Repeatability of measurements with a double-pass system

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PURPOSE: To evaluate the repeatability of measurements with a double-pass system.

SETTING: Rothschild Foundation, Paris, France.

METHODS: Eyes were separated into 2 control groups (<30 years old and >40 years), a post-refractive surgery group, and a cataract group. Measurements were performed using the Optical Quality Analysis System. The main outcome measures were the objective scattering index (OSI), the cutoff frequency of the modulation transfer function (MTF), and the Strehl ratio. The repeatability limit was obtained from the individual standard deviations.

RESULTS: Forty-two eyes were evaluated. The mean OSI value was 0.47 $\pm$ 0.11 (SD) in the younger control group, 1.73 $\pm$ 0.26 in the older control group, 1.34 $\pm$ 0.16 in the post-refractive surgery group, and 6.15 $\pm$ 0.50 in the cataract group. The mean cutoff MTF value was 39.44 $\pm$ 3.93 cycles per degree (cpd), 26.07 $\pm$ 3.89 cpd, 28.34 $\pm$ 2.84 cpd, and 13.3 $\pm$ 1.69 cpd, respectively, and the mean Strehl ratio, 0.234 $\pm$ 0.023, 0.146 $\pm$ 0.021, 0.169 $\pm$ 0.023, and 0.098 $\pm$ 0.010, respectively. The repeatability limit for the whole population was 0.841 (33.5%) for the OSI, 8.499 (31.1%) for the cutoff MTF, and 0.051 (31%) for the Strehl ratio.

CONCLUSIONS: The repeatability limit was good and equivalent for the OSI, the MTF, and the Strehl ratio values. There was a wide interval between the normal and pathologic threshold for OSI measurements, indicating that the reliability of the double-pass device complies with the requirements for quantitative assessment of scattering.

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The 2 leading causes of reduced optical quality of the human eye in clinical practice are uncorrected refractive abnormalities and increased media opacities that cause increased light diffusion.[1] Aberrometers measure optical aberrations of low and high degree but not the loss of ocular transparency. Thus, the optical quality estimation obtained with these aberrometers is only valid if ocular transparency is not altered. Another limitation of these systems is their low interreproducibility.[2–5] The Optical Quality Analysis System (Visiometrics)[1,6,7] is the only currently available device that allows direct objective measure of the effect of optimal aberrations and the loss of ocular transparency on the optical quality of the human eye. This double-pass system performs these measurements by analyzing the retinal image of a point source of light obtained after focalization of an infrared beam. This retinal image corresponds to the point-spread function (PSF).

The clinical applications of the double-pass system are numerous. The system can be used in all clinical situations in which it is important to quantify the reduction in the optical quality of the eye caused by an increase in higher-order aberrations and a reduction in the transparency of the ocular media. The direct measurement of ocular light diffusion is potentially relevant because it shows the objective effect of ocular media opacities on the light incident on the retina.

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It may be possible to confirm that mild opacities of the lens are responsible for visual symptoms in a phakic patient. Similarly, the role of posterior capsule opacification in the loss of vision in a pseudophakic eye can be confirmed by deterioration in the retinal PSF. Moreover, many studies[1,8–11] have concluded that Hartmann-Shack aberrometers may overestimate image quality in eyes affected by scattering (cataract, diffractive multifocal intraocular lenses).

Before relying on measurements by any device to diagnose a measured abnormality, it is necessary to ensure that repeated scans give consistent results. Repeatability, as adopted by the International Organization for Standardization,[12] is defined as a condition in which independent test results are obtained with the same method and equipment in the same subject by the same operator with the shortest possible time between successive readings.

To our knowledge, no comprehensive data on the repeatability of measurements obtained with the Optical Quality Analysis System have been published. Thus, we performed a study to assess repeatability of measurements obtained using the double-pass system.

SUBJECTS AND METHODS

This study was performed according to the tenets of the Declaration of Helsinki. All subjects provided informed consent after receiving an explanation of the nature and intent of the study. To be included, the subject had to have 10 successive measurements in 1 or both eyes.

The eyes were divided into 2 control groups, a post-refractive surgery group, and a cataract group. The first control group comprised eyes of subjects younger than 30 years who were emmetropic or ametropic with spectacle correction and with normal distance visual acuity (20/20 or better). Corneal regularity and the absence of topographic abnormalities were confirmed by Placido-based corneal topography. The second control group comprised eyes of subjects older than 40 years with no lens opacities detectable at the slitlamp, a corrected distance visual acuity (CDVA) of 20/20 or better, regular corneas, and no topographic abnormalities. The post-refractive surgery group comprised eyes that had uneventful laser in situ keratomileusis and 20/20 uncorrected distance visual acuity. To be included in 1 of the first 3 groups, the eye had to be free of ocular anomalies. The cataract group comprised eyes with impaired visual acuity caused by moderate to severe cataract.

The same experienced investigator performed all procedures. No medication was given to dilate the pupils, and no patient received topical drops or ointment.

Double-Pass System

The light source of the double-pass system is a 780 nm laser diode, which acts as a point object (Figure 1). After reflecting through a beam splitter, the light passes through 2 achromatic doublet lenses (lens 2 and lens 3) and through a mobile focus corrector, which has 2 mirrors attached to

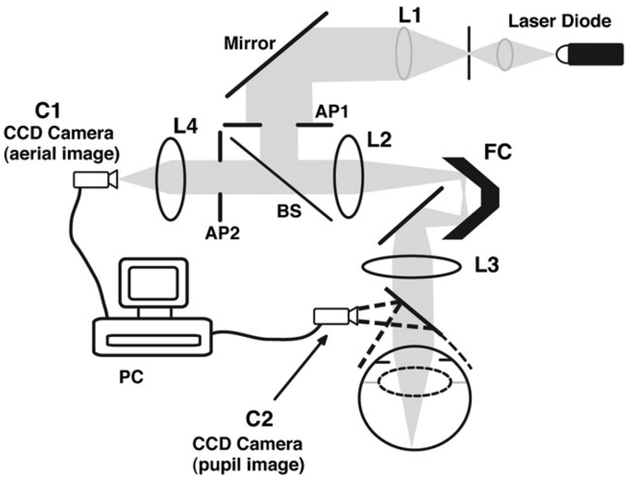

Figure 1. Schematic of the double-pass aberrometry system (AP1 = artificial pupil 1; AP2 = artificial pupil 2; BS = beam splitter; C1 = camera 1; C2 = camera 2; CCD = charge-coupled device; L1 = lens 1; L2 = lens 2; L3 = lens 3; L4 = lens 4; PC = personal computer).

it. Spherical refraction in the subject's eye is performed at the focus corrector by modifying the optical paths between lens 2 and lens 3. The eye forms the image of the point source on the retina. The optical pathway from the laser source to the retina constitutes the single pass of the system. The double pass is determined by the light on its way from the retina to a charge-coupled device (CCD) camera. The reflected light passes through the 2 doublet lenses and through the beam splitter, where 50% of light is lost. Light that passes through the beam splitter encounters the second artificial pupil. The effective exit pupil is the second artificial pupil or the natural pupil if it is smaller than the artificial pupil. An objective focuses the image on a CCD camera; a personal computer is used to grab and process the retinal images.

The double-pass system provides several measurements. The first is the modulation transfer function (MTF), which evaluates the ratio between the contrast in the retinal image of a sinusoidal grating and its original contrast as a function of the spatial frequency of the grating. The MTF value is the highest when the contrast in the image is the same as the contrast in the object. The value considered is the cutoff point of the MTF curve (cutoff MTF) on the x-axis; the results are given in cycles per degree (cpd), representing the highest spatial frequency at lower contrast. The classic definition of the cutoff frequency is an MTF value of zero. The MTF cutoff in the double-pass system is the frequency at which the MTF reaches a value of 0.01. Because the PSF images recorded by the double-pass instrument can be affected by high-frequency noise, which is inherent in the use of cameras, the frequency for very small MTF values may become unstable, potentially leading to artifacts. To avoid this problem, the device uses an MTF threshold value of 0.01, which corresponds to 1% contrast. Thus, the cutoff MTF in this paper refers to the frequency up to which the eye can image an object in the retina with a significant 1% contrast. Under optimum conditions (low level of optical aberration and diffraction), the maximum spatial frequency the human eye can detect is close to 60 cpd (the limit imposed by the retinal sampling).

The second measurement is the objective scattering index (OSI), which is an objective evaluation of intraocular

Table 1. Demographic characteristics by group.

Characteristic	Group			
	Control <30 Y	Control >40 Y	Post Refractive Surgery	Cataract
Subjects (n)	8	6	4	6
Eyes (n)	15	9	7	11
Mean age (y) ± SD	27.5 ± 2.8	53.1 ± 6.9	27.6 ± 4.1	67.3 ± 13.7
Male sex, n (%)	3 (37.5)	2 (33.3)	3 (75.0)	3 (50.0)
CDVA				
Value	1.0	1.0	1.0	0.46 ± 0.17*
Range	—	—	—	0.05 to 0.60

CDVA = corrected distance visual acuity
*Mean ± SD

scattered light. The index is calculated by evaluating the amount of light outside the double-pass retinal intensity PSF image in relation to the amount of light on the center. The higher the OSI value, the higher the level of intraocular scattering. According to the user's manual, the OSI value is lower than 0.5 in eyes with a normal degree of scattering (young eyes), between 1.5 and 4.0 in eyes that are developing cataract, and higher than 4 in eyes with mature cataract.

The third measurement is the Strehl ratio, which is an expression of the ratio of the central maximum of the illuminance of the PSF in the aberrated eye to the central maximum that would be found in the corresponding aberration-free system. It is the measure of the fractional drop in the peak of the PSF as a function of the wavefront error. A Strehl ratio of 1 indicates perfection.

Measurement Technique

The head of the subject was positioned on the chin rest and fixated on the center of a figure. The operator manually aligned the subject's pupil center with the optical axis of the device. Spherical correction within −11.00 and +5.00 diopters (D) of ametropia was automatically performed by the machine. Cylindrical refractive errors were corrected with a cylindrical trial lens. Twenty consecutive measurements were taken (10 OSI; 10 MTF and Strehl ratio); the pupil center was realigned between each measurement. Subjects were asked to blink before the measurement.

For each parameter (OSI, MTF, and Strehl ratio), the device took 6 measurements. It then calculated the mean of the measurements to provide the final results for each parameter. The operator can ignore 1 or more of the 6 measurements judged to be atypical to allow the machine to calculate a more accurate final result from the remaining measurements. However, this option was not used during our study (ie, all 6 measurements were always kept).

Repeatability Calculation

Repeatability is the closeness of agreement between the results of successive measurements of an identical test material performed under defined conditions. Conditions include the same operator, same apparatus, and a short time between analyses. The conditions under which these measurements were performed are known as the repeatability conditions. The results of the repeatability experiments can be used to calculate a standard deviation, called the repeatability standard deviation. This value is useful in determining a repeatability limit; a value less than or equal to the absolute difference between 2 test results obtained under repeatability conditions can be expected to lie within a probability of 95%.

The repeatability limit was calculated from the individual standard deviations as follows:

$$R = SD \times t_{0.05,n}$$

where R is the repeatability limit, SD is standard deviation, and t is the critical value of the Student t distribution at the 95% confidence level (t = 2.262 for 10 measurements).[13]

The mean repeatability limit in the population was calculated by adding the square of individual repeatability of each individual eye and calculating the root mean square of the mean value as follows:

$$R = \sqrt{\left(R^2 + R^2 + \ldots\ldots + R^2 + R^2\right)/N}$$

where N is the number of subjects in the study population. Repeatability is given with 95% confidence. In the remaining sections of the paper, the term *repeatability* is used as equivalent to the confidence interval of repeatability corresponding to the range of random errors determined at the 95% confidence level. Standard deviation and repeatability limit are expressed in absolute values and in percentage of the mean values of each tested parameter in the study population.

RESULTS

Forty-two eyes of 24 subjects were enrolled in the study. Table 1 shows the demographic data of the subjects and the number of subjects in each group. The mean age of the subjects was 44.4 years ± 18.9 (SD). The mean spherical equivalent of the attempted refractive correction in the post-refractive surgery group was −3.1 ± 1.4 D.

Table 2 shows the mean values for OSI, cutoff MTF, and Strehl ratio and the repeatability limit of each. The OSI was higher in the older control group (>40 years) than in the younger control group (<30 years). The cutoff MTF and the Strehl ratio decreased with age (Figure 2). There was a statistically significant

Table 2. Repeatability OSI, cutoff MTF, and Strehl ratio values.

	Group				
Parameter	Control <30 Y	Control >40 Y	Post Refractive Surgery	Cataract	All
Mean values ± SD					
OSI	0.47 ± 0.11	1.73 ± 0.26	1.34 ± 0.16	6.15 ± 0.50	2.51 ± 0.28
Cutoff MTF (cpd)	39.44 ± 3.93	26.07 ± 3.89	28.34 ± 2.84	13.3 ± 1.69	27.29 ± 3.23
Strehl ratio	0.234 ± 0.023	0.146 ± 0.021	0.169 ± 0.023	0.098 ± 0.010	0.165 ± 0.019
Repeatability limit (%)					
OSI	0.26 (56.1)	0.63 (36.5)	0.4 (29.7)	1.28 (20.9)	0.84 (33.5)
Cutoff MTF	9.54 (24.2)	9.62 (36.9)	6.79 (24.0)	5.11 (38.4)	8.49 (31.1)
Strehl ratio	0.053 (22.6)	0.053 (36.6)	0.059 (34.8)	0.030 (30.6)	0.051 (31.0)

cpd = cycles per degree; MTF = modulation transfer function; OSI = objective scattering index

difference in OSI values between the 2 control groups and between the younger control group and the post-refractive surgery group ($P<.001$, Kruskal-Wallis). There was no significant difference in OSI values between the older control group and the post-refractive surgery group ($P = .138$, Kruskal-Wallis) The repeatability limit (percentage of mean value) ranged between 20.9% and 56.1% for the OSI, between 20.4% and 38.4% for the cutoff MTF, and between 22.6% and 32.6% for the Strehl ratio. Thus, the limit was almost constant for the whole population, varying between 33.5% for the OSI, 31.1% for cutoff MTF, and 31% for the Strehl ratio.

DISCUSSION

Measurement validity or accuracy is dependent on 2 types of measurement uncertainties: systematic errors and random errors. The accuracy (validity) of an instrument indicates the closeness between the mean measured value and the true value of each measurement.

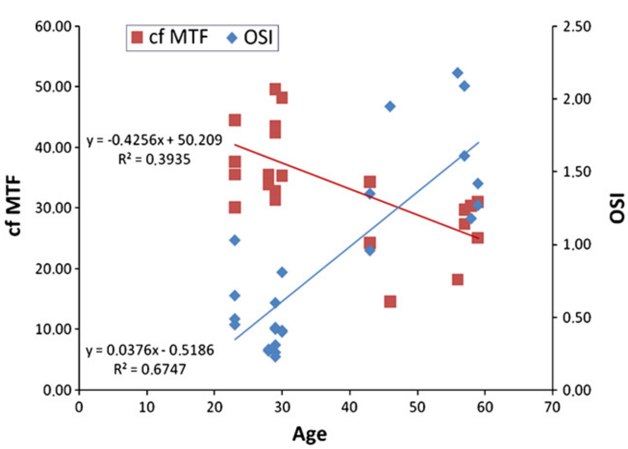

Figure 2. Objective scattering index (OSI) and cutoff MTF (cf MTF) as a function of age in normal eyes (2 control groups) (MTF = modulation transfer function).

The precision (repeatability, reliability) indicates the instrument's ability to repeat its own results.[14] Assessing the accuracy of the Optical Quality Analysis System double-pass device, defined as the trueness of the results, was not the primary goal of this study. However, accuracy testing is dependent on the repeatability of the device, which we did study.

The calibration of an instrument against known standards eliminates systematic errors. The errors associated with routine use of an instrument are random; these can be minimized by a detailed routine procedure and the use of repeated independent measurements. The determination of random errors leads to the identification of instrument measurement repeatability.

Measurements of the OSI, cutoff MTF, and Strehl ratio by the double-pass system had a good repeatability limit. For comparison, the repeatability limit of the Zernike coefficient computed for corneal wavefront reconstruction (pupil diameter of 4.5mm) varied in one study between 24% and 231%[4]; a repeatability limit of 50% is the highest acceptable value in biological metrics.[4] Because the standard values indicated by manufacturer of the double-pass system (OSI <0.5 for normal eyes, between 1.5 and 4.0 for mild to moderate cataract) specify a free interval between the normality and pathology thresholds higher than the repeatability limit, reliability of the double-pass measurements should not be affected. Therefore, the OSI results in normal young eyes did not reach a pathologic level, suggesting measurement consistency. In the normal group, the lowest cutoff MTF value was 14.5 cpd. This value is much lower than expected for a 46-year-old patient with a CDVA of 20/20. Although the MTF cutoff frequency with the system is defined by the frequency at which the MTF reaches the value of 0.01 (not 0 as in the classic definition), high-frequency noise from the instrument's camera may limit the precision of the calculation of the cutoff frequency value.

Repeatability error can be caused by operator- or patient-dependent factors. We thought that it would be interesting to eliminate aberrant measurements from the 6 captures performed by the machine during the initial acquisition to evaluate the effects on the instrument's repeatability. We applied this method in the young control group and found no difference in the final result; 5 of the 6 OSI measurements were always identical. The different measurement (present in 4 of 8 eyes) did not differ by more than 0.1 from the other 5 measurements. Thus, the mean value of the 6 measurements remained unchanged. A second source of error is noncycloplegic fixation, which can lead to accommodative spasm in the last measurements. Finally, any variation in the refractive formula used during the acquisition (patient's glasses, trial frame lenses) could affect the final results. In this study, the 10 measurements were performed using the same method of correction (trial lenses); thus, this variation did not affect the repeatability but may have affected the accuracy of the results. The possible variation in pupil diameter with time, individual, or age is known to affect MTF measurements. However, the effective exit pupil was fixed at 4.0 mm in our study and no eye had a pupil smaller than 4.0 mm during the measurements. Thus, pupil variation did not affect the repeatability or reliability of the results.

With almost every measuring device, the smaller the absolute value of the measured parameter, the more considerable the possible relative repeatability error. Because most OSI values in our young control group population were close to zero, the high repeatability error (56.1%) we observed may be the logical consequence of the low absolute values. Despite a low absolute value, the repeatability limit of the Strehl ratio was very good. Because this parameter is correlated only with the relative maximum height of the PSF intensity, it may be less affected by instrument variability than the OSI and cutoff MTF. The repeatability limit was not affected by age or other specific conditions (ie, previous refractive surgery or presence of cataract). Except in the young control group, the OSI varied between 20.9% and 38.4%. We found that the OSI and the cutoff MTF were correlated with age. Scattering increased with age, whereas the cutoff MTF decreased with age. This can be caused by an increase in corneal higher-order wavefront aberrations in older age[15] or by decreased ocular transparence that is undetectable at the slitlamp. Methods to estimate scattering in Hartmann-Shack raw images have been proposed, one of which is to calculate the brightness of pixels within an area containing each lenslet's PSF tail.[16] It would be interesting to compare the accuracy of measurements of the scattering level obtained with these methods with the accuracy of those obtained with the double-pass system. Because the system we used is based on a double pass of light through the eye's optics, the image is twice degraded. Even in a "perfect" eye, the PSF measurement would not be an Airy diffraction pattern; in addition, for the same pupil diameter on the 2 passes, the derived MTF would correspond to the square of the true ocular MTF. Thus, caution should be used when comparing our MTF measurements with those obtained with other devices.

Based on its numerous clinical applications, we believe the double-pass system will play an important role in daily clinical practice. Future studies should assess the normal range of values in eyes with various pathologies and evaluate the accuracy of the double-pass system in these cases.

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