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Effect of High Add Power, Medium Add Power, or Single-Vision Contact Lenses on Myopia Progression in Children
The BLINK Randomized Clinical Trial

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IMPORTANCE Slowing myopia progression could decrease the risk of sight-threatening complications.

OBJECTIVE To determine whether soft multifocal contact lenses slow myopia progression in children, and whether high add power (+2.50 D) slows myopia progression more than medium (+1.50 D) add power lenses.

DESIGN, SETTING, AND PARTICIPANTS A double-masked randomized clinical trial that took place at 2 optometry schools located in Columbus, Ohio, and Houston, Texas. A total of 294 consecutive eligible children aged 7 to 11 years with −0.75 D to −5.00 D of spherical component myopia and less than 1.00 D astigmatism were enrolled between September 22, 2014, and June 20, 2016. Follow-up was completed June 24, 2019.

INTERVENTIONS Participants were randomly assigned to wear high add power (n = 98), medium add power (n = 98), or single-vision (n = 98) contact lenses.

MAIN OUTCOMES AND MEASURES The primary outcome was the 3-year change in cycloplegic spherical equivalent autorefraction, as measured by the mean of 10 autorefraction readings. There were 11 secondary end points, 4 of which were analyzed for this study, including 3-year eye growth.

RESULTS Among 294 randomized participants, 292 (99%) were included in the analyses (mean [SD] age, 10.3 [1.2] years; 177 [60.2%] were female; mean [SD] spherical equivalent refractive error, −2.39 [1.00] D). Adjusted 3-year myopia progression was −0.60 D for high add power, −0.89 D for medium add power, and −1.05 D for single-vision contact lenses. The difference in progression was 0.46 D (95% CI, 0.29-0.63) for high add power vs single vision, 0.30 D (95% CI, 0.13-0.47) for high add vs medium add power, and 0.16 D (95% CI, −0.01 to 0.33) for medium add power vs single vision. Of the 4 secondary end points, there were no statistically significant differences between the groups for 3 of the end points. Adjusted mean eye growth was 0.42 mm for high add power, 0.58 mm for medium add power, and 0.66 mm for single vision. The difference in eye growth was −0.23 mm (95% CI, −0.30 to −0.17) for high add power vs single vision, −0.16 mm (95% CI, −0.23 to −0.09) for high add vs medium add power, and −0.07 mm (95% CI, −0.14 to −0.01) for medium add power vs single vision.

CONCLUSIONS AND RELEVANCE Among children with myopia, treatment with high add power multifocal contact lenses significantly reduced the rate of myopia progression over 3 years compared with medium add power multifocal and single-vision contact lenses. However, further research is needed to understand the clinical importance of the observed differences.

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Visual Abstract

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Supplemental content

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Group Information: Members of the BLINK Study Group are listed at the end of the article.

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Between 2000 and 2050, the worldwide prevalence of myopia is projected to increase from 23% to 54% and the prevalence of high myopia is projected to increase from 3% to 10%, based on a 2016 study.[1] Less time spent outdoors and increased near work time most likely explain the increased prevalence of myopia, although the specific attribute of outdoor time that protected people was unknown.[2] Myopia is associated with sight-threatening ocular sequelae, such as cataracts, retinal detachment, glaucoma, and choroidal atrophy.[3,4] Effective myopia control measures should therefore be implemented to reduce the risks associated with increasing myopia prevalence and high societal costs.

In the US, myopia typically begins between 8 and 10 years of age and progresses through 15 or 16 years of age.[5] Typical treatment involves single-vision glasses or contact lenses, but myopia control has become more standard, using orthokeratology,[6] soft multifocal contact lenses,[7] and low-concentration atropine.[8] Myopia control is typically prescribed at least until myopia progression is expected to stop naturally.

A modifiable risk factor for myopia progression is the optical profile of the eye. Specifically, focusing light in front of the retina slows eye growth in humans.[9,10] Soft multifocal contact lenses provide clear vision by focusing some light on the retina while simultaneously focusing some light in front of the retina to slow eye growth.[11-13] Higher add power contact lenses focus light further in front of the retina[14] and may lead to slower myopia progression than medium add power and nonmultifocal contact lenses (**Figure 1**). The Bifocal Lenses In Nearsighted Kids (BLINK) study randomly assigned children to wear single-vision (nonmultifocal) contact lenses or medium or high add power soft multifocal contact lenses for 3 years to determine whether commercially available soft multifocal contact lenses slow myopia progression and whether a higher add power provides more effective myopia control than a lower add power.

Key Points

Question Can soft multifocal contact lenses with a high add power slow myopia progression in children more than medium add power or single-vision contact lenses?

Findings In this randomized clinical trial that included 294 children aged 7 to 11 years with myopia (−0.75 D to −5.00 D), after 3 years, the use of high add power (+2.50 D) contact lenses resulted in myopia progression of −0.60 D, the use of medium add power (+1.50 D) contact lenses resulted in myopia progression of −0.89 D, and the use of single-vision contact lenses resulted in myopia progression of −1.05 D. The pairwise comparisons were statistically significant between high add power and single-vision contact lenses as well as between high add and medium add power contact lenses.

Meaning Among children with myopia, treatment with high add power multifocal contact lenses compared with medium add power multifocal and single-vision contact lenses reduced the rate of myopia progression over 3 years, but further research is needed to understand the clinical importance of the observed differences as well as long-term outcomes.

Methods

Study Oversight

Ethical approval was obtained from institutional review boards at The Ohio State University and the University of Houston. Written informed consent was provided by a parent/legal guardian, and written assent was provided by the participant. A data and safety monitoring committee oversaw the trial and reviewed the trial data for patient safety at regular intervals.

Study Design and Setting

This 3-year, double masked, 3-group, parallel randomized clinical trial of children with myopia was conducted in Houston, Texas, and Columbus, Ohio. The study protocol was summarized[15] and is available in Supplement 1. All investigators and key personnel were trained and certified on study procedures prior to study commencement. Participants were enrolled between September 22, 2014, and June 20, 2016. Follow-up was completed on June 24, 2019.

The study had 3 specific aims, but this article only addresses the first: (1) to compare the change in myopia between single-vision contact lens wearers and soft bifocal contact lens wearers to test the hypothesis that soft bifocal contact lenses slow myopia progression in a dose-dependent manner in children, (2) to determine whether peripheral defocus created by soft bifocal contact lenses is associated with myopia progression to test the hypothesis that peripheral myopic defocus slows myopia progression in children, and (3) to determine whether changes in ocular shape differ between children wearing single-vision and soft bifocal contact lenses to test the hypothesis that peripheral myopic defocus globally slows eye growth.

Eligibility Criteria

Eligible participants were aged 7 to 11 years; had myopia of −0.75 D to −5.00 D (spherical component by cycloplegic autorefraction), astigmatism less than 1.00 D cylinder, best-corrected visual acuity of 20/25 or better in each eye, binocular visual acuity of +0.1 logMAR (20/25) or better with +2.50 D add power soft multifocal contact lenses, and a clinically acceptable fit with study contact lenses at baseline; and were willing to participate in the study for 3 years. Participants were ineligible if they reported more than 1 month of gas permeable, soft bifocal, or orthokeratology contact lens wear; more than 1 month of myopia control (including atropine or bifocal spectacles); had systemic issues that could affect myopia or myopia progression; or if they were chronically using oral or ophthalmic steroids.[15]

Randomization and Masking

After verifying eligibility, REDCap[16] (a web-based electronic data capture system) issued a randomization assignment in a 1:1:1 ratio to wear single-vision contact lenses, medium add power (+1.50 D) soft multifocal contact lenses, or high

add power (+2.50 D) soft multifocal contact lenses. The randomization assignment was stratified by clinical site and age group (7-9 vs 10-11 y) using a random permuted block design with varying block sizes of 3 to 6. The data coordinating center verified the appropriate treatment group assignment after the unmasked examiner enrolled each participant. Masked examiners performed cycloplegic autorefraction and eye length measurements at annual visits. Participants and parents/legal guardians were masked by removing all contact lens labels prior to receiving the lenses, so it was nearly impossible to differentiate between single-vision and multifocal contact lenses.

Race/Ethnicity

Parents/legal guardians categorized their child's race/ethnicity according to National Institutes of Health–defined categories, because myopia prevalence and progression rates vary by race.[17]

Interventions

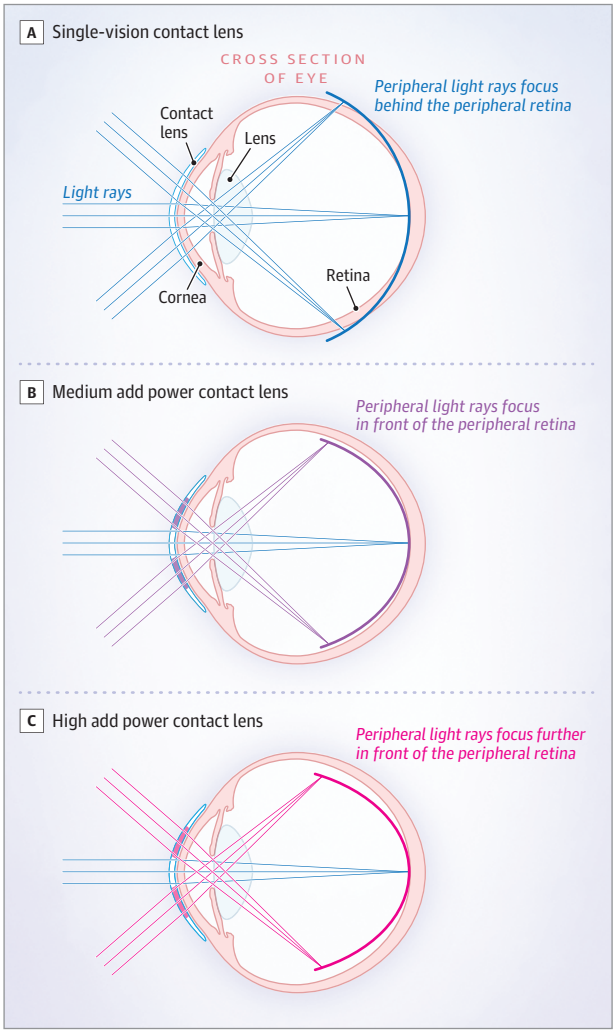
All participants wore Biofinity single-vision contact lenses, Multifocal D with a +1.50 D add power soft multifocal contact lenses, or Multifocal D with a +2.50 D add power soft multifocal contact lenses (CooperVision). All participants received contact lenses, solutions, and contact lens cases throughout the study at no charge; they also received updated spectacles at a reduced cost annually. Participants were encouraged to wear their contact lenses during the day as often as they could comfortably do so, but were restricted from overnight wear. A single-vision spectacle control group was not included to maximize masking to treatment group and because single-vision soft contact lenses do not alter myopia progression.[18]

Outcomes

The primary outcome was the 3-year change in spherical equivalent cycloplegic autorefraction (myopia progression). Ten measures of central refractive error were conducted on each eye with the Grand Seiko WAM-5500 Binocular Autorefractor/Keratometer (AIT Industries) and averaged.[19] Cycloplegia was achieved using 1 drop of 0.5% proparacaine or tetracaine followed by 2 drops of 1.0% tropicamide, separated by 5 minutes. Measurements were taken 25 minutes after the second drop of tropicamide. Participants fixated 20/30 size letters on a near-point test card viewed through a +4.00 D Badal lens. The letters were presented at the far point, then moved to a slightly blurred position to ensure relaxation of residual accommodation.[20]

Secondary outcomes presented in this article include axial elongation (eye growth), visual acuity, adverse events, and adherence. Other secondary outcomes not addressed in this article included accommodative lag (how accurately the eyes focus at near); peripheral measurements of refractive error and eye length under a variety of conditions (peripheral refractive error is believed to influence myopia progression and eye growth); choroidal thickness (blood vessels in the back of the eye that may signal changes in myopia); pupil size; aberrometry (measures very small changes in vision); and report of myopia risk factors, binocular vision and accommodation symptoms, and vision-specific quality of life (Supplement 1).

Figure 1. Theoretical Explanation of How Soft Multifocal Contact Lenses Slow Myopia Progression



Theoretical model showing that the peripheral rays through the distance portion of the single-vision contact lens focus behind the peripheral retina. The peripheral rays through the medium and high add portion of the multifocal contact lenses focus in front of the retina, acting as a cue to slow myopia progression and eye growth. The high add focuses further in front of the retina than the medium add, potentially acting as a stronger signal to slow eye growth.

The 3-year change from baseline in axial length (eye growth) was measured using the Lenstar LS 900 (Haag-Streit USA). The measurements were taken on each eye immediately after cycloplegic autorefraction, with the contralateral eye patched while fixating the internal red light. Five readings without a poor-quality warning indicator were obtained at baseline and each annual visit.

Visual acuity was measured using Bailey-Lovie logMAR visual acuity charts with luminance between 75 and 120 cd/m^2. Participants read the charts with both eyes open while wearing habitual refractive correction and a spherical overrefraction in a trial frame. From 4 m away, participants read

the first letter of every line until one was incorrectly read. Participants then read all 5 letters of each line, beginning 2 lines above the first letter missed, moving down the chart until 3 or more letters were missed on the same line. The same protocol was used at near using the Logarithmic Visual Acuity Chart 2000 "New ETDRS" near visual acuity chart (Precision Vision) held 40 cm from the eye.

Adherence was monitored by parental report of weekdays and weekend days that the participant usually wore contact lenses and the time the participant usually inserted and removed contact lenses during those periods. From that information, the number of hours per week that contact lenses were typically worn was calculated. The mean number of hours per day was calculated by dividing the hours per week by the number of days worn.

Adverse Events

Potential adverse events were reported by the unmasked examiner, and a final determination of the adverse event was conducted by the executive committee. Serious adverse events were defined as "fatal, life threatening, or resulted in a two-line loss of best corrected visual acuity or hospitalization." Severe adverse events were defined as "incapacitating or sight-threatening." Moderate adverse events "interfered with daily activities and/or were treated with prescription medication."

Sample Size

Sample size calculations assumed an α level of .05, 80% power, progression of −1.29 D over 3 years,[18] a 50% treatment effect (reducing the progression by 0.65 D for the high add power group), and a treatment effect for the medium add group that was halfway between the single-vision and the high add power group. A 30% to 50% reduction of myopia progression is generally considered to be clinically meaningful.[21] The sample size required was 24 participants per treatment group, or a total sample size of 72 participants. The ultimate sample size was determined by the second aim related to assessing changes in eye shape,[15] which required 89 participants per group, or a total sample size of 267 participants. Adjusting for 10% loss to follow-up[22,23] yielded a total sample size of 294 participants.

Statistical Analyses

We analyzed participants in their originally assigned treatment groups. Data from all participants who attended at least 1 subsequent annual visit were used to fit the models, regardless of whether a participant missed a visit. No missing outcomes were imputed. Repeated measures analyses using mixed linear models in SAS, version 9.4, Proc MIXED were undertaken to model myopia progression (primary outcome) and eye growth (secondary outcome). Models controlled for the baseline value of the outcome, clinic site, sex, age group (7-9 or 10-11 y), and eye (right or left). Site was fitted as a fixed effect. The repeated participant outcome measures result in clusters of correlated data. This correlation between eye and visit was modeled using a combination of unstructured and autoregressive covariance structures as described by Glynn and Rosner.[24] Linear model assumptions were checked. Additional details of the modeling are included in Supplement 2. The estimates of change assumed an equal mix of male and female participants, clinical sites, age groups, and right and left eyes, and that baseline values were equal to the mean values of those observed in the sample. Significant interactions that were retained in the model were between age group and time ($P < .001$; younger age group had a steeper slope) and treatment group and time ($P = .02$). The P values for the pairwise differences between treatment groups were adjusted using the step-down Bonferroni method.[25] Two-sided P values <.05 were considered statistically significant. Because of the potential for type I error due to multiple comparisons, findings for analyses of secondary end points should be interpreted as exploratory.

Using linear regression analyses, we examined whether wear time modified the effect of the treatment group on change in spherical equivalent to determine whether better adherence to treatment improved myopia control. Analyses of variance comparing treatment groups for different visual acuity measurements were conducted, and P values were adjusted using the step-down Bonferroni method as described above.

Post hoc analyses also compared the proportion of participants whose myopia progressed −1.00 D or more (the mean myopia progression of the control group) or eyes grew 0.36 mm or more (the equivalent of −1.00 D of myopia progression) by treatment group. The adjusted P values from the step-down Bonferroni method from Holm for 3 pairwise comparisons are presented.

Results

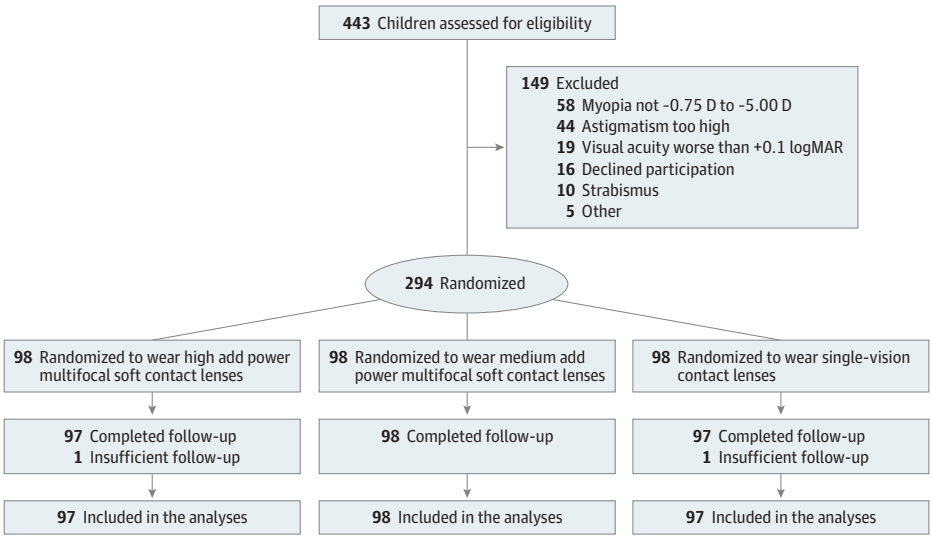
Of the 294 enrolled participants, 292 were included in the analyses (**Figure 2**) and 287 (97.6%) completed the 3-year visit. Overall, participants attended 861 of the 882 annual visits (97.6%). Complete data were available for 282 of 294 participants. Four participants did not attend the 1-year visit, 10 did not attend the 2-year visit, and 7 did not attend the 3-year visit.

Approximately 60% of the participants were female, the mean (SD) age was 10.3 (1.2) years, 60% were aged 10 or 11 years at baseline, 26% were Hispanic or Latino, and 68% were White.[15] The mean (SD) right eye cycloplegic spherical equivalent at baseline was −2.39 (1.00) D. Demographic and ocular characteristics of each treatment group at baseline are shown in **Table 1**.

Primary Outcome

For the high add power group, the mean myopia (mean value of both eyes) was −2.30 D at baseline and −2.84 D at 3 years, with a progression of −0.56 D (95% CI, −0.70 to −0.41). For the medium add power group, myopia was −2.46 D at baseline and −3.32 D at 3 years, with progression of −0.85 D (95% CI, −0.99 to −0.70). For the single-vision group, myopia was −2.45 D at baseline and −3.46 D at 3 years, with progression of −1.01 D (95% CI, −1.15 to −0.87) (**Figure 3**A and eFigure 1A in Supplement 3).

Figure 2. Flow of Participants in the BLINK Randomized Clinical Trial



Participants may have been excluded for multiple reasons, so the category numbers are greater than the number of excluded participants.

Table 1. Baseline Demographic and Ocular Characteristics in a Study of the Effect of High Add Power, Medium Add Power, or Single-Vision Contact Lenses on Myopia Progression in Children[a]

Characteristic	High add (+2.50 D; n = 98)	Medium add (+1.50 D; n = 98)	Single vision (n = 98)
Site, No. (%)			
Columbus, OH	46 (46.9)	48 (49.0)	49 (50.0)
Houston, TX	52 (53.1)	50 (51.0)	49 (50.0)
Age, y	10.3 (1.2)	10.3 (1.2)	10.3 (1.1)
7-9, No. (%)	39 (39.8)	39 (39.8)	39 (39.8)
10-11, No. (%)	59 (60.2)	59 (60.2)	59 (60.2)
Median (Q1-Q3)	10.2 (9.4-11.3)	10.5 (9.5-11.3)	10.5 (9.5-11.2)
Sex, No. (%)			
Female	64 (65.3)	49 (50.0)	64 (65.3)
Male	34 (34.7)	49 (50.0)	34 (34.7)
Ethnicity, No. (%)[b]			
Hispanic or Latino	26 (26.5)	26 (26.8)	25 (25.5)
Race, No. (%)[b]			
White	66 (67.3)	75 (76.5)	59 (60.2)
>1 race	13 (13.3)	7 (7.1)	11 (11.2)
Black or African American	5 (5.1)	7 (7.1)	17 (17.3)
Asian	9 (9.2)	7 (7.1)	9 (9.2)
American Indian or Alaska Native	3 (3.1)	1 (1.0)	1 (1.0)
Other	1 (1.0)	1 (1.0)	1 (1.0)
Native Hawaiian or other Pacific Islander	1 (1.0)	0	0
Right eye refractive error, D[c]			
Spherical equivalent	-2.28 (.90)	-2.43 (1.11)	-2.46 (.97)
Right eye biometry, mm			
Eye length[d]	24.43 (.74)	24.57 (.85)	24.45 (.83)
Anterior chamber depth[e]	3.97 (.21)	3.96 (.23)	4.00 (.23)
Lens thickness[f]	3.33 (.14)	3.34 (.13)	3.31 (.13)
Vitreous chamber depth[g]	17.13 (.77)	17.27 (.83)	17.14 (.82)

[a] Data are expressed as mean (SD) unless otherwise noted. All randomized participants are included.

[b] Parent/legal guardian report of participant based on categories defined by the National Institutes of Health.

[c] Based on cycloplegic autorefraction to paralyze the ciliary muscle of the eye so the participant cannot focus their eyes, which changes the prescription; ocular data differed between the right and left eye by less than 0.05 D and 0.05 mm.

[d] Anterior cornea to retina; normal range: 23.4-24.8 mm.[26]

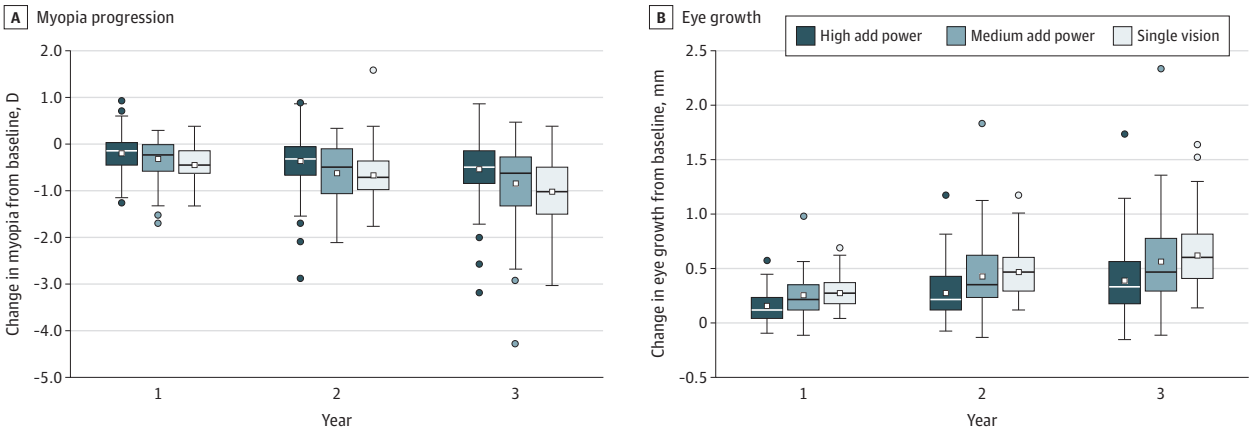
[e] Posterior cornea to anterior crystalline lens; normal range: 3.0-4.2 mm.[26]

[f] Anterior crystalline lens to posterior crystalline lens; normal range: 3.2-3.6 mm.[26]

[g] Posterior crystalline lens to retina; normal range: 16.1-17.5 mm.[26]

The 3-year adjusted (for baseline spherical equivalent, clinic site, sex, age group at randomization, and eye) mean myopia progression was −0.60 D for the high add power group, −0.89 D for the medium add power group, and −1.05 D for the single-vision group. The difference in progression was 0.46 D (95% CI, 0.29-0.63) between the high add power and

Figure 3. Myopia Progression and Eye Growth in a Study of the Effect of High Add Power, Medium Add Power, or Single-Vision Contact Lenses on Myopia Progression in Children



Box plots are shown in which the middle line represents the median change from baseline, boxes represent the interquartile range, whiskers extend to the most extreme observed values withing 1.5 × the interquartile range of the nearer quartile, and dots represent observed values outside that range. The data represent the mean change of the 2 eyes. A, More negative values indicate myopia progression. B, More positive values indicate eye growth.

single-vision groups, 0.16 D (95% CI, −0.01 to 0.33) between the medium add power and single-vision groups, and 0.30 D (95% CI, 0.13-0.47) between the high add and medium add power groups (**Table 2**). The 1- and 2-year mean and adjusted progression values are presented in eTable 1 in Supplement 3.

Secondary Outcomes

For the high add power group, mean axial length was 24.42 mm at baseline and 24.81 mm at 3 years, and the growth was 0.39 mm (95% CI, 0.32-0.46). For the medium add power group, mean axial length was 24.55 mm at baseline and 25.12 mm at 3 years, and the growth was 0.55 mm (95% CI, 0.49-0.62). Mean axial length was 24.43 mm at baseline and 25.08 mm at 3 years, and the growth was 0.62 mm (95% CI, 0.56-0.69), for the single-vision group (Figure 3B and eFigure 1B in Supplement 3).

The 3-year adjusted eye growth was 0.42 mm for the high add power group, 0.58 mm for the medium add power group, and 0.66 mm for the single-vision group. The difference in eye growth was −0.23 mm (95% CI, −0.30 to −0.17) between the high add power and the single-vision groups, −0.07 mm (95% CI, −0.14 to −0.01) between the medium add power and single-vision groups, and −0.16 mm (95% CI, −0.23 to −0.09) between the high add and medium add power groups (Table 2). The 1- and 2-year means and adjusted growth are presented in eTable 1 in Supplement 3.

At the final visit, the mean high-contrast distance logMAR visual acuity was −0.04 ($20/20^{+2}$) for the high add power group, −0.03 ($20/20^{+1}$) for the medium add power group, and −0.05 ($20/20^{+2}$) for the single-vision group (analysis of variance P = .13). The mean high-contrast near logMAR visual acuity was −0.07 ($20/15^{-2}$) for the high add power group,−0.07 ($20/15^{-2}$) for the medium add power group, and −0.08 ($20/15^{-2}$) for the single-vision group (analysis of variance P = .25). The mean low-contrast logMAR distance visual acuity was +0.07 ($20/25^{+2}$) for the single-vision group, which was statistically significantly better than the +0.10 (20/25) logMAR distance visual acuity for the high add power group (P = .04) and +0.10 (20/25) for the medium add power group (P = .01), but the differences were less than 2 letters (ie, not clinically meaningful).

Participants who wore their contact lenses wore them for a mean (SD) of 11.0 (4.4) hours per day. The correlation of responses between each 6-month visit ranged from 0.72 to 0.83. A treatment and wearing time interaction effect on myopia progression was not statistically significant (P = .29), indicating that longer wearing times did not enhance the effect of the +2.50 D add power.

Adverse Events

None of the ocular adverse events reported were serious or severe or caused permanent discontinuation of contact lens wear. All adverse events resolved with no reported loss of best-corrected visual acuity. Thirty-five ocular adverse events were moderate and were definitely or probably related to contact lens wear (eTable 2 in Supplement 3). The most common of these adverse events were giant papillary conjunctivitis (n = 9), infiltrative keratitis (n = 8), and ocular allergies (n = 7). There was no significant difference in those adverse events between the 3 treatment groups (P = .41).

Post Hoc Outcomes

The percentage of participants who progressed −1.00 D or more during the study was 16.8% (95% CI, 9.9%-25.9%) for the high add power group, 36.5% (95% CI, 26.9%-46.9%) for the medium add power group, and 51.0% (95% CI, 40.6%-61.4%) for the single-vision group. The percentage of participants who had eye growth more than 0.36 mm over 3 years was 47.4% (95% CI, 37.0%-57.9%) for the high add power group, 61.5% (95% CI, 51.0%-71.2%) for the medium add power group, and 80.2% (95% CI, 70.8%-87.6%) for the single-vision group (Table 2).

Table 2. Outcomes at 3 Years in a Study of the Effect of High Add Power, Medium Add Power, or Single-Vision Contact Lenses on Myopia Progression in Children

Outcome	High add (n = 97)	Medium add (n = 98)	Single vision (n = 97)	Mean difference (95% CI)	*P* value
Primary outcome					
Refractive error, D					
Baseline mean (SD)[a]	−2.30 (0.91)	−2.46 (1.09)	−2.45 (0.96)		
Year 3, mean (SD)[a]	−2.84 (1.22)	−3.32 (1.48)	−3.46 (1.20)		
3-y absolute change (95% CI)[b]	−0.56 (−0.70 to −0.41) (n = 95)[c]	−0.85 (−0.99 to −0.70) (n = 96)[c]	−1.01 (−1.15 to −0.87) (n = 96)[c]		
High add vs single vision				0.45 (0.25 to 0.66)	<.001
Medium add vs single vision				0.16 (−0.04 to 0.37)	.11
High add vs medium add				0.29 (0.09 to 0.50)	.01
3-y adjusted change (95% CI)[d]	−0.60 (−0.72 to −0.47)	−0.89 (−1.01 to −0.77)	−1.05 (−1.17 to −0.93)		
High add vs single vision				0.46 (0.29 to 0.63)	<.001
Medium add vs single vision				0.16 (−0.01 to 0.33)	.19
High add vs medium add				0.30 (0.13 to 0.47)	.004
Secondary outcomes					
Eye length, mm					
Baseline, mean (SD)[a]	24.42 (0.75)	24.55 (0.84)	24.43 (0.83)		
Year 3, mean (SD)[a]	24.81 (0.83)	25.12 (0.97)	25.08 (0.85)		
3-y absolute change (95% CI)[b]	0.39 (0.32 to 0.46) (n = 95)[c]	0.55 (0.49 to 0.62) (n = 95)[c]	0.62 (0.56 to 0.69) (n = 96)[c]		
High add vs single vision				−0.23 (−0.33 to −0.14)	<.001
Medium add vs single vision				−0.07 (−0.16 to 0.03)	.15
High add vs medium add				−0.16 (−0.26 to −0.07)	.002
3-y adjusted change (95% CI)[d]	0.42 (0.38 to 0.47)	0.58 (0.54 to 0.63)	0.66 (0.61 to 0.71)		
High add vs single vision				−0.23[e] (−0.30 to −0.17)	<.001
Medium add vs single vision				−0.07[e] (−0.14 to −0.01)	.09
High add vs medium add				−0.16 (−0.23 to −0.09)	<.001
Adverse events[f], No. (%)	14 (40.0)	8 (22.9)	13 (37.1)		.41[g]
Visual acuity, mean (95% CI), logMAR[h]					
High contrast distance	−0.04 (−0.06 to −.03)	−0.03 (−0.05 to −0.02)	−0.05 (−0.07 to −0.04)		.13[i]
High contrast near	−0.07 (−0.09 to −0.05)	−0.07 (−0.08 to −0.05)	−0.08 (−0.10 to −0.07)		.25[i]
Low contrast distance	+0.10 (+0.08 to +0.11)	+0.10 (+0.09 to +0.12)	+0.07 (+0.05 to +0.09)		
High add vs single vision				0.03 (0 to 0.05)	.04
Medium add vs single vision				0.03 (0.01 to 0.06)	.01
High add vs medium add				−0.01 (−0.03 to 0.02)	.58
Post hoc outcomes, No. (%) [95% CI]	**(n = 95)**	**(n = 96)**	**(n = 96)**		
Progress >1.00 D[j]	16 (16.8) [9.9 to 25.9]	35 (36.5) [26.9 to 46.9]	49 (51.0) [40.6 to 61.4]		
High add vs single vision				−34.2 (−46.7 to −21.7)	<.001
Medium add vs single vision				−14.6[e] (−28.5 to −0.7)	.04
High add vs medium add				−19.6[e] (−31.8 to −7.4)	.004
Eye growth >0.36 mm[k]	45 (47.4) [37.0 to 57.9]	59 (61.5) [51.0 to 71.2]	77 (80.2) [70.8 to 87.6]		
High add vs single vision				−32.8 (−45.7 to −20.0)	<.001
Medium add vs single vision				−18.8[e] (−31.3 to −6.2)	.01
High add vs medium add				−14.1 (−28.1 to −0.1)	.05

[a] Treatment group mean values include the mean value of both eyes (eg, 98 participants implies 196 measurements).

[b] Absolute changes are not simply 3-year measurements minus baseline measurements because a few participants were missing the 3-year measurements.

[c] A total of 287 of 294 participants attended the 3-year visit.

[d] Models were adjusted for baseline outcome value, eye (right or left), clinical site, sex, age group (7-9 vs 10-11 y), treatment × time, and age group × time interactions. The estimates of change assumed an equal mix of male and female participants, sites, age groups, and right and left eyes. They also assumed baseline values were equal to the mean values of the observed data (−2.40 D for refractive error and 24.5 mm for eye length).

[e] Values do not equal the simple difference between values in the table due to rounding.

[f] The 3 most common adverse events were giant papillary conjunctivitis (n = 9), infiltrative keratitis (n = 8), and ocular allergies (n = 7) (eTable 2 in Supplement 3).

[g] *P* value for χ^2 test of equality of proportions.

[h] Visual acuity with both eyes open at the last visit while wearing habitual correction and a spherical spectacle lens to adjust for myopia progression.

[i] *P* value for analysis of variance; *P* value corrected for multiple comparisons using the Bonferroni stepdown method.

[j] The average myopia progression of the single-vision control group was 1.00 D.

[k] The eye growth equivalent of 1.00 D of myopia progression is .36 mm.

Discussion

In this 3-year multicenter, randomized, double-masked clinical trial, commercially available center-distance soft multifocal contact lenses with a high add power slowed myopia progression by 0.45 D and eye growth by 0.23 mm compared with single-vision contact lenses, and slowed myopia progression by 0.29 D and eye growth by 0.16 mm compared with medium add power multifocal contact lenses.

Other soft multifocal contact lens myopia control studies reported a change in myopia progression that ranged from an increase of 10% to a decrease of 79%, and they reported slowing of eye growth ranging from no change to 79%.[7,9,27-36] The 43% slowing of myopia progression and 36% slowing of eye growth reported in this study were in the middle of the ranges previously reported. This study reported 0.23-mm slower eye growth compared with 0.32-mm slower eye growth in another 3-year randomized clinical trial when comparing the high add power group with the single-vision contact lens group.[7] This study used commercially available soft multifocal contact lenses, as opposed to proprietary lenses not available to the public, which were used in the other trial.

The high add power did not clinically alter the ability to see or result in a greater number of adverse events. Although these contact lenses were approved for wear by the US Food and Drug Administration (FDA) without age restriction, they did not have a specific FDA indication for myopia control and were prescribed off label.

Limitations

This study had several limitations. First, the adjusted myopic progression of the control group was −1.05 D, which is slower than the 3-year progression of other single-vision contact lens or spectacle wearers in the US, which ranges from −1.10 D to −2.19 D.[18,23,37,38] Younger participants and Asian children progress faster,[39] but demographics of the study sample cannot explain the slower progression of this study's control group compared with other myopia control studies conducted in the US. However, it may explain why the treatment effect was less than that of the other 3-year soft multifocal randomized clinical trial.[7] In that study, 32% of the participants were Asian, whereas less than 9% of the participants reported Asian ethnicity in the current study.

Second, the contact lenses used in this study were not individually adjusted for the amount of myopic defocus or the area of the retina that received myopic defocus to potentially maximize myopia control. Instead, the commercially available contact lenses were meant to provide myopic defocus for most participants.

Third, the duration of the study did not allow measurement of the participants' ultimate myopia, the effect of multifocal contact lens myopia control on the ocular morbidity associated with myopia, or myopia progression after removal of the multifocal contact lenses (rebound effect). A 3-year extension of the study during which all participants wear the high add power contact lenses will allow examination of the rebound effect.

Fourth, the dose-response result exhibited in this study only examined up to a +2.50 D add power. Speculation remains about whether add powers outside of the standard range may provide better myopia control.

Fifth, this study was designed to find a 50% slowing of myopia progression, a difference of 0.65 D between the high add power and single-vision contact lens wearers. The results indicated 45% slower progression, a difference of 0.45 D. A consensus paper by the International Myopia Institute indicated that a 40% slowing of myopia progression was clinically meaningful,[40] and a workshop organized by the FDA indicated that a 30% slowing may be clinically meaningful.[21] Although the myopia control effect reported in this study did not meet the standard for clinically meaningful myopia control set many years ago, it did meet the current standards of a rapidly evolving area of study.

Conclusions

Among children with myopia, treatment with high add power multifocal contact lenses significantly reduced the rate of myopia progression over 3 years compared with medium add power multifocal and single-vision contact lenses. However, further research is needed to understand the clinical importance of the observed differences.

ARTICLE INFORMATION

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Author Contributions: Drs Jones-Jordan and Walline had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
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Acquisition, analysis, or interpretation of data: All authors.
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Critical revision of the manuscript for important intellectual content: Walline, Mutti, Jones-Jordan, Sinnott, Giannoni, Bickle, Nixon, Berntsen.
Statistical analysis: Mutti, Jones-Jordan, Sinnott.
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REFERENCES

1. Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology*. 2016;123(5):1036-1042. doi:10.1016/j.ophtha.2016.01.006

2. Jones LA, Sinnott LT, Mutti DO, Mitchell GL, Moeschberger ML, Zadnik K. Parental history of myopia, sports and outdoor activities, and future myopia. *Invest Ophthalmol Vis Sci*. 2007;48(8):3524-3532. doi:10.1167/iovs.06-1118

3. Hayashi K, Ohno-Matsui K, Shimada N, et al. Long-term pattern of progression of myopic maculopathy: a natural history study. *Ophthalmology*. 2010;117(8):1595-1611, 1611.e1-1611.e4. doi:10.1016/j.ophtha.2009.11.003

4. Verkicharla PK, Ohno-Matsui K, Saw SM. Current and predicted demographics of high myopia and an update of its associated pathological changes. *Ophthalmic Physiol Opt*. 2015;35(5):465-475. doi:10.1111/opo.12238

5. Thorn F, Gwiazda J, Held R. Myopia progression is specified by a double exponential growth function. *Optom Vis Sci*. 2005;82(4):286-297. doi:10.1097/01.OPX.0000159370.66540.34

6. Cho P, Cheung SW. Retardation of Myopia in Orthokeratology (ROMIO) study: a 2-year randomized clinical trial. *Invest Ophthalmol Vis Sci*. 2012;53(11):7077-7085. doi:10.1167/iovs.12-10565

7. Chamberlain P, Peixoto-de-Matos SC, Logan NS, Ngo C, Jones D, Young G. A 3-year randomized clinical trial of MiSight lenses for myopia control. *Optom Vis Sci*. 2019;96(8):556-567. doi:10.1097/OPX.0000000000001410

8. Yam JC, Jiang Y, Tang SM, et al. Low-Concentration Atropine for Myopia Progression (LAMP) study: a randomized, double-blinded, placebo-controlled trial of 0.05%, 0.025%, and 0.01% atropine eye drops in myopia control. *Ophthalmology*. 2019;126(1):113-124. doi:10.1016/j.ophtha.2018.05.029

9. Sankaridurg P, Holden B, Smith E III, et al. Decrease in rate of myopia progression with a contact lens designed to reduce relative peripheral hyperopia: one-year results. *Invest Ophthalmol Vis Sci*. 2011;52(13):9362-9367. doi:10.1167/iovs.11-7260

10. Berntsen DA, Barr CD, Mutti DO, Zadnik K. Peripheral defocus and myopia progression in myopic children randomly assigned to wear single vision and progressive addition lenses. *Invest Ophthalmol Vis Sci*. 2013;54(8):5761-5770. doi:10.1167/iovs.13-11904

11. Berntsen DA, Kramer CE. Peripheral defocus with spherical and multifocal soft contact lenses. *Optom Vis Sci*. 2013;90(11):1215-1224. doi:10.1097/OPX.0000000000000066

12. Kang P, Fan Y, Oh K, Trac K, Zhang F, Swarbrick HA. The effect of multifocal soft contact lenses on peripheral refraction. *Optom Vis Sci*. 2013;90(7):658-666. doi:10.1097/OPX.0b013e3182990878

13. Ticak A, Walline JJ. Peripheral optics with bifocal soft and corneal reshaping contact lenses. *Optom Vis Sci*. 2013;90(1):3-8. doi:10.1097/OPX.0b013e3182781868

14. Rosén R, Jaeken B, Lindskoog Petterson A, Artal P, Unsbo P, Lundström L. Evaluating the peripheral optical effect of multifocal contact lenses. *Ophthalmic Physiol Opt*. 2012;32(6):527-534. doi:10.1111/j.1475-1313.2012.00937.x

15. Walline JJ, Gaume Giannoni A, Sinnott LT, et al; BLINK Study Group. A randomized trial of soft multifocal contact lenses for myopia control: baseline data and methods. *Optom Vis Sci*. 2017;94(9):856-866. doi:10.1097/OPX.0000000000001106

16. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010

17. French AN, Morgan IG, Burlutsky G, Mitchell P, Rose KA. Prevalence and 5- to 6-year incidence and progression of myopia and hyperopia in Australian schoolchildren. *Ophthalmology*. 2013;120(7):1482-1491. doi:10.1016/j.ophtha.2012.12.018

18. Walline JJ, Jones LA, Sinnott L, et al; ACHIEVE Study Group. A randomized trial of the effect of soft contact lenses on myopia progression in children. *Invest Ophthalmol Vis Sci*. 2008;49(11):4702-4706. doi:10.1167/iovs.08-2067

19. Thibos LN, Wheeler W, Horner D. Power vectors: an application of Fourier analysis to the description and statistical analysis of refractive error. *Optom Vis Sci*. 1997;74(6):367-375. doi:10.1097/00006324-199706000-00019

20. Zadnik K, Mutti DO, Friedman NE, Adams AJ. Initial cross-sectional results from the Orinda Longitudinal Study of Myopia. *Optom Vis Sci*. 1993;70(9):750-758. doi:10.1097/00006324-199309000-00012

21. Walline JJ, Robboy MW, Hilmantel G, et al. Food and Drug Administration, American Academy of Ophthalmology, American Academy of Optometry, American Association for Pediatric Ophthalmology and Strabismus, American Optometric Association, American Society of Cataract and Refractive Surgery, and Contact Lens Association of Ophthalmologists co-sponsored workshop: controlling the progression of myopia: contact lenses and future medical devices. *Eye Contact Lens*. 2018;44(4):205-211. doi:10.1097/ICL.0000000000000511

22. Walline JJ, Jones LA, Sinnott L, et al; ACHIEVE Study Group. Randomized trial of the effect of contact lens wear on self-perception in children. *Optom Vis Sci*. 2009;86(3):222-232. doi:10.1097/OPX.0b013e3181971985

23. Walline JJ, Jones LA, Mutti DO, Zadnik K. A randomized trial of the effects of rigid contact lenses on myopia progression. *Arch Ophthalmol*. 2004;122(12):1760-1766. doi:10.1001/archopht.122.12.1760

24. Glynn RJ, Rosner B. Regression methods when the eye is the unit of analysis. *Ophthalmic Epidemiol*. 2012;19(3):159-165. doi:10.3109/09286586.2012.674614

25. Holm S. A simple sequentially rejective multiple test procedure. *Scand J Statist*. 1979;6:65-70.

26. Gwiazda J, Marsh-Tootle WL, Hyman L, Hussein M, Norton TT; COMET Study Group. Baseline refractive and ocular component measures of children enrolled in the correction of myopia evaluation trial (COMET). *Invest Ophthalmol Vis Sci*. 2002;43(2):314-321.

27. Sankaridurg P, Bakaraju RC, Naduvilath T, et al. Myopia control with novel central and peripheral plus contact lenses and extended depth of focus contact lenses: 2 year results from a randomised clinical trial. *Ophthalmic Physiol Opt*. 2019;39(4):294-307. doi:10.1111/opo.12621

28. Ruiz-Pomeda A, Pérez-Sánchez B, Valls I, Prieto-Garrido FL, Gutiérrez-Ortega R, Villa-Collar C. MiSight Assessment Study Spain (MASS): a 2-year randomized clinical trial. *Graefes Arch Clin Exp Ophthalmol*. 2018;256(5):1011-1021. doi:10.1007/s00417-018-3906-z

29. Allen PM, Radhakrishnan H, Price H, et al. A randomised clinical trial to assess the effect of a dual treatment on myopia progression: the Cambridge Anti-Myopia Study. *Ophthalmic Physiol Opt*. 2013;33(3):267-276. doi:10.1111/opo.12035

30. Fujikado T, Ninomiya S, Kobayashi T, Suzaki A, Nakada M, Nishida K. Effect of low-addition soft contact lenses with decentered optical design on myopia progression in children: a pilot study. *Clin Ophthalmol*. 2014;8:1947-1956. doi:10.2147/OPTH.S66884

31. Pauné J, Morales H, Armengol J, Quevedo L, Faria-Ribeiro M, González-Méijome JM. Myopia control with a novel peripheral gradient soft lens and orthokeratology: a 2-year clinical trial. *Biomed Res Int*. 2015;2015:507572. doi:10.1155/2015/507572

32. Anstice NS, Phillips JR. Effect of dual-focus soft contact lens wear on axial myopia progression in children. *Ophthalmology*. 2011;118(6):1152-1161. doi:10.1016/j.ophtha.2010.10.035

33. Walline JJ, Greiner KL, McVey ME, Jones-Jordan LA. Multifocal contact lens myopia control. *Optom Vis Sci*. 2013;90(11):1207-1214. doi:10.1097/OPX.0000000000000036

34. Cheng X, Xu J, Chehab K, Exford J, Brennan N. Soft contact lenses with positive spherical aberration for myopia control. *Optom Vis Sci*. 2016;93(4):353-366. doi:10.1097/OPX.0000000000000773

35. Aller TA, Liu M, Wildsoet CF. Myopia control with bifocal contact lenses: a randomized clinical trial. *Optom Vis Sci*. 2016;93(4):344-352. doi:10.1097/OPX.0000000000000808

36. Lam CS, Tang WC, Tse DY, 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(1):40-45. doi:10.1136/bjophthalmol-2013-303914

37. Gwiazda J, Hyman L, Hussein M, et al. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. *Invest Ophthalmol Vis Sci*. 2003;44(4):1492-1500. doi:10.1167/iovs.02-0816

38. Correction of Myopia Evaluation Trial 2 Study Group for the Pediatric Eye Disease Investigator Group. Progressive-addition lenses versus single-vision lenses for slowing progression of myopia in children with high accommodative lag and near esophoria. *Invest Ophthalmol Vis Sci*. 2011;52(5):2749-2757. doi:10.1167/iovs.10-6631

39. Hyman L, Gwiazda J, Hussein M, et al. Relationship of age, sex, and ethnicity with myopia progression and axial elongation in the correction of myopia evaluation trial. *Arch Ophthalmol*. 2005;123(7):977-987. doi:10.1001/archopht.123.7.977

40. Wolffsohn JS, Kollbaum PS, Berntsen DA, et al. IMI: clinical myopia control trials and instrumentation report. *Invest Ophthalmol Vis Sci*. 2019;60(3):M132-M160. doi:10.1167/iovs.18-25955