Dynamic Changes in Ocular Zernike Aberrations and Tear Menisci Measured with a Wavefront Sensor and an Anterior Segment OCT

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PURPOSE. To measure dynamic change characteristics of spatial and temporal variations in the post-blink tear film of normal eyes.

METHODS. A wavefront sensor was used to measure dynamic changes in wavefront aberrations, up to the seventh order, for 10 seconds in a group of 33 normal young adults. Tear menisci were imaged with an anterior segment optical coherence tomography (AS-OCT) system and tear film break-up times (TFBUTs) were determined.

RESULTS. Systematic changes in main axis astigmatism ($R^2 = 0.933$, $P < 0.0001$), vertical coma ($R^2 = 0.935$, $P < 0.0001$) and spherical aberrations ($R^2 = 0.879$, $P = 0.0002$) occurred during the 10-second post-blink period. Both lower tear meniscus height and area increased by 10 seconds compared with the initial levels ($P < 0.0001$ for each). The change of vertical coma had significant correlation with the increase of lower tear meniscus areas during the 10-second post-blink period ($R^2 = 0.181$, $P = 0.014$). Subjects with TFBUTs $< 15$ seconds had significantly increased main axis astigmatism, vertical coma, and spherical aberrations by 10 seconds. Subjects with longer TFBUTs did not have any significant wavefront aberrations during that period.

CONCLUSIONS. Systematic changes in some Zernike aberrations after blinking are associated with the changes in tear menisci and TFBUT. There was a substantial individual variation in dynamic changes of Zernike aberrations, suggesting the necessity to explore individual differences in tear quality and tear performance. Dynamic wavefront measurement combined with anterior segment optical coherence tomography could provide a useful tool to understand spatial and temporal processes of the tear film in clinical practice. (Invest Ophthalmol Vis Sci. 2011;52:6050–6056) DOI:10.1167/iovs.10-7102

The optical system of the human eye is a component structure with the most anterior optical part consisting of a thin layer of tear film.1 The tear film is formed by blinking, through which tears that have accumulated in the tear menisci are spread over the corneal epithelium. The geometrical structure of the tear film, however, is by no means stable but constantly changes over time. Immediately after a blink, the tear film builds up quickly and then starts to thin due to a complex process involving evaporation, dewetting, surface tension gradients, and pressure-gradient flow of the tears.2 When the eye is opened for a sufficiently long period, the tear film breaks up at spots over the corneal surface.2 Both dynamic thinning and break-up of the tear film degrade the optical quality of the eye and consequently disturb visual performance.4–7 Break-up of the tear film can also generate problems for the cornea because the tear film moistens the cornea and protects it from invasion of microbes.8 Therefore, the study of tear film dynamics is of importance not only for understanding the optics of the eye but also for healthy care of the cornea.

Characterizing dynamic changes of the tear film, however, is challenging because the tear film is very thin, measured in micrometers, and it changes within seconds. In addition, the shape of the tear film is three-dimensionally irregular and locally inhomogeneous in its thickness, perhaps associated with the irregular shape of the anterior corneal surface.9 The irregularity of the tear film contributes to local differential changes from one area to another and makes it very difficult to be quantified.

Temporal change of the tear film has been traditionally assessed by its break-up time (BUT). In clinical practices, invasive observation with a slit-lamp combined with fluorescein instillation is still a widely used technique, while other methods are believed to be more precise due to their noninvasive nature.10 Further, the break-up time measurement does not provide any information about the temporal change of the tear film during the post-blink period, and it does not help to explain the localized nature of the tear film break-up.

Recent progress in optical coherence tomography (OCT) has made possible the in vivo imaging of tear film thinning.11,12 By using a real-time anterior segment OCT with an ultra-high axial resolution (approximately 3.0 μm), Palakuru et al. found that the tear film thickness increases significantly after each blink and then decreases when the eye blinked again in either a normal- or delayed-blinking paradigm.12 Under the delayed-blinking paradigm, tears in both upper and lower tear menisci increased in height and area after the eye was opened for a while. A recent study on normal eyes showed that the tear film thickness and the lower tear meniscus dimensions are correlated with the viscosity of artificial tears.13

Corneal topography is a traditional technique for assessing corneal geometrical properties by making use of the light reflected from the tear film. Therefore it is now possible to determine tear film stability from topographic variations.14–16 By continuously monitoring local variation in corneal power with a time resolution of one second, Goto et al. found that the tear film was more stable in the normal eyes than in the dry eyes.
eyes, as would be expected.\textsuperscript{14} Although the estimate of overall variation in corneal power provides a general measure of tear film stability, the result still did not show detail patterns of the local change in the tear film. By applying wavefront analysis of corneal measurements, Montes-Mico et al. were the first to successfully assess dynamic change in tear film shape from variations in corneal Zernike aberrations.\footnote{16} They found that after a blink, the tear film shape progressively changed from prolate to oblate. Rotationally asymmetric change in the tear film was also present due to a temporal variation in coma-like aberrations.

Recently, the Hartmann-Shack (HS) wavefront technique was used to continuously test dynamic variation in wavefront aberrations of the whole eye as an indirect measurement of the tear film performance. Continuous measurement of wavefront aberration is capable of assessing the tear film behavior because the tear film contributes to wavefront aberrations of the whole eye.\textsuperscript{7,17,18} Spatial change in the tear film is reflected in variation of wavefront aberrations as measured by the wavefront sensor. In a recent study,\textsuperscript{19} the HS wavefront sensor was combined with an anterior segment OCT (AS-OCT) system to simultaneously assess dynamic changes of the tear film. Changes in the root-mean-square (RMS) of the wavefront aberrations were positively correlated with the changes in tear meniscus dimensions in both normal and dry eye groups. However in that study, the relationship between the OCT measurements and the individual Zernike aberrations was not tested, and thus the specific spatial pattern of the tear film change was not examined. The aim of this study was to assess the dynamic change in Zernike aberrations of the whole eye in young normal subjects. Further, we explored the relationship of the changes in individual Zernike aberrations with changes in OCT measurements by using both AS-OCT and HS wavefront sensing.

**Subjects and Methods**

**Subjects**

Thirty-three healthy subjects who were students from the Optometry and Ophthalmology School in Wenzhou Medical College, Zhejiang, China, were enrolled in this study. None of them wore contact lenses in the preceding six months, and none had any eye complaints. Each one was given a full explanation of the whole procedure and signed an informed consent statement before participating in this study. This research was conducted in accordance with the tenets of the Declaration of Helsinki and the guidelines of Wenzhou Medical College Review Board. The subjects (15 male and 18 female) had a mean ± SD age of 23.0 ± 1.9 years (range, 21 to 29 years). Each subject completed a McMonnies dry eye survey, and for each, the total score was much lower than the critical score of 15. The mean score was 4.3 ± 2.9. Slit-lamp biomicroscopy and retinoscopy was performed for each subject, and no subject had any ophthalmic abnormalities. No histories of ocular diseases, trauma, or abnormal best corrected visual acuity were reported. The right eye of each subject was tested by the same examiner between 10:00 AM and 4:00 PM in a dim room where the temperature and humidity were controlled.

**Measurement of Wavefront Aberration**

Wavefront aberration was measured using a HS wavefront aberrometer (WASCA Asclepion Zeiss Wavefront Analyzer; Carl Zeiss Meditec AG, Jena, Germany). A multifocal acquisition mode was set to acquire the HS image at a speed of one test per second during a one-minute period. The subjects were asked to keep their heads stable and to hold their eyes open as long as possible once the test was started. During the test, each subject was instructed to fixate on a red target inside the machine while his/her eye was monitored by a video camera. At the end of the test, the examiner would check the blink recorded by the video camera and also the blink recorded by the wavefront sensor. If the blink numbers did not match, the data were excluded and another test was done 5 minutes later, but no more than three tests were taken within an hour.

**Measurement of Lower Tear Menisci**

Three edge touchpoints for deriving the lower tear meniscus height (LTMH) and lower tear meniscus cross-sectional area (LTMA).

**Measurement of Tear Film Break-up Time**

For this study population, the NITFBUT was 22.6 ± 17.86 seconds, which was not significantly different from the ITFBUT, 16.7 ± 13.40 seconds (P = 0.135). The NITFBUT was positively correlated with the ITFBUT (R² = 0.526, P < 0.001). Dynamic Changes in Zernike Aberrations

Our subjects were asked to keep their eyes open as long as possible once the experiment was started. The duration of the open eye period varied from one subject to another. Subjects with longer NITFBUTs and ITFBUTs tended to have longer interblink intervals (NITFBUT: R² = 0.345, P < 0.001; ITFBUT: R² = 0.301, P = 0.001). Every subject was able to maintain an open eye for at least 10 seconds before blinking; therefore we used data from that interval for further analysis.

For each wavefront measurement, 35 terms of Zernike coefficients of up to the seventh order were derived. Only Zernike aberration terms of the second order (Z\textsubscript{2,0} and Z\textsubscript{2,1}; oblique astigmatism; Z\textsubscript{2,2}, main axis astigmatism), third order (Z\textsubscript{3,0}, Z\textsubscript{3,1}, Z\textsubscript{3,2}, Z\textsubscript{3,3}, Z\textsubscript{3,4}, Z\textsubscript{3,5}), and fourth order (Z\textsubscript{4,0}, Z\textsubscript{4,1}, Z\textsubscript{4,2}, Z\textsubscript{4,3}, Z\textsubscript{4,4}, Z\textsubscript{4,5}, Z\textsubscript{4,6}) were considered in the analysis. The terms of Zernike aberrations within the 6.0 mm pupil diameter were derived from the wavefront sensor. Differences in mean values were tested using a paired sample t test. Correlations between measurements were analyzed with Pearson correlation analysis. These analyses were performed with statistical software (Statistical Procedures for the Social Sciences version 13.0 for Windows XP, SPSS Inc., Chicago, IL, USA.).

**Results**

**Tear Film Break-up Time**

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vertical coma; $Z_3^{-1}$, horizontal coma; $Z_3^{-3}$ and $Z_3^{-5}$, trefoil), and fourth order ($Z_4^0$, spherical aberration) make the largest contributions to the overall wavefront aberration. Therefore, we determined the results mainly for these aberration terms.

There was a substantial individual variation in the dynamic change of the Zernike aberrations. Dynamic changes occurred in Zernike coefficients of the second order ($Z_2^2$ and $Z_2^{-2}$, the astigmatism terms; Fig. 1, left panel), third order ($Z_3^{-5}$, $Z_3^{-1}$, $Z_3^1$, and $Z_3^3$, the trefoil and coma terms; Fig. 1, middle panel), and fourth order ($Z_4^0$, the spherical aberration term; Fig. 1, right panel) during the first 10-second postblink period. The data were assigned individual symbols for the different Zernike terms at each second, and the change trend was fitted with a second order polynomial function from the first second of the test. For some subjects, such as SWY and ZA, there were obvious changes in the Zernike terms (Fig. 1), especially in $Z_3^{-3}$, $Z_3^{-1}$, and $Z_4^0$, while other subjects, such as XCB and FJX, showed less variation.

In spite of substantial individual variation in Zernike aberration changes, systematic changes in some of the Zernike terms were observed for the 33 subjects (Fig. 2). There was a significant change toward a more negative direction in the main axis astigmatism $Z_2^2$ ($R^2 = 0.933, P < 0.0001$; Fig. 2, left panel) for this group of subjects while the oblique astigmatism $Z_2^{-2}$ was quite stable. The trefoil term $Z_3^{-3}$ and vertical coma $Z_3^{-1}$ both increased significantly during the 10-second period ($Z_3^{-3}$: $R^2 = 0.854, P = 0.003; Z_3^{-1}$: $R^2 = 0.935, P < 0.0001$; Fig. 2, middle panel). Meanwhile the trefoil term $Z_3^3$ and horizontal coma $Z_3^1$ were quite stable without showing any significant change. Spherical aberration $Z_4^0$ for this group of subjects increased significantly ($R^2 = 0.879, P = 0.002$; Fig. 2, right panel). The mean value of $Z_2^2$ decreased by 0.0262 μm by 10 seconds ($P = 0.022$).

**Figure 1.** Representative changes in seven Zernike aberrations during the 10-second postblink period for four normal subjects (SWY, ZA, XCB, and FJX). *Left*: dynamic changes of $Z_2^2$ (oblique astigmatism) and $Z_2^{-2}$ (main axis astigmatism). *Middle*: dynamic changes of third order (trefoil, vertical coma, horizontal coma, and trefoil respectively). *Right*: dynamic changes of $Z_4^0$ (spherical aberration).
while the vertical coma $Z_{31}$ was significantly increased by 0.0275 μm ($P = 0.019$). The mean values of both $Z_{33}$ and $Z_{40}$ at the 10-second point were also different from their corresponding initial values, but the differences were not significant ($P = 0.109$ and $P = 0.226$, respectively).

For all subjects, the variation of $Z_{40}$ was negatively correlated with NITFBUT and ITFBUT ($R^2 = 0.127$, $P = 0.042$; $R^2 = 0.147$, $P = 0.027$, respectively). Furthermore, ITFBUT was negatively correlated with changes of $Z_{33}$ ($R^2 = 0.150$, $P = 0.039$).

We divided our subjects into subgroups according to TF-BUTs. One group was composed of subjects ($n = 16$) with NITFBUT shorter than 15 seconds, and the other group was composed of subjects ($n = 17$) with NITFBUT equal to or greater than 15 seconds. There were differences in dynamic behavior of the Zernike aberrations of the two subgroups (Fig. 3).

For the group with shorter NITFBUTs (Fig. 3A), $Z_{22}$ ($P = 0.024$) and $Z_{31}$ ($P = 0.009$) at 10 seconds were significantly higher than the initial values. In contrast, the aberrations were quite stable for the group with longer NITFBUTs (Fig. 3B).

Except for $Z_{33}$, there were also variations of the total root-mean-square (tRMS) of the aberrations from the second to seventh orders during the first 10 seconds (Fig. 4). For all 33 subjects, the tRMS slightly decreased in the early seconds after blinking and then gradually increased to a level higher than that at the beginning ($P = 0.032$; Fig. 4, left panel). Subjects with shorter NITFBUTs had a significant increase in tRMS during the entire 10-second test period ($P = 0.019$; Fig. 4, middle panel). For subjects with longer NITFBUTs, the tRMS did not increase until the ninth second (Fig. 4, right panel). The results could imply that the systematic changes in Zernike aberrations for the entire group, as observed in Figure 2, were mainly contributed from the subjects with relatively shorter NITFBUT.

Dynamic Changes in Lower Tear Menisci

In general, LTMHs and LTMA increased with time during the 10-second postblink interval for the majority of our subjects. As an example, dynamic change in LTMH and LTMA for subject LX was illustrated in Figure 5, where the increase in tear dimensions with the time was clearly exhibited ($R^2 = 0.797$, $P = 0.004$ for LTMH; $R^2 = 0.924$, $P < 0.0001$ for LTMA). But, for our subjects, not everyone presented an increase in LTMH and LTMA, especially...
those with a relatively high baseline value of the LTMA. Overall, both LTMH and LTMA increased significantly by the end of the postblink interval (paired t test, $P < 0.0001$ for both, Table 1).

There was no significant correlation between the change in LTMA and the baseline LTMA. There was a weak negative correlation between the baseline LTMA and the ratio of LTMA and the baseline LTMA. There was a weak negative correlation between the change in LTMA and the ratio of LTMA and the baseline LTMA. There was a weak negative correlation between the tear film and the eyes with less baseline tear film. A faster change in the tear film might happen for the eyes with an initial high tear value than their initial values ($P = 0.034, P = 0.035$, respectively; Fig. 7). For the group with larger LTMA, there were no significant differences between the aberrations at 10 seconds and the beginning for any of the Zernike terms.

**DISCUSSION**

The structure of the tear film over the anterior corneal surface is neither temporally stable nor spatially regular. Adequate techniques with high time resolution and the ability to spatially assess irregular shapes are, therefore, required to precisely and accurately test tear performance. Wavefront analysis can assess complex spatial and temporal variation in optical structure, and thus provide a very interesting and useful method to investigate the tear behavior. However, in the majority of previous studies, analysis of wavefront dynamics was mainly focused on the RMS of the overall Zernike terms or the RMS of several specific Zernike terms, such as spherical-like or coma-like aberrations. In this study, we also analyzed the RMS change after blinking, as done in previous studies, and found similar patterns of RMS changes in the wavefront aberrations. However, while the RMS provides useful information about stability of the tear film, change in it does not specify local changes of the tear film that are already revealed in the changes of individual Zernike terms. Thus, the results of RMS analysis were not helpful in understanding the spatial variation of the tear film.

From the corneal Zernike aberrations derived from wavefront analysis, Montes-Mico et al. found systematic changes of the corneal Zernike spherical aberration during the postblink period. This indicated that the tear surface changed from prolate to oblate in shape after blinking. This type of tear film change was attributed to the thinning of the tear film more rapidly at the central area than at the periphery due to a greater rate of evaporation at the center of the palpebral aperture. In our study, from the measurements of wavefront aberrations in the whole eye, we found a trend for increased Zernike spherical aberration during the first 10 seconds of the postblink period. This result is consistent with the finding by Montes-Mico et al. and supports their approach.
hypothetical account about the mechanism underlying tear thinning processes. Interestingly, we also found that when subjects with shorter TFBUT were grouped together, they had significant increases in Zernike spherical aberrations during the 10-second postblink period. In contrast, the spherical aberration in the group with longer TFBUTs was quite stable. The difference in the change of spherical aberration between the two groups could imply that tears in eyes with shorter TFBUTs might evaporate faster than in eyes with longer TFBUTs.

There was a systematic increase in vertical coma ($Z_3^{-1}$) in this study for our subjects during the 10-second postblink interval, and it was accompanied with a decrease in the trefoil ($Z_3^{2}$), especially for the subgroup with shorter TFBUTs. The change could be due to a differential thinning of the tear film between the superior and inferior corneal area due to the effect of gravity, as suggested by Montes-Mico et al. 26

It might be of some concern that measurement of Zernike aberrations of the whole eye with the wavefront sensor alone is not adequate to characterize the dynamics of the tear film. This concern arises because aberrations of the whole eye are determined not only by the tear film but also by other post-tear factors such as the cornea and the crystalline lens. Thus, the dynamic change in spherical aberration and vertical coma as observed in this study might be due to a dynamic change in the cornea and lens. We have tested the dynamic change in tear dimensions and found a strong association between the changes in Zernike aberrations and the tear dimension. For example, the change in vertical coma was strongly correlated with the LTMA change. This result supports the idea that the dynamic changes in Zernike aberrations that we observed were closely linked to the dynamic changes of tear film. In addition, there was a correlation between the Zernike aberration change and NITFBUT. This further suggests that the change in Zernike aberrations is associated with the change in tear film shape. Thus, our results suggest that wavefront measurement of the whole eye is a useful method to explore tear film performance.

Based on the TFBUTs and the absence of symptoms, our subjects were normal with respect to dry eyes. However, as reflected in the change of Zernike aberrations, substantial individual variation in dynamic tear performance was observed among the 33 subjects. In contrast to subjects with NITFBUTs $\leq$ 15 seconds, subjects with NITFBUTs $>15$ seconds had $Z_2^{2}$ and $Z_3^{-1}$ aberrations that were significantly higher after 10 seconds. Similarly, in contrast to subjects with LTMA $>20,000 \mu m^2$, subjects with LTMA $<20,000 \mu m^2$ had $Z_2^{2}$ and $Z_3^{-1}$ aberrations that were significantly higher after 10 seconds. The results suggest that tear quality, and hence its behavior, differed from individual to individual among normal subjects, as suggested by Koh and Maeda.17 Thus some individuals with fast changes in Zernike aberrations might be at risk to develop dry eye. If this proves to be a reliable observation, the measurement of changes in dynamic wavefronts will be a very useful tool in dry eye diagnosis. Future study on this issue is therefore expected.

Conventional TFBUT tests characterize the tear stability in a general pattern. Changes in both wavefront aberrations and tear menisci are likely to have some relationship with the TFBUT measurements. 9, 24, 27, 28 We found a positive correlation between some of the Zernike aberrations and the NITFBUTs and also between the LTMA and the NITFBUTs. So the measurements of Zernike aberrations and tear dimensions are compatible with the conventional TFBUT in assessing stability of tear film. Moreover, the dynamic changes in Zernike aberrations and the LTMA clearly demonstrated the spatial and temporal pattern of tear film processing over the corneal surface during the postblink period. Therefore, the wavefront measurements combined with AS-OCT could be very useful to study the tear performance in both eye research and clinical care. Both techniques are noninvasive and fast. A combination of the two techniques could provide useful diagnostics in clinical practices, especially in wavefront-guided laser refractive surgery and contact lenses.

A methodological limitation of our study is that the measurements of wavefront aberrations and tear menisci were not simultaneously performed, so there would be concerns in associating the two measurements at different unmatched time periods. It would be better to simultaneously test both properties, and we are going to do so in a future study. For now, we have tested the repeatability of the Zernike aberrations for subjects who had more than two blinks within the one-minute test period. There was a high correlation between the measurements from the first interblink interval and the second interval. For example, the correlations for subject ZA were over 0.8 for the main Zernike terms ($R^2 = 0.910, P < 0.001$ for $Z_2^{2}$; $R^2 = 0.743, P = 0.001$ for $Z_3^{-3}$; $R^2 = 0.841, P < 0.001$ for $Z_3^{-5}$). So we believe the pattern of tear change in a single eye is quite repeatable. Therefore, our measurements are sufficiently valid to be used to explain tear film processes.

In summary, for whole eyes of young normal subjects, we observed systematic changes in Zernike aberrations after blinking. These changes were associated with changes in tear meniscus and TFBUT. The results confirmed observations in previous studies on spatial and temporal changes in the tear film and thus support the relevant theoretical explanations of dynamic tear processes. There were substantial individual variations in dynamic changes of the Zernike aberrations that were associated with changes in tear dimensions. The results suggest the necessity of exploring individual differences in tear quality and tear performance among normal eyes. Dynamic wavefront measurement combined with the AS-OCT for the assessment of tears at the tear meniscus could provide a useful tool to understand spatial and temporal processes of the tear film in clinical practices.

| TABLE 1. Lower Tear Meniscus Height and Area at Baseline and 10 Seconds after a Blink |
|---------------------------------|-----------------|-----------------|
| LTMH, µm                       | 233 ± 41        | 245 ± 42        |
| LTMA, µm²                      | 18,497 ± 7,451  | 19,635 ± 7,562  |

Baseline was measured immediately after a blink, n = 33 subjects.


