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The effect of aberrations on objectively assessed image quality and depth of focus

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The effects of aberrations on image quality and the objectively assessed depth of focus (DoF) were studied. Aberrometry data from 80 young subjects with a range of refractive errors was used for computing the visual Strehl ratio based on the optical transfer function (VSOTF), and then, through-focus simulations were performed in order to calculate the objective DoF (using two different relative thresholds of 50% and 80%; and two different pupil diameters) and the image quality (the peak VSOTF). Both lower order astigmatism and higher order aberration (HOA) terms up to the fifth radial order were considered. The results revealed that, of the HOAs, the comatic terms (third and fifth order) explained most of the variations of the DoF and the image quality in this population of subjects. Furthermore, computer simulations demonstrated that the removal of these terms also had a significant impact on both DoF and the peak VSOTF. Knowledge about the relationship between aberrations, DoF, image quality, and their interactions is essential in optical designs aiming to produce large values of DoF while maintaining an acceptable level of image quality. Comatic aberration terms appear to contribute strongly towards the configuration of both of these visually important parameters.

Introduction

The human eye's optical aberrations are omnipresent, but their exact role in many aspects of the process of vision is not fully understood (Artal, Benito, & Tabernero, 2006; Chen, Artal, Gutierrez, & Williams, 2007). It is well known that higher order aberrations (HOAs) affect the quality of the retinal image and this effect has been calculated for large populations of normal human eyes (Guirao, Porter, Williams, & Cox, 2002; Porter, Guirao, Cox, & Williams, 2001). The established relationship between HOAs and the eye's image quality has been the catalyst for a large number of studies focused on the benefits resulting from correcting HOAs for both normal (Williams et al., 2000; Yoon, Jeong, Cox, & Williams, 2004) and highly aberrated eyes (Sabesan et al., 2007; Sabesan & Yoon, 2009).

However, there is evidence in normal eyes, that the visual benefits (e.g., high-contrast acuity performance and contrast sensitivity) of correcting HOAs are relatively minor in many cases (Charman & Chateau, 2003; De Gracia, Marcos, Mathur, & Atchison, 2011; Guirao et al., 2002). Furthermore, there is also evidence to suggest that HOAs, if not encountered in pathological amounts, may not only be integral to human eye optics but may also provide basis for the robustness of the visual system (Artal et al., 2006) that otherwise could become unstable in the presence of internal retinal and crystalline lens fluctuations (Charman & Heron, 2015; Iskander, 2014), particularly given that HOAs are thought to provide the visual system with a cue to the sign of defocus (Wilson, Decker, & Roorda, 2002), and contribute towards the eye's normal depth

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of focus (DoF) (Artal, Marcos, Navarro, Miranda, & Ferro, 1995; Ramos-Lopez, Martínez-Finkelshtein, & Iskander, 2014). Previous research utilizing a variety of experimental and computational methods has established that while aberrations influence both image quality and the through-focus characteristics of the eye (Artal et al., 1995; Collins, Buehren, & Iskander, 2006; Ramos-Lopez et al., 2014; Schwiegerling, 2007), there is a trade-off between an optimal level of image quality and an optimal level of DoF (Marcos, Moreno, & Navarro, 1999; Yi, Iskander & Collins, 2010).

The balance between the eye's optical quality and DoF is extremely important in the design of many optical solutions for presbyopia, such as simultaneous vision intraocular or contact lenses, particularly for refractive (De Gracia, Dorronsoro, & Marcos, 2013) or diffractive lens designs. Other solutions, for instance, are based on abrupt phase changes (Ares García et al., 2008). The aim of all of these optical solutions is to provide the presbyope with optimal image quality across a wide range of vergences, with a typical approach involving inducing increased levels of particular aberrations (often spherical aberration), to enhance the DoF of the subjects.

There have been a number of previous studies examining the effect of aberrations on image quality and DoF, generally by utilizing a deformable mirror in order to manipulate subjects' monochromatic aberrations. Nevertheless, these investigations have focused primarily on the effect of spherical aberration, both primary and secondary (Benard, López-Gil, & Legras, 2010, 2011; Cheng, Bradley, Ravikumar, & Thibos, 2010; Rocha, Vabre, Chateau, & Krueger, 2009; Xu, Bradley, López-Gil, & Thibos, 2015). Comatic, trefoil, secondary astigmatic and tetrafoil aberrations have received much less attention, and there has been limited consensus on their effect on estimated image quality and DoF. For example, Rocha et al. (2009) indicated that trefoil and coma appeared to have no significant effect on the subjective DoF, whereas Legras, Benard, and López-Gil (2012) showed that both coma and spherical aberration had a significant impact on DoF. A selective approach, in terms of specific higher order wavefront aberration terms (e.g., only examining the impact of spherical aberration terms or a combination of only spherical aberration and coma) as employed in previous work has provided insights into the role of HOAs in image quality and DoF. However, these approaches overlook the potential effects of a number of naturally occurring aberration terms with the potential to substantially impact on the eye's normal image quality (e.g., coma, trefoil, and secondary astigmatism). Therefore, a more systematic and comprehensive analysis of all (to a certain degree) wavefront aberration terms is needed.

In this study, we therefore aimed to assess the influence of aberrations on objectively estimated image quality and DoF in a population of normal young adult subjects, employing a systematic analytical approach that considers a larger number of wavefront aberration terms than has been examined in previous works. This more comprehensive approach will generate knowledge that will assist in predicting the potential visual impact of aberrations for a range of applications (e.g., the visual effects of the decentration of an aberration-correcting contact lens on the eye), providing insights for future work aiming to manipulate higher order aberrations to expand the eye's DoF.

Methods

Subjects

Retrospective aberration data from 80 young adult participants aged between 18 and 33 years (mean $\pm$ *SD* $= 22.9 \pm 3.5$ years) previously collected as part of a study conducted at the School of Optometry & Vision Science, Queensland University of Technology, were analyzed in this study. All participants gave written informed consent, and were treated in accordance with the tenets of the Declaration of Helsinki. A non-cycloplegic subjective refraction performed on all subjects revealed spherical refractive errors ranging from -7.25 to $+0.75$ D (mean $\pm$ $SD = -0.80 \pm 1.68$ D), with no subject exhibiting astigmatism greater than 0.5 D (mean $\pm$ *SD* cylinder magnitude $= -0.17 \pm 0.11$ D, mean axis $1.4° \pm 19.0°$). All subjects exhibited best corrected visual acuity of logMAR 0.00 or better. Subjects were divided into three groups, based on their spherical refractive error: mild hyperopia to emmetropia ($+0.75$ D to 0.00 D), mild myopia (ranging from -0.25 to -1.50 D), and moderate to high myopia (with myopia greater than -1.5 D). Table 1 shows a summary of the main characteristics of each group. The three groups did not exhibit significant differences in terms of mean age ($p = 0.875$) or pupil diameter ($p = 0.108$).

Depth of focus computations

Repeated wavefront aberration measurements were collected and fit with Zernike polynomials up to and including eighth radial order from each subject's right eye only avoiding the potentially complicating factor of enantiomorphism which may occur when averaging data from right and left eyes (Smolek, Klyce, & Sarver 2002), during distance fixation, with a Complete Ophthalmic Analysis System (COAS, AMO Wavefront Sciences, Albuquerque, NM) and collected at a

Refractive group	Number of subjects	Sphere (D)	Cylinder (D)	Axis (°)	Age	Pupil diameter (mm)
Mild hyperopia to emmetropia	53	+0.04 ± 0.28	−0.16 ± 0.17	179.3 ± 19.6	22.8 ± 3.6	6.1 ± 0.8
Mild myopia	14	−0.88 ± 0.35	−0.25 ± 0.20	25.1 ± 15.4	23.4 ± 3.9	6.1 ± 0.7
Moderate to high myopia	13	−4.13 ± 1.73	−0.15 ± 0.16	118 ± 24.7	22.9 ± 2.9	5.6 ± 0.8

Table 1. Main characteristics (mean ± standard deviation) of the three refractive groups.

frequency of about 10 Hz over an approximate period of 10 seconds. All wavefront measurements were collected in dim room lighting to maximize the natural pupil size, and without pharmacological mydriasis or cycloplegia. Before averaging the data for each subject, blink and other possible artefacts were removed by examining the pupil diameter registered at each time instant. Individual wavefront data having a pupil size that was outside the range defined by each subject's mean pupil size plus/minus two standard deviations were removed. This resulted in a mean of 3.2 ± 2.6% of measurements being removed per subject.

All of the valid wavefront measurements for each subject were then averaged (Ginis, Plainis, & Pallikaris, 2004), and the Zernike coefficients were rescaled to a global minimum pupil diameter (Lundström, & Unsbo, 2007; Schwiegerling, 2002). In order to investigate the potential effect of pupil size, the data were analyzed over two different pupil diameters: 3.6 mm (the global minimum across all subjects after removing blink artefacts) and 4.6 mm (three mild hyperopic to emmetropic subjects had pupil diameters smaller than this and were removed from this aspect of the analysis).

Custom software written in Matlab (The MathWorks, Natick, MA) was used to compute the through-focus visual Strehl ratio based on the optical transfer function (VSOTF), of each subject, using an approach similar to that of Yi, Iskander, and Collins (2010, 2011). For each amount of defocus, the VSOTF was computed using Fourier methods (Thibos, Hong, Bradley, & Applegate, 2004), and these calculations were repeated for defocus levels ranging from −3 D to +3 D, in 0.0625 D steps. VSOTF is commonly used in these computations, since this objective image quality metric is known to correlate well with subjective measures of visual performance (Marsack, Thibos, & Applegate, 2004). In addition, the augmented version of the VSOTF addresses and solves some of its computational limitations (Iskander, 2006). The relative threshold values of 50%, DoF50, and 80%, DoF80 (used in a number of previous studies including Jansonius & Kooijman, 1998; Marcos et al., 1999; and Xu et al., 2015), were selected to evaluate whether the use of different thresholds affects the relationship between objectively assessed DoF and aberrations. The maximum of the through-focus VSOTF (Peak VSOTF) was also investigated. An example of calculating DoF using this approach is shown in Figure 1.

In order to systematically examine the impact of groups of aberrations of different magnitudes upon DoF and image quality, through-focus curves were calculated and analyzed for three different conditions: (a) HOAs and second order astigmatism; (b) Only HOAs; and (c) Only HOAs and excluding third order aberrations.

Population statistics

To determine if there were any significant differences in the magnitude of the aberrations, the calculated DoF and the Peak VSOTF among the refractive groups, a one-way ANOVA was performed for each of the two pupil diameters, following confirmation of normality (Jarque-Bera test) and equality of variance (Levene's test) of each dataset. For these calculations, the aberrations were grouped using a similar approach to Campbell (2003) that reduces the total number of terms considered by a factor of almost two and expresses them in a more clinically accessible way, but also retains the analytical power of the traditional Zernike approach. Here, second order astigmatism (c_{22}) root mean square (RMS), third order trefoil RMS (c_{33}), third order coma-like RMS (c_{31}), fourth order tetrafoil RMS (c_{44}), fourth order astigmatism RMS (c_{42}), spherical-like RMS (c_{460}, taking into account fourth and sixth Zernike radial orders), and fifth order coma

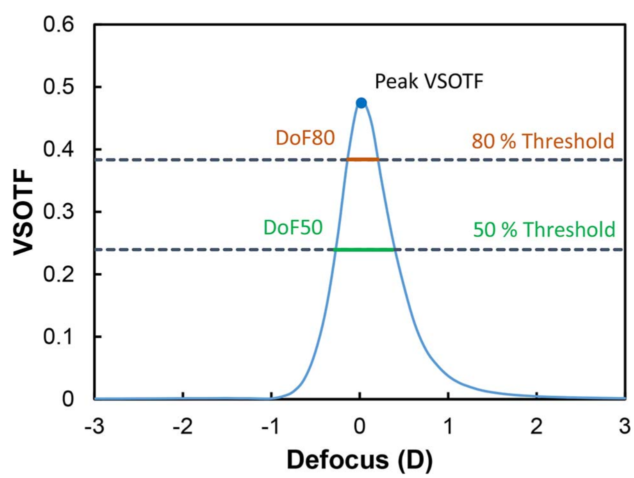

Figure 1. Estimation of the Depth of Focus (DoF) by means of the through-focus VSOTF for 50% and 80% thresholds.

RMS (c_{51}) were considered. These aberrations terms are related to the OSA standards for reporting aberrations of the eye (Thibos, Applegate, Schwiegerling, & Webb, 2002) as follows: c_{22} corresponds to $\sqrt{\left(C_2^{-2}\right)^2+\left(C_2^{+2}\right)^2}$, c_{33} is $\sqrt{\left(C_3^{-3}\right)^2+\left(C_3^{+3}\right)^2}$, c_{31} is $\sqrt{\left(C_3^{-1}\right)^2+\left(C_3^{+1}\right)^2}$, c_{44} is $\sqrt{\left(C_4^{-4}\right)^2+\left(C_4^{+4}\right)^2}$, c_{42} is $\sqrt{\left(C_4^{-2}\right)^2+\left(C_4^{+2}\right)^2}$, c_{460} is $\sqrt{\left(C_4^{0}\right)^2+\left(C_6^{0}\right)^2}$, and c_{51} is $\sqrt{\left(C_5^{-1}\right)^2+\left(C_5^{+1}\right)^2}$. Given the multiple statistical comparisons performed, a Bonferroni correction was applied in this analysis (resulting in $\alpha = 0.006$).

Relationship between DoF, optical quality and aberrations

To explore the relationship between different aberrations and the objectively assessed DoF, and also between these aberrations and the Peak VSOTF, stepwise forward regression (Efroymson, 1960) was used. Variables were entered in order starting from c_{22} and ending with c_{51}. This method performs a multilinear regression and keeps the statistically significant ($p < 0.05$) variables within the model, while the nonsignificant ($p > 0.05$) variables are rejected sequentially and do not appear in the final linear model. Therefore, this analysis provides a suitable way to explain the DoF and the Peak VSOTF by means of the aberrations that play the most significant role in the calculation of these parameters.

Impact of correcting aberrations on the DoF and the optical quality of the eye

In order to provide further insights on the impact of certain aberrations upon the DoF and the optical quality of the eye (i.e., the Peak VSOTF), simulations were performed in which different aberrations were corrected by removing the corresponding Zernike coefficients. For this purpose, aberrations were grouped in the same way as described above (Campbell, 2003).

Results

Population statistics

Regarding the distribution of aberrations among the three refractive groups, one-way ANOVA revealed no significant differences associated with refractive error for the mean of any of the aberration terms (Figure 2), the objectively assessed DoF (for each DoF50 and DoF80, Figure 3a) or the Peak VSOTF (for the HOAs + astigmatism case, Figure 3b), for the two considered pupil diameters (all $p > 0.056$). The ANOVA was repeated for the other two conditions (only HOAs and HOAs minus third order aberrations), which also showed no differences associated with refractive group. Given the lack of statistically significant differences in astigmatism and HOAs among the refractive groups for these values, all subjects were grouped together to form a single population for the remaining calculations. A posthoc power analysis revealed the sample size used had 95% power to detect a 0.005-micrometer difference in HOAs. A summary with the DoF and Peak VSOTF mean values (along with standard deviation) for the different conditions and pupil diameters is shown in Table 2, when the data from all refractive groups were pooled.

Relationship between DoF, optical quality and aberrations

Calculations with HOAs and second order astigmatism

A total of six stepwise regressions were performed regarding the DoF to examine the relationship between aberrations and the calculated DoF (at each pupil diameter and threshold level). For DoF50 and a pupil diameter of 3.6 mm, the stepwise forward regression revealed that the only aberration contributing significantly to the model was second order astigmatism ($p < 0.001$). The equation from the stepwise linear regression to predict the DoF50 in diopters, for a 3.6 mm pupil diameter was:

$$\mathrm{DoF50} = 0.615 - 1.269c_{22} \quad \left(\text{Model } R^2 = 0.275,\ p < 0.001\right) \qquad (1)$$

where c_{22} is the second order astigmatism RMS in micrometers. For DoF80, the aberration terms found to significantly contribute to the final model was fourth order astigmatism. In this case, the DoF80 (in diopters) can be obtained using the equation:

$$\mathrm{DoF80} = 0.356 - 3.209c_{42}, \quad \left(\text{Model } R^2 = 0.066,\ p = 0.022\right) \qquad (2)$$

Repeating the same, but using the 4.6 mm pupil diameter, the equation obtained for the DoF50 was

$$\mathrm{DoF50} = 0.537 + 0.374c_{22} + 2.375c_{460}, \quad \left(\text{Model } R^2 = 0.139,\ p < 0.001\right) \qquad (3)$$

with p values of 0.010 for the spherical-like RMS ($R^2 = 0.086$), and 0.036 for the second order astigmatism (R^2

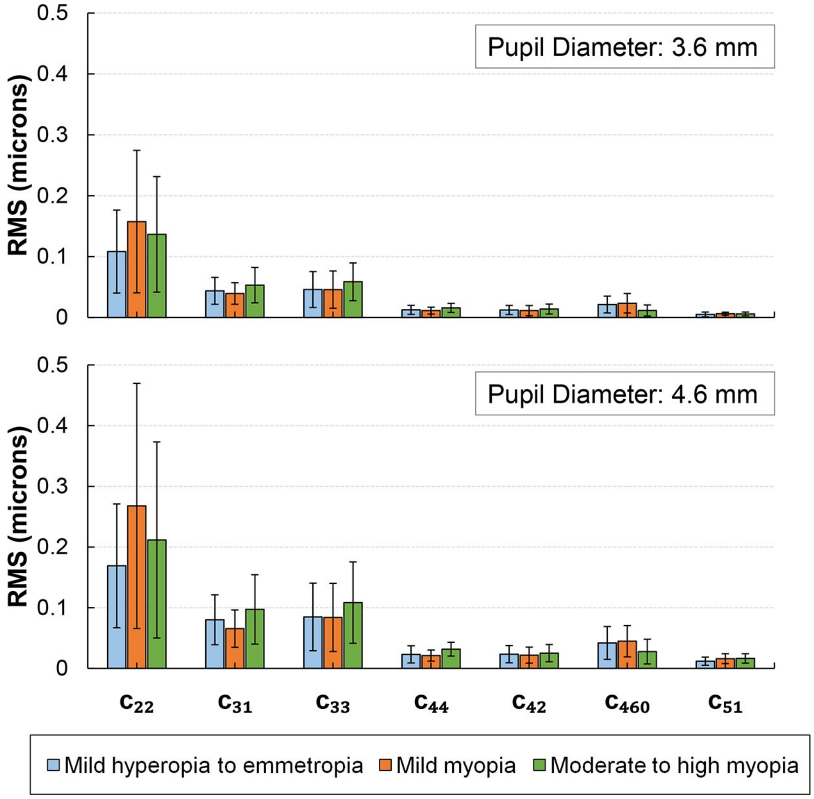

Figure 2. Mean RMS values of the grouped aberrations for each of the three refractive groups. Symbol c_{22} denotes second order astigmatism, c_{31} third order coma, c_{33} third order trefoil, c_{44} fourth order tetrafoil, c_{42} fourth order astigmatism, c_{460} fourth and sixth order spherical aberration, and c_{51} fifth order coma. Aberrations derived for both a 3.6 mm pupil diameter (top), and a 4.6 mm pupil diameter (bottom) are shown. Error bars represent $\pm$ one standard deviation.

increase = 0.053). For DoF80, the result was

$$\mathrm{DoF80} = 0.299 + 1.534c_{460} \quad \left(\text{Model } R^2 = 0.104,\ p = 0.004\right) \quad (4)$$

Correlations between the calculated values and those predicted by each of the linear models are shown in Figure 4. It is interesting to note that the predicted DoF values are not close to the calculated ones, which means the models in these particular cases are generally poor.

A similar stepwise regression analysis was performed, to examine the relationship between the aberrations and the objectively estimated retinal image quality (i.e., the Peak VSOTF) for the two pupil sizes. For both pupil sizes, second order astigmatism, third order coma, spherical-like, and fourth order astigmatism RMS were included in the linear models ($p < 0.05$ in all cases). Trefoil RMS was additionally included in the model for the 4.6 mm of pupil size. Correlations between the calculated values and those predicted by each one of the linear models are shown in the lower panel of Figure 4. The order in which these predictors were added for the smaller pupil was c_{22} ($R^2 = 0.577$), c_{31} (R^2 increase = 0.081), c_{42} (R^2 increase = 0.029), and c_{460} (R^2 increase = 0.022). For the larger pupil, the order was c_{22} ($R^2 = 0.424$), c_{460} (R^2 increase = 0.066), c_{31} (R^2 increase = 0.058), c_{42} ($R^2 = 0.026$), and c_{33} (R^2 increase = 0.024). It was observed that when the pupil size increases, the linear model is weaker, and therefore the predictions are worse.

Calculations with only HOAs

In order to study the effect of HOAs on DoF and image quality without the possibility of astigmatism masking the potentially important effects of other aberrations, the same analysis was repeated; however, this time only HOAs were considered for the calculations. For a pupil diameter of 3.6 mm, the equations from the stepwise linear regression to predict the different DoFs in diopters were

$$\mathrm{DoF50} = 0.391 + 8.147c_{31}, \quad \left(\text{Model } R^2 = 0.820,\ p < 0.001\right) \quad (5)$$

$$\mathrm{DoF80} = 0.184 + 5.903c_{31}, \quad \left(\text{Model } R^2 = 0.662,\ p < 0.001\right) \quad (6)$$

Repeating the same, but using the 4.6 mm pupil diameter, the equations obtained were

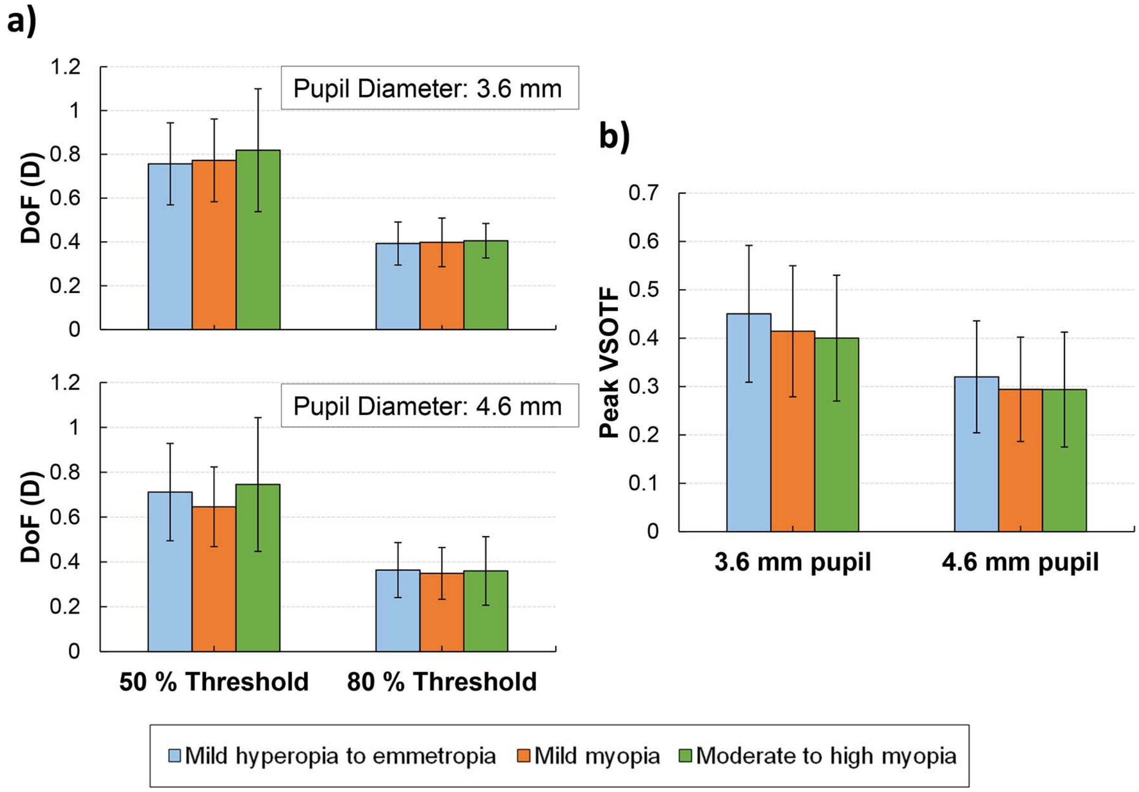

Figure 3. (a) Mean depth of focus (DoF) values for the three refractive groups calculated using a 50% and an 80% threshold. The DoF for both a 3.6 mm pupil diameter (top) and a 4.6 mm pupil diameter (bottom) is shown. (b) Peak VSOTF for the two pupil sizes and each refractive group. Error bars represent ± one standard deviation. These values correspond to the case HOAs + astigmatism.

$$\mathrm{DoF50} = 0.325 + 3.820c_{31} + 7.150c_{51},$$
$$\left(\mathrm{Model}\ R^2 = 0.662,\ p < 0.001\right) \quad (7)$$

with p values of < 0.001 for the third order coma ($R^2 = 0.627$), and 0.007 for the fifth order coma (R^2 increase $= 0.035$). For the 80 % threshold, the result was

$$\mathrm{DoF80} = 0.222 + 1.957c_{31}$$
$$\left(\mathrm{Model}\ R^2 = 0.453,\ p < 0.001\right) \quad (8)$$

Correlations between the calculated values and those predicted by each of the linear models are shown in Figure 5. In this case, more than 80% of the variance in DoF50 is explained using only the third order coma RMS at a 3.6 mm pupil. As the pupil size and the selected threshold increase, the linear models are weaker (lower R^2), giving as a result poorer predictions.

Regarding the Peak VSOTF, for the smaller pupil, the significant terms in order were: c_{31} ($R^2 = 0.780$; $p < 0.001$), c_{51} (R^2 increase $= 0.035$; $p < 0.001$), c_{33} (R^2 increase $= 0.035$; $p < 0.001$), and c_{460} (R^2 increase $= 0.026$; $p < 0.001$). In the larger pupil case, the terms selected were c_{31} ($R^2 = 0.563$; $p < 0.001$), c_{51} (R^2 increase $= 0.071$; $p < 0.001$), c_{460} (R^2 increase $= 0.068$; $p < 0.001$), and c_{33} (R^2 increase $= 0.017$; $p = 0.038$).

Calculations with HOAs only, excluding third order aberrations

Finally, the analysis was repeated once more, but this time third order aberrations were also removed. For a pupil diameter of 3.6 mm, the equations from the stepwise linear regression to predict the different DoFs in diopters were

	HOAs + astigmatism		HOAs		HOAs − third order	
Pupil (mm)	3.6	4.6	3.6	4.6	3.6	4.6
DoF50 (D)	0.76 ± 0.19	0.71 ± 0.22	0.78 ± 0.27	0.76 ± 0.28	0.48 ± 0.06	0.46 ± 0.12
DoF80 (D)	0.39 ± 0.10	0.36 ± 0.12	0.47 ± 0.22	0.40 ± 0.17	0.26 ± 0.02	0.24 ± 0.07
PeakVSOTF	0.45 ± 0.14	0.32 ± 0.12	0.54 ± 0.17	0.38 ± 0.14	0.87 ± 0.10	0.66 ± 0.15

Table 2. DoF and Peak VSOTF values (mean ± *SD*) for each of the conditions considered and for both pupil diameters.

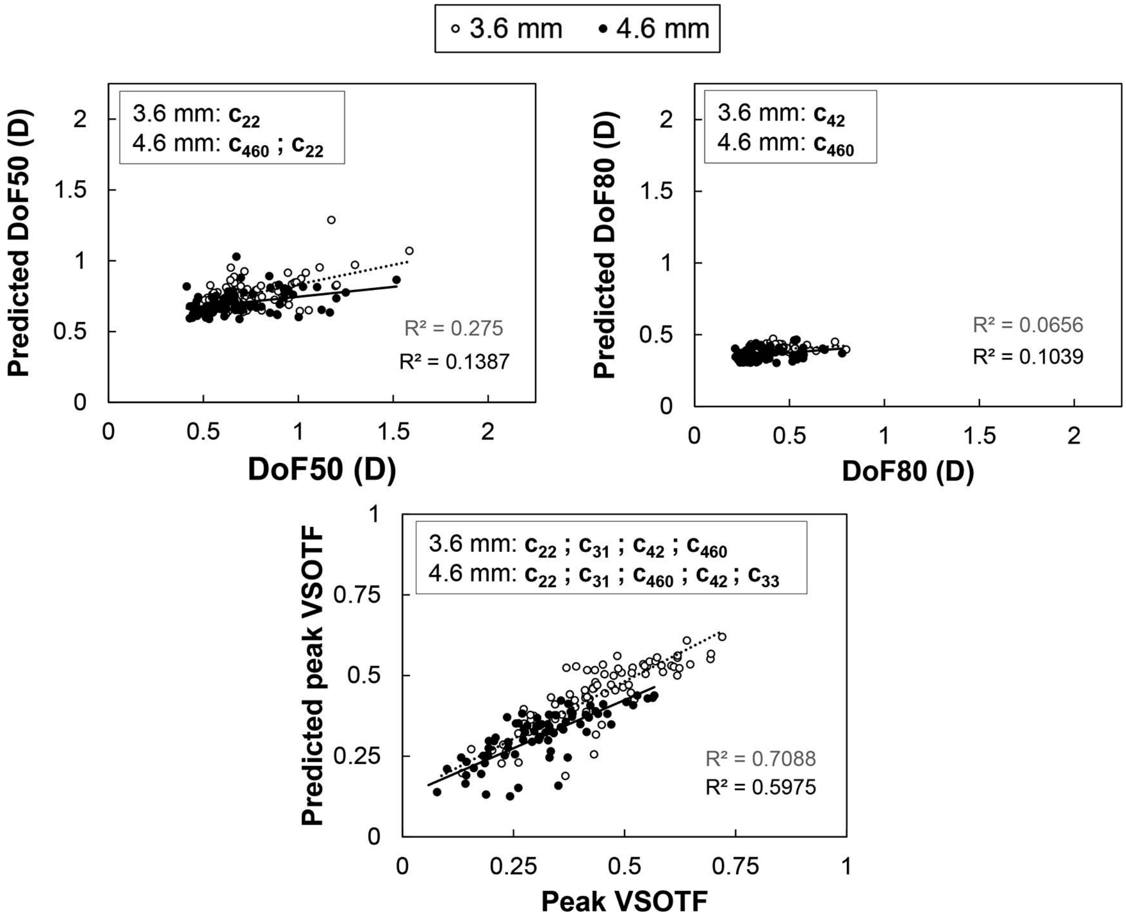

Figure 4. Correlations between the calculated depth of focus (DoF) and Peak VSOTF (considering HOAs + astigmatism), and the values predicted by the linear models for all pupils and thresholds. Solid lines represent the best linear fit to the data for a 4.6 mm pupil, whereas dotted lines correspond to the linear fit for 3.6 mm pupil. The lighter R2 corresponds to the small pupil. Notice that the axes scales can be different for each panel. Symbol c_{22} denotes second order astigmatism, c_{31} third order coma, c_{33} third order trefoil, c_{42} fourth order astigmatism, and c_{460} fourth and six order spherical aberration.

$$\mathrm{DoF50} = 0.366 + 2.149c_{460} + 1.1283c_{42} + 10.314c_{51}, \quad \left(\text{Model } R^2 = 0.723,\ p < 0.001\right) \quad (9)$$

with p values of < 0.001 for the fifth order coma ($R^2 = 0.485$), $p < 0.001$ for the spherical-like RMS (R^2 increase $= 0.220$), and 0.030 for the fourth order astigmatism term (R^2 increase $= 0.018$).

$$\mathrm{DoF80} = 0.220 + 0.821c_{460} + 0.546c_{42} + 3.790c_{51}, \quad \left(\text{Model } R^2 = 0.807,\ p < 0.001\right) \quad (10)$$

with p values of < 0.001 for the fifth order coma ($R^2 = 0.523$), $p < 0.001$ for the spherical-like RMS (R^2 increase $= 0.252$), and $p < 0.001$ for the fourth order astigmatism term (R^2 increase $= 0.032$).

For the 4.6 mm pupil diameter case, the equations obtained were

$$\mathrm{DoF50} = 0.235 + 3.965c_{460} + 5.038c_{51}, \quad \left(\text{Model } R^2 = 0.797,\ p < 0.001\right) \quad (11)$$

with p values of < 0.001 for the spherical-like term ($R^2 = 0.708$), and $p < 0.001$ for the fifth order coma (R^2 increase $= 0.089$). The result obtained for the 80% threshold was

$$\mathrm{DoF80} = 0.119 + 2.181c_{460} + 2.107c_{51}, \quad \left(\text{Model } R^2 = 0.624,\ p < 0.001\right) \quad (12)$$

The order in this case was spherical-like term ($R^2 = 0.582$; $p < 0.001$) and the fifth order coma (R^2 increase $= 0.042$; $p = 0.005$).

Regarding the Peak VSOTF, for the smaller pupil, the significant terms in order were c_{460} ($R^2 = 0.550$; $p < 0.001$), c_{51} (R^2 increase $= 0.273$; $p < 0.001$), c_{42} (R^2 increase $= 0.083$; $p < 0.001$), and c_{44} (R^2 increase $= 0.028$; $p < 0.001$). For the larger pupil, the terms selected were c_{460} ($R^2 = 0.582$; $p < 0.001$), c_{51} (R^2 increase $= 0.210$; $p < 0.001$), c_{42} (R^2 increase $= 0.084$; $p < 0.001$) and c_{44} (R^2 increase $= 0.044$; $p < 0.001$). The correlations between the calculated values and those predicted by each of the linear models are illustrated in

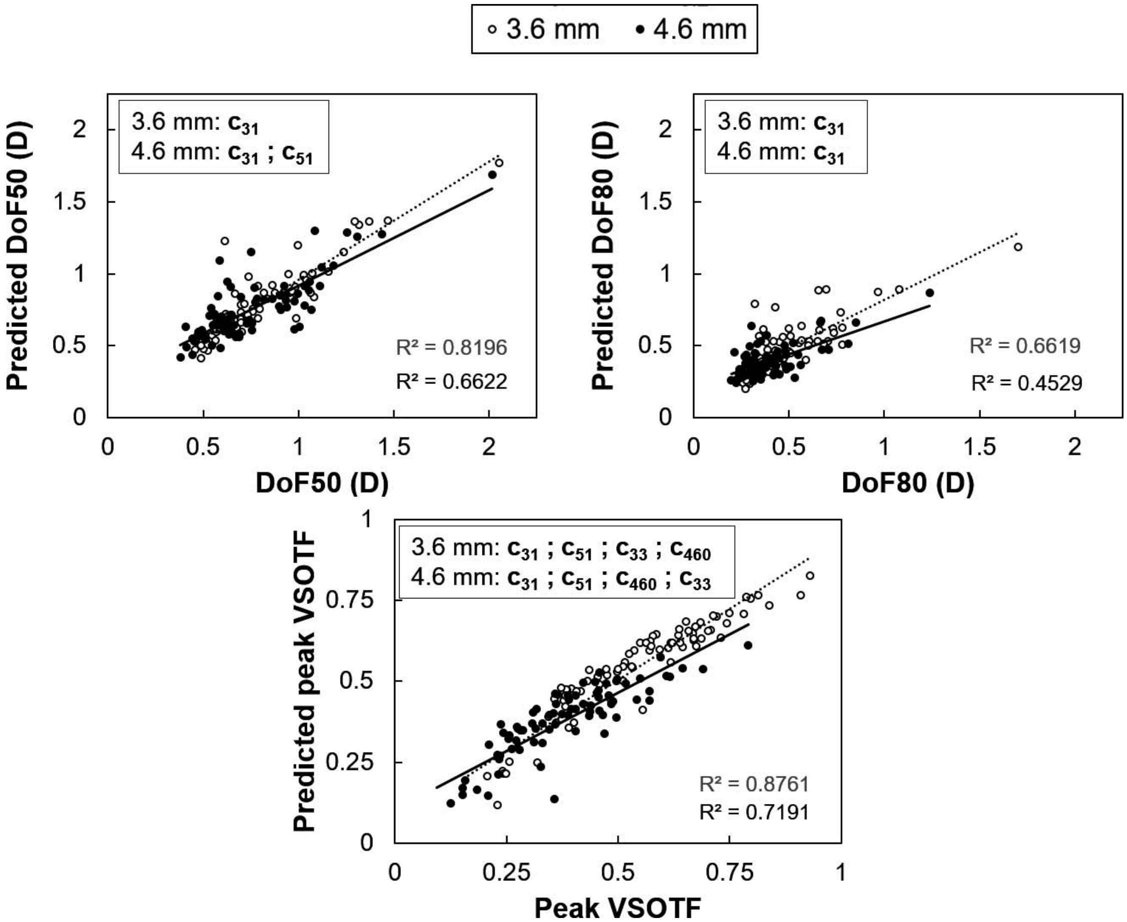

Figure 5. Correlations between the calculated depth of focus (DoF) and Peak VSOTF (considering only HOAs), and the values predicted by the linear models for all pupils and thresholds. Solid lines represent the best linear fit to the data for a 4.6 mm pupil, whereas dotted lines correspond to the linear fit for 3.6 mm pupil. The lighter R2 value corresponds to the small pupil. Notice that the axes scales can be different. Symbol c_{31} denotes third order coma, c_{33} third order trefoil, c_{460} fourth and sixth order spherical aberration, and c_{51} fifth order coma.

Figure 6. In this case, almost all the predictions are very good, since there are less aberration terms and their magnitude is smaller and less variable between subjects.

Impact of correcting aberrations on the DoF and the optical quality of the eye

Simulations examining the effect of correcting different aberrations on the DoF and the Peak VSOTF can be found in Figure 7. The additive effect of correcting these aberrations was studied, meaning that initially, second order astigmatism was removed, then third order coma, followed by the trefoil, and then sequentially the rest of the aberrations were removed until the fifth order coma. Hence, one term was removed each time. In general, when the optical quality improved, the DoF decreased, and the relationship between both follows a linear trend ($R^2 > 0.97$ for both pupil sizes and thresholds), as seen in the bottom row of Figure 7. This result highlights the trade-off that exists between optical quality and DoF. It is interesting to note that while removal of second order astigmatism resulted in an improvement in image quality, its removal also resulted on average in an increase in DoF whereas the removal of each of the other terms resulted in an improvement in image quality and a reduction in DoF. The aberration that had the largest impact on both parameters (DoF and Peak VSOTF) was the third order coma. This impact was larger than that caused by the second order astigmatism. For small pupils, the differences in the impact of the correction of several aberrations using the two different thresholds was minimal, whereas for larger pupils, small variations start to appear between thresholds, mainly from the correction of the spherical-like aberrations. It is also noticeable that for larger pupil diameters, the correction of aberrations with greater radial order, like the fifth order coma and the spherical-like aberrations has

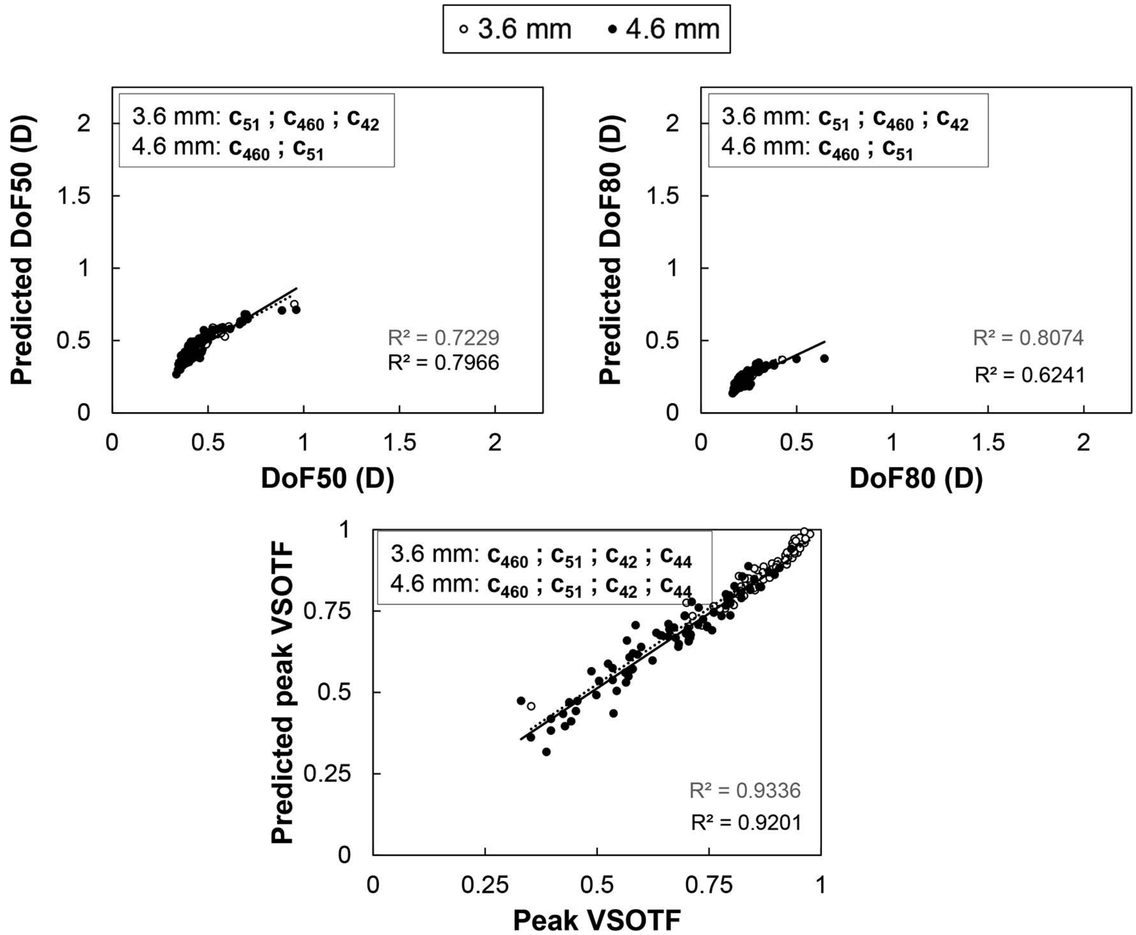

Figure 6. Correlations between the calculated depth of focus (DoF) and Peak VSOTF (HOAs – third order), and the values predicted by the linear models for all pupils and thresholds. Solid lines represent the best linear fit to the data for a 4.6 mm pupil, whereas dotted lines correspond to the linear fit for 3.6 mm pupil. The lighter R2 value corresponds to the small pupil. Notice that the axis scales are different. Symbol c_{44} denotes fourth order tetrafoil, c_{42} fourth order astigmatism, c_{460} fourth and sixth order spherical aberration, and c_{51} fifth order coma.

a larger impact on the optical quality of the eye compared to the smaller pupil analysis.

Another aspect of this analysis to consider is that the standard deviations obtained were quite high in some cases, indicating that the impact of the correction of different aberrations is highly subject-dependent. These DoF standard deviations ranged from 13% to 22% for the removal of all the terms, except the c_{22} which ranged between 42% and 67% for the 3.6 mm pupil, and from 14% to 67% for the larger pupil size. Regarding the Peak VSOTF, the standard deviation values grow with the removal of successive terms, reaching values up to 140% for the small pupil size, and up to 220% for the larger pupil, which emphasizes the high variability among subjects.

To better understand the impact of each aberration term on the DoF and the Peak VSOTF, regardless of their magnitude, the respective percentage of change in DoF and Peak VSOTF with the removal of each aberration term per micron of that term was calculated and is illustrated in Figure 8. The fifth-order coma term is the one that has the largest relative impact upon both DoF and image quality. This further highlights the importance of comatic terms in DoF and Peak VSOTF calculations.

Finally, using data from four exemplary subjects, Figure 9 illustrates the between subject variations observed in through-focus curve shape. In the case of subject #57, the calculated DoF is unlikely to be usable by that particular eye when the cylinder is not corrected. This is because the VSOTF, and hence image quality, presented extremely low values across all simulated focus levels. As suggested in previous studies (de Gracia et al., 2013; Yi et al., 2011), a VSOTF value of 0.12 or greater can be a good criterion for acceptable image quality. Values below this threshold correspond to poor optical quality, thus limiting the usability of DoF.

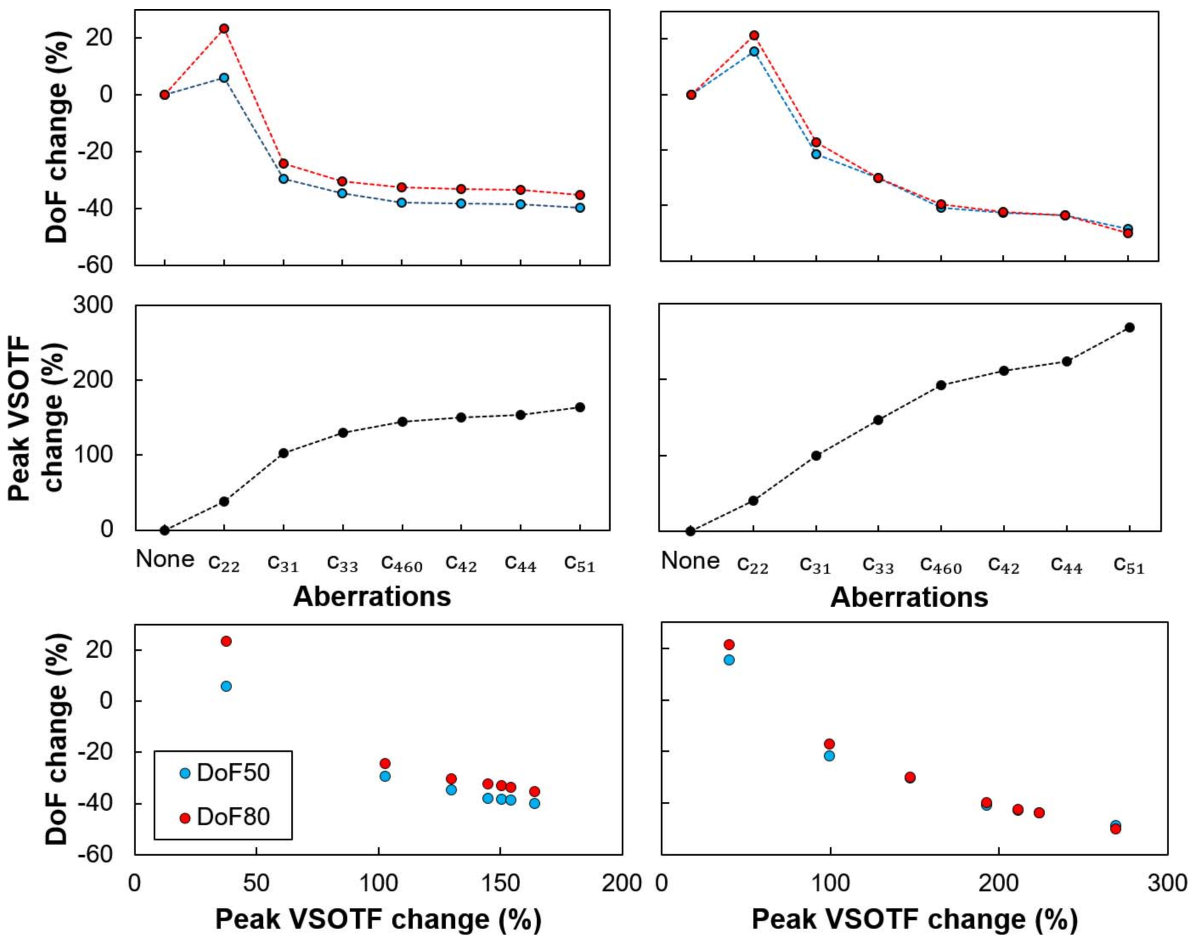

Figure 7. Top row: Change in depth of focus (DoF) expressed in percentage for all the thresholds after correcting the aberrations denoted in the x axis additively. Middle row: Percentage change in the value of the Peak VSOTF after the removal of the aberrations denoted in the x axis. Bottom row: Relationship between the change in DoF and the change in the Peak VSOTF. Columns correspond to the two different pupil diameters considered in this study: 3.6 (left) and 4.6 mm (right). Error bars have been omitted for the sake of clarity. Symbol c_{22} denotes second order astigmatism, c_{31} third order coma, c_{33} third order trefoil, c_{44} fourth order tetrafoil, c_{42} fourth order astigmatism, c_{460} fourth and sixth order spherical aberration, and c_{51} fifth order coma.

Discussion

In this study, we aimed to expand our understanding of the impact of HOAs on the human visual system, by examining the HOAs present in normal eyes holistically and connecting them to two objectively derived important parameters related to vision (i.e., the maximum of the through focus VSOTF and the DoF). We hypothesized that this more comprehensive analytical approach examining a larger range of aberration terms than most previous works, would reveal the potential importance of aberration terms (e.g., comatic terms) that may have been overlooked in previous studies focusing on only spherical-like terms. Our results demonstrate that both retinal image quality and DoF were strongly and statistically significantly dependent upon comatic terms irrespective of the pupil size and the threshold level used for determining the DoF. Interestingly, in our current study the comatic terms appeared to have a stronger association with DoF than the spherical-like terms, which have been the focus of a number of previous studies of DoF (Benard, López-Gil, & Legras, 2010; Yi, Iskander, & Collins, 2010). Note that unlike the works of Rocha et al. (2009) and Benard et al. (2010), who individually examined the influence of inducing relatively large magnitudes of each HOA coefficient in isolation (the latter also considered a combination of primary and secondary spherical aberration and coma), we employed a novel analytical method, using a stepwise forward regression and all available HOAs to arrive at our results.

The linear models obtained in this work generally appeared to be good predictors for DoF and Peak VSOTF (with R^2 values reaching up to ~0.8 for analyses considering HOAs only). However, poorer models were obtained for DoF when astigmatism was included in the calculations (R^2 values < 0.3). This is

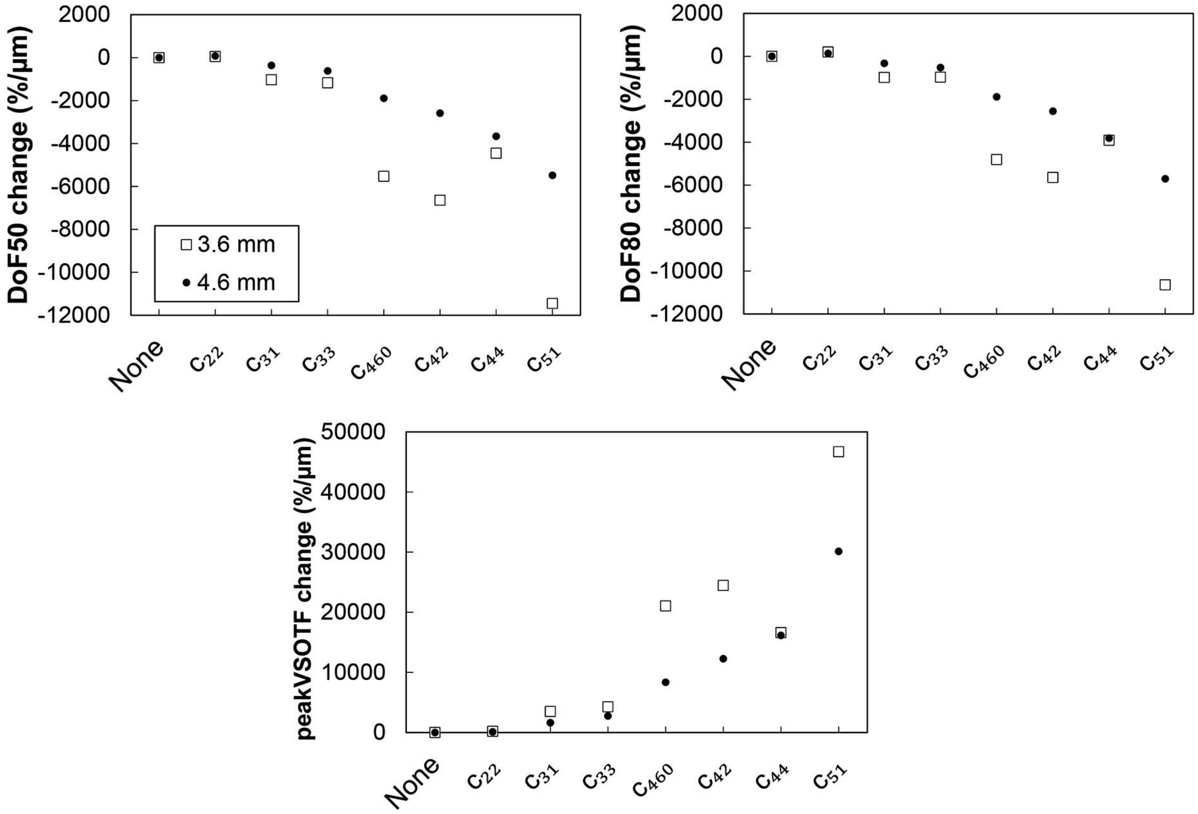

Figure 8. Top row: Change in depth of focus (DoF) for the two thresholds expressed in percentage per micron of aberrations after correcting the aberrations denoted in the X axis additively. Bottom panel: Percentage change per micrometer of aberration in the value of the Peak VSOTF after the removal of the aberrations denoted in the X axis. Error bars have been omitted for the sake of clarity. c_{22} denotes second order astigmatism, c_{31} third order coma, c_{33} third order trefoil, c_{44} fourth order tetrafoil, c_{42} fourth order astigmatism, c_{460} fourth and sixth order spherical aberration and c_{51} fifth order coma.

likely due to the fact that astigmatism was the aberration that presented the larger variation among subjects, and these larger interindividual differences may reduce the reliability of the linear predictions. Another trend that can be observed in the linear models is that they tend to become poorer when the pupil diameter increased. This trend likely occurs due to the fact that the magnitude of the aberrations and their variability among subjects increases with pupil size, which may result in a worsening of the outcomes from the linear models.

To the best of our knowledge, such an emphasis on the importance of comatic aberrations in the objectively determined through-focus characteristics of the human eye has not been previously observed. Our findings at least in part are likely to arise from the fact that coma represents one of the larger magnitude HOAs in our population for the pupil sizes examined, since it is known that, for low levels of aberrations, metrics like the Strehl ratio correlate linearly with the RMS (Wyant & Creath, 1992). However, other aberration terms that were of similar magnitude (e.g., trefoil) in our population did not appear to be as strongly linked to image quality and the DoF as were the comatic terms. Our analyses excluding third order terms also demonstrated a strong role of fifth order coma, despite its very low magnitude in our population. It is important to note that since our current study examined the association between naturally occurring aberrations and DoF, that the results cannot be directly extrapolated to suggest that coma and coma-like aberrations are the most effective for controlling the DoF of the eye. However, these findings do provide a catalyst for future work to explore in more detail the potential value of manipulating comatic terms for controlling DoF.

Tuning (rather than correcting) HOAs can be utilized in order to expand the through-focus optical characteristics of the eye. For example, Benard et al. (2011) reported optimizing subjective DoF by modifying the primary and secondary spherical aberration terms. There have also been more advanced developments for expanding the DoF in presbyopic eyes, with the use of multiple-zone multiple-phase optical designs (de Gracia et al., 2013; Fernández, Barbero, Dorronsoro, & Marcos, 2013). Most of these solutions, aimed at extending the eye's natural DoF, are based on tuning circularly symmetric aberrations. Our results provide

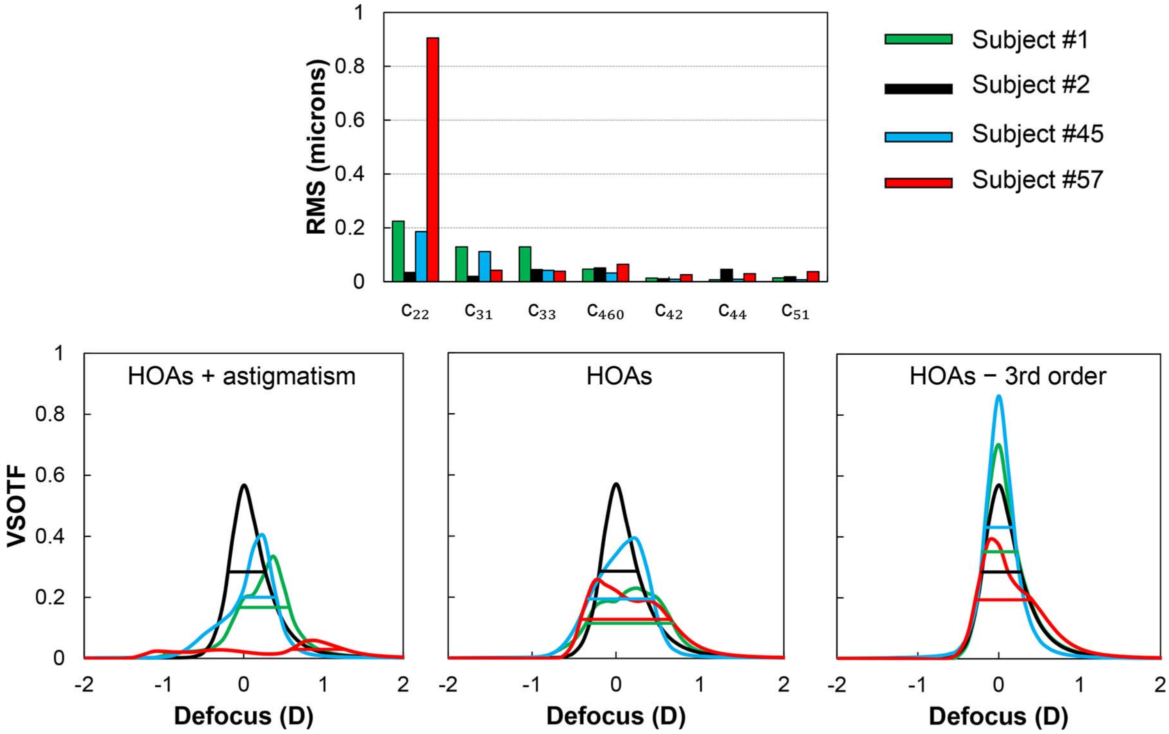

Figure 9. Top panel: RMS values in microns of each of the aberration terms considered in this study from four exemplary subjects. Bottom row: VSOTF through-focus curve and DoF50 (horizontal lines) for the same four subjects when considering different aberrations for its calculation. Symbol c_{22} denotes second order astigmatism, c_{31} third order coma, c_{33} third order trefoil, c_{44} fourth order tetrafoil, c_{42} fourth order astigmatism, c_{460} fourth and sixth order spherical aberration, and c_{51} fifth order coma.

some potentially useful insights for future work designing optical elements aiming to provide an extended DoF and suggest that the comatic aberrations, naturally strongly linked to the DoF, may also be considered for altering through-focus characteristics of the human eye. It should be noted, however, that our results also indicate that comatic terms also have a strong negative influence upon image quality, which emphasizes the important role of HOAs in the trade-off between retinal image quality and DoF in the optimal design of optical corrections. This suggests that in any future work utilizing comatic aberrations, careful tuning of aberrations will be required to arrive at an ideal optical correction providing a large DoF, while maintaining an acceptable level of image quality.

Aspects of our analysis examined second order astigmatism, which was also found to be significantly linked to both image quality and DoF in our population. These significant correlations are also likely to be related to the relatively high magnitude of astigmatism in our population compared to the HOAs. However, the correlations between second order astigmatism and DoF were found to be relatively weak, and removing astigmatism was also found to expand, rather than reduce the DoF in our population. These findings suggest that for the magnitude of astigmatism present in our current population, its presence significantly reduced image quality but did not appear to be useful in expanding the DoF.

A number of previous studies have examined the HOAs of normal populations, and previous research analyzing aberration data over similar pupil sizes and using similar groupings of aberration terms as our current study, has reported comparable levels of HOAs in normal eyes (Namba et al., 2015; Salmon & van de Pol, 2006). Our population of subjects also exhibited a wide range of (primarily) spherical refractive errors, and our analyses indicated that neither the mean levels of HOAs, the DoF, or the Peak VSOTF were significantly associated with refractive error. This suggests that despite the large variations in spherical refractive error (and hence ocular geometry), the mean optical quality associated with HOAs was similar across our population of subjects and not dependent upon the level of refractive error. This finding is consistent with a number of previous studies examining measures of HOAs (with distance fixation/relaxed accommodation) in subjects with different refractive errors (Artal et al., 2006; Cheng, Bradley, Hong, & Thibos, 2003; Hartwig, & Atchison, 2012; Namba et al., 2015; Porter et al., 2001; Salmon & van de Pol, 2006). However, other studies (Llorente, Barbero, Cano, Dorronsoro, & Marcos, 2004) including a substantially wider range of hyperopic refractive errors than our current work, have showed statistically significant differences in aberrations between myopes and hyperopes. In particular, they found differences in coma terms between refractive groups, which are of relevance to our current work. Such a dependence of the HOAs upon refractive error could potentially be one explanation for the previous finding of differences in DoF between myopes and hyperopes (Vasudevan, Ciuffreda, & Wang, 2006), amongst other factors.

It should be noted that our subjects were all young adults with normal vision and healthy eyes, and our results (that depend upon the natural profile of aberrations present in this population), therefore may not be generalizable to other populations. Given that the pattern and magnitude of HOAs are known to vary with age (Artal, Berrio, Guirao, & Piers, 2002), and with a variety of ocular conditions (e.g., Sabesan et al., 2007; Sabesan & Yoon, 2009), additional research is required to further understand the influence of HOAs upon image quality and DoF (and their interactions) in older populations and in those with larger than normal levels of HOAs. In our current research, we have used a purely computational approach to examine the relative impact of HOAs upon image quality and DoF. Therefore, future research using a systematic, experimental approach (e.g., manipulating or correcting specific HOAs using adaptive optics) is likely to augment our current findings and further expand knowledge of the influence of HOAs on the visual system.

Conclusions

We studied the effect that aberrations have upon the objectively assessed DoF and retinal image quality. Comatic aberration (third and fifth order) terms appear to play a very important role in the configuration of both of these visually important parameters, despite their smaller magnitude in comparison with other terms (e.g., second order astigmatism). The relationship between comatic aberrations and both DoF and image quality was generally stronger than that observed for the spherical-like aberrations.

Keywords: depth of focus, *image quality*, *aberrations*, *astigmatism*, *visual optics*

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