Analyses on the distribution and influence of higher-order aberrations both clinically and experimentally among varied refractive errors

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Abstract:

PURPOSE: The aim of this work is to determine and compare the distribution and influence of higher-order aberrations (HOAs) both clinically and experimentally between different refractive errors.

METHODS: Commercially available Shack–Hartmann aberrometer was employed to measure the HOA clinically in human eyes. Experimentally, HOA was measured in a model eye by simulating various refractive errors by constructing an aberrometer based on the same Shack Hartmann principle. One-way analyses of variance and simple regression were employed to analyze the distribution and influence of HOA among various refractive errors.

RESULTS: A total of 100 eyes were clinically measured for aberrations, of which 35, 50, and 15 eyes were emmetropes, myopes, and hyperopes, respectively. Out of the total root mean square (RMS) value, the HOAs found in the human eyes were 23%, 7%, and 26% and in the model eye, it was 20%, 8%, and 10% between emmetropes, myopes, and hyperopes, respectively. The mean higher-order RMS was almost similar between the groups and among various refractive errors. There was no statistical significance between the individual Zernikes except for the coma in both human and model eyes.

CONCLUSION: The mean HOA is similar amidst the different refractive errors. The presence of 23% HOA in emmetropes signifies that larger part of the human eye is capable of complying with HOA without compromising the image quality. This work signifies that HOA does not play an important role in image clarity for human eyes with regular refractive surface unlike irregular refractive surfaces.

Keywords:
Aberrations, emmetropia, higher-order root mean square, hyperopia, myopia, Shack–Hartmann principle

Introduction

Optical aberrations play a major role in the image quality perceived by the human retina.[¹‑³] There are various aberrations which consist of lower- and higher-order aberrations (HOAs) (LOAs and HOAs). Ninety-two percentage of vision correction is achieved by correcting the LOAs (defocus and astigmatism), whereas 7%–8% are still uncorrected and consist of HOAs such as coma, trefoil, and spherical aberrations.[⁴,⁵] Several aberrometers are used to measure these aberrations by using different principles, namely ray tracing, Tshering, and Shack–Hartmann.⁶ Clinically, HOAs are measured using commercially available aberrometers, which is based on Shack–Hartmann principle and can measure up to 8th order, though the visually significant HOAs are up to the 4th order.⁷ Experimental, the HOAs are measured by constructing an adaptive optics (AOs) system using the same Shack–Hartmann principle.

Hence, the aim of this work is to find out and compare the distribution and influence of HOA by both clinical and experimental methods in emmetropes, myopes, and hyperopes.
Methods

A prospective cohort study was done consisting of two cohorts, one each for clinical measurement and the experimental measurement and analyses of HOA. Based on the earlier works, the sample size was calculated. Using a simple random sampling in the first cohort, HOAs were clinically measured by a commercially available aberrometer on 100 randomly selected eyes from 100 subjects having various refractive errors. The tenets of the Declaration of Helsinki were followed, and all procedures were approved by the ethics committee of the institute. Informed consent was obtained from all the subjects. All the preliminary clinical examinations pertaining to history, visual acuity, binocular vision function, refraction, examination of the anterior segment, and intraocular pressure check followed by posterior segment assessment were performed. Contrast sensitivity was not measured. After completing the initial ocular examinations in the outpatient department of an eye hospital, 35 emmetropes, 15 hyperopes, and 50 myopes were recruited. Emmetropia was defined as spherical equivalent (SE) between $+0.25$ diopter sphere (DS) and $-0.25$ DS. Myopia was characterized as SE $\leq -0.50$ DS and hyperopia as $\geq +0.50$ DS. Zywave II Wavefront Aberrometer (Bausch and Lomb Zywave, Rochester, NY, USA) was used to measure the ocular aberrations. This uses a Shack–Hartmann principle with an infrared laser beam of 785 nm. The exit pupil of the eye was in conjugate with the charge-coupled device (CCD) detector, where the pupil plane gets focused by 76 microlenses as a 76-point centroid pattern. At each centroid point, the spatial displacement from the ideal position was used to determine the slope of the aberrated wavefront. Zernike terms were used to fit the slope data, and the coefficients were mathematically reconstructed in the Zywave aberrometer. It measures total wavefront aberration along with Zernike terms up to the 5th order for two pupil sizes, namely 5 and 6 mm. The measurements were taken by a qualified optometrist with experience in handling the aberrometer. To control the effect of accommodation, all pupils were dilated and fitted to 6-mm pupil size for recording the aberrations of all the eyes. Alignment of the aberrometer measurement axis with the eye’s primary line of sight was achieved by asking the subject to look at the center of the fixation target. After alignment, the room lights were dimmed and measurements were appropriated. Aberration measurements were recorded immediately after the final blink. All generated Zernike coefficients were corrected for enantiomorphism and later downloaded for offline analysis.

In the second cohort, HOAs were experimentally measured by constructing an AOs system (OKO Technologies, Polakweg, GG Rijswijk, Netherlands), and refractive errors were simulated in a model eye. The schematic representation of the experimental set up is shown in Figure 1. Light from a fiber-coupled superluminescent diode (SLD) of wavelength 633 nm was used as a test beam. The output from the fiber was collimated by lens L1 with initial beam size of 24 mm and focused on the model eye with 6-mm pupil diameter. To maintain the same pupil size as the first cohort for human eyes, pupil size was fixed at 6 mm for the model eye also. The exit aperture of the model eye was reimaged onto a lenslet array of the Shack–Hartmann wavefront sensor using lenses L2–L5, which also took care of beam resizing to fill the entire microlens array with the given input beam diameter. The conjugacy of two planes (at exit pupil of the model eye and at wavefront sensor) was maintained to measure the HOA as mentioned in detail in an earlier work. The wavefront sensor used in this work consisted of hexagonal array of 127 microlenses and a CCD camera. The focal length of the microlens array was 18 mm and the array pitch was 300 μm. The position of these spots varied when the input beam had aberrations compared to a perfect plane wavefront. By measuring the shift of the centroids of these spots, all the aberrations were calculated. Further, the wavefront reconstruction was performed by using “modal reconstruction” method, which means that the required wavefront was represented by a series expansion over a system of linearly independent basis functions, and the coefficients of expansion were calculated in terms on this basis. Singular value decomposition algorithm was used to construct an orthogonal basis. The reconstructed wavefront was then defined continuously throughout the whole aperture of the sensor, which was 3.9 mm in our wavefront sensor. Although optical aberrations up to 8th order could be measured, the data were analyzed up to 4th order only.

For simulating myopia, convex lenses of $-1.00$ DS–$-5.00$ DS in 1 DSM steps were placed in front of the model eye. For simulating hyperopia, concave lenses of $+1.00$ DS–$+5.00$ DS in 1 DSM steps were placed in front of the model eye. Aspheric lenses were used to simulate both myopia and hyperopia to reduce lens-induced HOA. With each lens, measurements were taken five times, and all the Zernike terms up to the 4th order were recorded. For emmetropia, the measurements were taken five times without any lens in front of the model eye.

All the Zernike terms measured by both the methods were recorded, compared, and analyzed using analyses of variance (ANOVA) with post hoc Games–Howell in SPSS 16 (IBM SPSS Statistics, Armonk, New York, United States of America). Simple linear regression was performed to analyze the influence of each HOA on different refractive errors. The amount of HOA out of total root mean square (RMS) was calculated in percentage. A significance level of 95% with $P = 0.05$ was applied for statistical tests.

Results

A total of 100 eyes were measured for HOA, out of which, 35, 50, and 15 eyes were emmetropes, myopes, and hyperopes, respectively. The mean age was found to be 23.57 ± 3.52, 35.16 ± 11.1, and 31.27 ± 9.91 years for emmetropes, myopes, and hyperopes, respectively. Both lower- and HOAs showed no significant correlation for lower-order RMS (LO RMS), defocus, and
horizontal astigmatism with $P < 0.05$, whereas there was no significant association of age with HOA. As the mean astigmatism in hyperopes was $< 0.75$ D, it was not compared with HOA. In myopes, the mean astigmatism was found to be $-1.68 \pm 0.91$ D cylinder (confidence interval [CI] $0.13, -3.50$) and showed statistical significance with higher order RMS (HO RMS) and secondary astigmatism with $P < 0.05$, whereas other aberrations were not statistically significant. From the subjective refraction findings, SE was calculated for myopes and hyperopes. The mean SE was found to be $-2.87 \pm 2.46$ D (CI $2.05, -7.79$) with minimum of $-0.50$ D and maximum of $-13.50$ D of myopia. For hyperopes, the mean SE was found to be $+0.88 \pm 0.51$ D (CI $1.90, -0.14$) with a minimum of $+0.50$ D and a maximum of $+2.50$ D. In the experimental method, the mean SE was found to be $-3.00 \pm 1.58$ D with a minimum of $-1.00$ D and a maximum of $-5.00$ D of myopia. For hyperopes, the mean SE was found to be $+3.00 \pm 1.58$ D with a minimum of $+1.00$ D and a maximum of $+5.00$ D.

The mean and standard deviation of all the Zernike terms for emmetropes, myopes, and hyperopes in both human eyes and model eye along with CIs are computed in Table 1. The HOA in emmetropes was 23%, 7% in myopes, and 26% in hyperopes among human eyes.

In the model eye, the HOAs distributed among were 20%, 8%, and 10% for the emmetropes, myopes, and hyperopes, respectively. For the total population, the HOA was found to be 19% in human eyes, whereas in the model eye, it was found to be 13%. The comparison of HOA between human eyes and model eye along with their distribution is shown in Figure 2. The RMS values for 3rd order and 4th order for both human eyes and model eye are shown in Figure 3.

A linear regression analysis was modeled between HO RMS and 2nd-, 3rd-, and 4th-order Zernike terms for all the human eyes among the three groups. It was found that there was a statistically significant influence on defocus, horizontal secondary astigmatism, 3rd-order RMS, and 4th-order RMS in emmetropes with $P < 0.05$, as shown in Figure 4a-d, respectively. For myopia, HO RMS was found to have a statistically significant influence with $P < 0.05$ for vertical quadrafoil, 3rd-order RMS, and 4th-order RMS as represented in Figure 5a-c accordingly. In hyperopes, HO RMS was found to have a statistically significant influence with $P < 0.05$ for 3rd-order RMS and 4th-order RMS as shown in Figure 6a and b, respectively.

Regression analysis was performed between SE and 2nd-, 3rd-, and 4th-order 16 Zernike terms for emmetropes, myopes, and hyperopes in all human eyes. It was found there was a statistically significant influence for LO RMS in myopes with a high positive correlation ($R = 0.95$). Whereas in hyperopes, SE was found to have statistically significant influence with $P < 0.05$ for LO RMS, HO RMS, and 3rd-order RMS. SE was found to have a low positive correlation with LO RMS ($R = 0.43$) and HO RMS ($R = 0.14$), while it showed a low negative correlation with 3rd-order RMS.

A one-way ANOVA applying post hoc (Games–Howell) was performed between all the groups for all the Zernike terms in human eyes. For emmetropes and myopes, the
mean values were found to have a statistically significant difference for defocus, horizontal coma, LO RMS, HO RMS, 3rd-order RMS, and 4th-order RMS with $P < 0.05$, though no statistically significant difference was found among other
have any statistically significant influence with $P > 0.05$ for all the Zernike terms including LO RMS, 3rd-order RMS, and 4th-order RMS. In hyperopes, HO RMS was found to have a statistically significant influence with $P < 0.05$ for LO RMS, 3rd-order RMS, and 4th-order RMS. LO RMS ($R = 0.50$) and 4th-order RMS ($R = 0.99$) showed moderate and high positive correlation with HO RMS, though 3rd-order RMS ($R = 0.37$) exhibited low negative correlation.

Regression analysis was performed between SE and the 2nd-, 3rd-, and 4th-order 16 Zernike terms among emmetropes, myopes, and hyperopes in human eyes. It was found that there was a statistically significant influence for defocus, vertical astigmatism, and vertical coma in myopes. Defocus ($R = 0.99$) showed a high positive correlation with SE, whereas vertical astigmatism ($R = 0.88$) and vertical coma ($R = 0.60$) showed high and moderate negative correlation accordingly. In hyperopes, the SE was found to have statistically significant influence with $P < 0.05$ for only defocus ($R = 0.99$), revealing a high negative correlation.

One-way ANOVA was performed between all the groups for all the Zernike terms in model eyes. Post hoc Games–Howell was applied. Among emmetropes and myopes, the mean values were found to have a statistically significant difference for defocus with $P < 0.05$, while for other Zernike terms, there was no statistically significant difference. For emmetropes and hyperopes, the mean values were not having any statistical significant difference between Zernike terms.

All emmetropes and myopes had best visual acuity of 6/6 and N6, whereas myopes had mean best-corrected visual acuity of $0.19 \pm 0.29$ Log MAR. Regression analyses were performed between best-corrected visual acuity and HO RMS for all emmetropes, myopes, and hyperopes, which revealed no statistical significance with $P < 0.05$.

In the model eye, regression analysis was performed between HO RMS and 2nd-, 3rd-, and 4th-order 15 Zernike terms between all the three groups of emmetropes, myopes, and hyperopes. In emmetropes, it was found that there was a statistically significant influence on horizontal secondary astigmatism, horizontal and vertical tetrafoil, LO RMS, 3rd-order RMS, and 4th-order RMS in emmetropes with $P < 0.05$. LO RMS ($R = 0.95$) and 3rd-order RMS ($R = 0.99$) revealed a high positive correlation with HO RMS, whereas 4th-order RMS ($R = 0.74$), vertical ($R = 0.86$), and horizontal tetrafoil ($R = 0.88$) showed a high negative correlation and horizontal secondary astigmatism ($R = 0.43$) displayed a low negative correlation. For myopia, HO RMS was not found to

Zernike terms. For myopes and hyperopes, the mean values were found to have a statistically significant difference for defocus with $P < 0.05$, while for other Zernike terms, there was no statistically significant difference. For emmetropes and hyperopes, the mean values were not having any statistical significant difference between Zernike terms.

Discussion

In earlier works,[4,5,10-12] HOA was found to be 8%–10% of the total RMS, albeit in this study it varied between the groups. In this work, the HOA was found to be 23%, 7%, and 26% for emmetropes, myopes, and hyperopes, respectively, in the human eyes. The HOA obtained from the experimental model eye was 20%, 8%, and 10% for emmetropes, myopes, and hyperopes, respectively.

The HOAs obtained in myopes between the human eyes and the model eyes are comparable due to the similar mean SE of both the groups. The presence of reduced percentage of HOA in both the cohorts in comparison with emmetropes and hyperopes is contributed by the increased magnitude of LOA.

Though the HOAs elicited by emmetropes in both the human eye and the model eye are almost similar, the very presence of approximately 20% is attributed to the reduced magnitude of LOA. The same pattern is observed in the human eye hyperopes exhibiting 26% HOA where the mean LOA is only +0.88 D, while for the model eye hyperope exhibited only 10% HOA where the mean LOA is +3.00 D.

The HOA was compared with SE of the groups and was found to have a statistically significant positive influence on LO RMS in

Figure 6: Association of 3rd- and 4th-order root mean square with higher-order root mean square in hyperopia for human eyes. (a) Association of 3rd-order root mean square with higher-order root mean square in hyperopia for human eyes. (b) Association of 4th-order root mean square with higher-order root mean square in hyperopia for human eyes.
### Table 1: The mean and standard deviation of all Zernike terms of emmetropes, myopes, and hyperopes for human eyes and model eye

| LO RMS (µm) | Human eye | Model eye |
|-------------|-----------|-----------|
| 0.42±0.30 (CI 1.02−0.18) | 0.60±0.22 (CI 1.04−0.16) |
| HO RMS (µm) | 0.11±0.05 (CI 0.20−0.02) | 0.13±0.02 (CI 0.18−0.09) |
| 3\(^{rd}\) order RMS (µm) | 0.14±0.06 (CI 0.27−0.01) | 0.19±0.04 (CI 0.28−0.11) |
| 4\(^{th}\) order RMS (µm) | 0.07±0.04 (CI 0.14−0.01) | 0.05±0.01 (CI 0.07−0.02) |

| Vertical astigmatism (µm) | 0.03±0.27 (CI 0.57−0.52) | 0.01±0.06 (CI 0.12−0.10) |
| Defocus (µm) | 0.05±0.68 (CI 1.41−1.31) | −0.05±0.15 (CI 0.24−0.35) |
| Horizontal astigmatism (µm) | 0.16±0.51 (CI 1.18−0.85) | −0.98±0.50 (CI 0.01−1.98) |
| Vertical trefoil (µm) | 0.13±0.14 (CI 0.40−0.14) | 0.02±0.02 (CI 0.06−0.02) |
| Vertical coma (µm) | −0.01±0.18 (CI 0.34−0.37) | −0.11±0.09 (CI 0.07−0.29) |
| Horizontal coma (µm) | −0.06±0.11 (CI 0.16−0.28) | −0.23±0.22 (CI 0.21−0.67) |
| Vertical quadrafoil (µm) | 0.01±0.06 (CI 0.13−0.11) | 0.03±0.02 (CI 0.07−0.02) |

| Myopia |
|-----------------|-----------------|
| LO RMS (µm) | 2.79±1.87 (CI 6.53−0.94) |
| HO RMS (µm) | 0.16±0.07 (CI 0.29−0.02) |
| 3\(^{rd}\) order RMS (µm) | 0.20±0.08 (CI 0.35−0.04) |
| 4\(^{th}\) order RMS (µm) | 0.10±0.07 (CI 0.25−0.04) |
| Vertical astigmatism (µm) | 0.09±0.61 (CI 1.31−1.13) |
| Defocus (µm) | −4.14±3.57 (CI 2.73−1.15) |
| Horizontal astigmatism (µm) | 0.25±1.12 (CI 2.49−1.99) |
| Vertical trefoil (µm) | 0.15±0.16 (CI 0.48−0.17) |
| Vertical coma (µm) | 0.01±0.22 (CI 0.45−0.42) |
| Horizontal coma (µm) | −0.17±0.18 (CI 0.19−0.53) |
| Horizontal trefoil (µm) | −0.04±0.14 (CI 0.24−0.32) |
| Vertical quadrafoil (µm) | −0.01±0.16 (CI 0.31−0.34) |
| Horizontal 2\(^{nd}\) astigmatism (µm) | 0.03±0.04 (CI 0.11−0.05) |
| Spherical aberration (µm) | −0.10±0.15 (CI 0.20−0.40) |
| V.2\(^{nd}\) astigmatism (µm) | 0.00±0.11 (CI 0.21−0.22) |
| H.Quadrafoil (µm) | −0.01±0.07 (CI 0.13−0.15) |

| Hyperopia |
|-----------------|-----------------|
| LO RMS (µm) | 0.44±0.31 (CI 1.06−0.19) |
| HO RMS (µm) | 0.12±0.06 (CI 0.25−0.01) |
| 3\(^{rd}\) order RMS (µm) | 0.15±0.09 (CI 0.33−0.03) |
| 4\(^{th}\) order RMS (µm) | 0.08±0.06 (CI 0.20−0.04) |
| Vertical astigmatism (µm) | 0.07±0.18 (CI 0.43−0.28) |
| Defocus (µm) | 0.08±0.60 (CI 1.29−1.12) |
| Horizontal astigmatism (µm) | −0.36±0.60 (CI 1.84−1.57) |
| Vertical trefoil (µm) | 0.14±0.13 (CI 0.41−0.12) |
| Vertical coma (µm) | 0.09±0.08 (CI 0.25−0.08) |
| Horizontal coma (µm) | −0.09±0.24 (CI 0.40−0.58) |
| Horizontal trefoil (µm) | −0.03±0.07 (CI 0.12−0.17) |
| Vertical quadrafoil (µm) | 0.00±0.04 (CI 0.08−0.08) |
| Horizontal 2\(^{nd}\) astigmatism (µm) | 0.01±0.03 (CI 0.07−0.04) |
| Spherical aberration (µm) | −0.14±0.15 (CI 0.16−0.44) |
| V.2\(^{nd}\) astigmatism (µm) | 0.00±0.06 (CI 0.11−0.11) |
| H.Quadrafoil (µm) | 0.00±0.05 (CI 0.10−0.10) |

RMS=Root mean square; LO RMS=Lower-order RMS; HO RMS=Higher-order RMS; CI=Confidence interval
myopes. This significance of LO RMS with SE is understandable, while HO RMS showed no significant relationship with SE in myopes. This is in accordance with the earlier work[13] where HO RMS in myopes showed no correlation, whereas, in other works,[14,15] it revealed that a positive correlation was found in HOA with increase in refractive errors. Another study presented that hyperopes had increased HOA when compared to myopes[16] and this work is in conjunction with the same. Although the SE of the myopic group in human eyes was up to –13.50 D when compared to the model eye of –5D, it resulted in almost equal amounts of HO RMS of 0.16 ± 0.07 in the human eye group and 0.10 ± 0.02 in the model eye group.

Though mathematically a statistical significance was found in 3rd-order RMS, 4th-order RMS, and few other LOA in both the cohorts, there was no statistical significance between the individual Zernike terms except for coma in human eyes between emmetropes and myopes and similarly in the model eye between myopes and emmetropes and hyperopes. Hence, in patients having irregular corneas such as keratoconus and post-LASIK ectasia, coma has to be analyzed in particular.

On analyzing the influence of the individual Zernike terms on HOA, only horizontal secondary astigmatism was influential in emmetropes and vertical quadrafoil was influential in myopes. There was no influence of any one particular Zernike term in hyperopes. Hence patients complaining of glare or starburst in spite of appropriate optical correction need to be analyzed for either of HOA.

Although the HOA percentage was less in myopes when compared to emmetropes and hyperopes in both the cohorts, the amount of mean HOA was almost equal in all the three groups, which was 0.11 ± 0.05, 0.16 ± 0.07, and 0.12 ± 0.06 for emmetropes, myopes, and hyperopes, respectively. In human eyes. Similar results were obtained in the model eye where the mean HOAs were 0.13 ± 0.02, 0.10 ± 0.02, and 0.18 ± 0.09 in emmetropia, myopia, and hyperopia, respectively.

In this study, mean HO RMS showed a statistically significant difference between the myopia-emmetropia groups, whereas previous studies showed no significance between the groups.[12,13,17]

As it is an established fact that HOA increases with pupil size,[1,8,19] pupil size analyses was not performed in this work. The amount of HOA exhibited in hyperopic human and model eyes were similar, which were not in accordance with previous studies.[20,21] This work revealed similar amounts of HOA for myopes in both human eyes and model eye, whereas earlier works reported myopic eyes to have increased levels of HOA.[22-27]

It is evident in this work that the mean HOA tend to be the same in any type of refractive error. Even in high myopes, HOA was almost similar with other refractive errors. Surprisingly, even emmetropes and hyperopes showed the same amount of HOA despite having good visual acuity of 6/6, indicating a strong debate on the significance of HOA on image quality for human eyes. In astronomy and image-capturing devices such as Optical coherence tomography (OCT), the image is made clearer and sharper by using AO technology. HOA correction gains importance and improves visual acuity where the surface is irregular due to ocular conditions such as keratoconus,[28,29] post-LASIK cases,[30,31] postcorneal injuries, post-PK cases,[32,33] dislocated or tilted Intraocular Lens (IOL).[34,35] and lenticous.

**Conclusion**

In regular surfaces of cornea and lens, HOA correction may not play a significant role in improving the visual acuity of the patients. However, the presence of 23% HOA out of total RMS in emmetropes for human eyes signifies that the human eye is capable of “adapting to HOA,” wherein the image quality is not compromised in spite of huge HOA. The factors for adaptation of the human eye for HOA can vary from dynamic pupil size changes, depth of focus, cone packing arrangements in fovea, etc., These factors were the limitations in finding out the precise HOA measurements in this study on which further exploration is necessary. This work signifies that HOA does not play an important role in image clarity for human eyes with regular refractive surface unlike irregular refractive surfaces.

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**Conflicts of interest**

There are no conflicts of interest.

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