Original Article

Comparison of higher order aberrations in amblyopic and non-amblyopic eyes in pediatric patients with anisometropic amblyopia

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Purpose: To compare the ocular higher order aberrations (HOAs) for the physiologic pupil size in amblyopic and non-amblyopic eyes of patients with anisometropic amblyopia in pediatric age group. **Methods:** Children between 5 and 15 years age having treatment naïve anisometropic amblyopia; after a detailed examination by a pediatric ophthalmologist; underwent assessment of wavefront aberrations for both amblyopic and non-amblyopic eyes at their physiologic pupil sizes using i-Trace ray tracing wavefront aberrometer. The axial lengths were also measured using IOL Master 500. The RMS values of the total ocular higher order aberrations (HOAs) and those arising from internal and corneal components of the two eyes were tabulated and compared to look for differences. Comparison of total ocular aberrations for pre-determined refractive error groups was also done for amblyopic and non-amblyopic eyes separately. **Results:** Eighty-eight eyes of 44 subjects were included for analysis. Mean pupil size was comparable in between amblyopic and non-amblyopic eyes (3.98 mm vs. 4.07 mm, $P = 0.346$). The mean axial lengths of the two eyes were comparable (amblyopic eyes 23.13 mm vs. non-amblyopic eyes 22.88 mm, $P = 0.419$). Significant differences in total HOAs and those arising from the internal optics (except spherical aberrations) of the eye were noted between the two eyes. There were no differences in the corneal HOAs. The total HOAs were comparable amongst the various refractive error groups for amblyopic and non-amblyopic eyes individually. **Conclusion:** There are significant differences in ocular HOAs between amblyopic and non-amblyopic eyes in children with anisometropic amblyopia.

Key words: Anisometropic amblyopia, aberrations, HOA, i-Trace

Access this article online
Website: www.ijo.in
DOI: 10.4103/ijo.IJO_1625_18
Quick Response Code:

Anisometropic Amblyopia is caused due to unequal cortical stimulation from the two eyes due uncorrected refractive error difference of ≥2D of Myopia, 1.5 D of Hyperopia or 1.5 D astigmatism.[1] Refractive error differences between the two eyes are caused due to structural differences in axial length, and/or corneal and lenticular curvature or thickness in the case of the latter. These structural differences usually manifest as a difference in spherical correction (defocus) and/or regular astigmatism (together comprising Lower Order Aberrations, LOAs) and are the primary reason for amblyogenesis. However, a difference in the Higher Order Aberrations (HOAs) present in these eyes might also contribute, albeit to a lesser degree, towards development of amblyopia and/or limiting complete recovery from amblyopia. Prior studies have attempted to identify and quantify these differences in the HOAs. But they lack consensus due to glitches in case definition and/or study design. In this study, we aim to compare the ocular HOAs for the physiologic pupil size in amblyopic and non-amblyopic eyes of patients with anisometropic amblyopia in pediatric age group.

Methods

The study was a cross sectional, observational study conducted between August 2016 and April 2017 at a tertiary eye care center in western India. Institutional Review Board and Ethics committee clearance was obtained prior to commencement of the study. An informed consent was obtained from the parents or guardians of the children for inclusion in the study.

Children between 5 and 15 years of age; referred to the Pediatric Ophthalmology clinic for amblyopia management after a minimum of 6 weeks of spectacle wear; who had a best corrected distance visual acuity (BCDVA) of 6/12 or worse in the amblyopic eye and an inter-ocular difference in BCDVA of 2 Snellen lines or more were included in the study. The difference in the spherical equivalent refraction had to be ± 2 D or more for inclusion in the study. History of past ocular surgery, prior amblyopia therapy, presence of latent or manifest squint, only one functional eye and diseases of cornea, lens or retina were criteria for exclusion. Children with developmental delay and those who were uncooperative for detailed examination were also excluded.

At presentation, a detailed refraction was done by a trained pediatric optometrist. The children were then screened by a pediatric ophthalmologist with special emphasis on orthoptic

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Manuscript received: 26.09.18; Revision accepted: 05.03.19

Cite this article as: Hoshing A, Samant M, Bhosale S, Naik AM. Comparison of higher order aberrations in amblyopic and non-amblyopic eyes in pediatric patients with anisometropic amblyopia. Indian J Ophthalmol 2019;67:1025-9.

evaluation, identification of media opacities and un-dilated examination of macula to look for gross macular pathologies.

If deemed suitable for inclusion in the study; ocular aberrations were measured for both eyes using i-Trace ray tracing wavefront aberrometer (Tracey Technologies) at the physiological pupil size in mesopic conditions. i-Trace aberrometer measures the total ocular aberrations by the ray tracing technology. It can then separate the aberrations into its corneal and internal optic components via proprietary algorithms using corneal topography data from the in-built Placido disc-based topographer.[2] It then presents the data in the form of RMS values for Total Eye, Corneal, and Internal Optics components separately which were used for comparison. The i-Trace also records the pupil size of the eye while measuring its aberrations. This was used to compare the intra-procedure pupil size between the two eyes.

Axial lengths of both eyes were measured by optical biometry using IOL Master 500 (Carl Zeiss Meditech). For both i-Trace and IOL master, the best of three consecutive studies was selected for data analysis. This was followed by a cycloplegic refraction and dilated examination by the pediatric optometrist and ophthalmologist, respectively. Age appropriate spectacle correction was prescribed to the subjects and this was considered for analysis of refractive error data. Identification, of any exclusion criteria or non-conformity to inclusion criteria after this repeat examination led to exclusion of the patients' data from the study protocol.

For the ease of comparison, eyes with Simple Hyperopia and Simple or Compound Hyperopic Astigmatism were grouped together as Hyperopic errors. Similar grouping of Myopic errors was done too. Eyes with Emmetropia and Mixed Astigmatism was analyzed separately. Snellen's visual acuities were converted to logMAR values for ease of calculation and data representation.

Data were compiled in a Microsoft Excel (MS Office 2007) spreadsheet and statistical analysis was done using IBM SPSS statistical software version 23. Categorical and ordinal data are presented as proportions. Means of continuous variable were compared using the Paired *t*-test instead of the Wilcoxon Signed Rank test as the Central Limits Theorem is applicable in this scenario. One way-ANOVA test was used to compare the mean aberration RMS values amongst the various refractive error groups for amblyopic and non-amblyopic eyes separately. Results are presented as table and charts as deemed fit.

Results

Eighty-eight eyes (44 Amblyopic and 44 Non-Amblyopic) of 44 patients were included in the data analysis. There were 18 boys and 26 girls. The median (min-max) age of the subjects was 9 (5–15) years.

Table 1 compares the mean refractive and anatomical parameters between the amblyopic and non-amblyopic eyes of the study subjects. Hyperopic errors, Myopic errors, and Mixed Astigmatism in the amblyopic eyes were present in 23/44 (52.2%), 13/44 (29.5%), and 8/44 (18.1%) subjects, respectively. The non-amblyopic eyes were emmetropic in 24/44 (54.5%) subjects. Hyperopic errors, Myopic errors, and Mixed Astigmatism were present in 6/44 (13.6%), 12/44 (27.2%), and 2/44 (4.5%) non amblyopic eyes, respectively.

The mean absolute spherical error in the hyperopic errors group for amblyopic eyes was 3.54 ± 1.59 D (95% Confidence Interval 2.89-4.18). The mean absolute spherical error in the myopic errors group was 7.09 ± 4.27 D (95% Confidence

Table 1: Comparison of Mean±S.D. refractive and anatomical parameters between the Amblyopic and Non amblyopic eyes of the study subjects. (*Values in parenthesis depict 95% Confidence Intervals. S.D. = standard deviation*)

Parameters ↓		Amblyopic Eyes (*n*=44)	Non Amblyopic Eyes (*n*=44)	*p*
Mean (SD) Absolute Spherical error in Diopters		4.28±3.20 (3.42, 5.31)	0.65±1.26 (0.31, 1.07)	< 0.001
Mean (SD) Absolute Cylindrical error in Dioptres		1.36±1.49 (0.92, 1.79)	0.50±0.85 (0.26, 0.78)	< 0.001
Mean (SD) logMAR Best Corrected Visual Acuity		0.57±0.28 (0.49, 0.65)	0.02±0.05 (0.01, 0.04)	< 0.001
Mean (SD) Pupil diameter while measuring ocular aberrations in millimeters		3.98±0.67 (3.77, 4.18)	4.07±0.64 (3.86, 4.24)	0.346
Mean (SD) Axial length in millimeters	Total group	23.13±2.24 (22.46, 23.79) (*n*=44)	22.88±0.79 (22.64, 23.11) (*n*=44)	0.419
	Hyperopic errors	21.60±0.89 (21.23, 21.96) (*n*=23)	22.34±0.84 (21.66, 23.01) (*n*=6)	0.07
	Myopic errors	26.11±1.45 (25.32, 26.89) (*n*=13)	23.38±0.78 (22.93, 23.82) (*n*=12)	< 0.001
	Mixed Astigmatism	22.69±0.71 (22.19, 23.18) (*n*=8)	22.75±0.28 (22.36, 23.13) (*n*=2)	0.91
	Emmetropia		22.78±0.71 (22.49, 23.06) (*n*=24)	n.a

Interval 4.76-9.41). In the mixed astigmatism group the mean absolute spherical error and mean absolute cylindrical error were 1.84 ± 1.38 D (95% Confidence Interval 0.88-2.79) and 3.25 ± 1.81 D (95% Confidence Interval 1.99-4.50), respectively.

The mean absolute spherical error difference between the eyes in the amblyopic hyperopic errors group was 2.89 ± 1.38 D (95% Confidence Interval 2.32-3.45). In the amblyopic myopic errors group, it was 6.21 ± 4.45 D (95% Confidence Interval 3.79-8.62). Only eyes with cylindrical correction in either of the two eyes were selected to calculate the mean absolute cylindrical error difference. It was 1.73 ± 1.61 D (95% Confidence Interval 0.61-2.84).

Table 2 depicts the comparison of the total ocular higher orders aberrations HOAs between the two eyes. Table 3 depicts similar comparison of the HOAs for the corneal and internal optics components. Significant difference in total ocular HOAs and HOAs from the internal optics, except spherical aberrations, between the amblyopic and non-amblyopic eyes is noteworthy.

Fig. 1 compares the total ocular aberrations amongst the various refractive error groups for amblyopic eyes and non-amblyopic eyes. It is evident that for both amblyopic and non-amblyopic eyes the higher order aberrations (except astigmatism) were not very different amongst the various types of refractive errors.

Table 2: Comparison of Mean±S.D. RMS values of Total Higher Order Aberrations (HOAs) in the two groups. (*Values in parenthesis depict 95% Confidence Intervals. S.D. = standard deviation*)

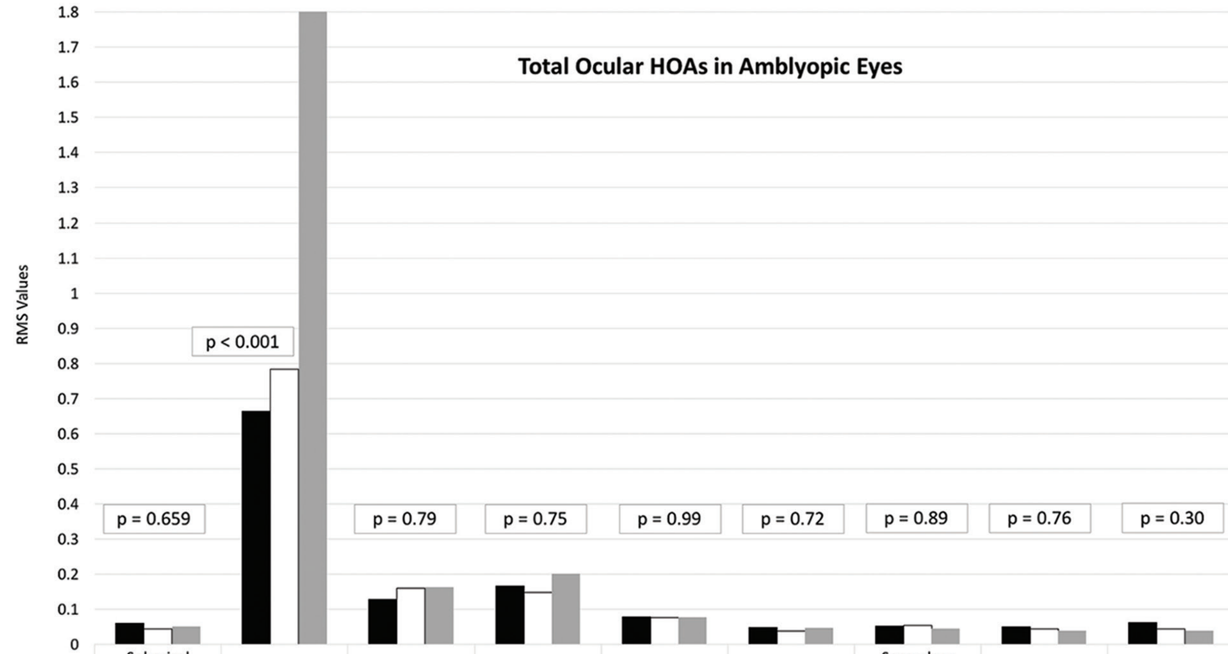
HOA ↓	Total Aberrations		
	Amblyopic Eye	Non Amblyopic Eye	*p*
Spherical aberration	0.054±0.04 (0.041, 0.067)	0.051±0.05 (0.037, 0.069)	0.827
Astigmatism	0.911±0.77 (0.699, 1.173)	0.363±0.37 (0.262, 0.485)	<0.001
Coma	0.144±0.15 (0.105, 0.193)	0.100±0.05 (0.082, 0.117)	0.06
Trefoil	0.166±0.15 (0.125, 0.213)	0.074±0.04 (0.061, 0.087)	<0.001
Tetrafoil	0.078±0.06 (0.060, 0.098)	0.038±0.02 (0.031, 0.044)	0.001
Pentafoil	0.045±0.03 (0.035, 0.056)	0.021±0.01 (0.017, 0.026)	<0.001
Secondary Astigmatism	0.052±0.04 (0.040, 0.064)	0.034±0.02 (0.027, 0.040)	0.006
Secondary Coma	0.047±0.03 (0.037, 0.059)	0.024±0.01 (0.021, 0.026)	0.001
Secondary Trefoil	0.052±0.04 (0.041, 0.065)	0.016±0.01 (0.013, 0.019)	<0.001

Discussion

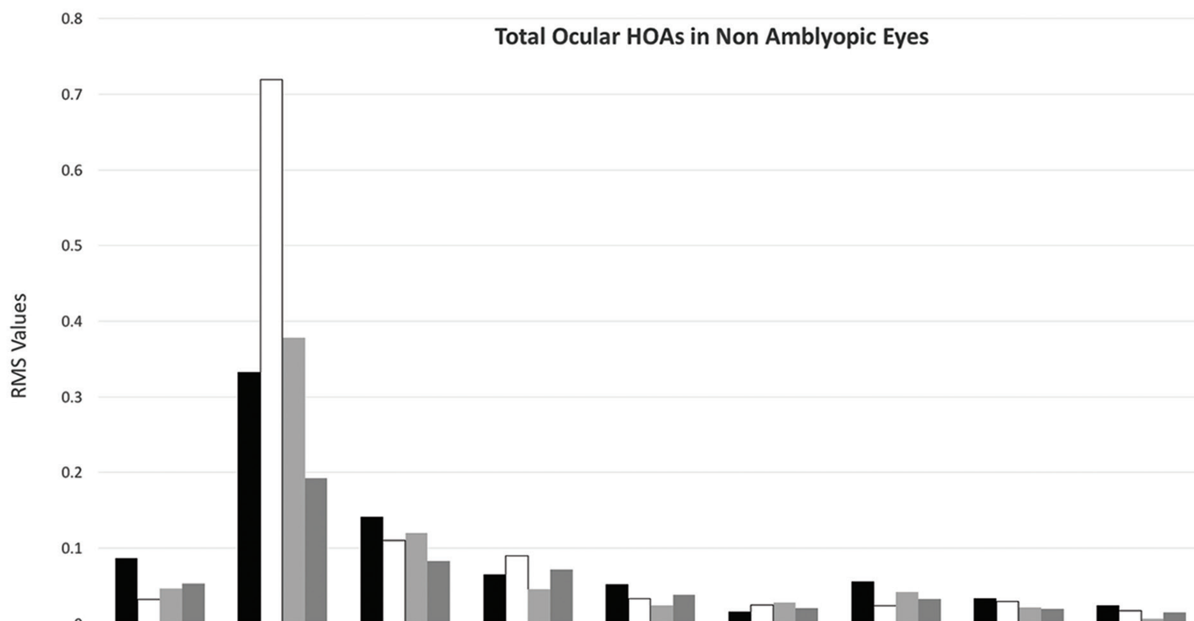
Our study demonstrated a significant difference in all total ocular HOAs between the amblyopic and non-amblyopic eyes in subjects with anisometropic amblyopia. In the past, other studies have tried to compare aberrations between amblyopic and non-amblyopic eyes. A study by Kirwan and O'Keefe found no difference in the HOAs in the amblyopic and fellow normal eyes.[3] They concluded that HOAs most probably do not play any role in the development of amblyopia. However, in their study there were equal number of patients with strabismic and anisometropic amblyopia. We believe that this heterogeneity in the study subjects led to spuriously negative result. In strabismus, the misalignment of the visual axis is the primary cause of amblyopia. The refractive components of the eye may or may not be affected and therefore may not show any significant difference in the HOAs when compared to the normal fellow eye. In anisometropic amblyopia alone there might be structural changes, major and/or minor, in the refractive components of the eye while still maintaining transparency. These will show up as differences in the wavefront aberrations between the amblyopic

Table 3: Comparison of Mean±S.D. RMS values of Corneal and Internal Higher Order Aberrations (HOAs) in the two groups. (*Values in parenthesis depict 95% Confidence Intervals. S.D. = standard deviation*)

HOA ↓	Corneal Component			Internal Optics Component		
	Amblyopic Eye	Non Amblyopic Eye	*p*	Amblyopic Eye	Non Amblyopic Eye	*p*
Spherical aberration	0.051±0.04 (0.040, 0.065)	0.058±0.04 (0.045, 0.073)	0.425	0.063±0.04 (0.050, 0.081)	0.062±0.05 (0.046, 0.078)	0.875
Astigmatism	0.629±0.53 (0.481, 0.795)	0.387±0.33 (0.297, 0.492)	0.006	0.541±0.39 (0.434, 0.665)	0.276±0.15 (0.231, 0.320)	<0.001
Coma	0.106±0.11 (0.075, 0.145)	0.081±0.08 (0.059, 0.105)	0.246	0.161±0.12 (0.128, 0.200)	0.095±0.05 (0.078, 0.113)	0.001
Trefoil	0.057±0.05 (0.042, 0.073)	0.045±0.03 (0.036, 0.055)	0.149	0.167±0.14 (0.127, 0.212)	0.069±0.04 (0.055, 0.084)	<0.001
Tetrafoil	0.022±0.01 (0.017, 0.028)	0.020±0.01 (0.016, 0.025)	0.648	0.074±0.06 (0.056, 0.097)	0.042±0.02 (0.034, 0.049)	0.004
Pentafoil	0.008±0.00 (0.006, 0.010)	0.007±0.00 (0.005, 0.009)	0.431	0.046±0.03 (0.035, 0.056)	0.023±0.01 (0.019, 0.028)	<0.001
Secondary Astigmatism	0.019±0.01 (0.014, 0.024)	0.017±0.01 (0.013, 0.020)	0.515	0.053±0.04 (0.040, 0.065)	0.034±0.02 (0.027, 0.043)	0.016
Secondary Coma	0.008±0.00 (0.005, 0.010)	0.007±0.00 (0.005, 0.010)	0.897	0.048±0.04 (0.036, 0.061)	0.024±0.01 (0.018, 0.030)	0.001
Secondary Trefoil	0.007±0.00 (0.005, 0.009)	0.007±0.00 (0.005, 0.009)	0.993	0.051±0.03 (0.040, 0.063)	0.017±0.01 (0.013, 0.021)	<0.001



	Spherical Aberration	Astigmatism	Coma	Trefoil	Tetrafoil	Pentafoil	Secondary Astigmatsim	Secondary Coma	Secondary Trefoil
■ Hyperopic Errors	0.0603	0.6634	0.1287	0.1656	0.0793	0.0483	0.0533	0.0509	0.0615
□ Myopic Errors	0.0453	0.7839	0.1599	0.1478	0.0761	0.0382	0.0538	0.0446	0.0448
■ Mixed Astigmatism	0.0517	1.8326	0.1626	0.2004	0.0778	0.0471	0.046	0.0399	0.0398



	Spherical Aberration	Astigmatism	Coma	Trefoil	Tetrafoil	Pentafoil	Secondary Astigmatism	Secondary Coma	Secondary Trefoil
■ Hyperopic Errors	0.0865	0.3324	0.1414	0.0656	0.0524	0.0159	0.0559	0.0336	0.0244
□ Myopic Errors	0.0321	0.7194	0.1107	0.0902	0.0334	0.0253	0.0241	0.0299	0.0178
■ Mixed Astigmatism	0.047	0.3782	0.1199	0.0458	0.0241	0.0281	0.0416	0.0219	0.0071
■ Emmetropia	0.0533	0.1921	0.083	0.0715	0.0379	0.0208	0.033	0.0198	0.0147

Figure 1: Comparison of Total Ocular HOAs amongst the various refractive error groups in amblyopic eyes and non-amblyopic eyes. (n = 23 and 6 for Hyperopic errors, n = 13 and 12 for Myopic Errors and n = 8 and 2 for Mixed astigmatism in amblyopic and non-amblyopic eyes respectively. For non-amblyopic eyes, n = 24 for Emmetropes)

eye and the fellow normal eye. Hence, we decided to include only anisometropic amblyopes in our study.

Aldebasi *et al*. found that amblyopic eyes had significantly greater RMS values for the whole eye aberrations.[4] However, they found statistically significant difference only in the 5th order RMS of pre-treated amblyopes versus the control emmetropes. No other HOA was found to be significantly different between the amblyopes or emmetropes. However, this paper too, doesn't clarify the type of amblyopes included. A careful perusal indicates the possibility of heterogenous sample of subjects. In our study, all HOAs except spherical aberration were significantly different between the two eyes.

The study by Prakash *et al*. found no significant difference between Zernike coefficients between normal and amblyopic eyes in patients with "idiopathic" amblyopia.[5] However, the reported refractive error range in the amblyopic and the fellow eyes of the subjects in this study suggests that they were not suffering from anisometropic amblyopia and were probably a mixed population. Furthermore, the authors chose to include the subjects after they had undergone a failed or partially successful treatment trial and hence, it might not be representative of the aberrations at baseline.

It is evident from Tables 2 and 3 that significant differences in the HOAs from the internal optical components contributed majorly to the differences in the total ocular HOAs between the amblyopic and non-amblyopic eyes. There was no significant difference in corneal HOAs between the two eyes. RMS values of corneal astigmatism were found to be significantly different. However, this was an expected outcome considering the significant differences in the refractive astigmatism of the two eyes. The same explanation is applicable for the significant difference in the RMS value of internal optics astigmatism too. Moreover, astigmatism by definition is a Lower Order Aberrations (LOA).

We chose to measure the aberrations for the physiological pupil size. We argued that as the patient develops amblyopia while functioning with the physiological pupil size; it is more prudent to study and measure the aberrations for that pupil size alone. Only then, we would be able to truly understand the amblyogenic potential of ocular aberrations, if any. There was no significant difference in the mean pupil size between the two eyes thus making them comparable at baseline. Other studies have chosen to measure the ocular aberrations with either dilated alone or with both un-dilated and dilated pupil sizes.

No significant difference in the spherical aberrations were noted between the two eyes. We attribute this finding to the small physiological pupil size that we chose for our study. It is a known fact that spherical aberrations get amplified with increasing pupil size.[6,7]

In our study, there was significant difference in the mean axial lengths between the myopic error groups of amblyopic and non-amblyopic eyes. The hyperopic amblyopic eyes were shorter than their non-amblyopic counterparts by 0.74 mm. Although this difference could account for a spherical error difference of >2 diopters; it does not reach statistical significance in our study. This could be due to the disparity in the number of eyes compared. In the mixed astigmatism group, there was no difference in the axial lengths. This could be explained by the fact that for the mean astigmatism subgroups, the mean spherical errors; which is a surrogate measure of the axial length; were comparable in the amblyopic and non-amblyopic eyes (1.8 ± 1.38 D in amblyopic arm vs. 0.87 ± 0.17 D in non-amblyopic arm; $P = 0.37$). The axial lengths for all amblyopic eyes average out due to the presence of longer myopic eyes and shorter hyperopic eyes in the calculation and thus do not appear significantly different from axial lengths of non-amblyopic eyes.

Lastly, we chose to compare whether the total HOAs were significantly different amongst the various refractive error groups for amblyopic and non-amblyopic eyes separately. Our analysis showed that only astigmatism was different between the refractive subgroups. Therefore, grouping the various errors together for the inter-eye comparison could not have confounded the results. Refractive error wise comparison of HOAs between the two eyes (subgroup analysis) was not attempted due to the lack of comparable number of subjects in each subgroup.

A relatively small sample is one of the shortcomings of our study. However, it is a side effect of maintaining stringent inclusion and exclusion criteria. We believe that a larger study sample with similar study criteria will help to fortify our findings. We have demonstrated significant differences of HOAs between amblyopic and non-amblyopic eyes of subjects with anisometropic amblyopia. However, whether these have any bearing on the development or treatment of amblyopia is yet to be proven. We believe that proving so is a daunting task with the current technology and research ethics.

The use of optical aids like wavefront customized spectacle correction and contact lenses might help to improve our understanding about the role of HOAs in development and treatment of amblyopia.

Conclusion

We conclude that there are significant differences in the HOAs between the amblyopic and non-amblyopic eyes in pediatric patients with anisometropic amblyopia. Majority of the HOA difference was generated by the internal optics of the eyes.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Wallace DK, Morse CL, Melia M, Sprunger DT, Repka MX, Lee KA, *et al*. Pediatric eye evaluations preferred practice pattern®. American academy of pediatric ophthalmology/strabismus preferred practice pattern pediatric ophthalmology panel. Ophthalmology 2018;125:P184-227.
2. Gomez AC, del Ray AV, Bautista CP, Ferrándiz AE, González DC, Burgos SC, *et al*. Principles and clinical applications of ray-tracing aberrometry. J Emmetropia 2012;3:96-110.
3. Kirwan C, O'Keefe M. Higher order aberrations in children with amblyopia. J Pediatr Ophthalmol Strabismus 2008;45:92-6.
4. Aldebasi HI, Fawzy SM, Alsaleh AA. Ocular aberrations in amblyopic children. Saudi J Ophthalmol 2013;27:253-8.
5. Prakash G, Sharma N, Saxena R, Choudhary V, Menon V, Titiyal JS. Comparison of higher order aberration profiles between normal and amblyopic eyes in children with idiopathic amblyopia. Acta Ophthalmol 2011;89:e257-62.
6. Kim JH, Lim T, Kim MJ, Tchah H. Changes of higher-order aberrations with the use of various mydriatics. Ophthalmic Physiol Opt 2009;29:602-5.
7. Fan R, He T, Qiu Y, Di YL, Xu SY, Li YY. Comparison of wavefront aberrations under cycloplegic, scotopic and photopic conditions using Wave Scan. Arq Bras Oftalmol 2012;75:116-21.