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PEDIATRICS

MiSight Assessment Study Spain (MASS). A 2-year randomized clinical trial

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Abstract

Purpose To compare myopia progression in children randomized to MiSight contact lenses (CLs) versus children corrected with single-vision spectacles (SV) over a 2-year period.

Methods Subjects aged 8 to 12 with myopia (−0.75 to −4.00 D sphere) and astigmatism (< −1.00 D cylinder) were assigned to the lens study group (MiSight) or the control group (single vision). Measurements of visual acuity and subjective refraction were taken at 6-month intervals, and axial length, anterior chamber, corneal power, and cycloplegic autorefraction were measured at the baseline, 12-month, and 24-month visits.

Results Eighty-nine subjects were recruited. Forty-fix children were assigned to the MiSight group, and 33 to the single-vision spectacle group. In total, 74 children completed the clinical trial, with the following parameters at the beginning of the study: $n =$ 41 in the MiSight group (age: 11.01 ± 1.23 years, spherical equivalent: −2.16 ± 0.94 D, gender: male: 21, female: 20) and $n = 33$ in the single-vision group (age: 10.12 ± 1.38 years, spherical equivalent: −1.75 ± 0.94 D, gender: male: 12, female: 21). After 2 years of follow-up, myopia progressed slowly in the MiSight group compared to the control group (0.45 D vs 0.74 D, $p < 0.001$) and there was less axial elongation in the MiSight group compared to the single-vision group (0.28 mm vs 0.44 mm, $p < 0.001$). Therefore, use of MiSight CLs produced lower myopia progression (39.32%) and lower axial growth of the eye (36.04%) at 2 years compared to spectacle use.

Conclusions MiSight contact lens wear reduces axial elongation and myopia progression in comparison to distance single-vision spectacles in children.

ClinicalTrials.gov Identifier: NCT01917110.

Keywords MiSight · Myopia · Contact lenses · Axial length · Children

Introduction

Myopia is currently a significant public health problem, affecting at least 25% of the world population, and is the most common refractive error in adolescents and young adults in most parts of the world [1–4]. The myopic eye is associated with an increased risk of developing ocular pathology. High levels of myopia (≤ −6 D) are associated with a range of ocular pathologies, such as retinal detachment, cataracts, macular degeneration, and glaucoma, which may lead to vision loss and even blindness [5–12]. While some of these complications are associated with adults, others can occur in myopic children's eyes as a consequence of rapid increase in the degree of myopia [13, 14]. Slowing the progression of myopia in children is an issue of particular interest to parents and to the

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scientific community. Several meta-analyses indicate that myopia progression can be significantly reduced by a range of interventions, as compared with single-vision spectacles or placebo. The most effective interventions are pharmacologic, such as atropine and pirenzepine (efficacy between 60% and 77% according to various studies) [15–21], followed by orthokeratology (efficacy between 37% and 56%) [22–25], peripheral defocus-modifying CLs (efficacy between 25% and 79%) [26–33], and progressive addition spectacle lenses (average efficacy 19%) [15, 16, 34, 35].

The mechanisms that support myopia control with CLs are based on the change in retinal peripheral defocus. This theory remains uncertain in humans, while in animals, results from several studies have demonstrated that the eye is capable of responding to myopic and hyperopic defocus by modifying axial length [36–40]. Myopic peripheral defocus with refractive-corrected central vision inhibits axial growth, and imposed hyperopic defocus accelerates eye growth [25]. These findings suggest that the mechanism behind defocus sign recognition and eye growth regulation is located inside the eye.

Over the last decade, there have been reports that relative peripheral myopia induced by CLs can slow myopia progression in children [26–33]. Two different types of CLs for myopia control have been studied: bifocal concentric lenses [26–29] and peripheral gradient lenses [30–33]. Both designs incorporate a central zone to correct myopic refractive error, but bifocal concentric lenses use a concentric zone of rings with plus power addition to simultaneously deliver peripheral myopic defocus, whereas peripheral gradient lenses simultaneously produce constant peripheral myopization defocus that increases gradually from the central optic axis toward the periphery [33–35].

Aller and Wildsoet [26] studied the progression of myopia with bifocal CLs. They have reported that Acuvue bifocal CLs are able to reduce ocular growth. Their results showed that the bifocal CLs achieved greater control over myopia progression and axial elongation (> 70%) compared with single-vision soft CLs. A crossover study conducted by Anstice and Phillips [27] reported that refractive bifocal (dual focus) CLs are effective in controlling progression of myopia and axial length: 37% and 49% respectively. Lam et al. [28] conducted a 2-year clinical trial in which those children wearing defocus-incorporated soft CLs (DISC) showed 31% less axial elongation than the single vision soft CL group. DISC CLs are refractive concentric bifocal CLs with 10 to 12 rings of alternating power over the optic zone. Walline et al. [30] reported a 29% regulation effect in axial length growth and a 50% regulation effect in the progression of refractive error in children wearing proclear multifocal dominant "D" CLs, as compared with the single-vision CL group. Sankaridurg et al. [31] performed a randomized clinical trial with Chinese children. The study group (soft gradient peripheral CLs) showed a 33% slower axial elongation compared with the control group (single-vision spectacles). Fujikado et al. [32] examined the effect of a low-addition progressive power lens with a decentered design on progression of myopia in young children, but their results show neither change in axial length nor refractive error in the new CL group compared with the control CL group. Pauné et al. [33] evaluated an experimental soft radial refractive gradient CLs. Their results show that the soft radial refractive gradient lens significantly decreased axial length elongation compared with a single-vision control group after 2 years of treatment.

In the current study we tested the efficacy of MiSight (CooperVision, Pleasanton, CA, USA) CLs in myopia control as measured by cycloplegic autorefraction and axial length. MiSight CLs contain a large central correction area of 3.36 mm surrounded by concentric zones of alternating distance and near powers. The dimension of the central correction area has been designed to provide good distance visual acuity. The near power is intended as a "treatment" zone to prevent myopic progression [35]. Efficacy of MiSight CLs in slowing the rate of progression of juvenile-onset myopia is also being studied in a prospective, randomized, double-masked, controlled multicenter study vs Proclear® 1 Day CLs [29] [see also Back A (2016) Optom Vis Sci 93: E-abstract 160035, for earlier stage in the same study].

Given the proliferation of myopia control studies over the past years, and the differences in their study designs, the goal of the current study was to determine whether wearing MiSight CLs can slow the rate of progress of myopia versus monofocal spectacles in white European children, aged 8 to 12, with moderate levels of myopia (−0.75 to −4.00D) and astigmatism (< −1.00D) and free of systemic or ocular disease over a 2-year period. Therefore, the primary outcome measure of MiSight Assessment Study Spain (MASS) was to compare progression of myopia and axial elongation between children wearing MiSight CLs and distance single-vision spectacles over a 2-year period. To the authors' knowledge, the MASS study is the first randomized controlled clinical trial to assess the efficacy of MiSight CLs wear versus single-vision spectacles in the reduction of myopia and axial length.

Methods

The protocol was approved by the CEI-R (Regional Research Ethics Committee of the Community of Madrid, Spain) and adhered to the tenets of the Declaration of Helsinki. The clinical trial was registered in Clinical Trials (ClinicalTrials.gov Identifier: NCT01917110). After receiving an explanation of the nature and possible consequences of the study, all parents provided signed permission for their children to participate, and participants provided written consent.

Participants

Children were recruited for and participated in this trial between September 2013 and June 2016. The study took place at two investigational sites, Novovision ophthalmologic clinic and the Universidad Europea [European University] of Madrid. Participants were 8 to 12 years old at the baseline visit. They had between −0.75 D and −4.00 D spherical component myopia and less than 1.00 D of astigmatism by cycloplegic autorefraction. Subjects were actively recruited from randomly selected schools, health care centers, and private clinics in the Madrid area. Subjects who were willing to participate were examined at a baseline visit to determine eligibility. Inclusion and exclusion criteria are shown in Table 1. At the initial baseline visit, all subjects underwent a full anterior segment examination, indirect fundus microscopy, and refractive evaluation to determine whether they were eligible to participate in the study. The children in both groups were examined by the same researcher using the same facilities, equipment, and methods.

Study procedures

The baseline visit data included case history, parental refractive status (non-cycloplegic autorefraction or record of recent prescription), subject's habitual visual acuity (distance and near) measured using 4 m and 40 cm ETDRS charts respectively, subject's non-cycloplegic autorefraction, manifest subjective refraction, best-corrected distance visual acuity, near visual acuity, ocular dominance measured using the Dolman method [41], biomicroscopy and fluorescein assessment, pupil diameter measured with a Colvard (Oasis Medical, Inc., USA) pupillometer, axial length, anterior chamber depth, and corneal power measured using an IOLMaster (Carl Zeiss Jena GmbH, Jena, Germany), cycloplegic autorefraction measured with an autorefractor (Topcon RM 8000, Japan), binocular and accommodative examination, and binocular indirect ophthalmoscopy.

Eligible subjects were sequentially randomized into either the study group (MiSight CLs) or the control group (single vision spectacles, Shamir, Spain). Personnel not directly related to the participants assigned subject numbers using a random-number table of 200 numbers. Researchers had no access to the randomization schedule. As participants entered the study, they were assigned a number in order of participation. This number was associated with a preassigned intervention group. If the participant had to be excluded, that subject number would be discarded and the next one used for the next participant, until the total number of participants was reached.

Subjects in the study group were fitted with MiSight CLs and asked to return for another visit (dispensing visit: 1–7 days after baseline) for lens insertion and removal training. The initial distance prescription of the CLs was determined by the spherical equivalent of the cycloplegic refraction, adjusted for vertex distance. Adjustments to the distance prescription were based on spherical over-refraction, which in turn was based on the highest positive power with optimum visual acuity. The centration and movement of the CLs were assessed in primary gaze with white light, diffuse and low-medium magnification, immediately after the blink, and the tightness of the CLs was assessed by digital push-up, white light, diffuse and low medium magnification. MiSight contact lenses were prescribed in a daily disposable wear pattern. Each subject was asked to wear their lenses for at least 6 days per week. Wearing time was not to exceed 15 h per day. Subjects could not sleep with their lenses in, and were told to discard them at the end of each wearing period and insert a fresh pair the following day

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Aged 8 to 12, both inclusive.	Current or prior contact lenses wear.
Understand and sign the Informed Consent Form.	Current or prior use of bifocals, progressive addition lenses, atropine, pirenzepine, or any other myopia control treatment.
Agree to fulfill the visit schedule and be able to keep all appointments as specified in the study protocol for the duration of the study.	Regular use of ocular medications and artificial tears.
Agree to accept either the control or test lenses as assigned by the randomization scheme.	Current uses of systemic medications, which may significantly affect contact lens wear, tear film production, pupil size, accommodation, or refractive state.
Be in good general health, based on his/her and parent's/guardian's knowledge.	A known allergy to fluorescein, benoxinate, proparacaine, or tropicamide.
Have best-corrected visual acuity by manifest refraction of + 0.10 logMAR (20/25 Snellen equivalent) or better in each eye.	A history of corneal hypoesthesia, corneal ulcer, corneal infiltrates, ocular viral or fungal infections, or other recurrent ocular infections.
A low-to-moderate level of refractive error (between 0.75 and 4.00D) and astigmatism (< 1.00D).	Strabismus by cover test at far (4 m) or near (40 cm) wearing distance correction.
	Systemic or ocular disease affecting ocular health.
	Keratoconus or an irregular cornea.
	CCLRU grade ≥ 2 for any given anterior segment ocular clinical signs.
	Having pathological myopia.
	Connective tissue disorders.

(daily wear use only). It was made clear that they had to remove their CLs if they experienced any signs or symptoms. They returned for follow-ups at 1 week, and at 1, 6, 12, 18, and 24 months. Subjects in the control group were prescribed standard, single-vision, spherocylindrical spectacles determined by cycloplegic refraction, with the highest positive power consistent with optimum visual acuity. They were asked to wear the spectacles at all times. The spectacles group was asked to return for follow-ups at 6, 12, 18, and 24 months. Measurements taken at each follow-up for both groups are shown in Table 2. At follow-up visits, children received new CLs or single-vision spectacles if over-refraction improved visual acuity by 3 logMAR letters, if there had been a change in refractive error of −0.25 D or greater, or, at the clinician's discretion, if the child experienced visual symptoms. In both groups, subjects received a new prescription for their CLs or spectacles, if a change was warranted. At each follow-up visit, the researcher asked the subject and parent/guardian to report any symptoms, problems, or complaints that had arisen since the previous visit.

Spectacles and CLs, as well as full ocular examinations, were provided free of charge to all subjects throughout the study. CooperVision S.L. provided the study contact lenses and the funding to carry out the clinical trial. Subjects could withdraw from the study at any time, and the researcher could decide whether a participant should be withdrawn in the event of significant symptoms such as discomfort, red eye, tearing or slit-lamp findings. Slit-lamp examination included assessment of the cornea, conjunctiva, eyelid, and lid margin of both eyes. Corneal and conjunctival integrity was confirmed with a fluorescein examination.

Table 2 Study visit plan

Procedures	Baseline	Dispense	Follow-up visits					
		Day 0*	1 week*	1 month*	6 months	12 months	18 months	24 months
Informed consent	X							
Case history	X	X	X	X	X	X	X	X
Lensometry	X							
Habitual visual acuity (distance and near)	X	X						
Subject non-cycloplegic autorefraction	X				X	X	X	X
Manifest subjective refraction	X				X	X	X	X
Best-corrected visual acuity (distance and near)	X				X	X	X	X
Cover test (distance and near), interpupillary distance and AC/A ratio	X					X		X
Stereo acuity	X					X		X
Ocular dominance	X							
Accommodative amplitude	X					X		X
Near point of convergence	X					X		X
Biomicroscopy	X	X	X	X	X	X	X	X
Randomization	X							
Contact lens corrected visual acuity (distance and near)*		X	X	X	X	X	X	X
Contact lens over-refraction*		X	X	X	X	X	X	X
Lens fit assessment*		X	X	X	X	X	X	X
Pupil diameter	X					X		X
Accommodative lag	X					X		X
Cycloplegic auto-refraction	X					X		X
Biometry	X					X		X
Binocular indirect ophthalmoscopy	X					X		X
Parental questionnaire of child's daily activities	X					X		X
Contact lens insertion and removal training / review*		X	X	X	X	X	X	X
Dispense study contact lens*		X	X	X	X	X	X	Xs
Complications & adverse events	Complete where applicable							
Study exit form	At 24 months if subject successfully completes the study, or when applicable if subject discontinues							

*Procedures and follow-up visits only for the MiSight Group

Contact lens design

MiSight is a soft (hydrophilic) CL composed of Omafilcon A material, with 8.7 mm base curve, 60% water content, non-ionic, with a total diameter of 14.2 mm comprising a 11.66 optic zone with four alternating distance and near zones (maximum treatment of +2.00 diopters) surrounding a central 3.36 mm distance zone diameter. This lens presents a 2D add power which renders a second focus in front of the retina at a distance of approximately 0.6 mm from the distance focus, intended to lie in the retina when viewing distant objects, assuming accurate accommodative response through the distance vision area of the lens. Therefore, the focus lying in front of the retina produced by the 2D add power of the treatment zones creates a defocused image in the retinal plane superimposed with the distance vision image. The test product is investigational in the United States and areas of Asia–Pacific, but is cleared for distribution in Canada and Europe (CE marked) [27]. It is a single-use, daily disposable lens.

Outcomes

The primary objective of this study was to quantify the effectiveness of the MiSight test CLs in slowing the rate of progression of youth-onset non-pathologic myopia as compared with monofocal ophthalmic control spectacles over a 2-year period. High or pathologic myopia has been defined as a myopia greater than 6 diopters or an axial length greater than 26 to 27 mm [5, 10]. This objective will be achieved by conducting a randomized clinical trial comparing myopia progression, as measured by cycloplegic autorefraction and axial length, in children treated with MiSight versus children treated with spectacles.

The primary outcome measure for progression of myopia was defined as the magnitude of change in the spherical equivalent refractive error relative to baseline, measured objectively with cycloplegia, three drops of cyclopentolate hydrochloride 1%, (Alcon Cusí, Masnou, Barcelona, Spain) instilled at 10-min intervals in each of the subjects' eyes, following the current protocol of the Novovision ophthalmologic clinic. Three auto-refraction measurements were taken using a Topcon RM-8000B autorefractor (Topcon Medical Systems, Inc., Oakland, NJ, USA) and the mean was calculated. Measures were expressed in power vector format [42] (M, J0, and J45), and the average M component was used as the spherical equivalent refractive error.

Progression of myopia was also defined as the change in axial length relative to baseline, measured with an IOL Master prior to cycloplegia. At least six separate measurements of axial length were recorded. Refraction under cycloplegia and axial length were measured at baseline and at the 12- and 24-month follow-up visits.

Sample size

The study sample size was calculated using statistical power analysis software Power and Precision v.4 (Biostat, Englewood, NJ, USA). It was based on data from previous clinical trials [27, 43, 44].

Taking a statistical power of 0.80 and assuming a standard deviation of the change in axial length over a 2-year period of 0.27 mm, a sample size of 28 subjects per group was needed to detect a difference in axial length variation equal to 0.22 mm at $P = 0.05$ [43, 44]. Previous studies have reported discontinuation rates of nearly 17% of subjects enrolled in clinical trials [44, 45]. Therefore, to account for attrition, this study sought to recruit at least 33 subjects per group.

Statistical analysis

Data for children who attended the 24-month visit were included in the analysis of progression of myopia. Data for the dominant eye only was used to avoid the confounding effect of using non-independent data from both eyes.

The differences between the two study groups in baseline demographics, refraction, binocular and accommodative and biometric data were subjected to analysis of variance (ANOVA), as well as the Brown–Forsythe F test depending on the result of Levene's test for homogeneity of variances. The Kruskal–Wallis test was also performed if the Kolmogorov–Smirnov test results rejected the hypothesis of data normality. A chi-squared test was used for qualitative data. Repeated measures analysis of variance tests (ANOVA) were used to compare changes in axial length and refractive error during the study period with the level of statistical significance set at 5%.

The SPSS 18 statistical software package for Windows was used for statistical data analysis.

The efficacy of myopic control of MiSight CLs was determined by dividing the difference in the two groups' mean spherical equivalent refraction changes by the mean spherical equivalent refraction change in the single vision group and then multiplying the result by 100% [28].

Results

Eighty-nine subjects were recruited for the study between September 2013 and June 2016. Forty-six children were allocated to the MiSight group and 33 to the single vision group (Fig. 1). At baseline, no significant differences between the two groups were found in refractive, biometric, or binocular vision assessment, except for age ($P < .05$) (Table 3). For this reason, the age variable was treated as a covariate to analyze its possible influence on the main variables using ANCOVA analysis. This analysis showed that the covariate age had no

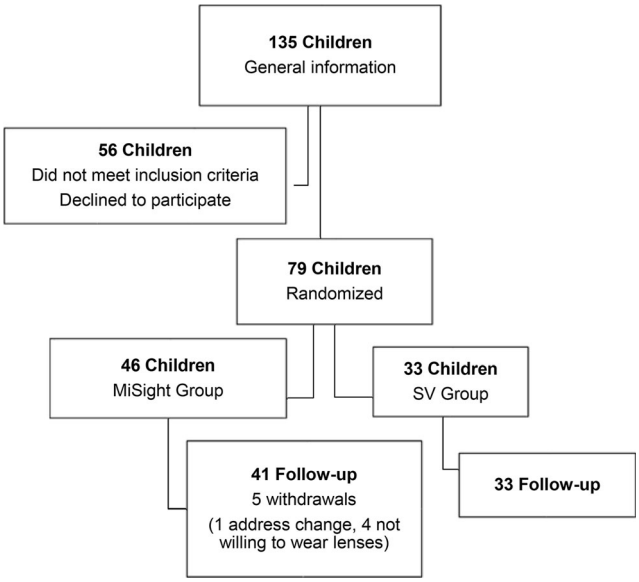

Fig. 1 Flow diagram of progress throughout the study. *MiSight*: contact lenses, *SV*: single vision spectacles

significant effect ($P \geq .05$), so it is understood that the mean difference cannot be attributed to the possible differences found between groups.

One participant was lost to follow-up before the 1-year visit. An additional four participants were lost to follow-up between the 1-year and 2-year visits. Data from these participants were not used in the analyses. When analyzing progression of myopia, data were included for 41 children in the MiSight group and 33 children in the single vision group. All withdrawals were from the MiSight group: one subject withdrew due to a change of address, and the other four left the study because they were not willing to wear CLs. Information on progression of myopia was not available for these children. There were zero withdrawals in the single vision group. Table 3 shows refractive and biometric data from the treatment and control groups at baseline, and shows statistical significance.

Over 1 year, the mean myopia progression was −0.18 D for the MiSight group (CI: 0.27 to 0.10) and −0.44 D for the single vision group (CI: 0.53 to −0.34) respectively ($P < .001$). Over 2 years, the mean myopic progression for the MiSight group was 0.45 D (CI: 0.27 to 0.64) and the mean for the single vision group was 0.74 D (CI: 0.53 to 0.95; $P < .001$). At the end of the treatment, the MiSight group showed significantly less myopic progression than the single vision group (mean difference = −0.29 D; 39.32%).

Over 1 year, the mean increase in axial length for the MiSight group was 0.12 mm (CI: 0.08 to 0.16) and that of the single vision group was 0.24 mm (CI: 1.95 to 0.28; $P < .001$). Over 2 years, the total increase in axial length was 0.28 mm (CI: 0.37 to 0.20) in the MiSight group and 0.44 mm (CI: 0.54 to 0.35) in the single-vision group ($P < .001$). The mean myopic progressions in the two groups over 2 years are shown in Fig. 2, and refractive status data can be seen in Table 4. This table shows cycloplegic autorefraction, factors J0 and J45, axial length and mean keratometry at baseline, the 12-month visit, and the 24-month visit for subjects who completed the 2-year study in either the MiSight or the single vision group.

The axial length changes were consistent with the refractive findings, and there was a statistically significant difference between the two groups (mean difference = 0.16 mm;

Table 3 Comparison of demographic and ocular components expressed as mean ± standard deviation (SD) for all subjects initially included in the study and participants who completed the study

	All			Completed		
	MiSight group($n = 46$)	SV group ($n = 33$)	*P* value	MiSight group($n = 41$)	SV group ($n = 33$)	*P* value
Age (years)	10.94 ± 1.24	10.12 ± 1.38	0.007	11.01 ± 1.23	10.12 ± 1.38	0.005
Spherical equivalent (D)	−2.10 ± 0.91	−1.75 ± 0.94	0.095	−2.16 ± 0.94	−1.75 ± 0.94	0.067
J0	0.07 ± 0.17	0.00 ± 0.12	0.038	0.07 ± 0.18	0.00 ± 0.12	0.059
J45	−0.02 ± 0.13	0.00 ± 0.12	0.638	−0.02 ± 0.12	0.00 ± 0.12	0.547
BCVA (LogMAR)	−0.06 ± 0.05	−0.07 ± 0.07	0.715	−0.06 ± 0.06	−0.07 ± 0.07	0.627
Best-corrected NVA (M)	0.40 ± 0.06	0.39 ± 0.03	0.683	0.4 ± 0.06	0.39 ± 0.03	0.276
Axial length (mm)	24.11 ± 0.57	24.00 ± 0.86	0.525	24.09 ± 0.55	24.00 ± 0.86	0.603
Anterior chamber (mm)	3.76 ± 0.20	3.76 ± 0.19	0.884	3.77 ± 0.19	3.76 ± 0.19	0.820
Mean keratometry (D)	44.16 ± 1.21	44.03 ± 1.59	0.693	44.24 ± 1.25	44.03 ± 1.59	0.533
Parental myopia			0.103			
One parent with myopia	23	12				
Both parents with myopia	14	8				

SV: single-vision spectacles; D: diopters; J0 and J45 vectorial components for astigmatism; BCVA: best-corrected visual acuity; NVAM: near visual acuity measured in M notation;

"*P*-value" refers to the statistical *P*-value

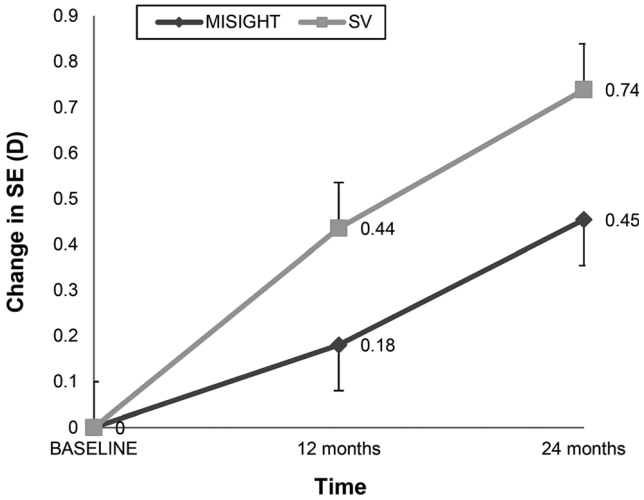

Fig. 2 Myopia progression SE (spherical equivalent) for the subjects who completed the study. *MiSight*: MiSight group, *SV*: single vision group

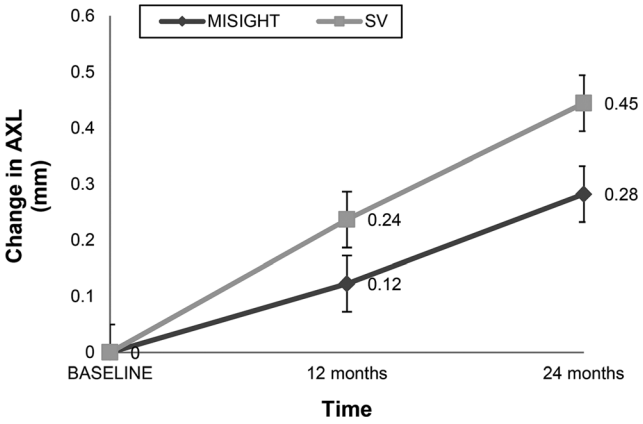

Fig. 3 Axial length elongation for the subjects who completed the study. *MiSight*: MiSight group, *SV*: single vision group

36.04%). The mean axial length change in the two groups is shown in Fig. 3, and further details of axial length are listed in Table 4. Keratometry did not show any significant changes during the study in any group ($P \geq .05$). Finally, the differences in axial length variation between groups were smaller than those we initially expected. With the sample size of 33 in control group and 41 in the MiSight group and a difference of axial length of 0.16 mm between groups, the study has power of 0.705 ($P = 0.05$).

The CL-wearing time in the MiSight group at the 6-month visit was 12.20 ± 1.82 h/day from Monday to Friday and 9.92 ± 3.62 on the weekend. At the 12-month visit, wearing time was 11.78 ± 2.08 from Monday to Friday and 7.25 ± 4.67 on the weekend. There was no significant correlation of myopia progression and lens-wearing time at the 6- and 12-month visits ($P > .05$). The average number of days per week that the CLs were worn was 6.40 ± 0.91 days/week at the 6-month visit and 6.34 ± 1.05 days/week at the 12-month visit.

Discussion

The present study shows that children wearing MiSight CLs had 39.2% lower progression of myopia and 36.4% lower axial elongation than children wearing single vision lenses over 2 years. Subjects and parents engaged enthusiastically in the study and responded well to initial introduction of the study design and protocol. For the MASS study, the subjects' baseline refractive and biometric data were markedly similar to baseline data from other studies assessing the effects of bifocal or multifocal CL wear on myopia progression in children [26–28, 30–33]. It is important to note that our study includes a large number of Caucasian children (87.3% of fathers and 86.1% of mothers were Caucasian), whereas most prior studies included only Asian subjects [28, 31, 32]. It is known that myopia has a higher prevalence and progression rate in East Asian children than in other ethnic groups [46]. Prevalence rates may be population-specific, so we believe our study may provide valuable information regarding Caucasian ethnicity. Although it is a randomized clinical trial and the CLs and spectacle lens groups had similar inclusion criteria for age and other features, there was a slight difference in age between the two

Table 4 Changes (mean ± SD) in cycloplegic autorefraction (SE), axial length (AXL) and mean keratometry at each visit in subjects who completed the 2-year study

	MiSight ($n = 41$) mean ± SD			SV ($n = 33$) mean ± SD			Two-year change between groups (mean)
	Baseline	12 months	24 months	Baseline	12 months	24 months	
Spherical equivalent	−2.16 ± 0.94	−2.34 ± 1.05	−2.61 ± 1.20	−1.75 ± 0.94	−2.18 ± 1.01	−2.48 ± 1.13	0.29
J0	0.07 ± 0.18	0.07 ± 0.16	0.11 ± 0.18	0.00 ± 0.12	−0.03 ± 0.15	0.00 ± 0.17	0.04
J45	−0.02 ± 0.12	0.10 ± 0.14	−0.02 ± 0.11	0.00 ± 0.12	0.03 ± 0.11	0.00 ± 0.12	0.04
Axial length	24.09 ± 0.55	24.21 ± 0.58	24.37 ± 0.59	24.00 ± 0.86	24.24 ± 0.86	24.45 ± 0.88	0.16
Keratometry	44.24 ± 1.25	44.17 ± 1.20	44.21 ± 1.23	44.03 ± 1.59	44.06 ± 1.57	43.93 ± 1.62	0.07

MiSight CLs, SV single vision; SE: spherical equivalent; J0 and J45 vectorial components for astigmatism, AXL: axial length

Table 5 Clinical studies of myopia control with soft contact lenses

Author	Change in SE (± SD) (D)				Change in AXL (± SD) (mm)				Follow-up period
	CLs	Control	Mean difference (D)	% effect	CLs	Control	Mean difference (mm)	% effect	
Aller et al. [26]	−0.22 ± 0.34	−0.79 ± 0.43	0.57	72	0.05 ± 0.14	0.24 ± 0.17	0.19	77	12 months
Anstice and Phillips [27]	Period 1: −0.44 ± 0.33 Period 2: −0.17 ± 0.35	Period 1: −0.69 ± 0.38 Period 2: −0.38 ± 0.38	Period 1: −0.25 ± 0.27 Period 2: −0.2 ± 0.34	Period 1: 37 Period 2: 54	0.11 ± 0.09	0.22 ± 0.10	0.11	Period 1: 49 Period 2: 80	12 months
Sankaridurg et al. [31]	0.57 ± 0.37	0.86 ± 0.47	0.29	34	0.27 ± 0.17	0.4 ± 0.19	0.13	33	24 months
Walline et al. [30]	−0.57 ± 0.06	−1.09 ± 0.06	0.52	50	0.29 ± 0.03	0.41 ± 0.03	0.12	29	12 months
Lam et al. [28]	0.59 ± 0.49	0.79 ± 0.56	0.2	25	0.25 ± 0.23	0.37 ± 0.24	0.12	32.4	24 months
Fujikado et al. [32]	−0.84 ± 0.42	−0.62 ± 0.43	0.22	26	0.09 ± 0.08	0.17 ± 0.08	0.08	47	12 months
Pauné et al. [33]	−0.56 ± 0.51	−0.98 ± 0.58	0.42	43	0.38 ± 0.21	0.52 ± 0.22	0.14	27	24 months

groups, with the spectacle lens group presenting a slightly younger baseline age than the CL group. However, when we adjusted for age in the analysis, the results were unaffected by this difference. Our results show that over 2 years the progression of myopia (spherical equivalent and axial length) was lower in the MiSight CL group than in the control group (0.45 D vs 0.74 D; 0.28 mm vs 0.44 mm respectively). Back A et al. (Back A (2016) Optom Vis Sci 93: E-abstract 160035) previously reported that, over 24 months of treatment, mean cycloplegic spherical equivalent progression was 0.54 D lower in the MiSight CL group, and the axial length growth in the MiSight group was 0.24 mm less. This difference could be because the Back et al. study included a large number of Asian subjects in the sample, and participants in the control group were wearing single vision daily disposable CLs instead of spectacles.

In relation to the prescription used by the participants, we determined it for both groups by cycloplegic refraction, but the MiSight group used spherical CLs and the control group used spherocylindrical spectacles. Although neither of the two groups had astigmatism greater than 0.75D and the toric contact lenses are used for astigmatism greater than 0.75D, we do not know whether the fact that the control group wore glasses with myopia and astigmatism could have influenced the results. Previously published studies of bifocal or multifocal CLs have reported reductions in myopic progression and axial length ranging from 25% to 70% (Table 5). To readily compare studies, the results are described in terms of mean differences measured in diopters and percentage change in progression by dividing the difference in progression of the combined experimental and control groups by the progression of the control group. All previous studies listed in Table 5 include monofocal CLs as a control group except Sankaridurg et al. [31] which, as in our study, includes a single-vision spectacle group. Although differences between these studies (ethnicity, age, duration, environmental conditions, method of measuring myopia progression and axial length, and contact lens design) can have significant effects on the outcomes, our results showed a greater effect of MiSight CLs on both ocular growth and myopia progression when compared with other 2-year follow-up studies, except for that of Pauné et al., which showed a 43% reduction in myopic progression (spherical equivalent) with soft radial refractive gradient CLs. Differences in myopia control may be due to differences in contact lens design (MiSight CLs have concentric rings of relative plus power, as opposed to the progressive increase in relative plus power of soft radial refractive gradient CLs).

After 12 months of treatment, the best results were shown by Aller [26] in 2016. Myopia progression in the Acuvue bifocal CL group was lower than in the control group, in terms of both refraction (72%) and axial length (77%). Both MiSight and Acuvue bifocal CLs include alternating rings of distance and near powers, but the results might differ because of differences in inclusion criteria (age and phoria). Aller et al.

included children from 8 to 18 years old, with an average age of 13.6 years and with 66% of the subjects aged 13 or older. It is known that younger children have higher myopia progression rates [47]. Only children with eso-associated near phoria were included in the Aller study. A high near esophoria and greater lag of accommodation have been identified as triggers for eye growth [48]. Aller calculated the addition of the Acuvue CLs with the minimum power necessary to reduce the near associated esophoria; this fact could have influenced the results, contributing to a smaller increase in axial length.

If we compare our results with other myopia control methods, reductions in myopia progression and eye elongation found in the MASS study are greater than those from previous studies with multifocal spectacle lenses in children. COMET II [48], a 3-year follow-up study, showed a mild treatment effect (0.28 D). Another shorter study (STAMP) [49] also reported a mild treatment effect over 12 months (0.18 D). Orthokeratology is another effective myopia control procedure. Studies have shown that the effect on axial length growth retardation is between 30% and 63% as compared with the single-vision lens or a monofocal CL [22–25]. However, the most effective myopia control intervention has been reported with muscarinic receptor antagonists such as pirenzepine and atropine at both high and low doses (from 1% to 0.01%) [15].

With regard to the number of participants who completed the study, the MASS study is the clinical trial with the lowest dropout rate. The dropout rate in the 24-month follow-up studies was higher than in ours: 42% in Pauné et al. [33] and in Lam et al. [28].

Our average days/week of wearing the CLs and the average time to wear CLs/day were similar to the Fujikado study [32] and greater than the study by Lam et al. [28]. We found no significant correlation between CL wearing time and myopia progression, while Lam et al. [28] showed that wearing time was a contributing factor to retardation of myopia progression. In their study, CLs were more effective in slowing progression of myopia when daily wearing time increased to at least 7 h. This difference may be due to the lower CL wearing time of participants in the Lam study (6.46 ± 2.16 h/day). Our participants used the CLs for 7 to 15 h per day from Monday to Friday, as confirmed at all study visits.

No clinical trial is without its limitations. Most of the current treatments for myopia control in children with contact lenses are based on the peripheral defocus. Previous studies have discussed the potential effect of the relative peripheral hyperopia on the myopia progression described above [36–40], but this theory still needs to be determined. Other factors may also have an influence, such as, for example, accommodative response or binocular vision. A limitation of our study is that we did not measure the myopic defocus induced with MiSight CLs, and we assumed that induced myopic defocus was sufficient to cover most of the retina. It would also have been interesting to measure the accommodative posture of the participants wearing MiSight CLs during near work, but it is difficult to obtain these measurements with the open-field autorefractometer due to the optical design of these CLs. There is also some controversy with regard to the finding of different meridians and the role of off-axis aberrations [50]. In this respect, the role of the spherical prescription of the MiSight group and the spheroclylindrical prescription of the control group could be taken into account for future research.

Clearly, further studies are required to: measure peripheral refraction and accommodation during CLs wear, determine the efficacy of MiSight CLs in slowing the progression of myopia over more than 2 years, establish treatment durations that will optimize reduction in progression of myopia, and determine the effect of discontinuing long-term lens wear on subsequent myopia progression.

In conclusion, our findings support the myopic progression control effect reported in previous studies [26–31] of soft multifocal center distance CLs. MiSight contact lens wear slowed myopia progression and axial elongation.

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Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (CEI-R, Regional Research Ethics Committee of the Community of Madrid, Spain) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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