·Clinical Research·

Reproducibility of optical quality parameters measured at objective and subjective best focuses in a double-pass system

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Abstract

• AIM: To evaluate intra-session repeatability and reproducibility of optical quality parameters measured at objective and subjective best focuses in a double-pass system.

• METHODS: Thirty Chinese healthy adults (19 to 40 years old) meeting our inclusion criterion were enrolled in the study. After a basic eye examination, two methods of optical quality measurement, based on subjective and objective best focuses were performed using the Optical Quality Analysis System (OQAS) with an artificial pupil diameter of 4.0 mm.

• RESULTS: With each method, three consecutive measurements of the following parameters: the modulation transfer function cutoff frequency (MTF_{cutoff}), the $Strehl^{2D}$ ratio, the OQAS values (OVs) at contrasts of 100%, 20%, 9% and the objective scatter index (OSI) were performed by an experienced examiner. The repeatability of each method was evaluated by the repeatability limit (RL) and the coefficient of repeatability (COR). Reproducibility of the two methods was evaluated by intra-class correlation coefficient (ICC) and the 95% limits of agreement (Bland and Altman analysis). Thirty subjects, seven females and twenty three males, of whom 15 right eyes and 15 left eyes were selected randomly for recruitment in the study. The RLs (percentage) for the six parameters measured at objective focus and subjective focus ranged from 8.44% to 15.13% and 10.85% to 16.26%, respectively. The CORs for the two measurement methods ranged from 8.27% to 14.83% and 10.63% to 15.93%, respectively. With regard to reproducibility, the ICCs for the six parameters of OQAS ranged from 0.024 to 0.276. The 95% limits of agreement obtained for the six parameters (in comparison of the two methods) ranged from -0.57 to 42.18 (MTF_{cutoff}), -0.01 to 0.23 ($Strehl^{2D}$ ratio), -0.02 to 1.40 ($OV_{100\%}$), -0.10 to 1.75 ($OV_{20\%}$), -0.14 to 1.80 ($OV_{9\%}$) and -1.46 to 0.18 (OSI).

• CONCLUSION: Measurements provided by OQAS with either method showed a good repeatability. However, the results obtained from the two different measurement methods showed a poor reproducibility. These findings suggest that it might be best to evaluate patients´ optical quality by OQAS using the best focus as chosen automatically by the instrument.

• KEYWORDS: optical quality; double-pass system; best focus; repeatability; reproducibility

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INTRODUCTION

Tear film with poor quality and stability, uncorrected refractive abnormalities and increased ocular media opacities that cause increased light diffusion are leading causes of reduced optical quality of the human eye [1-4]. An issue of increasing importance in the immediate future will involve methods to characterize and describe optical quality accurately in order to differentiate and evaluate outcomes of various therapies and procedures, especially those involving cataracts and refractive surgeries[2,5]. The most commonly used optical assessing instrument currently in use is the wave-front aberrometer, which is based on the Hartmann-Shack sensor. A major disadvantage of this technique is the lack of information on quite higher-order aberrations and scattering, due to limitations imposed by lens sampling[6]. As a result, in eyes where very high-order aberrations and scattered light are prominent, wave-front aberrometers may overestimate retinal image quality. In contrast, the double-pass (DP) technique, based on recording images of a monochromatic point source after reflection on the retina and DP through the ocular

media [2,3,7], provides a more complete and realistic evaluation of ocular optical quality since it incorporates information about both ocular aberrations and intraocular scattering that may affect the retinal image[6,8,9]. The Optical Quality Analysis System (OQAS™, Visiometrics SL, Tarrasa, Spain) is a new instrument based on the DP technique, that was developed to perform an objective evaluation of optical quality. This instrument enhances the assessment of optical quality by providing the retinal image corresponding to a point-source in near-infrared light consisting of a laser diode (λ=780 nm) coupled to an optical fiber [10]. In this way, the clinician has a better understanding of the visual problems of some patients [11]. Objective optical quality measurements, performed with a DP system have been demonstrated to be useful in several clinical applications, such as in patients who have undergone kerato-refractive and phakic IOL surgery[12-14], to evaluate presbyopia after photorefractive keratectomy[5], to grade nuclear cataract opacit [15], and to study the *in vitro* optical quality of foldable monofocal intraocular lenses.

Assessing the repeatability and reproducibility of measurements as obtained with a new instrument is essential in clinical practice. Several studies have demonstrated that OQAS is a clinical DP instrument with good intra- and inter-session repeatability over time [1,10]. However, we have found that when using OQAS, the target image at the best focus, as chosen automatically by the instrument, was oftentimes not the clearest one to the subject. In addition, no details were provided regarding the choice of best focus during the measurement of OQAS in these previous reports. This represents an important issue as it is well known that optical quality varies with different choices of focus. Accordingly, parameters measured at which focus may be accurate and true valves may not be known. Hence, we performed measurements at the best focus of each subject as chosen automatically by OQAS and the best focus with the target image being the clearest one for that subject in a sample of adult Chinese subjects. The repeatability of parameters as measured by each method and the reproducibility of parameters between the two methods in a DP system were assessed to determine the optimal focus for subjects during measurements. In this way, the results of this study can be used to generate guidelines and/or standard procedures for the OQAS examination.

SUBJECTS AND METHODS

Subjects This observational, cross-sectional, non-consecutive case study was conducted with voluntary, healthy subjects recruited from the medical staff of Beijing Tongren Hospital, Beijing, China. The research was performed according to the tenets of the Declaration of Helsinki and ethics approval was obtained from the Beijing Tongren Hospital Ethical Committee. All subjects provided informed consent after receiving a written and verbal explanation of the nature and intent of the study. Subjects were between 19 and 40 years old, had a best corrected visual acuity (BCVA) of 0.0 or better (logarithm of the minimum angle of resolution, logMAR); a spherical refraction within -0.50 and -8.00 diopters (D); a cylinder correction within ±2.00 D; a natural pupil diameter equal to or greater than 4 mm; no history of any ocular pathology other than refractive error, trauma, surgery and/or pharmacological treatment; and appeared to be of normal physical and mental health. Subjects with contact lens were asked to remove their lenses at least one day prior to testing.

Examinations Subjects underwent a complete optometric and ophthalmologic examination for both eyes (without cycloplegia). This assessment included objective refraction, subjective refraction, visual acuity examination using the Early Treatment Diabetic Retinopathy Study (EDTRS) logMAR E chart with a standard illumination box at a distance of 4 m, and slit-lamp examination to determine the following: uncorrected visual acuity (UCVA) and BCVA; manifest refractive error (including spherical power, cylindrical power and the axis); and media opacities (*e.g.* corneal scar or congenital lens opacity). Following these examinations, the retinal image quality of each subject was measured by means of the OQAS™II at 4-mm artificial pupil, which was controlled by means of a diaphragm wheel located inside the DP system. The diaphragm is conjugated with the pupil plane of the eye and therefore acts as an effective entrance pupil when the natural pupil of the eye is greater than the diaphragm diameter. It is recommended that in studies where data from both eyes are highly correlated, especially for normal eyes, only one eye per participant be used [16]. Hence, for OQAS examination, only one eye from each subject was chosen according to a random number sequence. The head of the subject was positioned on the chinrest and fixated on the center of a figure. The operator manually aligned the subject's pupil center with the optical axis of the device. The OQAS also incorporates a modified Thorner optometer, formed by 2 achromatic doublets, which can then be used to compensate for the patient's spherical refraction, ranging from -8.00 D to +6.00 D [2]. As a result, in our research, the spherical refractive error was corrected by means of internal lenses contained in OQAS through entering each subject's spherical refraction. Appropriate external cylindrical trial lenses on a holder placed in front of the eye were required for astigmatism $>$+0.50 D or $<$-0.50 D[2,3]. During the measurement, we used two different methods for the six parameters. In method A: after selecting *OBJECTIVE REFRACTION*, the system automatically chose the best retinal image acquired by the instrument as being the best focus. During this procedure, OQAS made a sweep to

identify the best point spread function (PSF) at different spherical corrections, as a means to compensate for any defocus. While maintaining the choice of the best focus according to that generated from the instrument, the six parameters were then obtained. In method B: images of the target were slowly changed and subjects asked which image was clearest. If they had trouble choosing an image, the procedure was repeated for one more time. If the subject still had trouble then the two or three images which seemed confusing were presented and the subject was instructed to select the clearest image and finish the measurement under this spherical refraction as the best focus. For each method, six consecutive measurements were taken (including three replicates each for "*Optical Quality*" and "*Scatter Meter*"); the pupil center was realigned between each measurement. Subjects were required to blink prior to each measurement to maintain a qualified tear film and blink freely during the examination.

The luminance of the room was approximately 42.0 lx (measured by digital lux meter, LX-1010B) during the testing.

Optical Quality Parameters Quantitative information about the optical quality of the eye was obtained from the PSF as recorded with the DP system. For each measurement, the PSF was calculated as the mean of 6 individual acquisitions. The modulation transfer function (MTF), which is the ratio of the image wave contrast to the object wave contrast for a particular spatial frequency, can be directly computed from the PSF [5,7,17,18]. In this study, we chose six parameters for analysis including the MTF cutoff frequency (MTF_{cutoff}), the $Strehl^{2D}$ ratio, the OQAS values (OVs) at contrasts of 100%, 20%, 9% and the objective scatter index (OSI). The MTF_{cutoff} is calculated as that corresponding to a 0.01 MTF value, as there is a certain level of background noise in the MTF profile that is computed from the real recorded DP image. The DP system computes the $Strehl^{2D}$ ratio in two dimensions ($Strehl^{2D}$ ratio), as the ratio between the areas under the MTF curve of the measured eye and that of the aberration-free eye [19]. A $Strehl^{2D}$ ratio of 1 indicates a perfect optical system that is limited only by diffraction [10]. The three OVs are normalized values of three spatial frequencies, which correspond to MTF values that describe the optical quality of the eye for three contrast conditions, commonly used in ophthalmic practice [11]: 100% ($OV_{100\%}$), 20% ($OV_{20\%}$), and 9% ($OV_{9\%}$). Specifically, $OV_{100\%}$ is directly related to the MTF_{cutoff} (*i.e.* the MTF_{cutoff} divided by 30 c/deg). The $OV_{20\%}$ and $OV_{9\%}$ values are computed in the same manner as that from smaller frequencies that are linked to 0.05 and 0.1 MTF values, respectively, which maintain the proportion at contrasts of 20% and 9% [10]. In general, OVs higher than 1 are associated with very high retinal image quality[11]. OSI is an index which corresponds to the degree of dispersion or diffusion. This occurs in an optic system when there is an opacity or discontinuity in some medium being traversed by light to allow objective evaluations of intraocular scattered light. It is calculated by evaluating the amount of light on the outside of the DP image in relation to the amount of light in the center [3]. In the particular case when the OQAS instrument was used, the central area selected was a circle of a radius of 1min of arc, while the peripheral zone was a ring set between 12 and 20min of arc [3,10]. The higher the OSI value, the higher the level of intraocular scattering. The OSI value is used for objective classification of cataract development. According to the user's manual, for eyes with a normal degree of scattering (non-cataract eyes), the OSI value is lower than 0.5; for eyes developing a cataract, the OSI value ranges between 1.5 and 4; and for eyes with a mature cataract the OSI value is greater than 4[1].

Statistical Analysis The data was performed using SAS 9.1.3 for Windows. All values are presented as means ± standard deviations (SDs) or median (and interquartile range). In t-tests used in this study, a $P<0.05$ was required for results to be considered statistically significant.

For statistical analysis, two approaches were applied to quantify the repeatability from replicated measurements as obtained by the same method in this study. A repeatability limit (RL), calculated from the individual SDs ($R=SD\times t_{0.05,\,n}$), is a value less than or equal to the absolute difference between test results as obtained under repeatability conditions[1]. In addition, a coefficient of repeatability (COR, 1.96 times the within-subject SD, S_w), which represents the error between two repeated measurements, was also calculated for repeatability assessment [19]. In the context of measuring individual eyes, a percentage of mean value for RL or COR of 50% is often selected as the highest acceptable value for metrological purposes in biology [20]. Two statistical analyses for comparisons between methods A and B were performed. The first was intra-class correlation coefficients (ICCs), which can be viewed as a measure of the correlation, consistency, or conformity for a dataset when it has multiple groups. ICCs range from 0 to 1 and are commonly classified as follows: ICC $\leqslant$0.75 means poor agreement; ICC 0.75-0.9 means moderate agreement; and ICC $>$0.90 means high agreement . The second approach was the Bland and Altman analysis, which is based on quantifying the variation of between-method differences in individual patients. This represents a standard analysis that is used in clinical comparisons involving two measurement methods [19]. The 95% limits of agreement, as estimated by a mean difference of values between two methods±1.96 SD of the differences (S_d), provide an interval within which 95% of differences

Table 1 Demographic characteristics and clinical data of subjects

Data	Age (a)	Gender (M/F)	UCVA	BCVA	Sph (D)	Cyl (D)	SE (D)	NP (mm)
$\bar{x} \pm s$	28.20±5.38		0.80±0.32	-0.02±0.05	-3.40±1.54	-0.26±0.38	-3.53±1.61	5.64±0.85
Number(%)		7(23.33)/23(76.67)						

UCVA: Uncorrected visual acuity; BCVA: Best corrected visual acuity; Sph: Spherical manifest refractive error; Cyl: Cylinder refractive error; SE: Spherical equivalent value; NP: Natural pupil diameter.

Table 2 Results of the measurements performed by method A and method B and *t*-test for the differences between two methods for the parameters provided by OQAS $\bar{x} \pm s$

Method	MTF_{cutoff}	$Strehl^{2D}$ ratio	$OV_{100\%}$	$OV_{20\%}$	$OV_{9\%}$	OSI
A	44.03±10.11	0.25±0.07	1.47±0.34	1.55±0.47	1.60±0.52	0.51±0.32
B	23.22±5.82	0.14±0.03	0.77±0.19	0.73±0.17	0.77±0.17	1.15±0.54
t	10.45	9.62	10.44	9.58	9.16	-8.40
P	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

SD: Standard deviation; MTF_{cutoff}: Modulation transfer function cutoff frequency; $OV_{100\%}$: OQAS value at contrast of 100%; $OV_{20\%}$: OQAS value at contrast of 20%; $OV_{9\%}$: OQAS value at contrast of 9%; OSI: Objective scatter index.

Table 3 Intra-session RLs and mean intra-session coefficients of repeatability for the parameters provided by OQAS

Data	Method	MTF_{cutoff}	$Strehl^{2D}$ ratio	$OV_{100\%}$	$OV_{20\%}$	$OV_{9\%}$	OSI
RL (%)	A	3.72(8.44)	0.03(11.63)	0.12(8.45)	0.15(9.35)	0.20(12.58)	0.08(15.13)
	B	3.41(14.69)	0.02(10.85)	0.11(14.68)	0.12(16.26)	0.12(15.70)	0.14(12.45)
COR (%)	A	3.64(8.27)	0.03(11.39)	0.12(8.28)	0.14(9.16)	0.20(12.33)	0.08(14.83)
	B	3.34(14.40)	0.02(10.63)	0.11(14.39)	0.12(15.93)	0.12(15.38)	0.14(12.20)

RL: Repeatability limit; COR: Coefficient of repeatability; MTF_{cutoff}: Modulation transfer function cutoff frequency; $OV_{100\%}$: OQAS value at contrast of 100%; $OV_{20\%}$: OQAS value at contrast of 20%; $OV_{9\%}$: OQAS value at contrast of 9%; OSI: Objective scatter index.

between measurements of the two methods are expected to lie [20]. According to the Bland and Altman analysis, the best approach to analyze the relationship between two measurements, is to plot the difference between those measurements against their mean values. The x axis shows the mean of the results of the two methods (A+B)/2, whereas the y axis represents the absolute difference between the two methods (B-A). If both measurements show perfect agreement, the mean of the differences would be zero, and all values would be concentrated around this line. The presentation of the 95% limits of agreement provides a visual representation of the extent that the two methods of measurement agree. The smaller the range between these two limits the better the agreement. The issue of how small this range should be to indicate an acceptable degree of agreement, depends on the clinical judgement.

RESULTS

Thirty subjects, seven females and twenty three males satisfied our criterion for inclusion and exclusion were enrolled in the study. The mean and SD in age was 28.2±5.4y with a range of 19 to 40y. Fifteen right eyes and fifteen left eyes were selected. The UCVA and the BCVA of the eyes ranged from +0.20 to +2.00 (logMAR) [median (interquartile range, IQR), +0.81(+0.60-+1.00)] and +0.10 to -0.10 (logMAR) [median (IQR), 0.00(-0.06-0.00)], respectively. The spherical manifest refractive error ranged from -0.50 to -7.00 D (mean±SD, -3.40±1.54 D), the cylinder diopter from 0.00 to -1.25 D [median (IQR), 0.00 (-0.50-0.00) D], and the spherical equivalent (SE) values from -0.50 to -7.00 D (mean±SD, -3.53±1.61 D). The natural pupil diameter varied from 4.00 to 7.25 mm (mean±SD, 5.64±0.85 mm). These data are summarized in Table 1.

Table 2 contains the mean and SD of the measurements from the two methods for each optical quality parameter as resulting from OQAS. As can be seen from the data of Table 2, the results of method A presented higher values of MTF_{cutoff}, $Strehl^{2D}$ ratio, $OV_{100\%}$, $OV_{20\%}$, $OV_{9\%}$ and lower value of OSI than those of method B. Statistically significant differences between methods A and B were obtained for each of the six parameters (*t*-test, $P < 0.0001$), as also shown in Table 2.

The limits of repeatability and mean CORs of parameters provided by OQAS of each measurement method as expressed in absolute values (and percentage) are presented in Table 3. The RLs (percentage of mean value) and CORs (percentage of mean value) for MTF_{cutoff}, $Strehl^{2D}$ ratio, $OV_{100\%}$, $OV_{20\%}$, $OV_{9\%}$ and OSI of method A and method B were all less than 50%.

The ICCs for reproducibility of the two methods for the six parameters were low, ranging from 0.024 to 0.276, as shown in Table 4. Also, Table 4 contains the results obtained for each parameter when the Bland and Altman analysis was used to compare the different methods. The mean of the differences ($mean_d$), SD of $mean_d$ and the corresponding 95% limits of agreement ($mean_d$±1.96 SD) for methods A and B are shown. The 95% limits of agreement of the six parameters were -0.57-42.18 for MTF_{cutoff}, -0.01-0.23 for

Table 4 Results of ICC and the Bland and Altman analysis between method A and method B

Data	MTF_{cutoff}	$Strehl^{2D}$ ratio	$OV_{100\%}$	$OV_{20\%}$	$OV_{9\%}$	OSI
ICC						
ICC (95% CI)	0.03 (-0.04, 0.13)	0.08 (-0.01, 0.21)	0.03 (-0.03, 0.13)	0.02 (-0.05, 0.13)	0.05 (-0.03, 0.18)	0.28 (0.12, 0.46)
P	0.25	0.07	0.25	0.32	0.18	0.00
B&A analysis						
$Mean_d \pm S_d$	20.81±10.91	0.11±0.06	0.69±0.36	0.83±0.47	0.83±0.50	-0.64±0.42
95% LOA	(-0.57, 42.18)	(-0.01, 0.23)	(-0.02, 1.40)	(-0.10, 1.75)	(-0.14, 1.80)	(-1.46, 0.18)

ICC: Intra-class correlation coefficient; CI: Confidence interval; B&A: Bland and Altman; $Mean_d$: Mean of differences; S_d: Standard deviation of $Mean_d$; LOA: Limits of agreement; MTF_{cutoff}: Modulation transfer function cutoff frequency; $OV_{100\%}$: OQAS value at contrast of 100%; $OV_{20\%}$: OQAS value at contrast of 20%; $OV_{9\%}$: OQAS value at contrast of 9%; OSI: Objective scatter index.

$Strehl^{2D}$ ratio, -0.02-1.40 for $OV_{100\%}$, -0.10-1.75 for $OV_{20\%}$, -0.14-1.80 for $OV_{9\%}$ and -1.46-0.18 for OSI. Figure 1 illustrates a representative example of the graphical method used to plot the differences in scores between the two methods against the mean for each subject for the six parameters as provided by OQAS, as advocated by Bland and Altman.

DISCUSSION

The repeatability of OQAS which represents the instrument's ability to replicate its own results was assessed in this research. The present results of RLs and CORs for the six parameters of methods A and B suggest a high degree of intra-class repeatability of each method used in the measurement of optical quality by the DP system as determined in a healthy sample of adult Chinese subjects. These findings are similar to those of previous studies by Vilaseca and Saad as based upon their data obtained using COR and RL[1,10]. However, in a study performed by Tomas *et al*[9], the consistency of measurements provided by OQAS seemed to be limited, particularly in eyes with poor optical quality, as evaluated by a within-subject SD (S_w) and intra-class correlation coefficient (ICC). The reason for the differences in conclusions may be due to the different methods of statistical analysis as applied for assessing repeatability. The results of our report suggest that repetitions of the measurements do not affect the final results, and instrument variability remains constant overtime.

A comparison of the repeatability of each method is relevant to method comparison because the repeatabilities of two methods of measurement limit the amount of agreement which is possible [19]. Lack of repeatability can interfere with the comparison of two methods as this will result in considerable variation in repeated measurements on the same subject.

As an ICC value of less than 0.75 indicates a poor agreement, the results of our study demonstrated that a poor degree of reproducibility exists between the two measurement methods. Furthermore, the results of the Bland-Altman analysis also revealed a poor agreement. For example, the mean difference and the 95% limits of agreement for MTF_{cutoff} were 20.81 and -0.57 to 42.18 with no value being outside the limits of agreement. Accordingly, the 95% limits of agreement for the six parameters were quite broad from a clinical perspective. In addition, about 3.3% of values for the $Strehl^{2D}$ ratio, 6.7% of the values for $OV_{9\%}$ and 6.7% of the values for OSI were outside the limits of agreement. With regard to method A, the mean values of the parameters provided by OQAS as related to optical quality and intraocular scattering suggested that there was a good optical quality in all eyes examined, which was similar to the results found in a healthy population of 18 to 30 years old as reported by Martinez-Roda *et al* [8]. In contrast, for method B, the mean values of the six parameters demonstrated a relatively poor optical quality, and the difference for each parameter between two methods was statistically significant ($P < 0.0001$). Therefore, for the sample included in this study, method A seems to be more reasonable and accurate.

However, an important question raised by these findings is that of why such a significant difference exists between the results of these two measurement methods? One reason may be related to longitudinal chromatic aberrations (LCA). The fact that there are differences in focus of human eyes for colors was first noted by Newton (1704). The optics of the eye cause different wavelengths of light to be differentially focused upon the retina. This phenomenon is due to LCA, that is, a wavelength-dependent change in refractive power of the eye (the ocular refractive power is higher for short wavelengths) [21-23]. The current view holds that chromatic aberration is the most important optical imperfection of the well corrected eye [24]. LCA has been found to be about 2 D over the effective range of the visible spectrum, with some differences across studies [22,25]. The DP system provides the retinal image corresponding to a point-source object in near-infrared light (λ=780 nm); and the parameters are computed from the best image in terms of optical quality corresponding to the subject's best focus as chosen automatically by the instrument. However, subjects are requested to casually look at the target (landscape with

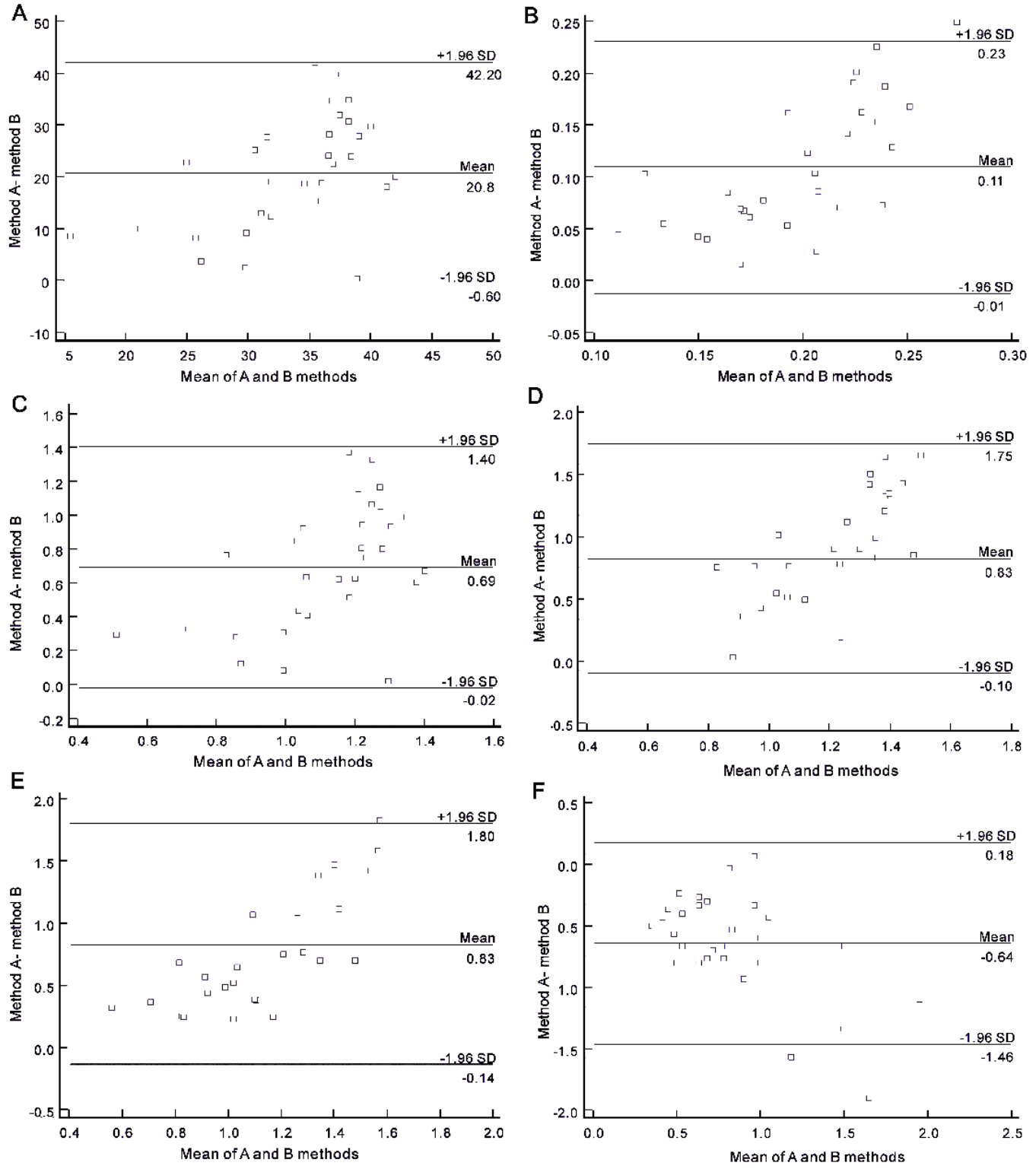

Figure 1 Plots showing the mean of the differences ($mean_d$) and the corresponding 95% CI when the two methods were compared for each parameter provided by OQAS A: MTF_{cutoff}; B: The $Strehl^{2D}$ ratio; C: $OV_{100\%}$; D: $OV_{20\%}$; E: $OV_{9\%}$; F: OSI.

house) in white light during the examination. The visible spectrum ranges between 400 and 760 nm, with 555 nm being the most sensitive light for the human eye. In one report, Lopez-Gil and Artal [26] found the chromatic differences in focus between 543 and 780 nm to be about 1 D in all the subjects tested. While, in another study as performed by Llorente *et al* [27], the average focus shift found between 787 nm and 543 nm was 0.72 D. As a result, at the best focus chosen automatically by OQAS, the image of the target is not the clearest one to the subject due to the influence of LCA. Also, as the subject perceives the clearest image of the target, the retinal image corresponding to the point-source object is not at the best focus. The effect of defocusing is a decrease of its MTF, except at the lowest (*i.e.* zero) and highest spatial frequencies transmitted [20]. Therefore, under such conditions, the parameters provided by

OQAS will not be optimal.

Another reason for the poor agreement may be related to eye accommodation. Accommodation is the action of the ciliary muscle to change crystalline lens shape for the focus of near objects on the retina [5]. In an accommodated eye, wave aberrations are expected to change because ocular structures, particularly the shape, position, and refractive index gradient of the crystalline lens changes during accommodation [28]. Such accommodation-induced changes in aberrations, which include changes of defocus, astigmatism, spherical aberration, and other higher order aberrations have been reported [28]. A review of the literature revealed a general tendency for spherical aberration to change in a negative direction with increases in accommodation, although large variability existed among individuals and studies [28]. In method A, parameters provided by OQAS were measured under conditions of free accommodation. However, in method B, when subjects tried their best to perceive the clearest image of the target, accommodation was inevitably performed, which may have resulted in variations in MTFs and other parameters.

Collating these findings, we attribute the poor reproducibility between the two measurement methods mainly to a combination of focus errors associated with accommodation and chromatic aberration between the wavelengths of the visible target and the infrared wavelength (780 nm) at which the PSFs were measured. Hence, we recommend that examiners always choose the best focus as generated by OQAS automatically and not to alter from this determination throughout the examination.

It has been proposed that variation in pupil diameter affects MTF measurements[1-3]. In this study, AP was fixed at 4.0 mm and no eye had a NP smaller than 4.0 mm during the measurements. Thus, pupil variation did not affect the repeatability of the results. Another consideration was that variations in the refractive formula used during the acquisition could have an effect on the final results. However, in this study, the three measurements were performed during each session using the same method of correction (external trial lenses or internal lenses contained in OQAS). Thus, this potential source of variation would not seem to affect the repeatability of our measurements.

There are some limitations in our study. One limitation was the small sample size which may skew the data representation and affect the statistical significance of the analyses. Another limitation was the characteristics of subjects enrolled. Factors like age, BCVA, and refractive state may exert a significant influence upon the results obtained. Thus the extent to which these findings are generalizable to the population as a whole awaits further research.

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REFERENCES

1 Saad A, Saab M, Gatinel D. Repeatability of measurements with a double-pass system. *J Cataract Refract Surg* 2010;36(1):28-33

2 Benito A, Perez GM, Mirabet S, Vilaseca M, Pujol J, Marin JM, Artal P. Objective optical assessment of tear-film quality dynamics in normal and mildly symptomatic dry eyes. *J Cataract Refract Surg* 2011;37 (8): 1481-1487

3 Artal P, Benito A, Perez GM, Alcon E, De Casas A, Pujol J, Marin JM. An objective scatter index based on double-pass retinal images of a point source to classify cataracts. *PLoS One* 2011;6(2): e16823

4 Montes-Mico R. Role of the tear film in the optical quality of the human eye. *J Cataract Refract Surg* 2007;33(9):1631-1635

5 Artola A, Patel S, Schimchak P, Ayala MJ, Ruiz-Moreno JM, Alio JL. Evidence for delayed presbyopia after photorefractive keratectomy for myopia. *Ophthalmology* 2006;113(5):735-741

6 Diaz-Douton F, Benito A, Pujol J, Arjona M, Guell JL, Artal P. Comparison of the retinal image quality with a Hartmann-Shack wavefront sensor and a double-pass instrument. *Invest Ophthalmol Vis Sci* 2006;47 (4):1710-1716

7 Castro JJ, Jimenez JR, Hita E, Ortiz C. Influence of interocular differences in the Strehl ratio on binocular summation. *Ophthalmic Physiol Opt* 2009;29(3):370-374

8 Martinez-Roda JA, Vilaseca M, Ondategui JC, Giner A, Burgos FJ, Cardona G, Pujol J. Optical quality and intraocular scattering in a healthy young population. *Clin Exp Optom* 2011;94(2):223-229

9 Tomas J, Pinero DP, Alio JL. Intra-observer repeatability of optical quality measures provided by a double-pass system. *Clin Exp Optom* 2012; 95(1):60-65

10 Vilaseca M, Peris E, Pujol J, Borras R, Arjona M. Intra- and intersession repeatability of double-pass instrument. *Optom Vis Sci* 2010; 87(9):675-681

11 Fernandez-Vega L, Madrid-Costa D, Alfonso JF, Montes-Mico R, Poo-Lopez A. Optical and visual performance of diffractive intraocular lens implantation after myopia laser in situ keratomileusis. *J Cataract Refract Surg* 2009;35(5):825-832

12 Vilaseca M, Padilla A, Pujol J, Ondategui JC, Artal P, Guell JL. Optical quality one month after verisyse and veriflex phakic IOL implantation and Zeiss MEL 80 LASIK for myopia from 5.00 to16.50 diopters. *J Refract Surg* 2009;25(8):689-698

13 Moreno LJ, Pinero DP, Alio JL, Fimia A, Plaza AB. Double-pass system analysis of the visual outcomes and optical performance of an apodized diffractive multifocal intraocular lens. *J Cataract Refract Surg* 2010;36(12): 2048-2055

14 Ondategui JC, Vilaseca M, Arjona M, Boniquet S, Cardona G, Guell JL, Pujol J. Retinal image quality three months after photorefractive keratectomy for myopia of up to -5.75 diopters. *J Emmetropia* 2011;2: 21-30

15 Ortiz D, Alio JL, Ruiz-Colecha J, Oser U. Grading nuclear cataract opacity by densitometry and objective optical analysis. *J Cataract Refract*

Surg 2008;34(8):1345-1352

16 McAlinden C, Khadka J, Pesudovs K. Statistical methods for conducting agreement (comparison of clinical tests) and precision (repeatability or reproducibility) studies in optometry and ophthalmology. *Ophthalmic Physiol Opt* 2011;31(4):330-338

17 Vilaseca M, Arjona M, Pujol J, Issolio L, Guell JL. Optical quality of foldable monofocal intraocular lens before and after injection: comparative evaluation using a double-pass system. *J Cataract Refract Surg* 2009;35(8):1415-1423

18 Palomino C, Carmona D, Castillo A, Genol I, Clariana A. Visual quality after presbyopia surgery. *J Emmetropia* 2010;1:74-80

19 Miranda MA, Radhakrishnan H, O'Donnell C. Repeatability of corneal thickness measured using an oculus pentacam. *Optom Vis Sci* 2009;86(3):266-272

20 Myles PS, Cui J. Using the Bland-Altman method to measure agreement with repeated measures. *Br J Anaesth* 2007;99(3):309-311

21 McLellan JS, Marcos S, Prieto PM, Burns SA. Imperfect optics may be the eye's defence against chromatic blur. *Nature* 2002;417(6885):174-176

22 Campbell FW, Gubisch RW. The effect of chromatic aberration on visual acuity. *J Physiol* 1967;192(2):345-358

23 Bedford RE, Wyszecki G. Axial chromatic aberration of the human eye. *J Opt Soc Am* 1957;47(6):564-565

24 Thibos LN, Bradley A, Zhang XX. Effect of ocular chromatic aberration on monocular visual performance. *Optom Vis Sci* 1991;68(8):599-607

25 Marcos S, Burns SA, Moreno-Barriusop E, Navarro R. A new approach to the study of ocular chromatic aberrations. *Vision Res* 1999;39(26):4309-4323

26 Lopez-Gil N, Artal P. Comparison of double-pass estimates of theretinal-image quality obtained with green and near-infrared light. *J Opt Soc Am A Opt Image Sci Vis* 1997;14(5):961-971

27 Llorente L, Diaz-Santana L, Lara-Saucedo D, Marcos S. Aberrations of the human eye in visible and near infrared illumination. *Optom Vis Sci* 2003;80(1):26-35

28 Cheng H, Barnett JK, Vilupuru AS, Marsack JD, Kasthurirangan S, Applegate RA, Roorda A. A population study on changes in wave aberrations with accommodation. *J Vis* 2004;4(4):272-280