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**Effects of indoor low humidity on eye discomfort and associated physiological responses
in soft contact lens and non-lens wearers**

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Abstract

Eye discomfort due to dryness is one of the major complaints reported in indoor spaces. The purpose of this study was to quantitatively evaluate the effect of low humidity on eye discomfort in soft contact lens (SCL) and non-CL wearers. In addition to subjective sensations, physiological parameters related to eye discomfort including tear-film parameters and blink patterns were comparatively evaluated between relative humidities of 10% and 45% at 23°C. For both the SCL and non-CL wearer groups, low humidity had a significant effect on some of the measured physiological parameters. The SCL group showed lower ocular surface temperature and larger temperature differential after blinking at 10% relative humidity (RH) than that at 45% RH, indicating faster tear evaporation. Furthermore, their tear films tended to be thinner and have a shorter break-up time at 10% RH than at 45% RH. The non-CL group showed a significantly higher blink frequency and longer eye-closure time at 10% RH than at 45% RH, presumably as a compensatory response to the disturbance of the tear film due to low

humidity. These results suggest the importance of humidity control in indoor spaces in terms of tear-film quality, which contributes to eye discomfort.

Keywords

Indoor environment; Humidity comfort; Dry eye; Tear film; Ocular surface temperature; Blink pattern

Introduction

Complaints related to dryness of the skin, eyes and mucous membranes have been commonly reported in offices and living spaces.¹⁻⁶ According to a survey conducted in Japan,⁴ 70% of office workers experienced discomfort due to dryness, especially during the cold and dry winter season. Generally, 40 – 60% relative humidity (RH) is considered appropriate humidity in terms of minimizing transmission and viability of some viruses and health risks from dust mites and mould.^{7,8} However, humidity in indoor spaces including living spaces, offices and aircraft cabins is often below this range.^{6,9-13} According to a recent survey,⁶ more than half of the offices in the mid-latitudes and above had average indoor humidity lower than 40% during the winter months, and in some buildings, it was even below 10%. This is due to the balance between the low absolute humidity of the outdoor air and the amount of humidification and ventilation. To address the problem of discomfort due to dryness, the indoor humidity should first be improved through adequate air conditioning.

Although ASHRAE¹⁴ suggests the existence of a lower comfort limit of humidity due to non-thermal factors such as dry skin and eyes, there is no consensus on the limit in air-conditioned indoor spaces. The subjective discomfort of occupants due to dryness might be an important criterion for determining the humidity target. Therefore, it is necessary to clarify the environmental conditions that cause discomfort in each part of the body. So far, some studies have attempted to determine the required humidity level regarding dryness of skin and mucous

membranes.^{15–19} In this study, we focus on the eye, for which complaints of discomfort are prominent.^{3–5}

Some previous studies have reported stronger eye discomfort or dryness sensation and more frequent blinks in low-humidity environments. However, the link between these symptoms and humidity is unclear, especially in relation to subjective discomfort.^{15–17,19–25} Wyon et al.¹⁷ conducted an experiment in which subjects were exposed to relative humidities of 5%, 15%, 25% and 35% at 22°C for 5 h. They reported a higher blink frequency and 3–7% degradation in office work performance at 5% RH compared to 35% RH, while subjective eye dryness and irritation were slight even at 5% RH. Sunwoo et al.¹⁶ conducted an experiment in which the subjects were transferred from 50% RH to 10%, 30% and 50% RH at 25°C. They reported a higher blink frequency after the transfer to 30% RH or less, while no significant change in subjective dryness sensation was observed. There have been reports of large individual differences in eye discomfort and blink frequency under low-humidity conditions, and there are also large variations due to factors other than humidity, such as tasks and emotional states.^{19,26}

One possible means of quantitatively evaluating the adverse effects of low humidity on eye comfort is to measure associated physiological parameters. The surface of the cornea is protected by two layers of the tear film, which is composed of an aqueous layer mixed with mucins and a surface lipid layer that contribute to the suppression of water evaporation from the aqueous layer.²⁷ Although the details of the mechanism are not yet clear, eye discomfort and blinking reflect the tear-film condition which is affected by surrounding environments; an unstable tear film is reported to cause more frequent blinking and more intense discomfort.^{28–32} The tear film formed by blinking gradually evaporates during eye-opening, resulting in dry spots on the cornea. A shorter tear-film break-up time (BUT), defined as the time elapsed

1 between eye-opening after a blink and the appearance of the first dry spot, indicates a more
2 unstable tear film.³³ In addition, tear film stability is interrelated with other tear-film parameters,
3 including tear film thickness and tear evaporation rate; in general, a thinner tear film and faster
4 tear evaporation suggest a more unstable tear film.^{27,34} Previous studies have reported that lower
5 humidity promotes tear evaporation³⁵ making the tear film more unstable,^{24,36} which may lead
6 to eye discomfort.

7
8 However, only a few studies have investigated the effect of humidity alone on the tear film, and
9 no consensus has been reached. For example, Abusharha and Pearce²⁴ exposed their
10 experimental subjects to 5% and 40% RH at 21°C and showed that extremely low humidity
11 affects tear evaporation rates and BUT. On the other hand, Wyon et al.¹⁷ reported that there was
12 no significant difference in BUT between 5% and 35% RH at 22°C. Although some previous
13 studies have used the mucous ferning test to assess tear film,¹⁷ this test is currently not widely
14 used because of some limitations that need to be overcome.³⁷ To evaluate the impact of low
15 humidity on eye discomfort based on its mechanism, while identifying important parameters
16 for the evaluation, a comprehensive measurement of tear-film parameters and subjective
17 sensations should be conducted.

18
19 Moreover, previous studies on contact lens wearers are particularly lacking despite the fact that
20 soft contact lens (SCL) wearers account for more than 10% of the total population in the United
21 States and Japan.^{38,39} A contact lens divides a tear film into two thin layers, the pre- and post-
22 lens tear films. Because of this, as some previous research suggests,^{20,40,41} physiological and
23 psychological responses to the surrounding environment of SCL wearers are expected to be
24 different from those of non-CL wearers. Maruyama et al.⁴¹ reported that the tear films on SCLs
25 became thinner as temperature and relative humidity decreased. López-de la Rosa et al.⁴²

showed that pre-lens tear film stability decreased as the barometric pressure and humidity decreased. However, no study has investigated the effects of humidity on the tear films of SCL wearers under constant air temperature and barometric pressure, which are considered to affect the tear film as well as humidity.

As described above, few studies have evaluated the effect of humidity alone on eye discomfort based on tear-film parameters, especially with regard to contact lens wearers. Therefore, as the first step for determining humidity targets needed to reduce or eliminate eye discomfort, the main objective of this study was to quantitatively evaluate the effect of low humidity on eye discomfort based on tear-film related physiological parameters in addition to subjective sensations. The secondary objective was to investigate the differences in physiological and psychological responses to low humidity between SCL and non-CL wearers; this will indicate how the influence of contact lenses should be considered in determining humidity targets. To achieve these objectives, we conducted a series of artificial climate chamber experiments. With other environmental conditions being constant, SCL and non-CL wearers were exposed to two humidity conditions. In addition to subjective sensations and blink patterns, several tear-film parameters including BUT were compared between the humidity conditions, and the difference between the SCL and non-CL wearing groups was also investigated.

Methods

Subjects

A total of 18 subjects participated in the experiment. They were young Asian men and women aged 21 to 31 years, 9 with naked eyes and 9 with SCLs. Table 1 shows the subjects' gender, age, SCL-wearing condition, average Ocular Surface Disease Index (OSDI) score and smoking habit. For the subjects wearing SCLs, the frequency of lens replacement and the water content

of the lens are also shown. The SCLs used by the subjects were all commercially available disposable lenses. The OSDI score evaluated the severity of subjective symptoms of dry eye with a score of 0 to 100 based on 12 questions related to eye discomfort and visual abnormalities in the week prior to the experiment.^{43,44} A total of 9 subjects, 4 SCL wearers and 5 non-CL wearers, scored 13 or higher, indicating the possibility of dry eye.³³ Two men had a smoking habit of less than 10 cigarettes per day.

Table 1. Subject profiles. The non-contact lens (CL) wearer group was named ‘N’ and the soft contact lens (SCL) wearer group was named ‘C’, numbered in ascending order of mean Ocular Surface Disease Index (OSDI) score indicative dry eye severity. The CL properties were obtained from the manufacturers’ published data.

ID	Gender	Age	Contact lens (CL) wear	Replacement schedule of CL	Water content of CL [%]	Mean OSDI score	Smoking habit (number of cigarettes per day)
N1	Male	23	non-CL			2.1	
N2	Male	24	non-CL			4.2	
N3	Male	22	non-CL			6.8	
N4	Male	23	non-CL			8.3	Yes (8)
N5	Male	25	non-CL			13.2	
N6	Male	24	non-CL			18.8	
N7	Male	22	non-CL			22.2	
N8	Female	31	non-CL			28.9	
N9	Male	22	non-CL			34.1	
C1	Male	23	SCL	1 day	60	0.0	
C2	Male	26	SCL	2 weeks	33	3.1	Yes (0–2)
C3	Male	23	SCL	1 day	33	7.3	
C4	Female	21	SCL	2 weeks	48	10.0	
C5	Male	24	SCL	2 weeks	58	10.0	
C6	Female	23	SCL	2 weeks	40	14.6	
C7	Female	25	SCL	2 weeks	40	14.8	
C8	Female	22	SCL	2 weeks	39	17.8	
C9	Female	22	SCL	1 day	60	21.9	

Experimental design

The experiment was conducted from January to February 2020 in an artificial climate chamber at Kobe University, Japan. Considering the effects of diurnal fluctuations in body temperature, tear secretion and blinking,⁴⁵ all experiments were conducted between 10 am and 2:30 pm. To investigate the significance of environmental improvements in low-humidity indoor spaces, two

humidity conditions were selected: 10% RH as the lowest reported level of humidity in indoor spaces and 45% RH as humidity that met the conventionally targeted range. After 30 min in a pre-room ($31 \pm 6\%$ RH at $22 \pm 1^\circ\text{C}$ with an air velocity of 0.14 ± 0.07 m/s), the subjects were exposed to 10% RH (0.0017 kg/kgDA) and 45% RH (0.0079 kg/kgDA) at 23°C with an air velocity of 0.16 ± 0.06 m/s for 60 min. The exposure time was determined based on Abusharha and Pearce's study,²⁴ in which a plateau in BUT was observed within 60 min. Each condition was performed on different days in random order. During the experiment, air temperature, black globe temperature, humidity (RS-14, Espec, Japan), and air velocity (Model6543, Kanomax, Japan) were measured 1,100 mm above the floor and automatically recorded at 10-s intervals. The clothing condition was not controlled. The estimated intrinsic clothing insulation⁴⁶ for each experiment was 0.93 ± 0.17 clo (mean \pm SD).

Physiological measurements

Physiological measurements were conducted using noncontact and non-invasive methods. Tear-film thickness and stability, ocular surface temperature and blink pattern were measured as physiological parameters. The thickness and stability of the tear film were measured using a video interferometer (DR-1 α , Kowa, Japan). The tear film was visualized by interference imaging with white LED light, and its dynamics were recorded for up to 30 s as a moving image (30 fps) after blinking. From the video, non-invasive tear-film BUT (NIBUT) was measured as an index of tear-film stability. Additionally, tear-film thickness was evaluated based on the grades used in ophthalmology, namely the interference grade for non-CL wearers^{47,48} and SCL wearers⁴¹ and the spread grade.^{48,49} The details of each grade are presented in Table 2. Spread grade classifies the speed and range of upward tear extension after eyelid opening into five grades, and the interference grade classifies the colour and pattern of the tear interference image of the tear film into five grades. These grades were assessed based on the time from the blink to the completion of the tear film extension as well as the RGB colour histogram of the tear

interference image.

Table 2. Grading scales for tear-film thickness immediately after blinking. Higher spread grade and higher interference grade values for non-contact lens (CL) wearers imply a thinner aqueous tear layer.^{47–49} Higher interference grade values for soft CL wearers imply a thinner tear film on the contact lens.⁴¹

	Grade	Appearance	Description
Spread grade	1	Quick and complete spread, quickly reaching the upper lid margin.	A higher grade implies less aqueous tear volume.
	2	Slow and complete spread.	
	3	Slow and partial spread, reaching > 1/2 the height of the image.	
	4	Slow and partial spread, reaching ≤ 1/2 the height of the image.	
	5	No spreading of Tear film.	
Interference grade for non-CL wearers	1	Grayish interference colour, uniform distribution.	0 to around 100 nm of lipid layer.
	2	Grayish interference colour, nonuniform distribution.	
	3	A few interference colours, nonuniform distribution.	100 to 185 nm of lipid layer.
	4	Many interference colours, nonuniform distribution.	185 to 370 nm of lipid layer.
	5	Corneal surface is partially exposed.	No lipid layer presence.
Interference grade for SCL wearers	1	Grayish interference colour with smooth expansion after blinking.	Normal lipid and aqueous layer.
	2	Colourful interference pattern beneath the grayish color.	Thin lipid layer and thin aqueous layer.
	3	Single colourful interference pattern.	Thin aqueous layer without lipid layer.
	4	The surface of the CL is partially exposed immediately after blinking.	Thin aqueous layer without lipid layer.
	5	CL surface is completely exposed immediately after blinking.	No tear film presence.

The ocular surface temperature was measured using infrared thermography (testo875-1i, Testo, Japan) with an emissivity of 0.98. Thermal images acquired 1 and 10 s after blinking were taken. The corresponding lowest temperatures in the cornea were recorded as OST1 and OST10, respectively, and a temperature differential of 9 s was calculated (OST1-OST10). As a reference, the forehead (between the eyebrows) skin temperature was continuously measured using a temperature sensor and data logger (LT-8, Gram, Japan).

The blink patterns of the subjects were recorded as 1-min video sequences (60 fps) using a digital video camera (HC-V480MS, Panasonic, Japan). In addition to blink frequency, median

1 blink duration and the sum of blink duration were computed using image analysis; the mode
2 palpebral fissure height and mode ocular surface area were also computed as the representative
3 values with eyes open (see Appendix A).

4 5 **Psychological measurements**

6 Fifteen words that express sensations related to eye discomfort were selected (Table 3). The
7 subjective intensity of each sensation was collected with the unipolar four-point scale as shown
8 in Figure 1 (0 = do not feel, 3 = strongly feel).

9
10 In addition, the discomfort onset time (DOT) was measured as the time from the last blink to
11 the onset of discomfort while keeping eyes open.⁵⁰

Table 3. Psychological sensations related to eye discomfort. Some of the items were originally expressed using the corresponding Japanese onomatopoeia.

Symptoms	Original Japanese onomatopoeia
1 Eye discomfort	
2 Eye dryness	
3 Itchy eye	
4 Irritated eye	hiri-hiri
5 Eye pain	
6 Pain behind the eye	
7 Gritty eye	goro-goro
8 Foreign body sensation	
9 Cool eye	suu-suu
10 Burning eye	
11 Eyestrain (Eye fatigue)	
12 Blurred vision	
13 Difficulty in opening the eye	
14 Watery eye	
15 Drowsiness	



Figure 1. Scale of subjective eye sensation votes

Experimental procedure

The experimental procedure is illustrated in Figure 2. The subjects were instructed to refrain from drinking alcohol the day before the experiment and from using eyelid makeup or eye drops on the day of the experiment, and to finish their last meal at least 1 h before the experiment.

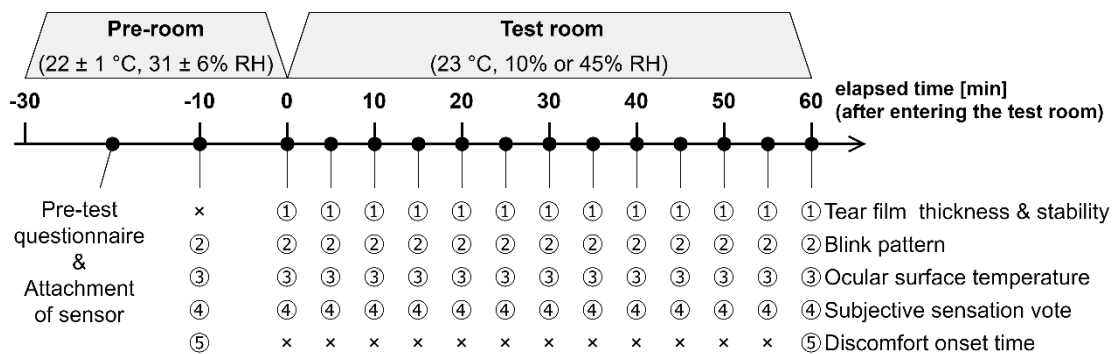


Figure 2. Experimental protocol

1 In the pre-room, following the pre-test questionnaire including the OSDI questionnaire, all
2 measurements except tear-film thickness and stability were conducted 10 min before entering
3 the test room. After entering, all measurement variables except for DOT were conducted every
4 5 min, and DOT was measured last before leaving the test room.

5
6 The measurements were performed according to the following procedures. First, for
7 interference imaging of the tear film, the subjects were instructed to keep their eyes open for
8 up to 30 s until tear-film break-up occurred, following a natural blink. After a 30-s recovery,⁵¹
9 they were asked to look directly at the video camera for 1 min to record the blink pattern. They
10 were then instructed to keep their eyes open for 10 s to measure the ocular surface temperature.
11 Finally, the subjective responses were collected. During the experiment, subjects were in a
12 sedentary position and were not allowed to drink anything. Between the measurement sets, they
13 were instructed not to keep their eyes closed and were allowed to read whatever they chose.

14
15 All procedures in this study were approved by the Human Ethics Committee of the Graduate
16 School of Engineering, Kobe University (01-11). The experiments were conducted after
17 obtaining informed consent from the subjects, based on the Helsinki Declaration.

18 19 **Statistical analysis**

20 Data obtained from the experiments were analyzed using non-parametric statistical analysis.
21 For both the SCL and non-CL wearers, the Wilcoxon signed-rank test was applied to compare
22 before and after entering the test room and between humidity conditions. The Wilcoxon rank-
23 sum test was applied to compare the SCL and non-CL wearer groups. For these analyses, the
24 average (median for ordinal scale data) of all data measured every 5 min was used as the
25 representative value during the 60-min exposure. All statistical analyses were conducted using
26 R software (version 4.0.3; <https://www.R-project.org/>) with a significance level of $P < 0.05$.

Results

We first checked the differences in the physiological and psychological results measured before entering the test room under each humidity condition. Of all measured items, except for the tear-film thickness and stability, the only ocular surface temperature in the non-CL wearer group showed a significant difference, being higher at 10% than at 45% RH ($P = 0.042$).

Comparisons of physiological and psychological responses between the humidity conditions are presented below.

Tear-film stability and thickness

Figures 3A, B and C show the results of the NIBUT, interference grade and spread grade respectively. Although there was no significant difference between the humidity treatments, only the SCL wearers tended to show a shorter NIBUT ($P = 0.098$), a higher interference grade ($P = 0.053$) and a spread grade ($P = 0.066$) at 10% than at 45% RH, which indicates destabilizing and thinning of the tear film on the front surface of contact lens (pre-lens tear film) under low-humidity conditions. In addition, the SCL wearers tended to have thinner lipid and aqueous layers with shorter NIBUT than that of non-CL wearers, regardless of the humidity condition. Seven out of nine SCL wearers showed an interference grade of 3 or above, which indicates thin tear films without a lipid layer.

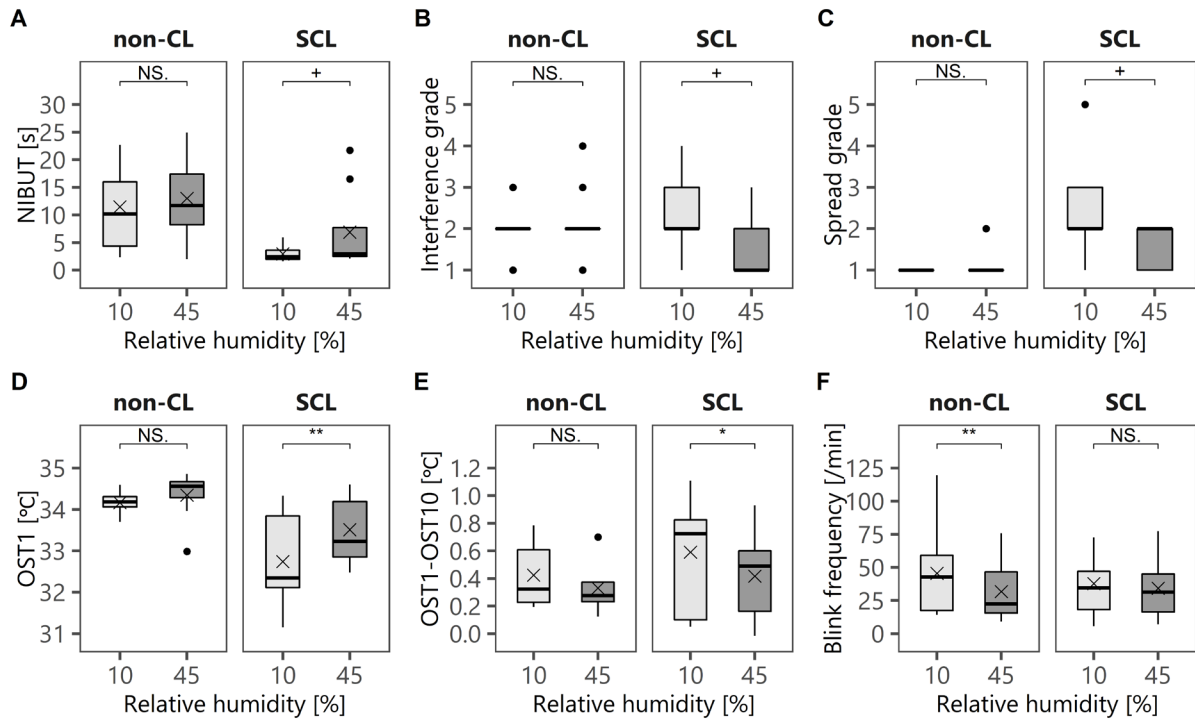


Figure 3. Comparison of (A) mean non-invasive break-up time (NIBUT), (B) median interference grade, (C) median spread grade, (D) mean OST1, (E) mean OST decline over 9 s (OST1-OST10), (F) mean blink frequency measured during 60-min exposure to 10% and 45% RH in soft contact lens (SCL) and non-CL wearers. OST1 and OST10 mean ocular surface temperature 1 s and 10 s after blinking, respectively. Box plots show median, interquartile range, minimum, maximum and outliers (•) with the mean value (×). *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$, + $P < 0.1$, NS. = not significant, Wilcoxon signed-rank test.

There was no significant difference in the NIBUT and thicknesses of the tear films of the non-CL wearers, while the thickness of each layer of the tear film was largely dependent on the individual; two subjects, N5 and N8, showed interference grades of 3 to 4 indicating a thick lipid layer, while others showed grades of 1 to 2 indicating thin to normal lipid layers. Although the spread grade ranged from 1 to 2, suggesting that there was no severe tear deficiency, subjects N5 and N6 tended to show a relatively high spread grade, implying thinner aqueous tear films. The tear-film properties of three non-CL subjects N5, N6 and N8 suggested the water-deficient dry eye type.^{52,53}

Ocular surface temperature

Figures 3D and E and Table 4 show the results of the ocular surface temperature measurements and the temperature decline over 9 s after blinking, which reflect the tear evaporation rate. In the SCL wearer group, the ocular surface temperatures both 1 and 10 s after blinking were significantly lower ($P = 0.008$, respectively), and the temperature differential was significantly greater ($P = 0.020$) under the 10% RH condition than that under the 45% RH condition. The average ocular surface temperature 1 s after blinking and the subsequent temperature differential was 33.5°C and 0.4°C at 45% RH compared to 32.7°C and 0.6°C at 10% RH, respectively (Table 4). Although the same pattern was observed in the non-CL wearer group, the difference between the humidity conditions was not statistically significant. In addition, the non-CL wearers showed significantly higher ocular surface temperatures and smaller temperature differentials compared to the SCL wearers.

Table 4. Summary of physiological measurements during 60-min exposure to 10% RH and 45% RH.

Measured items		Unit	Group	mean \pm bSD (wSD) or median \pm blQR (wlQR)		P
				10% RH	45% RH	
Tear-film stability	Non-invasive break-up time (NIBUT)	[s]	non-CL	11.5 \pm 7.1 (6.3)	13.0 \pm 7.9 (5.9)	+
			SCL	2.9 \pm 1.4 (2.5)	6.9 \pm 7.3 (4.7)	
Tear-film thickness	Interference grade	[-]	non-CL	2 \pm 0 (0.6)	2 \pm 0 (0.1)	+
			SCL	2 \pm 1 (0.9)	1 \pm 1 (0.8)	
	Spread grade	[-]	non-CL	1 \pm 0 (0.2)	1 \pm 0 (0.2)	+
			SCL	2 \pm 1 (0.6)	2 \pm 1 (0.8)	
Ocular surface temperature	Ocular surface temperature 1s after blinking (OST1)	[°C]	non-CL	34.2 \pm 0.3 (0.3)	34.3 \pm 0.6 (0.2)	**
			SCL	32.7 \pm 1.1 (0.3)	33.5 \pm 0.8 (0.3)	
	Ocular surface temperature 10s after blinking (OST10)	[°C]	non-CL	33.7 \pm 0.4 (0.3)	34.1 \pm 0.7 (0.3)	**
			SCL	32.1 \pm 1.4 (0.3)	33.1 \pm 1.0 (0.4)	
	OST1-OST10	[°C]	non-CL	0.4 \pm 0.3 (0.2)	0.3 \pm 0.2 (0.2)	**
			SCL	0.6 \pm 0.4 (0.2)	0.4 \pm 0.3 (0.2)	
Forehead skin temperature		[°C]	non-CL	33.7 \pm 0.8 (0.2)	33.8 \pm 0.4 (0.2)	
			SCL	33.3 \pm 0.8 (0.2)	33.4 \pm 0.5 (0.3)	
Blink pattern	Blink frequency	[/min]	non-CL	46 \pm 33 (9)	32 \pm 23 (7)	**
			SCL	38 \pm 24 (8)	34 \pm 24 (6)	
	Median blink duration	[s]	non-CL	0.18 \pm 0.03 (0.03)	0.18 \pm 0.02 (0.03)	
			SCL	0.18 \pm 0.06 (0.03)	0.16 \pm 0.04 (0.02)	
	Sum of blink duration (eye-closure time)	[s/min]	non-CL	8.5 \pm 6.8 (2.0)	5.8 \pm 4.1 (1.5)	*
			SCL	7.4 \pm 3.3 (2.0)	6.6 \pm 4.7 (1.7)	
	Mode palpebral fissure height	[mm]	non-CL	8.8 \pm 1.6 (0.3)	8.9 \pm 1.6 (0.3)	
			SCL	9.7 \pm 1.4 (0.4)	9.7 \pm 1.5 (0.6)	
	Mode ocular surface area	[cm ²]	non-CL	1.87 \pm 0.51 (0.10)	1.92 \pm 0.47 (0.08)	
			SCL	2.05 \pm 0.44 (0.11)	2.06 \pm 0.47 (0.17)	

SCL = soft contact lens wearers; non-CL = non-contact lens wearers; SD = standard deviation; bSD = between-subject SD; wSD = average value of within-subject SDs; IQR = interquartile range.
Values are presented as mean \pm between-subject SD (average value of within-subject SDs). The median and IQR are used instead of the mean and SD for grades (shown in italics).
*** P < 0.001, ** P < 0.01, * P < 0.05, and + P < 0.1, Wilcoxon signed-rank test.

Ocular surface temperatures are mainly affected by body temperature and latent heat loss due to tear evaporation.⁵⁴ In this study, as shown in Table 4, forehead skin temperature showed no significant difference between the humidity conditions, suggesting that there was no significant difference in body temperature between test conditions. Therefore, we infer that the observed ocular surface temperature responses under the low-humidity condition were mainly due to the increased tear evaporation rate. Furthermore, the effect of thermal comfort sensation on sensations related to eye discomfort¹⁵ was not significant.

Blink pattern

Figure 3F shows the results of the blink frequency. In the non-CL wearer group, blink frequency was significantly higher at 10% RH than that at 45% RH ($P = 0.008$). The average blink frequency was 32/min at 45% and 46/min at 10% RH (Table 4). In contrast, the difference between the humidity conditions was not significant in the SCL wearer group. Both groups showed large interindividual variations.

The results of the other blink parameters are listed in Table 4. Due to the influence of blink frequency, the sum of blink duration (total eye-closure time per minute) was also significantly different in the non-CL wearer group, which showed a higher value at 10% RH than that at 45% RH (mean = 8.5 compared to 5.8 s; $P = 0.039$). No significant differences were observed between the humidity conditions with respect to blink duration, palpebral fissure height or ocular surface area. However, a small portion of subjects showed a longer blink duration and a narrower palpebral fissure height at 10% RH compared to 45% RH.

Subjective responses

Figure 4 shows the results of the subjective sensation votes. Although there was high variability between individuals and no statistically significant difference for any of the variables, some subjects in both groups showed a clear psychological response to low humidity; for example, two subjects in each group declared that eye discomfort was “strongly felt” only at 10% RH condition. Similar results were obtained for eye dryness. Although the values of the overall vote were not high, the sensation votes for “irritated eye”, “difficulty in opening the eye” and “watery eye” tended to be higher at 10% RH than that at 45% RH.

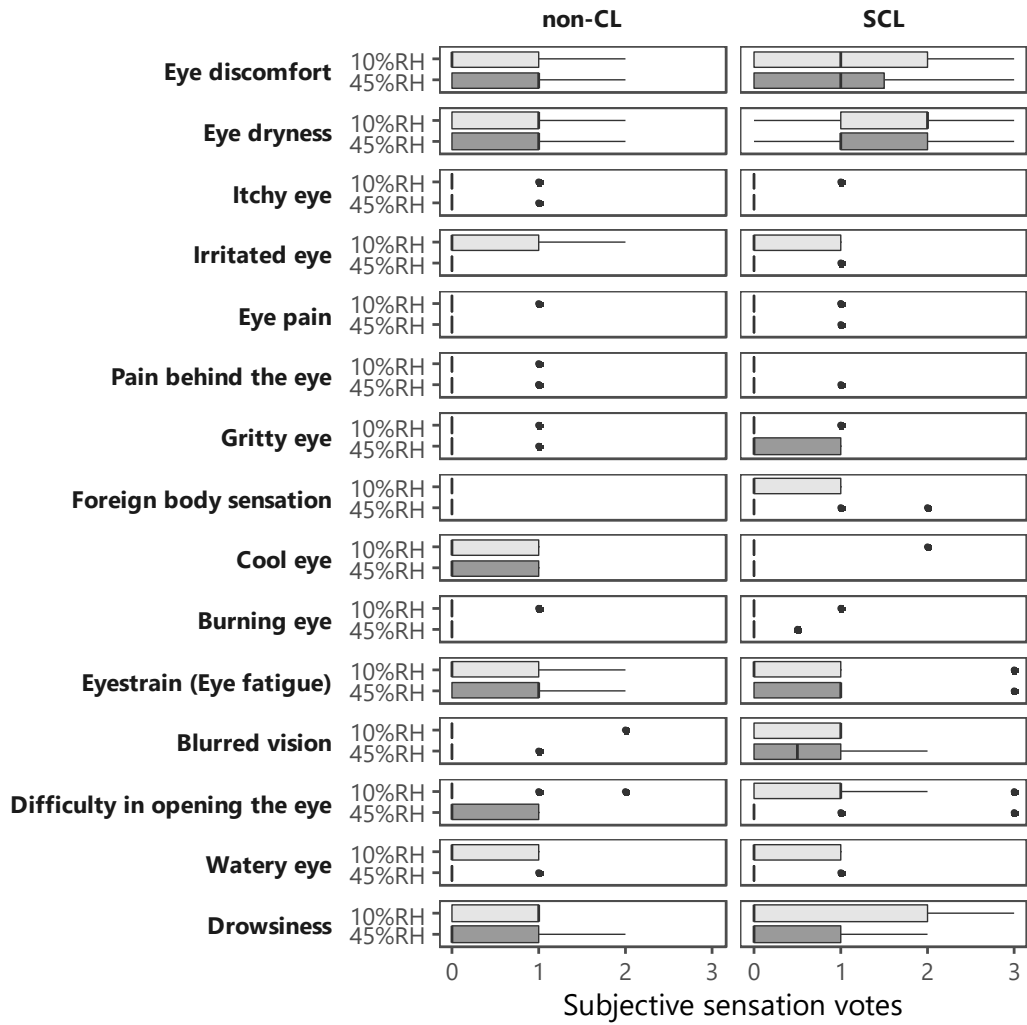


Figure 4. Median subjective sensation votes measured during 60-min exposure to 10% and 45% RH in soft contact lens (SCL) and non-CL wearers. Box plots show median, interquartile range, minimum, maximum and outliers (•). There were no statistically significant differences between the humidity conditions ($P > 0.1$).

Figure 5 shows the discomfort onset times from the last blink measured 60 min after entering the test room. Similar to blink frequency, a statistically significant difference was observed only in the non-CL wearer group, which showed a shorter time at 10% RH compared to 45% RH ($P = 0.008$).

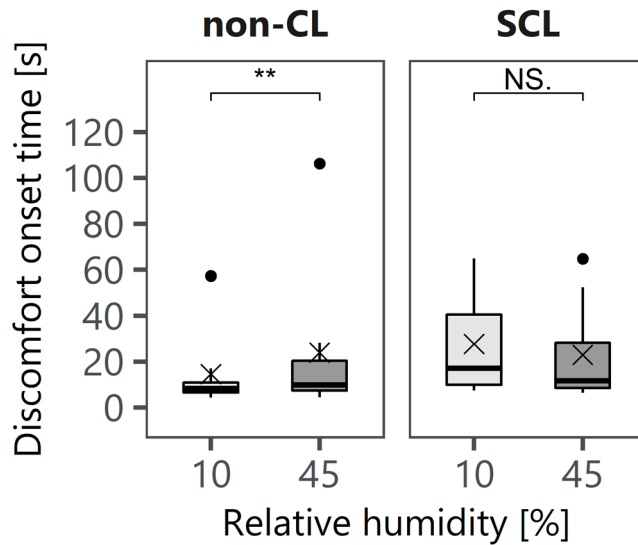


Figure 5. Comparison of discomfort onset time measured after 60-min exposure to 10% and 45% RH in soft contact lens (SCL) and non-CL wearers. Box plots show median, interquartile range, minimum and maximum, and outliers (•) with the mean value (×). *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$, + $P < 0.1$, NS. = not significant, Wilcoxon signed-rank test.

Discussion

Effect of low humidity on eye discomfort and associated physiological responses

The present study revealed the physiological and psychological responses related to eye discomfort to low humidity in both SCL wearers and non-CL wearers. In agreement with most previous studies,^{15–17,19,21,23} there was no clear tendency for subjective sensations to increase even at 10% RH. On the other hand, we found that low humidity affected some of the measured physiological parameters. This may be due to the less uncertainty of objective measurements than subjective voting with scales, in addition to the fact that subjective sensations arise from perceived physiological responses.

First, regarding the tear film, pre-lens tear film for the SCL wearers tended to be thinner and have a shorter BUT at 10% RH than that at 45% RH. Under 10% RH conditions, the mean

1 BUTs of all SCL wearers were less than 7 s, including two subjects who had mean BUTs of
2 more than 10 s under 45% RH conditions. The tear film with a BUT of less than 10 s is
3 considered unstable and is diagnosed as dry eye.⁵⁵ These results suggest that exposure to low
4 humidity reduces pre-lens tear-film stability. On the other hand, we found no significant
5 difference in the BUT and the tear-film thickness of the non-CL wearer group between different
6 humidity conditions. This is in contrast to the results of previous studies reporting that lower
7 humidities reduce the thickness of the tear film lipid layer on the naked eye.^{24,56} However, these
8 previous studies may conflate the effects of temperature and humidity, as lipid-layer thickness
9 is known to be affected by temperature.⁵⁷ To further understand the effect of low humidity on
10 the tear-film thickness of the naked eye, more detailed studies are required that focus on ocular
11 surface temperature.

12
13 The effect of low humidity on tear evaporation rate was examined based on ocular surface
14 temperature. Based on our results, the ocular surface temperature was lower and the temperature
15 drop over 9 s was larger at 10% RH than that at 45% RH, especially in the SCL wearer group.
16 This can be explained by an increase in tear evaporation due to thinning or break-up of the tear-
17 film lipid layer in addition to enhanced evaporation under low-humidity conditions.

18
19 In the case of blink patterns, blink frequency was significantly higher at 10% RH than that at
20 45% RH in the non-CL wearer group. Moreover, the sum of blink duration increased with the
21 number of blinks, which is likely to have an adverse effect on visual work performance. These
22 results are consistent with previous studies.^{15–17} Blink frequency is affected by tasks and gazing
23 positions.^{58,59} In this study, the subjects stopped reading and looked straight ahead during blink
24 recording. This may be one possible reason why the observed blink frequency tended to be
25 higher than values reported in previous studies.^{17,58} In the non-CL wearer group, there was also

a significant difference in the discomfort onset time from the last blink between the humidity conditions. Therefore, we infer that tear film homeostasis is maintained by the body perceiving disturbances of the tear film due to low humidity and, consequently, increasing the frequency of tear film reconstruction by blinking. Although no significant difference was observed in the blink durations or palpebral fissure heights between the humidity conditions, a few subjects did show a difference. Benedetto et al.⁶⁰ reported that forceful blinking increased the thickness of the tear film after blinking, and Takada⁶¹ reported that when the number of blinks was limited, each blink duration tended to be longer. Tsubota et al.^{62,63} showed that tear evaporation rates are suppressed when the eye is narrowed. Combined with these studies, our results suggest that the strength or duration of each blink, and the degree of eye-opening, are adjusted in addition to blink frequency to counter the low-humidity stimuli.

In conclusion, the results of this study suggest that increasing humidity from 10% RH to 45% RH, even for a one-hour exposure, improves the quality of the SCL wearer's tear film and reduces both the blink frequency and the eye-closure time of the naked eyes. This is one piece of the rationale for the significance of environmental improvement in low-humidity indoor spaces such as offices in winter and aircraft cabins, as it may consequently improve eye comfort and visual work performance. Furthermore, the measured physiological responses more clearly reflected the experimental humidity changes compared to the subjective responses. To determine humidity targets by quantifying the relationship between eye discomfort and humidity, the use of key physiological parameters, such as tear-film stability, ocular surface temperature and blink pattern was found to be effective, although the relationship between these physiological parameters and subjective discomfort sensation also should be quantified.

Difference between soft contact lens wearers and non-wearers

The present study also showed that the characteristics of the physiological responses to low

humidity differed between the non-CL wearer and SCL wearer groups. The pre-lens tear film of the SCL wearers showed a decrease in temperature and tended to show destabilizing and thinning due to low humidity, which was not clearly observed in the non-CL wearers. In contrast, regarding blink frequency and discomfort onset time from the last blink, only the non-CL wearer group showed a significant difference between the humidity conditions.

Possible reasons for the physiological changes in the pre-lens tear film of SCL wearers under low humidity are the higher tear evaporation rate and inadequate blink frequency. Given its thinner aqueous and lipid tear layer, we infer that pre-lens tear films more easily evaporate and become unstable under low humidity relative to tear films without CL. On the other hand, as pre-lens tear films and the corneal sensory nerves are separated by the lenses, thinning or breaking of the tear film is presumably difficult to detect. As a result, an inadequate frequency of tear-film reconstruction (by blinking) may accelerate tear-film thinning in SCL wearers.

Thinning of the pre-lens tear film leads to dehydration of the lens, which causes thinning of the post-lens tear film in contact with the cornea. This leads to increased friction between the lens and the palpebral conjunctiva during blinking and between the lens and cornea, causing discomfort.⁶⁴ In addition, it is expected that thinning of the tear film will progress as exposure time to low humidity increases. Therefore, the humidity levels required to reduce or eliminate eye discomfort may differ due to SCL wearing, especially with longer exposures expected in office spaces. Although many previous studies investigating required indoor humidity levels have not distinguished or discussed this aspect of the subjects wearing contact lenses, it is one of the important factors that should be considered.

Limitations and future studies

To the best of our knowledge, this is the first study to investigate the effect of humidity alone

on eye discomfort in both SCL and non-CL wearers in terms of the changes in the tear film. It also provides essential information that will aid future studies to determine the humidity target, as noted above. However, there are three major limitations in this study that could be addressed in future research.

The first limitation is the relatively small sample size. For the purposes of our study, we measured comprehensive physiological and psychological parameters instead of limiting the number of subjects. To reinforce our conclusions, the experiments should be repeated with larger sample sizes.

Secondly, our results may have been influenced by variations in subject profiles. We investigated the effect of humidity on eye discomfort in SCL wearers and non-CL wearers separately. This was because the wearing of CL changes the structure of the tear film, and previous studies^{20,40,41} have suggested that it could affect physiological and psychological responses to the environment. On the other hand, we did not strictly control the individual factors other than the wearing of contact lenses and age (such as dry eye severity, smoking habits, contact lens type and myopia), although their variations were not large and almost similar between the SCL and non-CL wearer groups. The influence of these individual factors is unknown, and should also be investigated in future studies.

Finally, because the present study focused on quantitatively evaluating the effect of low humidity on eye discomfort, the exposure did not faithfully reproduce the actual state of the occupants. The tests and the questionnaire were applied every 5 minutes during the 1-hour exposure. The impact of the environment on eye discomfort is expected to vary with the activities. For example, given that reduced blinking during visual display terminal work has

1 been reported,^{58,65} the adverse effect on eye comfort is likely to be greater when such work is
2 continued under low humidity. To predict eye discomfort sensations that might occur during a
3 full working day at the office, further study should be conducted.

5 **Conclusions**

6 To quantitatively evaluate the effect of low humidity on eye discomfort, SCL wearers and non-
7 CL wearers were exposed to 10% and 45% RH at 23°C. In addition to subjective discomfort
8 sensations, several physiological parameters related to eye discomfort, including tear break-up
9 time, ocular surface temperature and blink patterns were compared between humidity
10 conditions, and the difference between the SCL and non-CL wearing groups was also
11 investigated.

12
13 For both the SCL and non-CL wearer groups, we found no significant differences between the
14 humidity conditions in eye discomfort sensations, although a small portion of subjects reported
15 significant discomfort at 10% RH. In comparison, low humidity had a significant effect on some
16 of the measured physiological parameters. The SCL wearers showed significantly lower ocular
17 surface temperatures and greater temperature differentials after blinking at 10% RH than that
18 at 45% RH. Furthermore, their tear film on the front surface of contact lenses (pre-lens tear
19 films) tended to be thinner and have a shorter break-up time at 10% RH than that at 45% RH.
20 This suggests that low humidity increases evaporation rates of pre-lens tear films, reducing tear-
21 film stability. In contrast to the SCL wearers, the non-CL group showed significantly higher
22 blink frequencies, longer eye-closure times due to blinking, and shorter discomfort onset times
23 from the last blink at 10% RH than that at 45% RH. However, we found no significant
24 differences in tear-film parameters or ocular surface temperature between the humidity
25 conditions for this group.

1
2 The results of this study suggest that increasing humidity from 10% RH to 45% RH improves
3 the quality of the SCL wearer's tear film and reduces both the blink frequency and the eye-
4 closure time of the naked eye. This is one piece of the rationale for the significance of
5 environmental improvement in low-humidity indoor spaces, as it may consequently improve
6 eye comfort and visual work performance. By quantifying the relationship between the above
7 physiological parameters and subjective discomfort sensation, it may be possible to determine
8 indoor humidity targets.

9
10 Furthermore, the characteristics of the physiological response to low humidity differed between
11 the non-CL wearers and SCL wearers. We suggest that the pre-lens tear films of SCL wearers
12 easily evaporate and become unstable in low-humidity environments, which may have been
13 accelerated by an inadequate frequency of tear-film reconstruction by blinking. The difference
14 between non-CL and SCL wearers should be considered in future studies for investigating the
15 humidity levels required to reduce or eliminate eye discomfort.

16 17 **Authors' contribution**

18 K.I. and S.T. conceived the study. K.I. carried out the experiments and performed the analyses.

19 K.I. wrote the manuscript in consultation with S.T.. S.T. supervised the project.

20 21 **Declaration of conflicting interests**

22 The authors declare that there is no conflict of interest.

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Appendix A.

Blink patterns were quantified from a 1-min (60 fps) video sequence of the face using a free computer vision library, OpenCV (<https://opencv.org/>), and a machine learning library, Dlib (<https://opencv.org/>).

First, for every video frame, eye landmarks, p_i , were detected in the left eye⁶⁶ as shown in Figure A 1. The eye aspect ratio (EAR) between the palpebral fissure height, h_{eye} , and eye width, w_{eye} , is expressed as:

$$EAR = \frac{h_{eye}}{w_{eye}} = \frac{h_{eye,img}}{w_{eye,img}} = \frac{\|p_2 - p_6\| + \|p_3 - p_5\|}{2\|p_1 - p_4\|} \quad (1)$$

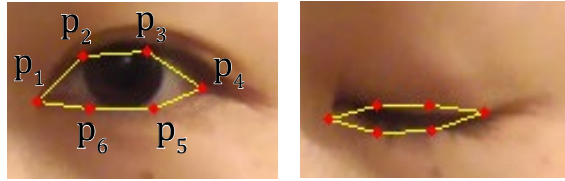
where $h_{eye,img}$ and $w_{eye,img}$ are palpebral fissure height and eye width on the image. If the EAR fell below a certain threshold (0.22) and then rose above this threshold, we judged that blinking had occurred.⁶⁷ This method was validated by comparing with manual blink counting. In addition to the blink frequency, median, and sum of duration for each blink, the mode palpebral fissure height and the mode ocular surface area were calculated. The palpebral fissure height is calculated as follows:

$$h_{eye} = \frac{w_{eye}}{w_{eye,img}} h_{eye,img} \quad (2)$$

w_{eye} was measured on a scale for each subject. Ocular surface area (S_{eye}) is calculated as follows:

$$S_{eye} = \left(\frac{w_{eye}}{w_{eye,img}} \right)^2 S_{eye,img} \quad (3)$$

where $S_{eye,img}$ is the ocular surface area surrounded by six landmarks on the image (Figure A 1).



1

2

Figure A 1. Open and closed eyes with detected landmarks, p_i .