〈Regular Article〉

Noninvasive measurement of tear film break-up time in eyes with high-water-content contact lenses

Hisataka FUJIMOTO[1, 2)]

1) Department of Ophthalmology, Kawasaki Medical School,
2) Department of Ophthalmology, Osaka University Graduate School of Medicine

ABSTRACT **Objective**: To evaluate changes in tear dynamics under soft contact lenses (SCLs) by measuring the noninvasive Keratograph break-up time (NIKBUT) in subjects wearing SCLs.

Methods: The study included 24 eyes of 12 subjects (10 women and 2 men; age range, 19-38 years) with experience wearing contact lenses and without ocular surface disease except for a refractive error. An infrared video-topographer was used to measure the NIKBUTs with and without high-water-content contact lens. The subjects were asked to grade their subjective feeling of dehydration on a scale of 0 to 3, with 0 indicating no dehydration and 3 indicating maximal dehydration.

Results: The eyes were divided into two groups: group A comprising 16 eyes that showed a significant decrease ($P < 0.05$) in the NIKBUTs with SCLs, and group B comprising eight eyes in which the NIKBUTs remained unchanged. The NIKBUTs without SCLs were significantly longer ($P < 0.001$) in group A than in group B. The subjective feelings of dehydration decreased significantly ($P < 0.001$) among subjects with SCLs in group B, whereas the subjective feelings remained unchanged among subjects in group A.

Conclusions: The NIKBUTs became relatively shorter with SCLs regardless of the basal NIKBUT of a bare eye. The changes in the NIKBUTs with SCLs could be classified into two groups. These findings offer new insights into the mechanism underlying SCL-induced complications. doi：10.11482/KMJ-E202046087 *(Accepted on June 22, 2020)*

Key words：Soft contact lens, Tear break-up time, Topographer, NIKBUT

Contact lenses are used worldwide for correcting ametropia and astigmatism. However, 50% of all contact lens users have symptoms of dryness and discomfort irrespective of whether they use daily-wear or extended-wear contact lenses[1-3)]. Many contact lens wearers experience significant levels of discomfort[4)], which is also the principal reason why wearers stop or reduce using their contact lenses[5-8)].

The principal symptoms of discomfort resemble those in patients with dry eye[4, 9)]. The report of the 2007 International Dry Eye WorkShop contained

Corresponding author
Hisataka Fujimoto
Department of Ophthalmology, Kawasaki Medical School, 577 Matsushima, Kurashiki, 701-0192, Japan

Phone : 81 86 462 1111
Fax : 81 86 462 1199

a definition of dry eye, as well as a classification scheme for different types of dry eye for clinical researchers[10]. The report suggested that contact lens dry eye should be considered a subclassification of the dry eye syndrome. Interactions between tear films and soft contact lenses (SCLs) play important roles in SCL-induced discomfort and symptoms, especially in wearers of high-water-content contact lens[11]. The tear film becomes unstable with the use of such lenses, whose use in low humidity also induces discomfort[12]. Eyes with lower tear film break-up time (BUT) have been reported to be unable to tolerate the use of contact lenses[13].

Recent technological advances have enabled us to evaluate the quantity and quality of the tear film. Several methods are now available to evaluate and quantify tear film parameters such as tear meniscus height (TMH), including slit-lamp evaluation with a graticule scale, optical pachymetry, video-meniscometry, and optical coherence tomography (OCT)[14−19]. Simultaneously, several noninvasive tear BUT tests have been developed to evaluate tear film stability. Consecutive topographic image recording techniques such as the tear film stability analysis system have also been applied to assess tear film stability[20, 21].

However, the tear film dynamics on SCLs are not well understood, even though they play an important role in contact lens-induced complications. The conventional BUT measurement using fluorescein is a well-established technique for assessing tear film stability, but it is not applicable for eyes with SCLs. Since the noninvasive tear break-up time tests do not require fluorescein instillation, these tests can help understand the unresolved tear film dynamics on SCLs.

In order to evaluate the changes in tear dynamics on SCLs, the noninvasive Keratograph break-up time (NIKBUT) of the tear film was measured in subjects wearing these lenses.

MATERIALS AND METHODS

The institutional review board of Osaka University Hospital approved the study, which adhered to the tenets of the Declaration of Helsinki. All subjects provided informed consent after they received an explanation of the nature and possible consequences of the study.

Subjects

Twenty-four eyes of 12 healthy subjects (10 women and 2 men; age range [mean ± standard deviation], 19-38 [28.2 ± 6.7] years) who had no ocular surface disease except for a refractive error were recruited for this study. All subjects were experienced contact lens wearers and had been wearing SCLs before participation in this study.

Tear film assessment using the Keratograph 5M

Keratograph 5M (Oculus GmbH, Wetzlar, Germany) equipped with a modified tear film scanning function was used for tear film assessment. With this device, the lower tear meniscus was imaged and the TMH was measured using an integrated ruler. In order to avoid the influence of the SCL's lower edge on the TMH, the TMHs were measured 4 o'clock and 8 o'clock positions and averaged, namely avoid 6 o'clock position.

The NIKBUT was measured to evaluate tear film stability. The principle underlying the NIKBUT and its measurement using the Keratograph have been described previously[22−24]. In brief, 22 mire rings are projected on the corneal surface, and the projected images are captured by videokeratoscopy. Corneal topographic data were continuously obtained after the subjects opened their eyes while simultaneously ensuring the subjects did not blink. By using an infrared Placido ring, the instrument can detect tear break-ups and calculate BUTs. The NIKBUT was measured as the time interval between an eye blink and the first perturbation caused by a grid projected onto the surface of the cornea, which the device detected automatically for up to 25 s. The subjects were instructed to keep their eyes open during NIKBUT measurements, and the recording was discontinued at the next blink.

Experimental protocol

In both eyes of each subject, the conventional BUT using fluorescein was measured first. On another day, the TMH and NIKBUT were measured without SCLs by using Keratograph 5M. The NIKBUTs were measured more than 5 times. In order to avoid reflex tearing, the NIKBUT measurements for each eye were performed with an interval of more than 5 min between measurements. Lower tear film meniscus images were captured once for each subject just before the series of NIKBUT measurements, and the TMH was measured using an integrated ruler.

Thirty minutes after wearing SCLs (Medalist 1 Day Plus; Bausch & Lomb, Tokyo, Japan), the NIKBUTs were measured again. This brand of contact lens has a high water content of 58.0% and a diameter of 14.2 mm, and it is classified by the U.S. Food and Drug Administration as a group II lens. The same base curve and lens power (8.6 mm and -2.0 diopters, respectively) were used for all subjects. The NIKBUTs were measured more than 5 times with an interval of more than 5 min.

The subjects were asked to grade their subjective feeling of dryness during the NIKBUT measurements with and without SCLs on a scale of 0 to 3, with 0 indicating no dryness and 3 indicating maximal dryness.

Statistical analysis

All statistical analyses were performed using MATLAB (The MathWorks, Inc., Natick, MA). Pearson correlation between the average values of the conventional BUT and the NIKBUT was examined. The NIKBUTs with and without SCLs were compared using the Kolmogorov-Smirnov test. The subjective feelings of dryness values with and without SCLs and the TMHs with and without SCLs were compared using the Kruskal-Wallis analysis of variance (ANOVA) test and Tukey honest significant difference (HSD) post-hoc test. $P < 0.05$ was considered significant for all analyses.

RESULTS

Correlation between the fluorescein BUT and NIKBUT measurements

The average fluorescein BUTs for each eye ranged from 3.4 to 24.3 (mean, 11.1) s, and the standard deviations (SDs) ranged from 1.1 to 10.3 (mean, 4.5) s. The average NIKBUTs for each eye ranged from 4.4 to 22.1 (mean, 10.4) s, and the SDs ranged from 1.2 to 10.6 (mean, 4.3) s. The correlation between the fluorescein BUTs and NIKBUTs is shown in Fig. 1 A significant correlation ($P = 1.5 \times 10^{-9}$, $R^2 = 0.816$) was confirmed.

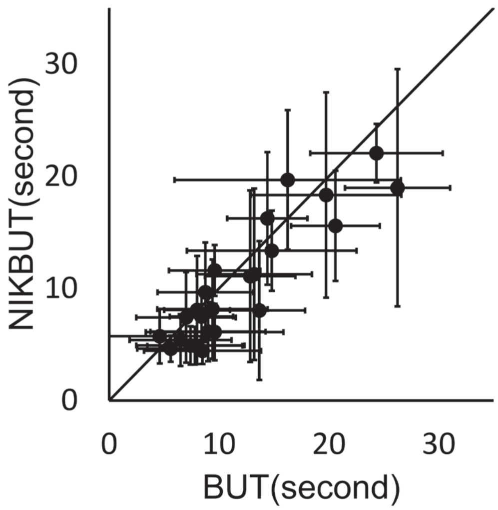

Fig. 1. Graph showing a comparison between the conventional break-up time (BUT) and noninvasive Keratograph break-up time (NIKBUT). More than 5 measurements were performed for each eye using both the conventional BUT with fluorescein and NIKBUT. The averaged values are plotted as black circles with error bars representing standard deviations. Each circle represents an eye. The plots are close to the identity line (solid line).

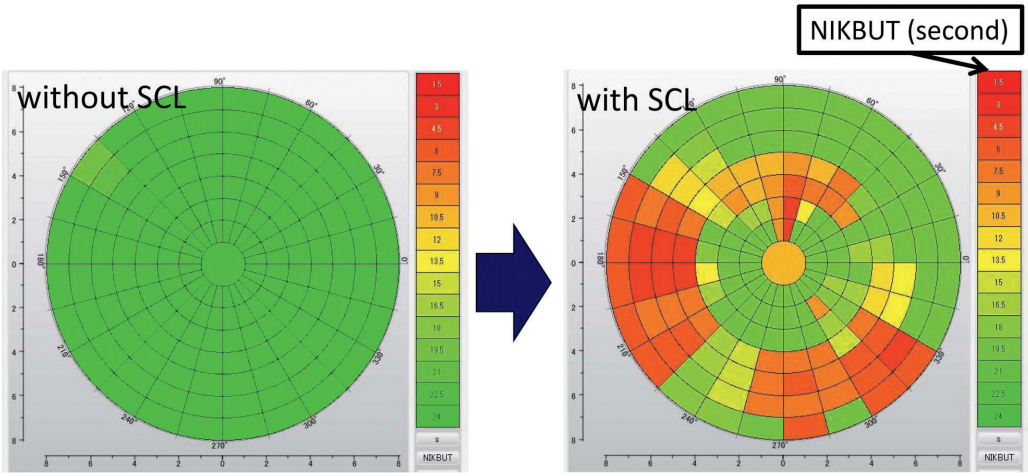

Fig. 2. Representative image of the right eye of a 35-year-old man showing changes in noninvasive Keratograph break-up time (NIKBUT) with the use of soft contact lenses (SCLs). The NIKBUTs for the same eye before and after high water-content SCL use are presented. The NIKBUTs are calculated as the first break-up time among all the segmented areas. A remarkable reduction in the NIKBUT induced by SCL use is observed.

The NIKBUT with and without SCLs

On the basis of the reduction in NIKBUTs induced by SCL wear (Fig. 2), the subjects' eyes were classified into two groups (Fig. 3). Group A comprised 16 eyes with a significant decrease ($P < 0.05$, Kolmogorov-Smirnov test) in the NIKBUTs measured while wearing SCLs (solid lines in Fig. 3), and group B comprised eight eyes with unchanged ($P \geq 0.05$, Kolmogorov-Smirnov test) NIKBUTs (dashed lines in Fig. 3). No eyes exhibited a significant increase in the NIKBUTs measured while wearing SCLs.

In group A, the average NIKBUTs with and without SCLs were 5.5 ± 0.4 s and 16.9 ± 2.9 s, respectively, showing a significant difference ($P < 0.05$, Kolmogorov-Smirnov test). In group B, the average NIKBUTs with and without SCLs were 5.9 ± 1.9 s and 7.1 ± 2.2 s, respectively, showing no significant difference ($P \geq 0.05$, Kolmogorov-Smirnov test). Moreover, the average NIKBUTs without SCLs were significantly longer in group A than in group B ($P = 2.9 \times 10^{-8}$, Kolmogorov-Smirnov test).

7 subjects had both group A eyes, 3 subjects had

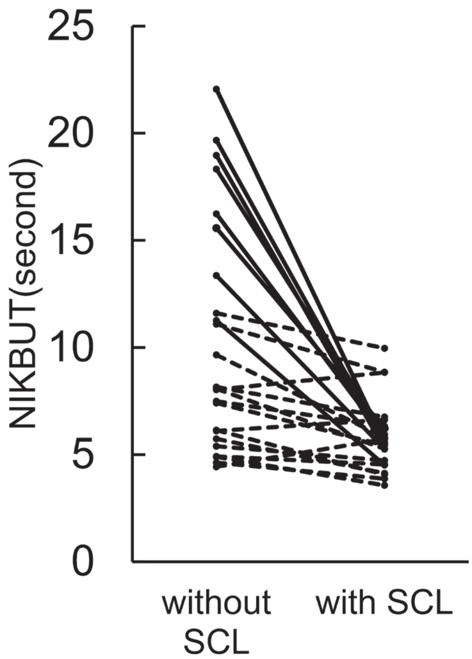

Fig. 3. Graph showing differences in noninvasive Keratograph break-up time (NIKBUT) with and without soft contact lenses (SCLs). The NIKBUT was measured more than 5 times for each eye with and without SCLs. Eyes with significant differences in the NIKBUTs ($P < 0.05$, Kolmogorov-Smirnov test) are plotted as solid lines (group A). Eyes without significant differences in the NIKBUTs ($P \geq 0.05$, Kolmogorov-Smirnov test) are plotted as dashed lines (group B).

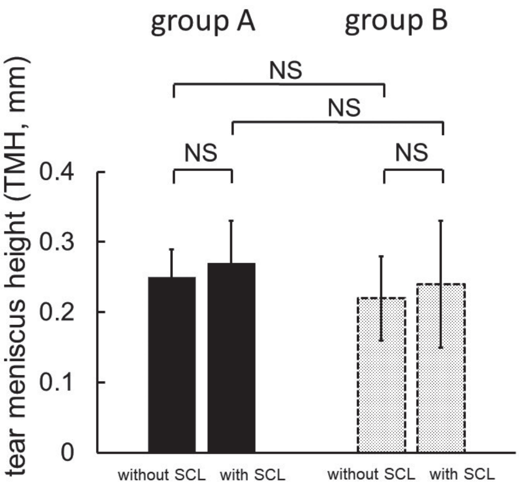

Fig. 4. Graph showing the tear meniscus heights (TMHs, mm) with and without soft contact lenses (SCLs). The TMHs show no significant differences ($P \geq 0.05$, Kruskal-Wallis analysis of variance test and Tukey honest significant difference post-hoc test) in all four conditions, i.e., with and without SCLs in groups A and B.

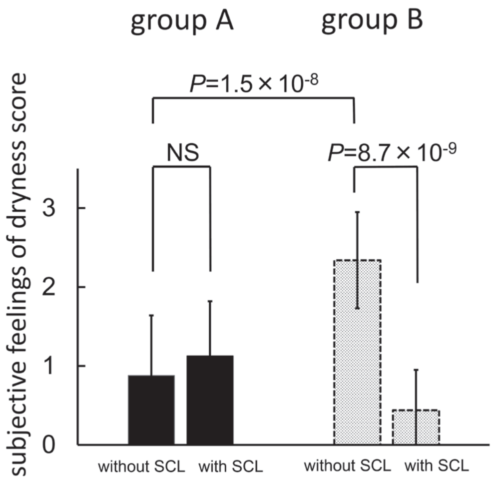

Fig. 5. Graph showing the scores of the subjective feelings of dryness. The patients' subjective feeling of dryness during the noninvasive Keratograph break-up time (NIKBUT) measurements with the eyes kept open are graded on a scale of 0 to 3, with 0 indicating no dryness and 3 indicating maximal dryness. Statistical comparisons were performed using the Kruskal-Wallis analysis of variance test and Tukey honest significant difference post-hoc test.

both group B eyes, and 2 subjects had both of the group A and group B eye.

TMH

In group A, the TMHs without and with SCLs were 0.25 ± 0.04 mm and 0.27 ± 0.06 mm, respectively. In group B, the TMHs without and with SCLs were 0.22 ± 0.06 mm and 0.24 ± 0.09 mm, respectively. Although the TMHs tend to be greater with SCLs in both groups A and B, the TMHs did not exhibit significant differences ($P \geq 0.05$, Kruskal-Wallis ANOVA test and Tukey HSD post-hoc test) between groups A and B with and without SCLs (Fig. 4).

Subjective ocular dryness

Subjective ocular dryness was scored at each NIKBUT measurement for each eye on a scale of 0 to 3, with 0 indicating no dryness and 3 indicating maximal dryness. In group A, the subjective ocular dryness score with SCLs (1.13 ± 0.69) did not differ from that without SCLs (0.88 ± 0.76) ($P \geq 0.05$, Kruskal-Wallis ANOVA test and Tukey HSD post-hoc test) (Fig. 5, left). In contrast, in group B, the subjective ocular dryness score without SCLs (2.34 ± 0.61) was significantly higher than that with SCLs (0.44 ± 0.51) ($P = 8.7 \times 10^{-9}$, Kruskal-Wallis ANOVA test and Tukey HSD post-hoc test) (Fig. 5, right). A comparison of the baseline ocular dryness score without SCLs showed that the score of group B (2.34 ± 0.61) was significantly greater than that of group A (0.88 ± 0.76) ($P = 1.5 \times 10^{-8}$, Kruskal-Wallis ANOVA test and Tukey HSD post-hoc test; Fig. 5).

DISCUSSION

Previous studies have shown a good correlation between the noninvasively measured BUT and fluorescein BUT when using several different equipment and Keratograph 5M[22, 23]. These results confirmed the positive correlation between the NIKBUT and conventional BUT. Therefore, the NIKBUT can be considered a sophisticated alternative to the conventional BUT.

In the current study, NIKBUTs were either lowered or remained unchanged when the subjects wore high-water-content SCLs. In fact, high-water-content SCLs are thought to aggravate dry eye and are considered risk factors for dry eye status[25]. These contact lenses may lose up to approximately 5% of their water content after 12 h of lens wear, whereas low-water-content lenses lose only approximately 1% of their water content within the same time period[26, 27]. However, tear fluid dynamics in a short time scale are not well understood. The results of this study revealed that even in eyes with normal BUTs, the NIKBUTs were shortened by the high-water-content SCLs. In contrast, in eyes with short BUTs, the NIKBUTs remained low when the high-water-content SCLs were used. Nevertheless, irrespective of whether the eyes had normal or short BUTs, the NIKBUTs were approximately less than 10 s with SCLs. This rapid tear film break-up is a possible reason why the high-water-content SCLs induce dry eye.

The tear film is known to become unstable when wearing high-water-content SCLs, especially in low humidity[12]. However, previous reports have not analyzed the basal BUTs and the effect of wearing SCLs. The current findings indicate that the NIKBUTs were significantly shortened by SCLs in eyes with originally normal BUTs, whereas NIKBUTs remained low and unchanged in eyes with originally short BUTs. This novel finding implies that the tear film dynamics and the SCL-induced pathology vary between eyes with normal and short BUTs.

Nichols et al. estimated that the tear film thickness in front of hydrogel contact lens (high-water-content contact lens) was 2.3 μm[28]. This value is almost half the natural tear film thickness. The reduced pre-contact lens tear film thickness may be the reason for the rapid drying up of the high-water-content SCL's surface in our results. However, the TMHs measured in our results remained unchanged regardless of wearing SCLs or the BUTs in bare eyes. This implies that the pre-contact lens tear film thickness is more important clinical feature than the TMH when wearing SCLs. On the other hand, previous reports indicate that wearing low-water-content SCLs reduced TMH using high-resolution OCT[29], but had limited effect on discomfort[13, 30]. This imply the discomfort mechanism is different between high and low -water-content SCLs conditions.

Studies have shown that wearing SCLs induce long-term discomfort[31, 32], especially in eyes with short BUTs[12]. Eyes with pre-contact lens BUTs less than 3 s are predicted to develop symptoms of discomfort in case of extended usage of SCLs[33]. In this study, short-term subjective feelings of dryness transiently improved when wearing high-water-content SCLs in eyes with short BUTs, even though their short NIKBUTs did not improve. These subjective feelings seem to be paradoxical, at the same time crucially may be important. Namely, the observed improvement in the subjective feelings of dryness when wearing SCLs may mask the discomfort. Moreover, the consequent decreases in nictitation reflex or eye blink result in progressive deterioration of dry eye. This may be another reason why high-water-content SCLs induced dry eye.

Recent research has shown that the quality of vision deteriorates when the tear film is disturbed even in normal eyes[34−36]. Serial measurements of topography or higher-order aberrations in patients with dry eye and healthy subjects have revealed that the dynamic changes that occur in the tear films after an eye blink have an effect on visual impairment[37−39]. Eye blink frequency is known to decrease 1 time per 10 seconds during visual display terminal (VDT) operation, which equates to 1 time per 3 seconds at the normal level[40]. In the present study, the NIKBUTs decreased to less than

10 s in almost all of the eyes when wearing high-water-content SCLs. The NIKBUT is shorter than the eye blink interval during VDT operation, which implies that the optical quality may be deteriorated during VDT operation in the later or ending period just before an eye blink. Consequently, careful consideration is needed when prescribing SCLs in the context of both the deterioration of dry eye and the visual function during VDT operation.

One limitation of the measurements performed in this study is the inability to evaluate the dynamics of the lipid layer of the tear film. Contact lens use may influence the lipid layer, which is thought to be play an important role in tear evaporation[41]. The simultaneous measurement of both tear film break-up and lipid layer dynamics would be very informative and should be explored further in future studies[42].

In summary, the NIKBUTs decreased to almost less than 10 s when wearing high-water-content SCLs, regardless of the basal NIKBUTs in bare eyes. In eyes with short BUTs, presumably including populations of patients with dry eye, the subjective feelings of dryness significantly improved when wearing high-water-content SCLs, even though the NIKBUTs remained short. These findings offer new insights into the mechanism underlying SCL-induced complications.

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CONFLICTS OF INTEREST AND SOURCE OF FUNDING

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