

# An investigation of non-invasive tear break up time and tear meniscus height of keratoconic versus non-keratoconic individuals



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Keratoconus is a debilitating condition where the cornea develops a conical shape rather than the characteristic round shape due to various physiological and structural changes taking place within the layers of the cornea. As a result of the pathogenesis of keratoconus, there are numerous changes that may occur within the tears of these patients. Research has shown changes in the tear metabolome, the presence of degradation products as well as loss of goblet cells into the tears. Could the changes occurring within the tear structure of these patients affect the results of various tear quantity and quality tests? Non-invasive tear break up time (NTBUT) is a diagnostic test used to determine the quality of the tear film and has been used extensively when diagnosing dry eye disease. This test is utilised in order to determine the time taken for the tear film to begin breaking apart, signalling thinning of the tears. Shorter break up times are therefore indicative of instability or changes occurring within the tear film which could be diagnostic of dry eye disease. Tear meniscus height (TMH) measurements have also been utilised in clinical practice, where these measurements provide an indication of the volume of tears contained within the upper and lower menisci. Lower tear volumes have been shown to be present in cases of dry eye disease where either tear production or tear drainage may be affected. Changes in the quality and quantity of the tear film in subjects with dry eye disease have been thoroughly investigated; however, the same cannot be said for subjects with keratoconus. Could the same findings be possible in subjects with keratoconus? Is it possible that the changes occurring within the tears of keratoconic subjects could lead to abnormal NTBUT and TMH measurements when compared to those of control subjects? Could the results of the NTBUT and TMH tests be related to one another? This study compares the NTBUT and TMH measurements of both keratoconic and control subjects by making use of a single type of instrumentation, namely the Oculus Keratograph 4 (OK4). The results of this study reveal that the values obtained for each of the two subject groups are not shown to be statistically significantly different and that there is no significant correlation between the NTBUT and TMH measurements when comparing keratoconic and control subjects.

## Introduction

The tear film functions as a vital component of a healthy ocular system. Changes in the tear film, either quality or quantity, may lead to a diagnosis of dry eye disease. Non-invasive tear break up time (NTBUT) and tear meniscus height (TMH) measurements are two of various tear tests used to investigate the normality of the tear film. In cases of a corneal ectasia such as keratoconus, tear parameters have not been extensively investigated. Could the physiological changes occurring in subjects diagnosed with keratoconus be linked to various other changes in terms of tear film test results? This study aims to determine whether a difference can be found when measuring the NTBUT and TMH in both keratoconic and non-keratoconic individuals and whether these two clinical tests may display a relationship with one another.

The tear film, being composed of three distinct layers, serves as a vital component of the eye. The tear film performs a multitude of utilities including cleansing, immunologic, refractive, antimicrobial and lubricating functions.<sup>1</sup> Most of the tear film is found to be contained within the tear menisci in contact with both the upper and lower lids.<sup>2</sup> Tear menisci may be defined as the area of tears found to be present at the margin of both lids and are responsible for the majority of the volume of tears present inside the ocular system.<sup>3</sup> Between 75% and 90% of the entire volume of the tear film, held in place by gravitational forces as well as surface tension, is found in the tear menisci.<sup>4,5</sup> The volume of tears found to be present reflects both the secretion and drainage system of the tear fluid, therefore allowing a diagnosis to be made regarding the functional status of the tear film.<sup>5</sup>

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Tears, produced by the glands within the ocular system, are initially found to be present within the tear menisci and are redistributed upon the process of blinking, thereby lubricating the front surface of the eye.<sup>6</sup> Various dimensions of the tear meniscus may be investigated including the height, area, depth as well as its curvature. The volume of tears contained within the tear menisci provides an accurate indication as to whether the tear film lacks in quantity (which may result in symptoms of dry eye disease). In most cases, the inferior tear meniscus is more commonly measured due to the ease of observation and measurement.<sup>2,5</sup> According to Santodomingo-Rubido et al.,<sup>4</sup> the inferior TMH in normal individuals tends to be approximately 130  $\mu\text{m}$ , while Bitton et al.<sup>7</sup> presented mean TMH measurements of between 240  $\mu\text{m}$  and 250  $\mu\text{m}$ . Nguyen et al.<sup>8</sup> measuring the lower TMH showed the mean values ranged between 140  $\mu\text{m}$  and 250  $\mu\text{m}$ .

NTBUT differs from the usual test of tear break up in that no fluorescein dye is used as this may disrupt the structure of the tear film and induce additional reflex tearing.<sup>9,10</sup> The non-invasive form of this test (NTBUT) involves the use of a regular grid-like pattern that is projected onto the anterior surface of the tear film. Discontinuity in this regular pattern reflects the disruption of the tear film.<sup>9</sup> The time taken for the first sign of discontinuity or irregularity to appear within this regular pattern is thought to represent the stability of the tear film.<sup>9</sup> Tear break up time lacks association when compared to symptoms. The sensitivity of break up time tests, however, shows a strong connection with dry eye disease.<sup>11</sup>

The normal values for tear break up time are shown to differ in the literature but generally are found to be between 10 and 15 s, with any value  $> 10$  s indicating normality.<sup>6,12,13</sup> A value of  $< 10$  s is indicative of dry eye, whether the invasive or non-invasive form of this test is used.<sup>14</sup> The correlations between various diagnostic testing methods have been investigated, and for example, when comparing the TMH versus NTBUT, no correlation exists between these two variables.<sup>15</sup> Nichols et al.<sup>15</sup> found NTBUT to be correlated with Schirmer test results and found that the height of the tear meniscus does not correlate with any of the other variables within their study. Wang et al.<sup>16</sup> differ in that a significant correlation was found to be present between NTBUT measurements and the lower tear meniscus volume. Could a significant connection be found between the NTBUT and lower TMH measurements when measured on patients with a corneal ectasia such as keratoconus? Keratoconus can be defined as a progressive, non-inflammatory corneal ectasia resulting in thinning and distortion of the anterior corneal surface.<sup>17,18</sup> Keratoconus is a progressive disorder, which may be bilateral but is asymmetric in most cases.<sup>17</sup> The extreme thinning that occurs within the cornea is a consequence of changes taking place within the corneal stroma.<sup>19</sup> Keratoconic patients present with irregular astigmatism as well as large amounts of myopia.<sup>19,20,21</sup> As keratoconus evolves, the cornea becomes oedematous due to a build up of fluid and scarring develops, which may cause detrimental effects to the vision of the

patient.<sup>22</sup> The pathogenesis of keratoconus is considered to be linked to oxidative stress within the corneal surface itself.<sup>18</sup> Both quality and quantity of the tear film have not been extensively investigated in keratoconic subjects. The purpose of this study was to investigate specific tear parameters (NTBUT and TMH) for two different subject groups, keratoconics and controls, in order to determine whether a significant relationship exists between the two groups.

## Method

The data obtained in this study included measurements taken on 25 keratoconic and 25 control subjects. The keratoconic subject group consisted of patients attending the contact lens clinic at the University of Johannesburg. Subjects consisted of 15 females and 10 males with an age range of 19–56 years (mean and standard deviation =  $25.08 \pm 10.63$  years). The control subject group consisted of first year students studying optometry at the University of Johannesburg. First year students were chosen as their schedule allowed for time to partake. The control group was made up of predominantly females with a mean age of approximately 19.28 years (standard deviation = 1.14 years). The study and its procedures were thoroughly explained to the potential subjects, and written informed consent was received from each subject before partaking in the study.

Within the keratoconic group of subjects, the presence of keratoconus was confirmed through the use of corneal topography scans as well as slitlamp biomicroscopy where signs characteristic of keratoconus could be observed. The control group of subjects were screened for any ocular pathology, use of certain medications as well as any contact lens wear that would result in exclusion from the study as these factors could influence the quantity and quality of the tear film. All measurements were taken using the Oculus Keratograph 4 (OK4).

With the subject seated comfortably behind the instrument, chin resting on the chin rest and forehead against the forehead rest, the NTBUT setting could be selected. Once initiated, the placido ring structure situated in front of the subject lights up presenting red LED lights and the subject is asked to fixate on the orange circle situated in the middle of the placido ring. The OK4 presents direction-giving arrows, signalling to the examiner the direction in which the joystick must be moved in order to focus the anterior surface of the eye. Once this has been achieved, the examiner instructs the subject to blink twice rapidly and thereafter to hold their eyes open for as long as possible. A reading is automatically obtained by the OK4, giving two separate values, the first being the initial time a discontinuity spot or irregular region is shown to appear and the second being the mean of the tear break up time. This procedure was repeated three times on both eyes of each of the 50 subjects in order to obtain average values. Of particular importance in this study was the value given for the first break up of the tear film. The three values for each eye were averaged in order to obtain one value for NTBUT (in each eye) for the 50 subjects partaking in the study.

Utilising the same instrument, TMH could be measured. The TMH function is applied, and in this case, there is no projection of LED lights. Instead, an infra-red camera is used in order to image the tear film. Only the lower tear meniscus was measured in this study, and therefore, the lower lid margin was focused before scans could be obtained. Due to the positioning of the instrument, in order to focus the lower lid margin, the subject was asked to fixate on the top half of the orange circle as part of the target was out of sight. Once the tear meniscus could be imaged clearly in the centre of the screen using the joystick situated in front of the examiner, images could be obtained by manually pressing the capture button on the OK4. Five photographs were obtained on each eye of the 50 subjects in order to calculate an average TMH measurement.

After the completion of the photographs using the OK4, each individual photograph was magnified to twice its original size in order to view the height of the tear meniscus. Using the tools and software available on the OK4, individual photographs were opened and each meniscus height was manually measured; these scans were saved with the measurements on them. The OK4 is calibrated such that the measurements are given in millimetres and can be converted to microns. In an attempt to ensure the consistency of the measurements, the same individual was responsible for measuring each scan in order to rule out variability amongst different individuals taking measurements. The scans were randomly measured so as to ensure that the individual taking the measurement was unaware to which subject group the specific scan belonged. Using these values for the NTBUT combined with the measurements taken for the TMH, a statistical analysis was done using SPSS (Statistical Package for Social Sciences).

## Results

The results presented below pertain to the data set obtained for the 50 subjects (100 eyes) partaking in this study.

Table 1 represents the normality tests performed on the data set, namely the Kolmogorov–Smirnov and Shapiro–Wilk tests. These tests were performed in order to determine whether the data samples conform to a normal distribution.

As can be observed from Table 1, most of the variables within this study are not shown to be normally distributed. The only variable shown to exhibit a normal distribution (as indicated by an \*) is the TMH measurements obtained for the control subject group. Due to the absence (mostly) of normality within the data set, non-parametric testing methods were chosen when analysing the data set.

From the descriptive statistics (seen in Table 2), it can be seen that the means of the NTBUT differ by a value of 0.2 s with the mean of the keratoconic group being larger than that of the controls. The median of the control group, however, is shown to be larger than that of the keratoconics, differing by 0.5 s. In terms of the TMH measurements, the mean of the keratoconic

**TABLE 1:** The Kolmogorov–Smirnov and Shapiro–Wilk test results are presented for both subject groups (keratoconic and control) for both the non-invasive tear break up time and the tear meniscus height measurements.

Test parameters	Kolmogorov–Smirnov		Shapiro–Wilk	
	Statistics	Significance	Statistics	Significance
<b>NTBUT</b>				
Keratoconic	0.189	0.021	0.796	0.00
Control	0.133	0.037	0.927	0.006
<b>TMH</b>				
Keratoconic	0.161	0.002	0.854	0.00
Control	0.106	0.20*	0.953	0.044

The test statistics and the significance levels are represented. A normal distribution being indicated by an asterisk (\*).

NTBUT, Non-invasive tear break up time; TMH, Tear meniscus height.

**TABLE 2:** Descriptive statistics for the two subject groups (keratoconics and controls) within this study.

Descriptive statistics	NTBUT (seconds)		TMH ( $\mu\text{m}$ )	
	Keratoconics	Control	Keratoconics	Controls
Mean and s.d.	4.9 $\pm$ 4.7	4.7 $\pm$ 3.2	268.5 $\pm$ 95.3	247.1 $\pm$ 42.8
Range	20	12	456	228
Median (interquartile range)	3.3 (5)	3.8 (4)	238 (101)	240 (59)

The means, standard deviations, ranges, medians and interquartile ranges are represented for each of the two groups.

Non-invasive tear break up time measurements are given in seconds while tear meniscus height measurements are given in microns ( $\mu\text{m}$ ).

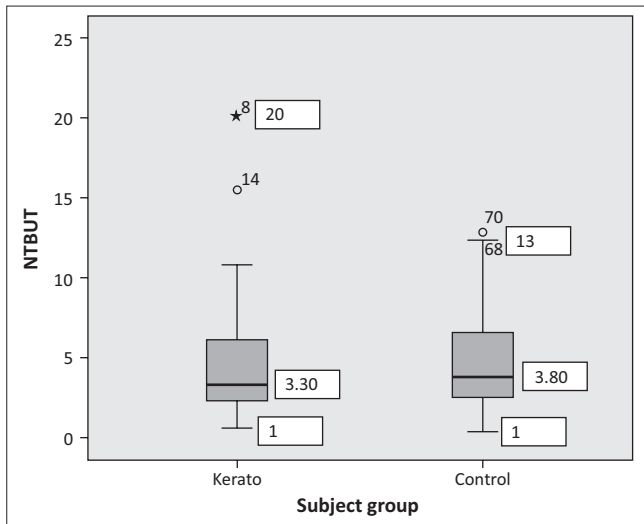
NTBUT, Non-invasive tear break up time; TMH, Tear meniscus height.

group is shown to be larger by approximately 21  $\mu\text{m}$ . The median values of the TMH are separated by 2  $\mu\text{m}$ , with the median of the control group being larger than that of the keratoconic group. The range of the TMH for the keratoconics is exactly double that of the control group.

The box and whisker plots represented in Figure 1 display the differences in the distribution of data measurements between the two groups for the NTBUT measurements. The dark line shown to pass through the centre of each box represents the median for each group, shown to be slightly larger in the control group. The minimum values for both groups are shown to be 1 second, while the maximum value for the keratoconics is shown to be 7 s longer than that of the control group.

A visual representation of the descriptive statistics given in Table 2 can be observed in Figure 2. The medians of the two groups, as can be seen by the thick black line passing through the box, are shown to be similar with a difference of only 2  $\mu\text{m}$ . The maximum values between the two groups are shown to differ by almost 200  $\mu\text{m}$ , with that of the keratoconics being larger. In terms of the minimum values, the controls display a larger value of 170  $\mu\text{m}$ , while the keratoconics have a minimum of 138  $\mu\text{m}$ .

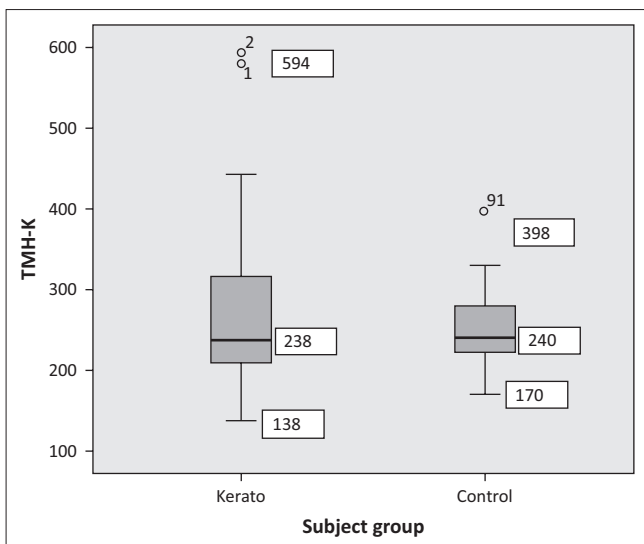
Table 3 represents the Mann–Whitney U tests used in order to determine whether a significant difference is shown to be present between the keratoconic and control groups. From the results in Table 3, it can be seen that the significance level for the NTBUT measurements is larger than 0.05, and therefore, the null hypothesis can be accepted. The null hypothesis states that the median of the keratoconic group is equal to the median of the control group, and therefore, no



The x-axis represents the two different subject groups, while the non-invasive tear break up time values are represented on the y-axis in seconds.

NTBUT, Non-invasive tear break up time.

**FIGURE 1:** Box and whisker plots representing the descriptive statistics for the non-invasive tear break up time measurements of the two subject groups (keratoconics vs controls).



The x-axis represents the two different subject groups, while the tear meniscus height measurement values are represented on the y-axis in microns ( $\mu\text{m}$ ).

TMH, Tear meniscus height.

**FIGURE 2:** Box and whisker plots representing descriptive statistics for the tear meniscus height measurements of the two subject groups (keratoconics vs controls).

**TABLE 3:** Non-parametric test statistics calculated for the non-invasive tear break up time and tear meniscus height measurements utilising the Mann-Whitney U test.

Test statistics	Mann-Whitney U	Z	Significance
NTBUT	547	-0.479	0.63
TMH	1207	-0.296	0.77

Represented are the test statistics as well as the significance levels used to determine whether a significant difference exists between the two subject groups, namely keratoconics and controls.

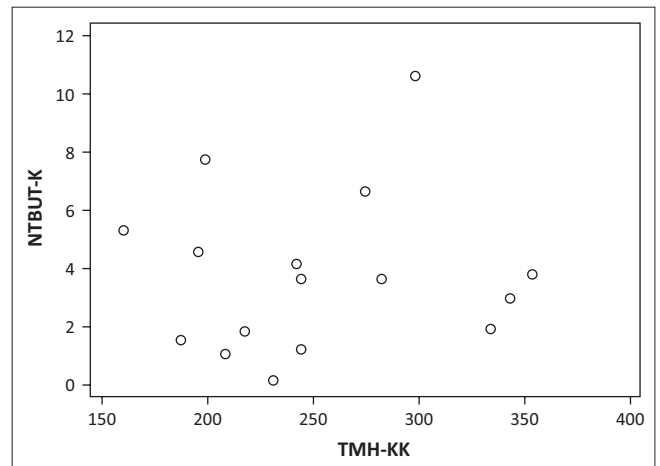
NTBUT, Non-invasive tear break up time; TMH, Tear meniscus height.

statistically significant difference is shown to be present between the two subject groups. The same can be shown for the TMH measurements, that is, there is no significant difference between the two subject groups as the null hypothesis can be accepted.

**TABLE 4:** Spearman's rank correlation calculated in order to determine the correlation between non-invasive tear break up time and tear meniscus height measurements of the two subject groups.

Spearman's Rank Correlation	Keratoconic	Control
Correlation coefficient ( $r$ )	0.05	-0.0506
$p$ -value	0.854	0.8101
95% confidence interval	-0.457 to 0.533	-0.437 to 0.352

The correlation coefficients, significance levels as well as the 95% confidence intervals for the correlation coefficients are represented.



Non-invasive tear break up time measurements are given in seconds, while tear meniscus height measurements are given in microns ( $\mu\text{m}$ ).

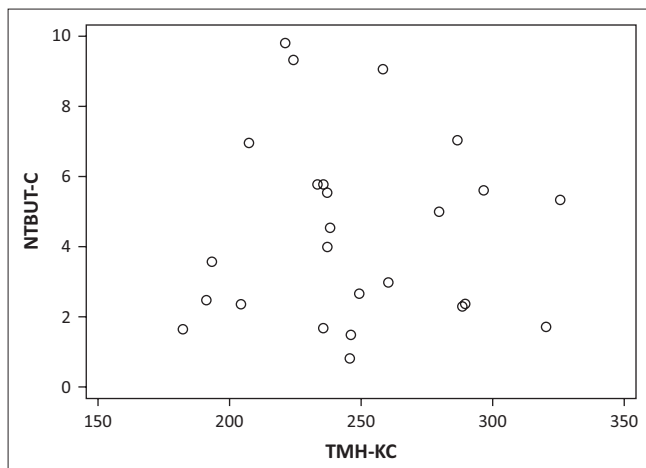
NTBUT, Non-invasive tear break up time; TMH, Tear meniscus height.

**FIGURE 3:** A scatter plot representing the data obtained for the non-invasive tear break up time versus tear meniscus height measurements, both obtained using the OK4 for the keratoconic subject group.

From Spearman's rank correlation in Table 4, it can be seen that in the keratoconic group of subjects, the correlation coefficient is 0.05. This correlation coefficient indicates no correlation between the two variables.<sup>23</sup> When looking at the significance level, this value is larger than 0.05, and therefore the null hypothesis can be accepted. The null hypothesis states that the two variables being tested do not display a significant correlation, and therefore it can be concluded that the correlation shown to be present is not statistically significant when looking at the NTBUT and TMH measurements in the keratoconics. In terms of the controls, the correlation coefficient also displays no correlation.<sup>23</sup> The significance level is shown to be a value of 0.81, which is larger than 0.05, and therefore the null hypothesis can be accepted. The very weak negative correlation shown to be present between these two variables is not statistically significant for the controls.

The scatter plot in Figure 3 represents the data measurements obtained when comparing NTBUT with TMH measurements in the keratoconics. These data do not seem to reflect a characteristic pattern and are shown to be distributed in a random fashion, thereby giving a visual representation of the lack of relationship between these two variables.

Looking at the data displayed in Figure 4, the conclusion appears to be the same as that for the keratoconic group. The data are distributed in a random fashion with no distinct pattern being observed. The lack of correlation, determined



Non-invasive tear break up time measurements are given in seconds while tear meniscus height measurements are given in microns ( $\mu\text{m}$ ).

NTBUT, Non-invasive tear break up time; TMH, Tear meniscus height.

**FIGURE 4:** A scatter plot representing for the data obtained for the non-invasive tear break up time versus tear meniscus height measurements, both obtained using the OK4 for the control group of subjects.

using Spearman's rank correlation (given in Table 4), can be observed when looking at the above scatter plot for the controls.

## Discussion and conclusion

The results of this study suggest that there is a lack of correlation between NTBUT and TMH measurements for both groups. When comparing the data between the two groups, the difference has not shown to be statistically significantly different. In general, NTBUT measurements of  $< 10$  s are indicative of dry eye disease.<sup>14</sup> Cox et al.<sup>24</sup> looked at the agreement between automated and traditional break up time measures and the repeatability of them and found that the average NTBUT measurement given by the OK4 showed better between-visit agreement compared to the first break up time measurement given. Jiang et al.<sup>25</sup> investigated the use of the Keratograph in order to measure the tear break up time in dry eye disease and subjects with age-related cataracts and their study revealed that the Keratograph proves to be an effective method for determining the tear film stability via NTBUT measurements. In this study, the mean NTBUT values for both the keratoconic and the control groups are shown to be shorter than 10 s, being 4.94 and 4.7 s, respectively. Utilising the Mann-Whitney U test, the results of which can be viewed in Table 3, it can be seen that no statistically significant difference is shown to exist between the NTBUT measurements of the two groups. This finding may suggest that the presence of keratoconus does not have a direct effect on the stability of the tear film, as indicated by the NTBUT values. It is thought that tear break up time would be shorter in cases of keratoconus, as the stability of the tear film decreases while the progression of keratoconus increases.<sup>26</sup>

TMH is indicative of tear volume and may therefore be used as a diagnostic criterion for dry eye disease.<sup>27</sup> Dogru et al.<sup>27</sup> demonstrated changes in the TMH owing to changes in the production and drainage of tears as is the case in dry eye disease. Due to the similarities found to be present in the tear

metabolome of keratoconic and dry eye subjects,<sup>28</sup> it has been thought that reduced TMH measurements would be found in keratoconic subjects. Sarac et al.<sup>21</sup> suggested that keratoconus is found to be similar to dry eye due to the release of collagen degradation products into the tears, altered surfacing of the tears across the cornea as well as squamous metaplasia of the conjunctival and corneal surfaces. When looking at the difference in descriptive statistics between the two subject groups in this study, the means are shown to be separated by an amount of approximately  $20 \mu\text{m}$ , while the median values only display a difference of  $2 \mu\text{m}$ . This falls in line with the conclusions determined by the Mann-Whitney U test (Table 3), where it was determined that no statistically significant difference exists between the two groups. In a similar study by Sarac et al.,<sup>21</sup> where the height of the tear meniscus was measured using optical coherence tomography (OCT), no statistically significant difference was found to be present between their keratoconics and controls.

The study by Dogru et al.,<sup>29</sup> where various clinical parameters were measured in keratoconic versus control subjects, showed significant differences between the two study groups. NTBUT measurements were shown to be significantly reduced in the keratoconics with a mean value of 6.8 s as opposed to 14.5 s for the control group.<sup>29</sup> Sarac et al.<sup>21</sup> found no significant difference between the height and the area of the tear meniscus when comparing keratoconic subjects with a group of control subjects. Carracedo et al.<sup>30</sup> also found that keratoconics have lower tear volumes compared to controls. They found no significant difference in TBUT measurements between the two groups<sup>30</sup>; however, using other findings such as the decreased mucin production in keratoconic tears, they concluded that keratoconics suffer from greater tear film instability compared to healthy individuals.

Due to the importance of both tear film measurement techniques (NTBUT and TMH), the correlations were calculated in order to determine whether a significant relationship exists between these two variables. In the study by Koh et al.,<sup>31</sup> it was determined that no significant correlation could be found between NTBUT measurements taken with the Keratograph 5M and TMH measurements taken using the same instrumentation. Nguyen et al.<sup>8</sup> performed a study where the correlation between TMH measurements and other clinical measurements of dry eye disease was compared. Nguyen et al.'s<sup>8</sup> study revealed that TMH measurements were significantly correlated with the results of the Schirmer test but no correlation could be found in terms of the NTBUT measurements. Ibrahim et al.<sup>32</sup> found a statistically significant correlation between the upper TMH as measured using an OCT and fluorescein break up time, when investigating these variables in subjects with dry eye disease. In the study by Golding et al.,<sup>33</sup> various tear meniscus parameters were compared to the break up time of the tear film in order to determine whether a relationship could be found. Golding et al.<sup>33</sup> found a statistically significant correlation between log of the NTBUT measurements and the curvature of the tear meniscus as well as the finding that

smaller radii of curvature were found to be associated with shorter break up times. In terms of TMH, Golding et al.<sup>33</sup> found a positive linear correlation between log of the NTBUT measurements and the height of the tear meniscus suggesting that lower tear volume is associated with a poor break up time. The reason for this association is thought to be a result of the influence that the volume of tears holds over the tensile strength of the tear film.<sup>33</sup>

When looking at the correlations calculated throughout this study, it can be seen that no statistically significant difference can be found when comparing the data of the two experimental groups. There is also a lack of significant correlation shown to exist between the NTBUT and TMH measurements for each of the two subject groups. It can be concluded that the presence of keratoconus does not have a significant effect on the results of either of these two tear film tests, being NTBUT and TMH measurements. This finding falls in line with various other items of research where the exact answers to keratoconus cannot be found. Optometry is still left somewhat in the dark when it comes to keratoconus and the various diagnostic components thereof.

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## Competing interests

The authors declare that they have no financial or personal relationships which may have inappropriately influenced them in writing this article.

## Authors' contributions

The study design was developed by both W.D.H.G. and D.L.N. Measurements were obtained by D.L.N. under the supervision of W.D.H.G. This article was written by D.L.N. under the supervision of W.D.H.G.

## References

- Murube J. Basal, reflex and psycho-emotional tears. *Ocul Surf.* 2009;7:60–65. [http://dx.doi.org/10.1016/S1542-0124\(12\)70296-3](http://dx.doi.org/10.1016/S1542-0124(12)70296-3)
- Johnson ME, Murphy PJ. Temporal changes in the tear menisci following a blink. *Exp Eye Res.* 2006;83:517–525. <http://dx.doi.org/10.1016/j.exer.2006.02.002>
- Benitez-del-Castillo JM, Lemp MA. *Ocular surface disorders.* London: JP Medical Ltd; 2013; p. 36–73, 237.
- Santodomingo-Rubido J, Wolffsohn JS, Gilmartin B. Comparison between graticule and image capture assessment of lower tear film meniscus height. *Cont Lens Anterior Eye.* 2006;29:169–173. <http://dx.doi.org/10.1016/j.clae.2006.05.004>
- Johnson ME, Murphy PJ. The agreement and repeatability of tear meniscus height measurement methods. *Optom Vis Sci.* 2005;82:1030–1037. <http://dx.doi.org/10.1097/O1.OPX.0000192352.78935.e0>
- Herranz RM, Corrales Herran RM. *Ocular surface: Anatomy and physiology disorders and therapeutic care.* Boca Raton, FL: CRC Press; 2012; p. 88.
- Bitton E, Keech A, Simpson T, Jones L. Variability of the analysis of the tear meniscus height by optical coherence tomography. *Optom Vis Sci.* 2007;84:903–908. <http://dx.doi.org/10.1097/OPX.0b013e3181560ba8>
- Nguyen P, Huang D, Li Y, et al. Correlation between optical coherence tomography-derived assessments of lower tear meniscus parameters and clinical features of dry eye disease. *Cornea.* 2012;31:680–685. <http://dx.doi.org/10.1097/ICO.0b013e3182261577>
- Sweeney DF, Millar TJ, Raju SR. Tear film stability: A review. *Exp Eye Res.* 2013;117:28–38. <http://dx.doi.org/10.1016/j.exer.2013.08.010>
- Ramos L, Barreira N, Mosquera A, Penedo MG, Yebra-Pimentel E, García-Resúa C. Analysis of parameters for the automatic computation of the tear film break-up time test based on CCLRU standards. *Comput Methods Programs Biomed.* 2014;113:715–724. <http://dx.doi.org/10.1016/j.cmpb.2013.12.003>
- Begley CG, Himebaugh N, Renner D, et al. Tear breakup dynamics: A technique for quantifying tear film stability. *Optom Vis Sci.* 2006;83:15–21. <http://dx.doi.org/10.1097/O1.OPX.0000195569.36185.f0>
- Chaudhuri Z, Vanathi M. *Postgraduate ophthalmology.* New Delhi: Jaypee Brothers Medical Publishers; 2012; p. 602.
- Zadnik K. *The ocular examination: Measurements and findings.* MI: W.B. Saunders; 1997; p. 205.
- Pleyer U, Foster CS. *Uveitis and immunological disorders.* Heidelberg: Springer Science and Business Media; 2006; p. 17.
- Nichols KK, Nichols JJ, Mitchell GL. The relation between tear film tests in patients with dry eye disease. *Ophthalmic Physiol Opt.* 2003;23:553–560. <http://dx.doi.org/10.1046/j.1475-1313.2003.00153.x>
- Wang MX, Swartz TS. *Irregular astigmatism: Diagnosis and treatment.* Thorofare, NJ: SLACK Incorporated; 2008; p. 55.
- Abolbashari F, Mohidin N, Hosseini SMA, Ali BM, Retnasabapathy S. Anterior segment characteristics of keratoconus eyes in a sample of Asian population. *Contact Lens Anterior Eye.* 2013;36:191–195. <http://dx.doi.org/10.1016/j.clae.2013.01.005>
- Saijyothi AV, Fowjana J, Madhumathi S, et al. Tear fluid small molecular antioxidants profiling shows lowered glutathione in keratoconus. *Exp Eye Res.* 2012;103:41–46. <http://dx.doi.org/10.1016/j.exer.2012.07.010>
- Joseph R, Srivastava OP, Pfister RR. Differential epithelial and stromal protein profiles in keratoconus and normal human corneas. *Exp Eye Res.* 2011;92:282–298. <http://dx.doi.org/10.1016/j.exer.2011.01.008>
- Assiri AA, Yousuf BI, Quantock AJ, Murphy PJ. Incidence and severity of keratoconus in Asir province, Saudi Arabia. *Br J Ophthalmol.* 2005;89:1403–1406. <http://dx.doi.org/10.1136/bjo.2005.074955>
- Sarac O, Soyugelen G, Gurdal C, Bostanci-Ceran B, Can I. Tear meniscus analysis with Fourier-domain optical coherence tomography in keratoconus. *Curr Eye Res.* 2011;36:528–533. <http://dx.doi.org/10.3109/02713683.2011.569869>
- Traboulsi EI. *Genetic diseases of the eye.* New York: Oxford University Press; 2011; p. 288.
- Pallant J. *SPSS survival manual.* Berkshire: Open University Press; 2005; p. 57, 291.
- Cox SM, Nichols KK, Nichols JJ. Agreement between automated and traditional measures of tear film breakup. *Optom Vis Sci.* 2015;92:257–263. <http://dx.doi.org/10.1097/OPX.0000000000000648>
- Jiang Y, Ye H, Xu J, Lu Y. Noninvasive Keratograph assessment of tear film break-up time and location in patients with age-related cataracts and dry eye syndrome. *J Int Med Res.* 2014;42:494–502. <http://dx.doi.org/10.1177/0300060513504701>
- Wang M. *Keratoconus and keratoectasia: Prevention, diagnosis and treatment.* Thorofare, NJ: SLACK Incorporated; 2010; p. 8.
- Dogru M, Karakaya H, Özçetin H, et al. Tear function and ocular surface changes in keratoconus. *Ophthalmology.* 2003;110:1110–1118. [http://dx.doi.org/10.1016/S0161-6420\(03\)00261-6](http://dx.doi.org/10.1016/S0161-6420(03)00261-6)
- Karamichos D, Zieske JD, Sejersen H, Sarker-Nag A, Asara JM, Hjortdal J. Tear metabolite changes in keratoconus. *Exp Eye Res.* 2015;132:1–8. <http://dx.doi.org/10.1016/j.exer.2015.01.007>
- Dogru M, Kakagawa N, Tetsumoto K, Katakami C, Yamamoto M. Ocular surface disease in atopic dermatitis. *Jpn J Ophthalmol.* 1999;43:53–57. [http://dx.doi.org/10.1016/S0021-5155\(98\)00061-6](http://dx.doi.org/10.1016/S0021-5155(98)00061-6)
- Carracedo G, Recchioni A, Alejandre-Alba N, et al. Signs and symptoms of dry eye in keratoconus patients: A pilot study. *Curr Eye Res.* 2015;40:1088–1094. <http://dx.doi.org/10.3109/02713683.2014.987871>
- Koh S, Ikeda C, Watanabe S, et al. Effect of non-invasive tear stability assessment on tear meniscus height. *Acta Ophthalmol.* 2015;93:135–139. <http://dx.doi.org/10.1111/aos.12516>
- Ibrahim OMA, Dogru M, Takano Y, et al. Application of Visante optical coherence tomography tear meniscus height measurement in the diagnosis of dry eye disease. *Ophthalmology.* 2010;117:1923–1929. <http://dx.doi.org/10.1016/j.ophtha.2010.01.057>
- Golding TR, Bruce AS, Mainstone JC. Relationship between tear-meniscus parameters and tear-film breakup. *Cornea.* 1997;16:649–661. <http://dx.doi.org/10.1097/00003226-199711000-00009>