BLIMP

Bifocal Lens Inhibition of Myopia Progression Study

MYOPIA CONTROL WITH A SOFT BIFOCAL CONTACT LENS

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ABSTRACT

Purpose: Evidence continues to accumulate regarding the role of the peripheral retina for regulating eye growth. Corneal reshaping contact lenses have been shown to effectively slow eye growth, and the hypothesized mechanism of treatment effect is relative peripheral myopia. Soft bifocal contact lenses with a distance center may provide a similar effect as corneal reshaping. The purpose of this study is to examine the one-year myopia control effects of soft bifocal contact lenses with a distance center.

Methods: 40 children with -1.00 to -6.00 D myopia, less than -1.00 D astigmatism, and healthy eyes were fit with Proclear Multifocal "D" lenses with a +2.00 add. This two-year study will compare the cycloplegic spherical equivalent myopic progression between the children wearing soft bifocal contact lenses to a historical control group matched on age and gender who wear soft spherical contact lenses. These results include only information from the right eye.

Results: Forty children were fit with soft bifocal contact lenses, and 28 have completed one year. Eight children have been discontinued (5 were lost to follow-up, 2 moved, and 1 had difficulty with insertion), and four have not yet completed one year. These results include only the 28 subjects and the matched controls. The average (±SD) age was 10.8 ± 0.75 years and 10.9 ± 0.88 years (p = 0.58), the average spherical equivalent was -2.45 ± 1.03 D and -2.29 ± 0.98 D (p = 0.56), and the average axial length was 24.4 ± 0.94 mm and 24.3 ± 0.94 mm (p = 0.62) for the soft bifocal and spherical contact lens wearers, respectively. After one year, the change in spherical equivalent was -0.39 ± 0.53 D for the soft bifocal wearers and -0.60 ± 0.32 D for the soft spherical wearers (p = 0.08). The change in axial length was 0.17 ± 0.21 mm for the soft bifocal wearers and 0.23 ± 0.17 mm for the soft spherical wearers (p = 0.32). With a sample size of 28 subjects, we have 75% power to detect a 50% reduction in spherical equivalent refractive error with a standard deviation of 0.50 D and assuming alpha = 0.05.

Conclusion: Over one year, the myopia progressed 35% slower for the soft bifocal contact lens wearers, but the results are not statistically significant for either the spherical equivalent refractive error progression or the axial elongation. The presentation will include a complete one year dataset and partial two-year results.

PURPOSE

- To compare axial elongation and myopia progression between soft bifocal and soft spherical contact lens wearers

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BACKGROUND

- Eye growth influenced by location of focus of light[1-3]
- Peripheral retina is more important to control eye growth than previously believed to be true[4-5]
- Corneal reshaping contact lenses slow eye growth in myopic children[6-7]
  - Mechanism of treatment effect is thought to be peripheral myopic blur
- Distance center soft bifocal contact lenses provide similar topographic profile as corneal reshaping (Figure)

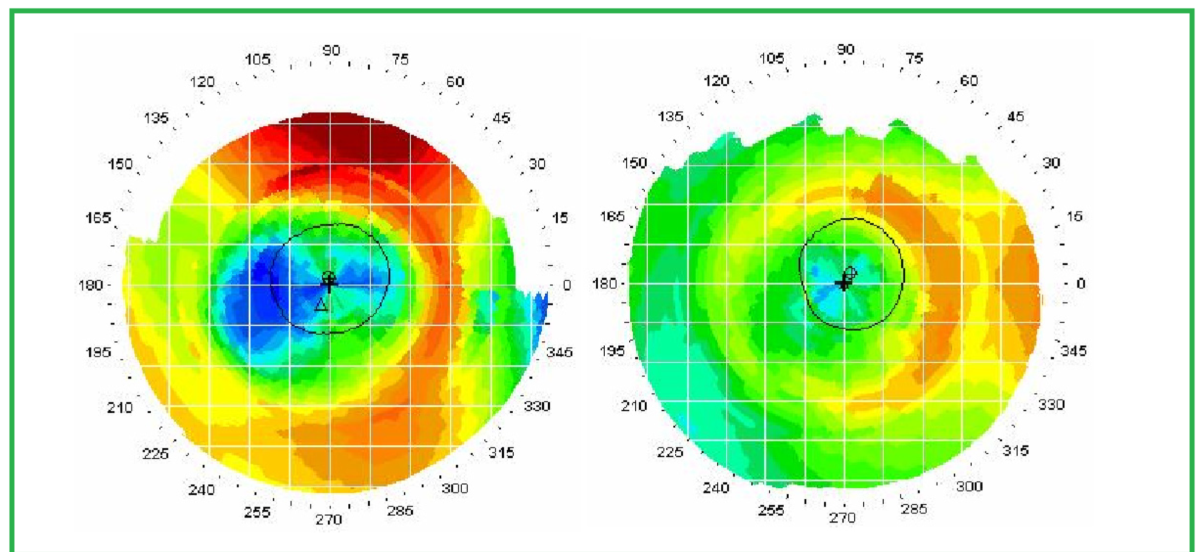

Figure. Corneal reshaping (left) and soft bifocal (right) contact lenses provide similar topographic results with a central flat portion surrounded by mid-peripheral steepening

- If both provide peripheral myopic blur, then soft bifocal contact lenses may slow myopia progression as well
- Anecdotal evidence that soft bifocal contact lenses slow myopia progression[8]
- Randomized clinical trial reports significant slowing of eye growth with soft bifocal contact lenses, but not published in peer-reviewed literature[9]

INCLUSION CRITERIA

- Sphere: –1.00 D to –6.00 D
- Cylinder: Less than 1.00 DC
- 20/20 or better best-corrected visual acuity in each eye
- No gas permeable contact lens wear
- No ocular or systemic health problems that could affect contact lens wear

Contact Lenses

	Soft Bifocal	Soft Spherical
Brand	Proclear Multifocal "D"	Acuvue 1 Day
Material	omafilcon A	etafilcon A
Water Content	62%	58%
Add Power	+2.00	N/A
Replacement	Monthly	Daily
dK	27	28

METHODS

- Age- and gender-matched to soft spherical lens wearer from ACHIEVE Study
- Baseline and annual examinations
- Cycloplegia: 25 minutes after two drops of 1% tropicamide, separated by 5 minutes
- Refractive error: 10 autorefractor readings while fixating 20/30 letters located beyond infinity on Badal track
- Axial length: five a-scan ultrasounds with equal lens peaks and abrupt retinal spike
- Average of two eyes

CONCLUSIONS

- 40 subjects enrolled
  - 32 completed one year
  - 14 completed two years so far
- Baseline characteristics: mean ± standard deviation

	Soft Bifocal	Soft Spherical	p-value
M (D)	−2.31 ± 1.05	−2.22 ± 0.97	0.75
J_0 (D)	0.00 ± 0.21	−0.07 ± 0.15	0.14
J_{45} (D)	+0.04 ± 0.08	+0.06 ± 0.08	0.54
Anterior Chamber Depth (mm)	3.82 ± 0.27	4.01 ± 0.24	0.002
Lens Thickness(mm)	3.45 ± 0.17	3.36 ± 0.17	0.05
Vitreous Chamber Depth (mm)	17.00 ± 1.03	16.94 ± 0.84	0.76
Axial Length (mm)	24.28 ± 0.99	24.30 ± 0.87	0.09

- One year change: mean ± standard deviation, controlling for baseline Anterior Chamber Depth and Lens Thickness

	Soft Bifocal (n=32)	Soft Spherical (n=32)	p-value
M	−0.37 ± 0.41	−0.61 ± 0.33	0.15
J0	+0.07 ± 0.16	+0.01 ± 0.11	0.08
J45	+0.01 ± 0.10	0.00 ± 0.12	0.71
Anterior Chamber Depth	+0.04 ± 0.09	−0.01 ± 0.07	0.88
Lens Thickness	−0.02 ± 0.09	0.00 ± 0.06	0.71
Vitreous Chamber Depth	+0.13 ± 0.15	+0.22 ± 0.16	0.08
Axial Length	+0.15 ± 0.13	+0.21 ± 0.16	0.12

- Two year change: mean ± standard deviation, controlling for baseline Anterior Chamber Depth and Lens Thickness

	Soft Bifocal (n=14)	Soft Spherical (n=14)	p-value
M	−0.55 ± 0.49	−1.10± 0.54	0.12
J0	+0.15 ± 0.19	+0.06 ± 0.11	0.09
J45	+0.01 ± 0.12	−0.02 ± 0.08	0.68
Anterior Chamber Depth	+0.05 ± 0.10	0.00 ± 0.10	0.57
Lens Thickness	−0.01 ± 0.15	−0.01 ± 0.05	0.24
Vitreous Chamber Depth	+0.28 ± 0.20	+0.48 ± 0.31	0.09
Axial Length	+0.32 ± 0.16	+0.47 ± 0.33	0.18

CONCLUSIONS

- Power Year 1: 73% to detect a significant difference with sample size of 32 (α = 0.05)
- Power Year 2: 77.6% to detect a significant difference with sample size of 13 (α = 0.05)
- At two years, the myopic progression is 50% slower for soft bifocal contact lens wearers (not statistically significant with preliminary data)
- At two years, axial elongation is 32% slower for soft bifocal contact lens wearers (not statistically significant with preliminary data)
- Trial completed July 2011, so stay tuned!

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Light Exposure Patterns in Children - A Pilot Study

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Purpose

- To examine the light exposure patterns of school-aged children in relation to refractive error.

Methods

- School-aged children (13-14 years old, n = 12) were issued with self-contained light meters that recorded the individual light exposure levels every 10 seconds (HOBO Pendant UA-002-064, Onset Computer Corporation, USA) [Fig. 1 and Fig. 2A].
- The ambient outdoor light levels were also recorded every 10 seconds over seven days (one period) [Fig. 2B].
- Measurements were made in three periods over three consecutive months in Southern Hemisphere winter (June, July, August).
- Cycloplegic autorefraction and axial length measurements were made at the beginning and end of the three month study.

Figure 1. Example of the self-contained light meter issued to the children.

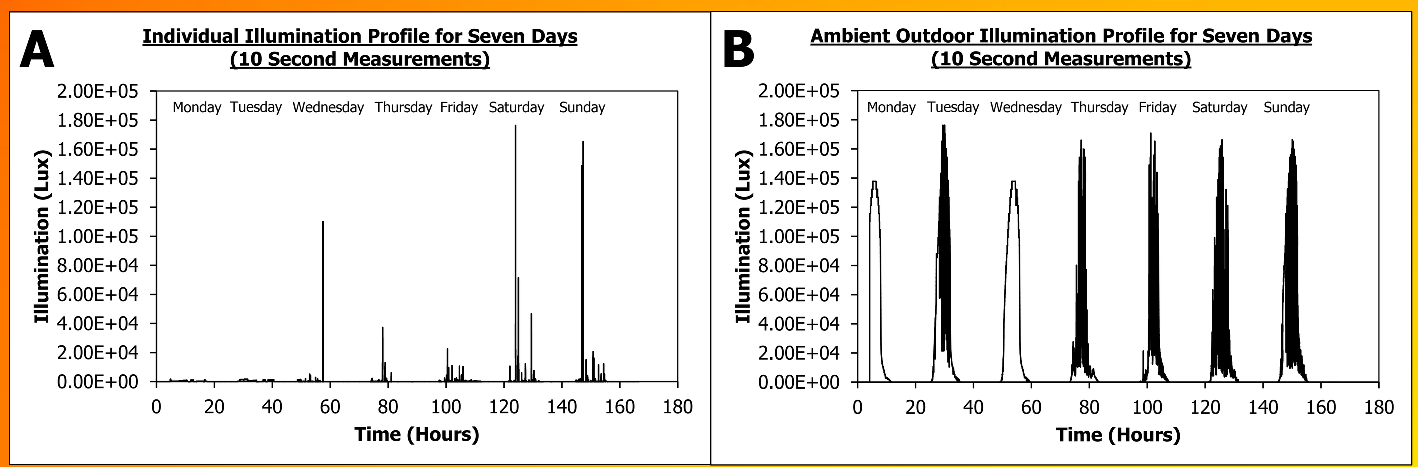

Figure 2. (A and B) Example seven day illumination profiles for individual (A) and ambient outdoor (B) light exposures. Measurements made every 10 seconds.

Results

- Individual light level recordings indicated that children spent only a small amount of time outside (5.88% ± 1.39% of the total time, or 10.65 ± 2.52 hours per week; mean ± 95% CI, n = 12). However, these outdoor periods accounted for a large proportion of their total light exposure (87.95% ± 3.72% of their total light exposure, or $4.72 \times 10^7 \pm 1.65 \times 10^7$ lux) [Fig. 3].
- The subjects were exposed to only 5.72% ± 1.86% of the total ambient outdoor light on average over the measurement period.
- **Refractive Error**: Refractive error was not significantly correlated with cumulative light exposure ($R^2 < 0.001$) [Fig. 4].
- **Change in Refractive Error**: There was no significant correlation between the change in refractive error and the cumulative light experienced over the three month measurement period ($R^2 = 0.0069$) [Fig. 5].

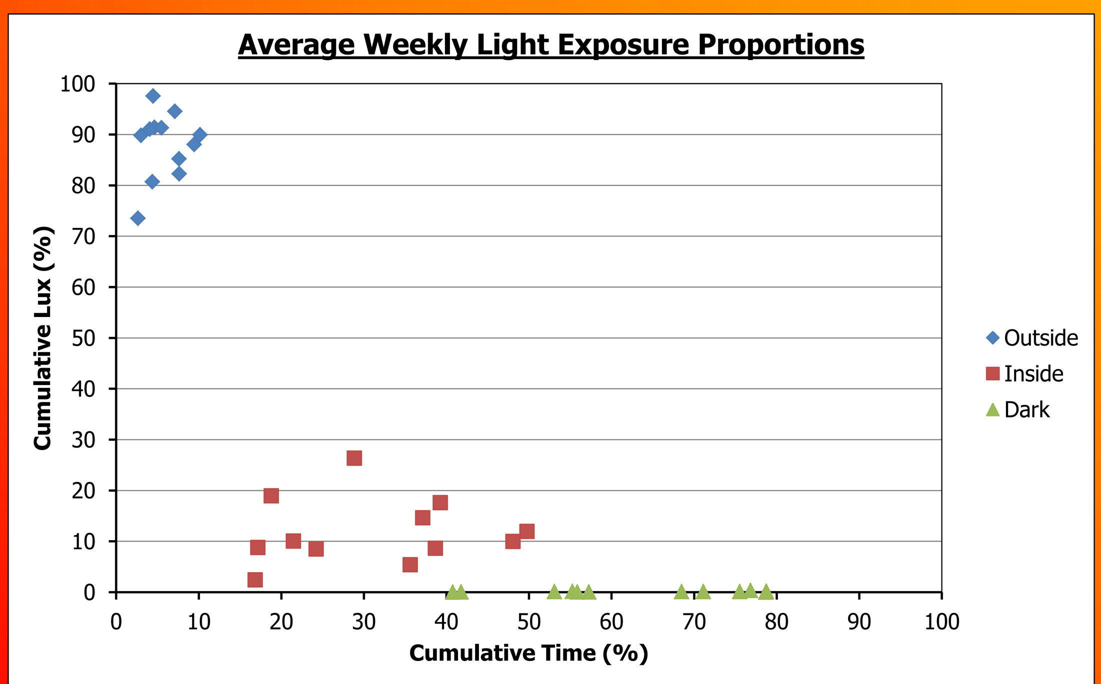

Figure 3. Proportion of the total average weekly light exposure coming from outdoor (> 1000 Lux), indoor (10-1000 Lux), and dark (< 10 Lux) exposure versus proportion of total average weekly time spent outdoors, indoors, and in the dark.

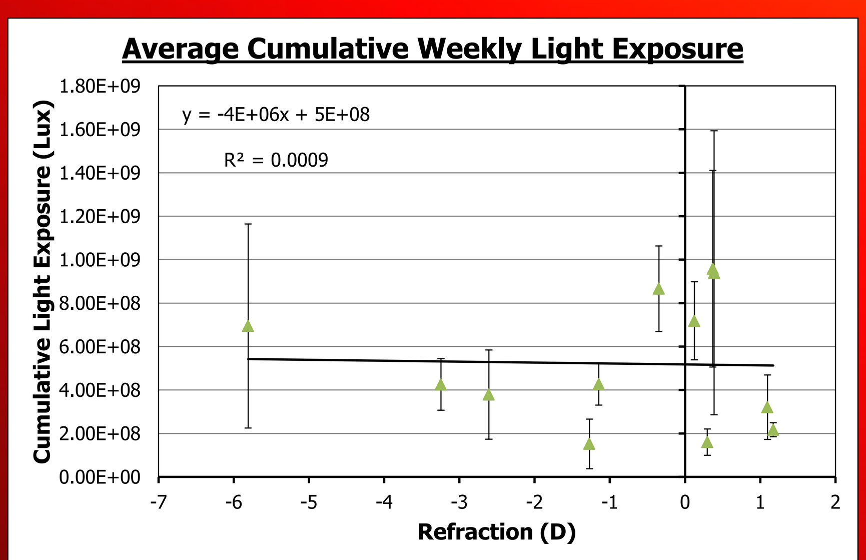

Figure 4. Average weekly light exposure as a function of refractive status. Each point represents the average of three measurement periods. Error bars are SEM. There was no correlation between refraction and the light received ($R^2 = 0.0009$).

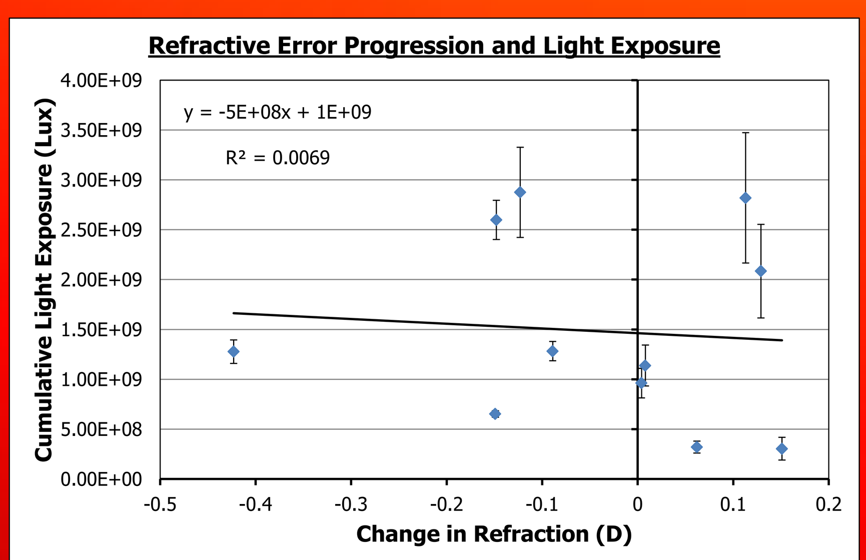

Figure 5. Change in refractive error over three months compared to the cumulative light exposure from three measurement periods (one week each). Refractive error progression is poorly correlated with light exposure ($R^2 = 0.0069$). Error bars are SEM.

- **Indoor Light**: There was a significant correlation between the amount of time spent indoors (between 10 and 1000 lux) and the cumulative light exposure obtained indoors ($R^2 = 0.945$) [Fig. 6].
- **Outdoor Light**: There was a poor correlation between the amount of time spent outdoors (>1000 lux) and the cumulative light exposure obtained outdoors ($R^2 = 0.296$) [Fig. 7].
- Modelling of weekly light exposure based on the average trends seen in figures 6 and 7 showed that a small amount of extra time spent outdoors can disproportionally affect the total light exposure received per week [Fig. 8].

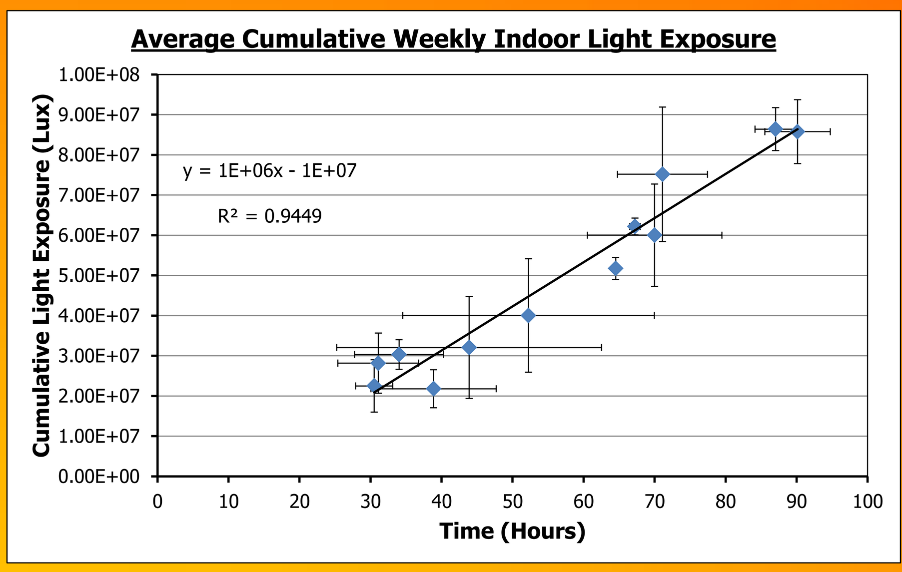

Figure 6. The average cumulative weekly light exposure received while indoors (10-1000 Lux). There is a strong correlation between the time spent indoors and the cumulative light exposure level ($R^2 = 0.9449$). Error bars are SEM.

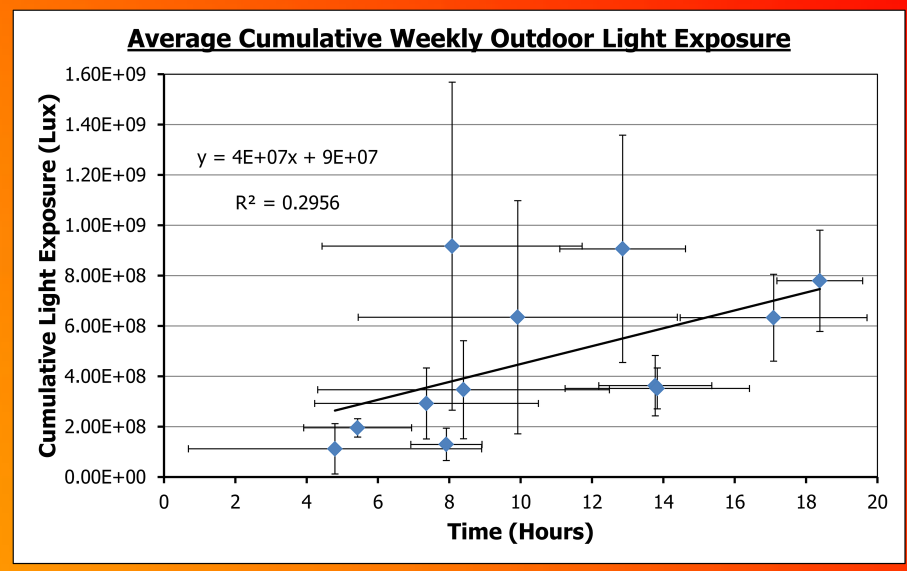

Figure 7. The average cumulative weekly light exposure received while outdoors (> 1000 Lux). There is a poor correlation between the time spent outdoors and the cumulative light exposure level ($R^2 = 0.2956$). Error bars are SEM.

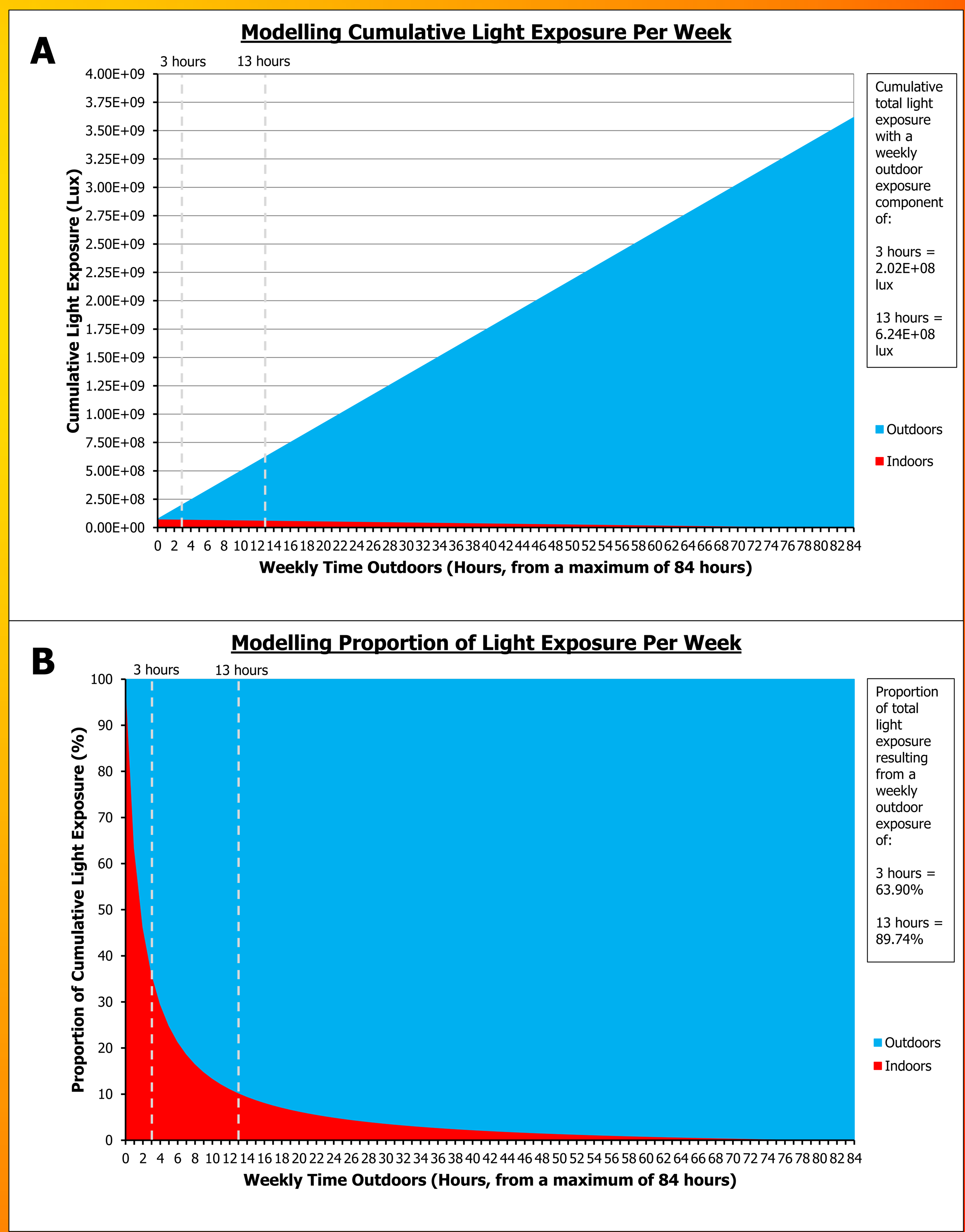

Figure 8. (A and B) Model showing cumulative light exposure (A) and proportion of total light exposure (B) experienced on average per week. The model is based on a 12:12 hour light:dark cycle, giving 84 hours of light per week. The amount of light received per hour from indoor (10-1000 lux) and outdoor (> 1000 Lux) exposures were calculated from the slopes in figures 6 and 7 (forced through zero) respectively. Comparison with data from Rose et al.[1], showing children in Singapore spend 3 hours/week outside while children in Sydney spend 13 hours/week outside, is also given.

Conclusions

- A small amount of time spent outdoors is associated with a large proportion of daily light exposure.
- While predictable levels of light exposure are obtained indoors, there is a great degree of variability in the amount of light received outdoors.
- A small amount of extra time spent outdoors can disproportionally affect the total light exposure received per day.
- Further investigations of the quality (e.g. spectral composition) and quantity (e.g. yearly exposure, differing seasons, etc.) of light received by school-aged children are warranted.

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Myopic reduction after sport activity

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Purpose

The aim of this study was to evaluate the influence of sport activity in refractive error and potentially related ocular parameters that could explain any significant change.

Introduction

In Europe the prevalence rates of myopia in adults and young adults vary around the 20% and 30% in south Europe and around 30 and 50% in north Europe. Such variability of myopia prevalence around the world could indicate some influence of the environmental factors as near work activities, education or light exposure. Rose et al found a significant association between the time spent in outdoor activity and myopia prevalence. They concluded that higher levels of total time spent outdoors were associated with less myopia and a more hyperopic mean refraction. Some other studies report the same association between outdoor activity and lower myopia prevalence rates and a more hyperopic refractive error. However these studies fail to prove the association between sport activities and refractive error.

Methods

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Age ranged from 15 to 54 years (mean ± SD, 25.7 ± 8.4)

Using the same procedure, the refractive error and the ocular parameters are measured before the subject staring their usual sport activity and repeated after one hour of sport activity. The sport activity was performed in a gym with a glass wall overlooking a garden. Each subject performed their sport activity as it normally does and was not required any activity in particular or any specific speed or performance requirement.

The refractive error was measured using an open field auto-refractor Grand Seiko Auto Ref/Keratometer WAM-5500. The ocular parameters including corneal curvature, anterior chamber depth (ACD), and axial length (AL) were assessed with IOL Master. Three readings of each parameter were taken and averaged.

Sphero-cylindrical refractive results were converted into vector representations by Fourier analysis, M, J0 and J45.

Myopia was defined as M≤ –0.50 D, emmetropia as M > –0.50 D and < +0.50 D and hyperopia as M ≥ +0.50 D.

Data were analyzed using the statistical package SPSS version 18.0

Results

Table 1. Mean (mean ± SD) values of the M, J0 and J45 components of refraction, corneal curvature, anterior chamber depth (ACD), and axial length (AL), before and after an hour of sport activity. Mean variations between the two measurements and statistical significance. Also present the values for all sample and for myopes, emmetropes and hyperopes, separately.

N=210	Refractive error group	Before	After	Mean difference	*p*
M	Myopes	-1.342 ± 0.939	-1.169± 0.976	0.173 ± 0.267	<0.001[a]
	Emmetropes	0.053 ± 0.231	0.130 ± 0.318	0.076 ±0.220	0.003 [b]
	Hyperopes	0.786 ±0.363	0.892 ± 0.685	0.106 ±0.438	0.596 [a]
				P= 0.007 [c]	
	All	-0.096 ± 0.969	0.014 ± 1.015	0.110 ± 0.312	<0.001[a]
J0	Myopes	0.487 ± 0.464	0.416 ± 0.475	-0.070 ± 0.112	<0.001[a]
	Emmetropes	-0.141 ± 0.152	-0.183 ± 0.179	-0.042 ± 0.118	0.001 [b]
	Hyperopes	-0.519 ± 0.190	-0.577 ± 0.351	-0.057 ± 0.230	0.435 [a]
				P=0.074 [c]	
	All	-0.088 ± 0.469	-0.142 ± 0.497	-0.054 ± 0.158	<0.001 [a]
J45	Myopes	-0.012 ± 0.020	-0.010 ± 0.017	0.002 ± 0.007	0.013 [a]
	Emmetropes	0.004 ± 0.008	0.004 ±0.009	0.001 ± 0.003	0.025 [a]
	Hyperopes	0.010 ± 0.011	0.012 ± 0.013	0.002 ± 0.009	0.184 [a]
				P= 0.081 [c]	
	All	0.002 ± 0.015	0.002 ± 0.015	0.001 ± 0.006	<0.001 [a]
Corneal curvature	Myopes	7.745 ± 0.233	7.750 ±0.232	0.005 ± 0.026	0.799 [b]
	Emmetropes	7.816 ± 0.232	7.815 ± 0.231	-0.001 ± 0.012	0.681 [b]
	Hyperopes	7.822 ± 0.270	7.824 ± 0.269	0.002 ± 0.021	0.334 [b]
				P=0.601 [c]	
	All	7.799 ± 0.245	7.801 ± 0.244	0.001 ± 0.022	0.386 [b]
ACD	Myopes	3.639 ± 0.536	3.679 ± 0.394	0.041 ± 0.487	0.649 [a]
	Emmetropes	3.359 ± 0.509	3.393 ± 0.493	0.034 ± 0.630	0.306 [a]
	Hyperopes	3.291 ± 0.493	3.334 ± 0.428	0.043 ± 0.418	0.221 [a]
				P=0.855 [c]	
	All	3.412 ± 0.528	3.451 ± 0.469	0.039 ± 0.536	0.106 [a]
AL	Myopes	24.229 ±0.799	24.235 ±0.797	0.006 ±0.016	0.011 [a]
	Emmetropes	23.585 ±0.700	23.583 ± 0.701	-0.003 ± 0.018	0.011 [a]
	Hyperopes	23.261 ±0.846	23.261 ± 0.831	0.000 ± 0.030	0.753 [b]
				P=0.383 [c]	
	All	23.658 ± 0.846	23.659 ± 0.848	0.003 ± 0.022	0.063 [b]

a) Wilcoxon signed rank test; b) Paired sample t test ; c) Kruskal Wallis test

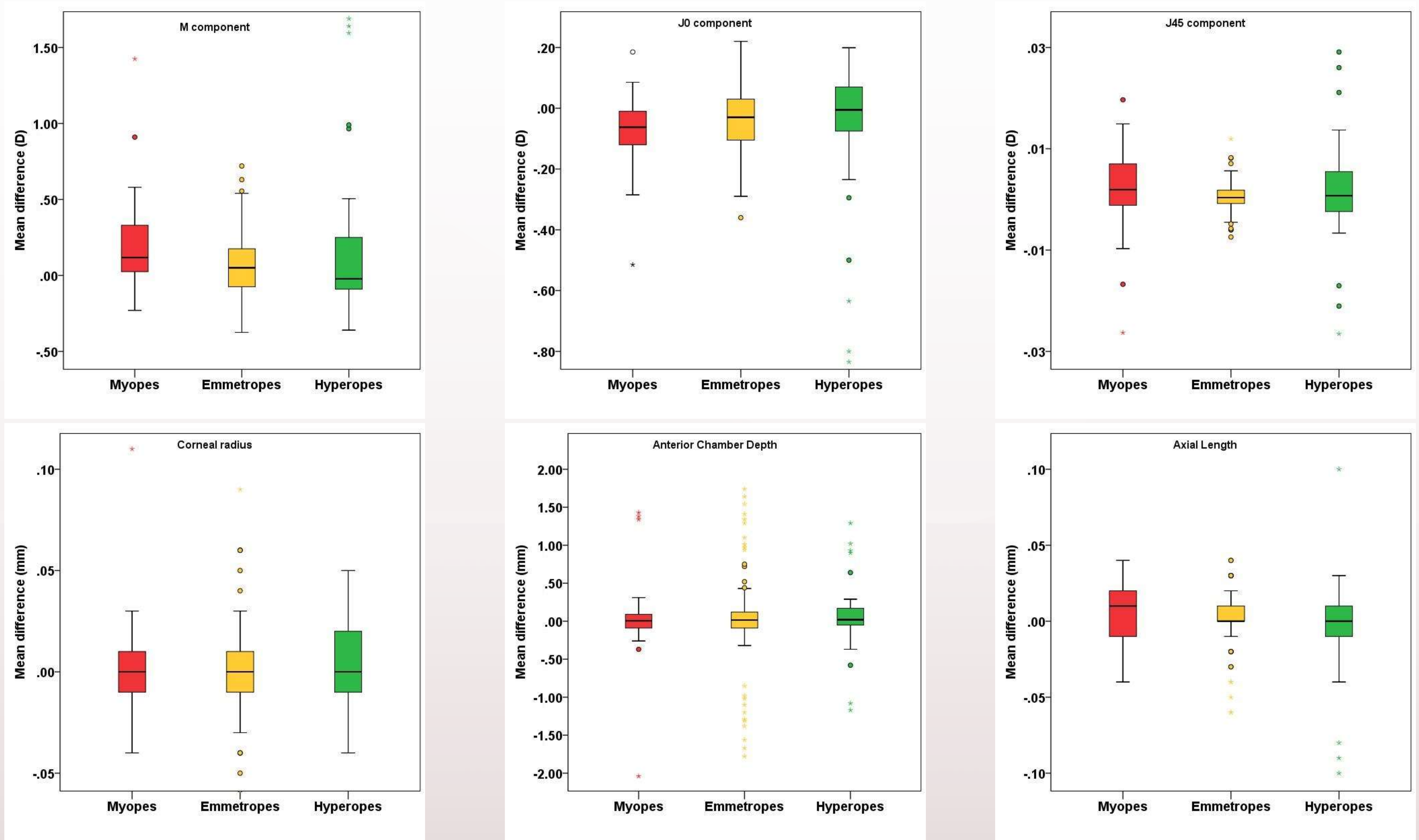

Figure 1. Graphic representation of the difference between measurements obtained before and after one hour of sport activity. Myopes, emmetropes and hyperopes are represented separately.

Considering the **all sample**, we found statistical significant changes after one hour of sport activity for all refractive parameters (M, J0 and J45). We verified a hyperopic shift (M= 0.110 D) after the sport activity and an increase of against-the-rule (or a decrease of with-the-rule) astigmatism (J0=-0.054D). For the astigmatism components, despite the differences were statistically significant the clinical significance were not relevant. For the ocular parameters as the corneal curvature, the axial length and the anterior chamber depth, we didn't found any difference statistically significant after the sport activity.

Considering **each refractive group separately** we verify that for the myopes and emmetropes the difference between the measurements obtained before and after the practice of sport activity is statistically significant for the M, J0 , J45 and for the AL. This means that the sport activity has less influence in the hyperopes than in the other two refractive groups.

Considering the **differences between refractive groups** we found that only the variation of the M is statistically significant (p=0.007), being the variation for the myopic group higher than that verified for the other two refractive groups.

Conclusions

With this work, we cannot establish a direct relation between myopia prevalence or degree and sport activity, but we can say that the practice of a sport activity induce a temporary myopic reduction and it is probably produced by changes in accommodation, since the ocular parameters remain unchanged. This effect, although in the opposite direction, is similar to what occurs after sustained near-work activities.

Sport activities could have some influence in temporary myopic reduction; however, it is necessary to study the effect over time of this refractive alteration.

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Reprint request

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Characteristics of multifocal electroretinogram (mfERG) in children with low to moderate myopia

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Purpose

To study functional change in children with low to moderate myopia by using global flash multifocal electroretinogram (mfERG).

Methods

Fifty-four children aged from 9 to 14 years (mean = 11 ± 1; median = 11) with refractive errors ranged from plano to -6 D underwent the global flash mfERG measurement at 96% contrast (Figure 1).

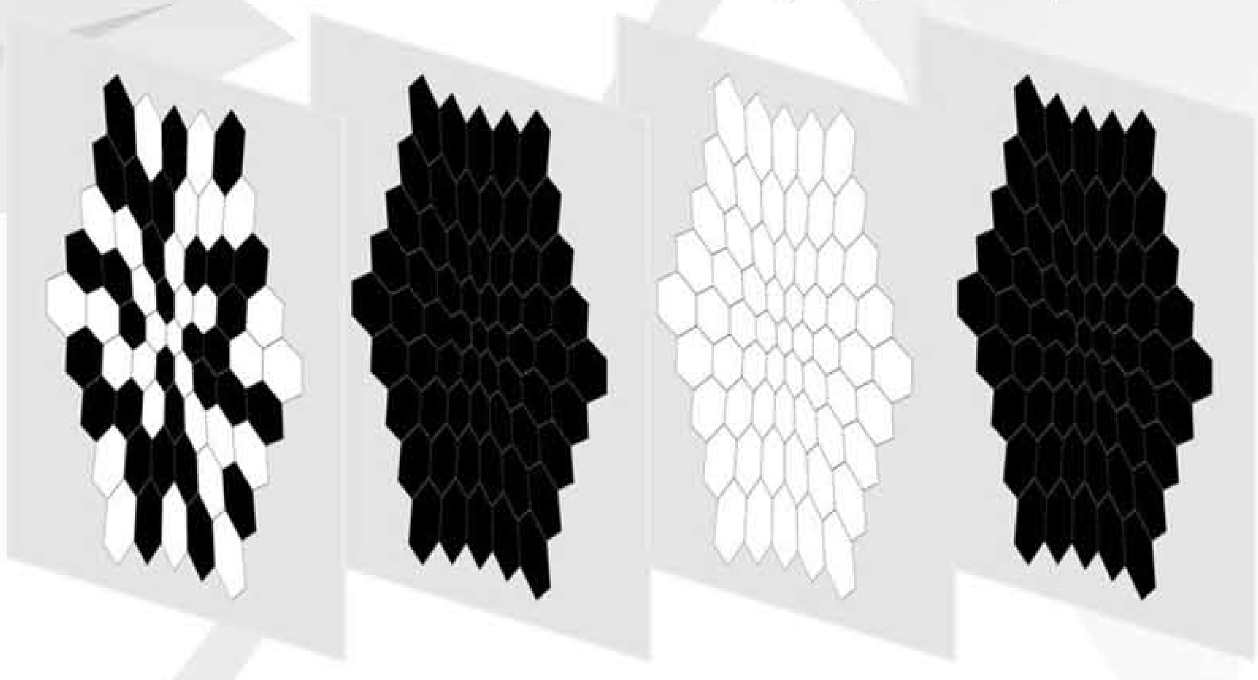

Figure 1: The global flash mfERG consisted of 4 video frames which was initiated with a frame of multifocal flashes, a dark frame, a global flash and a dark frame in each cycle.

The stimulus was made up of 61 hexagons scaled with eccentricity. The amplitude and implicit time of the direct (DC) and induced components (IC) were pooled into 5 regions for analyses (Figure 2). Stepwise multiple regression analysis was used to evaluate the contribution of refractive error and axial length to the mfERG responses.

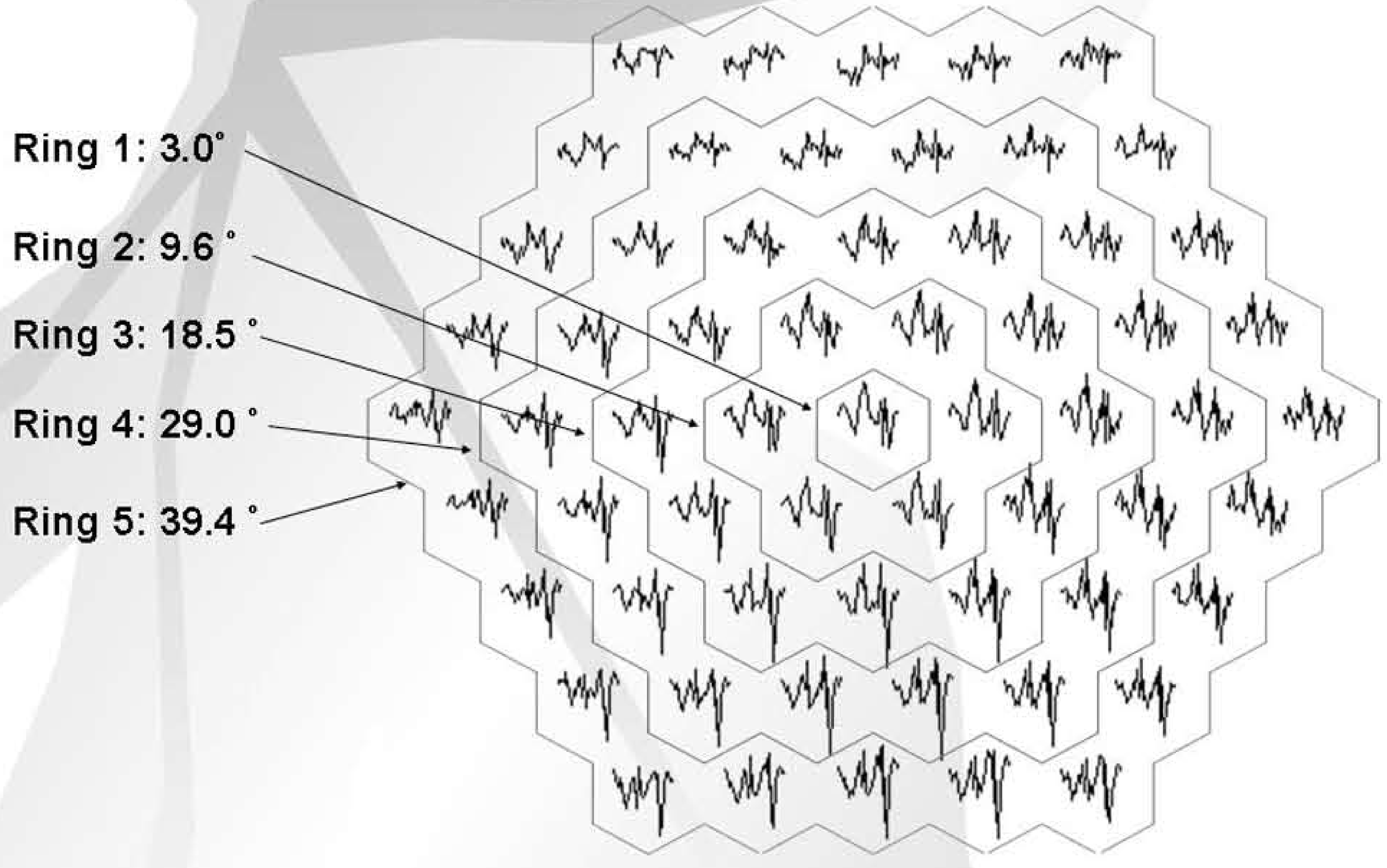

Figure 2 : The 61 local responses were pooled into 5 regions for analyses. The values beside each ring number represent the eccentricity in degree.

Results

The mean (± S.D.) spherical-equivalent refractive error and axial length of the children were, respectively, –2.64 ± 1.76 (range = 0.00 to -6.25; median = -2.38) D and 24.50 ± 0.95 (range = 22.77 to 27.23; median = 24.37) mm.

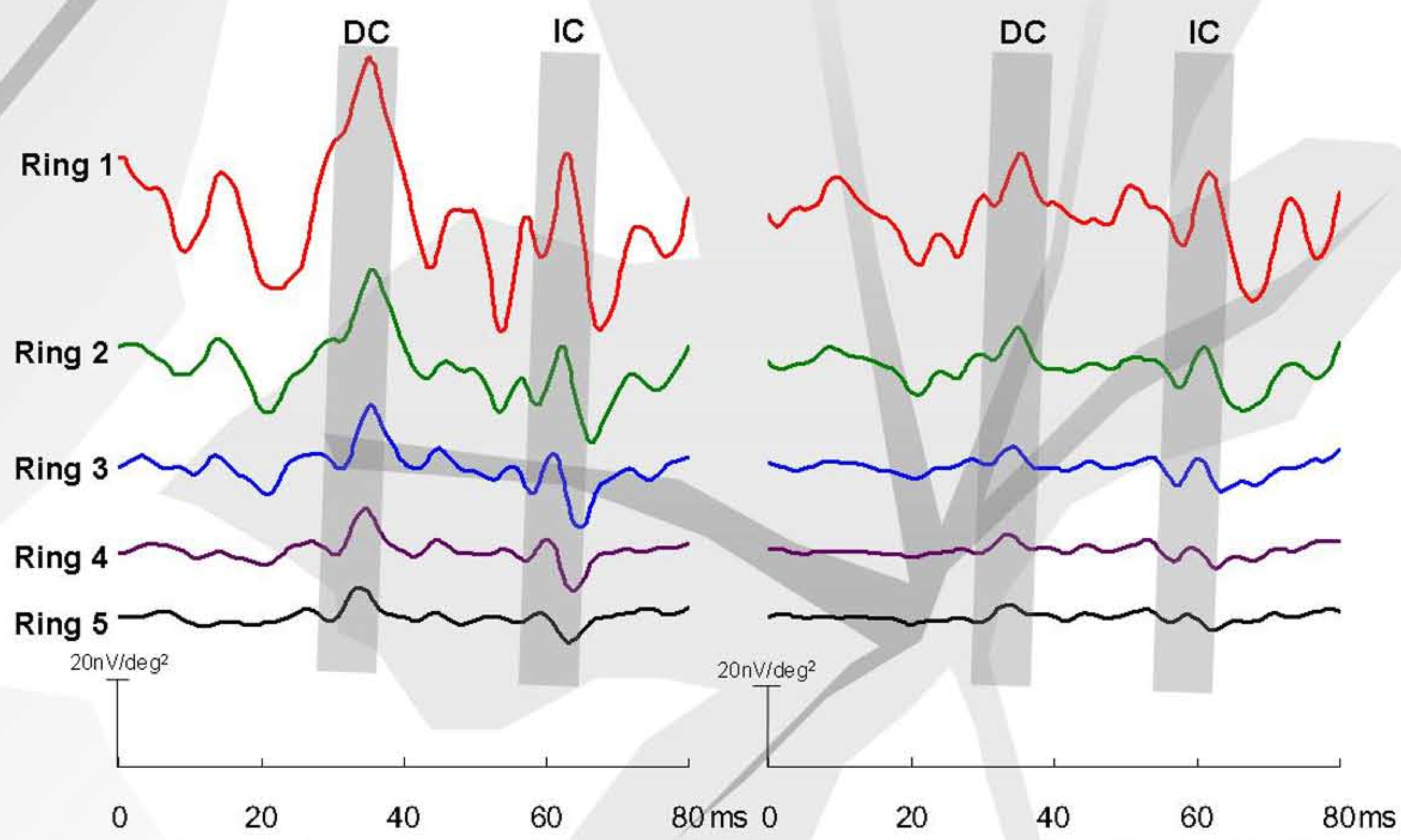

Figure 3: The typical global flash mfERG waveform from a low (SE = -0.50 D; AL = 22.97 mm) (left) and high myopic subjects (SE = -6.00 D; AL = 26.28 mm) (right).

Increasing axial length significantly reduced DC amplitude at the central region (adjusted R-square = 0.17, F = 12.02, p = 0.001) (Figure 4) but not the other retinal regions. Refractive error could not account for the extra reduction in the amplitude. On the other hand, neither refractive error nor axial length had significant impact on the amplitude of IC and the implicit times of IC and DC for all regions examined.

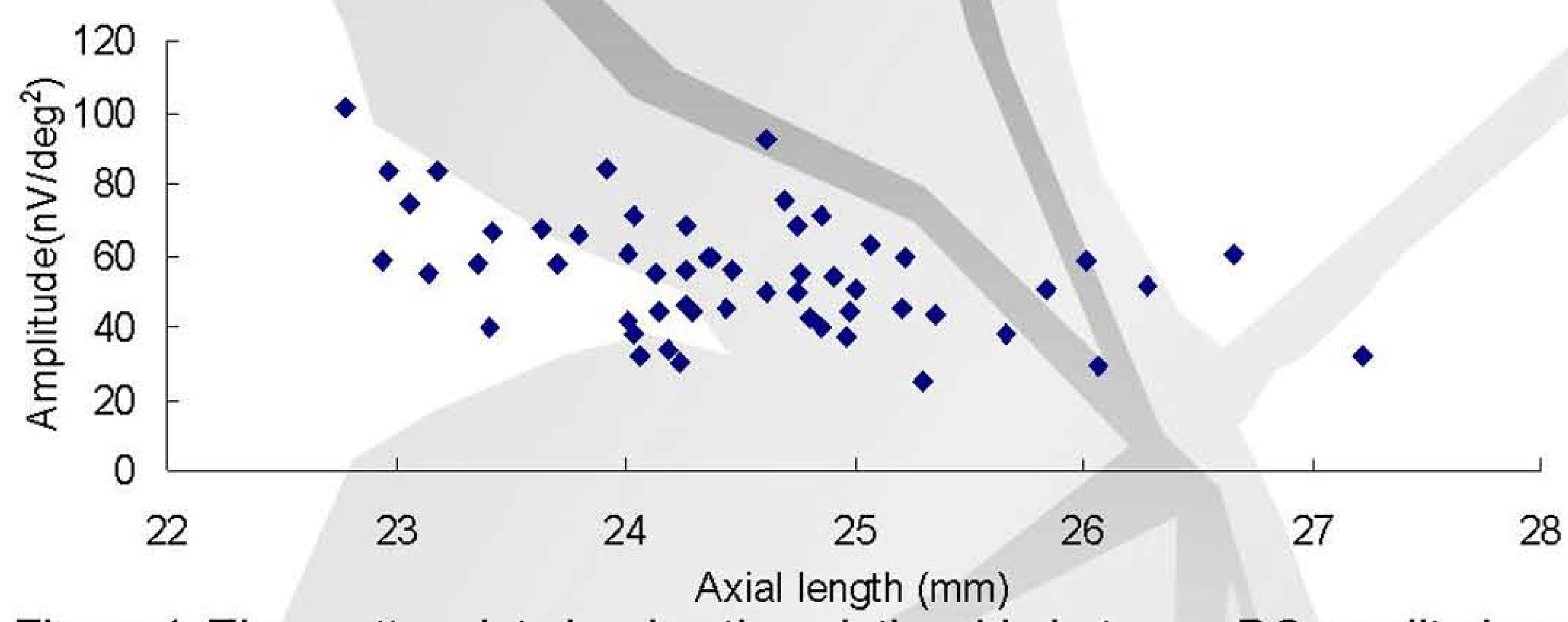

Figure 4: The scatter plot showing the relationship between DC amplitude and axial length (n = 54) (Adjusted R^2 = 0.17, p = 0.001).

Conclusions

In contrast to our previous study which showed that the paracentral IC responses reduced with increasing degree of myopia in adult[1], this study showed that only the central DC responses reduced with longer axial length in children. Further studies are needed to understand the underlying mechanism.

Acknowledgement

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Reference

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Two year follow-up of refractive error progression and optical component changes of college students

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PURPOSE

❖ To elucidate which aspects affect refractive error progression in young adulthood.

METHODS

❖ Cycloplegic refractive error was measured by Canon RK-F1. And anterior chamber depth(ACD), corneal radius(CR) and axial length(AL) were measured by IOLMaster on 74 eyes of 37 young adults in 2008 and 2010. Initial age ranged between 18 and 21.

RESULTS

❖ Table 1. Mean values of ocular components in 2008 and 2010.

	2008 (n=74 eyes)	2010 (n=74 eyes)	Difference
Variables	Mean±SD	Mean(±SD)	Mean(±SD)
SER (D)	-2.466±2.823	-2.772±3.153	0.305±0.430
CR(mm)	7.779±0.244	7.775±0.251	0.004±0.035
ACD(mm)	3.760±0.227	3.758±0.245	0.002±0.069
AL(mm)	24.722±1.439	24.767±1.446	-0.044±0.188
AL/CR ratio	3.178±0.168	3.185±0.171	-0.007±0.028

SER: spherical equivalent of refractive error, CR: corneal radius, AL: axial length, AL/CR ratio: axial length/corneal radius, ACD: anterior chamber depth.

❖ Myopia increased by an average of 0.305±0.430D(t=6.115, p=0.000) between 2008 and 2010[Table 1]. A significant correlation was found between changes in SE and CR(r=0.282, p=0.015) and in SE and AL/CR ratio(r=-0.240, p=0.039). But no significant correlation between change in SE and AL(r=-0.102, p=0.388) was found[Table 2].

❖ Table 2. The results of ordinal correlation(pearson's) for variable constants in ocular components changes.

		SER	CR	ACD	AL	AL/CR
SER (D)	r	1.000	0.282*	0.076	-0.102	-0.240*
	p		0.015	0.522	0.388	0.039
CR (mm)	r	0.282*	1.000	0.295*	-0.004	-0.517**
	p	0.015		0.011	0.972	0.000
ACD (mm)	r	0.076	0.295*	1.000	0.188	0.016
	p	0.522	0.011		0.108	0.891
AL (mm)	r	-0.102	-0.004	0.188	1.000	0.857**
	p	0.388	0.972	0.108		0.000
AL/CR ratio	r	-0.240*	-0.517**	0.016	0.857**	1.000
	p	0.039	0.000	0.891	0.000	

SER: spherical equivalent of refractive error, CR: corneal radius, AL: axial length, AL/CR ratio: axial length/corneal radius, ACD: anterior chamber depth.

❖ Classifying subjects into three groups(myopic, emmetropic, hyperopic) according to ±0.50D criteria, strong correlation between changes in SE and CR was found in emmetropic group(r=0.722, p=0.002), but no significant correlation between changes in SE and AL was found(r=-0.295, p=0.286)[Fig. 1]. In myopic group, correlation between changes in SE and CR was showed(r=0.287, p=0.048) but not between changes in SE and AL(-0.046, p=0.756)[Fig. 2]. In hyperopic group, no correlation between changes in SE and CR or AL was found.

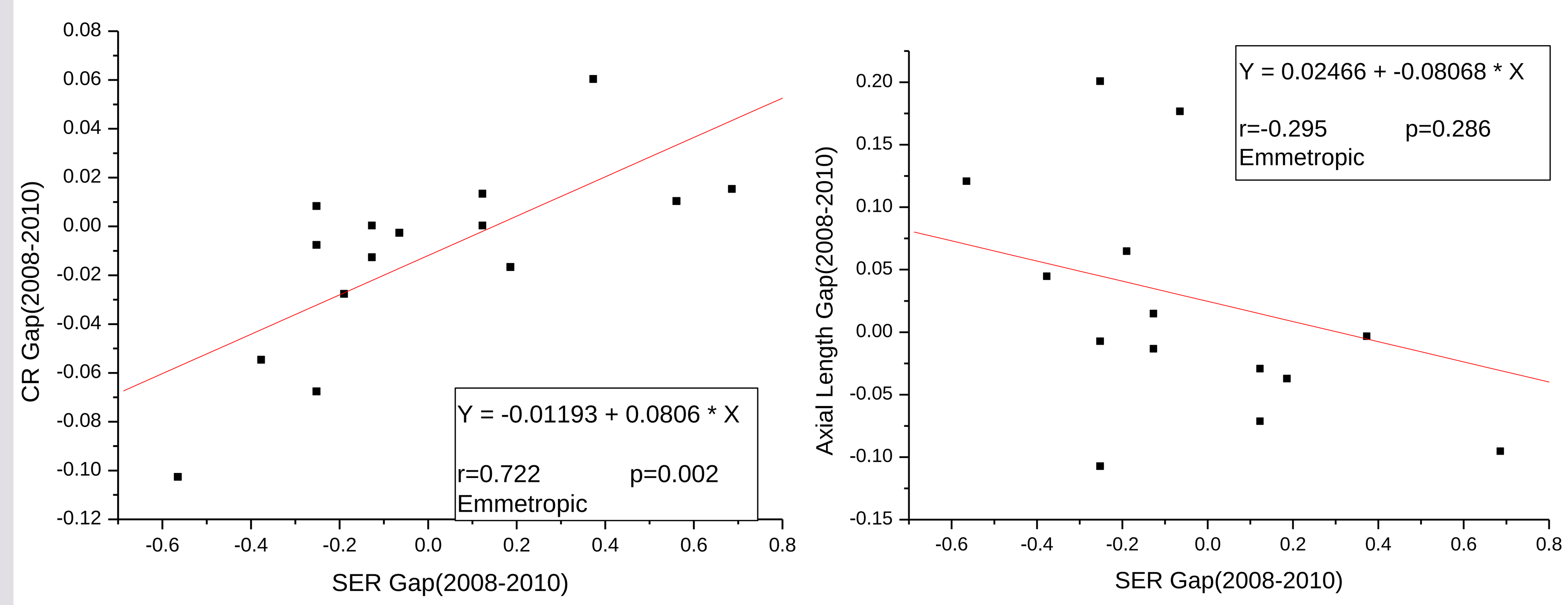

Figure 1. Correlation of ocular component changes in Emmetropic Group.

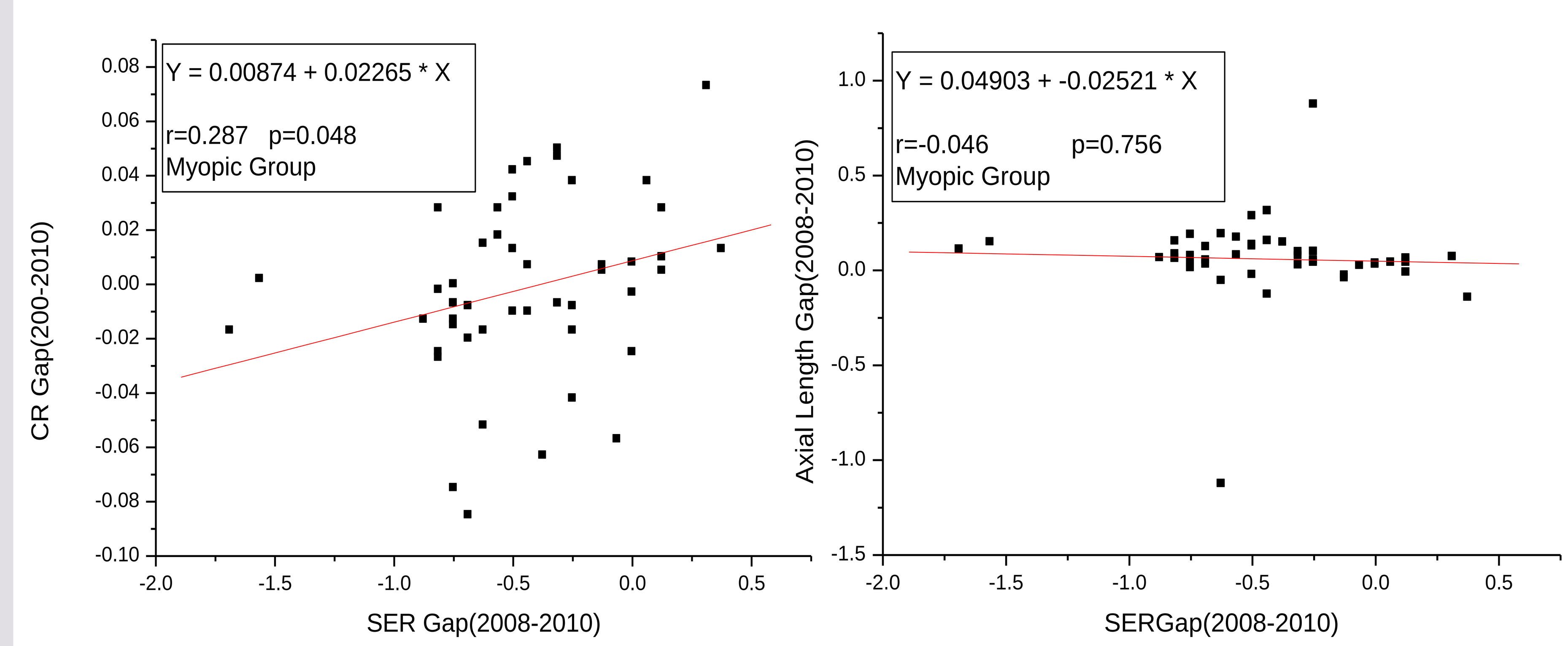

Figure 2. Correlation of ocular component changes in Myopic Group.

❖ Statistically, myopia progressed the most significantly in myopic group(t=7.599, p=0.000) for two years.

DISCUSSION AND CONCLUSIONS

❖ Changes in SE, corneal radius and AL/CR ratio were significantly correlated each other and changes in CR is the most essential factor for myopia progression in young adults. Myopia progression in young adulthood is more common in myopic eyes. It, therefore, is presumed that adulthood myopia is related to not axial length elongation but corneal radius steepening.

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Differential protein expression using two-dimensional salt plug mass spectrometry techniques

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Introduction

The risks of myopia emergence and development can be classified to nature and nurture[1]. Chick (Gallus Gallus) as a well-established myopic animal model is used to study the mechanism of nurture in myopia[2]. The rapid advancement of proteomic technology provides a powerful tool and new sight to investigate the effect of proteins in myopic chicks[3].

In this study we aim to study the retinal protein expressions in lens induced myopia (LIM) and lens induced hyperopia (LIH) chicks using two-dimensional salt plug mass spectrometry (2D-LCMS) coupled with isotope coded protein labeling (ICPL).

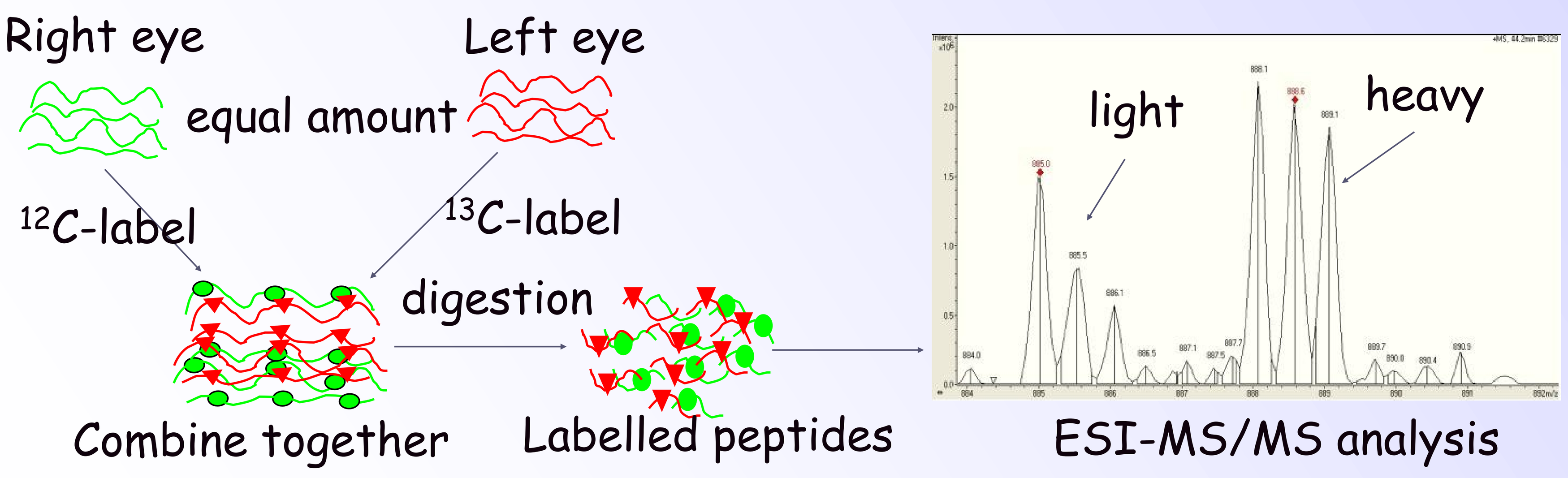
Methods

Samples preparation

The right eyes of white leghorn chicks (3 days old, n=5) wore -10D lens and left eyes with +10D lens for 3 days. Refractive error and eye parameter before and after the treatment were measured using a streak retinoscope and high frequency ultrasonography respectively. Retina tissues were harvested and homogenised in Guanidine-HCl buffer using a dismembrator with liquid nitrogen. The protein concentration of each retina sample was measured using 2-D Quant Kit™.

Isotope coded protein labelling (ICPL)

Equal amount of proteins from both eyes were labelled with ^{12}C-Nic-reagent (right eye) and ^{13}C-Nic-reagent (left eye) respectively and mixed according to SERVA ICPL Kit. The mixture was in-solution digested by trypsin and endoproteinase GluC overnight.



Two-dimensional (2-D) salt plug

Using HCTultra IonTrap Mass Spectrometry, 22ug protein mixture was loaded into a strong cation-exchange (SCX) column as a 1st-dimension separation and subsequently separated in a reversed-phase (RP) column for 2nd-dimension separation. The concentrations of NaCl range from 1mM to 1M. After separation the samples were sent to Electrospray Ionization Tandem Mass Spectrometry (ESI-MS/MS) for detection. Peptides labelling for isotope pairing (SILE pair detection) and protein quantification were performed in WARP-LC™ software. International Protein Index (IPI) database of chick was used for peptide sequences searching to get the protein IDs.

Results

Fig.1 Refractive error and axial length changes (Mean±SEM, n=5) after 3 days lens wearing (R: -10D & L: +10D, compared to left eye, ***as p<0.001 using paired t-test)

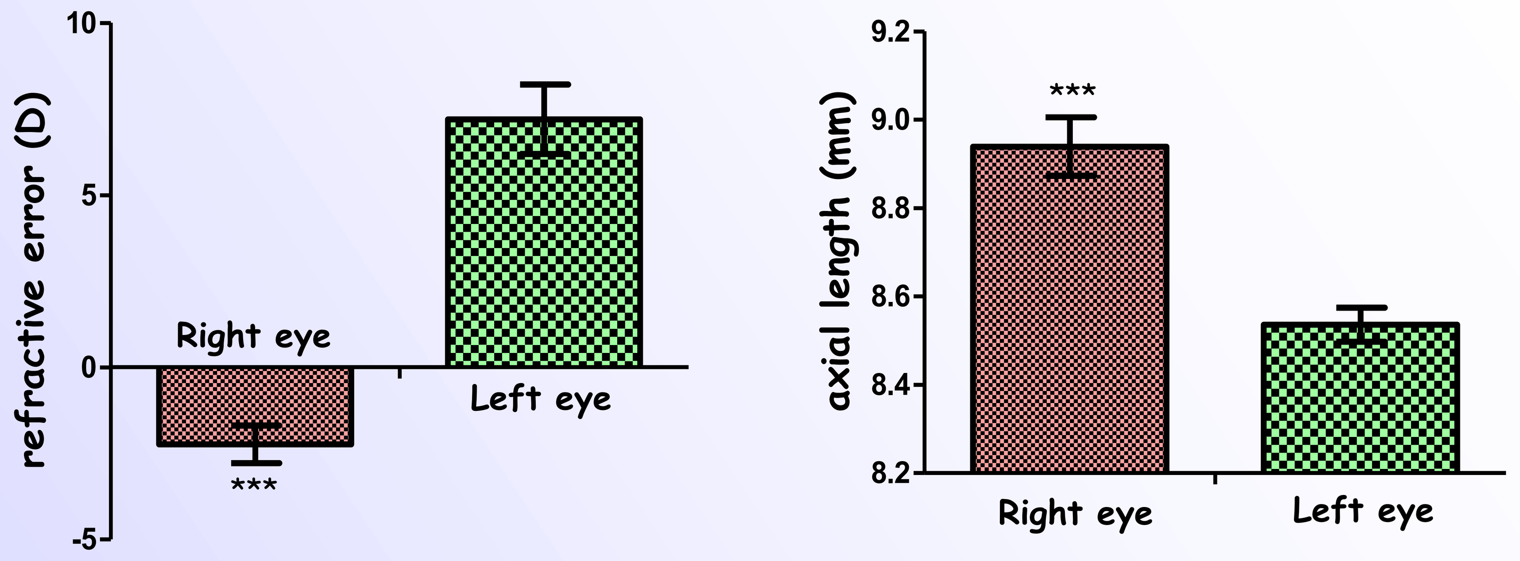


Fig.2 ESI-MS/MS results of ICPL data using 2-D salt plug separation. Total 789 proteins were identified, in which 544 protein Ids (70.2%) have paired ratios and 127 IDs have more than 3 paired rations. 16 protein IDs were selected using our criterion (at least 3 paired-ratios & ratios >1.35 or <0.7).

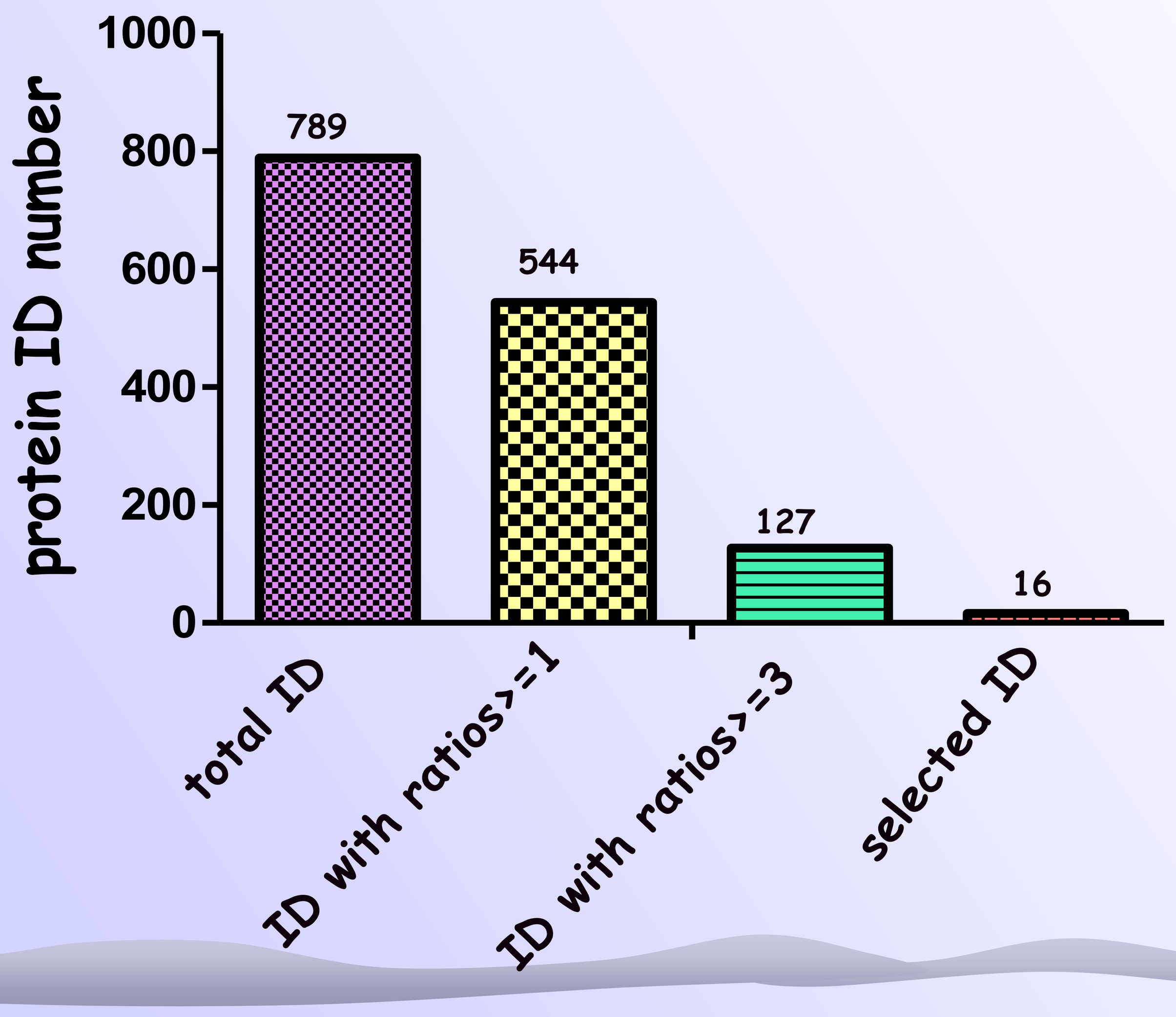


Table.1 Differentially expressed protein candidates

Expression	IPI number	Gene Symbol	ratio	protein name	MW	#bands
UP	IPI00573583	MYO1F	2.11±0.38	CBBMIB(Brush border myosin IB)	126.64	3
UP	IPI00581757	NEB	1.57±0.23	nebulin	765.25	5
UP	IPI00600745	GOLGB1	1.88±0.59	golgin B1, golgi integral membrane protein	318.65	3
UP	IPI00594463	KIF15	1.60±0.27	kinesin family member 15	163.36	3
UP	IPI00596489	TTN Connection	2.51±0.66	Titin/Connection(Fragment)	911.65	5
UP	IPI00590269	IBTK	2.34±0.52	inhibitor of Bruton agammaglobulinemia tyrosine kinase	152.84	4
UP	IPI00594691	CMYA5	1.76±0.31	cardiomyopathy associated 5	477.58	3
UP	IPI00586709	TLN1	1.65±0.13	Talin-1	273.78	3
UP	IPI00582908	ANK3	2.14±0.56	ankyrin 3	475.85	4
UP	IPI00580771	TRIP11	3.55±1.09	thyroid hormone receptor interactor 11	227.65	5
UP	IPI00597865	GCC2	2.79±0.99	GRIP and coiled-coil domain containing 2	196.95	3
UP	IPI00588012	ZMYM3	2.01±0.43	zinc finger, MYM-type 3	158.07	3
DOWN	IPI00588305	CEP152	0.69±0.06	centrosomal protein 152kDa	206.82	3
DOWN	IPI00602741	ASPM	0.70±0.14	asp (abnormal spindle) homolog, microcephaly associated (Drosophila)	986.17	5
DOWN	IPI00599953	RREB1	0.62±0.29	RAS-responsive element-binding protein 1	181.36	3
DOWN	IPI00594389	CCDC41	0.69±0.17	coiled-coil domain containing 41	91.09	3

Conclusions

2-D salt plug mass spectrometry showed its good usability as a protein separating technique in analytical researches. We have found 16 differentially expressed protein candidates in this experiment using this proteomic approach. Some of these proteins may play an important role in the development of chick eyes and further studies are needed to elucidate the mechanism of them.

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Wavefront aberration sensitivity of intraocular lens implantation position in myopic eyes

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1. Introduction

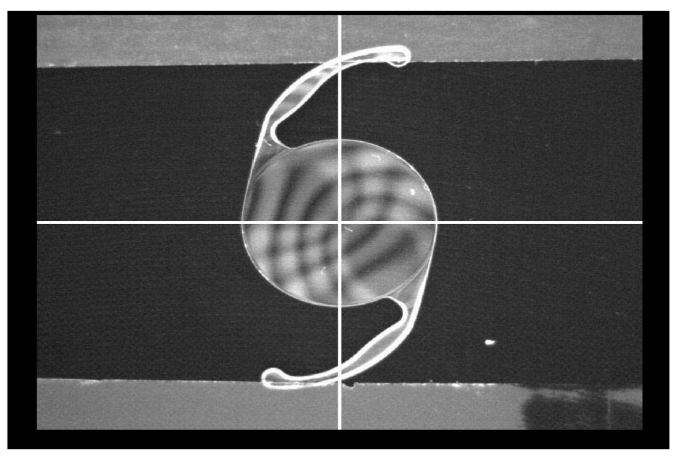


Fig. 1. An isolated IOL. Its central disk is the functional optical power zone plus its edge. Its two arms connected to the edge are usually called haptics, which has small elasticity and can hold the IOL in its position e. g. in the crystalline lens capsular bag to replace the original lens.

Cataract patients usually need intraocular lens (IOL) with proper optical power to replace their less transparent or opaque crystalline lens. IOL is therefore an artificial human eye lens. Fig. 1 shows a photo of an isolated IOL.

The necessary IOL power calculation and prediction are generally based on biometrics of cataractous eyes and surgical protocols. Any IOL implantation error such as de-centrations, tilts, axial shifts, rotation and/or combinations of these, reduces the vision quality of the pseudophakic eyes.

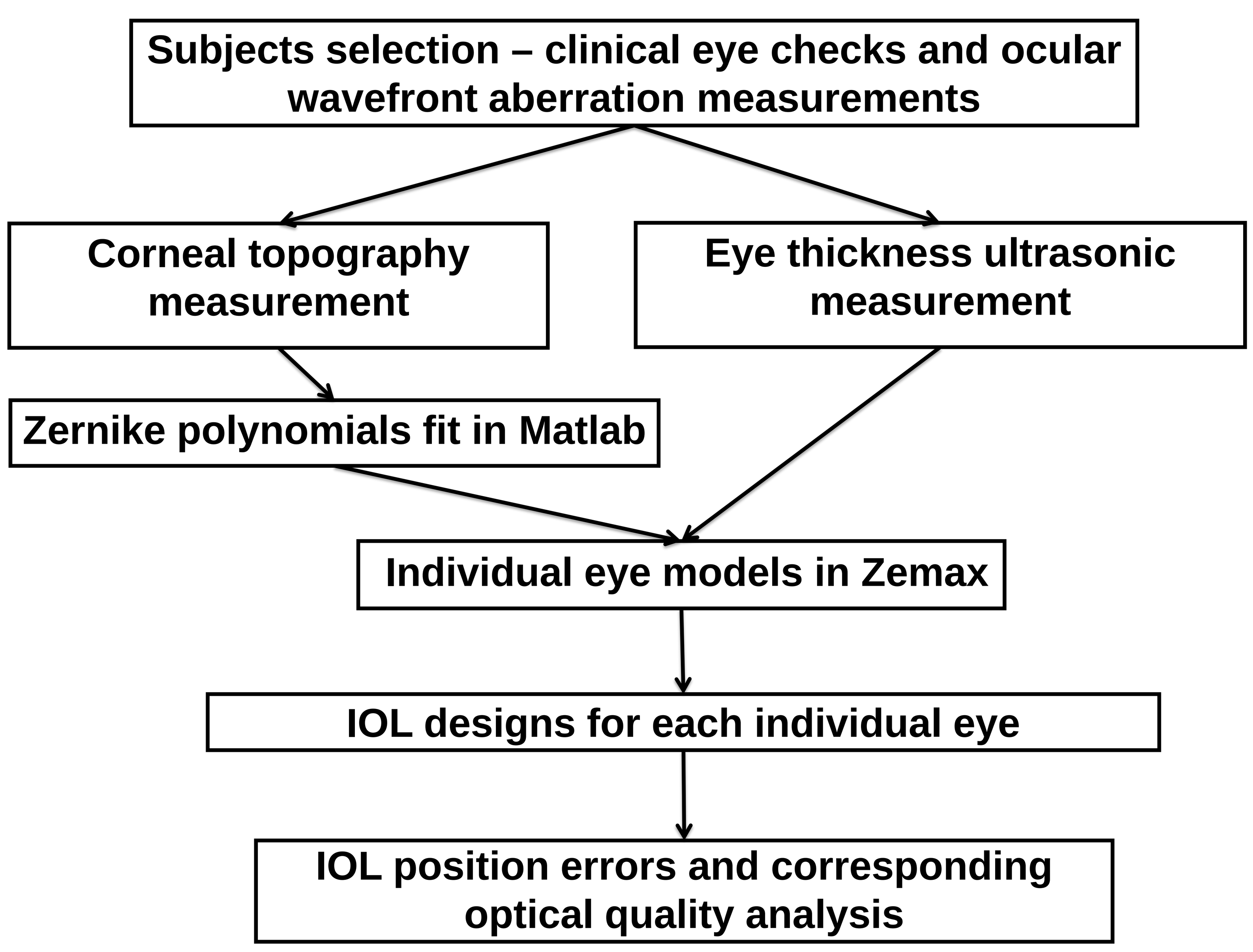
Previous studies (e. g. Ref. [1], [2]) have separately considered some of the IOL position errors by use of biometric measurement and/or statistical data. In this study, we use new method based on random mixture of all possible IOL position errors to understand the sensitivity of IOL to its implantation position in individual pseudophakic eyes. We focus on IOLs that are designed for myopic eyes.

2. Purpose

To use real eye's biometric data to theoretically calculate the influence of IOL's implantation position errors on pseudophakic eye's monochromatic wavefront aberrations for individual myopic eyes.

3. Methods

Fig. 2. Working flow chart of individual eye model construction for analysing aberration effect of IOL's implantation errors



Individual optical eye models (Ref. [3]) were constructed to design IOLs and analyse pseudophakic eye's optical quality. We used individual eye's biometric data measured by corresponding instruments.

Fig. 2 shows a flow chart for constructing individual eye optical model, and customized designed IOLs hereby were incorporated into these eye models aiming to provide proper optical power correction. In this study, we selected 9 eyes data from 6 subjects who have no other eye pathology except myopia, and their ocular wavefront aberrations are in normal range. Nine individual models were constructed for these eyes and different IOL designs were invesgated. These designs included: a) the IOLs which only corrected the eye's sphere refractive error; b) which corrected sphere plus cylinder errors; c) which corrected sphere plus spherical errors and d) which corrected all wavefront aberrations up to 17 ophthalmic Zernike terms. Although only monochromatic aberrations and their changes at 546 nm wavelength were calculated by ray-tracing method, chromatic effect of all components in the models were included to cover wavelengths shift. Zernike coefficients describing the aberrations and the root mean square (RMS) value was calculated from these coefficients for estimation of optical quality. Pupil size of 5.2 mm and 6 meters distance object were used in the calculation. Five field points within 2 degree visual field were combined together to estimate RMS value of wavefront aberrations.

The pseudophakic eyes' IOL position errors, i.e. decentrations, tilts, rotation, shift from its nominal position and/or mixture of all of these errors, were modelled following Gaussian normal distributions. In each individual eye model, they were randomly mixed together with each of them covering ranges of typical cataract surgery conditions. Fig. 3 illustrates one individual optical model eye with a displaced IOL in it.

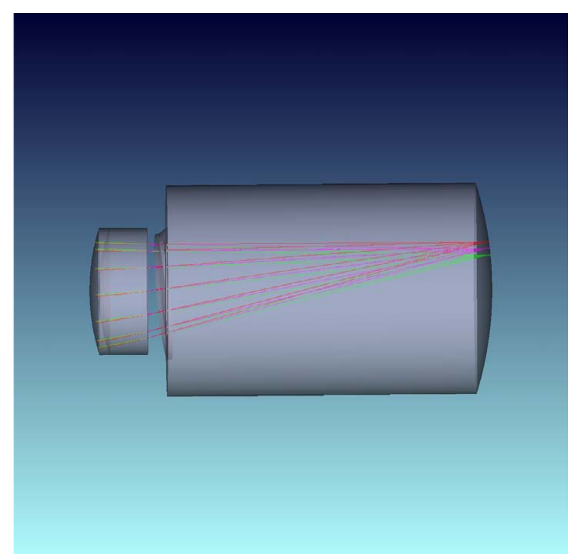


Fig. 3. An individual optical eye model. The corneal anterior and posterior surfaces locate at the left side of this picture. Then a short distance to the right covers by the anterior chamber of the eye and is followed by the iris and posterior chamber, and then by a displaced IOL (may include decentrations, tilts, rotation, shift). The vitreous body is the longest part of the eye. The rays passing through all these parts reach the fovea of the retina, possibly carrying aberrations induced by all parts especially by the displaced IOL.

4. Results

Fig. 4 shows averaged nine individual eyes' wavefront aberration RMS values with four types of IOL design. For IOL at its nominal position (best correction position), IOLs with sphere plus cylinder correction, sphere plus spherical correction and full correction can provide significantly better quality compared to sphere only correction IOL ($p < 0.05$). If IOL implantation position is displaced from its nominal position by means of random displacement mixture, sphere plus spherical and full corrections are significantly more sensitive to their position change than sphere only correction ($p < 0.05$), while sphere plus cylinder correction has no significant difference with sphere only correction IOL ($p > 0.05$) .

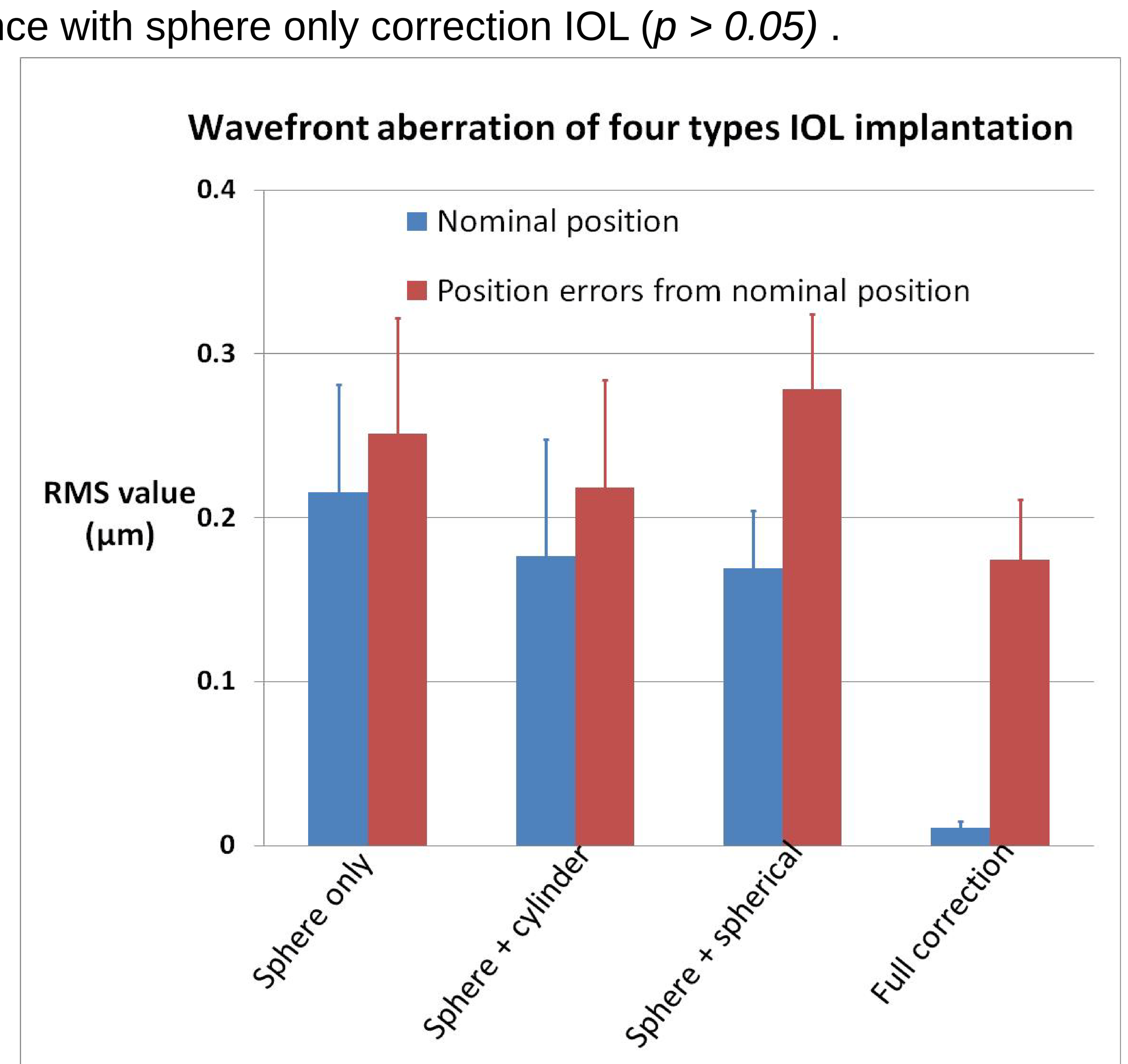


Fig. 4. Four types of IOL implantation at nominal positions and with errors for nine myopic eyes.

5. Conclusions

In general, for the myopic eyes, sphere only correction IOL is most robust to its implantation position errors than customized IOLs, while customized IOLs offer better correction than sphere only one.

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Longitudinal observations on the role of the peripheral refraction profile in myopia development

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INTRODUCTION

In recent years the roles of peripheral refraction and ocular shape in the development of myopia are subject of increased interest and discussion (Charman, 2005; Stone and Flitcroft, 2004; Wallman and Winawer, 2004).

Hoogerheide (1971) showed that pilots with relative peripheral hyperopia had the greatest risk of developing myopia.

Smith *et al.* (2007, 2005) demonstrated in investigations in monkeys that the peripheral retina can influence refractive development and that an intact fovea is not essential for emmetropisation.

In this context the aim of the present study was to investigate longitudinally whether relative peripheral refraction is a causative factor in the development of myopia.

METHODS

- 4-year longitudinal study on refractive development conducted in private optometric practice in Duisburg, Germany
- 140 subjects between 5 and 20 years with visual acuity of 6/6 or better
- Exclusion criteria: ocular or systemic disease, strabismus, astigmatism > 2D, anisometropia > 2D, RGP lens wear
- Measurements at baseline and after 2 and 4 years:
  - Non-cycloplegic mean spherical equivalent refractive error (MSE) centrally and peripherally (25° temporal) using an open-field infrared autorefractor (Shin-Nippon Nvision-K 5001)
  - Axial length (AL) using partial coherence interferometry (Zeiss IOLMaster)

RESULTS

Baseline data

- Baseline MSE between -5.88D and +3.45D
- 44 hyperopes (HYP), 61 emmetropes (EMM) and 35 myopes (MYO)[1]
- MYO had *hyperopic* relative peripheral refraction (RPR) while HYP and EMM had *myopic* RPRs (*Table 1*)

Year 4 data

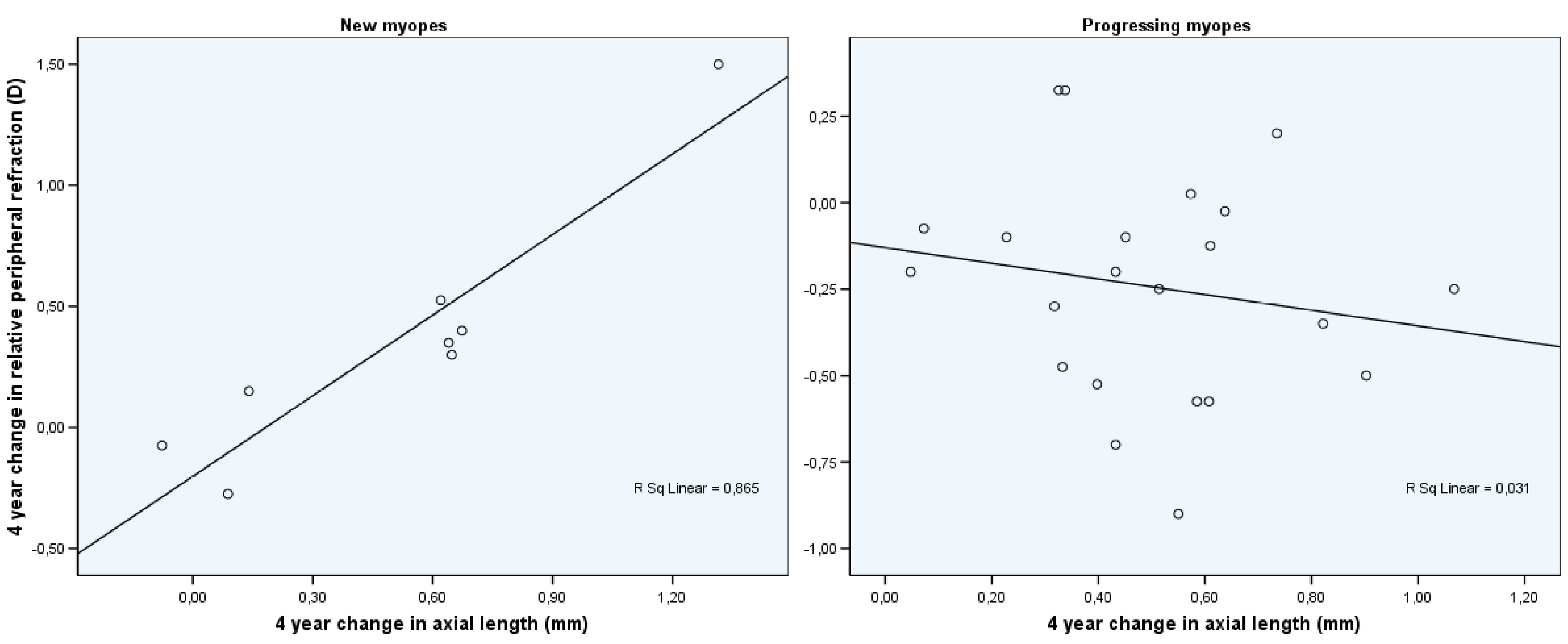
- 105 subjects completed the year 4 examinations
- 8 EMM became myopic and 22 MYO had progressing myopia[2] (*Table 2)*
- No statistically significant differences (p>0.05) in baseline RPR between either the stable emmetropes and new myopes or between the stable and progressing myopes
- No statistically significant differences (p>0.05) in 4-year refractive (*Figure 1*) or axial development (*Figure 2*) between subjects with a hyperopic RPR compared to those with a myopic RPR for both the MYO and EMM subgroups
- Significant correlation between axial/refractive development and changes in RPR in the new myopes (*Figure 3*) but not in the progressing myopes (*Figure 4*)

	Mean central refraction (D)	Mean axial length (mm)	Mean relative periph. refr. (D)
Myopes	-2.36±1.37	24.68±1.09	0.32±0.73
Emmetropes	0.19±0.28	23.06±0.92	-0.34±0.80
Hyperopes	0.94±0.60	22.70±0.77	-0.66±0.85

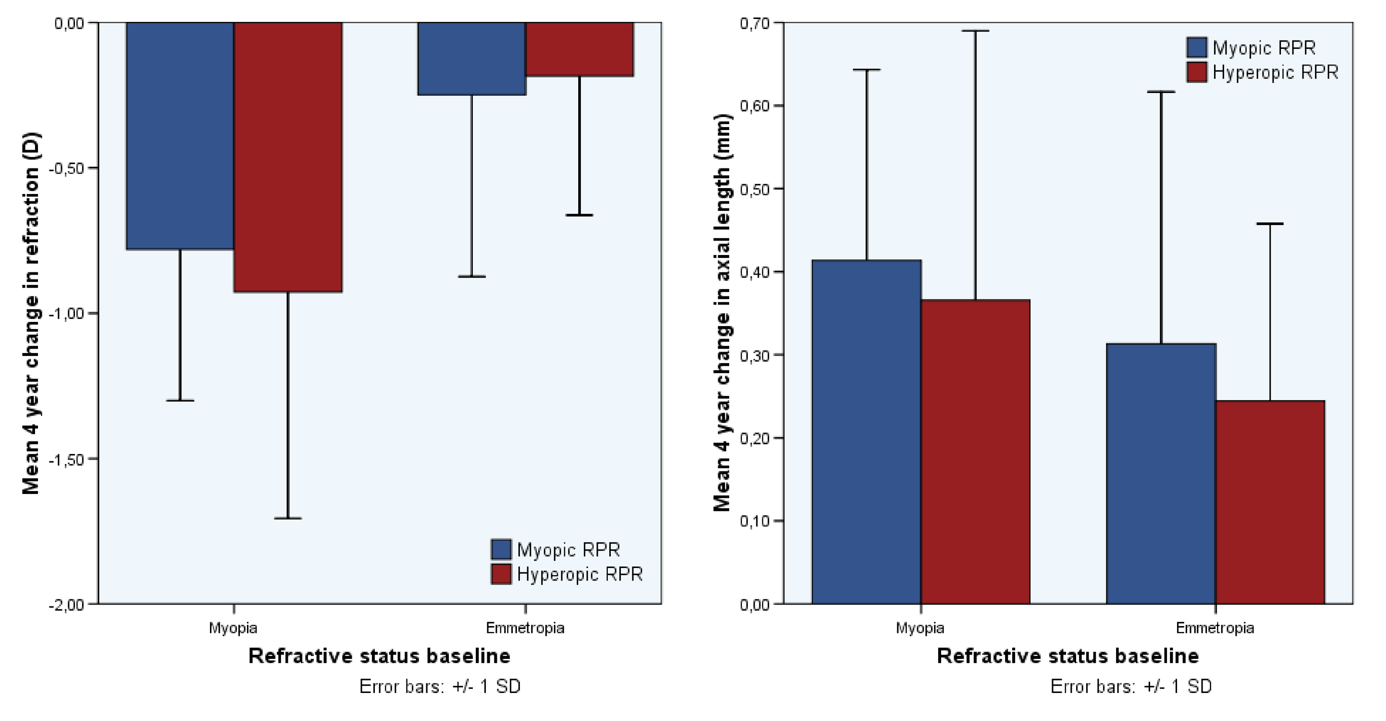
Table 1. Baseline refraction and axial length in all groups

	Changes in mean central refraction (D)	Changes in mean axial length (mm)
New myopes	-1.08±0.78 (p<0.01)	0.51±0.44 (p<0.05)
Progressing myopes	-1.19±0.61 (p<0.01)	0.50±0.25 (p<0.01)

Table 2. 4-year changes in refraction and axial length in new and progressing myopes



Figures 3 and 4. Changes in RPR during eye growth in the new and progressing myopes



Figures 1 and 2. Changes in refraction and axial length compared in subjects with *myopic* relative periph. refraction (RPR) and *hyperopic* RPR in the baseline myopes and emmetropes

[1] HYP = MSE > 0.50D, MYO = MSE < -0.50D

[2] Negative change of MSE > 0.50D

CONCLUSIONS

Consistent with previous peripheral refraction investigations, myopic eyes demonstrated a relative hyperopic peripheral profile while hyperopic eyes showed relative peripheral myopia.

Longitudinal data support the association between myopia formation and concomitant changes towards a more hyperopic relative peripheral refraction.

While the relative hyperopic peripheral profile is a normal anatomical attribute of myopic eyes there is no evidence for it to be a risk factor for the development of myopia.

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Psychophysical measurements of blur adaptation in myopia

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Purpose

- To investigate the differences in blur adaptation between myopic and non-myopic participants using both sinusoidal grating and letter acuity measurements.
- To determine whether exposure to visual tasks of varying visual demand affects blur adaptation in these groups.

Figure 1. A screen capture of the action computer game simulating the difference in image quality between the in-focus view (left half of image) and the blurred image (right half of image). Note the loss of clearly defined edges under blur.

Methods

- Refractive error was measured under cycloplegia at least one day prior to blur adaptation measurements. Contact lenses were used to provide correction during later experimental sessions.
- Acuity thresholds were measured in 13 adult participants (7 myopes, 6 non-myopes) using computer-generated sinusoidal gratings (40% contrast) and a high contrast logMAR (Bailey-Lovie) letter chart.
- Acuity thresholds were measured immediately prior to, and following induction of 1.00D myopic blur. A period of one hour of blur adaptation was undertaken while the participant performed either a visually demanding task (fast-paced action computer game) [Fig. 1], or a less visually demanding task (slow-paced geometric puzzle game) at a viewing distance of 3 m.
- Acuity thresholds were re-measured immediately following the period of blur adaptation both with and without blur.

Results

- Following blur adaptation, both myopic and non-myopic participants showed a significant improvement in letter acuity with the blur in place of -0.052 logMAR and -0.084 logMAR respectively (mixed ANOVA, $F_{(1.9)} = 5.94$, P=0.037) regardless of the visual task [Fig. 2a].
- On removal of the blur, myopic participants returned to baseline letter acuity while the non-myopic participants showed a significant improvement over baseline letter acuity (-0.046 logMAR, P=0.018) [Fig. 2a].
- The type of video game played during blur adaptation had no significant effect on the above outcome however the non-myopic group exhibited a trend for a greater blur adaptation effect with the action game [Fig. 2b] than with the puzzle game [Fig. 2c]
- No significant change in grating acuity was found following blur adaptation, irrespective of the adaptation task (action vs puzzle game) or of the participant's refractive status (myopic vs non-myopic) [Figs 3a, 3b, 3c].

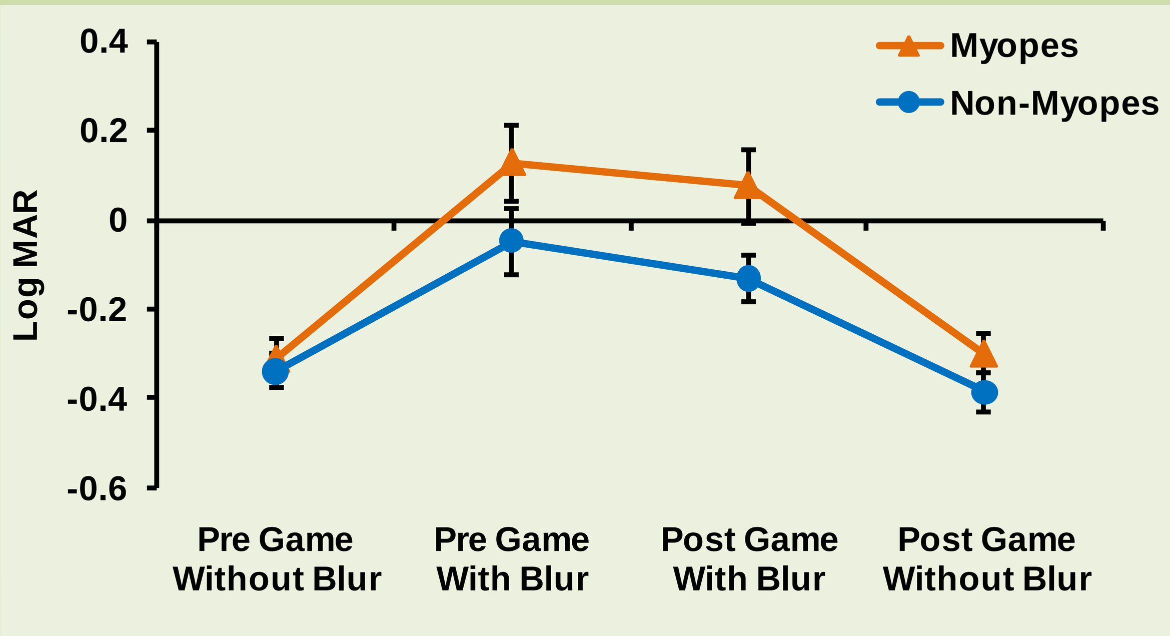

Figure 2a. Letter acuity measurements as a function of blur condition and refractive status. Myopic and non-myopic groups both show a significant improvement in letter acuity under blur following visual adaptation.

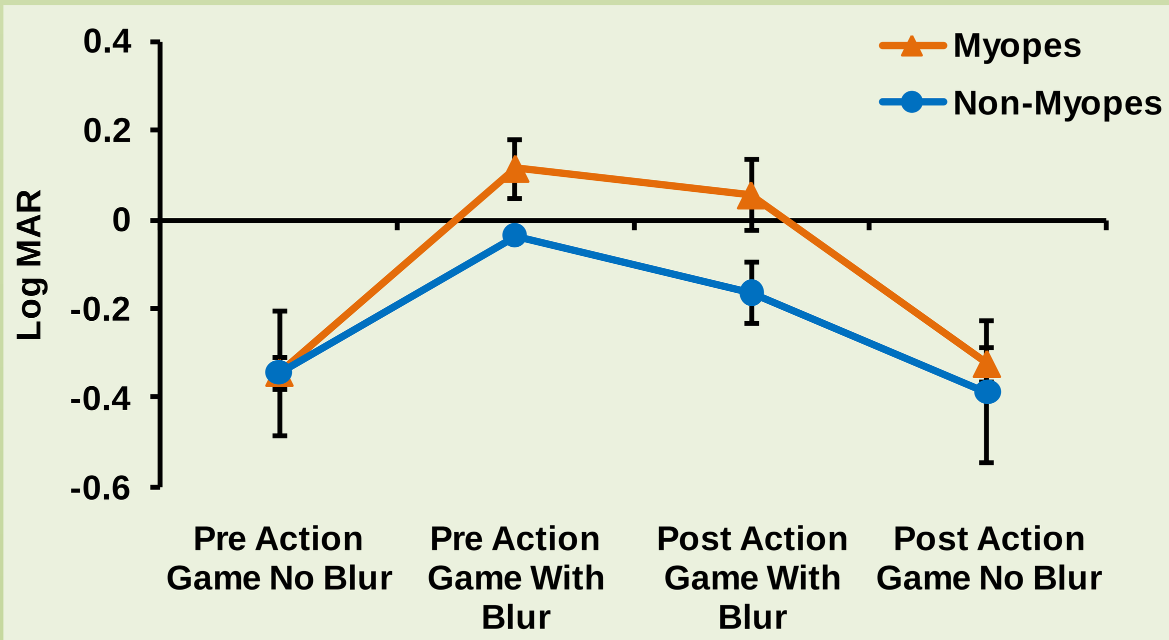

Figure 2b. Letter acuity measurements for the fast-paced action game adaptation task. The non-myopic group exhibits a trend for a greater blur adaptation effect than the myopic group.

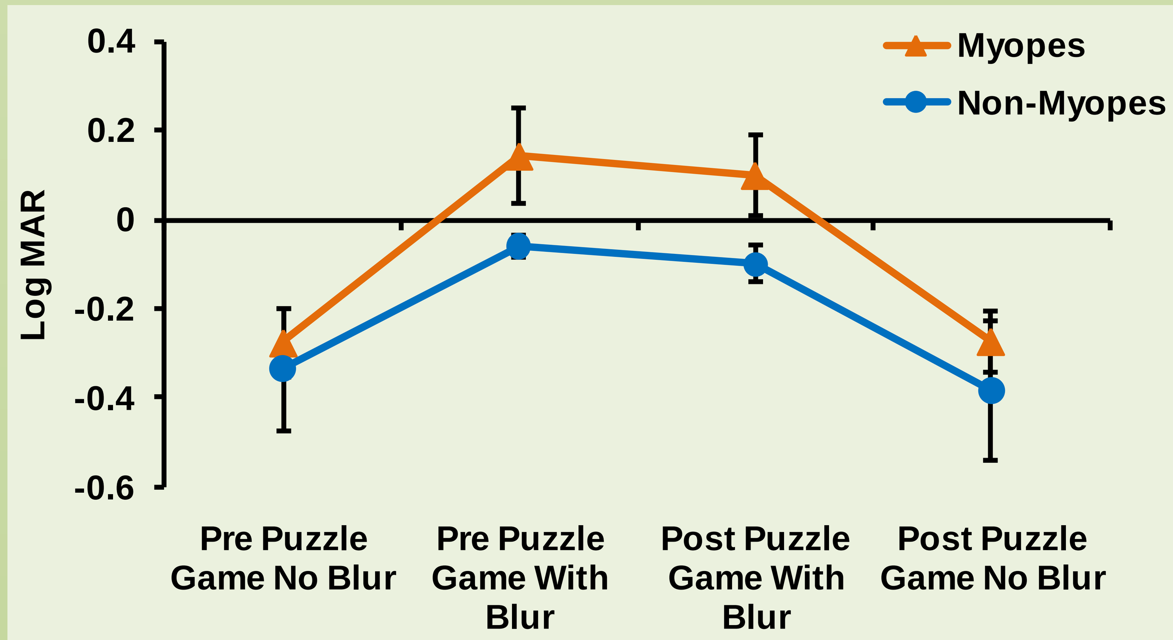

Figure 2c. Letter acuity measurements for the slow-paced puzzle game adaptation task. The non-myopic and myopic groups exhibit a parallel trend in acuity improvement following blur adaptation.

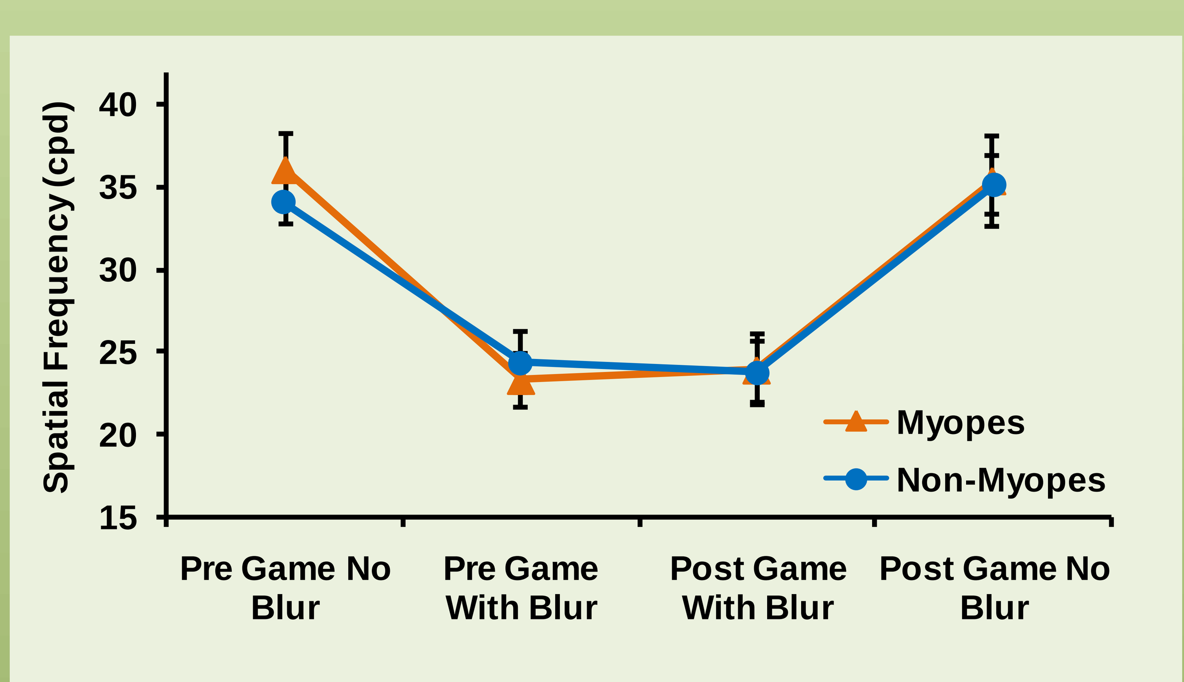

Figure 3a. Grating acuity measurements as a function of blur condition and refractive status. Myopic and non-myopic groups showed no significant improvement in grating acuity following visual adaptation.

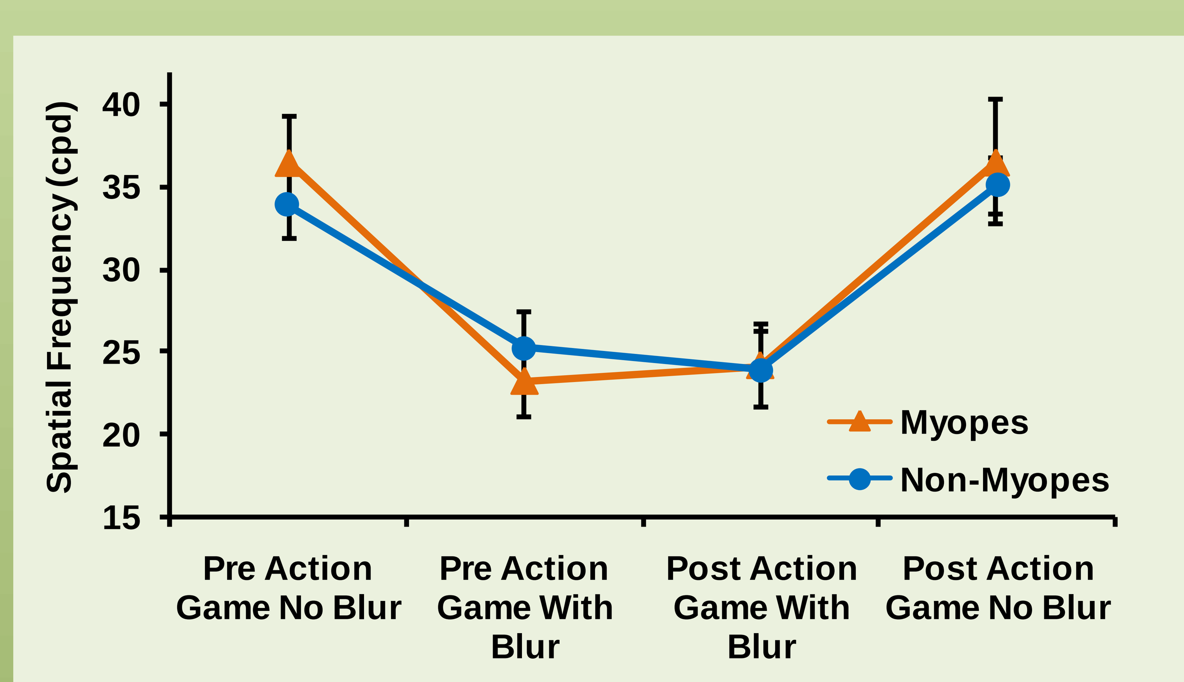

Figure 3b. Grating acuity measurements for the fast-paced action game adaptation task.

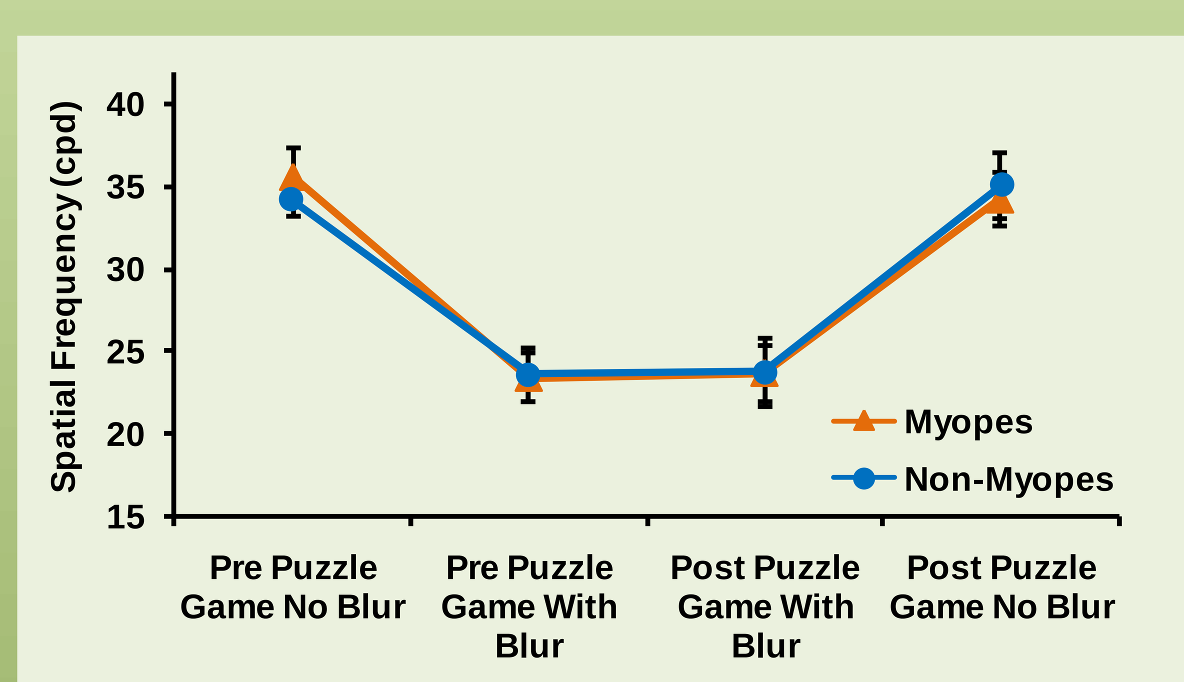

Figure 3c. Grating acuity measurements for the slow-paced puzzle game adaptation task.

Conclusions

- The observed increase in letter acuity following a one hour period of induced blur is consistent with previous findings that the visual system is capable of rapidly adapting to a degraded visual stimulus.
- The differential response of myopic observers to removal of blur (when measured by letter acuity) suggests that this group is less able to adapt to blur.
- The differences in adaptation found using high-contrast letters versus sinusoidal gratings suggests that the underlying adaptation mechanism is based on modulating edge-detection sensitivity.
- Variation in blur adaptation between myopic and non-myopic observers may be related to the effectiveness of emmetropisation in these two groups.

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ROC Curve Analysis of Visual Acuity and Auto Refractometer screening for Refractive Error in Elementary School Children

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Purpose

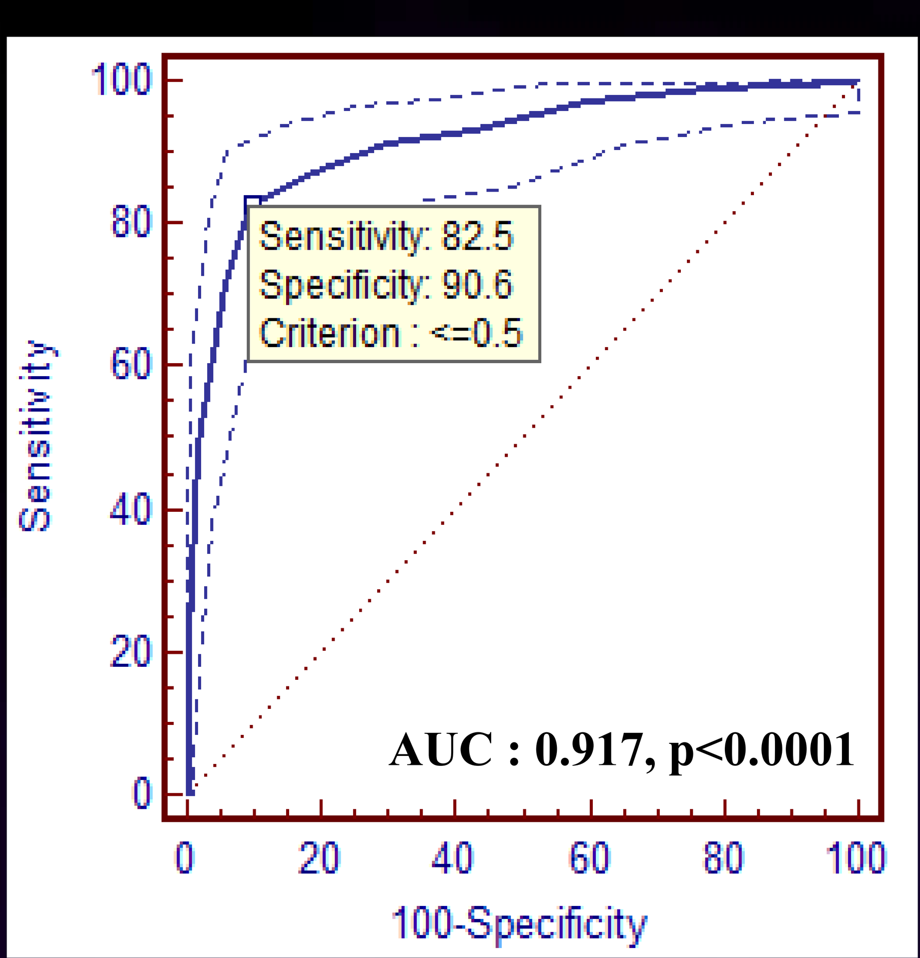
To evaluate the optimal cutoff point for visual acuity and auto refrac tion result to screen for refractive errors in elementary school children.

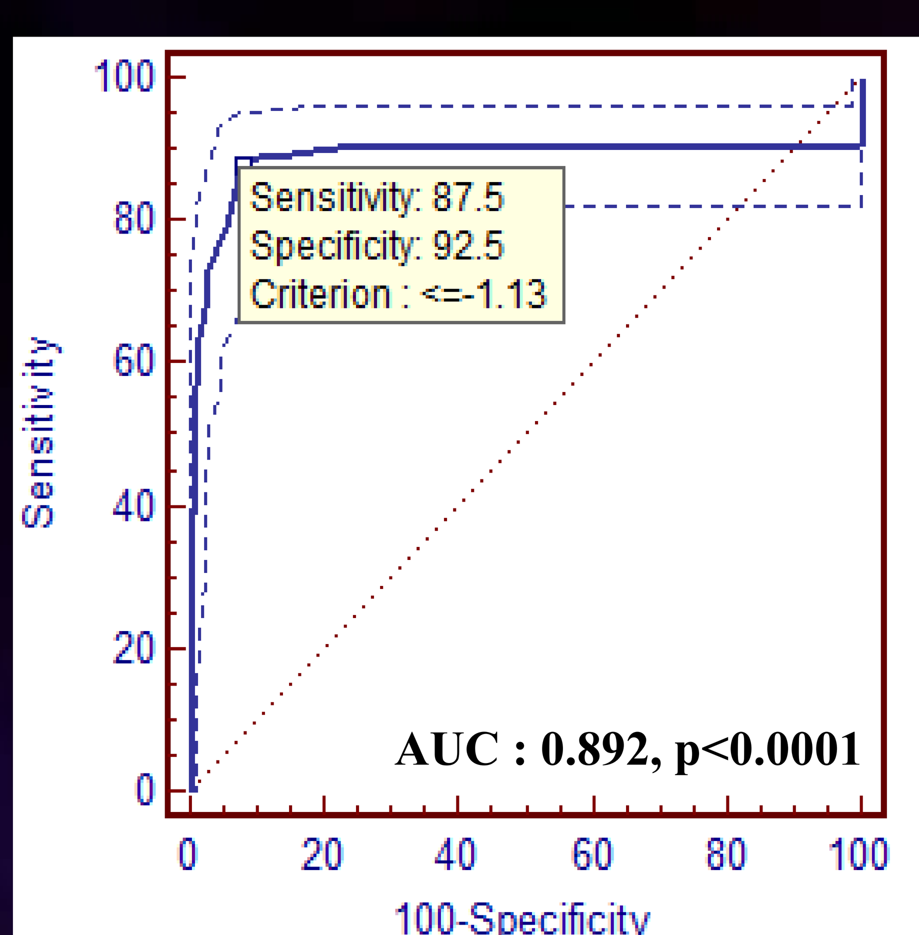
Subjects and methods

For a sample of elementary school children, unaided visual acuity with standard distance visual acuity chart, auto refraction and subjective refraction were performed without optical corrections. For subjective refraction(assumed as gold standard) of at least -1.00D, -0.75D and -0.50D for myopia criteria, optimal cut-off point and sensitivity/specificity of visual acuity and auto refraction was calculated by receiver operator characteristics curve, respectively.

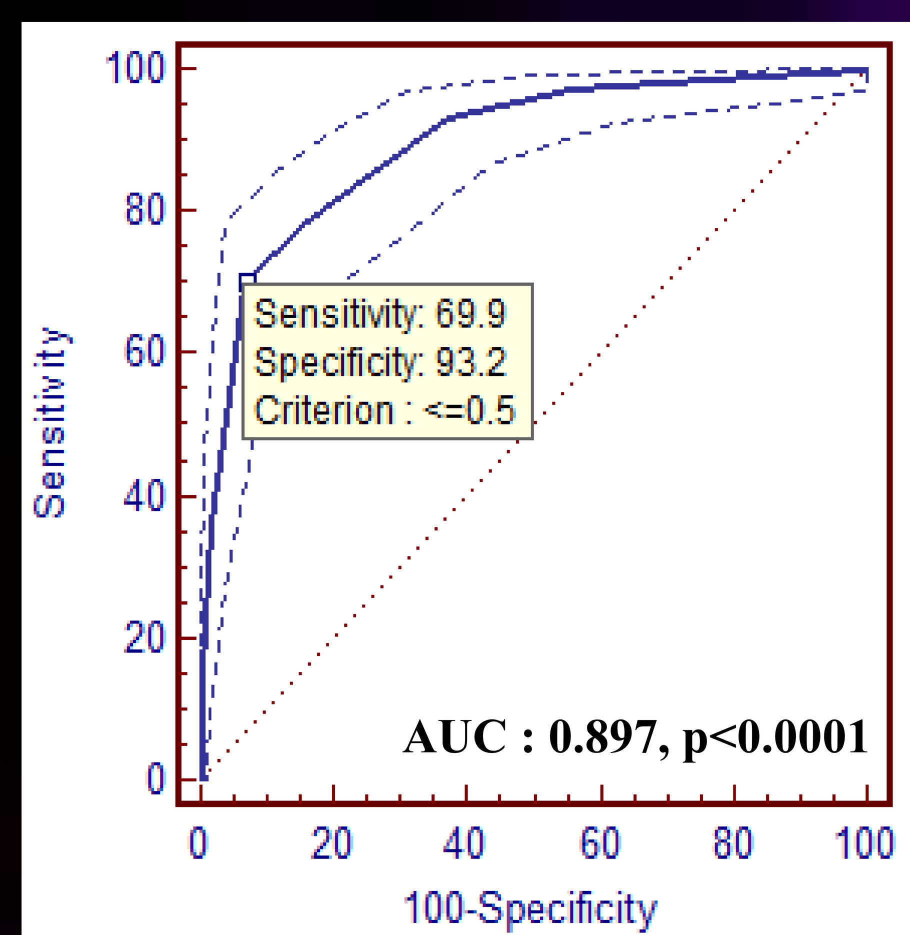
Result

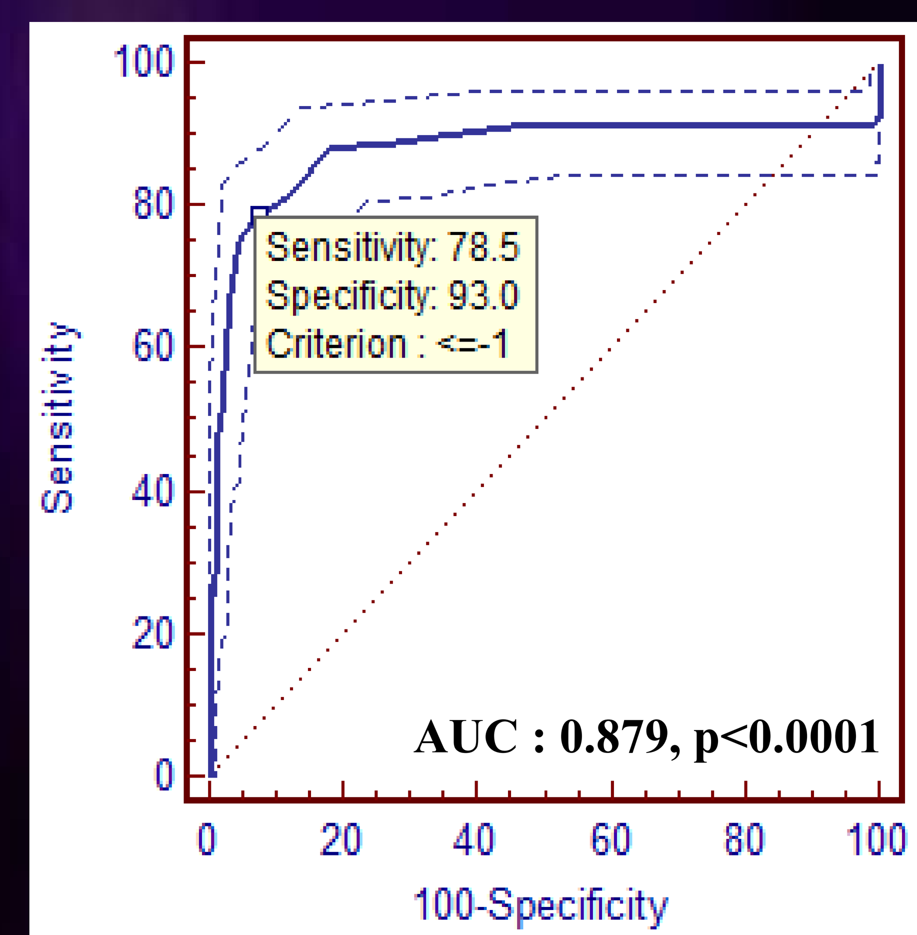
Total 293 children were tested. Sensitivity/specificity of optimal cut-off point of each myopia criteria was obtained for visual acuity and auto refraction. For at least -1.00D of subjective refraction criteria, optimal cut-off point of visual acuity was 0.5(sen:82.5%, spec:90.6% AUC:0.917), auto refraction was -1.13D(sen:87.5%, spec:92.5%, AUC:0.892).



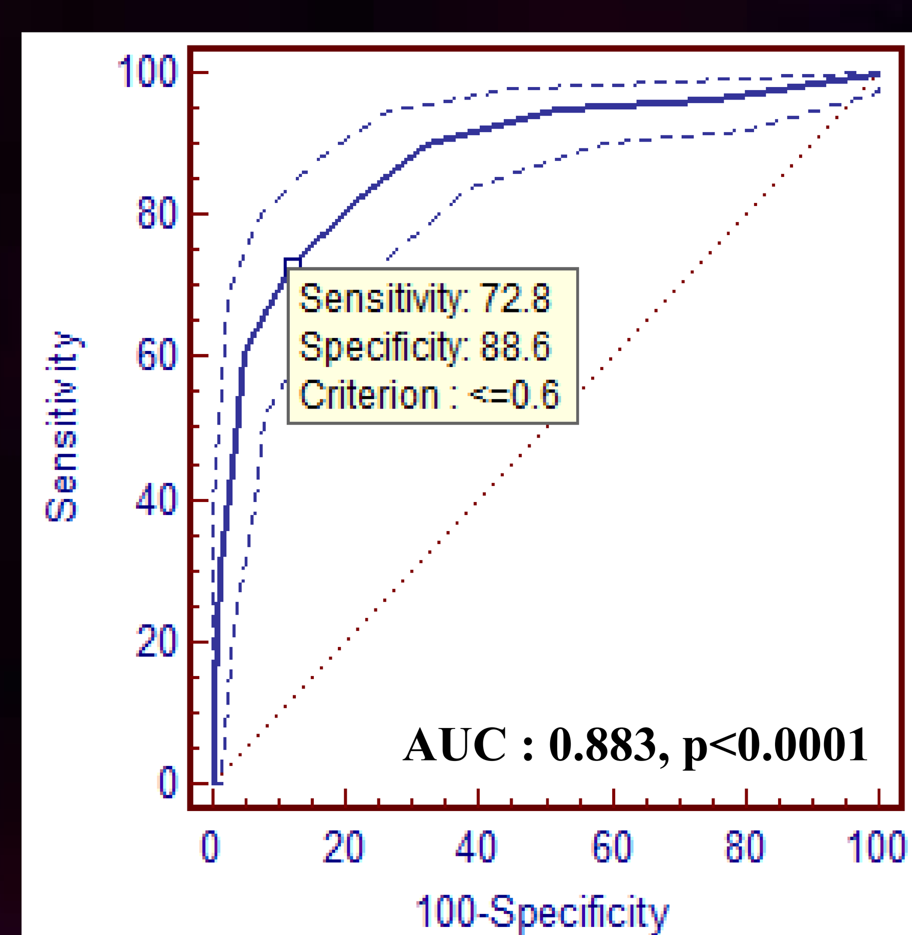


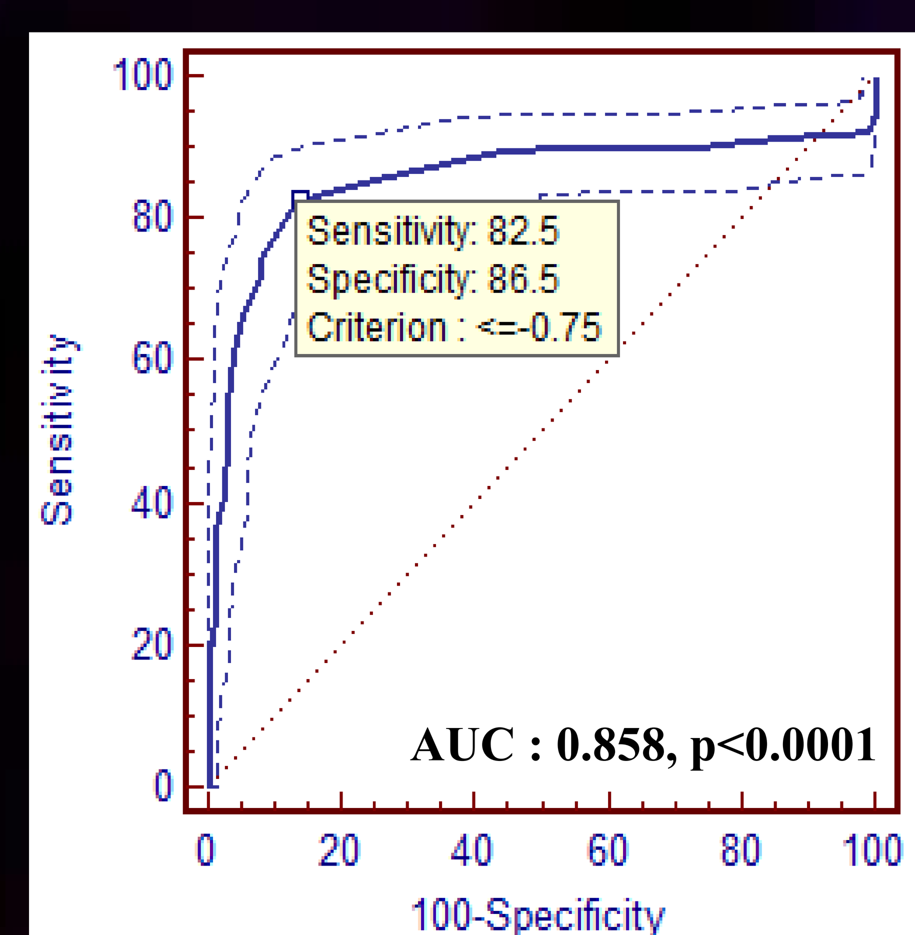
For at least -0.75D criteria, visual acuity was 0.5(sen:69.9%, spec:93.2% AUC:0.897), auto refraction was 1.00D(sen:78.5%, spec:93.0%, AUC:0.879).





For at least -0.50D criteria, visual acuity was 0.6(sen:72.8%, spec:88.6% AUC:0.883), auto refraction was -0.75D(sen:82.5%, spec:86.5%, AUC:0.858).





Conclusions

To screen for refractive errors with visual acuity and auto refraction in elementary school children, the optimal cut-off point were recommended as decimal visual acuity of 0.5, and auto refraction of -1.13D, respectively.

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