input; dashed lines, defocused peripheral input. (**b**) Schematic diagram. The size of central clear zone is 9 mm; each ring width is 2.80 mm. Distribution of power varies depending on frame shape and size.

Outcome measurements

The primary study outcome was the mean change in SER from baseline to the 24- month visit. An interim analysis was performed after all subjects reached the 1-year follow-up time point. This report presents the results of the interim analysis of the study. Participants will remain blinded to their treatment assignment until all participants have completed the 24-month follow-up period, the data are cleaned, and the database is locked. The secondary outcomes included the mean change in axial length (AL) (mm) from baseline at the 12-month visit, the change in vision-related quality of life (QOL) from baseline to the 12-month visit and the incidence of adverse events related to MSL.

MSL spectacle lens design

All spectacle lenses were made of polycarbonate. Myoslow (Crystal Optic Industries Ltd., Acre, Israel) is a spectacle lens based on the peripheral defocus mechanism of action, designed to provide the same optical image as the Defocus Incorporated Soft Contact (DISC) lens for myopia control that imposes myopic defocus on both the central and peripheral retinas (Fig. 3).

The design is based on the assumption that targeted myopic defocus, produced by the 396 mid-peripheral lenslets with a positive power, slows down the axial elongation. This resulting optical image is similar to that produced by the DISC, consisting of a central correction zone and a series of alternating defocusing and correction zones spreading towards the perimeter in a 50:50 ratio, with the defocusing zones at + 2.5 D and the corrective zones matching the distance prescription. Regular single vision spectacle lenses were used as a control group (Crystal Optic Industries Ltd., Acre, Israel).

Enrollment and sample size calculation

The sample size calculation assumed that myopia progression in the control arm would be 0.55 D per year and the Myoslow group would have a 50% reduction in progression compared to the control group (0.275 D per year). Using 2:1 random treatment allocation (treatment: control), a sample size of 40 in the control arm and 80 in the Myoslow arm (total 120) has 80% power to detect a difference of 0.55 D progression in the control arm versus 0.275 D progression in the Myoslow arm with a common standard deviation of 0.5 using a two group t-test with a 5% two-sided significance level. Accounting for 4% drop out, the total sample size required was calculated as 125.

Each of the participating medical centers referred potentially eligible participants to a screening visit. An advertisement approved by the ethics committee was also used for recruitment. Participants were included in the trial if they met the following criteria:

- age 6–12 years.
- cycloplegic SER between − 1.00 to -5.00 D.
- astigmatism and anisometropia of 1.50 D or less.
- monocular best corrected visual acuity (BCVA) of 6/7.5 (0.1 logMAR) or better at distance for both eyes.

Children with strabismus and abnormalities in binocular vision, eye and systemic disorders or previously treated for myopia were excluded.

The first participant was enrolled on January 3, 2023. Eligible enrolled participants were assigned to either receive MSL or SV treatment using the Electronic Data Capture (EDC) randomization platform (clinxl.ennov.com) using block randomization with a block size of 6. Masked examiners, optometrists or orthoptists, performed all the study measurements. Spectacles were not labelled to identify the assigned treatment. Masking

was maintained for all study measurements for investigators, examiners, participants, and parents or guardians. No physical differences between the two lenses are discernible with the naked eye. The examiners were instructed not to examine the lenses with the lensometer. Data were anonymized, with only outcome variables and treatment group provided for interim analysis by the study manager. Spectacles were provided at no cost.

Study procedures and data collection

SER (calculated by the sum of the spherical power plus half the cylindrical power of the refractive error) was based on the cycloplegic refraction. Visual acuity measurement was obtained using an M&S, Smart system 2 (M&S technologies, Niles IL, USA) at the Sheba Medical Center and at the Assuta Medical Center. AL measurements obtained using either IOL MASTER – 700 (Carl Zeiss Meditec, Jena, Germany) at the Sheba Medical Center or an OA-2000 (Tomey, Nagoya, Japan) at the Assuta Medical Center. The two instruments were confirmed to produce similar measurements[56,57]. Each subject was measured at each visit with the same instrument, either IOL master or Tomey OA 2000. Vision related QOL was accessed using the questionnaire PREP2[58], administered during the screening, the 6-month and 12-month follow up visits.

Cycloplegia was induced with the instillation of Tropicamide 1% once, Phenylephrine 2.5% once, and Cyclopentolate 1% instilled 3 times every 5 min. If the patient's residual accommodation was 2D or less, it confirmed that adequate cycloplegia has been achieved.

Eye deviation was measured using the standard manual cover test following a PEDIG protocol[59]. Stereopsis was measured using the standard Fly test. Eye motility was measured using a standard fixation target manual test. BCVA was measured using either a M&S system (M&S Technologies Inc., Niles, IL, USA) at the Sheba Medical Center or a Snellen chart at the Assuta Medical Center following a PEDIG protocol[59]. Fundus examination was performed using either a slit lamp (Topcon (AIT-16, IJssel, The Netherlands) at the Sheba Medical Center or a Righton (model MW50D) at the Assuta Medical Center. Pupil responses were measured using a manual retinoscope at the Sheba Medical Center or the Welch Allyn screener (Spot, Hill-Rom Holdings, Inc., Chicago, IL, USA) at the Assuta Medical Center.

All participants were asked to wear the spectacles throughout the day, every day. Compliance was monitored by monthly parent questionnaires. The average daily wearing hours were calculated based on the total daily wearing time in a month. Caregivers of the participants were also asked monthly regarding the average daily number of hours the participant was exposed to daylight, spent reading or using a tablet and watching television.

Statistical analysis

There was no statistically significant difference between the right and the left eye data. The analysis of change from baseline in SER and AL at 12 months was performed for the full analysis set. The full analysis set includes all randomized participants that received the spectacles and had at least one post baseline measurement. A mixed model repeated measures (MMRM) model was constructed for the analysis of change from baseline in SER with baseline SER, age at enrollment, gender, parental myopia, treatment group, visit, and treatment group by visit interaction as fixed effects and eye as a random effect in the model (parametric analysis). The change from baseline was measured in each eye. The mixed model for repeated measurements allows for estimation of the change from baseline taking into account both the repeated measurements over time and the repeated measurements across eyes by specifying both the within patient correlation and the between patient correlation in the model[60]. Change from baseline in both the right and left eyes at the 6 month and 12 month timepoints were included in the model. A similar MMRM model was built for the change from baseline in AL with baseline AL included instead of baseline SER. A comparison of the baseline characteristics between the two treatment arms was performed using a chi-square test for categorical variables and an independent t-test for continuous variables. The correlation between the change from baseline to 12 months in SER and the change from baseline to 12 months in AL was examined using Pearson's correlation coefficient.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Received: 30 June 2025; Accepted: 7 October 2025
Published online: 13 November 2025

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Acknowledgements

The authors thank Leah Price, PhD, the study biostatistician (LBPrice Statistical Consulting, Karmiel Israel) and Naomi Berdugo (ClinXL, Ltd. Bet Shemesh Israel), the study data manager.

Author contributions

All authors have approved the submitted version of the manuscript, have agreed both to be personally accountable for their own contributions and to ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated, resolved, and the resolution documented in the literature. Specific contributions were: T.W.-J.: conceptualization, methodology, validation, investigation, resources, writing – review & editing, supervision; S.S.: investigation, supervision; N.G.: investigation; N.F.: investigation; Y.C.: data curation, writing – original draft, project administration; O.Z.: funding acquisition, resources, methodology; C.S.: conceptualization, methodology, validation, investigation, resources, writing – review & editing, supervision.

Funding

Supported by Crystal Optic Industries Ltd., Acre, Israel. The sponsor participated in designing the study; conducting it; data management; data analysis; interpreting the data; and preparation, review, and approval of the manuscript.

Declarations

Ethics approval and consent to participate

This trial was approved by the Sheba Medical Center's and the Assuta Medical Center's ethics committees prior to the beginning of the trial and conducted according to the applicable Good Clinical Practice and local regulatory requirements (ClinicalTrials.gov Identifier: NCT06553404; date of first registration: 11/8/2024; MOH Identifier: MOH_2022-11-09_012170, available at my.health.gov.il/CliniTrials; date of first registration: 09/11/2022). Assent and informed consent were obtained from the children and both parents prior to participation in the study.

Competing interests

T.W.-J., S.S., N.G. and N.F. declare no competing interests. Y.C. and C.S. have consulted for Crystal Optic Industries Ltd., Acre, Israel and received compensation. O.Z. has received compensation as an employee of Crystal Optic Industries Ltd.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-23501-1.

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