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Repeatability of a commercially available adaptive optics visual simulator and aberrometer in normal and keratoconic eyes

Running head: Repeatability of adaptive optics visual simulator measurement in normal and aberrated eyes.

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Abstract

Purpose: To evaluate the repeatability of aberration measurement obtained by Hartmann-Shack aberrometer combined with an visual adaptive optics (VAO) simulator in normal and keratoconic eyes.

Methods: Fifty normal eyes and forty-two eyes of grade I and II keratoconus, as per the Amsler-Krumeich classification, were included in the study. To evaluate the repeatability, three consecutive measurements of ocular aberrations were obtained by a single operator. Zernike analyses up to fifth order for a pupil size of 4.5mm were performed. Statistical analyses included the intra-class correlation coefficient (ICC) and within-subject standard deviation (SD).

Results: For intra-session repeatability, ICC value for sphere and cylinder was 0.94 and 0.93 in normal eyes, respectively. The same was 0.98 and 0.97 in keratoconic eyes, respectively. The ICC for root mean square of higher order aberration (HOA_{RMS}) was 0.82 in normal and 0.98 in keratoconus eyes. For third order aberrations (trefoil and coma), the ICC values were >0.87 for normal eyes and >0.92 in keratoconus. The ICC for spherical aberration was 0.92 and 0.90 in normal and keratoconus eyes, respectively.

Conclusions: VAO provided repeatable aberrometry data in both normal and keratoconic eyes. For most of the parameters, the repeatability in early keratoconus eyes was somewhat better than the normal individuals. The repeatability of the Zernike terms was acceptable for third order (trefoil and coma) and spherical aberrations. Therefore, VAO was a suitable tool to perform repeatable aberrometric measurements.

Key Words: Adaptive Optics, Repeatability, Keratoconus, Aberration

Introduction

Aberrations are unique features of a patient's eye, which arise from refractive interfaces, e.g., cornea, lens.[1] Aberrations can affect the quality of vision.[1] Aberrations are known to increase in keratoconus and other ectatic disorders.[2-4] Adaptive optics (AO) technology could play an important role in determining the best combination of aberrations to maximize the quality of vision . When corrected with AO, visual quality and contrast sensitivity can be improved beyond the limits of spectacles and contact lenses in normal eyes. A new prototype device that combined Hartmann-Shack aberrometer and deformable mirror was demonstrated in 2002.[6] The device was capable of measuring and modifying the ocular aberrations for functional vision testing of the patient.[6,7] Subsequently, the device was modified to replace the deformable mirror with a liquid crystal on silicon light modulator to perform specific modulation of aberrations.[8-10] The test-retest variability of the aberrometer in the commercial device was assessed in normal eyes.[11] However, repeatability of this device on keratoconic eyes needs to be assessed. This is particularly important for surgical treatments such as wavefront guided, where ablation volume is computed based on reliable measure of ocular aberrations. Therefore, the purpose of the current study was to analyze intra-session repeatability of the device for lower and higher order aberrations in normal and keratoconic eyes.[12]

Methods

This was a prospective study, approved by the Narayana Nethralaya eye hospital ethics committee, Bengaluru, India. The research followed the tenets of the Declaration of Helsinki and all participants gave written informed consent. Hundred and fifteen normal eyes of 115 patients and 92 keratoconus eyes (grade I and II severity on Amsler-Krumeich classification[13,14]) of 92 patients were recruited for the study. Only normal eyes with a corrected distance visual acuity of 20/20 or better, spherical error less than −5 Diopters (D) and astigmatism less than 4 D were included. Keratoconus was diagnosed on the basis of clinical signs such as scissoring of the red reflex or an abnormal retinoscopy reflex, Fleischer's ring, Vogt's striae and topographic evidence.[15] Exclusion criteria included the presence of progressive myopia, advanced keratoconus, active ocular disease, diabetic retinopathy, contact lens wear or any other ocular diagnosis that may alter the optical quality. All subjects underwent complete ocular examination before the test.

Measurements of ocular aberrations were obtained using the Visual adaptive optics (VAO, Voptica S.L., Murcia, Spain) simulator. The device measured the refraction in Diopters and the root mean square of higher order aberration (HOA_{RMS}) in μm for a pupil size of 4.5 mm. The device software provided an output up to 8th order Zernike decomposition of the aberrations. However, the current study was limited up to 5th order to maintain clinical relevance since most Zernike coefficients of order 5 and above were generally very small in magnitude compared to order 4 and lower. After proper focus and alignment, three measurements were obtained by the same experienced operator using the same method for normal and keratoconic eyes. Defocus (sphere), astigmatism, trefoil (Z_6 and Z_9), coma (Z_7 and Z_8), spherical aberration (Z_{12}) and the total higher order aberrations (HOA_{RMS}) were assessed using the device.

Statistical analysis

Statistical analyses were performed using MedCalc statistical software version 16.8 (MedCalc Software, Inc., Mariakerke, Belgium) and included within-subject standard deviation (SD). The SD was calculated as the square root of the mean square error.[16] An intra-class correlation coefficient (ICC), a measure of the repeatability of measurements, was also performed.[17] This correlation measured the relative homogeneity within groups (between the repeated measurements) in relation to the total variation. The ICC approached 1.0, when the variability within repeated measurements was zero. Low intra-observer repeatability is generally assumed, when ICC is below 0.75. The three measurements for each participant were considered to account for intra-session repeatability.

Results

The sample size of normal and keratoconic eyes for this study was sufficient (within 10% confident limit).[18] In this study, the mean age of the normal eyes was 27.3 ± 4.3 years (range 16 to 40). Three measurements each for sphere (defocus), cylinder (astigmatism), RMS_{HOA} and Zernike polynomials trefoil (Z_6 and Z_9), coma (Z_7 and Z_8), spherical aberration (Z_{12}) are summarized in Table 1. The mean value with 95 % confidence interval and the mean standard deviation (SD) across subjects for a given measurement were assessed**. Table 1** also shows ICC for all the parameters. ICC above 0.8 was obtained for many parameters suggesting good repeatability in normal eyes (sphere: 0.99, cylinder: 0.99, RMS_{HOA}: 0.80). Further, lower-order aberrations (sphere and cylinder) were associated with better repeatability than higher-order aberrations in normal eyes. ICC of axis of cylinder was low (0.71). Therefore, ICC was calculated for sub-group of eyes based on magnitude of cylinder. For eyes with cylinder less than 0.5D, ICC was only 0.49. For eyes with cylinder greater than 1.0D, the ICC improved to 0.84. For eyes with cylinder greater than 2D, ICC was 0.83. Thus, magnitude of cylinder was critical in obtaining repeatable measurements of axis.

In keratoconus patients (51 female and 41 males) with a mean age of 26.7 ± 10.8 years (range 14 to 42), all the relevant parameters are summarized in **Table 2**. ICC value of more than 0.9 was obtained for all the parameters (sphere: 0.94, cylinder: 0.96, RMS_{HOA}: 0.95), suggesting high repeatability in grade I and grade II keratoconus patients. In this cohort, the ICC was comparable for both lower and higher order aberrations. In keratoconus subjects, ICC of axis was greater than the ICC of axis in normal eyes (0.95) due to greater magnitude and abnormal curvature.

Discussion

Hartmann-Shack aberrometer can give excellent results for total ocular aberrations.[19]A highly repeatable measurement of aberrations will help tremendously in designing optical corrections using wavefront-guided corneal surgery,[20] aberration-correcting contact lenses,[21] and wavefront-based custom intraocular lenses.[22] In this study, the ICC value for sphere and cylinder was 0.94 and 0.93 in normal eyes, respectively. The same was 0.98 and 0.97 in keratoconus eyes, respectively. The value of ICC for RMS_{HOA} indices was 0.82 and 0.98 in normal and keratoconus eyes, respectively. The ICC for third order aberrations was >0.87 and >0.92 in normal and keratoconus eyes, respectively. The ICC for spherical aberration was 0.92 and 0.90 in normal and keratoconus eyes, respectively. Thus, overall the device achieved high and similar repeatability in both normal and keratoconus eyes, respectively.

Another study evaluated the inter-session and intra-session repeatability of aberration in normal individuals using VAO. [11] They reported ICC values of 0.99 and 0.97 for sphere and cylinder, respectively. However, the ICC for RMS_{HOA} was 0.61, which implied that lower-order aberrations had better repeatability than higher-order aberrations. Overall, better results were obtained with RMS values than with some of the individual Zernike coefficients (**Tables 1 and 2**). Some other commercial instruments based on Hartmann-Shack sensors were comparable to our study. In a study on Zywave (Bausch and Lomb, Rochester, NY), ICC of total HOA’s and second-order terms were greater than 0.94. The ICC for third-order terms was high (ICCs > 0.87).[23] In iDesign aberrometer (AMO, Inc., Santa Ana, California, United States), the ICC for sphere and cylinder was 0.999 and 0.995 D, respectively.[24] Another study evaluated the repeatability of Topcon KR-1W.[25] For intra-session repeatability, excellent ICC was obtained (ICC >0.87), except for internal primary coma (ICC = 0.75) and 3rd order (ICC = 0.72) HOA.[25]

Studies suggested that measurement errors may occur in keratoconus patients with Hartmann-Shack devices.[26] A study used the IRX3 (Imagine Eyes, Paris, France) to compare the aberrometry-derived refractive error in patients with keratoconus and normal eyes (n = 12 aged 33.6 ± 4.2 years). The lower order and higher order aberrations measured in keratoconic eyes showed high variability compared to measurements in normal eyes.[27] In this study, most of the parameters had comparable repeatability in normal and keratoconic eyes though keratoconic eyes had somewhat better repeatability. However, whether a similar trend will remain for higher grades of keratoconus is unknown at this point. Another study reported better repeatability (good to moderate) in keratoconic eyes than in normal eyes (moderate to poor).[28] However, this study established that VAO demonstrated good performance in terms of single session, intra-user repeatability for refractive and wavefront parameters. A future study comparing this devise with the other Hartmann Shack aberrometers could be worthwhile. The study conclusions may not apply to eyes with more advanced stages of the disease.

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Table 1: Parameters in normal eyes (n=115)

		Exam 1	Exam 2	Exam 3	ICC
Sphere(D)	Mean [95% CI of mean]	-1.82 [-2.20, -1.44]	-1.81 [-2.20, -1.43]	-1.82 [-2.21, -1.44]	0.99
	Standard deviation	2.05	2.07	2.09	
Cylinder(D)	Mean [95% CI of mean]	-0.72 [-0.90, -0.55]	-0.76 [-0.94, -0.57]	-0.73 [-0.92, -0.55]	0.99
	Standard deviation	0.94	0.99	0.98	
Axis (degrees)	Mean [95% CI of mean]	92.94 [81.62, 104.26]	92.23 [81.20, 103.27]	90.16 [78.92, 101.40]	0.71
	Standard deviation	61.29	59.75	60.85	
HOA_{RMS}	Mean [95% CI of mean]	0.18 [0.17, 0.20]	0.17 [0.15, 0.18]	0.18 [0.17, 0.20]	0.80
	Standard deviation	0.09	0.08	0.10	
Z6	Mean [95% CI of mean]	-0.05 [-0.06,-0.04]	-0.05 [-0.06, -0.04]	-0.05 [-0.06, -0.04]	0.85
	Standard deviation	0.06	0.06	0.07	
Z7	Mean [95% CI of mean]	-0.02 [-0.04, 0.0]	-0.02 [-0.03, 0.0]	-0.02 [-0.04, 0.0]	0.95
	Standard deviation	0.10	0.10	0.10	
Z8	Mean [95% CI of mean]	0.0 [-0.02, 0.0]	0.0 [-0.01, 0.01]	0.0 [-0.017, 0.01]	0.81
	Standard deviation	0.065	0.063	0.065	
Z9	Mean [95% CI of mean]	0.0 [-0.01, 0.01]	0.02 [0.0, 0.03]	0.0 [-0.01, 0.02]	0.86
	Standard deviation	0.07	0.06	0.07	
Z12	Mean [95% CI of mean]	0.02 [0.01, 0.025]	0.01 [0.0, 0.02]	0.02 [0.0, 0.03]	0.91
	Standard deviation	0.05	0.05	0.06	

CI = Confidence interval, ICC = Intra-class correlation coefficient, D = Dioptres, HOA_{RMS} = Root mean square of Higher order aberration, Z6 = vertical trefoil, Z7= vertical coma, Z8 = horizontal coma, Z9 = horizontal trefoil, Z12 = Spherical aberration

Table 2: Parameters in keratoconus eyes (n=92)

		Exam 1	Exam 2	Exam 3	ICC
Sphere (D)	Mean [95% CI of mean]	-1.77 [-2.32, -1.22]	-1.88 [-2.42, -1.34]	-1.82 [-2.36, -1.28]	0.94
	Standard deviation	2.53	2.48	2.48	
Cylinder (D)	Mean [95% CI of mean]	-3.51 [-4.11, -2.90]	-3.42 [-4.02, -2.83]	-3.43 [-3.98, -2.88]	0.96
	Standard deviation	2.79	2.76	2.51	
Axis (degrees)	Mean [95% CI of mean]	93.02 [81.36, 104.68]	90.70 [78.99, 102.42]	90.62 [78.96, 102.28]	0.95
	Standard deviation	53.7	54.0	53.8	
HOA_{RMS}	Mean [95% CI of mean]	0.72 [0.61, 0.83]	0.72 [0.61, 0.83]	0.72 [0.62, 0.83]	0.98
	Standard deviation	0.51	0.51	0.50	
Z6	Mean [95% CI of mean]	-0.01 [-0.10, 0.07]	-0.03 [-0.12, 0.06]	-0.02 [-0.10, 0.06]	0.89
	Standard deviation	0.39	0.41	0.35	
Z7	Mean [95% CI of mean]	-0.37 [-0.45, -0.30]	-0.35 [-0.44, -0.26]	-0.40 [-0.48, -0.31]	0.88
	Standard deviation	0.33	0.40	0.40	
Z8	Mean [95% CI of mean]	0.01 [-0.04, 0.06]	0.03 [-0.02, 0.07]	0.03 [-0.02, 0.08]	0.90
	Standard deviation	0.33	0.40	0.40	
Z9	Mean [95% CI of mean]	0.07 [0.0, 0.14]	0.03 [-0.04, 0.10]	0.02 [-0.04, 0.08]	0.95
	Standard deviation	0.34	0.32	0.26	
Z12	Mean [95% CI of mean]	-0.08 [-0.12, -0.05]	-0.09 [-0.12, -0.05]	-0.07 [-0.11, -0.03]	0.87
	Standard deviation	0.16	0.18	0.18	

CI = Confidence interval, ICC = Intra-class correlation coefficient, D = Dioptres, HOA_{RMS} = Root mean square of Higher order aberration, Z6 = vertical trefoil, Z7= vertical coma, Z8 = horizontal coma, Z9 = horizontal trefoil, Z12 = Spherical aberration