Spherical Aberration Customization to Extend the Depth of Focus With a Clinical Adaptive Optics Visual Simulator

Lucía Hervella, MSc; Eloy A. Villegas, PhD; Consuelo Robles, MSc; Pablo Artal, PhD

ABSTRACT

PURPOSE: To evaluate the use of the VAO adaptive optics visual simulator (Voptica SL, Murcia, Spain) for customization of spherical aberration to increase depth of focus.

METHODS: Through-focus visual acuity with both high- and low-contrast letters from +1.00 to -3.00 diopters (D) was measured in 17 dilated eyes with three different induced amounts of spherical aberration for a 4.5-mm pupil diameter: control (0 μm), -0.15 μm, and -0.30 μm.

RESULTS: The defocus curves followed the same behavior with both values of contrast, but the visual acuity was 0.2 logMAR lower with low contrast. The mean values of high-contrast logMAR visual acuity at far, intermediate (67 cm), and near (40 cm) were -0.10, 0.11, and 0.37 for control, 0.04, 0.00, and 0.15 for -0.15 μm, and 0.23, 0.00, and 0.06 for -0.30 μm conditions. The 95% confidence interval ranged from ±0.14 to ±0.45 logMAR and the middle 50% of the distribution was approximately 0.2 logMAR.

CONCLUSIONS: Negative values of spherical aberration extend the depth of focus in different ways depending on each patient. The VAO is a new instrument that allows the visual customization of spherical aberration to enhance depth of focus.

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Every day, more presbyopic patients demand surgical solutions to achieve spectacle independence. A monovision technique can be used in corneal refractive surgery[1] or with intraocular lenses (IOLs),[2] but its success depends on the ability of each patient to get used to a considerable amount of defocus monocularly.

Multifocal IOLs[3] allow the patients to see clearly and binocularly at two or three viewing distances with bifocal or trifocal designs, respectively. However, multifocal IOLs have major limitations, such as limited visual acuity at intermediate distances, loss of contrast sensitivity, and unwanted or disturbing visual effects such as glare and halos.[4]

Optical profiles with extended depth of focus have also been used to mitigate the effects of presbyopia. Extended depth of focus IOLs[5,6] are designed to maintain good values of visual acuity from far to intermediate distances but are worse at near distances in comparison with trifocal diffractive designs. In corneal refractive surgery, the presbyopic laser in situ keratomileusis (PresbyLASIK) technique[7-10] uses aspheric ablation profiles to increase the depth of focus, but this procedure is mainly indicated for hyperopia and needs to be combined with monovision to guarantee good vision at all distances.

The induction of spherical aberration is an effective alternative to increase the depth of focus.[11] The spheri-

From Laboratorio de Optica, Departamento de Física, Universidad de Murcia, Murcia, Spain (LH, EAV, CR, PA); and Voptica SL, Murcia, Spain (LH, CR).

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Correspondence: Eloy A. Villegas, PhD, Laboratorio de Optica, Campus de Espinardo, Centro de Investigación en Optica y Nanofisica, Universidad de Murcia, 30100 Murcia, Spain. E-mail: villegas@um.es

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cal aberration of the commercially available monofocal IOLs ranges between positive and negative values[10,12] increasing or partially or totally compensating for the positive values of the cornea.[13] Light-adjustable IOLs change the refraction and the spherical aberration of the eye after cataract surgery. In this type of IOL, different values of spherical aberration can be adjusted to customize the depth of focus.[9] In corneal refractive surgery, myopic and hyperopic ablation patterns provide positive and negative shifts in the ocular spherical aberration values, respectively.[11,14] Corneal asphericity can be programmed in hyperopic refractive surgery to achieve negative values of ocular spherical aberration that increase the depth of focus.[7]

Although both positive and negative spherical aberration can significantly shift and expand a patient's overall depth of focus,[15] they have different effects on through-focus retinal image quality. The best option for each patient could depend on how different factors affect the visual performance of each one. An individual eye has a distinct wavefront aberration pattern[16,17] that plays a defining role in determining its potential for visual performance and its neural adaptation.[18,19] The amount of spherical aberration suitable for patients to customize and improve their vision according to their needs should be measured, because it varies from patient to patient. Adaptive optics technology allows us to visually simulate any optical profile to find the best solution for each patient.

In this study, an adaptive optics visual simulator was used to measure through-focus visual acuity with different controlled levels of induced negative spherical aberration and to explore the potential benefit of customization of spherical aberration.

PATIENTS AND METHODS

This prospective study was approved by the ethics committee of the University of Murcia and all procedures conformed to the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants after written and oral explanations were given. Inclusion criteria comprised no current ocular pathology, no history of ocular surgery, astigmatism of less than 3.00 diopters (D), and not using ocular drugs that may affect vision.

All participants' pupils were dilated, and accommodation was paralyzed with tropicamide 1%. Although the participants were younger than typical individuals with presbyopia, their accommodative ability was fully impaired due to the cycloplegia. Previous studies have showed that the cycloplegic effect of cyclopentolate is significantly stronger than that of tropicamide in children and hyperopic patients, but not in emmetropic and myopic adults.[20-22] In the current study, the participants were adults with refractions ranging from +0.38 to -4.63 D; therefore, the use of tropicamide to paralyze the accommodation should have had the same effect as cyclopentolate.

ADAPTIVE OPTICS VISUAL SIMULATOR

All measurements of the study were taken using the VAO adaptive optics visual simulator (Voptica S.L., Murcia, Spain). The set-up of this clinical instrument has already been described.[23,24] The VAO combines optical measurements and visual testing within the same compact instrument. It incorporates a Hartmann-Shack sensor[25] to measure objective refraction and wavefront aberrations of the eye with a high degree of repeatability.[26] A liquid crystal on silicon[27] spatial light modulator permits correction or induction of any optical phase profile, optically placing the stimuli at any required distance. An organic light-emitting diode acted as a micro display to present visual stimuli (optotype) to the patient.[28] The instrument performs subjective refraction[29] and induces different amounts of higher order aberrations (HOAs). In this study, through-focus visual acuity was measured for different simulated values of spherical aberration.

EXAMINATION PROTOCOL AND MEASUREMENTS

All measurements were taken at least 20 minutes after instilling two drops of tropicamide 1% in each participant. Visual testing was performed monocularly using the VAO for a 4.5-mm pupil size. The pupil size was chosen as a compromise between photopic and mesopic pupil size in daily life. Although the pupil diameter of 6 mm is too large and uncommon in people's daily routines, the use of this pupil size to study corneal and ocular aberrations is widespread. Analytical calculations for scaling Zernike expansion coefficients to different pupil sizes show that the values of Z_1^2 can be scaled by multiplying the ratio between the pupil sizes raised to the fourth power.[30] So, the conversion factor of Z_1^2 values from 4.5 to 6 mm is 3.[16] Thus, -0.15 and -0.30 µm for a 4.5-mm pupil correspond to -0.47 and 0.95 µm for a 6-mm pupil.

Three consecutive Hartmann-Shack measurements were taken using the VAO. The mean objective refraction from the Hartmann-Shack images was used as a starting point to perform subjective refraction. Sphere was refined in steps of ±0.25 D and, according to clinical standards, the endpoint of subjective refraction was the maximum plus that gave the best visual acuity. Cylinder from Hartmann-Shack images was corrected directly because its value agrees with that obtained in subjective refinement using the Jackson

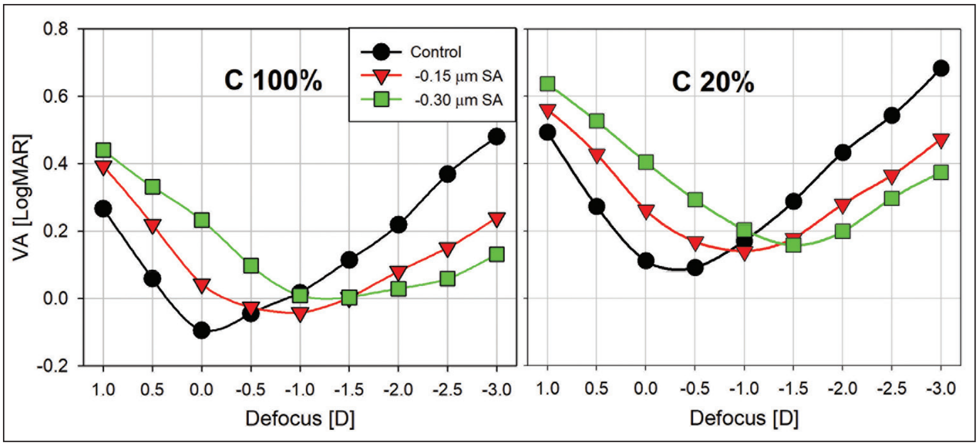

Figure 1. Mean values of through-focus visual acuity (VA) in logMAR units of all patients for control (0 µm), -0.15 µm, and -0.30 µm conditions of spherical aberration (SA) at 100% (C 100%) and 20% of contrast (C 20%) as a function of defocus in diopters (D).

cross-cylinder test.[29] Then, through-focus visual acuity spanning from +1.00 to -3.00 D in steps of 0.50 D was measured under three different amounts of simulated spherical aberration: control (0 µm), -0.15 µm, and -0.30 µm. The sum of spherical aberration values of the eye and the values induced by the VAO had to give the simulated amounts of spherical aberration (ie, all participants were affected by the same values of spherical aberration without changing the other participants' HOAs). Each condition was tested for high (100%) and low (20%) contrast. For this study, intermediate and near distances were considered at 67 and 40 cm, respectively.

Statistical Analysis

The statistical analysis was performed using the R Core Team software (R Foundation for Statistical Computing, Vienna, Austria, 2016). The Shapiro–Wilk test was used to assess normality of all variables analyzed. Non-parametric statistics were applied in non-normally distributed variables. Differences between variables were obtained using the Student's *t* test for normally distributed variables and the Wilcoxon signed-rank test for non-normally distributed variables. All statistical tests were two-tailed, and *P* values of less than .05 were considered statistically significant. The 95% confidence interval of visual acuity for each defocus value was calculated by multiplying the standard deviation by 1.96.

To obtain statistically significant results according to a power analysis for comparing paired differences, a sample size of 17 eyes was required to achieve a power of 0.80 and a two-tailed alpha level of 0.05, assuming expected values of mean and standard deviation of 0.15 and 0.20 logMAR, respectively.

The box plot was used as a standardized approach to display the distribution of our data, summarizing minimum value, first quartile, median, third quartile, maximum value, and outliers.

RESULTS

The right eyes of 17 healthy participants (6 women and 11 men) were included in the study, with a mean age of 30.2 ± 5.7 years (range: 23 to 43 years), manifest mean spherical equivalent error of -1.58 ± 1.49 D (range: 0.38 to -4.63 D), and cylinder of -0.57 ± 0.53 D (range: -2.25 to 0.00 D).

The mean of the root mean square (RMS) for HOAs was 0.12 ± 0.04 µm (range: 0.07 to 0.20 µm), the mean RMS for third order aberrations was 0.10 ± 0.03 (range: 0.05 to 0.15 µm), and the mean of spherical aberration was 0.03 ± 0.04 µm (range: -0.04 to 0.12 µm) for all patients.

Mean through-focus visual acuity for the three optical conditions with 100% and 20% contrast letters are shown in **Figure 1**. High-contrast visual acuity at far distance decreased significantly ($P < .05$) for the -0.15 µm (0.04 ± 0.08 logMAR) and -0.30 µm (0.23 ± 0.16 logMAR) conditions in comparison with the control condition (-0.10 ± 0.07 logMAR). At intermediate distance, visual acuity improved significantly ($P < .05$) with negative values of spherical aberration, from 0.11 ± 0.09 logMAR in the control condition to 0.00 ± 0.09 logMAR in both the -0.15 µm and -0.30 µm conditions. Visual acuity at near distance improved significantly ($P < .05$) as values of negative spherical aberration increased: 0.37 ± 0.23, 0.15 ± 0.16, and 0.06 ± 0.09 logMAR for control, -0.15 µm, and -0.30 µm conditions, respectively. Although there was a significant deterioration in values of low-contrast visual acuity, the defocus curves followed the same behavior as those of high-contrast visual acuity, with similar differences (approximately 0.20 logMAR), for the three optical conditions and all defocus values. There were no statistically significant differences ($P > .05$) between the differences of the three conditions, indicating that the increase of spherical aberration similarly affected the through-focus visual acuity independently of the contrast letters. Spherical aberration induced signifi-

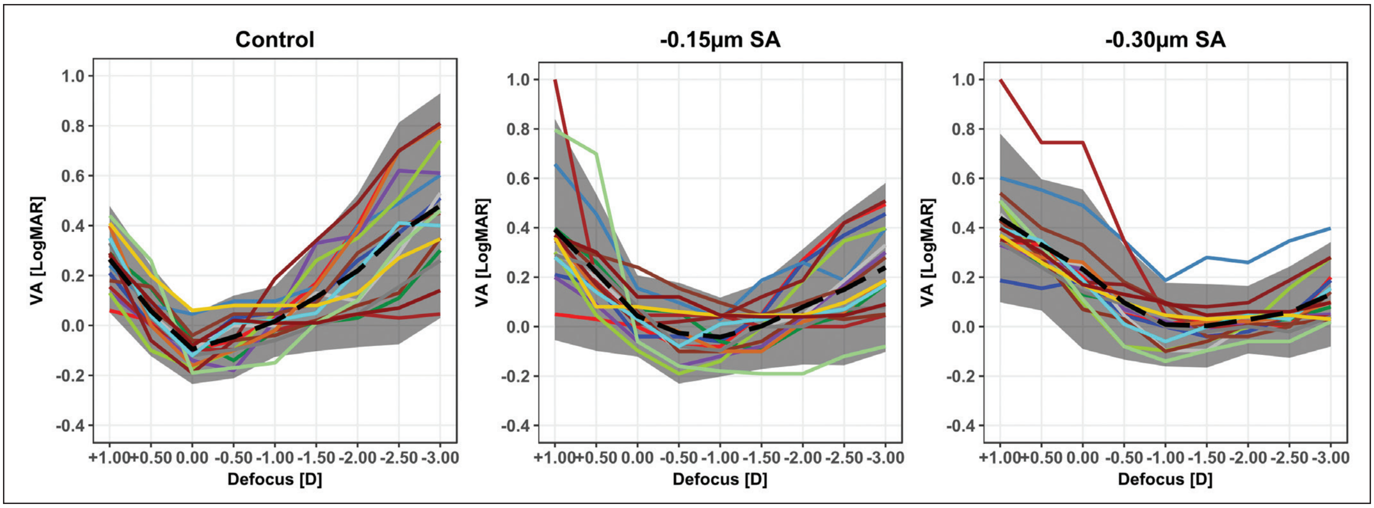

Figure 2. Visual acuities (VA) of all patients (color lines) expressed in logMAR units and 95% confidence intervals (CIs) (shaded areas) as a function of defocus in diopters (D) for control (0 μm), -0.15 μm, and -0.30 μm conditions of spherical aberration (SA) conditions.

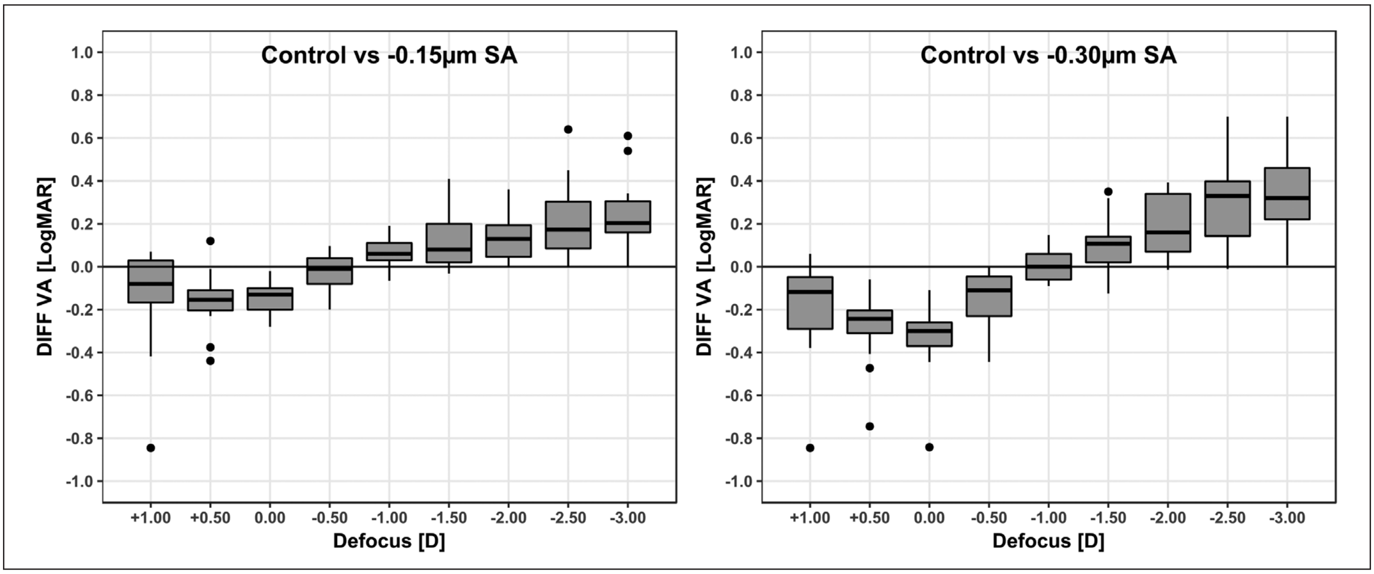

Figure 3. Boxplot of the differences of visual acuities (DIFF VA) in logMAR units between control (0 μm) and -0.15 μm conditions of spherical aberration (SA) and control and -0.30 μm conditions of SA as a function of defocus in diopters (D). In the box plots, the more negative boundary of the box indicates the 25th percentile, the black line within the box marks the median, and the more positive boundary of the box indicates the 75th percentile. Vertical lines above and below the box delimit the maximum and minimum values. Points above and below the box indicate outliers.

cant myopic shifts ($P < .05$) of -1.09 ± 0.50 and -1.43 ± 0.42 D for high contrast and -1.00 ± 0.59 and -1.38 ± 0.48 D for low contrast.

As shown in **Figure 2**, there was a high intersubject variability in visual acuity at all defocus values and optical conditions of spherical aberration. For high-contrast visual acuity, the 95% confidence interval increased as visual acuity worsened, ranging between ±0.14 and ±0.45 logMAR, with mean values of ±0.14, ±0.22, and ±0.44 logMAR for the control condition, ±0.16, ±0.17, and ±0.31 logMAR for the -0.15-µm condition, and ±0.32, ±0.17, and ±0.18 for the -0.30-µm condition at far, intermediate, and near distances, respectively. In general, the intersubject variability of low-contrast visual acuity was larger: ±0.41, ±0.26, and ±0.44 logMAR for the control condition, ±0.46, ±0.22, and ±0.38 logMAR for the -0.15-µm condition, and ±0.33, ±0.16, and ±0.20 for the -0.30-µm condition at far, intermediate, and near distances, respectively.

Figure 3 shows boxplots with the differences in visual acuity between three optical conditions for all defocus values. In almost all participants, the shaded boxes (ie, the middle 50% of the distribution) were positive at near and intermediate distances, indicating a better visual acuity with spherical aberration. These enhancements depended on each participant, with shaded boxes of approximately 0.2 logMAR achieving more than 0.4 logMAR of 100th percentile for some defocus values.

DISCUSSION

Due to the current methods to correct presbyopia and increased patient expectations, the specific needs of the patients should be taken into consideration to find the optimum solution. In surgical procedures, adequate selection of both the technique and the optical profile could improve postoperative patient satisfaction. In this study, the ideal combination of spherical aberration and defocus was found for each patient from simulating though-focus visual acuity with different values of negative spherical aberration.

Positive and negative spherical aberration extend the depth of focus in different ways. Positive spherical aberration induces an extra positive power in the pupil periphery with respect to the central zone, whereas negative spherical aberration provides an opposite effect of more power in the central zone (central myopic shift). Pupil size diminishes at near viewing distances, so visual performance improves if a myopic shift is induced in the central area of the pupil. Previous clinical results[31] in pseudophakic patients implanted with light-adjustable IOLs demonstrated the benefit of induced negative values of spherical aberration to increase the depth of focus. In the current study, the pupil size of 4.5 mm was fixed as a mean value used in daily life at far distance in photopic and mesopic conditions. In daily conditions, the size of the pupil will be smaller at intermediate and near distances, so the visual performance should be better than those obtained in our simulations.

On the other hand, the pupil size depends on each person and on other variables such as viewing distance and illumination. Therefore, in most people, it is not possible to choose a pupil that covers all daily activities. The aim of our study was to explore the use of a new instrument to simulate and customize the spherical aberration to increase the depth of focus. The fixation of pupil size allows us to compare the visual simulations of different participants while avoiding the effect of multiple variables on pupil diameter.

The aim of this study was to study visual acuity for different net values of spherical aberration (0, -0.15, and -0.30 µm) in participants with normal values of HOAs. The ocular RMS of HOAs ranged between 0.07 and 0.20 µm and the RMS of third-order aberrations ranged between 0.05 and 0.15 µm for a 4.5-mm pupil diameter. These values of HOAs were within the normal range for a young and healthy population, as was reported in previous studies. From a review of 17 major studies, Bruce and Catania[32] determined the normative reference ranges of RMS in young healthy participants should be less than 0.18 and 0.30 µm for all HOAs, less than 0.18 and 0.29 µm for third-order aberrations, and less than 0.07 and 0.15 µm for spherical aberration with 4- and 5-mm pupil diameters, respectively. Another study[33] with 24,000 healthy patients found a mean value of RMS of HOAs of 0.18 ± 0.08 µm at a 4.5-mm pupil diameter, which was slightly higher than our value of 0.12 ± 0.04 µm.

The effect of negative values of spherical aberration on defocus curves could be different depending on the contrast of the letters. As expected and previously reported,[34] the low-contrast visual acuity was worse in all defocus values, but the deterioration was the same (approximately 0.2 logMAR) for the three values of spherical aberration, which is in agreement with previous experiments inducing different levels of blur with positive lenses.[35] Consequently, visual acuity was better for high contrast letters in all conditions, but the performance for both contrast values was practically the same.

The enhancement of depth of focus by inducing spherical aberration has been previously reported.[7,15,31,36-38] We found that adding negative spherical aberration led to a substantial benefit at near and intermediate visual acuity, whereas far visual acuity decreased for both conditions of spherical aberration in comparison with the control condition. Nonetheless, the defocus curve with the same value of spherical aberration is different for each participant. Therefore, the values of spherical aberration and defocus used to increase the depth of focus in corneal refractive surgery[38] and in cataract surgery with light-adjustable IOLs[35] should be controlled and, if possible, individualized, to customize the visual quality at different viewing distances.

In the current study, we observed that in some participants the optimum visual performance could be achieved with the combination of spherical aberration and a small myopic shift. The optimum values of spherical aberration and defocus should be chosen considering an adequate visual acuity criterion at different distances according to the daily needs of patients. For each patient, we evaluated the visual acuity at far, intermediate, and near distances for the three conditions of spherical aberration (0, -0.15, and -0.30 µm spherical aberration) in combination with two values of defocus (0.00 and 0.50 D). As an example of through-focus customization, we selected the optimum solution for each individual patient following this criterion: visual acuity should be 0.2 logMAR or better at far, intermediate, and near distances.

In some participants, this criterion was fulfilled in more than one condition. In this study, although visual performance could be optimized at any viewing distance, we chose to optimize near visual acuity in these cases by selecting the condition with the best visual acuity at 40 cm. **Figure A** (available in the online version of this article) shows the percentage of participants who fulfilled our criteria for each combination of defocus and spherical aberration. For both defocus values combined with the control condition of spherical aberration, there were no patients who fulfilled these criteria. The outcomes showed an adequate solution of compromise between the three viewing distances with mean values of visual acuity of 0.13 ± 0.07, -0.02 ± 0.08, and 0.05 ± 0.08 logMAR at far, intermediate, and near distances, respectively. Presby-LASIK allows increased values of spherical aberration in the non-dominant eye to improve the near vision, reaching values of 0.1 logMAR for far and intermediate distances and 0.3 logMAR for near distance.[8] In comparison with previous studies using extended depth of focus and trifocal IOLs,[39,40] our example of customization showed a better visual acuity at intermediate distance, similar at near distance, and worse at far distance.

Our study shows that the adaptive optics visual simulator can be used to determine the visual acuity benefit of inducing different amounts of spherical aberration and that this benefit was dependent on individual participants. We have demonstrated the feasibility and numerous advantages of using an adaptive optics visual simulator to choose the optimum solution for each patient, therefore obtaining the best outcomes, an additional option for individualized patient care.

AUTHOR CONTRIBUTIONS

Study concept and design (LH, EAV, PA); data collection (LH, EAV, CR); analysis and interpretation of data (LH, EAV, CR, PA); writing the manuscript (LH, EAV); critical revision of the manuscript (LH, EAV, CR, PA); statistical expertise (LH, EAV, CR); supervision (LH, EAV, PA)

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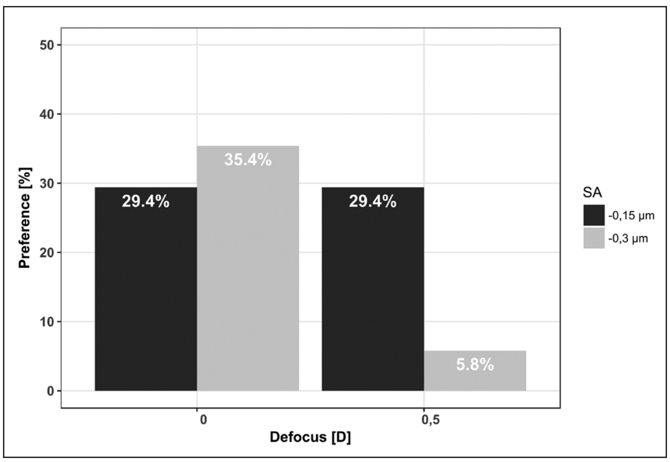

Figure A. Percentage of people for whom visual acuity (VA) was better than 0.2 logMAR for all distances and that had the best near VA for different amount of defocus (diopters) and spherical aberration (SA) in micrometers.