Article

Effectiveness of a Spectacle Lens with a Specific Asymmetric Myopic Peripheral Defocus: 12-Month Results in a Spanish Population

Miguel Ángel Sánchez-Tena [1,2], **Jose Miguel Cleva** [3,*], **Cesar Villa-Collar** [4,*], **Marta Álvarez** [3], **Alicia Ruiz-Pomeda** [1], **Clara Martinez-Perez** [2], **Cristina Andreu-Vazquez** [4], **Eva Chamorro** [3] and **Cristina Alvarez-Peregrina** [1]

[1] Department of Optometry and Vision, Faculty of Optics and Optometry, Universidad Complutense de Madrid, 28037 Madrid, Spain; masancheztena@ucm.es (M.Á.S.-T.); alicru04@ucm.es (A.R.-P.); cristina_alvarez@ucm.es (C.A.-P.)
[2] ISEC LISBOA-Instituto Superior de Educação e Ciências, 1750-179 Lisbon, Portugal; clara.perez@iseclisboa.pt
[3] Clinical Research Department, Indizen Optical Technologies, 28002 Madrid, Spain; malvarez@iot.es (M.Á.); evachamorro@iot.es (E.C.)
[4] Faculty of Biomedical and Health Science, Universidad Europea de Madrid, 28670 Madrid, Spain; cristina.andreu@universidadeuropea.es
* Correspondence: jmcleva@iot.es (J.M.C.); villacollarc@gmail.com (C.V.-C.)

Abstract: Background: Different designs of ophthalmic lenses have been studied to control the progression of myopia in children. This study aims to evaluate the short-term efficacy of a new design of ophthalmic lens with asymmetric myopic peripheral defocus (MPDL) on myopia progression in children compared to a control group wearing a single-vision lens (SVL). Methods: Children aged 5 to 12 with myopia up to -0.50 D, astigmatism and anisometropia under 1.50 D, and corrected visual acuity over 20/20 were randomized to either the study group (MPDL) or control group (SVL). The myopia progression was evaluated by measuring axial length (AL) growth (IOL Master; Zeiss) over a period of one year. Results: Ninety-two subjects were recruited. Forty-six children were randomly assigned to the control group, and 46 to the study group. In total, 83 children completed the clinical trial, with a mean age of 10.81 [9.53–11.92] years, among which 59.04% were female. After one year of treatment, there was less AL elongation in the study group compared to the control group (0.16 ± 0.16 mm vs. 0.24 ± 0.16 mm, $p = 0.034$). Conclusions: The MPDL significantly reduced the absolute growth of AL by 39% ($p = 0.014$) and relative growth of AL by 37.3% ($p = 0.012$) after 12 months in comparison to the control group in a Spanish population.

Keywords: myopic peripheral defocus lenses; children; efficacy; myopia

Citation: Sánchez-Tena, M.Á.; Cleva, J.M.; Villa-Collar, C.; Álvarez, M.; Ruiz-Pomeda, A.; Martinez-Perez, C.; Andreu-Vazquez, C.; Chamorro, E.; Alvarez-Peregrina, C. Effectiveness of a Spectacle Lens with a Specific Asymmetric Myopic Peripheral Defocus: 12-Month Results in a Spanish Population. *Children* **2024**, *11*, 177. https://doi.org/10.3390/children11020177

Academic Editor: Hee-Young Choi

Received: 30 November 2023
Revised: 10 January 2024
Accepted: 26 January 2024
Published: 1 February 2024

Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

1. Introduction

Myopia is one of the most common eye conditions [1–3] and its prevalence is increasing worldwide [4,5]. The onset of myopia in early childhood is closely related to high myopia in adulthood [5,6]. Low myopia (up to -2.75 D) and moderate myopia (-3.00 D to -5.75 D) have the potential to progress to high myopia (-6.00 D and more) with a corresponding axial length (AL) of around 26.0 mm [7] without appropriate intervention, which can have severe consequences for an individual's ocular health. High myopia is associated with a greater risk of developing retinal detachment, myopic macular degeneration, glaucoma, and, in some cases, lead to blindness [8].

It is expected that the prevalence of high myopia will increase substantially worldwide, with its incidence expected to grow from 399 million in 2020 to 516 million by 2030 [3,9]. Consequently, pathological myopia is predicted to become the leading cause of permanent vision impairment and blindness worldwide. This growing awareness of the potential complications of high myopia has led to a global call for myopia control strategies. Therefore, it

is important to detect myopia at an early stage and take measures to decrease its incidence and progression, especially among young children.

Myopia onset and progression are now understood to result from a complex interplay of visual, environmental, and genetic factors that regulate the growth of the eye in response to visual stimuli [10]. Animal studies have played a crucial role in helping us to understand myopia and develop treatment strategies [11]. Animal models have shown that emmetropization is an active process based on visual feedback and have robustly demonstrated that inducing myopic defocus inhibits eye growth, while hyperopic defocus promotes it [12]. Research with various species, including rhesus monkeys [13], marmosets [14], chicks [15], and guinea pigs [16], indicates that myopic defocus, achieved with a dual-power or multifocal lens, can inhibit or even reverse myopic eye growth. Notably, myopic defocus is considered to be the key mechanism in several contemporary myopia control strategies, including orthokeratology, multifocal soft contact lenses, and spectacle lenses.

A recent meta-analysis assessed the comparative efficacy of different optical and pharmacological interventions, showing that they may slow refractive change and reduce AL elongation [17]. Optical interventions such as ophthalmic lenses, soft contact lenses, and orthokeratology aim to alter retinal defocus by inducing myopic defocus to slow myopia progression. These optical interventions were evaluated in a meta-analysis that concluded they are effective in controlling childhood myopia progression; however, treatment effects were greater during the first 12 months of treatment and reduced over time [18].

The new designs of ophthalmic lenses recently developed to control myopia progression can be divided into two groups: peripheral myopic defocus and diffusion optics technology. Both designs are based on the two mechanisms studied for myopia progression: peripheral hyperopic defocus and abnormal cone contrast signaling in the retina [19]. Within the first category, we can include progressive peripheral defocus ophthalmic lenses [20–23] and defocus incorporated multiple segments (DIMS) [24], highly aspherical lenslets target (HALT) [25,26], and cylindrical annular refractive element (CARE) [27] spectacle lenses, while the second category includes diffusion optics technology (DOT) spectacle lenses [28].

This study presents a new ophthalmic lens design based on a specific asymmetric myopic peripheral defocus (MPDL), with an ovoidal blur-free central area surrounded by a progressive power distribution producing asymmetrical myopic defocus.

The study aims to evaluate if the proposed design can slow myopia progression in schoolchildren compared to a control group corrected with a single-vision lens (SVL).

2. Materials and Methods

A prospective, double-blind, randomized clinical trial (RCT) was carried out to evaluate the efficacy of a new ophthalmic lens design developed by IOT for myopia control at the Novovision Clinic in Madrid (Madrid, Spain).

The study included children aged between 5 to 12 years old who met certain criteria: cycloplegic spherical equivalent (SE), defined as sphere + ½ cylinder, had to be lower than −0.50 D; astigmatism had to be less than 1.50 D; anisometropia had to be less than 1.50 D, and visual acuity had to be equal to or greater than 20/20. Children who had previously received any treatment for myopia control, had any ocular pathology, were using drugs that could affect pupil size, or had any systemic disease that could affect vision were excluded from the study.

The study recruited 100 myopic children who were randomly assigned to either the treatment or control group. The treatment group wore the MPDL, while the control group wore a standard spherical SVL.

The MPDL comprised an ovoidal blur-free central area with a horizontal size of 7 mm and a peripheral treatment area consisting of an asymmetrical horizontal myopic defocus with an addition value of +1.50 D at 25 mm nasally and +1.80 D at 25 mm temporally. Additionally, the lens also featured a myopic defocus inferiorly with a value of +2.00 D.

The spherical equivalent and cylinder power distribution maps for a plano prescription are shown in Figure 1.

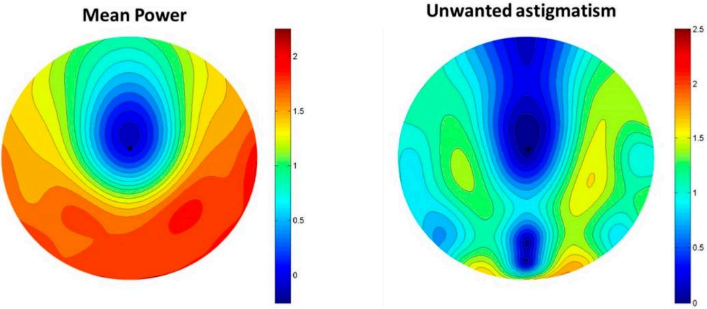

Figure 1. Spherical equivalent and cylinder power distribution maps for a plano prescription of the new design of ophthalmic lens for myopia control.

All lenses were manufactured by free-form technology in index 1.6 with anti-reflective coating considering the children’s prescription, monocular pupillary distances, and pupil heights. FreeFormDesigner software version 10.5 (IOT, Madrid, Spain) was used for all lens calculations.

Lenses were fitted to spectacle frames that ranged in horizontal size from 41 mm to 55 mm and in vertical size from 30 mm to 48 mm. As would be expected and advised by the optician, younger children generally selected smaller frames than older children.

The procedures followed in the RCT and the instruments used were:

- Sociodemographic questionnaire: Participants’ parents completed a questionnaire that included information regarding age (date of birth), gender, ocular and medical health records, ocular surgeries, history of parents’ myopia, age of myopia onset, history of myopia progression, and previous eye treatments.
- Objective refraction: Performed using an autorefractometer after cycloplegia using 3 drops of cyclopentolate.
- Biometry: AL was measured with the optical biometer IOL Master® (Carl Zeiss Meditec, Jena, Germany)
- Binocular vision: Distance and near vision phoria were measured using Von Graefe’s technique, the amplitude of accommodation was measured using the Sheard method, and the accommodative lag was measured using MEM retinoscopy.
- Wearability questionnaires: All of the children, with parental assistance, completed questionnaires to assess their satisfaction with the spectacles, record the time of use, and document any issues associated with the spectacles or any adverse effects.

During the first visit, the optometrist provided information about the study to the parents of the children, who then signed a written consent form after any doubts were addressed. The optometrist also checked that the children met the inclusion criteria. Baseline measurements were also taken. All children underwent an ophthalmology exam to evaluate their ocular health, and their cycloplegic autorefraction, binocular vision, and AL were recorded in the case report form. Additionally, parents completed a sociodemographic questionnaire, and the children selected frames for their spectacles.

The second visit was scheduled for the collection of the spectacles, which the children were required to wear throughout the day. The optometrist checked the fitting of the spectacles and gave each child a wearability questionnaire to complete and return at the next visit. Children whose refraction changed by more than 0.50 D during the study or who suffered an adverse incident, such as broken frames or scratched lenses, were provided with a new pair.

Wearability questionnaires were collected at 6 and 12 months following the second visit, and the children also underwent a cycloplegic autorefraction, binocular vision, and AL assessment, which was recorded in the case report form.

Table 1 shows a summary of the data collected at each visit.

Table 1. Schedule of assessments and examination items.

Visit		**V0**	**V1**	**V2**	**V3**
Consent form signed		X			
Basic Information	Demographics	X			
	History	X			
Refraction	Subjective Refraction	X		X	X
	Cycloplegic autorefraction	X		X	X
Visual acuity	Uncorrected visual acuity	X		X	X
	Best corrected visual acuity	X		X	X
Eye examination	Keratometry	X			
	Slit lamp examination	X			
	Fundus examination	X			
	Intraocular pressure measurement	X			
	Axial length	X		X	X
Binocular vision	LAG	X		X	X
	Accommodation Amplitude	X		X	X
	Phoria (distance and near)	X		X	X
Spectacle fitting	Frame position and lens condition		X		
Questionnaire	Lifestyle	X			
	Wearability			X	X

The RCT was approved by the Institutional Ethics Committee of Hospital Clínico San Carlos (Madrid, Spain) and adhered to the tenets of the Declaration of Helsinki. The trial was registered on ClinicalTrials.gov (accessed on 25 January 2024) with ID NCT05250206.

A comparative statistical analysis of absolute (mm) and relative (%) AL growth between the MPDL and SVL groups was performed using STATA$^{®}$ software v.14. Absolute AL growth was calculated as the median relative difference after 6 and 12 months of treatment: (AL at 6 m − baseline AL)/baseline AL × 100 and (AL at 12 m − baseline AL)/baseline AL × 100. The significance level was set as p-value < 0.05. The efficacy of the MPDL was evaluated by comparing the means of relative AL growth in children treated with MPDL to that of children treated with SVL.

3. Results

Out of 100 children who were assessed for eligibility, 92 were enrolled and randomized into two groups. The control group consisted of 46 children using SVL, and the study group included 46 children wearing MPDL. The flowchart in Figure 2 shows the enrollment and follow-up visits, indicating that 9 of the participants did not complete the study (4 in the SVL group and 5 in the MPDL group), resulting in a dropout rate of 9.8%. Finally, the

83 children analyzed were divided into 42 (50.6%) in the control group with SVL and 41 (49.4%) in the study group with MPDL.

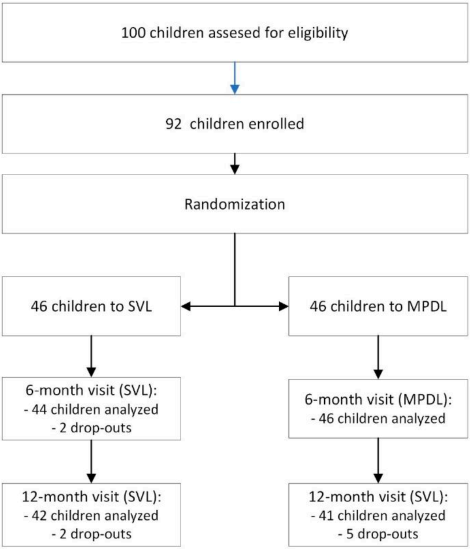

Figure 2. Randomized clinical trial flow chart with participant randomization, treatment group assignment, and follow-up visits. SVL: Single-vision lens; MPDL: Asymmetric myopic peripheral defocus lens.

Table 2 presents the baseline parameters of the entire sample and each study group. The age of the children who participated in the study ranged from 6.4 to 13.7 years, with 59.0% being girls. The initial axial length in the study group was 24.17 ± 0.91 mm, while it was 23.98 ± 0.82 mm in the control group. As for the initial spherical equivalent, it was −2.63 ± 1.28 D in the MPDL group and −2.01 ± 1.03 D in the SVL group.

The fitting characteristics of the children varied as a result of different face physiognomies, leading to a range of distances from the pupil to the nasal side of the frame of 20 ± 2 mm (from 16 to 24 mm), to the temporal side of 30 ± 3 mm (from 24 to 35 mm), to the superior side of 14 ± 4 mm (from 8 to 23 mm), and to the inferior side of 26 ± 3 mm (from 20 to 32 mm). Figure 3 shows an illustrative example of the fitting characteristics of 2 participants of the study with extremely different face physiognomies, indicating the distances from the pupil to the nasal, temporal, superior, and inferior sides of the edge of the frame. In example A, the maximum positive defocus was 1.78 D, and in example B, the maximum positive defocus was 1.98 D.

Table 2. Baseline characteristic of the sample.

Baseline Characteristics *	**Total (n = 83)**	**MPDL (n = 41)**	**SVL (n = 42)**	***p*-Value** **
Age (Median [Q1, Q3])	10.81 [9.53–11.92]	11.7 [9.97–11.98]	10.49 [8.76–11.32]	0.022
Gender (n, %)				0.212
Boys	41.0 (34)	34.1 (14)	47.6 (20)	
Girls	59.0 (34)	65.9 (27)	52.4 (22)	
Initial cycloplegic refraction (Mean ± SD)	−2.32 ± 1.20	−2.63 ± 1.28	−2.01 ± 1.03	0.018
Initial axial length (Mean ± SD)	24.07 ± 0.86	24.17 ± 0.91	23.98 ± 0.82	0.329
Myopic parents (%, n)				0.657
0	40.3 (31)	36.8 (14)	43.6 (17)	
1	37.7 (29)	36.8 (14)	38.5 (17)	
2	22.1 (17)	26.3 (10)	18.0 (7)	
Hours/week outdoors (Median [Q1, Q3])	6.5 [2.5–10]	6 [3–10]	7 [2–10.50]	0.604
Hours/week doing homework (Median [Q1, Q3])	6 [2.5–10]	6 [2.5–12]	5.5 [3–10]	0.697
Computer Hours/Week (Median [Q1, Q3])	3 [0.5–8]	4 [1–7]	2.25 [0–8]	0.652
Sleeping hours (Mean ± SD)	9.58 ± 0.71	9.52 ± 0.59	9.64 ± 0.82	0.461

* Weekday hours during the school term. ** *p*-value of the comparison between MPDL and SVL groups (Chi-square test for qualitative variables, or Student's *t*-test for independent samples or Mann–Whitney U test, according to normality, for quantitative variables.

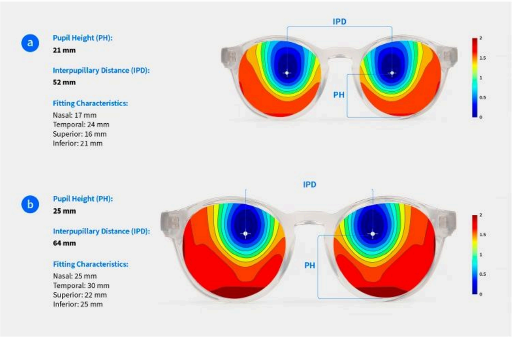

Figure 3. Fitting characteristics of 2 participants of the study with extremely different face physiognomies, indicating distances from the pupil to the nasal, temporal, superior, and inferior sides of the edge of the frame. (**a**) Seven-year-old participant wearing a frame with horizontal size of 41 mm, vertical size of 37 mm, and bridge of 18 mm. (**b**) Eleven-year-old participant wearing a frame with horizontal size of 55 mm, vertical size of 47 mm, and bridge of 14 mm.

Based on subjective prescription changes over or equal to 0.25 D during the 12-month duration of the study, the optical prescription was updated in 18 children from the SVL group and 15 children from the MDPL group. Additionally, 1 child in the SVL group and 0 children in the MDPL group required more than one change of lenses. The mean

change in prescription was −0.36 ± 0.43 D in the SVL group and −0.25 ± 0.18 D in the MDPL group.

After 6 months of treatment, the SE increased by a mean of 0.07 ± 0.22 diopters in the group of children who wore MPDL, while it increased by −0.09 ± 0.27 diopters in the group of children who wore SVL. The difference in the increase between the two groups was found to be statistically significant, with a *p*-value of 0.0034.

One year after treatment, the SE increased by −0.00 ± 0.31 diopters in the MPDL group and −0.25 ± 0.32 diopters in the SVL group. The difference in the increase between the two groups was found to be statistically significant, with a *p*-value of 0.0005. These changes represented a relative growth of 1.0 ± 16.1% in the MPDL group versus 16.4 ± 19.1% in the SVL group (*p* = 0.0002).

Table 3 shows the AL values for each group in all visits, as well as the relative changes.

Table 3. Axial length by group in all visits.

	MPDL (n = 41)	**SVL (n = 42)**	***p*-Value**
Initial axial length (Mean ± SD)	24.17 ± 0.91	23.98 ± 0.82	0.329
6-month visit axial length (Mean ± SD)	24.23 ± 0.93	24.10 ± 0.84	0.507
12-month visit axial length (Mean ± SD)	24.32 ± 0.95	24.22 ± 0.85	0.610
Axial Length Change at 6 Months			
Absolute axial length change (mm)	0.06 ± 0.09	0.12 ± 0.11	0.018
Relative change in axial length (Mean)	0.27 ± 0.42	0.51 ± 0.53	0.026
Relative change in axial length (Median [Q1, Q3]) (AL at 6 months—AL at baseline/AL at baseline) × 100 (%)	0.20 [0.07–0.35]	0.36 [0.16–0.74]	0.020
Change in Axial Length at 12 Months			
Absolute axial length change (mm)	0.14 ± 0.14	0.23 ± 0.15	0.014
Relative change in axial length (Mean)	0.61 ± 0.64	0.98 ± 0.65	0.012
Relative change in axial length (Median [Q1, Q3]) (AL per year—AL at baseline/AL at baseline) × 100 (%)	0.57 [0.20–0.87]	0.74 [0.54–1.31]	0.010

SVL: Single-vision lens; MPDL: asymmetric myopic peripheral defocus lens.

After 6 months, the AL of the eye increased by 0.06 ± 0.09 mm in the group that received MPDL, while it increased by 0.12 ± 0.11 mm in the group that received SVL (*p* = 0.018). This resulted in a relative growth rate of 0.20% [0.07–0.35] in the MPDL group compared to 0.36% [0.16–0.74] in the SVL group (*p* = 0.02). After 1 year, the AL increased by 0.14 ± 0.14 mm in the MPDL study group and by 0.23 ± 0.15 mm in the SVL control group (*p* = 0.014), representing a relative growth of 0.57% [0.20–0.87] in the MPDL group versus 0.74% [0.54–1.31] in the SVL group (*p* = 0.01). Figure 4A,B visually display these relative changes.

The efficacy of the MPDL was evaluated by comparing the means of relative AL growth in children treated with MPDL to that of children treated with SVL. During the first 6 months of treatment, children in the MPDL group showed a mean value of relative increase in AL of 0.27 ± 0.42%, while children in the SVL group showed a mean value of relative increase of 0.51 ± 0.53%. The MPDL proved to significantly reduce the relative growth of AL by 46.9% (*p* = 0.026).

After 12 months, the mean value of relative increase in AL was 0.98 ± 0.65% for children in the SVL group and 0.61 ± 0.64% for children in the MDPL group. The MPDL significantly reduced the relative growth of AL by 37.3% (*p* = 0.012).

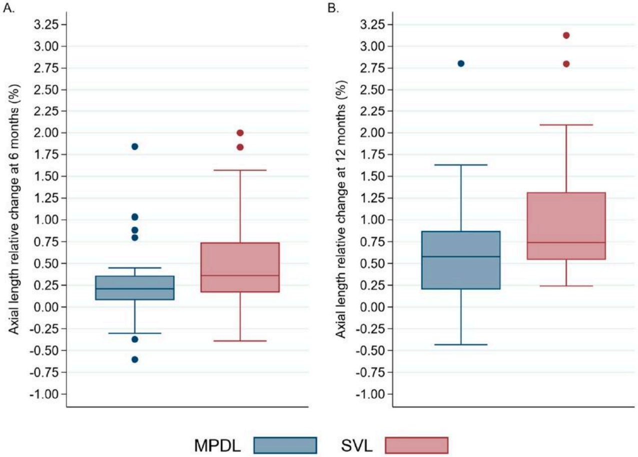

Figure 4. (**A**) Axial length relative change at 6 months (%), and (**B**) axial length relative change at 12 months (%). SVL: Single-vision lens; MPDL: Asymmetric myopic peripheral defocus lens.

Regarding the factors associated with relative AL growth, univariate linear regression analyses indicated that factors such as sex, presence of one or two parents with myopia, time spent outdoors, hours spent doing homework or in front of the computer, daily hours of sleep, and initial spherical equivalent did not have significant impacts on the relative growth of AL over 6 and 12 months of treatment. However, it was observed that the age of the child at the beginning of the study influenced the relative growth of AL in both groups (6-month regression coefficient: −0.066, 95% CI: −0.124 to −0.007; 12-month regression coefficient: −0.134, 95% CI: −0.210 to −0.058), with the relative growth being lower in children with MPDL compared to children with SVL (regression coefficient at 6 months: −0.238, IC 95%: −0.447 a −0.029; regression coefficient at 12 months: −0.364, IC 95%: −0.646 a −0.083).

Multivariate analysis confirmed the effect of age, showing that, for each additional year of the child's age at baseline, relative growth was lower at both 6 months (regression coefficient: −0.065, 95% CI: −0.125 to −0.004) and 12 months of treatment (regression coefficient: −0.133, 95% CI: −0.212 to −0.054). In addition, multivariate regression analysis revealed that regardless of the child's age and AL at the beginning of treatment, the relative growth of AL in children in the MPDL group tended to be lower after 6 months (regression coefficient: −0.238, 95% CI: −0.447 to −0.029) and was significantly lower at 12 months (regression coefficient: −0.275, 95% CI −0.548 to −0.001) compared to that in children in the SVL group (Figure 5).

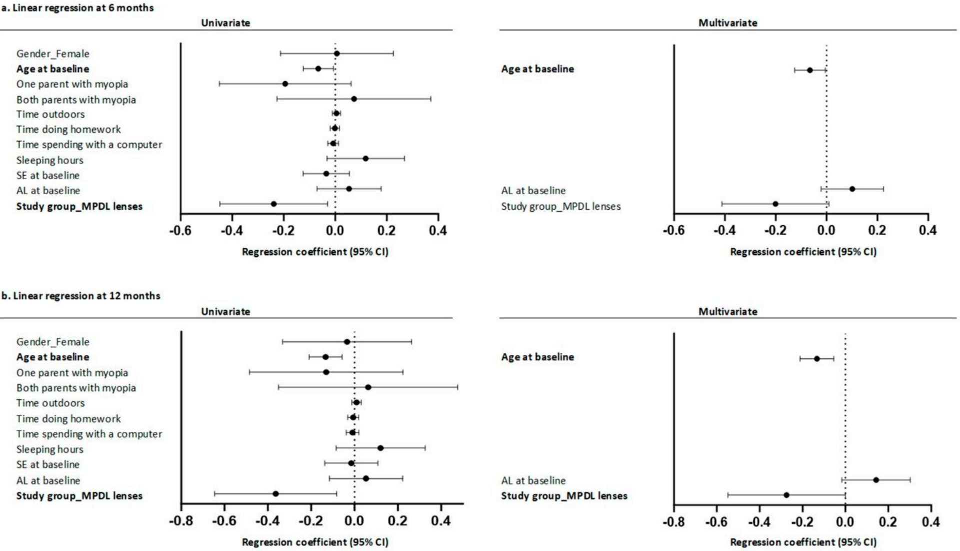

Figure 5. Factors associated with the relative growth of axial length at (**a**) 6 months and (**b**) 12 months following the start of the study.

4. Discussion

The use of spectacle lenses for managing the progression of myopia has been well studied in recent years, demonstrating different levels of efficacy between different lens designs.

Sankaridurg et al. [20] showed no significant differences in the rate of progression of myopia in Chinese children between the control group that used SVL and the group that used one of three types of lens based on reducing peripheral hyperopic defocus, using central apertures of 20 mm, 14 mm, and 10 mm in diameter combined with a positive additional peripheral power of 1 D, 2 D, or 1.9 D, respectively. Later, Kanda et al. [22] tested MyoVision lenses, which have an asymmetric design with a central aperture of 20 mm in diameter and a positive additional peripheral power of 1.9 D. The study performed with Japanese children did not show significant differences in the progression of myopia or ocular elongation between the control group (SVL) and the group wearing MyoVision lenses.

Although these lenses seemed to not have enough efficacy to reduce myopia progression, there are other studies with different designs of ophthalmic lenses that have shown effectiveness in controlling AL progression in juvenile-onset myopes, such as peripheral progressive defocus lenses (perifocal and Shamir Myopia Control lenses) [21,23], lenslets (DIMS and HALT) [24,25], rings (CARE) [27], or diffusion optics (DOT) [28], not only in Asian populations [24,25,27] but also in Caucasian populations [21,29].

Analyzing the results of the above-mentioned studies in more detail, perifocal lenses were studied in a Russian population, showing significant differences against SV lenses. These peripheral progressive defocus lenses consisted of a central area for full prescription correction of 10 mm in diameter surrounded by asymmetric horizontal progressive defocus reaching a maximum addition of 2.50 D at 25 mm of the temporal side and +2.00 D at 25 mm of the nasal side [21].

Shamir Myopia Control lenses were studied in children from Israel, showing significant differences in the progression of AL during 1 year of follow-up compared to an SVL group. This design has a similar power distribution to the one used in our study, with a central region for full prescription correction with a horizontal width of 10 mm and a positive power that gradually increases up to 1–3 D at different peripheral areas of the lens [23].

DIMS technology has been thoroughly researched, with data available for up to 6 years in Chinese children [30]. The DIMS spectacle lens has a central aperture of 9 mm in diameter for full prescription correction surrounded by a treatment area of 33 mm in diameter with multiple lenslets of 3.5 D positive power [31]. The data from 6 years of follow-up on DIMS lenses demonstrated that there was no rebound effect when the treatment stopped, with myopia control maintained throughout the entire study duration [30]. DIMS lenses have also demonstrated similar efficacy in European children and adolescents treated with a combined method of DIMS and atropine [29].

HALT lenses include a central area for full prescription correction with a central aperture of 10 mm in diameter surrounded by a treatment area with 11 concentric rings formed by aspherical lenslets (diameter of 1.1 mm) with positive power between 3.50 D for lenslets of the peripheral ring and 6.00 D for central rings. HALT lenses have also undergone thorough examination in Chinese children, with data available for up to 4 years [32]. Another study on HALT spectacle lenses in Vietnamese children concluded their effectiveness in slowing myopia progression, with no indication of myopia rebound upon discontinuation [33].

CARE technology consists of a central optical area for myopia correction and a treatment area formed by concentric rings. The design for children under 10 has a 7 mm diameter central zone and a mean surface power of +4 D, and the design for children older than 10 has a 9 mm diameter central zone and a mean surface power of +3.80 D [27]. CARE lenses significantly reduced AL elongation in Chinese children over 1 year compared with SVL [27].

Finally, DOT technology consists of a 5 mm diameter central zone surrounded by translucent microscopic diffusers (diameter of 0.14 mm) to scatter light, with the intent of reducing contrast and therefore reducing the relative activity difference between L and M cones. Two investigational DOT lenses with two different diffusion densities (test 1 and test 2) have been studied, showing effectiveness in controlling myopia progression and axial elongation in North American children compared with SVL [28].

The lens used in this study, MPDL, was developed based on hyperopic defocus theory, with an oval central zone of 7 mm in horizontal width providing full prescription correction surrounded by an asymmetric peripheral defocus treatment area, reaching an addition of +1.50 at 25 mm nasally, +1.80 D at 25 mm temporally, and +2.00 D at the bottom of the lens. After 1 year of treatment, the MPDL study group showed an average eye growth of 0.14 mm, and the control group showed 0.23 mm ($p = 0.014$), corresponding to an absolute efficacy of 39%. The progressions in the control and treatment groups were less than the average obtained with Asian populations using DIMS, HALT, and CARE lenses (change in AL from 0.30 to 0.36 mm). This could be due to the differences between the ethnicities and ages of the populations studied, with the average age of the children in this study being slightly older. It has been demonstrated that the progression of myopia depends on age and race, with AL elongation decreasing as age increases and greater in Asian children compared to non-Asian children [34]. However, studies with Caucasian populations have shown similar rates of AL progression in children not treated with methods to control the progression of myopia, with progression of 0.24 mm in Spanish children [35] and 0.34 mm in 9-year-old European myopes [36].

Our results showed an absolute AL change between the MPDL and SVL groups of 0.09 mm over 1 year. With the same follow-up duration, several studies using peripheral progressive defocus lenses in Chinese [20] and Japanese [22] populations have not shown statistically significant results in the progression of myopia compared to the use of SVL. However, the results of Tarutta et al. [21] with perifocal lenses in Russian children and Yuval et al. [23] with Shamir Myopia Control lenses in Israeli children showed similar results, with an AL change between the study lens group and the SVL group of 0.09 mm and 0.11 mm, respectively. In comparison with other myopia management spectacle lenses, our results in a Spanish population showed, in general, lower AL change between the MPDL and SVL groups than in studies performed in other regions with other lenses. Lam et al. [24] showed a difference in AL progression between the DIMS group and SVL group of 0.21 mm in Chinese children. Bao et al. showed a difference in AL progression between the SVL control group and HALT group of 0.23 mm [25] in Chinese children. Liu et al. showed that treatment with CARE lenses significantly reduced the rate of AL elongation, with a difference of 0.10 mm between the CARE and SVL groups [27] in Chinese children. And Rappon et al., in the CYPRESS study with North American children, demonstrated that DOT test lenses significantly reduced the progression of AL by averages of 0.15 mm and 0.11 mm for the test 1 and 2 lenses, respectively, compared to SVL [28].

The efficacy results of myopia control treatments have historically been presented as percentage of efficacy, involving a simple comparison between the increase occurring in the control group versus the study group. This percentage of reduction in progression as an index to describe treatment effect has been considered misleading. Given the influence of certain parameters, such as children's age and treatment duration, recent studies recommend showing the efficacy of a lens based on the relative growth of AL [37]. In this sense, the MPDL showed a 37.3% decrease in the relative growth of AL. The difference in efficacy between the different ophthalmic lens studies could be due to various reasons, such as differences in the designs of the lenses used, differences in the characteristics of the study population (age, ethnicity, etc.), or differences in the methodology used. In this sense, for improved accuracy and relevance, this study has used relative growth to calculate efficacy, therefore the initial values of AL have been considered.

Regarding the lens design, most of the lenses previously described have a central area providing full prescription correction (of greater or smaller diameter depending on the

design) and a peripheral area with positive addition that aims to create a myopic blur in the peripheral retina. All of the designs of these spectacle lenses (MPDL, DIMS, HALT, SMC, perifocal, and CARE lenses) align with the theory of creating simultaneous myopic retinal defocus during both distance and near viewing with an optical central zone between 7 and 10 mm in diameter surrounded by an addition range from 1.50 D to 3.80 D. Smaller central zone diameters could cause vision problems and discomfort when wearing the lenses. Another aspect to consider in lens design is the myopic defocus, the magnitude and distribution of which could directly impact the effectiveness of the lens. Previous studies have suggested that creating different retinal peripheral defocuses could play an important role in controlling myopia [38,39], and it has been shown that using high add power multifocal contact lenses resulted in a considerable decrease in the rate of myopia progression when compared to medium add power [40].

On the other hand, the existing research does not include any trials of these new designs of ophthalmic lenses in the Spanish population. There are three studies with Caucasian populations, two of them evaluated the efficacy of DIMS in slowing the progression of myopia, the first in German children combined with atropine [29] and the second in English children [41], and the other showed the effect of wearing perifocal glasses in Russian children [21]. In this sense, our study is the first to show efficacy data for a spectacle lens for myopia management in Spanish subjects.

Regarding the limitations of this study, one of them is the absence of stratification in the randomization process, which led to differences in both initial age and initial refraction. The second one is the age range of the sample; future research would ideally involve analyzing the results by age group. The follow-up time should also be extended, as it has been observed in many studies [18] that the effectiveness during the first year of treatment is greater than that in the second and following years of follow-up. Future research should focus on increasing the follow-up period to show the long-term efficacy of the MPDL and any possible rebound effects. This extension has already been approved by the ethics committee. Finally, it would be also interesting for future analysis to examine the influence of the frame and fitting characteristics on the efficacy of the lens, as well as the influence of the convergence in the adaptation and efficacy of the MDPL.

In summary, today myopia is not only treated as a refractive error but also as an ocular disorder that requires effective intervention. To prevent severe myopia and its associated complications, various optical treatments have been explored to slow down the progression of myopia, showing clinically meaningful reductions in myopia progression [42]. Myopia management spectacles are a popular choice because they can be easily fitted even for younger children. Moreover, spectacles have minimal to no side effects in comparison to alternative optical treatments like contact lenses or pharmaceutical therapies such as atropine. The optimal intervention will be clinically selected based on effectiveness and depending on the geographical location [11,31].

Related to spectacle lenses to control the progression of myopia in children, the current study provides the first randomized, double-blind study of a 1-year clinical trial carried out in a European population, with Spanish children wearing an asymmetric myopic defocus ophthalmic lens design, showing that the study group experienced significantly less ocular elongation compared to the SVL group.

5. Conclusions

The MPDL is effective in myopia control in a Spanish population, showing reductions in absolute growth of AL by 50% and 39% after 6 and 12 months of treatment, respectively, and in relative growth of AL by 46.9% and 37.3% after 6 and 12 months of treatment, respectively.

Author Contributions: Conceptualization, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; methodology, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; software, C.A.-V.; validation, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; formal analysis, C.A.-V.; investigation, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C., C.M.-P. and C.V.-C.; resources, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; data curation, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C., A.R.-P., C.M.-P. and C.V.-C.; writing—original draft preparation, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C., A.R.-P. and C.V.-C.; writing—review and editing, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C., A.R.-P. and C.V.-C.; visualization, C.A.-P., M.Á.S.-T., J.M.C., M.Á., A.R.-P., E.C. and C.V.-C.; supervision, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; project administration, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; funding acquisition, J.M.C., M.Á. and E.C. All authors have read and agreed to the published version of the manuscript.

Funding: All expenses associated with the study were funded by Indizen Optical Technologies (IOT).

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of Hospital Clínico San Carlos (Madrid, Spain) (protocol 19/366-R_P, date of approval 26 April 2021). The trial is registered on ClinicalTrials.gov (accessed on 25 January 2024) with ID NCT05250206.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to to specific ethical and privacy considerations.

Conflicts of Interest: Indizen Optical Technologies (IOT) serves as the driving force behind this research study. Authors J.M.C., M.Á., E.C., were employed by the company Indizen Optical Technologies (IOT). The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Morgan, I.G.; French, A.N.; Ashby, R.S.; Guo, X.; Ding, X.; He, M.; Rose, K.A. The epidemics of myopia: Aetiology and prevention. *Prog. Retin. Eye Res.* **2018**, *62*, 134–149. [CrossRef] [PubMed]
2. Resnikoff, S.; Jonas, J.B.; Friedman, D.; He, M.; Jong, M.; Nichols, J.J.; Ohno-Matsui, K.; Smith, E.L., III; Wildsoet, C.F.; Taylor, H.R.; et al. Myopia—A 21st Century Public Health Issue. *Investig. Ophthalmol. Vis. Sci.* **2019**, *60*, Mi–Mii. [CrossRef] [PubMed]
3. Holden, B.A.; Fricke, T.R.; Wilson, D.A.; Jong, M.; Naidoo, K.S.; Sankaridurg, P.; Wong, T.Y.; Naduvilath, T.; Resnikoff, S. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. *Ophthalmology* **2016**, *123*, 1036–1042. [CrossRef] [PubMed]
4. Saw, S.-M.; Matsumura, S.; Hoang, Q.V. Prevention and management of myopia and myopic pathology. *Investig. Ophthalmol. Vis. Sci.* **2019**, *60*, 488–499. [CrossRef] [PubMed]
5. Grzybowski, A.; Kanclerz, P.; Tsubota, K.; Lanca, C.; Saw, S.-M. A review on the epidemiology of myopia in school children worldwide. *BMC Ophthalmol.* **2020**, *20*, 27. Available online: https://pubmed.ncbi.nlm.nih.gov/31937276/ (accessed on 20 October 2023). [CrossRef] [PubMed]
6. Recko, M.; Stahl, E.D. Childhood myopia: Epidemiology, risk factors, and prevention. *Mo. Med.* **2015**, *112*, 116–121. [PubMed]
7. Xu, L.; Wang, Y.X.; Wang, S.; Jonas, J.B. Definition of high myopia by parapapillary atrophy. The Beijing Eye Study. *Acta Ophthalmol.* **2010**, *88*, e350–e351. [CrossRef] [PubMed]
8. Jonas, J.B.; Jonas, R.A.; Bikbov, M.M.; Wang, Y.X.; Panda-Jonas, S. Myopia: Histology, clinical features, and potential implications for the etiology of axial elongation. *Prog. Retin. Eye Res.* **2023**, *96*, 101156. [CrossRef]
9. Swenor, B.; Varadaraj, V.; Lee, M.J.; Whitson, H.; Ramulu, P. World Health Report on Vision: Aging Implications for Global Vision and Eye Health. *Innov. Aging* **2020**, *4* (Suppl. S1), 807–808. [CrossRef]
10. Németh, J.; Tapasztó, B.; Aclimandos, W.A.; Kestelyn, P.; Jonas, J.B.; De Faber, J.T.H.; Januleviciene, I.; Grzybowski, A.; Nagy, Z.Z.; Pärssinen, O.; et al. Update and guidance on management of myopia. European Society of Ophthalmology in cooperation with International Myopia Institute. *Eur. J. Ophthalmol.* **2021**, *31*, 853–883.
11. Sankaridurg, P.; Berntsen, D.A.; Bullimore, M.A.; Cho, P.; Flitcroft, I.; Gawne, T.J.; Gifford, K.L.; Jong, M.; Kang, P.; Ostrin, L.A. IMI 2023 Digest. *Investig. Ophthalmol. Vis. Sci.* **2023**, *64*, 7. [CrossRef]
12. Wallman, J.; Winawer, J. Homeostasis of Eye Growth and the Question of Myopia. *Neuron* **2004**, *43*, 447–468. [CrossRef] [PubMed]
13. Arumugam, B.; Hung, L.-F.; To, C.-H.; Holden, B.; Smith, E.L. The Effects of Simultaneous Dual Focus Lenses on Refractive Development in Infant Monkeys. *Investig. Opthalmology Vis. Sci.* **2014**, *55*, 7423–7432. [CrossRef] [PubMed]
14. Benavente-Perez, A.; Nour, A.; Troilo, D. The Effect of Simultaneous Negative and Positive Defocus on Eye Growth and Development of Refractive State in Marmosets. *Investig. Opthalmology Vis. Sci.* **2012**, *53*, 6479–6487. [CrossRef] [PubMed]
15. Ashby, R.; Ohlendorf, A.; Schaeffel, F. The Effect of Ambient Illuminance on the Development of Deprivation Myopia in Chicks. *Investig. Opthalmology Vis. Sci.* **2009**, *50*, 5348–5354. [CrossRef] [PubMed]

16. McFadden, S.A.; Tse, D.Y.; Bowrey, H.E.; Leotta, A.J.; Lam, C.S.; Wildsoet, C.F.; To, C.-H. Integration of Defocus by Dual Power Fresnel Lenses Inhibits Myopia in the Mammalian Eye. *Investig. Opthalmology Vis. Sci.* **2014**, *55*, 908–917. [CrossRef]
17. Lawrenson, J.G.; Shah, R.; Huntjens, B.; E Downie, L.; Virgili, G.; Dhakal, R.; Verkicharla, P.K.; Li, D.; Mavi, S.; Kernohan, A.; et al. Interventions for myopia control in children: A living systematic review and network meta-analysis. *Cochrane Database Syst. Rev.* **2023**, *2023*, CD014758.
18. Sarkar, S.; Khuu, S.; Kang, P. A systematic review and meta-analysis of the efficacy of different optical interventions on the control of myopia in children. *Acta Ophthalmol.* 2023; *early view*. [CrossRef]
19. Ma, J.-X.; Liu, Q.-P.; Tian, S.-W. Effectiveness of peripheral defocus spectacle lenses in myopia control: A Meta-analysis and systematic review. *Int. J. Ophthalmol.* **2022**, *15*, 1699–1706. [CrossRef]
20. Sankaridurg, P.; Donovan, L.; Varnas, S.; Ho, A.; Chen, X.; Martinez, A.; Fisher, S.; Lin, Z.; Smith, E.L.I.; Ge, J.; et al. Spectacle Lenses Designed to Reduce Progression of Myopia: 12-Month Results. *Optom. Vis. Sci.* **2010**, *87*, 631–641. [CrossRef]
21. Tarutta, E.P.; Proskurina, O.V.; Tarasova, N.A.; Milash, S.V.; Markosyan, G.A. Long-term results of perifocal defocus spectacle lens correction in children with progressive myopia. *Vestn. Oftalmol.* **2019**, *135*, 46–53. [CrossRef]
22. Kanda, H.; Oshika, T.; Hiraoka, T.; Hasebe, S.; Ohno-Matsui, K.; Ishiko, S.; Hieda, O.; Torii, H.; Varnas, S.R.; Fujikado, T. Effect of spectacle lenses designed to reduce relative peripheral hyperopia on myopia progression in Japanese children: A 2-year multicenter randomized controlled trial. *Jpn. J. Ophthalmol.* **2018**, *62*, 537–543. [CrossRef]
23. Yuval, C.; Otzem, C.; Laura, B.-S.; Shirel, R.; Dana, G.-N.; Atalia, W.; Noam, B.; Nir, E.; Yair, M. Evaluating the Effect of a Myopia Control Spectacle Lens Among Children in Israel: 12-Month Results. *Am. J. Ophthalmol.* **2024**, *257*, 103–112. [CrossRef]
24. Lam, C.S.Y.; Tang, W.C.; Tse, D.Y.-Y.; Lee, R.P.K.; Chun, R.K.M.; Hasegawa, K.; Qi, H.; Hatanaka, T.; To, C.H. Defocus incorporated multiple segments (DIMS) spectacle lenses slow myopia progression: A 2-year randomised clinical trial. *Br. J. Ophthalmol.* **2020**, *104*, 363–368. [CrossRef] [PubMed]
25. Bao, J.; Yang, A.; Huang, Y.; Li, X.; Pan, Y.; Ding, C.; Lim, E.W.; Zheng, J.; Spiegel, D.P.; Drobe, B.; et al. One-year myopia control efficacy of spectacle lenses with aspherical lenslets. *Br. J. Ophthalmol.* **2022**, *106*, 1171–1176. [CrossRef]
26. Bao, J.; Huang, Y.; Li, X.; Yang, A.; Zhou, F.; Wu, J.; Wang, C.; Li, Y.; Lim, E.W.; Spiegel, D.P.; et al. Spectacle Lenses with Aspherical Lenslets for Myopia Control vs Single-Vision Spectacle Lenses: A Randomized Clinical Trial. *JAMA Ophthalmol.* **2022**, *140*, 472–478. [CrossRef] [PubMed]

27. Liu, X.; Wang, P.; Xie, Z.; Sun, M.; Chen, M.; Wang, J.; Huang, J.; Chen, S.; Chen, Z.; Wang, Y.; et al. One-year myopia control efficacy of cylindrical annular refractive element spectacle lenses. *Acta Ophthalmol.* **2023**, *101*, 651–657. [CrossRef]
28. Rappon, J.; Chung, C.; Young, G.; Hunt, C.; Neitz, J.; Neitz, M.; Chalberg, T. Control of myopia using diffusion optics spectacle lenses: 12-month results of a randomised controlled, efficacy and safety study (CYPRESS). *Br. J. Ophthalmol.* **2022**, *107*, 1709–1715. [CrossRef]
29. Nucci, P.; Lembo, A.; Schiavetti, I.; Shah, R.; Edgar, D.F.; Evans, B.J.W. A comparison of myopia control in European children and adolescents with defocus incorporated multiple segments (DIMS) spectacles, atropine, and combined DIMS/atropine. *PLoS ONE* **2023**, *18*, e0281816. [CrossRef]
30. Lam, C.S.Y.; Tang, W.C.; Zhang, H.Y.; Tse, D.Y.Y.; To, C.H. Myopia control in children wearing DIMS spectacle lens: 6 years results. *Investig. Ophthalmol. Vis. Sci.* **2022**, *63*, 4247.
31. Lam, C.S.Y.; Tang, W.C.; Qi, H.; Radhakrishnan, H.; Hasegawa, K.; To, C.H.; Charman, W.N. Effect of defocus incorporated multiple segments spectacle lens wear on visual function in myopic chinese children. *Transl. Vis. Sci. Technol. Transl. Vis. Sci. Technol.* **2020**, *9*, 11. [CrossRef]
32. Drobe, B.; Xue, L.; Huang, Y.; Lim, E.W.; Bao, J. Spectacle lenses with highly aspherical lenslets for myopia control: 4-year clinical trial results. *Investig. Ophthalmol. Vis. Sci.* **2023**, *64*, 4162.
33. Sankaridurg, P.; Weng, R.; Tran, H.; Spiegel, D.P.; Drobe, B.; Ha, T.; Tran, Y.H.; Naduvilath, T. Spectacle Lenses with Highly Aspherical Lenslets for Slowing Myopia: A Randomized, Double-Blind, Cross-Over Clinical Trial: Parts of these data were presented as a poster at the Annual Research in Vision and Ophthalmology meeting, 2022. *Am. J. Ophthalmol.* **2023**, *247*, 18–24. [CrossRef] [PubMed]
34. Shamp, W.; Brennan, N.A.; Bullimore, M.A.; Cheng, X.; Maynes, E. Influence of Age and Race on Axial Elongation in Myopic Children. *Investig. Ophthalmol. Vis. Sci.* **2022**, *63*, 257.
35. Ruiz-Pomeda, A.; Pérez-Sánchez, B.; Valls, I.; Prieto-Garrido, F.L.; Gutiérrez-Ortega, R.; Villa-Collar, C. MiSight Assessment Study Spain (MASS). A 2-year randomized clinical trial. *Graefe's Arch. Clin. Exp. Ophthalmol.* **2018**, *256*, 1011–1021. [CrossRef] [PubMed]
36. Tideman, J.W.L.; Polling, J.R.; Vingerling, J.R.; Jaddoe, V.W.V.; Williams, C.; Guggenheim, J.A.; Klaver, C.C.W. Axial length growth and the risk of developing myopia in European children. *Acta Ophthalmol.* **2018**, *96*, 301–309. [CrossRef] [PubMed]
37. Brennan, N.A.; Toubouti, Y.M.; Cheng, X.; Bullimore, M.A. NC-ND license Efficacy in myopia control. *Prog. Retin. Eye Res.* **2021**, *83*, 100923. [CrossRef]
38. Yu, X.; Zhang, B.; Bao, J.; Zhang, J.; Wu, G.; Xu, J.; Zheng, J.; Drobe, B.; Chen, H. Design, methodology, and baseline data of the Personalized Addition Lenses Clinical Trial (PACT). *Medicine* **2017**, *6*, e6069. [CrossRef] [PubMed]
39. Smith, E.L. Optical treatment strategies to slow myopia progression: Effects of the visual extent of the optical treatment zone. *Exp. Eye Res.* **2013**, *114*, 77–88. [CrossRef]

40. Walline, J.J.; Walker, M.K.; Mutti, D.O.; Jones-Jordan, L.A.; Sinnott, L.T.; Giannoni, A.G.; Bickle, K.M.; Schulle, K.L.; Nixon, A.; Pierce, G.E.; et al. Effect of high add power, medium add power, or single-vision contact lenses on myopia progression in children: The BLINK randomized clinical trial. *JAMA J. Am. Med. Assoc.* **2020**, *324*, 571–580. [CrossRef]
41. McCullough, S.; Barr, H.; Fulton, J.; Logan, N.S.; Nagra, M.; Pardhan, S.; Richardson, P.; Saunders, K.; Whayeb, Y.; Williamson, P.; et al. 2-Year Multi-Site Observational Study of MiYOSMART myopia control spectacle lenses in UK children: 1-year results. *Investig. Ophthalmol. Vis. Sci.* **2023**, *64*, 4945.
42. Wolffsohn, J.S.; Whayeb, Y.; Logan, N.S.; Weng, R.; the International Myopia Institute Ambassador Group. IMI—Global Trends in Myopia Management Attitudes and Strategies in Clinical Practice—2022 Update. *Investig. Ophthalmol. Vis. Sci.* **2023**, *64*, 6. [CrossRef] [PubMed]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

children

MDPI

Article

Efficacy of Asymmetric Myopic Peripheral Defocus Lenses in Spanish Children: 24-Month Randomized Clinical Trial Results

Clara Martinez-Perez [1,*], Miguel Ángel Sánchez-Tena [1,2], Jose Miguel Cleva [3], Cesar Villa-Collar [4], Marta Álvarez [3], Eva Chamorro [3] and Cristina Alvarez-Peregrina [2]

[1] School of Management, Engineering and Aeronautics, ISEC LISBOA—Instituto Superior de Educação e Ciências, Alameda das Linhas de Torres, 179, 1750-142 Lisbon, Portugal; masancheztena@ucm.es

[2] Department of Optometry and Vision, Faculty of Optics and Optometry, Universidad Complutense de Madrid, 28037 Madrid, Spain; cristina_alvarez@ucm.es

[3] Clinical Research Department, Indizen Optical Technologies, 28002 Madrid, Spain; jmcleva@iot.es (J.M.C.); malvarez@iot.es (M.Á.); evachamorro@iot.es (E.C.)

[4] Faculty of Biomedical and Health Science, Universidad Europea de Madrid, 28670 Madrid, Spain; villacollarc@gmail.com

* Correspondence: clara.perez@iseclisboa.pt

Abstract: Background/Objectives: Asymmetric myopic peripheral defocus lenses (MPDLs) have proven to be effective in slowing the progression of myopia in Spanish children over a period of 12 months. The purpose of this study was to assess the MPDL spectacles'

efficacy in slowing myopia progression over a 24-month period in children. **Methods**: This study extends the follow-up period of the double-masked, prospective, and randomized clinical trial previously published to 24 months. Children from 6 to 12 years were assigned to two groups: a control group wearing spherotorical single vision lenses (SVLs) or a treatment group wearing MPDL lenses. Inclusion criteria included children with myopia less than −0.50 D, astigmatism below 1.50 D, and best-corrected visual acuity of at least 20/20. Participants underwent cycloplegic autorefractive examination and axial length (AL) measurements at the baseline and six and twelve months in the study already published, and twenty-four months later in the present study. Lifestyle factors, including outdoor activities and digital device use, were also assessed. Baseline characteristics, including age, refractive error, and AL, were comparable between groups. Dropout rates were 15.9%, with 14 participants lost to follow-up, distributed equally between the two groups. **Results**: After 24 months of follow-up, 69 children remained in this study, comprising 34 participants in the SVL cohort and 35 in the MPDL cohort. Over 24 months, the MPDL group showed significantly less AL elongation than the SVL group (0.27 ± 0.23 mm and 0.37 ± 0.24 mm; $p = 0.0341$). The mean relative AL increase was 1.10 ± 0.95% in the MPDL group, compared to 1.56 ± 1.02% in the SVL group ($p = 0.0322$). Younger children exhibited faster AL growth, while digital device use and outdoor activities did not affect AL changes. **Conclusions**: MPDL spectacle lenses substantially slowed myopia progression over a 24-month period, with 28.7% less progression in absolute AL growth and 29.8% in relative AL growth compared to SVL. These results indicate that MPDL lenses are an effective method for slowing myopia progression.

Academic Editors: Hee-Young Choi, Sara Jayne McCullough and Lesley Doyle

Received: 17 December 2024
Revised: 1 February 2025
Accepted: 5 February 2025
Published: 6 February 2025

Citation: Martinez-Perez, C.; Sánchez-Tena, M.Á.; Cleva, J.M.; Villa-Collar, C.; Álvarez, M.; Chamorro, E.; Alvarez-Peregrina, C. Efficacy of Asymmetric Myopic Peripheral Defocus Lenses in Spanish Children: 24-Month Randomized Clinical Trial Results. *Children* **2025**, *12*, 191. https://doi.org/10.3390/children12020191

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

Keywords: myopia; axial length; spectacle lenses

1. Introduction

One of the most prevalent ocular disorders globally is myopia [1–3], and its incidence rates are rapidly increasing across the globe [4,5]. The earlier onset of myopia is strongly associated with the progression to severe levels of myopia in adulthood [5,6]. Low and moderate myopia can develop into high myopia of −6.00 D or greater if not addressed in time [7]. This progression can result in severe long-term ocular health issues. Severe myopia has been linked to an increased likelihood of experiencing complications such as glaucoma, myopic macular degeneration, retinal detachment and, in extreme cases, irreversible vision loss [8].

The global incidence of high myopia is expected to rise considerably, with an increase estimated at 117 million people from 2020 to 2030 [3,9]. As a result, pathological myopia is projected to become the main cause of blindness and irreversible vision impairment in the world. The growing concern regarding the potential complications associated with high myopia has intensified the call for effective myopia control measures. Early detection and effective intervention to manage myopia and slow its progression, particularly in children, have thus become critical.

The initiation and progression of myopia are governed by a combination of visual, environmental, and genetic factors that modulate eye growth in response to visual inputs [10]. Research involving animal models has been instrumental in deepening our knowledge of myopia and advancing the development of effective treatment approaches [11]. Research using these models has demonstrated that emmetropization is a visually guided process, where myopic defocus decelerates eye growth and hyperopic defocus accelerates it [12]. Research on animals such as rhesus monkeys [13], marmosets [14], chicks [15], and guinea pigs [16] has shown that myopic defocus, induced by multifocal or dual-power lenses, can slow down or even reverse eye growth associated with myopia. This principle forms the basis of various myopia control strategies, including orthokeratology (OK), spectacle lenses, and multifocal soft contact lenses.

A recent meta-analysis reviewed the effectiveness of current treatments, both pharmacological and optical alternatives, revealing their efficacy in slowing myopia progression by reducing refractive changes and axial length (AL) elongation [17]. Optical interventions for myopia management such as spectacle lenses, soft contact lenses, and OK work by modifying retinal defocus, specifically inducing myopic defocus to slow the progression of myopia. The meta-analysis concluded that these optical interventions are effective in managing childhood myopia, with the most significant effects observed in the first 12 months of use, followed by a decrease in effectiveness over time [18].

Recently developed ophthalmic spectacle lenses designed to control myopia progression can be grouped into three categories: simultaneous defocus, contrast management, and peripheral addition designs [18,19]. The first group includes lenses like defocus incorporated multiple segment (DIMS) [20], highly aspherical lenslets target (HALT) [21,22], and cylindrical annular refractive element (CARE) [23] lenses. The second group is composed of the diffusion optics technology (DOT) lenses [24]. The third group includes lenses that produce progressive peripheral defocus [25–29].

In a previously published study [29], the effectiveness of a new ophthalmic lens design featuring asymmetric myopic peripheral defocus (MPDL, MyoLess®, IOT, Madrid, Spain) was evaluated over 12 months in a cohort of Spanish children. The results showed a significant reduction in AL elongation for the group treated with MPDL compared to the control group with single-vision lenses (SVLs). After one year, the MPDL group exhibited an AL elongation of 0.14 ± 0.14 mm, compared to 0.23 ± 0.15 mm in the control group, representing a 39% reduction in absolute AL growth ($p = 0.014$).

The current research builds on previous work, aiming to expand it to a two-year period to examine the sustained efficacy of MPDL lenses in slowing the progression of myopia.

2. Materials and Methods

This is a double-masked, prospective, randomized clinical trial conducted at Novovision (Madrid, Spain). The study was initially planned to follow children for one year to evaluate the efficacy of MDPL lenses for myopia control. This is an extension of the follow-up to 24 months, following the same methodology already published [29].

The inclusion criteria were children aged five to twelve years with a cycloplegic spherical equivalent refraction (SE) less than or equal to 0.50 diopters, astigmatism less than or equal to 1.50 diopters, anisometropia less than or equal to 1.50 diopters, and corrected visual acuity (VA) greater than or equal to 20/20.

Children were randomly assigned at the beginning of the study to the intervention group fitted with MPDL lenses and the control group using SVL. The MPDL lenses have a 7 mm central zone free of defocus and an asymmetric myopic defocus zone of +1.50 D at 25 mm nasally, +1.80 D at 25 mm temporally, and +2.00 D in the lower region. The lenses were made using freeform technology and were customized for each child based on their prescription, pupillary distances, and pupillary heights. The defocus pattern was identical for all children.

The Ethics Committee of Hospital Clínico San Carlos in Madrid, Spain, granted approval for the randomized controlled trial, ensuring compliance with the ethical guidelines outlined in the Declaration of Helsinki. Additionally, the trial was officially documented on ClinicalTrials.gov under the registration ID NCT05250206.

2.1. Visual Examination

At the 24-month visit, SE, AL, and VA evaluations were performed following identical criteria to previous follow-up visits. For SE, the Canon Full Auto Ref-keratometer RK-F1 (Canon, Tokyo, Japan) was used after administering three drops of cyclopentolate to induce cycloplegia. For AL, the IOL Master® optical biometer (Carl Zeiss Meditec, Jena, Germany) was used. The best corrected VA was measured monocularly at distance vision. Additionally, data from the baseline visit were considered for determining factors associated with AL growth: demographics (age and gender), family history of myopia (number of parents with myopia), and children's lifestyle (time on digital devices and time outdoors). Table 1 shows the data collected at each visit.

Table 1. Assessment and examination schedule.

Visit		Baseline	Dispensing	6 Months	12 Months	24 Months
Signed parental consent form		X				
Basic information	Demographic data	X				
	Medical records	X				
Refraction	Subjective refraction	X		X	X	X
	Cycloplegic autorefraction	X		X	X	X
VA	Uncorrected VA	X		X	X	
	Best-corrected VA	X		X	X	X
Eye evaluation	Keratometry	X				
	Biomicroscopy	X				
	Ocular fundus	X				
	IOP	X				
	AL	X		X	X	X
Binocular vision	Accommodation lag evaluation	X		X	X	
	Accommodation amplitude			X	X	
	Distance and near phorias	X		X	X	
Spectacle fitting	Evaluation of frame alignment and lens condition		X			
Questionnaires	Lifestyle	X				
	Wearability			X	X	

VA: visual acuity; IOP: Intraocular pressure; AL: axial length.

Table 1. *Cont.*

2.2. Statistical Analysis

The relative (%) and absolute (mm) AL values were statistically compared between children wearing MPDL and SVL lenses. Relative AL growth refers to the percentage change in AL relative to the baseline measurement for each individual. It was calculated using the following formula:

$$(\text{AL at 24 months} - \text{baseline AL})/\text{baseline AL}$$

Statistical analysis was conducted using Python (version 3.13.1). Continuous variables were analyzed according to their distribution: means were analyzed through Student's *t*-test, while median values were analyzed employing the Mann–Whitney U statistical method. Categorical data, including factors like gender distribution and parental myopia, were assessed using the Chi-square test. To identify factors associated with relative AL growth, such as age and other sociodemographic and lifestyle factors, univariate and multivariate linear regression analyses were performed. The significance level was set at a *p*-value of less than 0.05.

3. Results

The baseline and one-year results of this study have already been published by Sánchez-Tena et al. [29]. Initially, 92 children were recruited and randomly assigned to two groups: the SVL and MPDL groups were the control and treatment, respectively. During the first year, nine participants dropped out (five from the MPDL cohort and four from the SVL cohort), leading to an attrition rate of approximately 10%. The analysis included 83 children (42 with SVL and 41 with MPDL). In the second year, an additional 14 children left the study (6 from the MPDL cohort and 8 from the SVL cohort). Factors contributing to withdrawal included starting a new treatment after the 12-month study (six children from each group), relocating (one child from the control group), and missing follow-up visits (one child from the control group) (Table 2). Ultimately, 69 children completed the two-year follow-up (35 with MPDL and 34 with SVL), with a mean age of 10.0 ± 1.8 years (ranging from 6 to 12 years). Power analysis determined that a sample size of 34 participants per group would provide 80% power, based on a one-sided test with a 5% Type I error threshold. This calculation assumes a mean difference between groups of 0.14 mm with a standard deviation (SD) of 0.23 mm. The flowchart of the RCT is shown in Figure 1, and the baseline demographic and clinical characteristics of the participants are presented in Table 3.

Table 2. Summary of dropout reasons and potential impacts on statistical power.

Reason for Dropout	SVL Group (n)	MPDL Group (n)	Total (n)	Potential Impact on Statistical Power
Started a new treatment after 12 months	6	6	12	May introduce bias if participants had faster progression rates.
Relocated	1	0	1	Minimal impact due to low frequency.
Missed follow-up visits	1	0	1	Minimal impact due to low frequency.
Total	8	6	14	Attrition rate remains below threshold to affect power significantly.

100 children assesed for eligibility

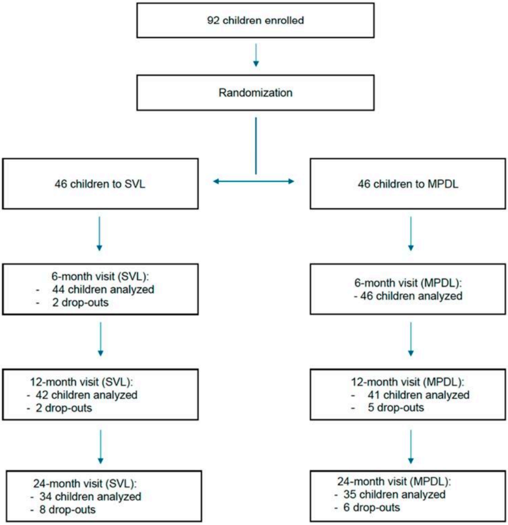

Figure 1. Revised flowchart of the randomized clinical trial illustrating participant allocation and follow-up visits over the 24-month period. MPDL: asymmetric peripheral myopic defocus lens; SVL: single-vision lens.

Table 3. Baseline characteristics of the sample.

	MPDL	SVL	*p*-Value
Mean age (years)	10.4 ± 1.8	9.6 ± 1.8	0.046 *
Median age (years)	11.0 [2.5]	10.0 [2.0]	
Age range (years)	6–12	6–12	
Gender distribution			0.274 ‡
Female	23	17	
Male	12	17	
Mean axial length (mm)	24.12 ± 0.94	23.94 ± 0.84	0.400 †
Median axial length (mm)	24.05 [1.44]	23.83 [1.23]	
Mean cycloplegic refraction (D)	−2.57 ± 1.21	−2.00 ± 1.04	0.039 †
Median cycloplegic refraction (D)	−2.50 [1.63]	−1.81 [1.72]	

Family history of myopia			
One myopic parent	15	13	
Both myopic parents	10	16	0.187 ‡
Neither parent	9	5	

* U—Mann–Whitney; † *t*—Student; ‡ Chi—cuadrado.

After two years of follow-up, no significant differences were observed between the two eyes; therefore, only data from the right eye were used for statistical analysis (Table 4 and Figure 2). Over the 24-month period, the SVL group exhibited an AL increase of 0.37 ± 0.24 mm (95% CI: 0.29 to 0.45 mm), whereas the MPDL group showed a smaller increase of 0.27 ± 0.23 mm (95% CI: 0.19 to 0.35 mm; $p = 0.0341$). The absolute difference in AL elongation between the groups was 0.10 mm (95% CI: −0.01 to 0.21 mm). This corresponded to a median relative growth of 1.32% [0.93–2.12] in the SVL group versus 0.93% [0.42–1.72] in the MPDL group ($p = 0.0322$). The mean relative AL increase was 1.10 ± 0.95% (95% CI: 0.77 to 1.43%) in the MPDL group, while it was 1.56 ± 1.02% (95% CI: 1.20 to 1.92%) in the SVL group. The use of MPDL lenses resulted in a significant reduction in absolute AL growth by 28.7% and in relative mean AL growth by 29.8% compared to the SVL group.

Table 4. Axial length change at 2 years: Comparison between SVL and MPDL.

	SVL	MPDL	*p*-Value
Change in Axial Length between Initial and 24 Months			
Absolute change (mean ± SD) (mm)	0.37 ± 0.24	0.27 ± 0.23	0.0341
Relative change (mean ± SD) (%)	1.56 ± 1.02	1.10 ± 0.95	0.0322
Relative change (median [Q1, Q3]) (%)	1.32 [0.93–2.12]	0.93 [0.42–1.72]	0.0322

The change in mean cycloplegic refraction at the 2-year follow-up was 0.43 ± 0.49 D in the control group (95% CI: 0.26 to 0.60 D) and 0.20 ± 0.43 D in the MPDL group (95% CI: 0.05 to 0.35 D).

Regarding the factors linked to relative AL growth, univariate linear regression analyses revealed that associations with variables such as gender, parental myopia, outdoor time, hours spent using digital devices, and the initial spherical equivalent had no significant impact on the relative AL growth between the baseline and 24 months. However, the age of the child at enrollment affected the proportional increase in axial length during both periods (regression coefficient for baseline to 24 months: −0.275, 95% CI: −2.232 to 1.681). The negative regression coefficient (−0.275) indicates that for each additional year of age at

the start of the study, the relative AL growth was lower. This suggests that AL increases more in younger children, which could imply that myopia progression is faster in this group. As such, the efficacy of the MPDL lens in controlling AL growth may be greater in younger children, who experience a faster progression rate. The regression coefficient was −0.275, with a 95% CI of −0.393 to −0.158 for the period between the baseline and 24 months (Figure 3).

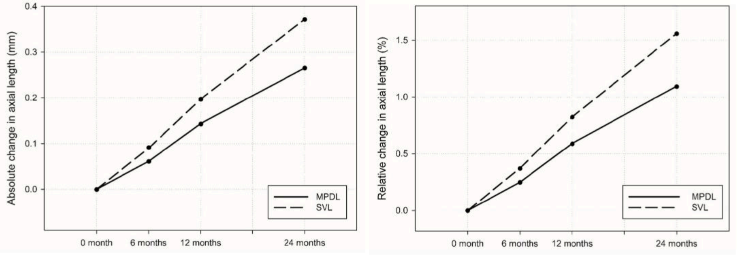

Figure 2. Absolute and relative axial length change from the baseline to 24 months; SVL: single-vision lens; MPDL: asymmetric myopic peripheral defocus lens.

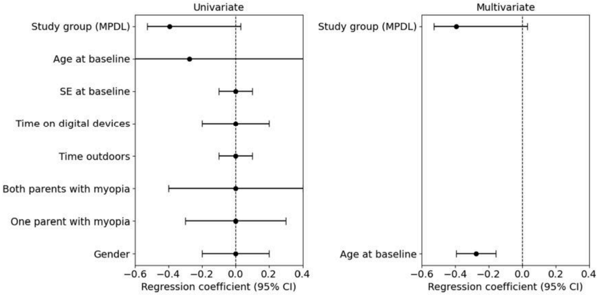

Figure 3. Factors related to AL relative growth at 24 months.

4. Discussion

In this study, it was found that after two years, MPDL spectacle lenses reduced the absolute AL growth by 28.7% and the relative AL growth by 29.8% compared to SVL, suggesting that MPDL lenses maintain efficacy over time and provide sustained intervention to slow myopia progression. The current study provides results after 24 months of treatment from the first RCT carried out in a Caucasian population, evaluating MPDL lenses. Note that when comparing our results with other studies on the efficacy of myopia control lenses over two years, we observed several differences that may be attributed to population characteristics. Currently, to our knowledge, there are few published studies assessing the two-year efficacy of myopia control spectacle lenses in European populations.

Lam et al. [20] carried out research on the efficacy of lenses incorporating defocus incorporated multiple segments (DIMSs) within a population of Chinese participants. These lenses are designed with a central 9 mm aperture, surrounded by a 33 mm treatment zone embedded with multiple +3.5 D positive power lenslets. The results after two years showed a change of 0.55 ± 0.02 mm in AL for the SV group, compared to 0.21 ± 0.02 mm for the treatment group, resulting in a difference of 0.34 mm.

Similarly, Bao et al. [22] investigated the effectiveness of HALT lenses in a population of Chinese participants. These lenses are designed with a central zone dedicated to full prescription correction and a 10 mm diameter aperture at the core. This central area is encircled by a treatment zone comprising 11 concentric rings, each containing aspherical lenslets measuring 1.1 mm in diameter. These lenslets have positive powers ranging from +3.50 D in the peripheral rings to +6.00 D in the central rings. After 2 years of follow-up, they found an AL increase of 0.69 ± 0.04 mm in the SV group, compared to 0.34 ± 0.03 mm in the treatment group, with a difference of 0.35 mm.

In contrast, studies conducted in non-Asian populations have shown somewhat different results. The study by Rappon et al. [30] on DOT lenses in the United States observed that after two years of follow-up, there was an AL increase of 0.53 ± 0.33 mm in the SV group, compared to 0.33 ± 0.23 mm in the treatment group, with a difference of 0.20 mm. DOT technology features a central zone with a diameter of 5 mm, surrounded by translucent microscopic diffusers (0.14 mm in diameter) designed to scatter light. This helps reduce contrast and, consequently, reduces the disparity in activity between the L and M cones.

A recent study by Lembo et al. [31] evaluated the effectiveness of DIMS and HALT lenses in slowing myopia progression over a 2-year period in a European population. This retrospective cohort study assessed axial length (AL) elongation in two groups: 73 children wearing DIMS lenses (mean age: 11.2 ± 2.3 years) and 73 children wearing HALT lenses (mean age: 11.4 ± 2.4 years). At the 2-year follow-up, the mean AL increase was 0.29 ± 0.63 mm for the DIMS group and 0.32 ± 0.72 mm for the HALT group. Similar findings have been reported in other studies on European populations evaluating myopia control interventions using contact lenses. For instance, the study by Ruiz-Pomeda et al. [32] analyzed the efficacy of MiSight lenses in a Spanish cohort of 46 children (mean age: 11.0 ± 1.2 years) and observed a mean AL increase of 0.28 mm (95% CI: 0.20 to 0.37) over 2 years in the MiSight group. Additionally, the multicenter study by Chamberlain et al. [33] reported that a group of 70 children (mean age: 10.1 ± 1.3 years) treated with MiSight contact lenses exhibited a mean AL increase of 0.23 ± 0.03 mm over 2 years. These results align with our findings in children wearing MPDL lenses (mean age: 10.4 ± 1.8 years), where the mean AL elongation was 0.27 ± 0.23 mm over the same period.

Our study showed a variation after two years of follow-up of 0.27 ± 0.23 mm in AL in the MPDL group and 0.37 ± 0.24 mm in the SVL group, which resulted in a difference of 0.10 mm or an efficacy of 29% in reducing AL growth, which are somewhat lower than the effects observed in the Asian studies. Lam et al. [34] reported a 62% reduction in AL elongation with DIMS lenses over a two-year period, while Gao et al. [35] showed that HALT lenses achieved a reduction of approximately 51%. These differences could be attributed to the specific population characteristics in our study. In this sense, it is well-established that the progression of myopia varies significantly between Asiatic and non-Asiatic populations. Studies have consistently shown that individuals of East Asian descent, particularly those from countries such as China, Japan, and South Korea, tend to experience more rapid myopia progression compared to populations from Western countries [36,37]. This difference in progression rates has been attributed to a combination of genetic, environmental, and lifestyle factors. In East Asia, the high prevalence of myopia is often linked to increased near-work activities, such as additional time spent on reading,

studying, and using digital devices, as well as limited outdoor activity [38,39]. In contrast, populations from non-Asian regions, such as Europe and North America, generally show slower rates of myopia progression [40]. In Spain, for instance, the greater number of sunlight hours and a lifestyle that often involves more outdoor activities may contribute to a slower progression of myopia. Children in Spain are typically exposed to more natural light, which has been suggested to have a protective effect against myopia progression [41,42]. These differences in progression rates highlight the need to consider ethnicity, lifestyle, and environmental factors when assessing the efficacy of myopia control interventions.

On the other hand, our cohort represents a population with a relatively lower risk of myopia progression compared to what is typically reported in the literature. In our study, children in the control group experienced an increase of 0.37 mm in AL after two years of follow-up. However, according to a model for non-Asian populations [43], an increase of 0.46 mm in AL would be expected over the same period in a population with an average age, like that of our sample. This aligns with the characteristics of a lower-risk population, where the progression of myopia tends to be slower.

Additionally, it is important to consider potential biases introduced by dropouts in the study. Data from children who completed the one-year follow-up [29] showed an increase in AL of 0.14 mm in the MPDL group and 0.23 mm in the control group. The control group values were consistent with the virtual control group, which predicts an AL growth of 0.23 mm after one year of follow-up for children with an average age equivalent to that of our sample. However, in the remaining sample that completed the two-year follow-up, the AL growth of the control group was considerably smaller than expected in the virtual control group. Specifically, our study showed an increase in AL of 0.14 mm in the MPDL group and 0.20 mm in the control group after 1 year of follow-up and, according to the model, an increase of 0.25 mm in AL for the control group for the same period would be expected. Therefore, while the 0.1 mm reduction in AL elongation observed in our study is modest compared to other interventions, it is consistent with the effects expected in a low-risk population.

When comparing optical treatments with pharmacological ones, it is evident that both have advantages and limitations in controlling myopia progression. MPDL demonstrated a significant 29–30% reduction in myopia progression in our study. Pharmacological therapies such as low-concentration atropine (0.05%) have shown greater efficacy in several studies, achieving up to a 50% reduction in myopia progression over two years [44,45]. However, it is important to note that many of these studies, such as the LAMP2 trial, were conducted in Asian populations, where the effects of atropine may differ compared to non-Asian populations [44]. On the other hand, although atropine could be more effective, this therapy presents drawbacks such as the need for daily instillation, side effects like photophobia and near-focusing difficulties, and potential adherence barriers in children and families. In contrast, MPDL lenses offer a non-invasive option with better acceptance among parents and children, as they eliminate the need for topical medications. The use of spectacle lenses for myopia management has been extensively studied in recent years and is currently one of the preferred options for myopia control due to their ease of fitting, even for younger children. Additionally, spectacles generally have fewer or no side effects compared to other optical treatments like contact lenses or atropine. This balance between convenience, side effects, and efficacy must be carefully considered when choosing a treatment, as each approach can be tailored to the individual needs and preferences of patients and their families. Future studies could further explore parents' perceptions of these treatments and how these preferences influence therapy selection.

Regarding lens design, most of the lenses discussed feature a central zone that fully corrects the prescription, with the diameter varying by design, and a peripheral zone with

a positive addition to create myopic blur on the peripheral retina. These spectacle lenses are designed to induce simultaneous myopic retinal defocus for both distance and near vision. The central optical zone typically ranges from 7 to 10 mm in diameter, surrounded by an addition of 1.50 D to 3.80 D. A smaller central zone diameter can cause visual discomfort and issues when wearing the lenses. Another crucial aspect of lens design is the myopic defocus, as its magnitude and distribution can significantly impact lens performance. Previous research has indicated that varying peripheral retinal defocus is vital in controlling myopia progression [46,47]. Additionally, studies have shown that high-add power multifocal contact lenses significantly reduce the rate of myopia progression compared to medium-add power lenses [48]. MPDL is a freeform lens with an optical zone of 7 mm and an asymmetrical progressive peripheral positive defocus of +1.50 D at 25 mm nasally, +1.80 D at 25 mm temporally, and +2.00 D in the lower region. The lenses were designed with the goal of finding an optimal configuration that minimizes the optical area while maximizing the region with plus power and reaching a high level of defocus power that is wearable for the user in order to ensure compliance with the treatment. The positive power added to the lower part of the lens serves to expand the plus defocus area for distance vision while maintaining appropriate comfort for near vision. The asymmetrical positive defocus between the nasal and temporal areas of the lens was incorporated to better align with the morphological characteristics of the myopic retina. It is well-established that the retina exhibits asymmetry, particularly between the nasal and temporal retinal hemifields, with differences observed in anatomical neural features, peripheral refraction, and AL growth [49–51]. It has been proposed that retinal sensitivity may differ between the nasal and temporal hemifields, with the nasal region potentially playing a more crucial role in the mechanisms driving eye growth in response to hyperopic defocus [51]. To determine the final power distribution of the lens, various prototypes were developed and tested in a series of trials with young adults. The lens selected for this study was the one that provided the best balance between comfort and design characteristics.

Finally, several factors of the present study have been identified as limitations and deserve discussion. Firstly, baseline data show a significant difference in the mean age between the two groups, with children in the MPDL group being slightly older than those in the SVL group. Although this age difference persisted throughout the 24-month period, our analyses controlled for this variable to ensure that the observed differences in myopia progression were not solely influenced by age. Secondly, while the study duration of two years is considerable, it is shorter compared to other studies, such as the CYPRESS trial evaluating DOT lenses over four years [52], or DIMS studies reporting data spanning up to six years in Chinese pediatric populations [53]. A longer evaluation period could provide a more comprehensive perspective on the long-term efficacy and safety of MPDL lenses in controlling myopia. Another limitation is the dropout rate of 16.7%, which could affect the robustness of the results. Initially, this study was planned for one year, but the extension to two years led to some participants discontinuing treatment after the first year. Furthermore, this study was conducted at a single center in Madrid, which may limit the generalizability of the findings to other regions with different demographic and environmental characteristics. However, the inclusion of a diverse sample in terms of age and gender improves the generalizability of the findings despite these limitations.

5. Conclusions

This research is the first two-year, randomized, double-blind clinical trial in Europe to evaluate the use of ophthalmic lenses with an asymmetric myopic peripheral defocus design. The results confirm the effectiveness of MPDL spectacle lenses in controlling myopia in a cohort of Spanish children, demonstrating a 28.7% reduction in the absolute

growth in AL and a 29.8% reduction in relative AL growth compared to the control group wearing SVL. These results are clinically relevant, as they provide optometrists with a non-invasive, spectacle-based option for managing myopia progression in children. Given their efficacy and ease of use, MPDL lenses could serve as an alternative or complement to pharmacological interventions, particularly for children or families preferring non-pharmacological approaches.

Future research should focus on validating these findings through multi-center trials that encompass diverse populations and environmental conditions. Longer follow-up periods would also help to assess the sustained efficacy and safety of MPDL lenses, as well as their long-term impact on the risk of developing high myopia and associated complications.

Author Contributions: Conceptualization, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; methodology, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; software, C.M.-P.; validation, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; formal analysis, C.M.-P.; investigation, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C., C.M.-P. and C.V.-C.; resources, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; data curation, C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C., C.M.-P. and C.V.-C.; writing—original draft preparation, C.M.-P.; C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; writing—review and editing, C.M.-P., C.A.-P., M.Á.S.-T., J.M.C., M.Á., E.C. and C.V.-C.; visualization, C.A.-P., M.Á.S.-T., M.Á., J.M.C., C.V.-C. and E.C.; supervision, J.M.C., M.Á.S.-T., M.Á., C.A.-P., C.V.-C. and E.C.; project administration, J.M.C., M.Á.S.-T., M.Á., C.A.-P., C.V.-C. and E.C.; funding acquisition, E.C., M.Á. and J.M.C. All authors have read and agreed to the published version of the manuscript.

Funding: This study was fully financed by Indizen Optical Technologies (IOT).

Institutional Review Board Statement: The study is registered on ClinicalTrials.gov under the identifier NCT05250206 (accessed 25 January 2024) and received formal approval from the Ethics Committee at Hospital Clínico San Carlos, Madrid, Spain (Protocol 19/366-R_P, approved on 26 April 2021). All procedures were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Informed Consent Statement: Written consent was obtained from all participants before their involvement in the research.

Data Availability Statement: The data generated in this study can be requested from the corresponding author. However, public access is restricted due to ethical considerations and the need to maintain participant confidentiality.

Conflicts of Interest: This research was funded by IOT. Authors M.Á., E.C. and J.M.C. were employed by IOT. The remaining authors confirm that no commercial or financial relationships influenced the conduct of this research.

References

1. Morgan, I.G.; French, A.N.; Ashby, R.S.; Guo, X.; Ding, X.; He, M.; Rose, K.A. The epidemics of myopia: Aetiology and prevention. *Prog. Retin. Eye Res.* **2018**, *62*, 134–149. [CrossRef]
2. Resnikoff, S.; Jonas, J.B.; Friedman, D.; He, M.; Jong, M.; Nichols, J.J.; Ohno-Matsui, K.; Smith, E.L., III; Wildsoet, C.F.; Taylor, H.R.; et al. Myopia—A 21st Century Public Health Issue. *Investig. Ophthalmol. Vis. Sci.* **2019**, *60*, Mi–Mii. [CrossRef]
3. Holden, B.A.; Fricke, T.R.; Wilson, D.A.; Jong, M.; Naidoo, K.S.; Sankaridurg, P.; Wong, T.Y.; Naduvilath, T.; Resnikoff, S. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. *Ophthalmology* **2016**, *123*, 1036–1042. [CrossRef]
4. Saw, S.-M.; Matsumura, S.; Hoang, Q.V. Prevention and management of myopia and myopic pathology. *Investig. Ophthalmol. Vis. Sci.* **2019**, *60*, 488–499. [CrossRef]
5. Grzybowski, A.; Kanclerz, P.; Tsubota, K.; Lanca, C.; Saw, S.-M. A review on the epidemiology of myopia in school children worldwide. *BMC Ophthalmol.* **2020**, *20*, 27. [CrossRef] [PubMed]

6. Recko, M.; Stahl, E.D. Childhood myopia: Epidemiology, risk factors, and prevention. *Mo. Med.* **2015**, *112*, 116–121. [PubMed]
7. Xu, L.; Wang, Y.X.; Wang, S.; Jonas, J.B. Definition of high myopia by parapapillary atrophy. The Beijing Eye Study. *Acta*

Ophthalmol. **2010**, *88*, e350–e351. [CrossRef]

8. Jonas, J.B.; Jonas, R.A.; Bikbov, M.M.; Wang, Y.X.; Panda-Jonas, S. Myopia: Histology, clinical features, and potential implications for the etiology of axial elongation. *Prog. Retin. Eye Res.* **2023**, *96*, 101156. [CrossRef]
9. Swenor, B.; Varadaraj, V.; Lee, M.J.; Whitson, H.; Ramulu, P. World Health Report on Vision: Aging Implications for Global Vision and Eye Health. *Innov. Aging* **2020**, *4* (Suppl. S1), 807–808. [CrossRef]
10. Németh, J.; Tapasztó, B.; Aclimandos, W.A.; Kestelyn, P.; Jonas, J.B.; De Faber, J.T.H.; Januleviciene, I.; Grzybowski, A.; Nagy, Z.Z.; Pärssinen, O.; et al. Update and guidance on management of myopia. European Society of Ophthalmology in cooperation with International Myopia Institute. *Eur. J. Ophthalmol.* **2021**, *31*, 853–883. [CrossRef]
11. Sankaridurg, P.; Berntsen, D.A.; Bullimore, M.A.; Cho, P.; Flitcroft, I.; Gawne, T.J.; Gifford, K.L.; Jong, M.; Kang, P.; Ostrin, L.A. IMI 2023 Digest. *Investig. Ophthalmol. Vis. Sci.* **2023**, *64*, 7. [CrossRef] [PubMed]
12. Wallman, J.; Winawer, J. Homeostasis of Eye Growth and the Question of Myopia. *Neuron* **2004**, *43*, 447–468. [CrossRef] [PubMed]
13. Arumugam, B.; Hung, L.-F.; To, C.-H.; Holden, B.; Smith, E.L. The Effects of Simultaneous Dual Focus Lenses on Refractive Development in Infant Monkeys. *Investig. Opthalmol. Vis. Sci.* **2014**, *55*, 7423–7432. [CrossRef] [PubMed]
14. Benavente-Perez, A.; Nour, A.; Troilo, D. The Effect of Simultaneous Negative and Positive Defocus on Eye Growth and Development of Refractive State in Marmosets. *Investig. Opthalmol. Vis. Sci.* **2012**, *53*, 6479–6487. [CrossRef]
15. Ashby, R.; Ohlendorf, A.; Schaeffel, F. The Effect of Ambient Illuminance on the Development of Deprivation Myopia in Chicks. *Investig. Opthalmol. Vis. Sci.* **2009**, *50*, 5348–5354. [CrossRef]
16. McFadden, S.A.; Tse, D.Y.; Bowrey, H.E.; Leotta, A.J.; Lam, C.S.; Wildsoet, C.F.; To, C.-H. Integration of Defocus by Dual Power Fresnel Lenses Inhibits Myopia in the Mammalian Eye. *Investig. Opthalmol. Vis. Sci.* **2014**, *55*, 908–917. [CrossRef] [PubMed]
17. Lawrenson, J.G.; Shah, R.; Huntjens, B.; E Downie, L.; Virgili, G.; Dhakal, R.; Verkicharla, P.K.; Li, D.; Mavi, S.; Kernohan, A.; et al. Interventions for myopia control in children: A living systematic review and network meta-analysis. *Cochrane Database Syst. Rev.* **2023**, *2023*, CD014758. [CrossRef]
18. Sarkar, S.; Khuu, S.; Kang, P. A systematic review and meta-analysis of the efficacy of different optical interventions on the control of myopia in children. *Acta Ophthalmol.* **2023**, *102*, e229–e244. [CrossRef]
19. Ma, J.-X.; Liu, Q.-P.; Tian, S.-W. Effectiveness of peripheral defocus spectacle lenses in myopia control: A Meta-analysis and systematic review. *Int. J. Ophthalmol.* **2022**, *15*, 1699–1706. [CrossRef]
20. Lam, C.S.Y.; Tang, W.C.; Tse, D.Y.-Y.; Lee, R.P.K.; Chun, R.K.M.; Hasegawa, K.; Qi, H.; Hatanaka, T.; To, C.H. Defocus incorporated multiple segments (DIMS) spectacle lenses slow myopia progression: A 2-year randomised clinical trial. *Br. J. Ophthalmol.* **2020**, *104*, 363–368. [CrossRef] [PubMed]
21. Bao, J.; Yang, A.; Huang, Y.; Li, X.; Pan, Y.; Ding, C.; Lim, E.W.; Zheng, J.; Spiegel, D.P.; Drobe, B.; et al. One-year myopia control efficacy of spectacle lenses with aspherical lenslets. *Br. J. Ophthalmol.* **2022**, *106*, 1171–1176. [CrossRef]
22. Bao, J.; Huang, Y.; Li, X.; Yang, A.; Zhou, F.; Wu, J.; Wang, C.; Li, Y.; Lim, E.W.; Spiegel, D.P.; et al. Spectacle Lenses with Aspherical Lenslets for Myopia Control vs Single-Vision Spectacle Lenses: A Randomized Clinical Trial. *JAMA Ophthalmol.* **2022**, *140*, 472–478. [CrossRef]
23. Liu, X.; Wang, P.; Xie, Z.; Sun, M.; Chen, M.; Wang, J.; Huang, J.; Chen, S.; Chen, Z.; Wang, Y.; et al. One-year myopia control efficacy of cylindrical annular refractive element spectacle lenses. *Acta Ophthalmol.* **2023**, *101*, 651–657. [CrossRef] [PubMed]
24. Rappon, J.; Chung, C.; Young, G.; Hunt, C.; Neitz, J.; Neitz, M.; Chalberg, T. Control of myopia using diffusion optics spectacle lenses: 12-month results of a randomised controlled, efficacy and safety study (CYPRESS). *Br. J. Ophthalmol.* **2022**, *107*, 1709–1715. [CrossRef]
25. Sankaridurg, P.; Donovan, L.; Varnas, S.; Ho, A.; Chen, X.; Martinez, A.; Fisher, S.; Lin, Z.; Smith, E.L.I.; Ge, J.; et al. Spectacle Lenses Designed to Reduce Progression of Myopia: 12-Month Results. *Optom. Vis. Sci.* **2010**, *87*, 631–641. [CrossRef] [PubMed]
26. Tarutta, E.P.; Proskurina, O.V.; Tarasova, N.A.; Milash, S.V.; Markosyan, G.A. Long-term results of perifocal defocus spectacle lens correction in children with progressive myopia. *Vestn. Oftalmol.* **2019**, *135*, 46–53. [CrossRef]
27. Kanda, H.; Oshika, T.; Hiraoka, T.; Hasebe, S.; Ohno-Matsui, K.; Ishiko, S.; Hieda, O.; Torii, H.; Varnas, S.R.; Fujikado, T. Effect of spectacle lenses designed to reduce relative peripheral hyperopia on myopia progression in Japanese children: A 2-year multicenter randomized controlled trial. *Jpn. J. Ophthalmol.* **2018**, *62*, 537–543. [CrossRef] [PubMed]
28. Yuval, C.; Otzem, C.; Laura, B.-S.; Shirel, R.; Dana, G.-N.; Atalia, W.; Noam, B.; Nir, E.; Yair, M. Evaluating the Effect of a Myopia Control Spectacle Lens Among Children in Israel: 12-Month Results. *Am. J. Ophthalmol.* **2024**, *257*, 103–112. [CrossRef] [PubMed]

29. Sánchez-Tena, M.A.; Cleva, J.M.; Villa-Collar, C.; Álvarez, M.; Ruiz-Pomeda, A.; Martinez-Perez, C.; Andreu-Vazquez, C.;

Chamorro, E.; Alvarez-Peregrina, C. Effectiveness of a Spectacle Lens with a Specific Asymmetric Myopic Peripheral Defocus: 12-Month Results in a Spanish Population. *Children* **2024**, *11*, 177. [CrossRef]

30. Rappon, J.; Neitz, J.; Neitz, M.; Chung, C.; Chalberg, T.W. Two-year effectiveness of a novel myopia management spectacle lens with full-time wearers. *Investig. Ophthalmol. Vis. Sci.* **2022**, *63*, 408.
31. Lembo, A.; Schiavetti, I.; Serafino, M.; Caputo, R.; Nucci, P. Comparison of the performance of myopia control in European children and adolescents with defocus incorporated multiple segments (DIMS) and highly aspherical lenslets (HAL) spectacles. *BMJ Paediatr. Open* **2024**, *8*, e003187. [CrossRef] [PubMed]
32. Ruiz-Pomeda, A.; Pérez-Sánchez, B.; Valls, I.; Prieto-Garrido, F.L.; Gutiérrez-Ortega, R.; Villa-Collar, C. MiSight Assessment Study Spain (MASS). A 2-year randomized clinical trial. *Graefes Arch. Clin. Exp. Ophthalmol.* **2018**, *256*, 1011–1021. [CrossRef]
33. Chamberlain, P.; Peixoto-de-Matos, S.C.; Logan, N.S.; Ngo, C.; Jones, D.; Young, G. A 3-year Randomized Clinical Trial of MiSight Lenses for Myopia Control. *Optom. Vis. Sci.* **2019**, *96*, 556–567. [CrossRef]
34. Lam, C.S.; Tang, W.C.; Lee, P.H.; Zhang, H.Y.; Qi, H.; Hasegawa, K.; To, C.H. Myopia control effect of defocus incorporated multiple segments (DIMS) spectacle lens in Chinese children: Results of a 3-year follow-up study. *Br. J. Ophthalmol.* **2022**, *106*, 1110–1114. [CrossRef]
35. Gao, Y.; Lim, E.W.; Drobe, B. Impact of myopia control spectacle lenses with highly aspherical lenslets on peripheral visual acuity and central visual acuity with peripheral gaze. *Ophthalmic Physiol. Opt.* **2023**, *43*, 566–571. [CrossRef]
36. Gwiazda, J.E.; Hyman, L.; Norton, T.T.; Hussein, M.E.; Marsh-Tootle, W.M.; Manny, R.; Wang, Y.; Everett, D.; COMET Group. Accommodation and related risk factors associated with myopia progression and their interaction with treatment in COMET children. *Investig. Ophthalmol. Vis. Sci.* **2004**, *45*, 2143–2151. [CrossRef]
37. Saw, S.M.; Gazzard, G.; Shih-Yen, E.C.; Chua, W.H. Myopia and associated pathological complications. *Ophthalmic Physiol. Opt.* **2005**, *25*, 381–391. [CrossRef] [PubMed]
38. Sherwin, J.C.; Reacher, M.H.; Keogh, R.H.; Khawaja, A.P.; Mackey, D.A.; Foster, P.J. The association between time spent outdoors and myopia in children and adolescents: A systematic review and meta-analysis. *Ophthalmology* **2012**, *119*, 2141–2151. [CrossRef]
39. Dirani, M.; Chan, Y.H.; Gazzard, G.; Hornbeak, D.M.; Leo, S.W.; Selvaraj, P.; Zhou, B.; Young, T.L.; Mitchell, P.; Varma, R.; et al. Prevalence of refractive error in Singaporean Chinese children: The strabismus, amblyopia, and refractive error in young Singaporean Children (STARS) study. *Investig. Ophthalmol. Vis. Sci.* **2010**, *51*, 1348–1355. [CrossRef] [PubMed]
40. Lanca, C.; Saw, S.M. The association between digital screen time and myopia: A systematic review. *Ophthalmic Physiol. Opt.* **2020**, *40*, 216–229. [CrossRef] [PubMed]
41. Wu, P.C.; Tsai, C.L.; Wu, H.L.; Yang, Y.H.; Kuo, H.K. Outdoor activity during class recess reduces myopia onset and progression in school children. *Ophthalmology* **2013**, *120*, 1080–1085. [CrossRef]
42. Williams, K.M.; Bertelsen, G.; Cumberland, P.; Wolfram, C.; Verhoeven, V.J.; Anastasopoulos, E.; Buitendijk, G.H.; Cougnard-Grégoire, A.; Creuzot-Garcher, C.; Erke, M.G.; et al. Increasing Prevalence of Myopia in Europe and the Impact of Education. *Ophthalmology* **2015**, *122*, 1489–1497. [CrossRef] [PubMed]
43. Brennan, N.A.; Shamp, W.; Maynes, E.; Cheng, X.; Bullimore, M.A. Influence of age and race on axial elongation in myopic children: A systematic review and meta-regression. *Optom. Vis. Sci.* **2024**, *101*, 497–507. [CrossRef]
44. Yam, J.C.; Zhang, X.J.; Zhang, Y.; Yip, B.H.K.; Tang, F.; Wong, E.S.; Bui, C.H.T.; Kam, K.W.; Ng, M.P.H.; Ko, S.T.; et al. Effect of Low-Concentration Atropine Eyedrops vs Placebo on Myopia Incidence in Children: The LAMP2 Randomized Clinical Trial. *JAMA* **2023**, *329*, 472–481. [CrossRef] [PubMed]
45. Lee, S.H.; Tseng, B.Y.; Wang, J.H.; Chiu, C.J. Efficacy and Safety of Low-Dose Atropine on Myopia Prevention in Premyopic Children: Systematic Review and Meta-Analysis. *J. Clin. Med.* **2024**, *13*, 1506. [CrossRef] [PubMed]
46. Yu, X.; Zhang, B.; Bao, J.; Zhang, J.; Wu, G.; Xu, J.; Zheng, J.; Drobe, B.; Chen, H. Design, methodology, and baseline data of the Personalized Addition Lenses Clinical Trial (PACT). *Medicine* **2017**, *6*, e6069. [CrossRef]
47. Smith, E.L. Optical treatment strategies to slow myopia progression: Effects of the visual extent of the optical treatment zone. *Exp. Eye Res.* **2013**, *114*, 77–88. [CrossRef] [PubMed]
48. Walline, J.J.; Walker, M.K.; Mutti, D.O.; Jones-Jordan, L.A.; Sinnott, L.T.; Giannoni, A.G.; Bickle, K.M.; Schulle, K.L.; Nixon, A.; Pierce, G.E.; et al. Effect of high add power, medium add power, or single-vision contact lenses on myopia progression in children: The BLINK randomized clinical trial. *JAMA J. Am. Med. Assoc.* **2020**, *324*, 571–580. [CrossRef] [PubMed]
49. Curcio, C.A.; Allen, K.A. Topography of ganglion cells in human retina. *J. Comp. Neurol.* **1990**, *300*, 5–25. [CrossRef] [PubMed]
50. Logan, N.S.; Gilmartin, B.; Wildsoet, C.F.; Dunne, M.C. Posterior retinal contour in adult human anisomyopia. *Investig. Ophthalmol. Vis. Sci.* **2004**, *45*, 2152–2162. [CrossRef] [PubMed]
51. Faria-Ribeiro, M.; Queirós, A.; Lopes-Ferreira, D.; Jorge, J.; González-Méijome, J.M. Peripheral refraction and retinal contour in stable and progressive myopia. *Optom. Vis. Sci.* **2013**, *90*, 9–15. [CrossRef] [PubMed]

52. Laughton, D.; Hill, J.S.; McParland, M.; Tasso, V.; Woods, J.; Zhu, X.; Young, G.; Craven, R.; Hunt, C.; Neitz, J.; et al. Control of myopia using diffusion optics spectacle lenses: 4-year results of a multicentre randomised controlled, efficacy and safety study (CYPRESS). *BMJ Open Ophthalmol.* **2024**, *9*, e001790.35. [CrossRef] [PubMed]
53. Lam, C.S.Y.; Tang, W.C.; Zhang, H.Y.; Tse, D.Y.Y.; To, C.H. Myopia control in children wearing DIMS spectacle lens: 6 years results. *Investig. Ophthalmol. Vis. Sci.* **2022**, *63*, 4247.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.