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Optical quality and intraocular scattering in a healthy young population

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Background: We objectively assessed the optical quality and intraocular scattering by means of parameters provided by a clinical double-pass system in healthy young subjects and thereby we obtained new reference data for clinical diagnosis. We calculated normal values of neural contrast sensitivity function (nCSF) from the measured modulation transfer function (MTF) and the contrast sensitivity function (CSF).
Methods: Eligible subjects were healthy adults aged from 18 to 30 years with a logMAR visual acuity (VA) of 0.0 or better and normal values of CSF. Optical quality measurements for a 4.0 mm pupil were performed using the Optical Quality Analysis System (OQAS) based on the double-pass technique. The following parameters were analysed: the modulation transfer function cutoff frequency (MTF_{cutoff}), the $Strehl^{2D}$ ratio, the OQAS values (OV) at 100, 20 and nine per cent contrasts and the objective scatter index (OSI).
Results: A total of 178 volunteers responded to the call, of whom 181 eyes were finally part of the study taking into account the criteria for inclusion. The values for the optical quality parameters were: 44.54 ± 7.14 cpd (MTF_{cutoff}), 0.27 ± 0.06 ($Strehl^{2D}$ ratio), 1.48 ± 0.24 ($OV_{100\%}$), 1.58 ± 0.32 ($OV_{20\%}$), 1.64 ± 0.39 ($OV_{9\%}$), and 0.38 ± 0.19 (OSI). The nCSF calculated was 1.76 ± 0.21 (3 cpd), 2.13 ± 0.23 (6 cpd), 2.01 ± 0.28 (12 cpd) and 1.86 ± 0.33 (18 cpd).
Conclusion: The normal values provided can be a useful tool for discriminating healthy eyes from early abnormal ones in which the optical quality or sensory function is impaired.

Key words: aberrations, contrast sensitivity, intraocular scattering, optical quality, visual acuity

In the past decade, wavefront aberrometers have become widely used for determining ocular higher-order aberrations, since their use has been linked to customised wavefront-guided LASIK.[1,2] These instruments, which are usually based on the Hartmann-Shack sensor,[3,4] generally consist of a microlens array, conjugated with the eye's pupil and a camera placed at its focal plane. If a plane wavefront reaches the microlens array, the image recorded with the camera is a perfectly regular mosaic of spots. If a distorted (that is, aberrated) wavefront reaches the sensor, the pattern of spots is irregular. The displacement of each spot is proportional to the derivative of the wavefront over each microlens area. From the images of the spots, the wavefront aberration can be computed by Fourier transformation and the modulation transfer function (MTF), which represents the loss of contrast produced by the eye's optics as a function of spatial frequency, can also be calculated.

In recent years, the double-pass technique has been shown to be a useful tool for comprehensively evaluating the optical quality of the eye.[5–7] Double-pass systems are based on recording images from a point-source object after reflection on the retina and a double pass through the ocular media. In contrast to wavefront aberrometry, the double-pass systems directly compute the modulation transfer function from the acquired double-pass retinal image by Fourier transformation, allowing the complete characterisation of the optical quality of the eye, mainly degraded by higher-order ocular aberrations and scattered light. Because of the differences between both technologies, recent studies suggest that wavefront aberrometers may overestimate retinal image quality in eyes where higher-order aberrations and scattered light are prominent.[8]

The Optical Quality Analysis System (OQAS, Visiometrics SL, Spain)[9] is the only instrument based on the double-pass technique that is currently available for use in daily clinical practice. It is based on the asymmetric scheme of the double-pass technique, that is, with different entrance and exit pupil sizes,[10] enabling the detection of both symmetric and asymmetric aberrations. Asymmetric aberrations such as coma cannot be measured by a conventional symmetric double-pass system.

This system has been used to evaluate the optical quality of eyes in several situations, such as in patients who have undergone kerato-refractive and phakic IOL surgery,[11–13] in patients with keratitis,[14] to evaluate presbyopia after photorefractive keratectomy[15] and to study the *in vitro* optical quality of foldable monofocal intraocular lenses.[16] Moreover, a study of the repeatability of this system was also performed recently.[17] The authors found good repeatability limits (close to 30 per cent) in a control group of patients, a post-refractive surgery group and a cataract group.

The Optical Quality Analysis System computes the modulation transfer function from the double-pass images that are acquired. It also provides many other optical quality parameters (MTF cutoff frequency [MTF_{cutoff}], Strehl ratio [$Strehl^{2D}$ ratio], and Optical Quality Analysis System values [OV] at contrasts of 100, 20 and nine per cent) to simplify the study of the optical quality of the eye. Furthermore, it allows intraocular scattering to be quantified by means of the OSI parameter (objective scatter index).

Although several studies[18–20] have already analysed the optical performance of the eye in a normal healthy population, a reference database with normal values for the specific parameters provided by the Optical Quality Analysis System does not exist yet, making it difficult to clinically analyse the results.

As the optical quality of the eye is affected by natural degradation with age,[21,22] this process should be carried out among subjects of different age ranges. As a first approach to this goal, in this study we report normal values for the optical quality and intraocular scattering parameters provided by the double-pass based system measured in a healthy homogeneous sample population aged between 18 and 30 years. Furthermore, we provide normal values for the neural contrast sensitivity function (nCSF), which is computed as the ratio between the measured contrast sensitivity function (CSF) and the modulation transfer function.

METHODS

Healthy young volunteers aged from 18 to 30 years were recruited for this prospective, observational, cross-sectional, non-consecutive case study from the staff and students of the Universitat Politècnica de Catalunya (UPC). Subjects with no history of ocular pathology or surgery underwent a standardised examination at the University Vision Centre (CUV) between March and November 2009. The research followed the tenets of the Declaration of Helsinki. All subjects gave their written informed consent after receiving a written and verbal explanation of the nature of the study. Ethical committee approval was obtained.

Criteria for inclusion in the study were a logMAR visual acuity (VA) of 0.0 or better, normal contrast sensitivity function values in mesopic conditions, a spherical manifest refractive error from -6.00 D to +3.00 D and a cylinder below 2.00 D inclusive. Moreover, we only analysed patients with a pupil diameter of 4.0 mm or more in mesopic conditions, as this was the value used in the optical quality measurements.

For all subjects, we assessed the manifest refractive error, logMAR VA with a Bailey-Lovie chart and contrast sensitivity function with the CSV-1000E test (VectorVision, Greenville OH, USA) at frequencies of three, six, 12 and 18 cycles per degree (cpd) measured in mesopic conditions.[23] No lens opacities were detected with direct slitlamp observation. The natural pupil diameter was also measured by means of the double-pass system used in this study. Furthermore, this system was used to measure optical quality in the study population, with an artificial pupil of 4.0 mm in diameter as stated above. Measurements were conducted by two trained examiners and the first eye that was measured was randomly selected. The measurements took approximately 45 minutes.

We used the modulation transfer function profile computed by the double-pass system and the clinically measured contrast sensitivity function to calculate the nCSF corresponding to each eye as the ratio between the contrast sensitivity function and the modulation transfer function at spatial frequencies of three, six, 12 and 18 cpd.

Double-pass system

The optical quality and intraocular scattering were measured using the Optical Quality Analysis System with the subject's retinal image optimally focused. The patients' refractive errors were corrected during these measurements: the spherical refractive error was automatically corrected by the double-pass system and astigmatism over 0.50 D was corrected with an external cylindrical lens. The size of the artificial pupil is controlled by means of a diaphragm wheel located inside the double-pass system. Room illumination was kept low during testing.

The double-pass system provided the retinal image corresponding to a point-source object in near-infrared light consisting of a laser diode (l = 780 nm)

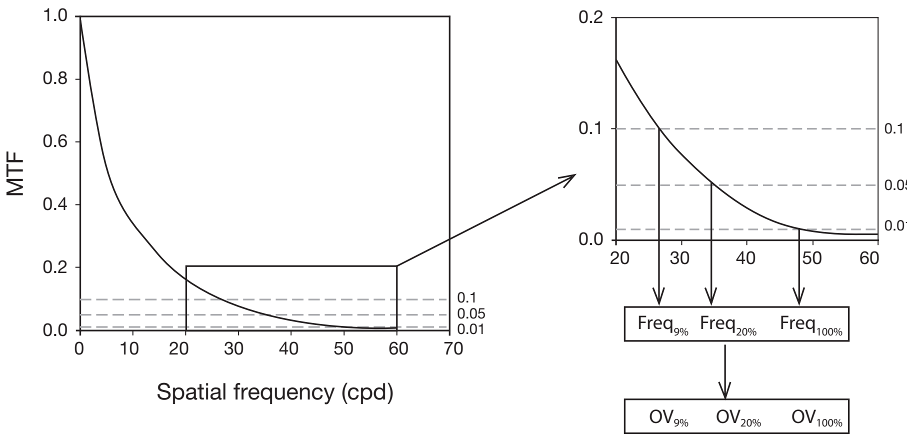

Figure 1. Schematic diagram showing the computation of $OV_{100\%}$, $OV_{20\%}$ and $OV_{9\%}$ from the modulation transfer function curve. The three spatial frequencies from which they are derived ($freq_{100\%}$ or MTF_{cutoff}, $freq_{20\%}$, $freq_{9\%}$), which correspond to modulation transfer function values of 0.01, 0.05 and 0.1, respectively, are also shown.

coupled to an optical fibre. Near-infrared light is used because it is more comfortable for the subject and provides retinal image quality estimates that are comparable to those obtained with visible light.[24] From the retinal image of each analysed eye the monochromatic modulation transfer function was computed. A two-dimensional radially averaged profile of the modulation transfer function is used to describe the complete eye's optical quality in the double-pass instrument. Moreover, to facilitate the clinical use of the device and the comparison of retinal image quality among subjects, the system also provides several simpler parameters that are related to the modulation transfer function profile: the MTF_{cutoff}, the $Strehl^{2D}$ ratio and the OQAS values (OV) at 100, 20 and nine per cent contrasts.

The MTF_{cutoff}[17] is calculated as that corresponding to a 0.01 modulation transfer function value, as there is a certain background noise in the modulation transfer function profile that is computed from the real recorded double-pass image.

In the visual optics field, the Strehl ratio[25–27] is often computed in the frequency domain as the ratio between the volumes under the modulation transfer function curve of the measured eye and that of the aberration-free eye, which provides overall information on the eye's optical quality. The double-pass system computes the Strehl ratio in two dimensions (2D) ($Strehl^{2D}$ ratio) as the ratio between the areas under the modulation transfer function curve of the measured eye and that of the aberration-free eye, as accepted in the literature.[22] This computation has a lower cost in time, which makes this approach more suitable for clinical practice.

The three OVs[11] are normalised values of three spatial frequencies that correspond to the modulation transfer function values of optical quality for three contrast conditions commonly used in ophthalmologic practice: 100 per cent ($OV_{100\%}$), 20 per cent ($OV_{20\%}$) and nine per cent ($OV_{9\%}$). These values can be used to obtain more specific information on the performance of the eye's optics at different contrasts, which may remain hidden when more general parameters that integrate the information along all available spatial frequencies are considered, such as the Strehl ratio. Specifically, $OV_{100\%}$ is directly related to the modulation transfer function cutoff frequency (it is the modulation transfer function cutoff frequency divided by 30 cpd) and therefore to the patient's visual acuity, although it is not affected by retinal and neural factors. $OV_{20\%}$ and $OV_{9\%}$ are computed in the same way from smaller frequencies linked to 0.05 and 0.1 modulation transfer function values, respectively, which maintain the proportion of contrasts at 20% and 9% (Figure 1). Therefore, they inform us about the shape of the modulation transfer function profile at lower frequencies than the modulation transfer function F cutoff. In addition, these two additional frequencies have been normalised so that the values obtained are comparable to standard decimal visual acuity values.

The system also quantifies intraocular scattered light by means of the OSI parameter,[17,28–30] which is computed as the ratio of the amount of light within an annular area of 12 and 20 minutes of arc and that recorded within one minute of arc of the central peak in the acquired double-pass image (Figure 2).

Statistical analysis

The statistical analysis of the data was performed using Minitab software (version 15.0, Minitab Inc, USA) for Windows. The Kolmogorov-Smirnov test was used to evaluate the normal distribution of all variables. Balanced analysis of variance was used to analyse the influence on the results of spherical equivalent, cylinder, age, sex, right and left eyes and pupil diameter. The influence of the examiner was also analysed. A p value of 0.05 was considered to be statistically significant.

The mean (± SD, standard deviation) and the corresponding range (minimum and maximum) are given for each analysed variable. The upper or lower limits of normal are defined at the 95% level of agreement by mean $\pm 1.96 \times$ SD.[31]

Finally, we report the normal values based on the normal probability at the 95% level of agreement for the nCSF at spatial frequencies of three, six, 12 and 18 cpd.

RESULTS

A total of 178 volunteers were responding to the call made but 17 were excluded in the previous interview and 38 were excluded to maintain parity between the two trained examiners throughout the

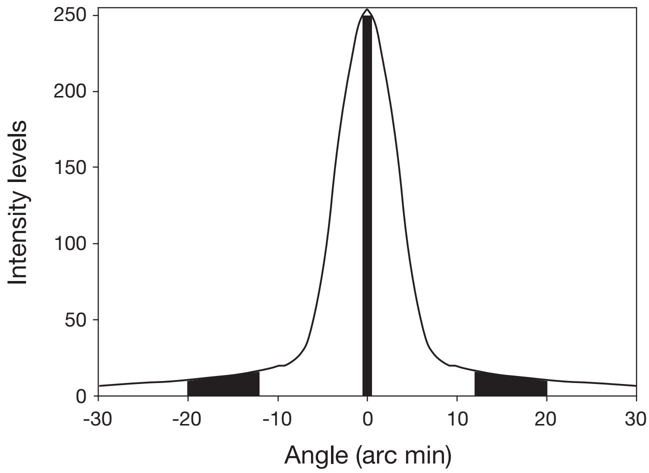

Figure 2. Schematic diagram showing the computation of objective scatter index from the double-pass image acquired. Black areas correspond to the amount of light within an annular area of 12 and 20 minutes of arc and that recorded within one minute of arc of the peak.

Parameter	Sex	Eye	n	Mean		SD		Range (Min-max)	Normal limits
VA	F	R	45	-0.14	-0.14	0.07	0.07	-0.30–0.00	-0.28–0.00
		L	57	-0.14		0.07			
	M	R	41	-0.13		0.07			
		L	38	-0.14		0.07			
CSF 3 cpd	F	R	45	1.61	1.57	0.22	0.20	1.49–1.78	1.18–1.96
		L	57	1.56		0.20			
	M	R	41	1.57		0.19			
		L	38	1.55		0.19			
CSF 6 cpd	F	R	45	1.76	1.78	0.24	0.21	1.70–1.84	1.37–2.19
		L	57	1.78		0.21			
	M	R	41	1.78		0.20			
		L	38	1.79		0.20			
CSF 12 cpd	F	R	45	1.35	1.37	0.22	0.26	1.25–1.54	0.86–1.88
		L	57	1.40		0.28			
	M	R	41	1.40		0.25			
		L	38	1.33		0.26			
CSF 18 cpd	F	R	45	0.99	0.95	0.24	0.29	0.81–1.10	0.38–1.52
		L	57	0.96		0.26			
	M	R	41	0.94		0.29			
		L	38	0.88		0.31			

Table 1. VA and CSF (log) at different spatial frequencies. Sex, eye (R/L), number of samples (n), mean, standard deviation (SD), range (minimum-maximum) and upper and lower normal limits (at the 95% level of agreement) are specified.

analysis (the examiners carried out 48.8 and 51.2 per cent of the examinations). Finally, we examined 246 eyes of 123 persons, of whom 65 were discarded taking into account the criteria for inclusion, leaving 181 eyes validated for the study (56.4 per cent female).

The mean age was 22.47 ± 3.04 years (range: 18 to 30 years) and subjects had a spherical equivalent of 1.07 ± 1.39 D (range: -6.00 to +3.00 D). Specifically, 83 emmetropic eyes and 98 eyes with ametropia were measured. A total of 54 eyes had a cylindrical refractive error but only 18 eyes showed astigmatism higher than 0.50 D. The natural pupil diameter measured under mesopic conditions (illuminance value at the pupil's plane was 23.3 ± 1.4 lx) was 6.9 ± 0.8 mm (range: 4.5 to 8.5 mm).

In this study, all analysed variables (demographics, clinical data and optical quality parameters) were normally distributed ($p > 0.15$).

The mean, standard deviation, corresponding ranges and normal limits at the 95% level of agreement for the VA and CSF are given in Table 1. No statistically significant differences were observed for these variables, when the influence of the spherical equivalent, cylinder, age, sex, eye and pupil diameter were tested ($p > 0.05$), thus proving the homogeneity of the sample population. The examiner did not have a statistically significant influence on the results.

Table 2 shows the statistics of the optical quality and intraocular scattering parameters provided by the double-pass system as well as the corresponding normal cut-offs. No statistically significant differences were observed for the optical quality parameters, when the influence of the spherical equivalent, cylinder, age, sex and eye were tested, as well as when the influence of the examiner was analysed ($p > 0.05$). An exception was found for the influence of age on the objective scatter index ($p = 0.001$). The influence of pupil diameter was not analysed, as all optical quality parameters were measured using a 4.0 mm pupil.

Figure 3 shows the calculated nCSF profile at frequencies of three, six, 12 and

Parameter	Sex	Eye	n	Mean		SD		Range (Min-max)	Normal limits
MTF_{cutoff}	F	R	45	45.50	44.54	6.89	7.14	24.22–55.93	30.54–58.53
		L	57	44.30		7.30			
	M	R	41	44.60		7.20			
		L	38	43.71		7.31			
$Strehl^{2D}$ ratio	F	R	45	0.28	0.27	0.06	0.06	0.15–0.42	0.15–0.39
		L	57	0.26		0.06			
	M	R	41	0.27		0.06			
		L	38	0.25		0.05			
OV 100%	F	R	45	1.52	1.48	0.23	0.24	0.81–1.86	1.01–1.95
		L	57	1.48		0.24			
	M	R	41	1.49		0.24			
		L	38	1.47		0.24			
OV 20%	F	R	45	1.64	1.58	0.31	0.32	0.85–2.24	0.95–2.21
		L	57	1.56		0.33			
	M	R	41	1.59		0.33			
		L	38	1.50		0.31			
OV 9%	F	R	45	1.73	1.64	0.39	0.39	0.83–2.60	0.88–2.40
		L	57	1.60		0.40			
	M	R	41	1.68		0.40			
		L	38	1.54		0.32			
OSI	F	R	45	0.36	0.38	0.17	0.19	0.00–1.12	0.00–0.75
		L	57	0.39		0.22			
	M	R	41	0.38		0.17			
		L	38	0.41		0.18			

Table 2. Optical quality and intraocular scattering parameters provided by the double-pass system (MTF_{cutoff}, $Strehl^{2D}$ ratio, $OV_{100\%}$, $OV_{20\%}$, $OV_{9\%}$, and objective scatter index). Sex, eye (R/L), number of samples (n), mean, standard deviation (SD), range (minimum-maximum), and upper and lower normal limits (at the 95% level of agreement) are specified.

18 cpd. Table 3 reports the statistics of this function and the normal limits found for normal healthy young subjects. No statistically significant differences were observed for the nCSF, when the influence of the spherical equivalent, cylinder, age, sex, eye and pupil diameter were tested ($p > 0.05$). The examiner did not have a statistically significant influence in this case.

DISCUSSION

The mean VA values measured in this study were close to others found in similar studies. Elliot, Yang and Whitaker[32] obtained a mean value of -0.13, Arditi and Cagenello[33] of -0.10 with a maximum of -0.3 and Stonecipher and Kezirian[34] of 6/4.5 (-0.10). In addition, the contrast sensitivity functions closely agreed with those provided by the manufacturer of the CSV-1000E test, which are 1.61 (3 cpd), 1.66 (6 cpd), 1.08 (12 cpd) and 0.56 (18 cpd), respectively. The manufacturer's values were collected as baseline (pre-operative) measurements in an FDA clinical trial for refractive surgery, which was based on the evaluation of 156 normal eyes (79 patients) with an age range of 21 to 55 years (36.6 ± 9.02 years). The slightly diminished values for high frequencies may be due to the broader range of ages that were included in the FDA study. The lower normal limits found for both the VA and the contrast sensitivity functions (Table 1) seem to be consistent with the values commonly used in daily clinical practice.

For the parameters MTF_{cutoff}, $Strehl^{2D}$ ratio, $OV_{100\%}$, $OV_{20\%}$ and $OV_{9\%}$, which account for the optical quality of the eye, the upper limit found has no clinical significance (it is the lower limit rather than the upper limit that matters when distinguishing normal from abnormal performance). The lower limit of normal for the MTF_{cutoff} was 30.54 cpd. A similar value was expected, as it is usually assumed that a 30 cpd cutoff frequency in the CSF corresponds to 6/6 visual acuity.[35] For the $Strehl^{2D}$ ratio, the lower limit of normality was 0.15. This value closely agrees with that found by other authors in young eyes, which measured Strehl ratios of 15 per cent for a 4.0 mm pupil in the fovea.[27] For the OVs, the criteria of normal probability established the following lower limits: 1.01 ($OV_{100\%}$), 0.95 ($OV_{20\%}$), and 0.88 ($OV_{9\%}$). As these parameters are normalised so that the values obtained are comparable to standard decimal visual acuities,[11] values similar to or higher than 1 are usually associated with high optical quality. A slightly larger variability between subjects was observed for parameters related to low contrasts, such as $OV_{20\%}$ and $OV_{9\%}$ (Table 2). Among the 181 evaluated eyes, only five (MTF_{cutoff}), 0 ($Strehl^{2D}$ ratio), 5 ($OV_{100\%}$), 3 ($OV_{20\%}$) and 1 ($OV_{9\%}$) eyes were located outside the specified normal ranges.

For the objective scatter index, the upper normal limit established (0.75) is the one with clinical relevance, as it quantifies the amount of scattered light present in the eye. This parameter has been used in previous studies to establish an objective gradation for cataracts.[28] The studies concluded that, in general, objective scatter index values below 2 are usually recorded in eyes with low scattering, values from 2 to 5 correspond to eyes with moderate diffused light and values above 5 are usually linked to eyes with very high scattering, such as eyes with a mature cataract. In our study, only four eyes were over the specified upper normal range.

Previous studies have demonstrated that intraocular scattering is highly affected by the subject's age.[22,23,36] In this work, the objective scatter index was also shown to be influenced by age (a p value of 0.001

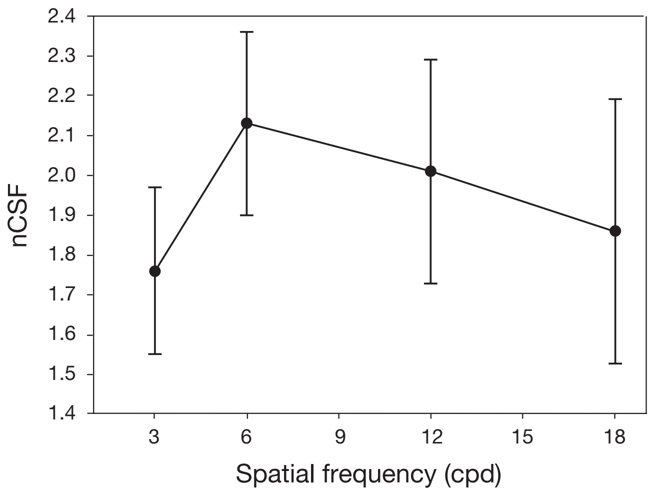

Figure 3. nCSF profile calculated from the double-pass images and the measured contrast sensitivity function. The mean and standard deviation are provided for spatial frequencies of 3, 6, 12 and 18 cpd.

Parameter	Sex	Eye	n	Mean		SD		Range (Min-max)	Normal limits
nCSF 3 cpd	F	R	45	1.77	1.76	0.22	0.21	1.27–2.30	1.35–2.17
		L	57	1.75		0.22			
	M	R	41	1.75		0.20			
		L	38	1.74		0.20			
nCSF 6 cpd	F	R	45	2.08	2.13	0.25	0.23	1.40–2.78	1.68–2.58
		L	57	2.15		0.22			
	M	R	41	2.12		0.22			
		L	38	2.15		0.21			
nCSF 12 cpd	F	R	45	1.94	2.01	0.25	0.28	0.99–2.85	1.46–2.56
		L	57	2.05		0.31			
	M	R	41	2.02		0.28			
		L	38	2.00		0.26			
nCSF 18 cpd	F	R	45	1.85	1.86	0.34	0.33	0.73–3.07	1.21–2.51
		L	57	1.89		0.30			
	M	R	41	1.83		0.35			
		L	38	1.85		0.34			

Table 3. nCSF (Log) at different spatial frequencies. Sex, eye (R/L), number of samples (n), mean, standard deviation (SD), range (minimum-maximum) and upper and lower normal limits (at the 95% level of agreement) are specified.

was found when we analysed the influence of the subject's age on the results). A wider range of ages should be analysed to establish the correct relationship between these two variables, due to the limited range of ages analysed in this study.

The results obtained for the nCSF showed that the visual system has its maximum efficiency in intermediate frequencies at the neural stage, as expected (Table 3, Figure 3). The mean results obtained are very close to those previously found for other authors that directly measure the nCSF using the interference fringe technique[37] and a laser interference system,[38] as well as those indirectly calculated from the modulation transfer function measured by means of laser ray tracing.[39] The lower limits of normal proposed in this study are in general less restrictive than the standard 95% confidence limits used in some of these works.

In conclusion, these results show the usefulness of the double-pass technique in evaluating the optical quality of the eye by means of the modulation transfer function and related parameters as well as the intraocular scattering. The study allowed us to establish the normal limits in healthy young subjects for the objective optical quality and intraocular scattering parameters provided by the double-pass system, which may facilitate addressing patients' ocular problems. Our data provide a new basis for evaluating optical quality in clinical environments and can be a reference for discriminating healthy from early abnormal eyes, in which the optical quality or sensory function is impaired. Furthermore, we demonstrated that the double-pass technique is a powerful tool for correctly predicting the nCSF. The data gathered here are representative of healthy young adults. Future studies in this area should focus on other age ranges.

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CONFLICT OF INTEREST

Dr Jaume Pujol is an investor and consultant for Visiometrics SL. The other authors have no conflict of interest with the companies of instruments used in this study.

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