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PEDIATRICS

Binocular and accommodative function in the controlled randomized clinical trial MiSight® Assessment Study Spain (MASS)

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Abstract

Purpose To evaluate the binocular and accommodative function in children wearing dual focus (DF) MiSight® contact lenses (CLs) for myopia control compared with children wearing single-vision (SV) spectacles.

Methods This was a randomized, controlled clinical trial involving subjects aged 8 to 12, with myopia ranging from − 0.75 to − 4.00D and astigmatism < 1.00D, allocated to MiSight® study CLs group or control group wearing SV. Binocular and accommodative function was determined at baseline, 12-, and 24-month visits, assessed by the following sequence of tests: distance and near horizontal phoria, accommodative convergence/accommodation (AC/A) ratio, stereopsis, accommodative amplitude (AA), and accommodative response (AR) at 33, 25 and 20 cm.

Results Seventy-four children completed the study: 41 in the CL group and 33 in the SV group. CLs group did not show any significant differences in binocular and accommodative measurements throughout the study. In control group, distance and near phoria, stereopsis, AC/A and AR at 20 cm did not show any significant change, but AA, AR at 33 cm and AR at 25 cm were greater at 24-month visit compared with baseline ($p < 0.05$).

Conclusions DF lenses do not change the binocular and accommodative function in children wearing dual focus CLs.

Trial registration NCT01917110

Keywords Binocular vision · Accommodation · Dual focus contact lenses · Children

Introduction

Changing myopia prevalence figures are consistent with the increased role that environmental influences play in the development of myopia. Some studies have associated myopia with an increase in near work activity [1–4]. Other studies point to outdoor activities as a protective factor against the development of myopia [5–8]. Although the specific factors contributing to myopia development and progression are unresolved, visual experience seems to play a central role and has refocused attention on the possibility that myopia progression can and should be controlled [9]. In animal models, multifocal lenses incorporating zones of positive power were found to inhibit eye growth, even though the positive zones are in the periphery of the lenses [10–12]. Translated to human myopia, these observations raised the possibility of increased progression with standard corrective spectacles and soft contact lenses [13].

Since myopia control contact lenses (CLs) are intended to be worn by children, who have very different accommodative

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and binocular systems than adults, it is critical to understand whether accommodation and binocular function is affected by the use of various designs of CLs in children [14, 15]. It is well known that switching from spectacles to CLs affects the convergence and accommodative demands [16–18]. Hunt et al. reported that a group of adult myopes exerted greater accommodative and vergence effort for viewing near targets when wearing CLs compared with spectacles lenses [19]. A study of university students found higher values of esophoria and accommodative lag and lower negative fusional vergence for near vision when wearing soft CLs, as compared with spectacles [20]. And esophoria myopic children exhibited a stronger trend towards exophoria when they changed from spectacles to CLs [21]. When overnight orthokeratology lenses (OK) are used to control myopia, it has been reported that accommodative and binocular function is not altered for either a short or a long period of treatment [22, 23].

MiSight CL is a soft (hydrophilic) CL with a concentric design. It contains a large central correction zone surrounded by a series of treatment and correction concentric zones of alternating distant and near powers, which together produce two focal planes. The optical power of the correction zones corrects the refractive error while the treatment zones produce 2.00 diopters (D) of simultaneous myopic retinal defocus during both distance and near viewing, maintaining good visual acuity [24]. Several studies have demonstrated the efficacy of concentric design CLs in myopia control [9, 24, 25], while others have shown the security and good quality of life provided by MiSight CLs [26, 27], but to the best of our knowledge, there are no studies that evaluate accommodative and binocular outcomes with this type of bifocal CLs and compare these results with SV spectacle use.

The differences in binocular and accommodative status between CLs and SV spectacles can be an important clinical consideration in relation to myopia control. Therefore, the aim of this study is to determine the effect of MiSight CLs used to control myopia in binocular vision and accommodation in children, as compared with children wearing SV spectacles.

Materials and methods

This study was part of the MiSight® Assessment Study Spain (MASS) [24], designed to assess the efficacy and subjective acceptance of MiSight® CLs versus distance SV spectacles in myopic children over a 2-year period. 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), where the outcome measures and the eligibility criteria can be consulted. After receiving an explanation of the nature and possible consequences of the study, informed consent was obtained from all individual participants included in the study.

Healthy subjects of European descent, 8 to 12 years of age, with moderate levels of myopia (− 0.75 to − 4.00D) and astigmatism (< − 1.00D) and free of systemic or ocular disease, were recruited for this study. At the baseline visit, all subjects underwent a full anterior segment examination, indirect fundus microscopy, binocular and accommodative function assessment, and refractive evaluation. All the measurements were performed in the same office, in the same order by the same researcher using the same facilities, equipment, and methods for all patients. Eligible subjects were sequentially randomized into either the study group (MiSight CLs) or control group (SV spectacles, Shamir, Spain).

Subjects in CL group were instructed to wear their lenses for at least 6 days per week, without exceeding 15 h per day in daily replacement use. It was made clear that they had to remove their contact lenses if they experienced any sort of problem. To check compliance, study group subjects were asked their average CLs wearing time from Monday to Friday and at weekends, average number of days per week that CLs were worn, and about their CLs experience at each follow-up visit. All of this information was recorded in the form of a questionnaire given to the subjects and their parents.

Subjects in the CL group 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 (Monofocal Shamir Alite, 1.56 HMC) and were asked to wear them at all times. The SV group was asked to return for follow-ups at 6, 12, 18, and 24 months.

Baseline, 12, and 24 month visits included case history, 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, biomicroscopy and fluorescein assessment, 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.

Binocular and accommodative function was assessed for both groups wearing trial frame with the best subjective refraction to achieve the best visual acuity. Far and near phoria were measured using the cover test technique at 6 m and 40 cm, respectively. With the subject wearing their refractive correction and viewing the fixation target, a unilateral cover-uncover test was conducted to test for strabismus. This was followed by an alternating cover test, and the horizontal phoria was neutralized using prism lenses, the magnitude (Δ) and direction (eso/exo/ortho) of the horizontal phoria being recorded.

The interpupillary distance (mm) was assessed with an interpupillometric ruler. The AC/A ratio was assessed with the calculated method [28] taking into account the values of far and near phoria, considering the exo values as negative and the eso as positive, interpupillary distance in centimeters, fixation distance, and reading distance in meters (in our case 0.4 m). Near point of convergence (NPC) was assessed using a standard push-up technique. An accommodative target with a 20/30 single letter used as fixation stimulus was moved toward the patient at 1–2 cm/s. Subjects were encouraged to try to keep the target single. The break and recovery values were measured and recorded in centimeters. The break value was considered as the average of three measurements in which the examiner observed one eye deviate, and the recovery value was defined as the average of three measurements in which the subject reported regaining single vision. If there was no subjective report of diplopia, the points at which the patient objectively lost and regained ocular alignment were recorded as the break and recovery [15, 29]. Stereoacuity was assessed with the Randot SO-002 test and polarizing spectacles [28]. The accommodative response was assessed using the binocular auto refractor/Keratometer WAM-5500 (Grand Seiko Co, Ltd., Hiroshima, Japan) at three stimulus distances: 33 cm, 25 cm, and 20 cm, giving accommodative demands at 3D, 4D, and 5D, respectively. Subjects were instructed to focus binocularly on the middle letter of the 20/30 line of a near ETDRS chart at each distance, and to keep the letters as clear as possible viewing the near chart through the spherical equivalent non-cycloplegic subjective refraction in a trial frame positioned at 12 mm from the subject's eye. The researcher took five measurements of the dominant eye and the procedure was repeated in the same way at 33, 25, and 20 cm distance. The final AR was calculated taking into account the effective accommodative demand obtained following the formula described in previous reports [30, 31]. The accommodative demand can differ according to the degree of refractive error, the power of the correcting lens, and the back vertex distance of the correcting lens.

$$\text{Accommodative demand} = ((1/DT) - LENS + Rf + (DL \times (1/DT) \times (LENS - Rf))) / (1 - (DL \times (LENS + Rf)))$$

$$\text{Accommodative response} = (Rf / (1 - (DL \times RX)) - (LENS / (1 - (DL \times LENS))) - R$$

where R = WAM 5500 instrument reading (D), Rf = spherical equivalent of the refractive power of the lens at complete correction (D), DT = distance between the corneal apex and the accommodation target (m), DL = distance between the corneal apex and the lens (0.012), and LENS = spherical equivalent of the refractive power of the spectacle or contact lens used (D). The difference between the accommodative demand and the accommodative response was regarded as the accommodative error (lag or lead).

Binocular push-up accommodation was measured with the subject wearing non-cycloplegic subjective refraction in a trial frame following Donder's push-up method. Subjects were instructed to view the middle letter of the 1.0-M line of the near chart at 40 cm. The chart was moved closer at a rate of ~ 1 to 2 cm/s until the subject could not make out the letters clearly. We measured and recorded the distance of the near target from the subject to the nearest 0.5 cm and repeated three measurements that were averaged and converted to diopters [20]. All the tests were administered consistently by the same optometrist to avoid variability between examiners.

Statistical analysis

Statistical analysis of data was performed using SPSS statistical software package SPSS 18 for Windows. Data corresponding to children who attended the 24-month visit were included in the analysis. The level of statistical significance was taken as 5%. Differences in all the binocular and accommodative parameters were assessed in each group over time (baseline vs. 24th visit). General linear model (GLM) repeated measures were applied, where the within-subjects factor is time. The assumption that the variance-covariance matrix is circular was subjected to Mauchly's test of sphericity. If this assumption is rejected, GLM repeated measures use the univariate F statistic, corrected by epsilon index.

The differences between the two study groups in each visit were assessed by Student's t test, depending on the assumption of homogeneity of variances (Levene's test).

Results

Eighty-nine subjects were recruited for the study between September 2013 and June 2016. Forty-six children were allocated to MiSight group and 33 to the SV correction modalities. Table 1 shows the data of subjects in the CLs and SV groups who initially were included in the study and those who completed the study. In total, 74 children completed the study: $n = 41$ in the MiSight group and $n = 33$ in the SV group. At baseline, no significant differences between the two groups were found in refractive and biometric assessment, except for age ($p < .05$). 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 significant effect ($p \geq .05$), so it is understood that the mean difference cannot be attributed to the possible differences found between groups.

Table 2 shows the means and standard deviation of the refractive error (spherical equivalent, J0 and J45) and axial length for the two follow-up groups.

CLs 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

Table 1 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. "*p* value" refers to the statistical *p* value

	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 ± 1.5	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; *statistically significant values

weekend. At the 24-month visit, wearing time was 11.69 ± 2.12 from Monday to Friday and 8.45 ± 4.50 on the weekend. The average number of days per week that the CLs were worn was 6.40 ± 0.91 days/week at the 6-month visit, 6.34 ± 1.05 days/week at the 12-month visit, and 6.32 ± 1.08 days/week at the 24-month visit.

Table 3 shows the mean values and standard deviation for binocular and accommodative assessment for all the participants who completed the 24 months follow-up for the MiSight group and for the SV group. It includes far and near horizontal phoria, near vertical phoria, NPC (break and recovery points), far interpupillary distance, stereopsis, AC/A ratio, AA, and AR at 33, 25, and 20 cm. Both groups were checked for binocular and accommodative function differences at baseline, 12- and 24-month visits. No significant differences between the two groups were found, except for the AR measured at 25 cm at baseline ($p < .05$).

All the binocular and accommodative parameters were compared over the time. The means and standard deviations of all these values are shown in Table 4. The *p* value did not show any statistically significant differences in the MiSight group for any of the studied parameters apart from interpupillary distance, but did in the SV group for interpupillary distance, AA and AR measured at 33 and 25 cm.

In order to present what happened to individual subjects for both groups, the scatter plot graphs (Figs. 1 and 2) analyze the relationship between near phoria and AC/A ratio at baseline, compared with the 24 month visit. Table 5 shows the degree of correlation of some of the binocular and accommodative parameters measured at baseline, compared with the 24-month visit.

Discussion

Over the 2 years of follow-up, in the MiSight group none of the parameters of binocular vision and accommodation underwent significant changes except for interpupillary

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

	MiSight (*n* = 41) Mean ± SD			SV (*n* = 33) Mean ± SD			2-year change between groups
	Baseline	12 months	24 months	Baseline	12 months	24 months	Mean
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

Table 3 Comparison of binocular vision and accommodative data expressed as mean ± standard deviation (SD) for the participants who completed the study at baseline (3.1), at 12-month visit (3.2) and 24-month visits (3.3). "*p* value" refers to the statistical *p* value

Baseline	MiSight group ($n = 41$)	SV group ($n = 33$)	*p* value
Distance phoria (Δ)	− 0.24 ± 1.43	− 0.79 ± 2.69	0.268
Near horizontal phoria (Δ)	0.49 ± 4.11	− 1.06 ± 4.42	0.124
Near vertical phoria (Δ)	0.00 ± 0.00	0.05 ± 0.26	0.325
NPC break (cm)	3.40 ± 3.52	2.80 ± 3.24	0.452
NPC recovery (cm)	6.39 ± 7.08	5.08 ± 5.54	0.388
Far DIP (mm)	57.61 ± 3.32	56.85 ± 3.80	0.361
Stereopsis (sec. of arc)	30.24 ± 12.09	38.18 ± 31.77	0.145
AC/A ratio	6.05 ± 1.48	5.58 ± 1.21	0.140
Amplitude of accommodation (D)	13.88 ± 3.58	12.40 ± 2.55	0.05
Accommodative response 33 cm (D)	1.08 ± 0.61	1.24 ± 0.75	0.304
Accommodative response 25 cm (D)	1.24 ± 0.66	1.59 ± 0.79	0.040*
Accommodative response 20 cm (D)	1.34 ± 0.64	1.64 ± 0.94	0.105
12-month visit	MiSight group ($n = 41$)	SV group ($n = 33$)	*p* value
Distance phoria (Δ)	0.12 ± 1.71	− 0.97 ± 3.01	0.069
Near horizontal phoria (Δ)	0.00 ± 2.89	− 0.24 ± 6.14	0.836
Near vertical phoria (Δ)	0.00 ± 0.00	0.06 ± 0.35	0.325
NPC break (cm)	3.76 ± 2.98	3.68 ± 3.73	0.919
NPC recovery (cm)	5.76 ± 4.44	6.05 ± 5.40	0.798
Far DIP (mm)	57.90 ± 3.18	57.48 ± 3.63	0.600
Stereopsis (sec. of arc)	34.02 ± 21.04	29.70 ± 8.00	0.231
AC/A ratio	5.74 ± 0.96	6.01 ± 1.90	0.433
Amplitude of accommodation (D)	14.18 ± 2.26	13.90 ± 2.88	0.642
Accommodative response 33 cm (D)	1.13 ± 0.50	1.19 ± 0.55	0.630
Accommodative response 25 cm (D)	1.27 ± 0.57	1.35 ± 0.74	0.595
Accommodative response 20 cm (D)	1.13 ± 0.62	1.40 ± 0.95	0.149
24-month visit	MiSight group ($n = 41$)	SV group ($n = 33$)	*p* value
Distance phoria (Δ)	− 0.26 ± 1.14	− 1.39 ± 4.17	0.137
Near horizontal phoria (Δ)	− 0.53 ± 3.67	− 1.33 ± 7.66	0.581
Near vertical phoria (Δ)	0.00 ± 0.00	0.06 ± 0.35	0.325
NPC break (cm)	3.37 ± 3.29	2.93 ± 3.11	0.563
NPC recovery (cm)	4.89 ± 4.84	4.93 ± 5.05	0.970
Far DIP (mm)	58.90 ± 2.94	58.90 ± 2.94	0.323
Stereopsis (sec. of arc)	31.75 ± 21.56	28.33 ± 9.90	0.404
AC/A ratio	5.84 ± 1.38	5.84 ± 2.16	0.996
Amplitude of accommodation (D)	12.99 ± 2.87	12.59 ± 2.93	0.560
Accommodative response 33 cm (D)	0.86 ± 0.71	0.64 ± 0.95	0.260
Accommodative response 25 cm (D)	1.13 ± 0.58	1.21 ± 0.66	0.604
Accommodative response 20 cm (D)	1.31 ± 0.67	1.29 ± 0.65	0.905

*Statistically significant values

distance, as could be expected due to the growth of the subjects in 2 years. In the SV group, interpupillary distance, AA and AR 3D and 4D showed significant changes.

Mean distance phoria values for both groups were more exophoric over time, although not statically significant. Mean near phoria for MiSight group at baseline was esophoric, orthophoric at 12 month follow-up and exophoric at the end of the treatment, and for the SV group mean near phoria was more exophoric over the study period ($p > 0.05$). Mean values of distance and near phoria could be more exophoric wearing CLs or after OK treatment [22] due to the effect of addition lenses on the reduction in accommodation demand and, consequently, in accommodative convergence. The increase in exophoria induced by multifocal CLs at near distance is in agreement with previous reports that suggest children are utilizing positive addition provided by

Table 4 Changes (mean ± SD) in binocular and accommodative data results at each visit in subjects who completed the 2-year study

	MiSight ($n = 41$) Mean ± SD				SV ($n = 33$) Mean ± SD			
	Baseline	12 months	24 months	*p* value	Baseline	12 months	24 months	*p* value
Distance phoria	−0.24 ± 1.43	0.12 ± 1.71	−0.26 ± 1.14	0.343	−0.79 ± 2.69	−0.97 ± 3.01	−1.39 ± 4.17	0.300
Near phoria	0.49 ± 4.11	0.00 ± 2.89	−0.53 ± 3.67	0.217	−1.06 ± 4.42	−0.24 ± 6.14	−1.33 ± 7.66	0.393
Near vertical phoria	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00		0.05 ± 0.26	0.06 ± 0.35	0.06 ± 0.35	0.325
NPC (break point)	3.40 ± 3.52	3.76 ± 2.98	3.37 ± 3.29	0.777	2.80 ± 3.24	3.68 ± 3.73	2.93 ± 3.11	0.150
NPC (recovery point)	6.39 ± 7.08	5.76 ± 4.44	4.89 ± 4.84	0.441	5.08 ± 5.54	6.05 ± 5.40	4.93 ± 5.05	0.278
Far DIP	57.61 ± 3.32	57.90 ± 3.18	58.90 ± 2.94$^{\alpha}$	0.000*	56.85 ± 3.80	57.48 ± 3.63$^{\sigma}$	58.15 ± 3.55$^{\alpha}$	0.003*
Stereopsis (sec. of arc)	30.24 ± 12.09	34.02 ± 21.04	31.75 ± 21.56	0.156	38.18 ± 31.77	29.70 ± 8.00	28.33 ± 9.90	0.272
AC/A	6.05 ± 1.48	5.74 ± 0.96	5.84 ± 1.38	0.372	5.58 ± 1.21	6.01 ± 1.90	5.84 ± 2.16	0.356
AA	13.88 ± 3.58	14.18 ± 2.26	12.99 ± 2.87	0.132	12.40 ± 2.55	13.90 ± 2.88	12.59 ± 2.93	0.009*
Accommodative response 3D (D)	1.08 ± 0.61	1.13 ± 0.50	0.86 ± 0.71	0.070	1.24 ± 0.75	1.19 ± 0.55	0.64 ± 0.95	0.002*
Accommodative response 4D (D)	1.24 ± 0.66	1.27 ± 0.57	1.13 ± 0.58	0.397	1.59 ± 0.79	1.35 ± 0.74	1.21 ± 0.66	0.040*
Accommodative response 5D (D)	1.34 ± 0.64	1.13 ± 0.62	1.31 ± 0.62	0.140	1.64 ± 0.94	1.40 ± 0.95	1.29 ± 0.64	0.196

SD, standard deviation; σ, statistically significant values between baseline and 12 month visits; α, statistically significant values between 12 and 24 month visits; *statistically significant values over the study period (baseline, 12, and 24 months)

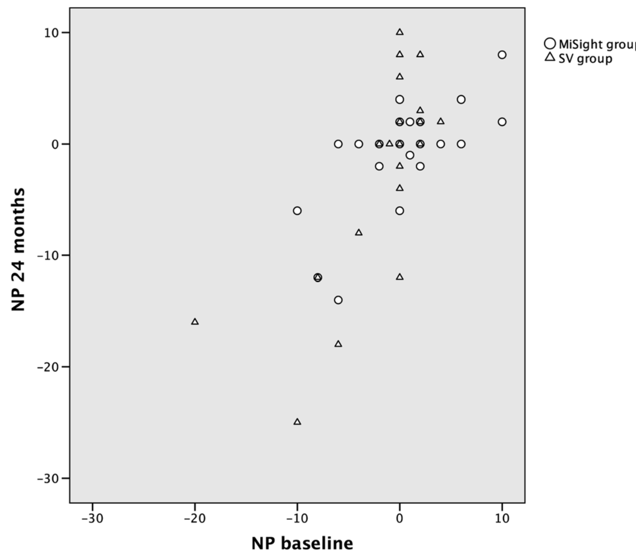

Fig. 1 Scatter plot for near horizontal phoria (NP) at baseline and 24-month visit

the multifocal design to relax their accommodation [9, 32]. Although we did not find significant differences in the mean values of distance and near phoria in the MiSight group subjects, they showed an exophoric tendency after wearing MiSight CLs.

Mean value of NPC (break and recovery) [33], AC/A ratio [34] and stereopsis [28] presented normal values in both groups in all the follow-ups. There were no significant differences in these parameters between both groups over time. Although there is some disagreement regarding age-related changes in the AC/A ratio over time, some authors have reported [35, 36] no changes in the AC/A ratio, as was the case with our results.

Although no significant changes in binocular and accommodative, parameters were observed in the MiSight group in

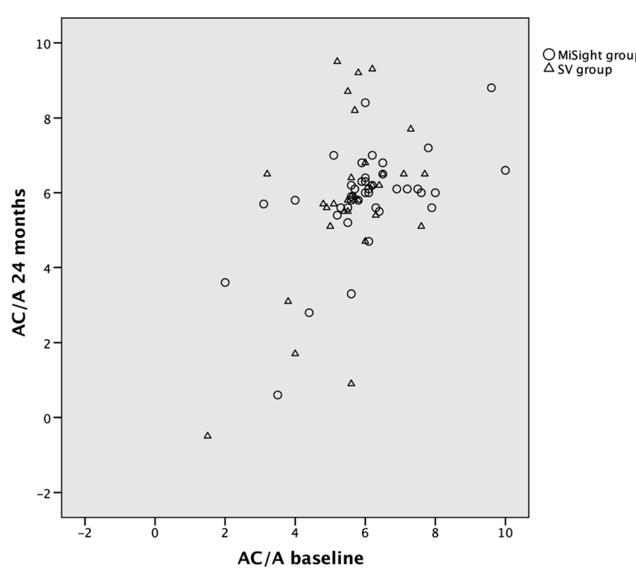

Fig. 2 Scatter plot for AC/A ratio at baseline and 24-month visit

Table 5 Correlation data for binocular and accommodative parameters for both groups

	MiSight group		SV group	
	Pearson's coefficient	*p* value	Pearson's coefficient	*p* value
Distance phoria	0.868	0.000*	0.880	0.000*
Near phoria	0.632	0.000*	0.737	0.000*
Stereopsis	0.394	0.012*	− 0.092	0.611
AC/A ratio	0.568	0.000*	0.512	0.002*
AA	0.207	0.201	0.317	0.072
Accommodative response 3D	0.308	0.053	0.087	0.629
Accommodative response 4D	− 0.003	0.984	0.356	0.042
Accommodative response 5D	0.212	0.189	0.011	0.951

*Statistically significant values

terms of mean values, individual changes were examined in terms of linear regression. It might be expected that some individuals could respond to the new image profile provided by the MiSight CLs while others do not. The scatter plot (Figs. 1 and 2) gives us information about the individual values of the selected variables (near phoria, AC/A ratio) showing a significant correlation in the MiSight group for these variables, as was expected.

In the MiSight group, the AA decreased over 2 years but not significantly, unlike in the spectacle group, where there were statistically significant changes between baseline and 12 month visits and between 12 and 24 month visits. According to previous reports, these findings were to be expected due to the different myopia compensation methods used, which involved CLs wearers having to accommodate more than spectacle users [16, 17, 19, 37].

When comparing accommodative results over time for both groups and their relation to myopia control, age can be a confusing factor. The accommodation system can vary with age to make optimal use of the available AA and the eye's depth of focus [38]. In this regard, it has been reported that AA decreases with age [28, 38, 39], so a decrease in AA over 2 years in the spectacle group may be a normal finding. On the other hand, there was no significant change in AA in the CLs group, which could be due to the greater accommodation effort that CLs wearers have to make, as compared with SV spectacles.

We assessed the AR at several stimulus demands in order to represent possible differences in accommodative effort among children. Previous reports have shown the tendency of myopic children to work at closer reading distances [40]. The average AR of the subjects for both groups was higher as demand increased, as has also been reported previously [39]. This may result in hyperopic retinal defocus that can trigger axial elongation and myopia, but our results did not show any statistical differences in AR between groups, except for the measurement at 25 cm, which was greater in the SV group at baseline.

Factors that could influence the measurement, such as the instrument used and the instructions given to the subjects were identical for both groups. Therefore, we find it difficult to explain this difference in the measurement at 25 cm, especially given that this difference did not occur in the measurement at 33 and 20 cm.

AR in the MiSight group did not suffer any statistical changes over time, while in the SV group we found a significant decrease in the AR 3D and AR 4D at follow-up visits. AR 3D changed between 12 and 24 month visits, and AR at 4D between baseline and 24 month visit, with values falling as time passed.

In relation to this measurement, our results are in correlation with previous studies that have reported a very small reduction in this parameter with age [38, 41]. Some studies have reported that subjects who are already myopic, or at risk of developing myopia, have large accommodative lag [42, 43], and an increase in the accommodative lag and the resulting hyperopic retinal defocus have been hypothesized as factors in myopic progression [44]. On the other hand, Mutti et al. suggested that accommodative lag was a result of myopia rather than a cause [37, 45]. In this regard, although there is no statistical difference between AR in the two groups for any of the follow-up visits (apart from AR 4D at baseline), SV group shows a slight tendency to present greater accommodative LAG than the MiSight group. It is known that there is an increase in LAG values when multifocal lenses are used, compared with monofocal CLs use [46]. Once again, this increase seems to be due to the positive addition, which affects accommodation and, due to the multifocal CLs design that induces positive spherical aberration. It has been shown that this positive spherical aberration could increase the depth of focus. These effects are not present in SV group. In fact, we did not find any significant changes in AR values in MiSight group. This difference in relation to the literature could be due to the fact that our AR measurements were performed without CLs, and therefore our values are not influenced by lens design per se. However, our results suggest that the use of this design has influenced AR in children wearing MiSight CLs. Our results indicate that myopia progression is higher in SV group than in MiSight group, and it has been found that lower values of LAG interfere with the regulation of axial elongation in myopic eyes [47]. In addition, several studies showed [48–50] that the effect of a plus addition can be more successful in slowing myopia progression in children with esophoria. Our work [24] reports that subjects who wore MiSight CLs during 2 years experienced lower myopia progression than the SV group ($p \le 0.05$) (Table 2), perhaps due to the action of the + 2.00D addition of MiSight CLs and its effect on peripheral retina defocus.

In conclusion, our results suggest that MiSight CLs are an effective treatment for myopia control in children, with no changes in binocular and accommodative function induced by this type of CLs over 2 years of follow-up. This lack of change in the binocular and accommodative function in our MiSight group tallies with Felipe-Márquez et al. [22, 23], who, in the only previous study to have analyzed such changes with a CLs for myopia control, reported that OK induced no changes in the ocular accommodative function and minimal changes in the binocular system.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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.

References

1. Saw SM, Wu HM, Seet B, Wong TY, Yap E, Chia KS, Lee L (2001) Academic achievement, close up work parameters, and myopia in Singapore military conscripts. Br J Ophthalmol 85:855–860
2. Mutti DO, Mitchell GL, Moeschberger ML, Jones LA, Zadnik K (2002) Parental myopia, near work, school achievement, and children's refractive error. Invest Ophthalmol Vis Sci 43:3633–3640
3. Ip JM, Saw S-M, Rose KA, Morgan IG, Kifley A, Wang JJ, Mitchell P (2008) Role of near work in myopia: findings in a sample of Australian school children. Invest Ophthalmol Vis Sci 49:2903–2910. https://doi.org/10.1167/iovs.07-0804
4. Fernández-Montero A, Olmo-Jimenez JM, Olmo N, Bes-Rastrollo M, Moreno-Galarraga L, Moreno-Montañés J, Martínez-González MA (2015) The impact of computer use in myopia progression: a cohort study in Spain. Prev Med 71:67–71. https://doi.org/10.1016/j.ypmed.2014.12.005
5. Sherwin JC, Reacher MH, Keogh RH, Khawaja AP, Mackey DA, Foster PJ (2012) The association between time spent outdoors and myopia in children and adolescents: a systematic review and meta-analysis. Ophthalmology 119:2141–2151. https://doi.org/10.1016/j.ophtha.2012.04.020
6. Guggenheim JA, Northstone K, McMahon G, Ness AR, Deere K, Mattocks C, Williams C (2012) Time outdoors and physical activity as predictors of incident myopia in childhood: a prospective cohort study. Invest Ophthalmol Vis Sci 53:2856–2865. https://doi.org/10.1167/iovs.11-9091
7. Torii H, Kurihara T, Seko Y, Negishi K, Ohnuma K, Inaba T, Tsubota K (2017) Violet light exposure can be a preventive strategy against myopia progression. Ebiomedicine 15:210–219. https://doi.org/10.1016/j.ebiom.2016.12.007
8. Rose KA, Morgan IG, Ip J, Kifley A, Huynh S, Smith W, Mitchell P (2008) Outdoor activity reduces the prevalence of myopia in children. Ophthalmology 115:1279–1285. https://doi.org/10.1016/j.ophtha.2007.12.019
9. Aller TA, Liu M, Wildsoet CF (2016) Myopia control with bifocal contact lenses: a randomized clinical trial. Optom Vis Sci 93:344–352. https://doi.org/10.1097/opx.0000000000000808
10. Liu Y, Wildsoet C (2011) The effect of two-zone concentric bifocal spectacle lenses on refractive error development and eye growth in young chicks. Invest Ophthalmol Vis Sci 52:1078–1086. https://doi.org/10.1167/iovs.10-5716
11. Liu Y, Wildsoet C (2012) The effective add inherent in 2-zone negative lenses inhibits eye growth in myopic young chicks. Invest Ophthalmol Vis Sci 53:5085–5093. https://doi.org/10.1167/iovs.12-9628
12. Benavente-Perez A, Nour A, Troilo D (2014) Axial eye growth and refractive error development can be modified by exposing the peripheral retina to relative myopic or hyperopic defocus. Invest Ophthalmol Vis Sci 55:6765–6773. https://doi.org/10.1167/iovs.14-14524
13. Smith EL 3rd (1998) Spectacle lenses and emmetropization: the role of optical defocus in regulating ocular development. Optom Vis Sci 75:388–398
14. Jimenez JR, Durban JJ, Anera RG (2002) Maximum disparity with acuvue bifocal contact lenses with changes in illumination. Optom Vis Sci 79:170–174
15. Scheiman M, Wick B (2008) Clinical management of binocular vision: heterophoric, accommodative, and eye movement disorders. Wolters Kluwer Health/lippincott Williams & Wilkins, Philadelphia
16. Alpern M (1949) Accommodation and convergence with contact lenses. Am J Optom Arch Am Acad Optom 26:379–387
17. Robertson DM, Ogle KN, Dyer JA (1967) Influence of contact lenses on accommodation: theoretic considerations and clinical study. Am J Ophthalmol 64:860–871
18. Carney LG, Woo GC (1977) Comparison of accommodation with rigid and flexible contact lenses. Am J Optom Physiol Optic 54:595–597
19. Hunt OA, Wolffsohn JS, García-Resúa C (2006) Ocular motor triad with single vision contact lenses compared to spectacle lenses. Cont Lens Anterior Eye 29:239–245
20. Jimenez R, Martinez-Almeida L, Salas C, Ortiz C (2011) Contact lenses vs spectacles in myopes: is there any difference in accommodative and binocular function? Graefes Arch Clin Exp Ophthalmol 249:925–935. https://doi.org/10.1007/s00417-010-1570-z

21. Fulk GW, Cyert LA, Parker DE, West RW (2003) The effect of changing from glasses to soft contact lenses on myopia progression in adolescents. Ophthalmic Physiol Opt 23:71–77
22. Felipe-Marquez G, Nombela-Palomo M, Palomo-Alvarez C, Cacho I, Nieto-Bona A (2017) Binocular function changes produced in response to overnight orthokeratology. Graefes Arch Clin Exp Ophthalmol 255:179–188. https://doi.org/10.1007/s00417-016-3554-0
23. Felipe-Marquez G, Nombela-Palomo M, Cacho I, Nieto-Bona A (2015) Accommodative changes produced in response to overnight orthokeratology. Graefe's Arch Clin Exp Ophthalmol 253:619–626. https://doi.org/10.1007/s00417-014-2865-2.
24. Ruiz-Pomeda A, Perez-Sanchez B, Valls I, Prieto-Garrido FL, Gutierrez-Ortega R, Villa-Collar C (2018) MiSight Assessment Study Spain (MASS). A 2-year randomized clinical trial. Graefes Arch Clin Exp Ophthalmol. https://doi.org/10.1007/s00417-018-3906-z
25. Anstice NS, Phillips JR (2011) Effect of dual-focus soft contact lens wear on axial myopia progression in children. Ophthalmology 118: 1152–1161. https://doi.org/10.1016/j.ophtha.2010.10.035
26. Ruiz-Pomeda A, Pérez-Sánchez B, Prieto-Garrido FL, Gutiérrez-Ortega R, Villa-Collar C (2018) MiSight Assessment Study Spain: adverse events, tear film osmolarity, and discontinuations. Eye Contact Lens. https://doi.org/10.1097/ICL.0000000000000484
27. Pomeda AR, Pérez-Sánchez B, Cañadas Suárez MDP, Prieto Garrido FL, Gutiérrez-Ortega R, Villa-Collar C (2017) MiSight Assessment Study Spain: a comparison of vision-related quality-of-life measures between MiSight contact lenses and single-vision spectacles. Eye Contact Lens. https://doi.org/10.1097/ICL.0000000000000413
28. Jiménez R, Pérez MA, García JA, González MD (2004) Statistical normal values of visual parameters that characterize binocular function in children. Ophthalmic Physiol Opt 24:528–542
29. Scheiman M, Gallaway M, Frantz KA, Peters RJ, Hatch S, Cuff M et al (2003) Nearpoint of convergence: test procedure, target selection, and normative data. Optom Vis Sci 80:214–225
30. Gwiazda J, Thorn F, Bauer J, Held R (1993) Myopic children show insufficient accommodative response to blur. Invest Ophthalmol Vis Sci 34:690–694
31. Nakatsuka C, Hasebe S, Nonaka F, Ohtsuki H (2005) Accommodative lag under habitual seeing conditions: comparison between myopic and emmetropic children. Jpn J Ophthalmol 49: 189–194
32. Kang P, Wildsoet CF (2016) Acute and short-term changes in visual function with multifocal soft contact lens wear in young adults. Cont Lens Anterior Eye 39:133–140. https://doi.org/10.1016/j.clae.2015.09.004
33. Maples WC, Hoenes R (2007) Near point of convergence norms measured in elementary school children. Optom Vis Sci 84:224–228
34. Gwiazda J, Grice K, Thorn F (1999) Response AC/A ratios are elevated in myopic children. Ophthalmic Physiol Opt 19:173–179
35. Ciuffreda KJ, Rosenfield M, Chen HW (1997) The AC/a ratio, age and presbyopia. Ophthalmic Physiol Opt 17:307–315
36. Mutti DO, Jones LA, Moeschberger ML, Zadnik K (2000) AC/A ratio, age, and refractive error in children. Invest Ophthalmol Vis Sci 41:2469–2478
37. Jiménez R, Martínez-Almeida L, Salas C, Ortíz C (2011) Contact lenses vs spectacles in myopes: is there any difference in accommodative and binocular function? Graefe's Arch Clin Exp Ophthalmol 249:925–935. https://doi.org/10.1007/s00417-010-1570-z
38. Chen AH, O'Leary DJ (2002) Are there age differences in the accommodative response curve between 3 and 14 years of age? Ophthalmic Physiol Opt 22:119–125
39. Anderson HA, Glasser A, Manny RE, Stuebing KK (2010) Age-related changes in accommodative dynamics from preschool to adulthood. Invest Ophthalmol Vis Sci 51:614–622. https://doi.org/10.1167/iovs.09-3653
40. Sreenivasan V, Irving EL, Bobier WR (2011) Effect of near adds on the variability of accommodative response in myopic children. Ophthalmic Physiol Opt 31:145–154. https://doi.org/10.1111/j.1475-1313.2010.00818.x
41. Mordi JA, Ciuffreda KJ (1998) Static aspects of accommodation: age and presbyopia. Vis Res 38:1643–1653
42. Charman WN, Radhakrishnan H (2009) Accommodation, pupil diameter and myopia. Ophthalmic Physiol Opt 29:72–79. https://doi.org/10.1111/j.1475-1313.2008.00611.x
43. Abbott ML, Schmid KL, Strang NC (1998) Differences in the accommodation stimulus response curves of adult myopes and emmetropes. Ophthalmic Physiol Opt 18:13–20
44. Norton TT, Gamlin PD (1999) The near response, emmetropia and myopia. Ophthalmic Physiol Opt 19:79–80
45. Mutti DO, Mitchell GL, Hayes JR, Jones LA, Moeschberger ML, Cotter SA et al (2006) Accommodative lag before and after the onset of myopia. Invest Ophthalmol Vis Sci 47:837–846
46. Gong CR, Troilo D, Richdale K (2017) Accommodation and phoria in children wearing multifocal contact lenses. Optom Vis Sci 94: 353–360. https://doi.org/10.1097/OPX.0000000000001044.
47. Paune J, Thivent S, Armengol J, Quevedo L, Faria-Ribeiro M, Gonzalez-Meijome JM (2016) Changes in peripheral refraction, higher-order aberrations, and accommodative lag with a radial refractive gradient contact lens in young myopes. Eye Contact Lens 42:380–387. https://doi.org/10.1097/icl.0000000000000222
48. Goss DA (1986) Effect of bifocal lenses on the rate of childhood myopia progression. Am J Optom Physiol Optic 63:135–141
49. Goss DA, Grosvenor T (1990) Rates of childhood myopia progression with bifocals as a function of nearpoint phoria: consistency of three studies. Optom Vis Sci 67:637–640
50. Fulk GW, Cyert LA, Parker DE (2000) A randomized trial of the effect of single-vision vs. bifocal lenses on myopia progression in children with esophoria. Optom Vis Sci 77:395–401