Variability of Higher Order Wavefront Aberrations After Blinks

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ABSTRACT

PURPOSE: To investigate the rapid alterations in value and fluctuation of ocular wavefront aberrations during the interblink interval.

METHODS: Forty-two volunteers were examined with a WASCA Wavefront Analyzer (Carl Zeiss Meditec AG) using modified software. For each subject, 150 images (about 6 frames/second) were registered during an interblink period. The outcome measures were spherical and cylindrical refraction and root-mean-square (RMS) values for spherical, coma, and total higher order aberrations. Fifth order polynomials were fitted to the data and the fluctuation trends of the parameters were determined. We calculated the prevalence of the trends with an early local minimum (type 1). The tear production status (Schirmer test) and tear film break-up time (BUT) were also measured.

RESULTS: Fluctuation trends with an early minimum (type 1) were significantly more frequent than trends with an early local maximum (type 2) for total higher order aberrations RMS (P= .036). The incidence of type 1 fluctuation trends was significantly greater for coma and total higher order aberrations RMS (P= .041 and P= .003, respectively) in subjects with normal results in the BUT or Schirmer test than in those with abnormal results. In the normal subjects, the first minimum of type 1 RMS fluctuation trends occurred, on average, between 3.8 and 5.1 seconds after blink.

CONCLUSIONS: We suggest that wavefront aberrations can be measured most accurately at the time after blink when they exhibit a decreased degree of dispersion. We recommend that a snapshot of wavefront measurements be made 3 to 5 seconds after blink. [J Refract Surg. 2009;25:59-68.]

The wavefront analyzer is an important diagnostic tool in modern refractive corneal ablation surgery. New excimer lasers, wavefront analyzers, and a precise knowledge of the features of ocular higher order aberrations are premises for the successful outcome of treatment.

The role of the oculist is to explore the physiological characteristics of ocular aberrations. The age-dependent changes in aberrations can cause difficulties in predicting the long-term effectiveness of refractive surgery.1,2 Moreover, the short-term variability of ocular aberrations can hamper their exact measurement. For example, the accommodation process mostly influences the spherical aberrations,3 and it is well known that tear film break-up also affects the wavefront map (eg, the videokeratographic map).4-7 Changes in topographic results in the early period after blink have been well described,8-10 but relatively little information is available concerning alterations in the total ocular aberrations measured with a wavefront analyzer in this period. Snapshot wavefront measurements are usually made in the first few seconds after blink.

To our knowledge, the first published results on sequential wavefront measurements in the early interblink period were those of Koh et al,11 who distinguished three different patterns of alteration.

These previous results stimulated us to investigate the early changes in ocular wavefront aberrations after blink with a high number of wavefront images per second. The aims of the present study, therefore, were to examine changes in the...
total ocular wavefront aberration after blink in young volunteers, and to determine the time or period suitable for preparation of snapshots with the wavefront analyzer; these results may furnish a good reflection of the refractive characteristics of the examined eye.

MATERIALS AND METHODS

STUDY PARTICIPANTS

Forty-two volunteers participated in this prospective study, which followed the tenets of the Declaration of Helsinki. All participating subjects were advised of the nature and aims of the examination, and signed informed consent was obtained. The study was approved by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics.

No participant had any known ophthalmic disease. Each person underwent slit-lamp examination of the anterior segment, and uncorrected and best spectacle-corrected visual acuity was determined. Exclusion criteria were ocular trauma, previous ophthalmological surgery, acute allergy with eye symptoms, diabetes mellitus, keratoconus, or cataract. Soft contact lens wear was stopped at least 3 days before the investigation. Five women who were taking oral contraceptive pills were not excluded.

Tear status was detected by means of the Schirmer test without anesthesia and by measuring the tear film break-up time (BUT). The results of the Schirmer test at 1, 3, and 5 minutes were recorded. The tear BUT was determined by a fluorescein-imbibed strip technique. A normal tear status was defined as a Schirmer value $\geq 10$ mm after 5 minutes, BUT $\geq 10$ seconds, and no fluorescein staining. The Schirmer test and BUT determination were performed after the wavefront measurements to avoid any effects of these examinations on the tear film. The participants were asked whether they had any subjective eye symptoms in the past month before examination. The tear film status was classified on the basis of BUT and Schirmer tests, as subjective complaints are generally not in correlation with clinical signs.\(^1\)

EXPERIMENTAL PROCEDURE

Wavefront data were examined with a Hartmann-Shack wavefront aberrometer (WASCA Asclepion Zeiss Wavefront Analyzer, SW 1.41.6.; Carl Zeiss Meditec AG, Jena, Germany). The Zernike coefficients were determined up to the sixth order and spherical and cylindrical refraction were measured. To avoid instrument-induced myopia and spontaneous accommodation, a distant fixation target was used: green luminous spots were arranged in a circle with a diameter of 4 cm at a distance of 5 m. The humidity and temperature in the examination room were measured. The room was darkened and the measurements were taken under scotopic conditions because of the natural pupil dilatation. No pharmaceutical dilating agents were employed. All records were made between 1 and 5 PM to avoid diurnal fluctuations in the wavefront data.\(^1\)

The patient’s head was fixed by using a common head and chin rest and an adjustable supporting band stabilized from behind. By this means, movement of the head, especially the backward and forward deviations that could cause false results, was minimized.

A single record was first made on both eyes of the participants so they could become familiar with the apparatus and environment of the examination. The head of the subject was stabilized and he/she was asked to look straight ahead. The examined eye saw a red spot in the measuring apparatus, whereas the fellow eye looked at the fixation target. The position of the measuring apparatus was varied until the subject saw the red spot in the middle of the green circle. He/she was then asked to look at the distant fixation target and 150 images were registered during an interval of approximately 25 seconds. During the recording, the subject was asked to make a complete blink on the examiner’s request, keep his/her eyes open, and to fixate continuously. The subject was additionally asked not to speak or move during recording. If the subject was not able to keep his/her eyes open during examination, the recording was excluded and the examination procedure was repeated as the instability could have caused reflex tearing. The subjects were requested to blink several times between recordings to avoid influence of the previous examination on the tear film.

DATA ANALYSIS

The first part of the participants’ records, up to the complete blink, was removed. If the eye on the first image after the complete blink was not fully opened, this part was also removed. Only those records were used that did not include a complete or an incomplete blink in the first 15 seconds after the first requested complete blink.

Wavefront data were derived for a 4-mm diameter pupil. We analyzed the temporal changes in the spherical and cylindrical refractions, as well as coma, spherical, and total higher order root-mean-square (RMS) values. Spherical and coma RMS were calculated (the root of the sum of the squares) from the coefficients $Z_0^0$, $Z_0^0$, and $Z_0^1$, $Z_1^0$, $Z_1^0$, and $Z_1^1$, respectively.\(^1\) The total higher order aberrations RMS included all coefficients from the third to the sixth order. The wavefront aberrometer was not able to...
record sequential measurements with fixed frequency, but the times of measurements were detected with 10^{-2}-second accuracy.

The mean value and range of the measured parameters were calculated in 3-second periods (Fig 1), which demonstrate the general pattern of alterations in refractive errors and aberrations of the whole examined population. The differences of the mean values and ranges between 3-second periods were analyzed with Fisher’s sign test (STATISTICA, version 7.1; StatSoft Inc, Tulsa, Okla). A P value <.01 was regarded as statistically significant due to multiple comparisons.

To analyze the individual characteristics, fifth-order polynomial trend lines were fitted with commercial statistical software (SPSS, version 12.01 for Windows; SPSS Inc, Chicago, Ill) by polynomial regression to the first 15-second sequence of the time series parameters. The polynomials were called value trends (Fig 2A). The suitability of the order of polynomial trends was analyzed on the basis of residual plots and number of extremes, and was found to be appropriate. The fluctuation around the value trends was assessed by the absolute differences between the original data and the value trend line (see Fig 2A). The changes in time of the fluctuation were modeled by fifth-order polynomials fitted by ordinary polynomial regression to the absolute differences. Note that in short time intervals where the value trends are nearly constant, the fluctuation trends approximate the average absolute differences (mean deviations). Therefore, the fluctuation trends can be interpreted as mean deviation trends. The order of the fluctuation polynomial trends was again fitted on the basis of residual plots.

The first local minimum and maximum values in each polynomial trend line were determined. Extremes at least 10% smaller or larger than the first value of the trend were called relevant local minimum or maximum, respectively. Trends were regarded as regular trend lines if they had a relevant local minimum or maximum value after the first 0.5 second, but before the last 0.5 second of the examined 15-second period. In this way, we rejected the excessively small changes and artifacts due to the well-known type of mathematical modeling error that is common at the beginning or end of the time domain in regression models. We determined the rate of trend lines that had a local relevant minimum value before a local relevant maximum or had only a local relevant minimum. These trends were regarded as type 1 (see Fig 2). Regular trends, which had only a relevant maximum pattern or had a first local relevant maximum before a relevant minimum, were regarded as type 2 (see Fig 2). The fluctuation trends allowed the classification of different fluctuation types and made possible the examination of correlation between tear film status and alterations in higher order aberrations.

We examined the percentage of type 1 value trend occurrences among the records with type 1 fluctuation trends. Exact binomial tests were applied for the analysis. A P value <.05 was regarded as statistically significant.

We compared the examination outcomes of participants with a normal tear status and those that had abnormal BUT or Schirmer test results. The rates of
different type trends among groups were compared by means of Fisher’s exact test. A P value <.05 was regarded as statistically significant.

**RESULTS**

In 11 of the 42 volunteers, we noticed failure during the sequential measurement; records did not contain the first purposeful complete blink in 4, and 7 participants were not able to keep his/her eyes open during the record, which contained involuntary complete or incomplete blinks. These failures did not show correspondence with tear film status. Seven participants had correct recording in repeated examination, but finally we excluded 4 of the 11. We succeeded in recording suitable sequential measurements of the right eyes of 38 participants (20 women and 18 men), with a

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**Figure 2.** Total higher order aberrations root-mean-square (RMS) values (thin dashed lines) with the fitted value trends (bold dashed lines) showing absolute differences between the original data and the value trend line (thin dotted lines) and the fitted fluctuation trends (bold dotted lines). **A** Represents a value trend with fluctuation trends of a 25-year-old woman with normal tear status. **B** Represents a value trend with fluctuation trend of a 20-year-old man with normal tear status. **C** Represents a value trend with fluctuation trend of a 26-year-old man with abnormal tear status. **D** Represents a value trend with fluctuation trend of a 24-year-old woman with normal tear status.
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mean age of 25.1 ± 2.6 years (range: 20 to 30 years). The average temperature and humidity in the examination room were 26.8 ± 1.5°C and 31.9 ± 7.9%, respectively. Mean uncorrected visual acuity was 20/50 (logMAR; 0.35) for the right and 20/50 (logMAR; 0.37) for the left eyes. The range of spherical equivalent refractive error was from −6.25 to 0.25 diopters (D) for the right and from −7.50 to 0.0 D for the left eyes. Best spectacle-corrected visual acuity of each of the included subjects was 20/20 (logMAR; 0). Three subjects reported eye symptoms during the month before examination. One woman reported occasional itching, one man reported eye dryness with tiredness despite normal tear status, and another woman had eye tiredness with abnormal tear status.

Mean values of the 3-second periods did not exhibit significant differences in the first 15 seconds after blink, except in cases of spherical refractive error (Fig 3). For the cylindrical diopter and coma and total higher order aberrations RMS, the range of measured data decreased significantly after the first 3 seconds (Fig 4).

For all examined parameters, the rates of type 1 trends among the regular value trends were >50%, but significantly >50% only in the case of the cylindrical refractive error (P = .011) (Table 1). In the course of statistical analysis of the spherical refractive error, the results on one subject were rejected because the sign of his spherical diopter changed and an artificial minimum value appeared. The proportions of the type 1 trends among the regular fluctuation trend lines were at least 50% for all parameters and significantly >50% for total higher order aberrations RMS (P = .036) (Table 1). The percentages of the type 1 value trend occurrences among the records with type 1 fluctuation trends were >50%, and the results of the cylindrical refractive error were statistically significant (P = .029) (Table 1).

The percentages of the type 1 fluctuation trend for total higher order aberrations and coma RMS were significantly higher for the subjects with normal tear status than for those with abnormal results (P = .003 and P = .041, respectively) (Table 2). Average times of the first local minimum of the type 1 value and fluctuation trends for subjects with normal tear status are presented in Figure 5. Average times
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were unable to analyze the difference in time of the first local minimum of type 1 trends between subjects with a normal or an abnormal tear status due to the small number of cases.

**DISCUSSION**

Ocular higher order aberrations display short time variability, which limits designed wavefront-guided refractive surgery. In earlier studies, Mirshahi et al.19 and Cheng et al.20 had found that the repeatability of Hartmann-Shack aberrometry was not satisfactory, but more recent authors reported better results.21,22 Our own investigation demonstrated broad ranges of coma and total higher order aberrations RMS relative to the mean value in the first 3 seconds, but the range of measured data narrowed after the first few seconds.

These averaged results are easy to survey, but they conceal the individual characteristics of the examined volunteers, which were revealed by the trends. In addition, a great range could be caused by monotone decrease or increase of values or great fluctuation, and the usage of the trends took rigorous analysis. The value and fluctuation trends were easy to analyze and utilized the extra information from frequent measurements. Regarding the RMS value trends, we did not detect a typical pattern among the examined population. Only for the fluctuation trend of total higher order aberrations RMS was the type 1 pattern seen for a larger proportion of the individual participants. This type 1 fluctuation trend followed the pattern of averaged results. However, the participants with normal tear status exhibited mostly type 1 fluctuation trends in coma and total higher order aberrations RMS. In the normal subjects, the average times of the first minimum of the type 1 RMS fluctuation trends were between 3.8 and 5.1 seconds after blink. Thus, estimation of the mean values of coma and total higher order aberrations RMS via snapshot wavefront measurements may involve greater error in the first few seconds than in 3 to 5 seconds after eye opening.

**Figure 4.** A) Average range (black circles) of wavefront total higher order aberrations (HOA) root-mean-square (RMS) in 3-second periods after blink. Solid black lines indicate total higher order aberrations RMS, dashed black lines indicate coma RMS, and dotted black lines indicate spherical RMS. Solid and dashed gray lines indicate statistically significant differences (P<.006 [*], **, ***, †, ††) by multiple comparisons with Fisher’s sign test. B) Average range (black circles) of refractive errors in 3-second periods after blink. Solid and dashed black lines indicate cylindrical and spherical refractive errors, respectively. Solid gray lines indicate statistically significant differences (P<.0007 [§, §§, §§§, §§§§] by multiple comparisons with Fisher’s sign test).
Our results may be particularly valuable relating to the measurement of coma RMS. Lewis and Krueger reported that the standard deviation of coma aberrations was largest in repeated measurements: 37% of the mean coma RMS value. Faithful determination of coma aberrations is important in refractive surgery. These aberrations are related to symptoms such as double vision. Oshika et al found that the value of coma-like aberrations may be correlated with the loss of contrast sensitivity in normal patients. The importance of our results is determined by the technical limits of customized corneal ablations, which may be revised by the outcome of technical developments aimed at optimizing excimer laser appliances.

There are many possible causes of the typical pattern of changes. Cheng et al reported that the short time variability in human wavefront aberrations reflects the instability of the tear film, microfluctuations of accommodation, and small fixational eye movements. The most obvious reason may be tear film alterations. Montés-Micó et al observed a decrease–increase–type trend in the temporal changes in corneal coma-like and total higher order aberrations RMS measured by videokeratography in both normal and dry eye patients. The time at which the minimum coma-like and total higher order aberrations RMS occurred correlated well with the measured tear BUT. Montés-Micó et al measured significantly higher ocular coma aberrations with a wavefront analyzer in dry eye patients as compared with normal patients. Koh et al also examined the early variations in ocular wavefront aberrations. They demonstrated the influence of the tear film dynamics on ocular aberrations measured with a wavefront analyzer. Our results are in accordance with the conclusions of Montés-Micó et al and Koh et al. We found relationships between the type of the fluctuation trends of coma and total ocular higher order aberrations RMS and tear film dynamics. The type 1 trend may describe the process in which the tear layer reached its most regular state a few seconds after blink and from that point started thinning. We consider that the surface will be the most regular when the lipid layer spreads over the surface; the tear layer builds up and a steady state evolves. It does not necessarily follow that decreased values of wavefront aberrations can be measured in this state but, despite the fluctuation, we may determine the ocular aberrations with a wavefront analyzer are more accurate at this time than earlier or later. The wavefront aberrometer measures aberrations of the whole eye, in contrast with the videokeratograph, which examines the anterior surface of the cornea and can detect changes in the tear film more directly. The effect of the tear film build-up process on a wavefront map may be more moderate than in videokeratography.

In this small, normal subpopulation with abnormal tear status, we can not distinguish whether the qualitative (BUT) or the quantitative (Schirmer) tear abnormality is accountable for the type 2 fluctuation trend. However, Montés-Micó et al found correlation between the tear BUT and the time at which minimum corneal higher order aberrations was observed. Additionally, Koh et al found a maximum spike in total higher order aberrations and coma-like RMS during the first seconds after blink in a 42-year-old woman after punctal occlusion, which was caused by excessive retention of tear film. On the basis of these results, it seems that the quality of tear film shows correlation with the temporal procession of changes in higher order aberrations after blink and the quantity of tear film exercises an influence on the pattern of the alteration. Further studies are necessary to examine the changes in the patients.
Higher order aberrations after blink in numerous dry eye patients classified according to the damaged glands and tissues.29

The accommodation process also has a considerable influence on refractive error. We could not completely preclude the possibility of the effects of accommodation on the temporal changes in ocular aberrations in our study. Cheng et al3 found that spherical aberration, coma, and primary astigmatism varied with accommodation, but the direction and value of the change in the spherical aberration were only proportional to the change in the accommodation response. In our study, we employed a distant fixation target to avoid accommodation, and the largest alteration during an interblink period was smaller than 1.00 D. Cheng et al3 concluded that higher order aberrations (excluding defocus) changed the accommodative level only moderately up to 3.00 D. Similar to the studies of Koh et al11 and Montés-Micó et al,30 we did not use cycloplegic drops due to the possibility that the components could influence the results of measurements. The influence of small eye movements requires further examination.

Using a wavefront analyzer, Ginis et al31 found a higher instrument noise level for a 3-mm pupil with a “direct” method of recalculation than when a “scaling” method of recalculation was used. This was attributed to the reduced number of sensor elements (approximately 600 sample points within a diameter of 6 mm and 150 sample points within 3 mm). They stated that the wavefront changes related to tear film quality did not interfere with the detected dispersion in the early period. We used the standard software procedure to recalculate the data and determined the Zernike coefficients for a pupil diameter of 4 mm. This method could induce variance in the measurement of the higher order aberrations coefficient. The number of sensor elements involved in the measurement was more for a 4-mm than for a 3-mm pupil, so the fitting

### TABLE 2

<table>
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<tr>
<th>Parameter Tear Status</th>
<th>Type 1 Fluctuation Trends (n) (%)</th>
<th>Type 2 Fluctuation Trends (n) (%)</th>
<th>Total Number (%)</th>
<th>P Value</th>
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<td>12 (50)</td>
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<td>Abnormal</td>
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<td>3 (37.5)</td>
<td>8 (100)</td>
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<td>Total</td>
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<td>Total HOA RMS</td>
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<tr>
<td>Total</td>
<td>23</td>
<td>14</td>
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NS = not significant, HOA = higher order aberrations, RMS = root-mean-square
*Statistically significant.
error was moderate. A pupil diameter of 4 mm was the largest that could be used without exclusion of any subjects. We did not employ any pharmaceutical dilating agents as these drops might exert a troublesome effect on the tear film.

Our results were variable and did not show rigorous resemblance among the participants, as can be seen in the results of Montés-Micó et al. The tear film alteration, microfluctuations of accommodation, small eye movements, and instrument noise also influence the variability of wavefront measurements. The typical pattern in the fluctuation of aberrations is mostly caused by the tear film, whereas other factors produce temporary additional changes.

In contrast with higher order aberrations, fluctuation trends of the spherical and cylindrical refractive errors did not exhibit typical trends. We found a significantly higher rate of type 1 value trends only in the cylindrical refractive error. The percentages of the type 1 value trend occurrences among the records with type 1 fluctuation trends were high, but we did not detect a relation between the tear status and the cylindrical refraction results. The interpretation of these results necessitates additional examination.

As far as we are aware, this was the first examination of temporal changes in the fluctuation of aberration measured with a Shack-Hartmann wavefront aberrometer. The new outcome of this study was the determination of a regular pattern of the temporal changes in the fluctuation of ocular wavefront aberrations. It is important to establish a period suitable for creation of the preoperative snapshot of the wavefront map used to correct ocular higher order aberrations. Knowledge of this common, regular pattern allows a more reliable wavefront map to be made before refractive surgery. In this study, we did not examine the repeatability of the changing pattern. However, the great prevalence of the type 1 fluctuation trend in normal patients predestines the great incidence of this pattern in repeated examination. Comparative studies would be useful to find the optimal period after blink in which to capture the wavefront map for the best outcome of customized corneal refractive surgery. It is necessary to examine the repeatability of a wavefront map in different periods after blink.

It appears advisable to produce several snapshots

Figure 5. Average times of minimum values of A) type 1 fluctuation and B) value trends in volunteers with normal tear status. RMS = root-mean-square, HOA = higher order aberrations, SE = standard error, SD = standard deviation
of the wavefront map before refractive surgery, recorded at approximately equal intervals after blink. We suggest this interval be about 3 to 5 seconds.

REFERENCES


