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Correlations among upper and lower tear menisci, non-invasive tear break-up time and Schirmer's test

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Abstract

Purpose—The aim was to determine the relationships among tear meniscus parameters, non-invasive tear break-up time (NITBUT), and Schirmer's test.

Design—Experimental study.

Methods—Thirty-six subjects were tested on one randomly selected eye. Real-time corneal optical coherence tomography (OCT) was used to image the upper and lower tear menisci during normal and delayed blinking followed by measurement of NITBUT and Schirmer's test. Digital images of the eye were taken for measuring the lid lengths to estimate tear volume in the menisci.

Results—Compared to normal blinking, significant increases of tear menisci occurred during delayed blinking (post hoc, $p < 0.01$). NITBUT was weakly but significantly correlated with the height ($r = 0.36$, $P = 0.03$) and area ($r = 0.37$, $P = 0.03$) of the lower tear meniscus during normal blinks. NITBUT was also correlated with the lower tear meniscus volume ($r = 0.45$, $P < 0.05$) and total tear meniscus volume ($r = 0.43$, $P < 0.05$) during normal blinking. Schirmer's test was not significantly related to any parameters of the tear menisci, volumes, or NITBUT; however, it was negatively correlated with the age of the subjects ($r = -0.47$, $P = 0.004$). The age was negatively correlated with the upper tear meniscus (r ranged from 0.36 to 0.37 for the radius, height and area, $P < 0.05$) measured during delayed blinking.

Conclusions—NITBUT appears correlated with the lower tear meniscus during normal blinking, and the Schirmer's test appears not correlated with the non-invasively measured tear meniscus.

Five keywords

tear meniscus; tear break-up; Schirmer's test; optical coherence tomography

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Dr. Wang had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis as well as the decision to submit for publication.

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C. Contributions to authors: Design of the study (JW, JA); Conduct and data analysis of the study (JW, JP and JA).

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The epithelium on the ocular surface requires constant coverage with tear fluid for the purposes of hydration, anti-microbial protection, nutrient supply, and waste removal. A stable pre-corneal tear film is essential for maintenance of the regular optical surface and clear vision. This is accomplished by adequate amount of tears on the ocular surface and conjunctival sac which are constantly renewed by fresh secretions from the lacrimal glands and removal by drainage. The importance of evaluation of the lower tear meniscus in the diagnosis of aqueous tear deficiency has long been recognized.¹⁻³ Objective estimates of the lower tear meniscus with newer instruments may have improved the accuracy compared to the earlier subjective observations.^{4, 5} Measurements of the lower tear meniscus height, radius, and cross-sectional area are good indicators of tear volume.^{1, 5-9} In these previous studies, upper tear meniscus was not imaged and studied, mainly due to the extreme difficulty of imaging the upper tear meniscus in a non-invasive way.^{6, 10} Thanks to the technological advancements, recently both upper and lower tear menisci were imaged simultaneously by custom anterior segment optical coherence tomography (OCT).^{11, 12} With this development, the correlations between the tear menisci around both eyelids and other conventional tear tests routinely used in clinics for the diagnosis of dry eye can be studied for the first time. The aim of this study was to determine the relationship among tear menisci measured with anterior segment OCT, non-invasive tear break-up time (NITBUT) obtained using a Keeler Tearscope, and Schirmer's test.

Subjects and methods

The research review boards of the University of Rochester and University of Miami approved this study. Thirty-six subjects (20 women and 16 men, mean $\pm$ standard deviation age: 45.1 ± 15.4 years, range: 20 - 70 years) in good health and with no history of contact lens wear, current ocular diseases or previously diagnosed dry eye were recruited in Rochester, NY. Each subject provided informed consent and was treated in accordance with the tenets of the Declaration of Helsinki.

Subjects were tested between 10:00 AM and 4:00 PM in a small consulting room, where central air conditioning and humidifiers were used to control the temperature (15 to 25°C) and humidity (30 to 50%). All tests were performed on one randomly selected eye of each subject. Preliminary anterior segment examination was done to exclude any current ocular diseases. OCT imaging was conducted and followed by NITBUT and Schirmer's test with local anaesthesia.

A real-time corneal OCT, developed as described previously,¹¹ was used to perform a vertical 12 mm scan across the central cornea (apex) including upper and lower menisci simultaneously. The subjects were asked to look at an external target (a red dot) and were exposed only to ambient room light. OCT images were recorded while the subjects were asked to blink normally (normal blink session). Afterwards, the subjects were asked to delay the blinks as long as possible (delayed blink session) whereupon the OCT imaging was repeated.

Five minutes after OCT scanning, NITBUT was performed using a Keeler Tearscope (Keeler, UK) with a grid filter, mounted on a slit-lamp and connected to a TV monitor. The subject was seated in front of the slit lamp and asked to look straight ahead. After a few blinks, subjects were asked to hold the eye open as long as possible. The investigator observed the reflection of the grid from the cornea on the TV monitor. The time from eye opening to the first discontinuity of the grid was noted. Three readings were taken and the average of the three readings in seconds was taken as the NITBUT. No fluorescein was added during the test.

Five minutes after the NITBUT test, Schirmer's test was performed. One minute after instillation of a drop of proparacaine, any visible fluid on the lower lid margin was gently wiped off with a cotton swab. A filter paper strip (Haag-Street, UK) was placed in the lower fornix

near the lateral canthus to avoid corneal stimulation and left in place for 5 minutes. Subjects were asked to blink normally during the procedure. After 5 minutes the filter paper was removed and the amount of wetting was measured in millimeters.

To calculate tear volume of the menisci around both eyelids, digital images of the eye with a reference scale were taken using a camera mounted on the slit-lamp for measuring the lid lengths. The estimation of tear meniscus volume was obtained by multiplying tear meniscus area and the eyelid length, assuming the tear meniscus was uniform across the entire eyelids, as used by Mainstone et al.¹ As the lids are curved in the third dimension, a multiplication factor of 1.294, suggested by Tiffany et al,¹³ was used to convert the lengths of upper and lower lids measured with two dimensional images into three dimensional values.

The imaging process to yield meniscus variables was described in detail previously.¹¹ Briefly, the first good OCT image showing both upper and lower menisci immediately succeeding two consecutive blinks during normal and delayed blinking sessions, was used to obtain meniscus results using custom software. Six variables were obtained including upper tear meniscus curvature (UTMC), height (UTMH) and cross-sectional area (UTMA), and lower tear meniscus curvature (LTMC), height (LTMH) and cross-sectional area (LTMA). Upper and lower lid lengths were processed from the digital images using custom software and a reference scale. Image processing and data analysis were done at University of Miami.

Data analysis was conducted using a statistical package (Statistica; StatSoft, Inc., Tulsa, OK). Data are presented as means $\pm$ standard deviations. Repeated measures analysis of variance (Re-ANOVA) was used for overall effects, and post hoc paired t-tests were used to determine whether there were pair-wise differences ($P < 0.05$). Pearson's correlation coefficient was used to determine the correlation between variables.

Results

Compared to normal blinking, significant increases of the height and cross-sectional area of the upper and lower tear menisci occurred during the delayed blinking session (post hoc test, $p < 0.01$, Figure 1 and Table). There were no significant differences of all measured parameters between the male and female (t-test, $P > 0.05$). The average NITBUT was 16.7 ± 7.6 seconds and Schirmer's test was 17.6 ± 10.1 seconds. NITBUT was weakly but significantly correlated with LTMH ($r = 0.36$, $P = 0.03$) and LTMA ($r = 0.37$, $P = 0.03$) measured during normal blinks (Fig. 2). NITBUT was also correlated with the lower tear meniscus volume ($r = 0.45$, $P < 0.05$) and total tear meniscus volume ($r = 0.43$, $P < 0.05$) measured during normal blinking. Upper tear meniscus measured during normal blinking was found not related with the NITBUT ($P > 0.05$). There were no significant correlations between NITBUT and tear meniscus parameters measured during delayed blinking session.

Schirmer's test was not significantly correlated with the parameters of the tear menisci (Fig. 3), tear meniscus volumes, or NITBUT, however, it was negatively correlated with the age of the subjects ($r = -0.47$, $P = 0.004$, Fig. 4). Age also was negatively correlated with the upper tear meniscus (r ranged from 0.36 to 0.37 for UTMH, UTMA, and UTMC, $P < 0.05$) measured during delayed blinking session (Fig. 5).

Discussion

Many clinical tests are used to evaluate the tear system and ultimately to diagnose dry eye. These tests include tear break-up time for tear stability,^{14, 15} Schirmer's test for tear production,¹⁶ and ocular surface staining to evaluate the damage on the ocular surface.¹⁷ Conflicting results between these tests are often observed and agreements among these tests are proven poor.^{17, 18} Multiple tear tests are usually used along with dry eye symptoms to

diagnose the tear disorder.^{18, 19} Some issues in these clinical tests may contribute to the poor specification and sensitivity. The tear system is highly dynamic and may be influenced by many internal and external factors. The use of fluorescein might cause reflex tearing, resulting in great variation.^{20, 21} Local anesthetics might alter the tear system, including tear secretion and drainage, possibly resulting in the conflicting results in Schirmer's test. Tear meniscus measurements made by slit lamp, especially for the lower tear meniscus, have been used to evaluate the tear system for a long time.²² The measurement is normally a one-time snapshot during the inter-blink period. Although the tear system is dynamic, the static measurements showed a reduced meniscus in dry eye patients.¹ Obviously, the tear meniscus keeps changing from time to time and is affected by many factors, like tear secretion, lid length, location of the punctum and location of the grey line that limits the anterior extension of tears on lid margin,²³ palpebral aperture,⁸ and lacrimal drainage.²⁴ Using real-time OCT in this study, both upper and lower tear menisci parameters were obtained immediately after normal blinking and delayed blinking. The relationships between these tear meniscus results and clinical tests such as tear break-up time and Schirmer's test, could provide further information about the tear system for better understanding the clinical implications of these tear meniscus measurements.

NITBUT using the Tearscope was introduced to monitor the stability of the tear film.²⁵ It is a non-invasive method that observes and images the specular reflection of the tear film surface when a cold-cathode light is projected onto it. A similar device used to obtain NITBUT has a large dome with many straight lines in a grid pattern and has more than 90% specificity and sensitivity.²⁶ NITBUT was measured using a modified Topographic Modelling System by Mainstone et al.,¹ who found that the lower tear meniscus, imaged with a camera, was correlated with NITBUT. Khurana et al.²⁷ reported a similar relationship between fluorescein tear break-up time and the subjectively graded lower tear meniscus. In contrast, Savini et al.⁶ found no relationship between lower tear meniscus height measured with a commercial posterior segment OCT and fluorescein break-up time. In the present study, we used a video Tearscope to monitor the tear stability in an attempt to determine the relationship between it and tear menisci measured with the OCT. NITBUT correlated with LTMH and LTMA measured during normal blinking (baseline) but not during delayed blinking (reflex tearing). It appears that a larger lower tear meniscus renders longer tear break-up time, possibly due to a thicker tear film. The relation between tear film thickness and lower tear meniscus was demonstrated when artificial tears were instilled into the eye in our previous study.¹¹ However, the relationship might be lost during reflex tearing as we found during the delayed blink session in present study. This phenomenon might explain the contradiction of the relationship between tear break-up time and tear meniscus in the literature.^{1, 6, 27} It is unclear whether tear break-up time was altered during reflex tearing since we did not measure NITBUT during the delayed blink session. Further studies are needed to examine this point, ideally with simultaneous measurements of NITBUT and tear menisci. Interestingly, there was no evidence of a relationship between upper tear meniscus and NITBUT in this study. This might be due to the limitation of space hosting the upper tear meniscus. The upper meniscus also showed much less changes compared to the lower tear meniscus during delayed blinking, which is consistent with results found after instillation of artificial tears in a previous study.¹² NITBUT was also correlated with total tear meniscus volume at baseline, which could mean that the greater tear menisci around both eyelids may result in longer tear break-up times among individuals. However, Wang et al.²⁶ found no correlation between fluorophotometrically measured total tear volume and NITBUT measured with an illuminated grid pattern. The disagreement could be explained by the different methodologies and the use of fluorescein in Wang et al.'s study.

The relationship between Schirmer's test and the tear meniscus has been studied previously.^{6, 8, 23, 27, 28} Lamberts et al.²³ found Schirmer's test with and without topical anaesthesia was not correlated with LTMH measured with a reticule on a slit-lamp eye piece. Doughty et al.⁸ also found no relationship between LTMH measured using a video camera and a short (1

minute) Schirmer's test. In contrast, Khurana et al.,²⁷ reported a positive correlation between Schirmer's test and the lower tear meniscus. Savini et al.⁶ observed a significant relationship between the OCT-estimated LTMH and a modified Schirmer's test in a group comprised of healthy and dry eye patients. We found no relationship between the Schirmer's test and tear meniscus variables in our study during either normal or delayed blink sessions. The lack of correlation between the Schirmer's test and tear meniscus measurements in the present study may be due to the use of topical anesthetic during the test. The increase in tear meniscus during delayed blinking indicated that increased tear volume may be due to reflex tearing. The anesthetic blocks reflex tearing, therefore the lack of correlation is not surprising. Jordan and Baum²⁸ reported that lower tear meniscus height measured with a reticule decreased significantly after topical anaesthesia, indicating that a reduction in tear secretion reduced lower tear meniscus height. Another reason for the conflicting results may be that the tear meniscus measured in various studies might not be at the same time after blink. The variation of the tear meniscus during blinking might cause these conflicting results. Lamberts et al.²³ found LTMH is influenced by many variables like tear flow, lid length, location of the punctum and location of the grey line which limits the anterior extension of tears on lid margin. Palpebral aperture height also might affect LTMH.⁸ In this study, the tear meniscus was measured immediately after eye opening. The results might differ from others using different methods.^{6, 8, 27}

Age as a factor impacting the tear system has been well documented.^{23, 26, 29-31} Schirmer's test decreased with aging eyes in the present study and other previous studies.^{23, 26, 29-31} Some studies reported significantly negative relationship between age and tear stability measured as tear thinning time³² and NITBUT.²⁶ However, we found no significant relationship between age and NITBUT, though this might have been due to small sample size of the study population. Interestingly, a negative relationship between age and upper tear meniscus during delayed blink was present. This might indicate that less reflex tearing occurs during delayed blinking in elderly, which is consistent with observations made by Mishima et al.²

There are some limitations in this study. Tear film thickness was not obtained by applying a drop of gel onto the eye for indirect calculation of the tear film, as done in previous studies.^{11, 12} The use of the gel might interfere with other tests which were conducted after OCT imaging. Additionally, reflex tearing during delayed blinking might have some impact on the NITBUT and Schirmer's test that followed. However, the impact may have been minimized by the gap of 5 minutes between the tests. During the Schirmer's test, the contralateral eye was not anaesthetized. Any irritation of that eye might induce sympathetic reflex secretion in both eyes. Other possible errors related to the OCT method were discussed previously.^{11, 12} In normal subjects, the test results of the tear like NITBUT and Schirmer's test usually are with a small range, therefore the relations between these tests and the measurements of the tear menisci may not be detected. In the present study, a group of participants with a wide range of the age was tested and the results of the NITBUT and Schirmer's test were found with a wide range (Fig. 2 and 3). Further studies are warranted with a large sample size including subgroups like dry eye. The time of eye opening was not standardized in this study. Greater variation of the increase (reflex tearing) in the tear menisci was expected during delayed blinking since the increase may be larger in some subjects who could hold their eye longer. The relation between the inter-blink interval and the increase of the tear menisci was not the aim of this study. Further studies may be needed.

In summary, NITBUT appears to correlate with the lower tear meniscus measured at baseline, and the invasive Schirmer's test was not correlated with either tear meniscus measured non-invasively. Age was inversely correlated with the Schirmer's test and the upper tear meniscus

imaged during delayed blinking. Further studies will be needed to test these relationships in patients with dry eye and other conditions, like punctal occlusion.

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Biography

Dr. Wang's Biosketch

Jianhua (Jay) Wang, MD, PhD is an assistant professor in the Bascom Palmer Eye Institute at the University of Miami. Prior to the current position, he worked as a research assistant professor at the University of Rochester, after he obtained his PhD on vision science from the University of Waterloo, Canada. Dr. Wang also earned a MD degree in China. His conducts research on optical coherence tomography for imaging the anterior segment of the eye.

Figure 1. Changes in the upper and lower menisci during normal and delayed blinking
 A vertical 12 mm scan across corneal apex was performed using optical coherence tomography. Images were obtained immediately after normal and delayed blinks. Cornea (CO), upper eyelid (UL) and lower eyelid (LL), upper tear meniscus (UTM) and lower tear meniscus (LTM) are marked on the images. Note the greater size of upper and lower menisci during delayed blinking compared to that during normal blinking. Bars denote to 500 μ m.

Figure 2. Correlations between non invasive tear breakup time (NITBUT) and lower tear meniscus height (LTMH) and area (LTMA) during normal blinking (n = 36 eyes)
 The correlation of NIBUT with LTMH and LTMA was weak but significant.

Figure 3. Correlation between Schirmer's test and lower tear meniscus height (LTMH) and area (LTMA) during normal blinking (n = 36 eyes)
Schirmer's test was not significantly correlated with either LTHM or LTMA.

Figure 4. Relations between Schirmer's test and non invasive tear breakup time (NITBUT) and age (n = 36 eyes)

Though the correlations were weak, the inverse relationship of Schirmer's test with age was significant. No significant relationship was found between NITBUT and age.

Figure 5. Relations between age and upper tear meniscus height (UTMH) and area (UTMA) during delayed blinking session (n = 36 eyes)

Though the correlations were weak, the inverse relationships of UTMH and UTMA with age were significant.

Table

Tear meniscus variables immediately after blink during normal and delayed blinking sessions in 36 subjects (36 eyes)

		Normal blinking After blink	Delayed blinking After blink	P Value
UTMC (μm)	Mean	254	282	0.06
	SD	82	101	
UTMH (μm)	Mean	267	301	0.003
	SD	54	58	
UTMA (μm^2)	Mean	20463	26794	0.002
	SD	8298	11423	
LTMC (μm)	Mean	455	800	0.05
	SD	401	1158	
LTMH (μm)	Mean	339	459	0.006
	SD	149	306	
LTMA (μm^2)	Mean	35920	72498	0.02
	SD	34053	98175	

UTMC = upper tear meniscus curvature

UTMH = upper tear meniscus height

UTMA = upper tear meniscus area

LTMC = lower tear meniscus curvature

LTMH = lower tear meniscus height

LTMA = lower tear meniscus area