



Pre-contact lens and pre-corneal tear film kinetics

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ABSTRACT

Purpose: Contact lenses (CL) insulate the corneal surface from the environment. It is possible that they influence the corneal sensory mechanism that contribute to spontaneous blinking. The study objective was to quantify the pre-CL and pre-corneal tear film kinetics (TFK) over blink period.

Methods: The study population was 202 soft CL wearers, 133 non-lens wearers. TFK were quantified via post-hoc masked analysis of HD Tearscope videos. The parameters were: Non-Invasive Break Up Time (NIBUT), Exposed Area % at initial break (EA 1st Break) and at blink (EA Blink), Interblink period (IB), Protective Index (PI) and exposure speed of surface dehydration (ES mm²/s). The TFK of CL wearers were compared to non-lens wearers. The hypothesis was that pre-CL TFK was inferior to pre-corneal, specifically greater tear film anomalies presence at blink.

Results: The pre-corneal NIBUT was longer than pre-CL NIBUT (9.1 vs. 5.1s, $p < 0.001$). The EA 1st Break was smaller for pre-corneal than pre-CL (0.003 vs. 0.43%, $p < 0.001$). The mean IB time was similar for pre-CL and pre-corneal (9.4 vs. 9.8s, $p = 0.213$). The EA Blink % was smaller for pre-corneal than pre-CL (0.03 vs. 6.66%, $p < 0.001$). The ES was faster for pre-CL than pre-corneal (0.339 vs. 0.004, $p < 0.001$). The PI was greater for pre-corneal than pre-CL (99.9 vs. 97.1%, $p < 0.001$).

Conclusions: Pre-CL TFK were significantly inferior than pre-corneal, confirmed the hypothesis. The NIBUT was shorter. Once the initial break occurred, ES was faster, and EA was much greater for pre-CL than pre-corneal. The differences identified may be an aetiological component of CL discomfort and the relationship between TFK and discomfort in contact lens wearers should be investigated.

1. Introduction

A functional tear film is required to keep the anterior epithelium of the cornea moist, to provide protection against dust and microorganisms, to transport waste away and to provide a smooth optical surface allowing clear vision [1–5]. Since exposure of the tear film to the environment affects its stability [6,7], it has to be reformed on a continuous basis aided by blinking, and ideally the interval between blinks should be shorter than the time that is taken for the tear film to become unstable [8].

The pre-corneal tear film has conventionally been recognized as being a tri-layered structure approximately 3 μm thick [9,10], consisting of an inner mucous layer, a middle aqueous layer and an outer lipid layer [3,11]. More recently a lack of distinction between these layers has been recognized and in the recently published Dry Eye Workshop II Tear Film Report, the pre-corneal tear film is more accurately described as comprising a single dynamic functional unit with the muco-aqueous component being closest to the epithelial cells and an

overlying lipid layer at the air interface [12]. At the inner interface between the tear film and the ocular surface there is a glycocalyx formed by the expression of transmembrane mucins from the epithelial cells of the cornea and conjunctiva [13]. Both these transmembrane mucins, and the gel-forming mucins of the inner mucous layer are known to play an integral part in spreading and stabilizing the pre-corneal tear film between blinks [1,3]. The main physical function of the aqueous component is to lubricate the ocular surface and evaporation of the aqueous is retarded by the overlying lipid [6]. This lipid layer is composed of an outermost non-polar component with polar lipids providing surfactant properties at the interface between the aqueous and lipid layers [14,15], which further stabilizes the tear film [15].

Contact lenses can have both biophysical interactions with the tear film and can result in biochemical changes to the tear film. A detailed review of these interactions has recently been reported by the Contact Lens Interactions with the Tear Film Subcommittee of the TFOS International Workshop on Contact Lens Discomfort [16]; therefore,

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only a summary of the key pertinent impacts is provided. When a contact lens is inserted into the eye the pre-corneal tear film is split into a pre-contact lens tear film and a post-contact lens tear film [17]. It has been reported that initially the pre-contact lens tear film is thicker than the pre-corneal tear film without a contact lens in place [18]; however, once any reflex tearing has subsided, the thickness has decreased to approximately 2 μm as compared with 3 μm for the pre-corneal tear film [9,17,18], and the post-lens tear film has most consistently been reported to be 1–3 μm centrally. [10,17,18]. In addition to overall changes in thickness, a disruption of the outermost lipid layer has also been reported with contact lens wear [19–21], along with an accompanying decrease in tear film stability which is typically characterized by a decrease in tear break up time [22–25]. An increase in evaporation rate of 1.2–2.6 times has also been reported [26–28].

An important effect of the presence of a contact lens on tear film regeneration, that has until recently been largely ignored, is its insulating effect on the corneal sensory mechanism. Pre-corneal tear film evaporation leads to corneal surface cooling and increased osmolarity; both changes are detected by the corneal cold receptors, in turn leading to reflex blinking to maintain tear film homeostasis [35–39]. Whereas the pre-contact lens tear film temperature is lower than the corneal temperature, the temperature of the post contact lens tear film is higher, potentially affecting the blink reflex mechanism [40,41].

Most assessments of tear film stability concentrate on the period of time during which the tear film is performing well, and comparisons between contact lens wearers and non-lens wearers have shown differences in the non-invasive break up time. [22–24,42]. To date, there is no information regarding differences between the pre-contact lens and pre-corneal with respect to the severity of the tear film anomaly at the time of the break, the length of time during which the compromised tear film is present before the natural blink and the severity of the tear film anomaly at the time of the blink. These parameters are jointly referred to as the Tear Film Kinetics (TFK) and have been characterized using a non-invasive, post hoc analysis technique that is able to evaluate tear film dynamics during the full interblink period [43].

The objective of this study was to quantify the TFK over Inter Blink (IB) Period in both contact lens and non-contact lens wearers. The hypothesis was that contact lens TFK are inferior to corneal TFK with the greatest difference occurring at the time of the blink.

2. Methods

2.1. Study design and procedures

The study population comprised 202 soft contact lens wearers and 133 non-lens wearers attending the Ocular Technology Group - International (OTG-i) research clinic for routine screening visits prior to enrolment into its database of prospective study participants. The subjects had normal eyes, other than the need for vision correction. Throughout the study, the tenets of the Declaration of Helsinki were adhered to, informed consent was provided prior to any procedures being conducted. This study was a retrospective analysis of the OTG-i existing database. OTG-i did apply for ethics committee approval through the UK centralised National Health System (NHS) - Health Research Authority (HRA) Integrated Research Application System (IRAS) and the decision was made by the Research Ethics Committee that the analysis of existing database did not require ethics approval. Therefore, this study was exempted from ethical review.

Contact lens wearing subjects attended the visit wearing their habitual contact lenses. All subjects initially completed the Ocular Surface Disease Index (OSDI) questionnaire; [44] contact lens wearers were instructed to complete the questionnaire based upon their contact lens wearing experiences in the preceding one-week period. The lipid layer of the pre-contact lens or pre-corneal tear film was viewed with a Topcon SL-D4 slit lamp biomicroscope (Topcon, Newbury, UK) at 25 times magnification with illumination provided by the Tearscope Plus

(Keeler, Windsor, UK), prior to any other invasive assessments of the tear film or ocular adnexa being conducted. Video segments were captured for both the right and left eyes over a period of at least three natural blinks using the Topcon DV-3 high resolution digital video camera, which has a frame rate of 24 s^{-1} , and Topcon IMAGeNet i-base software. Programmable settings were used to ensure consistent lighting levels across subjects.

All videos were subsequently coded in a non-identifiable manner by an unmasked technician (contact lens or non-contact lens wearer, eye, subject demographics etc.) for subsequent post hoc analysis by trained, masked investigators. The digital videos were initially viewed with VSDC Free Video Editor (version 1.4.10 and the time that elapsed from opening the eyes until the first break in the lipid layer occurred was measured for each of three interblink periods. The TFK were measured for the blink interval associated with the median of these measurements. An image of the tear film was then captured at the time of the first break and for the time point corresponding to the last image with the eye fully open immediately prior to the next blink. For each image highlighting of area(s) of break in the lipid layer was subsequently made with Image J Version 1.49 an open source software made available by the NIH (<https://imagej.nih.gov/ij/>) and a proprietary automated image analysis routine was used to quantify the break characteristics. Examples of the first break in the lipid layer, corresponding to the NIBUT, and the breaks in the tear film immediately prior to the next spontaneous blink, as highlighted by Image J, are shown in Fig. 1A and B respectively.



A



B

Fig. 1. A: First break in the lipid layer, corresponding to the NIBUT. B: The breaks in the tear film immediately prior to the next spontaneous blink.

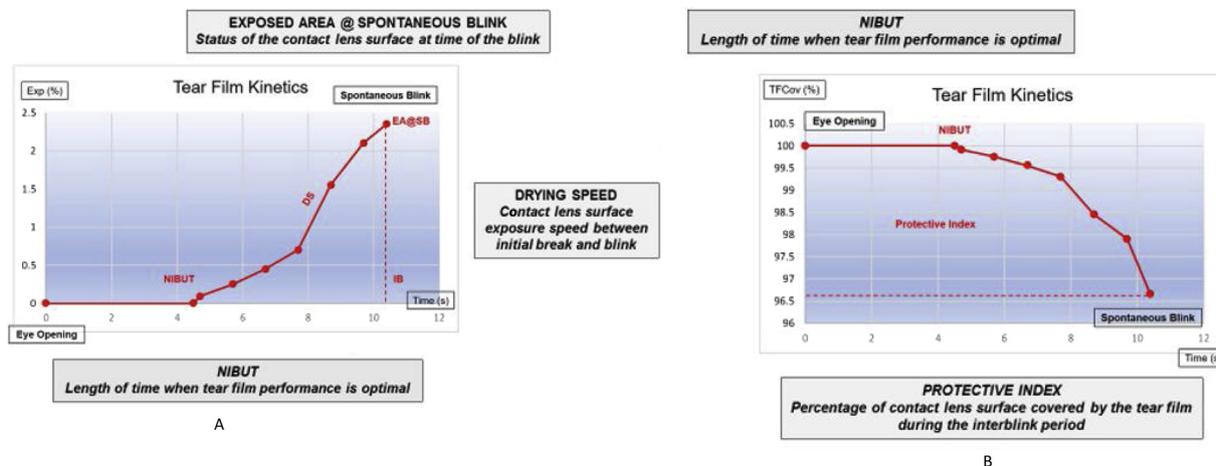


Fig. 2. A: Tear Film Kinetics (TFK) Parameters, NIBUT = Non-Invasive Tear Break Up Time. B: Tear Film Kinetics (TFK) Parameters NIBUT = Non-Invasive Tear Break Up Time, EA 1st Break = Exposed Area at First Break.

The parameters analyzed for each of the videos of the pre-contact lens and pre-corneal tear films are represented graphically in Fig. 2A and B. The Non-Invasive Break Up Time (NIBUT) is the time in seconds between eye opening and the appearance of the first visible break in the lipid layer of the pre-contact lens or pre-corneal tear film. The Interblink Time (IB) is the time in seconds between eye opening and the start of the subsequent blink. The Exposed Area at the First Break (EA 1st Break) corresponds to the percentage of the contact lens or corneal surface over which there is a break in anterior to the lens (pre-contact lens) or anterior to the cornea (pre-corneal) tear film and hence exposure of the contact lens or corneal surface to the atmosphere when the first break is detected. The time of the first break is when a break is observed, hence the exposed area at the time of the first break is never zero. The Exposed Area at Blink (EA Blink) corresponds to the percentage of the contact lens or corneal surface over which there is a break in the pre-contact lens or pre-corneal tear film and hence exposure of the surfaces to the atmosphere at the time of the natural blink. The Exposure Speed (ES), which relates to surface dehydration, is the increase in the contact lens or corneal surface that is exposed to the atmosphere (not covered by the tear film) between the first break and the natural blink; it is recorded in mm²/s. In addition, the Protective Index (PI) was calculated; this corresponds to the percentage of the contact lens or corneal surface that is not exposed to the atmosphere (i.e. fully covered by the tear film) during the entire interblink period.

2.2. Statistical analyses

The data were first tested for normality and transformed if necessary and where possible. For those parameters which were normal either prior to or post transformation, a Mixed Linear Model (MLM) was used and for the parameters that could not be normalized a Generalized Linear Model (GLM) was used. The models used were as follows:

- i NIBUT: the data were transformed (LOG of NIBUT)) and a MLM was carried out;
- ii IB: the data were transformed (LOG of IB) and a MLM was carried out;
- iii EA 1st Break data were fitted in a GLM with Tweedie (1.5) Distribution and identity as a link function;
- iv EA Blink data were fitted in a GLM with Tweedie (1.5) Distribution and identity as a link function;
- v PI data were transformed (1/PROTECTIVE INDEX) to fit in a GLM with Tweedie (1.5) Distribution and identity as a link function;
- vi Average ES data were fitted in a GLM with Tweedie (1.5) Distribution and identity as a link function.

In all cases where individual data were available for each eye these were included in the Mixed Generalized Estimating Equation Model (A Mixed Generalized Linear Model with repeated factors). The fixed factors were contact lens wear status (Pre-contact lens for contact lens wearer vs. pre-corneal for Non-contact lens wearer), wear status and eye. The subject identification number was a random factor. The covariance structure was chosen as exchangeable. In all cases Bonferroni adjustments were used for multiple post hoc comparisons. The criterion for statistical significance was $p < 0.05$.

3. Results

3.1. Study population

The demographics for the contact lens wearing and non-contact lens wearing groups are presented in Table 1. The non-contact lens wearing group was significantly older than the contact lens wearing group with a mean difference of 7.8 years ($p < 0.001$) but similar in their gender distribution ($p = 0.518$). The OSDI score was significantly higher for the non-contact lens wearers than for the contact lens wearers ($p < 0.001$) and there was a higher proportion of asymptomatic contact lens wearers (OSDI $\leq 12 = 59\%$; OSDI $> 12 = 41\%$) than non-wearers (OSDI $\leq 12 = 32\%$; OSDI $> 12 = 68\%$).

The contact lens wearers comprised 47% daily disposable wearers, 13% two weekly replacement wearers and 40% monthly replacement wearers; 47% wore hydrogel materials and 53% silicone hydrogel materials and the mean reported daily wearing time was 11.0 ± 3.4 h.

Table 1 Subject Demographics for Contact Lens Wearers (CLW) and Non Wearers (NW).

Variable	CLW	NW
Number (n)	202	133
Age (years)		
Mean \pm SD	29.5 \pm 9.4	37.3 \pm 12.9
Median	26	35
Range	18 to 62	18 to 64
Sex		
Male	67 (33%)	48 (36%)
Female	135 (67%)	86 (64%)
OSDI score		
Mean \pm SD	14.2 \pm 14.2	25.5 \pm 21.4
Median	9.2	19.1
Range	0 to 65.1	0 to 93.8
Symptom status (OSDI)		
Asymptomatic (≤ 12)	59%	32%
Symptomatic (> 12)	41%	68%

Table 2
Study Results Summary.

	NIBUT (s)	Exposed Area (%) 1stBreak	Interblink Time (s)	Exposed Area (%) at Blink	Exposure Speed (mm ² /s)	Protective Index (%)
Contact Lens Wearers (CLW)						
Number (n)	404	404	404	404	404	404
Mean	5.12	0.430	9.35	6.66	0.339	97.06
Median	3.50	0.010	7.30	0.08	0.004	99.99
Std. Dev	5.37	3.595	7.92	17.22	0.853	8.45
Minimum	0.10	0.000	0.30	0.00	0.000	23.82
Maximum	41.40	61.000	65.60	100.00	6.550	100.00
Non-lens wearers (NW)						
Number (n)	266	266	266	266	266	266
Mean	9.05	0.003	9.84	0.03	0.004	99.99
Median	6.30	0.000	6.60	0.00	0.000	100.00
Std. Dev	8.21	0.014	8.81	0.12	0.015	0.05
Minimum	0.50	0.000	1.40	0.00	0.000	99.28
Maximum	66.20	0.031	66.20	2.00	0.130	100.00

The modality, material distributions and daily wearing time are representative of a contact lens wearing population in the United Kingdom. A summary of study results can be found in Table 2.

3.2. Non-invasive break up time characteristics

The frequency distribution of the NIBUT in the contact lens wearers and non-contact lens wearers is represented graphically in Fig. 3. In cases where there was no observable tear film break during the IB period the NIBUT was reported as the IB time. The distribution is positively skewed for both groups but the mean NIBUT was 44% shorter for the contact lens wearers than the non-lens wearers (mean 5.1 versus 9.1 s, $p < 0.001$).

The frequency distribution for the EA 1st Break is represented graphically in Fig. 4. There was no observable break during the IB period for 47% of the contact lens wearers and 86% of the non-contact lens wearers. When a break was observed, the mean EA 1st Break was generally very small, measuring 1% or less of the area of observation for 96% of the subjects; however the mean EA 1st Break was significantly smaller for the non-contact lens wearers than the contact lens wearers (0.003% versus 0.430%, $p < 0.001$).

3.3. Tear film characteristics at the spontaneous blink

The frequency distribution of the IB time is represented graphically in Fig. 5. The IB time ranged from less than 2 s to greater than 45 s; however, the mean IB time was similar for the contact lens wearers and non-contact lens wearers (9.4 and 9.8 s respectively, $p = 0.213$).

The frequency distribution for the EA Blink is represented graphically in Fig. 6. As stated earlier, there was no observable break during the IB period for 47% of the contact lens wearers and 86% of the non-

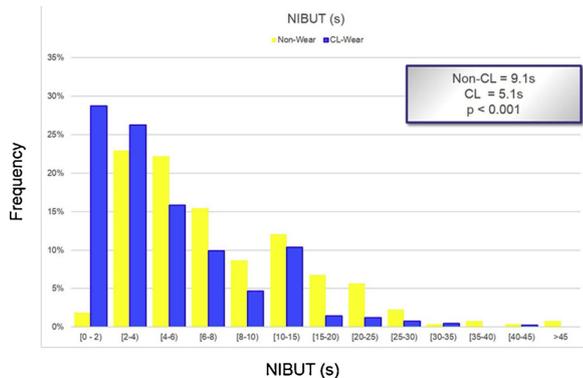


Fig. 3. Frequency distribution of Non Invasive Break Up Time (NIBUT) in seconds for contact lens wearers and non-contact lens wearers.

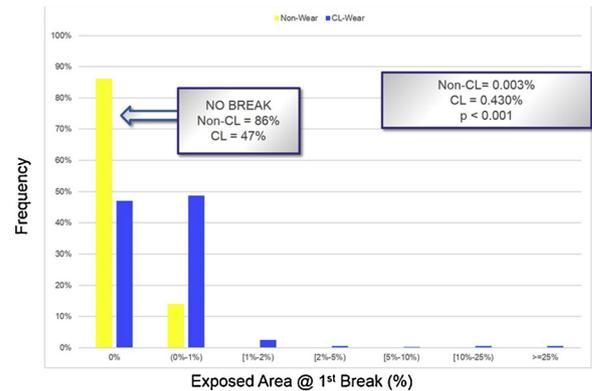


Fig. 4. Frequency distribution for Exposed Area (EA) at 1st Break for contact lens wearers and non-lens wearers.

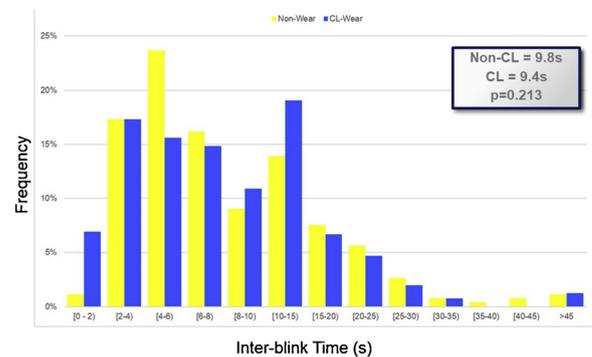


Fig. 5. Frequency distribution of Inter Blink Time in seconds for contact lens wearers and non-lens wearers.

contact lens wearers. When a break was observed, the mean EA Blink was significantly smaller for the non-contact lens wearers than the contact lens wearers (0.03% versus 6.66%, $p < 0.001$). The maximum EA Blink for the non-lens wearers was 1%, whereas the EA Blink was greater than 1% in 32% of wearers and greater than 10% in 15% of wearers.

3.4. Surface dehydration characteristics

The average exposure speed was significantly faster for the contact lens wearers than the non-lens wearers (0.339 mm²/s versus 0.004 mm²/s, $p < 0.001$). The distribution of exposure speed for the two groups is represented graphically in Fig. 7.

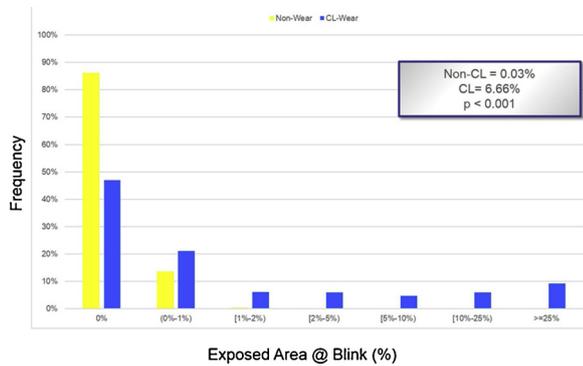


Fig. 6. Frequency distribution of the Exposed Area at blink as a percentage of visible area for contact lens wearers and non-lens wearers.

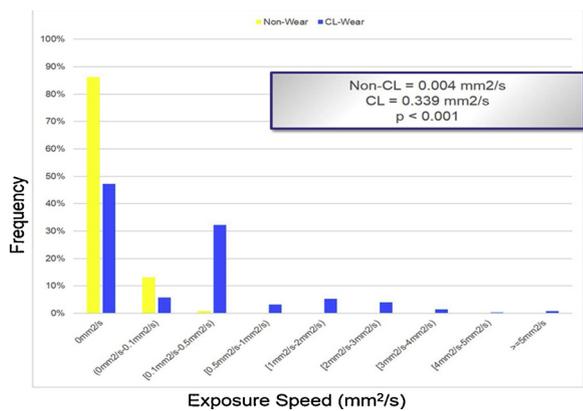


Fig. 7. Frequency distribution of Exposure Speed for contact lens wearers and non-lens wearers.

3.5. Protective index

The Protective Index was significantly higher for the non-contact lens wearers than the contact lens wearers (99.9% versus 97.1%, $p < 0.001$) and for 14% of contact lens wearers more than 5% of the contact lens was exposed to the atmosphere (not covered by the tear film) during the entire interblink period. The frequency distribution of the Protective Index is represented graphically in Fig. 8.

Overall the hypotheses tested during the study were demonstrated and the TFK of the pre-contact lens tear film were shown to be inferior to those of the pre-corneal tear film.

3.6. Non-invasive break up time vs. inter blink correlation

The analysis of the correlation between NIBUT and IB times

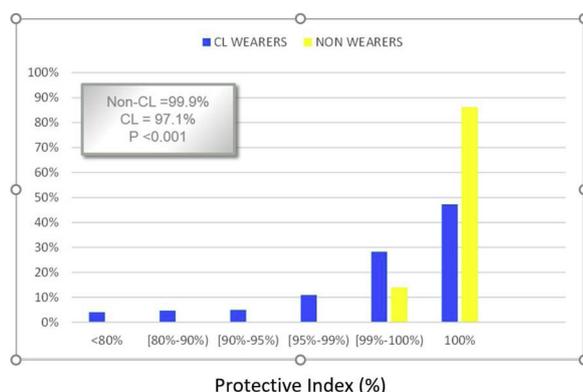


Fig. 8. Frequency distribution of the Protective Index (PI).

revealed some marked differences between the contact lens wearers and non-wearers. For the pre-corneal tear film of non-contact lenses wearers NIBUT and IB were very highly correlated ($r = 0.935$, $p < 0.001$). In contrast, for contact lens wearers the correlation between NIBUT and IB was moderate to strong ($r = 0.600$, $p < 0.001$), suggesting a different mechanism being involved in spontaneous blinking for contact lens wearers and non-wearers. Further, the pre-corneal NIBUT-IB correlation was very strong and similar for both symptomatic ($r = 0.941$, $p < 0.001$) and asymptomatic ($r = 0.930$, $p < 0.001$) groups, but the pre-contact lens NIBUT-IB correlation was weaker for the symptomatic ($r = 0.487$, $p < 0.001$) than the asymptomatic ($r = 0.630$, $p < 0.001$) wearing group.

4. Discussion

The contact lens and non-contact lens population differed in two ways: the latter had a mean age that was 8 years older and had a greater preponderance of symptomatic subjects. Such characteristics within a population are associated with potentially greater tear film anomalies. Hence, any findings presenting greater tear film anomalies in contact lens wearers than non-wearers in this study cannot be attributed to differences in population demographics.

The hypothesis tested in this study was that contact lens TFK are inferior to corneal TFK, with the greatest difference occurring at the time of the blink. This hypothesis was supported by the results of the study. The pre-contact lens tear film NIBUT was on average 44% shorter than the pre-corneal tear film, while the exposed area at the time of the break was statistically different between the two groups, the amplitude was small for both groups (0.003% vs. 0.43%) and the difference not considered clinically significant.

In contrast, the difference in EA Blink, the percentage of the surface not covered by the tear film at the time of the blink, was both statistically and clinically highly different; the average exposure being 0.03% for the pre-corneal tear film and 6.6% for the pre-contact lens tear film respectively. Further, for the pre-contact lens tear film an exposure greater than 1% was recorded in 32% of the cases and an exposure greater than 10% was recorded in 15% of cases.

An additional difference between the pre-ocular and pre-contact lens tear films was the rate of expansion of the exposed surface area following the initial break, with the rate of expansion of the exposed surface area being much greater for the pre-contact lens tear film. This finding points to the poorer capability of the contact lens surface as compared to the corneal surface to resist dehydration once an initial break in the tear film has occurred. It is acknowledged that dehydration is not the sole mechanism underpinning tear fluid withdrawal from the lens surface, however under the conditions of the current work, it is likely to be dominant.

Importantly the correlation between the initial break and the occurrence of the spontaneous blink, which was nearly perfect for the pre-corneal tear film, was considerably poorer for the pre-contact lens tear film. This may indicate a modified blink control mechanism for the pre-contact lens tear film compared with the pre-corneal tear film.

The current literature indicates that there is an association between ocular surface sensitivity and spontaneous blinking as follows. Cold receptors, which constitute 10%–15% of all corneal receptors, have a dynamic response characteristic that can detect a change in temperature as small as 0.5 °C [30]; the same receptors also detect increases in tear film osmolarity. The latest literature suggests that cold receptors have a leading role in detecting changes (cooling and increased osmolarity) that occur because of tear film evaporation. Based upon this, the TFOS DEWS II Working group on Pain and Sensation hypothesized that cold receptors play a leading role in initiating spontaneous reflex blinking and associated lacrimal production [29].

The contact lens divides the tear film into pre (anterior surface) and post (posterior surface) contact lens tear films; whereas the pre-contact lens tear film is cooler than the pre-corneal tear film, the post-contact

lens tear film is warmer than the pre-corneal tear film [31,32].

Hence, a possible mechanism for a disassociation between surface break and spontaneous blinking is that the contact lens partially insulates the corneal surface from environmentally induced tear film changes normally detected by the cold receptors leading to the initiation of spontaneous blinking. Due to this, spontaneous blinking efficiency is affected, leading to a very large contact lens surface area being unprotected by the tear film at the time of the spontaneous blink in a proportion of wearers. The current study showed the presence of large surface area not covered by the tear film at the time of the blink to be unique to contact lenses, this was not observed for the pre-corneal tear film of the large proportion of non-contact lens wearing population that included a significant prevalence of dry eye sufferers.

Blinking occurs over 10,000 times per day and at every blink, friction occurs between the leading eyelid margin and the corneal or contact lens surface. The eyelid, cornea or contact lens friction is controlled by the lubrication afforded by the tear film. When a continuous tear film is present, hydrodynamic lubrication occurs and the friction is very low. The opposite occurs when the tear film is broken and large areas of the contact lens surface are exposed, in such a case mixed and boundary lubrications, which are associated with much higher friction, occur [33]. In an earlier study, differences in tear film kinetics between symptomatic and asymptomatic contact lens wearers, representing differences in on eye lubrication have been demonstrated. Symptomatic contact lens wearers have a significantly shorter break up time and significantly greater surface exposure at the time of the blink than asymptomatic contact lens wearers [34].

Considering the findings in this study of a poorer correlation between the initial break and the occurrence of the spontaneous blink for symptomatic than for asymptomatic contact lens wearers and the findings in the previous study of greater symptomatology in the presence of poorer contact lens surface wettability indicative of greater friction at blink, it is proposed that a loss of spontaneous blinking homeostasis may play a significant role and may lead to compromised tear film kinetics and contact lens discomfort. Future studies should investigate the association between compromised spontaneous blinking and tear film kinetics with contact lens discomfort.

5. Conclusion

The current study which compared the TFK over the full spontaneous interblink period has proved that the pre-contact lens TFK were significantly inferior than the pre-corneal TFK. The non-invasive break up time was significantly shorter, and once the initial break had occurred, the speed at which the surface is no longer covered by the tear film was much greater for the pre-contact lens than the pre-corneal tear film. In addition, the extent of the exposed contact lens surface at the time of the blink was much greater than the extent of the exposed corneal surface. It is therefore hypothesized that the presence of the contact lens partially dampens the corneal cold receptor mechanism that controls spontaneous blinking. The implication of the loss of spontaneous blinking homeostasis is that a significant percentage (15%) of wearers are not able to compensate, the loss of synchronization between tear film break-up (thinning) and spontaneous blinking leading to the presence of a non-continuous tear film over the contact lens surface which has been previously associated with contact lens discomfort.

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