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ORIGINAL ARTICLE

Effect of peripheral defocus on axial growth and modulation of refractive error in children with anisohyperopia

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Abstract

Purpose: To establish whether axial growth and refractive error can be modulated in anisohyperopic children by imposing relative peripheral hyperopic defocus (RPHD) using multifocal soft contact lenses.

Methods: This study is a prospective, controlled paired-eye study with anisohyperopic children. Axial growth and refractive error were observed without intervention for the first 6 months of the 3-year trial with participants wearing single vision spectacles. Then, participants wore a centre-near, multifocal, soft contact lens (+2.00 D add) in their more hyperopic eye for 2 years, with a single vision contact lens worn in the fellow eye if required. The 'centre-near' portion of the contact lens in the more hyperopic eye corrected distance refractive error while the 'distance' portion imposed hyperopic defocus in the peripheral retina. Participants reverted to single vision spectacles for the final 6 months.

Results: Eleven participants, mean age of 10.56 years (SD 1.43; range 8.25–13.42), completed the trial. No increase in axial length (AL) was found during the first 6 months in either eye ($p > 0.99$). Axial growth across the 2-year intervention period was 0.11 mm (SEM 0.03; $p = 0.06$) in the test eye versus 0.15 mm (SEM 0.03; $p = 0.003$) in the control eye. AL was invariant during the final 6 months in both eyes ($p > 0.99$). Refractive error was stable during the first 6 months in both eyes ($p = 0.71$). Refractive error change across the 2-year intervention period was −0.23 D (SEM 0.14; $p = 0.32$) in the test eye versus −0.30 D (SEM 0.14; $p = 0.61$) in the control eye. Neither eye demonstrated a change in refractive error during the final 6 months ($p > 0.99$).

Conclusions: Imposing RPHD using the centre-near, multifocal, contact lens specified here did not accelerate axial growth nor reduce refractive error in anisohyperopic children.

KEYWORDS
anisometropia, axial growth, contact lenses, hyperopia, peripheral defocus, refractive error

INTRODUCTION

The visual consequences of hyperopia[1–5] and anisometropia,[6,7] namely strabismus and amblyopia, are well documented. The prevalence of anisometropia varies by ethnicity and geographical location. The proportion of anisometropes among White children in the UK at age 6–7 years is around 9%, with a similar level found at 12–13 years of age. Additionally, it is more common in those with moderate hyperopia.[8] In Australia, the prevalence is reported as 1.6% in 6-year-old children,[9] versus 6.7% in 4- to 13-year-old American Indians[10] and 9.9% in 7- to 18-year-old Taiwanese children.[11] The pathological implications associated with eyes of short axial length (AL), the predominant feature in hyperopia,[12] have also been established,[13–15] including predisposition to angle closure glaucoma[13,15] and vascular abnormalities, such as central and branch retinal vein occlusion.[14]

Until recently,[16] attempts to modulate refractive error in children with hyperopia have been absent from the literature and remain unaddressed in those with anisohyperopia.

Stochastic factors appear to play a role in the aetiology of refractive errors as inferred by the existence of anisometropia.[6] In anisometropes, despite sharing the same genome, and for the most part, similar environmental exposure, each eye emerges with a different refractive error. Anisometropia can be present early in life with subsequent ocular development complicated by amblyopia.[6,7] However, anisometropia often develops later; it seems that the regulated pattern of growth at around the age of 6 years exhibits increasing variability between individuals and between the two eyes of an individual.[6]

The ability to modulate axial growth in a range of species by imposing single vision, full-field relative hyperopic and myopic defocus has been widely reported.[17–21] Furthermore, the literature demonstrates that short-term changes in AL and choroidal thickness occur in response to hyperopic defocus in humans.[22–26] The progression of myopia and axial growth can be slowed in children and adolescents using soft multifocal or dual-focus contact lenses.[27–30] These contact lenses are designed to impose myopic defocus through the outer optic zone, while simultaneously correcting distance refractive error through the central optic zone. More recently, work from the present authors has shown the ability to accelerate axial growth in children with isohyperopia using centre-near multifocal contact lenses to impose relative peripheral hyperopic defocus (RPHD).[16]

The ability to modulate refractive error and axial growth in children with anisohyperopia by imposing RPHD has not yet been tested. Given that axial growth can be accelerated in children with isohyperopia by imposing hyperopic defocus using multifocal contact lenses,[16] applying a similar principle to anisohyperopes is a natural extension to this work.

Key points

- Unlike similar work with isohyperopes, the rate of eye growth did not increase using the multifocal soft contact lens specified in the present study for children with anisohyperopia.
- The reduction in refractive error did not accelerate using the multifocal soft contact lens specified in the present study for children with anisohyperopia.
- Earlier intervention and imposing a greater degree of peripheral defocus is an opportunity for future work to build upon the findings in the present study.

METHODS

Prior to commencing the research, ethical approval was obtained from both the National Health Service Health Research Authority and Aston University Research Ethics Committees with the study designed to follow the tenets of the Declaration of Helsinki. Each participant, and their parent or guardian where appropriate, was given detailed information regarding the nature of the study, both verbally and in written form; this allowed informed consent and assent to take place prior to participation. Participants were required to complete a short questionnaire[31] to ensure they met the inclusion criteria. The programme of research was registered as a clinical trial: ClinicalTrials.gov NCT02686879. Suitable candidates for the study were recruited by displaying notices at the research sites. Potential participants were also sourced through a database search at the research venues to identify individuals who met the age and refractive error inclusion criteria.

Participants aged between 8 and <16 years were recruited. Axial growth and refractive error were observed without intervention for the first 6 months of the trial with participants wearing their habitual spectacle correction during this period. Between the 6- and 30-month time points of the 3-year trial, participants wore a centre-near multifocal soft contact lens in their more hyperopic eye for a minimum of 10 h per day for 6 days per week. A single vision contact lens was worn in the fellow eye if required, that is if the level of hyperopia in this eye required refractive correction. Monthly disposable, comfilcon A multifocal contact lenses (Biofinity, coopervision.com) with a centre-near design and a +2.00 D add were worn throughout the intervention period in the more hyperopic (intervention) eye and an equivalent single vision contact lens (monthly disposable, comfilcon A) was worn in the fellow (control) eye if required. The power of the central portion of the intervention lens was selected to correct distance refractive error while simultaneously exposing the retina to RPHD from the outer distance zone (see Figure 1). A +2.00 D add was selected in line with previous refractive error modulation studies[27,28,32] to strike a balance between ensuring adequate visual performance[33] while imposing peripheral defocus at a level sufficient to test the hypothesis.[30] The power profile of the Biofinity centre-near lens design has a measured add close to its nominal value at +1.83 D for +2.00 D.[34] The intervention was withdrawn for the remaining 6 months of the trial and participants reverted to optimal single vision spectacle lens correction as determined at the penultimate visit using standard objective and subjective refraction. Changes to axial growth and refractive error were measured at the final visit.

Inclusion and exclusion criteria are summarised in Table 1 and are in line with earlier work in children with isohyperopia.[16] Full details of primary and secondary outcomes' measures, including time points, are provided in Tables 2–5 and Figures 2 and 3. Key parameters

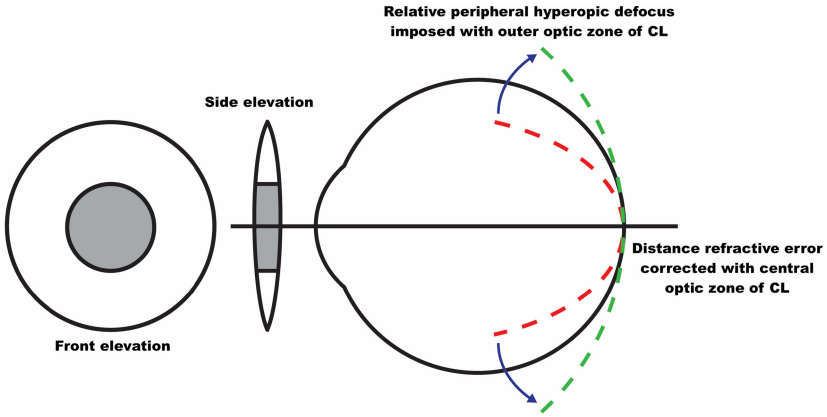

FIGURE 1 Schematic to demonstrate the concept of relative peripheral hyperopic defocus imposed in the more hyperopic eye with a centre-near multifocal contact lens (CL) while the full refractive error is corrected centrally.[16]

TABLE 1 Summary of inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Between 8 and <16 years of age	Previous contact lens wear
Parents must have read, understood and signed the informed consent form	Participating in another clinical study
Participants must have read, understood and signed the consent or assent form as appropriate	Regular use of medication to treat ocular conditions
Participants agreed to wear contact lenses for a minimum of 10 h per day, 6 days per week for the 2-year intervention period	Current use of systemic medication that could impact upon successful contact lens wear or affect focusing ability
Be in good general health with no contraindications to contact lens wear	Participants who were unable to provide informed consent without the aid of an interpreter due to lack of funding available for the provision of this facility
Maximum manifest spherical refractive error of +6.00 D	Findings identified during contact lens assessment that would preclude contact lens wear
Maximum manifest cylindrical refractive error of −1.00 D	Known ocular or systemic disease. Participants with amblyopia/strabismus were not excluded
Manifest anisometropia of >1.00 D (mean spherical error)	
Minimum manifest mean spherical refractive error of +2.00 D in the more hyperopic eye	
Be competent at handling contact lenses and understand the instructions given to ensure safe wear	

TABLE 2 Axial length (AL) at each visit.

Time point (months)	AL (mm)	
Baseline	21.67 (SEM 0.20)	22.19 (SEM 0.21)
6	21.70 (SEM 0.19)	22.27 (SEM 0.21)
12	21.74 (SEM 0.19)	22.30 (SEM 0.21)
18	21.77 (SEM 0.19)	22.35 (SEM 0.21)
24	21.80 (SEM 0.18)	22.34 (SEM 0.20)
30	21.81 (SEM 0.19)	22.42 (SEM 0.22)
36	21.84 (SEM 0.19)	22.43 (SEM 0.22)
	Intervention eye ($n = 11$)	Control eye ($n = 11$)

Note: The intervention period is shaded orange.
Abbreviation: SEM, standard error of the mean.

TABLE 3 Post-cycloplegic, objective central mean spherical equivalent refractive error at each visit.

Time point (months)	Refractive error (D)	
Baseline	+5.28 (SEM 0.44)	+3.37 (SEM 0.35)
6	+5.06 (SEM 0.46)	+3.28 (SEM 0.37)
18	+4.95 (SEM 0.41)	+3.02 (SEM 0.39)
30	+4.83 (SEM 0.45)	+2.98 (SEM 0.41)
36	+4.94 (SEM 0.56)	+3.01 (SEM 0.44)
	Intervention eye ($n = 11$)	Control eye ($n = 11$)

Note: The intervention period is shaded orange.
Abbreviation: SEM, standard error of the mean.

TABLE 4 Summary of secondary outcome measures for the test eye group and the control eye group.

	Baseline		6 months		12 months	
Measure	**Test**	**Control**	**Test**	**Control**	**Test**	**Control**
Unaided DV LogMAR	0.18 (0.04)	−0.01 (0.02)	0.19 (0.04) $p > 0.99$	−0.02 (0.02) $p > 0.99$	0.17 (0.04) $p > 0.99$	−0.01 (0.02) $p > 0.99$
Spectacle DVA LogMAR	0.06 (0.04)	−0.09 (0.02)	0.06 (0.04) $p > 0.99$	−0.07 (0.01) $p = 0.96$	0.03 (0.04) $p > 0.99$	−0.09 (0.01) $p > 0.99$
Spectacle NVA LogMAR	0.28 (0.02)	0.19 (0.02)	0.25 (0.02) $p > 0.99$	0.18 (0.01) $p > 0.99$	0.27 (0.02) $p > 0.99$	0.16 (0.02) $p > 0.99$
Spectacle stereoacuity (sec of arc)	78.00 (9.17)	84.00 (9.80) $p > 0.99$	90.00 (10.00) $p > 0.99$	72.00 (8.00) $p > 0.99$	78.00 (9.17) $p > 0.99$	72.00 (8.00) $p > 0.99$
Contrast sensitivity with spectacles			1.51 (0.02)	1.58 (0.02)		
CC (mm)	7.78 (0.10)	7.76 (0.09)	7.79 (0.09) $p > 0.99$	7.79 (0.09) $p = 0.95$	7.79 (0.10) $p > 0.99$	7.79 (0.09) $p > 0.99$
ACD (mm)	3.33 (0.09)	3.45 (0.08)	3.35 (0.09) $p = 0.21$	3.48 (0.08) $p = 0.06$		
Amplitude of accommodation (D)	11.01 (0.48)	11.33 (0.38)	10.94 (0.37) $p > 0.99$	11.11 (0.37) $p > 0.99$	10.74 (0.40) $p > 0.99$	11.54 (0.26) $p > 0.99$
Accommodative lag with spectacles (D)	0.78 (0.10)	0.93 (0.06) $p > 0.99$	1.04 (0.12) $p > 0.99$	0.93 (0.12) $p > 0.99$	1.00 (0.10) $p > 0.99$	1.10 (0.08) $p > 0.99$
MSE relative peripheral refraction temporal 30° (D)	−2.40 (0.46)	−1.45 (0.30)	−2.68 (0.54) $p > 0.99$	−1.81 (0.51) $p > 0.99$		
MSE relative peripheral refraction nasal 30° (D)	−0.55 (0.48)	−0.39 (0.26)	−1.15 (0.44) $p = 0.49$	−0.69 (0.41) $p > 0.99$		
MSE relative peripheral refraction superior 20° (D)	−0.43 (0.27)	−0.36 (0.26)	−0.45 (0.32) $p > 0.99$	−0.41 (0.25) $p > 0.99$		
MSE relative peripheral refraction inferior 20° (D)	−0.71 (0.13)	−0.21 (0.17)	−0.26 (0.27) $p = 0.88$	−0.05 (0.21) $p > 0.99$		

Note: *p* Values are for within-subject differences between consecutive measures. Values within parentheses are SEM.

Abbreviations: ACD, anterior chamber depth; CC, corneal curvature; DV, distance vision; DVA, distance visual acuity; MSE, mean spherical equivalent; NVA, near visual acuity.

included measures of unaided distance vision and distance visual acuity (DVA) at 6 m along with near visual acuity at 0.25 m undertaken with high contrast logMAR charts and determined using a by-letter scoring method (0.02 logMAR units per letter). Biometric assessment included measures of AL, anterior chamber depth (ACD) and corneal curvature (CC) and was taken using the IOLMaster 500 (zeiss.com).[35] For AL, 10 measurements were taken per eye and the composite value recorded. Subjective refraction was recorded prior to instillation of cyclopentolate hydrochloride 1% using standard optometric techniques. Measures of accommodative lag were also obtained (prior to cycloplegia) using the Grand Seiko WAM-5500 autorefractor (grandseiko.com).[36] Participants were asked to view a high-contrast Maltese cross, 25 mm in size, binocularly at a distance of 0.33 m while wearing their contact lens correction, with measures of accommodative lag taken from the dominant eye only,[37] which was determined with the commonly used hole-in-the-card test to achieve a binary outcome.[38] Amplitude of accommodation was assessed using a Royal Air Force rule with the mean of three push-up and three pull-down measures reported.[39,40] Objective central refraction was measured 30 min after instillation of the cycloplegic agent using the Grand Seiko WAM-5500 autorefractor while viewing a diffuse target at a 6 m equivalent distance. Post-cycloplegic peripheral refraction measures were undertaken using the same instrument at 30° temporally, 30° nasally, 20° superiorly and 20° inferiorly. Here, participants were asked to fixate on high-contrast Maltese crosses, 25 mm in size, in photopic conditions (440 lux) which were placed on a wall at 1.64 m to achieve the desired eccentricity for each of the four peripheral measures. Non-cycloplegic measures of peripheral refraction were also taken with contact lenses in situ. Central contrast sensitivity was recorded monocularly with spectacle and contact lens correction using a computerised version of the Pelli–Robson chart (thomson-software-solutions.com) at a distance of 1 m. Stereoacuity was measured using the TNO Randot Stereotest (Edition 15, lameris-group.nl) at a distance of 0.4 m with the spectacle and contact lens correction.

18 months		24 months		30 months		36 months	
Test	**Control**	**Test**	**Control**	**Test**	**Control**	**Test**	**Control**
0.16 (0.04) $p=0.80$	−0.03 (0.02) $p>0.99$	0.15 (0.04) $p>0.99$	−0.04 (0.02) $p>0.99$	0.17 (0.04) $p=0.86$	−0.03 (0.03) $p>0.99$	0.17 (0.05) $p>0.99$	−0.04 (0.03) $p>0.99$
0.03 (0.04) $p>0.99$	−0.10 (0.01) $p>0.99$	0.03 (0.04) $p>0.99$	−0.11 (0.01) $p>0.99$	0.07 (0.04) $p=0.10$	−0.09 (0.01) $p=0.22$	0.08 (0.04) $p>0.99$	−0.06 (0.01) $p>0.99$
0.25 (0.02) $p>0.99$	0.17 (0.01) $p>0.99$	0.21 (0.02) $p>0.99$	0.11 (0.02) $p=0.04$	0.22 (0.02) $p>0.99$	0.11 (0.02) $p>0.99$	0.22 (0.02) $p>0.99$	0.13 (0.02) $p>0.99$
90.00 (10.00) $p>0.99$							
				1.54 (0.03) $p>0.99$	1.61 (0.02) $p=0.50$	1.53 (0.04) $p>0.99$	1.62 (0.03) $p>0.99$
7.82 (0.09) $p=0.22$	7.79 (0.08) $p>0.99$	7.81 (0.10) $p>0.99$	7.81 (0.09) $p>0.99$	7.79 (0.10) $p>0.99$	7.80 (0.08) $p>0.99$	7.79 (0.09) $p>0.99$	7.78 (0.09) $p>0.99$
3.37 (0.09) $p=0.07$	3.49 (0.08) $p>0.99$			3.36 (0.09) $p>0.99$	3.48 (0.08) $p>0.99$	3.37 (0.09) $p>0.99$	3.47 (0.08) $p>0.99$
11.31 (0.50) $p>0.99$	11.30 (0.29) $p>0.99$	10.95 (0.46) $p>0.99$	11.54 (0.38) $p>0.99$	11.02 (0.37) $p>0.99$	11.18 (0.31) $p>0.99$	10.79 (0.40) $p>0.99$	11.62 (0.29) $p>0.99$
1.16 (0.12) $p>0.99$							
−2.24 (0.64) $p>0.99$	−1.27 (0.70) $p>0.99$			−2.15 (0.70) $p>0.99$	−1.27 (0.51) $p>0.99$	−2.18 (0.76) $p>0.99$	−1.50 (0.53) $p>0.99$
−1.11 (0.52) $p=0.51$	−0.96 (0.43) $p>0.99$			−2.18 (0.81) $p=0.65$	−0.98 (0.60) $p>0.99$	−1.47 (0.66) $p=0.70$	−0.94 (0.45) $p>0.99$
−0.86 (0.45) $p>0.99$	−0.52 (0.37) $p>0.99$			−0.66 (0.40) $p>0.99$	−0.56 (0.33) $p>0.99$	−0.54 (0.41) $p>0.99$	−0.60 (0.29) $p>0.99$
−0.16 (0.34) $p>0.99$	−0.36 (0.35) $p>0.99$			−0.62 (0.17) $p>0.99$	−0.60 (0.35) $p>0.99$	−0.86 (0.12) $p>0.99$	−0.52 (0.41) $p>0.99$

Statistical analyses

All data were analysed using commercially available software, SPSS, v. 25, (ibm.com). Sample size calculation indicated that a total of 11 participants would be required to achieve 80% power for an effect size of 0.25 at a significance level of 5% using a mixed factor repeated measures ANOVA design (G*Power 3.1, psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower). Data were examined with the Bonferroni correction applied throughout.[41–43]

RESULTS

In total, 11 participants were recruited, comprising eight females and three males with an age range at baseline of 8.25–13.42 years, mean 10.56 years (SD 1.43 years); these data were normally distributed (Kolmogorov–Smirnov, $Z=0.18$, $p=0.20$). All participants completed the trial and reported compliance with the prescribed wearing schedule. There were no adverse events related to contact lens wear. All participants required contact lens correction in both eyes. The primary outcome measures were changed to AL and post-cycloplegic central refractive error which are detailed in Tables 2 and 3 and Figures 2 and 3. Secondary outcome measures are summarised in Tables 4 and 5.

Overall, AL changed over time ($F_{(6,60)}=14.81$, $p<0.001$), although an interaction between factors demonstrated that this occurred in the control eye only ($F_{(6,60)}=2.61$, $p=0.03$). For the intervention eye, AL did not change from baseline to the 6-month time point ($p>0.99$), throughout the 2 years of intervention ($p=0.06$) or after the intervention was withdrawn for the final 6 months of the trial ($p>0.99$). For the control eye, AL did not change significantly from baseline to the 6-month time point ($p=0.05$). Axial growth accelerated throughout the 2 years of intervention ($p=0.003$) but did not change once the intervention was withdrawn for the final 6 months of the trial ($p>0.99$). Observed power was 0.82. AL data from baseline to the end point of the

TABLE 5 Summary of outcomes comparing spectacle versus contact lens measures for the test eye group (T) and the control eye group (C).

	6 months		12 months		18 months		24 months		30 months	
Measure	**Spectacle**	**Contact lens**	**Spectacle**	**Contact lens**	**Spectacle**	**Contact lens**	**Spectacle**	**Contact lens**	**Spectacle**	**Contact lens**
DVA: spectacle versus contact lens	T 0.06 (0.04) C −0.07 (0.01)	T 0.24 (0.04) C 0.02 (0.02)	T 0.03 (0.04) $p = 0.54$ C −0.09 (0.01) $p > 0.99$	T 0.16 (0.03) $p = 0.08$ C 0.00 (0.02) $p > 0.99$	T 0.03 (0.04) $p > 0.99$ C −0.10 (0.01) $p > 0.99$	T 0.17 (0.04) $p > 0.99$ C −0.03 (0.02) $p > 0.99$	T 0.03 (0.04) $p > 0.99$ C −0.11 (0.01) $p > 0.99$	T 0.16 (0.04) $p > 0.99$ C −0.03 (0.02) $p > 0.99$	T 0.07 (0.04) $p = 0.05$ C −0.09 (0.01) $p = 0.20$	T 0.19 (0.04) $p > 0.99$ C −0.04 (0.02) $p > 0.99$
NVA: spectacle versus contact lens	T 0.25 (0.02) C 0.18 (0.01)	T 0.30 (0.02) C 0.22 (0.01)	T 0.27 (0.02) $p > 0.99$ C 0.16 (0.02) $p > 0.99$	T 0.25 (0.02) $p > 0.99$ C 0.20 (0.00) $p > 0.99$	T 0.25 (0.02) $p = 0.82$ C 0.17 (0.01) $p > 0.99$	T 0.24 (0.02) $pp = 0.01$ C 0.19 (0.01) $p > 0.99$	T 0.21 (0.02) $p = 0.38$ C 0.11 (0.02) $p > 0.99$	T 0.24 (0.02) $p > 0.99$ C 0.16 (0.00) $p > 0.99$	T 0.22 (0.02) $p > 0.99$ C 0.11 (0.02) $p > 0.99$	T 0.22 (0.01) $p > 0.99$ C 0.17 (0.01) $p > 0.99$
Stereoacuity: spectacle versus contact lens			90.00 (10.00)	168.00 (39.80)			78.00 (9.17) $p = 0.17$	114.00 (16.61) $p = 0.10$		
Contrast sensitivity: spectacle versus contact lens	T 1.51 (0.02) C 1.58 (0.02)	T 1.53 (0.03) C 1.54 (0.02)							T 1.54 (0.03) $p = 0.51$ C 1.61 (0.02) $p = 0.17$	T 1.51 (0.03) $p = 0.80$ C 1.60 (0.02) $p = 0.10$
Accommodative lag: spectacle versus contact lens			1.04 (0.12)	1.70 (0.09)			1.00 (0.10) $p = 0.74$	1.60 (0.11) $p = 0.44$		
Central contact lens power		T +3.59 (0.42) C +2.00 (0.39)		T +3.41 (0.44) $p = 0.12$ C +1.89 (0.41) $p = 0.53$		T +3.25 (0.46) $p = 0.02$ C +1.75 (0.43) $p = 0.25$		T +3.07 (0.43) $p = 0.04$ C +1.66 (0.43) $p = 0.38$		T +3.14 (0.47) $p > 0.99$ C +1.68 (0.45) $p > 0.99$
Peripheral refraction—contact lenses in situ temporal 30° (D)				T +2.69 (0.40) C +0.98 (0.28)						
Peripheral refraction—contact lenses in situ nasal 30° (D)				T +2.25 (0.53) C +0.77 (0.24)						
Peripheral refraction—contact lenses in situ superior 20° (D)				T +1.03 (0.40) C +0.01 (0.35)						
Peripheral refraction—contact lenses in situ inferior 20° (D)				T +1.57 (0.45) C +0.39 (0.37)						

Note: *p* Values are for within-subject differences between consecutive measures. Values within parentheses are standard error of the mean (SEM).

Abbreviations: DVA, distance visual acuity; NVA, near visual acuity.

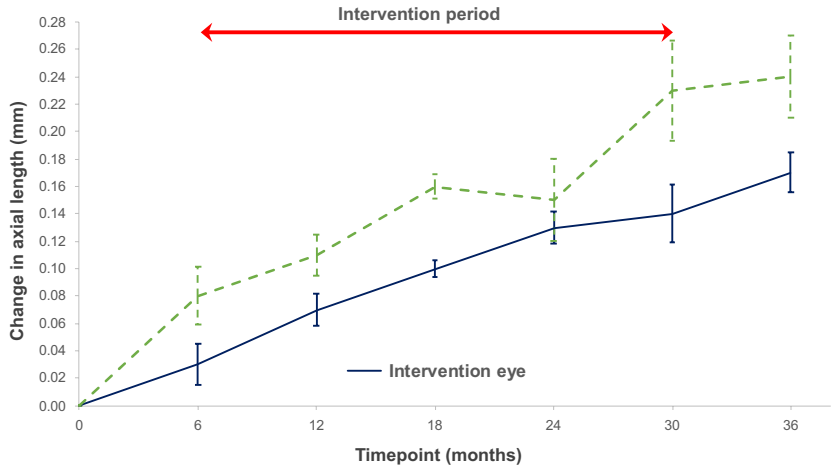

FIGURE 2 Change in axial length (mean ± SEM).

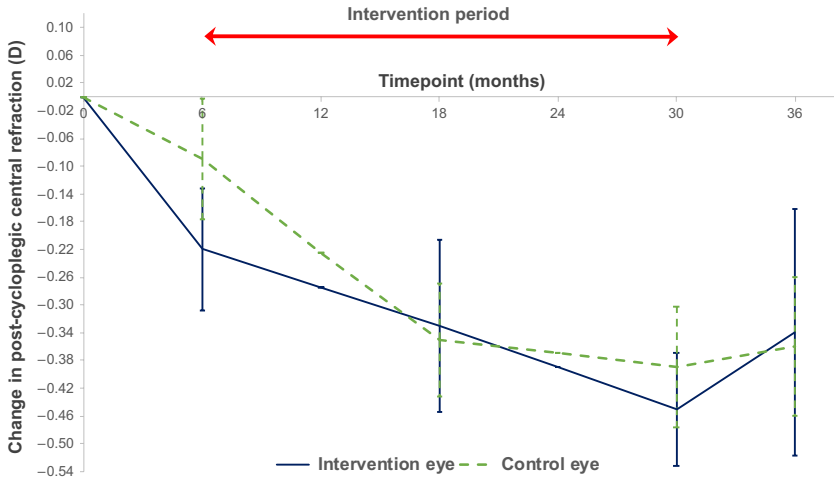

FIGURE 3 Change in post-cycloplegic, objective central mean spherical equivalent refractive error (mean ± SEM).

trial are detailed in Table 2, with changes over time illustrated in Figure 2.

Post-cycloplegic mean spherical equivalent central refractive error decreased over time ($F_{(4,40)} = 4.60$, $p = 0.004$) with an interaction between factors demonstrating that this was similar in both the intervention eye and the control eye ($F_{(4,40)} = 0.32$, $p = 0.86$) and the observed power was 0.11. Refractive error data from baseline to the end point of the trial are given in Table 3, with changes over time provided in Figure 3.

DISCUSSION

This paired-eye clinical trial has explored for the first time whether the interocular differences in AL and refractive error at baseline can be reduced in children with anisohyperopia by imposing RPHD unilaterally in the more hyperopic eye, with the fellow eye serving as a control. Measurements of peripheral refraction with the multifocal contact lens in situ showed that the intended level of RPHD was achieved in the intervention eye. Nevertheless, despite the imposition of RPHD, AL did not increase significantly over time. Intriguingly, the AL in the control eye did increase over the trial period, and in fact, the interocular difference in AL was greater at the point of exit from the trial than at baseline. The findings here are in contrast to similar work with isohyperopes[16] where axial growth accelerated with the imposition of RPHD.

While mean post-cycloplegic refractive error decreased over time, this was by a similar amount in both the intervention and control eyes. As with AL, there was a failure to close the gap between the interocular difference in refractive error measured at baseline, although this outcome measure did not achieve statistical power. It is also worth observing the variability associated with measurement of refraction,[44] which may be a factor in this outcome. The lack of response to the imposition of RPHD may be due to a failure of eyes with high levels of hyperopia to emmetropise early in life; a theory postulated in earlier work where

these hyperopes are 'left behind' rather than being regulated towards emmetropia.[6]

Stereoacuity was similar to both spectacles and contact lenses, which is in keeping with findings from earlier work showing that stereoacuity appears to be preserved in multifocal contact lens wear compared to single vision correction, albeit in a presbyopic cohort.[45] In terms of contrast sensitivity, measures were similar to spectacles compared with both single vision and multifocal contact lenses and did not change over time; this offers reassurance that visual performance appears adequate for young wearers with this form of correction.

With respect to anterior eye parameters, as with previous refractive error modulation work in myopes,[29,46] CC did not change over time in either eye. Similarly, ACD did not change over time suggesting that the longitudinal increase in AL observed in the control eye was likely to be due to vitreous chamber depth changes.

Accommodative lag with spectacle correction in the intervention eye did not change over time although it was significantly less than with contact lenses, which may reflect the fact that hyperopes would be expected to converge less through the former mode of correction. The finding here is interesting given that impaired lag has been implicated as a driver for axial growth progression in myopes;[47,48] nevertheless, this does not appear to be the case here.

As with previous work,[49–54] peripheral refraction was relatively myopic in all four quadrants in both the intervention and control eyes and did not change over time. Importantly, the trial demonstrated that centre-near multifocal contact lenses offer a viable method to induce defocus in anisohyperopes compared to the control eye fitted with a single vision contact lens. However, the role of peripheral defocus in the manipulation of axial growth remains uncertain, and the primary outcomes observed here for anisohyperopes fail to add clarity.

All participants completed the trial, which supports the findings from earlier work that children can successfully and safely transition into contact lens wear[55] and also adapt well to wearing a multifocal design unilaterally. While participants appeared to comply with the wearing regime outlined in Table 1, this was a self-reported measure.

While the imposition of RPHD appears to influence axial growth in isohyperopes,[16] the same does not hold true for anisohyperopes using the paradigm outlined in the present work. It seems that, unlike isohyperopes, the unique growth patterns typically experienced by anisohyperopes[7] are resistant to the influence of RPHD, at least in this age demographic and at the magnitude of defocus tested here. In the present trial, a single power, 'off-the-shelf' presbyopic design was used. Intervention with a tailored design using a smaller central zone and higher add power to impose greater levels of peripheral defocus may have greater impact on the modulation of axial growth and refractive error in these children.

For anisohyperopes, instinctively, the eye closer to emmetropia (the control) would be regarded as the 'normal' eye. However, given that the mean growth rate for the more hyperopic eye in the present work was closer to the expected norm,[56] should the control eye be considered as the 'abnormal' one of the pair? With this in mind, perhaps the primary endeavour should be to slow down growth in the *least* hyperopic eye, rather than attempting to accelerate growth in the more hyperopic eye. Taking this further, imposing competing defocus models could potentially yield the greatest result for anisohyperopes; that is to say, using myopic defocus to slow down growth in the least hyperopic eye, with the opposite approach taken in the fellow eye.

It remains to be seen whether earlier intervention and taking a more aggressive approach to defocus would yield more promising results; this provides an opportunity for future work to help avoid the near lifelong visual impairment that these individuals otherwise face.

AUTHOR CONTRIBUTIONS

Ian G. Beasley: Conceptualization (equal); data curation (lead); formal analysis (lead); investigation (lead); methodology (equal); project administration (lead); resources (supporting); validation (lead); visualization (lead); writing – original draft (lead); writing – review and editing (lead). **Leon N. Davies:** Conceptualization (supporting); formal analysis (supporting); investigation (supporting); methodology (supporting); project administration (supporting); resources (supporting); supervision (supporting); visualization (supporting); writing – original draft (supporting); writing – review and editing (supporting). **Nicola S. Logan:** Conceptualization (equal); data curation (supporting); formal analysis (supporting); funding acquisition (lead); investigation (supporting); methodology (equal); project administration (supporting); resources (lead); supervision (lead); validation (supporting); visualization (supporting); writing – original draft (supporting); writing – review and editing (supporting).

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CONFLICT OF INTEREST STATEMENT

The authors confirm that they do not have any commercial interest relevant to the subject of the paper. The contact lenses in the study were supplied free of charge by CooperVision. CooperVision did not sponsor the research and does not support or have an opinion regarding any of the content in the paper.

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REFERENCES

1. Kulp MT, Ying GS, Huang J, Maguire M, Quinn G, Ciner EB, et al. Associations between hyperopia and other vision and refractive error characteristics. *Optom Vis Sci*. 2014;91:383–9.
2. Klimek DL, Cruz OA, Scott WE, Davitt BV. Isoametropic amblyopia due to high hyperopia in children. *J AAPOS*. 2004;8:310–3.
3. Ingram RM. Refraction as a basis for screening children for squint and amblyopia. *Br J Ophthalmol*. 1977;61:8–15.
4. Ip JM, Robaei D, Kifley A, Wang JJ, Rose KA, Mitchell P. Prevalence of hyperopia and associations with eye findings in 6- and 12-year-olds. *Ophthalmology*. 2008;115:678–85.
5. Colburn JD, Morrison DG, Estes RL, Li C, Lu P, Donahue SP. Longitudinal follow-up of hypermetropic children identified during preschool vision screening. *J AAPOS*. 2010;14:211–5.
6. Flitcroft DI. Emmetropisation and the aetiology of refractive errors. *Eye*. 2014;28:169–79.
7. Flitcroft I, McCullough S, Saunders K. What can anisometropia tell us about eye growth? *Br J Ophthalmol*. 2020;105:1211–5.
8. O'Donoghue LO, McClelland JF, Logan NS, Rudnicka AR, Owen CG, Saunders KJ. Profile of anisometropia and aniso-astigmatism in children: prevalence and association with age, ocular biometric measures, and refractive status. *Invest Ophthalmol Vis Sci*. 2013;54:602–8.
9. Huynh SC, Wang XY, Ip J, Robaei D, Kifley A, Rose KA, et al. Prevalence and associations of anisometropia and aniso-astigmatism in a population based sample of 6 year old children. *Br J Ophthalmol*. 2006;90:597–601.
10. Dobson V, Harvey EM, Miller JM, Clifford-Donaldson CE. Anisometropia prevalence in a highly astigmatic school-aged population. *Optom Vis Sci*. 2008;85:512–9.
11. Shih YF, Hsiao CH, Wen SH, Lin LL, Chen CJ, Hung PT. Prevalence of anisometropia in Taiwanese schoolchildren. *J Formos Med Assoc*. 2005;104:412–7.
12. Strang NC, Schmid KL, Carney LG. Hyperopia is predominantly axial in nature. *Curr Eye Res*. 1998;17:380–3.
13. Lowe RF. Aetiology of the anatomical basis for primary angle-closure glaucoma. Biometrical comparisons between normal eyes and eyes with primary angle-closure glaucoma. *Br J Ophthalmol*. 1970;54:161–9.
14. Szigeti A, Schneider M, Ecsedy M, Nagy ZZ, Récsán Z. Association between retinal vein occlusion, axial length and vitreous chamber depth measured by optical low coherence reflectometry. *BMC Ophthalmol*. 2015;15:45. https://doi.org/10.1186/s12886-015-0031-1
15. Xu L, Cao WF, Wang YX, Chen CX, Jonas JB. Anterior chamber depth and chamber angle and their associations with ocular and general parameters: the Beijing eye study. *Am J Ophthalmol*. 2008;145:929–36.
16. Beasley IG, Davies LN, Logan NS. The effect of peripheral defocus on axial growth and modulation of refractive error in hyperopes. *Ophthalmic Physiol Opt*. 2022;42:534–44.
17. Schaeffel F, Glasser A, Howland HC. Accommodation, refractive error and eye growth in chickens. *Vision Res*. 1988;28:639–57.
18. Wildsoet C, Wallman J. Choroidal and scleral mechanisms of compensation for spectacle lenses in chicks. *Vision Res*. 1995;35:1175–94.
19. Norton TT, Siegwart JT Jr, Amedo AO. Effectiveness of hyperopic defocus, minimal defocus, or myopic defocus in competition with a myopiagenic stimulus in tree shrew eyes. *Invest Ophthalmol Vis Sci*. 2006;47:4687–99.
20. Smith EL III, Hung LF. The role of optical defocus in regulating refractive development in infant monkeys. *Vision Res*. 1999;39:1415–35.
21. Tkatchenko TV, Shen Y, Tkatchenko AV. Mouse experimental myopia has features of primate myopia. *Invest Ophthalmol Vis Sci*. 2010;51:1297–303.
22. Read SA, Collins MJ, Sander BP. Human optical axial length and defocus. *Invest Ophthalmol Vis Sci*. 2010;51:6262–9.
23. Chakraborty R, Read SA, Collins MJ. Hyperopic defocus and diurnal changes in human choroid and axial length. *Optom Vis Sci*. 2013;90:1187–98.
24. Moderiano D, Do M, Hobbs S, Lam V, Sarin S, Alonso-Caneiro D, et al. Influence of the time of day on axial length and choroidal thickness changes to hyperopic and myopic defocus in human eyes. *Exp Eye Res*. 2019;182:125–36.
25. Delshad S, Collins MJ, Read SA, Vincent SJ. The human axial length and choroidal thickness responses to continuous and alternating episodes of myopic and hyperopic blur. *PLoS One*. 2020;15:e0243076. https://doi.org/10.1371/journal.pone.0243076
26. Delshad S, Collins MJ, Read SA, Vincent SJ. Effects of brief periods of clear vision on the defocus-mediated changes in axial length and choroidal thickness of human eyes. *Ophthalmic Physiol Opt*. 2021;41:932–40.
27. Anstice NS, Phillips JR. Effect of dual-focus soft contact lens wear on axial myopia progression in children. *Ophthalmology*. 2011;118:1152–61.
28. Chamberlain P, Logan N, Jones D, Gonzalez-Meijome J, Saw S-M, Young G. Clinical evaluation of a dual-focus myopia control 1 day soft contact lens: 6-year results. American Academy of Optometry Annual Meeting. 2020.
29. Lam CSY, Tang WC, Tse DY-Y, Tang YY, To CH. Defocus incorporated soft contact (DISC) lens slows myopia progression in Hong Kong Chinese schoolchildren: a 2-year randomised clinical trial. *Br J Ophthalmol*. 2014;98:40–5.
30. Walline JJ, Walker MK, Mutti DO, Jones-Jordan LA, Sinnott LT, Giannoni AG, 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*. 2020;324:571–80.
31. Beasley IG. The effect of peripheral defocus on axial growth and modulation of refractive error in Hyperopes. PhD thesis, Aston University. 2021.
32. Walline JJ, Greiner KL, McVey ME, Jones-Jordan LA. Multifocal contact lens myopia control. *Optom Vis Sci*. 2013;90:1207–14.
33. Sha J, Bakaraju RC, Tilia D, Chung J, Delaney S, Munro A, et al. Short-term visual performance of soft multifocal contact lenses for presbyopia. *Arq Bras Oftalmol*. 2016;79:73–7.
34. Kim E, Bakaraju RC, Ehrmann K. Power profiles of commercial multifocal soft contact lenses. *Optom Vis Sci*. 2017;94:183–96.
35. Santodomingo-Rubido J, Mallen EA, Gilmartin B, Wolffsohn JS. A new non-contact optical device for ocular biometry. *Br J Ophthalmol*. 2002;86:458–62.
36. Sheppard AL, Davies LN. Clinical evaluation of the Grand Seiko Auto Ref/Keratometer WAM-5500. *Ophthalmic Physiol Opt*. 2010;30:143–51.
37. Flitcroft D, Morley JW. Accommodation in binocular contour rivalry. *Vision Res*. 1996;37:121–5.
38. Lopes-Ferreira D, Neves H, Queiros A, Faria-Ribeiro M, Peixoto-de-Matos SC, González-Méijome JM. Ocular dominance and visual function testing. *Biomed Res Int*. 2013;2013:238943. https://doi.org/10.1155/2013/238943
39. Rosenfield M, Cohen AS. Repeatability of clinical measurements of the amplitude of accommodation. *Ophthalmic Physiol Opt*. 1996;16:247–9.
40. Burns DH, Allen PM, Edgar DF, Evans BJW. Sources of error in clinical measurement of the amplitude of accommodation. *J Optom*. 2020;13:3–14.
41. Cohen J. The effect size. Statistical power analysis for the behavioral sciences. Abingdon: Routledge; 1988. p. 77–83.
42. Armstrong RA, Davies LN, Dunne MCM, Gilmartin B. Statistical guidelines for clinical studies of human vision. *Ophthalmic Physiol Opt*. 2011;31:123–36.
43. Armstrong RA. Statistical guidelines for the analysis of data obtained from one or both eyes. *Ophthalmic Physiol Opt*. 2013;33:7–14.
44. Bullimore MA, Fusaro RE, Adams CW. The repeatability of automated and clinician refraction. *Optom Vis Sci*. 1998;75:617–22.
45. Ferrer-Blasco T, Madrid-Costa D. Stereoacuity with balanced presbyopic contact lenses. *Clin Exp Optom*. 2011;94:76–81.
46. Aller TA, Liu M, Wildsoet CF. Myopia control with bifocal contact lenses: a randomized clinical trial. *Optom Vis Sci*. 2016;93:344–52.
47. Mutti DO, Mitchell GL, Hayes JR, Jones LA, Moeschberger ML, Cotter SA, et al. Accommodative lag before and after the onset of myopia. *Invest Ophthalmol Vis Sci*. 2006;47:837–46.

48. Chakraborty R, Ostrin A, Benavente-Perez A, Verkicharla PK. Optical mechanisms regulating emmetropisation and refractive errors: evidence from animal models. *Clin Exp Optom*. 2020;103: 55–67.
49. Verkicharla PK, Mathur A, Mallen EAH, Pope JM, Atchison DA. Eye shape and retinal shape, and their relation to peripheral refraction. *Ophthalmic Physiol Opt*. 2012;32:184–99.
50. Atchison DA, Li SM, Li H, Li SY, Liu LR, Kang MT, et al. Relative peripheral hyperopia does not predict development and progression of myopia in children. *Invest Ophthalmol Vis Sci*. 2015;56:6162–70.
51. Gilmartin B, Nagra M, Logan NS. Shape of the posterior vitreous chamber in human emmetropia and myopia. *Invest Ophthalmol Vis Sci*. 2013;54:7240–51.
52. Atchison DA, Charman WN. Can partial coherence interferometry be used to determine retinal shape? *Optom Vis Sci*. 2011;88:601–7.
53. Charman WN, Radhakrishnan H. Peripheral refraction and the development of refractive error: a review. *Ophthalmic Physiol Opt*. 2010;30:321–38.
54. Schmid GF. Association between retinal steepness and central myopic shift in children. *Optom Vis Sci*. 2011;88:684–90.
55. Bullimore MA. The safety of soft contact lenses in children. *Optom Vis Sci*. 2017;94:638–46.
56. Breslin KMM, O'Donoghue L, Saunders KJ. A prospective study of spherical refractive error and ocular components among Northern Irish schoolchildren (The NICER study). *Invest Ophthalmol Vis Sci*. 2013;54:4843–50.

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