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# Ocular thermography and clinical measurements in symptomatic and asymptomatic soft contact lens wearers

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**SIGNIFICANCE:** Symptoms of dryness and discomfort are the main reasons for contact lens dropout. Clinical tests for this purpose are invasive or subjective. Ocular thermography may help to assess the ocular discomfort and dryness in a noninvasive and objective manner.

**PURPOSE:** This study aimed to investigate the relationship of ocular thermography with clinical measurements in habitual symptomatic and asymptomatic soft contact lens wearers.

**METHODS:** Forty habitual contact lens wearers were evaluated in two age- and gender-matched asymptomatic and symptomatic groups (Contact Lens Discomfort Questionnaire scores  $\leq 8$  and  $\geq 14$ , respectively). Clinical measurements took place during visit 1 (with contact lens *in situ* and after contact lens removal) and at baseline after a 2-week washout period (visit 2). The Ocular Surface Disease Index (OSDI) questionnaire, noninvasive tear breakup time, bulbar conjunctival hyperemia, and corneal staining were assessed. Thermal cooling rate was computed in the central and lower cornea during natural blinking (30 s) and sustained eye opening (10 s).

**RESULTS:** Dry eye symptoms (OSDI score) were significantly higher in the symptomatic group during contact lens wear ( $p < 0.001$ ) and at baseline ( $p = 0.001$ ). Thermal cooling rate was significantly higher in the symptomatic group in the lower cornea (10 s,  $p = 0.013$ ) with the contact lens *in situ* and in the central cornea (30 s,  $p = 0.045$ ) after contact lens removal. At baseline, dry eye symptoms (OSDI score) significantly correlated with cooling rate in the central cornea region for the symptomatic group (30 s:  $r = -0.5$ ,  $p = 0.03$ ; 10 s:  $r = -0.63$ ,  $p = 0.005$ ). Noninvasive tear breakup time correlated with cooling rate in the central cornea region at baseline in the symptomatic group (30 s,  $r = 0.6$ ,  $p = 0.005$ ; 10 s,  $r = 0.55$ ,  $p = 0.018$ ). Cooling rate in the central cornea region (10-s duration,  $p < 0.0001$ ) and noninvasive tear breakup time ( $p < 0.0001$ ) were identified as significant predictor variables for dry eye symptoms at baseline.

**CONCLUSIONS:** Noninvasive tear breakup time and thermal cooling rate were identified as significant predictor variables for contact lens-induced dry eye. These findings may suggest the potential for the additional application of ocular thermography in the evaluation of contact lens discomfort.

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Contact lens discomfort, particularly toward the end of the day, affects up to half of contact lens wearers with variable frequency and magnitude. This issue represents the primary cause of discontinuation from contact lens wear.<sup>1–3</sup> End-of-day discomfort and dry eye symptoms are the most common complaints<sup>4,5</sup> leading to discontinuation rates ranging from 21 to 64% among wearers.<sup>3,6–8</sup> Dry eye symptoms as the most common reason for contact lens discomfort have a prevalence ranging between 31 and 55%, depending on the study population, contact lens material, diagnostic criteria, and clinical tests,<sup>2,3,6,9,10</sup> as well as their combination. Because of discomfort and dryness sensation, 15% of contact lens wearers eventually stop wearing contact lenses.<sup>11</sup>

The presence of a contact lens in the eye divides the tear film into a pre- and post-contact lens tear film, leading to thinning and a decrease in overall tear volume and its stability.<sup>5,12,13</sup> By thinning of the pre-contact lens tear film, the tear film evaporation rate accelerates and ocular surface temperature decreases.<sup>14</sup> This may also lead to increased tear osmolarity, ocular surface inflammation, ocular dryness, and discomfort.<sup>15</sup> Temperature decrease across the ocular surface, i.e., thermal cooling rate, may be recorded with means of noninvasive infrared thermography.<sup>16</sup>

Although the relationship between ocular surface temperature decrease and tear film instability has been well established in dry eye patients,<sup>17–21</sup> it remains less investigated in contact lens wearers, particularly in symptomatic compared with asymptomatic groups. Itokawa et al. showed good correlations between ocular surface temperature decrease (during a 10-s period of sustained eye opening) and noninvasive tear breakup time over the contact lens surface,<sup>11</sup> confirming that ocular thermography measurement may be useful for the tear film evaluation in contact lens wear.

Kim et al. showed that a faster thermal cooling rate is related to accelerated evaporation, which was higher in symptomatic contact lens wearers, although not reaching statistical significance.<sup>22</sup> Furthermore, in healthy participants without contact lens wear, a faster ocular surface cooling rate was observed in eyes with shorter maximum interblink periods, indicating thermal cooling rate as a potential initiating factor for ocular discomfort.<sup>23</sup>

This study extends on previous research works by exploring associations between contact lens-induced dry eye symptoms and noninvasive measurement of thermal cooling rate over the ocular surface in a cohort of symptomatic and asymptomatic contact lens wearers in automated way. An infrared thermal imaging system was developed that measures the temporal variation of ocular surface temperature in a noninvasive, noncontact, quick, quantitative, and automated manner. With means of automatic detection of blinks, the onset of the cooling cycle was accurately identified. The relevance of thermal cooling rate

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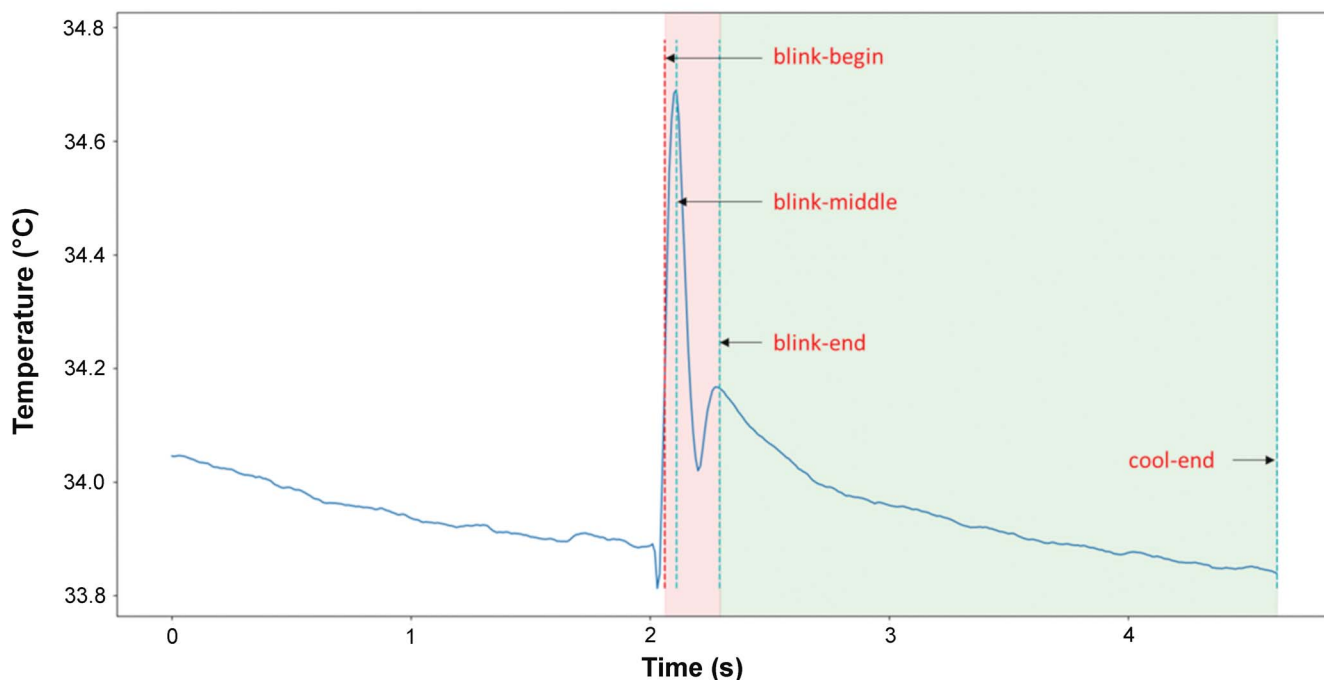


FIGURE 1. Automatic blink detection on sustained eye opening.

with sensations of discomfort of habitual contact lens wearers was explored in parallel to other clinical tests carried out in this study.

## METHODS

### Ocular thermography system

The thermal camera system was FLIR camera A655sc (Teledyne FLIR, Wilsonville, OR) with an additional 25° macro lens (640 × 480 pixel resolution; frame rate, 100 Hz). A chin rest was attached to the camera mounting system in order to stabilize the head during measurements. The FLIR Research IR software (version 4.40, Teledyne FLIR, Wilsonville, OR) was used to annotate the thermal data sequences. By using FLIR SDK software (FLIR ATLAS SDK, version 5, Teledyne FLIR, Wilsonville, OR), proprietary software backend was developed in order to automatically process and analyze thermal data.

### Automatic blink detection, annotation, and analysis

In order to capture the dynamic changes of temperature, the time points for when the blink starts and when the blink ends were identified. Blinking is a periodic phenomenon that can be recorded based on the temperature changes on the ocular surface. Algorithms were developed to detect the blinks automatically. Fig. 1 shows the full blink cycle including the blink itself and when the eye is open. The light red region corresponds to the blink duration time for one complete blink. The green region corresponds to the time period when the eye is open between blinks. Upon initiation of a blink, the maximum temperature variation (red dotted line, blink-begin) is recorded. When the eye is closed, the much higher temperature of the eyelid is recorded (blink-middle line). The second highest peak (blink-end) corresponds to the point where the eye is fully open and the cooling process on the ocular surface starts. At the end of the cycle (cool-end), the ocular surface reaches its lowest temperature.

Two corneal regions were selected as regions of interest on the ocular surface: a circular region with a diameter of 4 mm in the central cornea, equidistant from the lower lid and the upper

lid, and an elliptical region fitted to the lower part of the cornea (Fig. 2). This elliptical region is fitted between the central cornea (4 mm) and the outer circle with a diameter of 8 mm. The annotation of the regions of interest was carried out manually with the FLIR Research IR software.

The central cornea region is the most exposed region of the ocular surface to the outer environment and the most studied region in the previous research works.<sup>11,19</sup> The lower part of the cornea is also interesting to investigate for the purposes of contact lens fitting and the heat variations in this region.

Two measurement types were implemented in this study. In order to capture the natural blinking pattern, the participants were asked to blink normally for a duration of 30 s in front of thermal camera. In order to capture the longer duration of ocular surface evaporation, the participants were subsequently asked to blink once and then keep the eye open for a duration of 10 s.

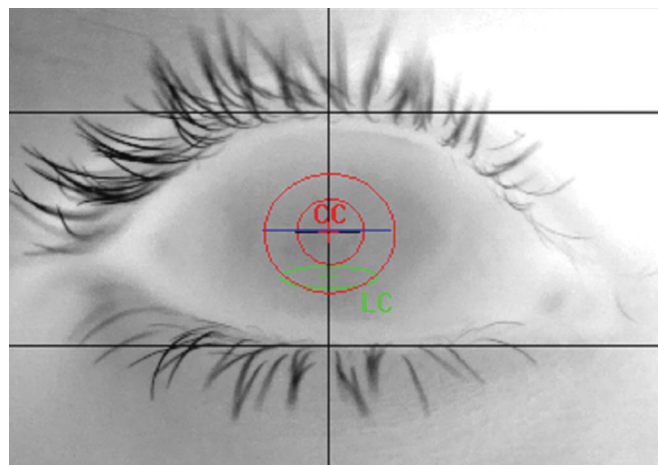


FIGURE 2. Corneal regions analyzed with thermography. CC = central cornea; LC = lower cornea.

## Cooling rate analysis

Different approaches were investigated in the literature to study dynamic temperature changes during a blink cycle. Su et al. captured the dynamic change of temperature by recording the difference between the temperature at the start of the blink and the end of a blink cycle in a 6-s period.<sup>24</sup> Mori et al. modeled the dynamic temperature change as an exponential phenomenon.<sup>21</sup> Li et al. chose linear modeling to explain the cooling phenomenon over the blink cycle.<sup>16</sup> Although linear modeling may not accurately reflect the nature of a cooling cycle, it is more suitable for clinical interpretation. For this reason, linear modeling was applied for the analysis on dynamic changes of temperature. The obtained parameter as the coefficient of linear model is introduced as the thermal cooling rate. With the applied linear model, the parameter can be interpreted that, with 1-unit increase in time, the temperature will drop to the amount of the obtained coefficient on the ocular surface, considering the other factors constant. To capture the temperature decay during the initial phase of cooling, linear fitting was applied in the time interval of 500 milliseconds from the start of cooling cycle (blink-end line in Fig. 1). For natural blinking with the duration of 30 s, the cooling rate values were averaged for all the blink cycles. The goodness of fit was measured by  $R^2$  values with a threshold above 0.7. Higher  $R^2$  values (closer to 1) indicate better fitting and explainability of this linear model.

## Study protocol

This was a prospective exploratory single-center study with two arms and was reviewed by an independent ethical review board (Swiss ethics commission) and conforms with the principles and applicable guidelines for the protection of human subjects in biomedical research. Volunteers were recruited from the patient pool of the Optometry Department, University of Applied Sciences in Olten, Switzerland. Optometrists or those studying optometry were not eligible for participation. Study recruitment was based on contact lens comfort levels in habitual contact lens wearers, with the 8-item Contact Lens Discomfort Questionnaire (CLDEQ-8).<sup>25</sup> Group A was the asymptomatic group with a discomfort score no greater than 8, and group B was the symptomatic group with a discomfort score of at least 14 points. There was an equal number of participants in the two study groups with matched age range and gender distribution between the two groups. Study measurements took place during and immediately after contact wear following a minimum of 6 hours of contact lens wear on the day (visit 1) and again after a washout phase of cessation of contact lens wear ( $14 \pm 2$  days; visit 2). The washout period was implemented in order to restore the normal physiology of the ocular surface following contact lens wear. The measurements during visit 1 were conducted with the contact lens *in situ* and immediately after its removal, to investigate the effect of lens presence for thermal cooling rate, noninvasive tear breakup time measurement, and discomfort sensation by the end of day with contact lens wear.

Any possible bias arising from the examiner was minimized by application of objective software programs for grading or determining variables. Examiners were masked to which groups the individual participants belonged to.

Inclusion criteria were binocular visual acuity of at least 0.80 with the contact lens *in situ*, no eye drops or eye makeup at the day of measurement, no hot drink intake 1 hour before measurements, no high-impact activities (such as sport activities) on the day of measurement, habitual (silicone) hydrogel disposable contact lens wear (minimum of 5 days per week and 8 hours per day), and good contact lens fitting characteristics.<sup>26</sup>

Exclusion criteria were systemic disease that may affect ocular health, such as diabetes; injury and history of operations on the anterior segment of the eye; regular application of systemic or ocular

medication known to affect the tear film, specifically on the day of measurement; and overnight contact lens wear.

## Measurement procedures

All participants invited to take part in the study received an information sheet explaining the nature of the study. They completed the CLDEQ-8 prior to visit 1 and returned it to a person who was not involved in the study measurement procedures, in order to mask the group distribution to the examiner during all procedures. Also prior to visit 1, all participants received five fresh pairs of contact lenses, which they wore on each of the four preceding days and on the day of measurements (the same contact lens type that they normally wore). This means that they replaced their contact lens on each of these 5 days, even if individual lenses were meant to be worn for more than 1 day. This ensured that factors from lens spoilage, lens care solutions, and regimen practices in contact lens care were excluded.

At visit 1, all participants confirmed that they had received and read the patient information sheet before signing it. In addition, they completed the Ocular Surface Disease Index (OSDI) questionnaire. They were also asked to estimate their duration of habitual contact lens wear (in months) and how many hours per day they spend on average in front of a computer screen. Consequently, the following measurements were carried out during visit 1 with the contact lens *in situ*: slit-lamp examination for evaluation of the anterior segment, visual acuity (high contrast logMAR visual acuity), contact lens performance assessment after a minimum wear of 6 hours on the day of visit (wettability and fitting characteristics), and ocular surface thermography (thermal cooling rate over the contact lens with FLIR camera [FLIR A655sc], noninvasive tear breakup time obtained with the Keratograph 5M [NIK BUT; Oculus GmbH, Wetzlar, Germany]). Consequently, the contact lenses were removed, and the following measurements were carried out: ocular surface thermography, noninvasive tear breakup time, bulbar conjunctival hyperemia, and corneal staining.

After a washout period of no lens wear for  $14 \pm 2$  days, all participants returned for baseline visit 2, and the same measurements as during visit 1 after contact lens removal were carried out. In addition, the OSDI questionnaire was completed again by all participants. All measurements were carried out on the right eye during both visits.

Procedure descriptions for all clinical measurements are as follows:

- CLDEQ-8: Standardized questionnaire for the evaluation of discomfort symptoms arising during contact lens wear<sup>25</sup>
- OSDI questionnaire: Standardized evaluation of dry eye symptoms<sup>27</sup>
- Contact lens performance assessment: Fitting characteristics were evaluated according to the guideline published by Wolffsohn et al.<sup>26</sup>
- Bulbar conjunctival hyperemia was evaluated by using an objective assessment system, delivering the Ocular Redness Index with a score of 0 to 100, whereby pictures were white balanced, image color was standardized, and the redness score was analyzed with the ImageJ software (U.S. National Institute of Health, Bethesda, MD).<sup>28</sup>
- Corneal staining was evaluated with sodium fluorescein dye using a cobalt blue excitation filter and a yellow barrier filter according to the two-factor Centre for Ocular Research & Education corneal staining scale (type and extent of staining) and averaged to provide a global staining score for five corneal regions on a scale of 0 to 10,000.<sup>29</sup>
- Measurements with placido-based topographer Oculus Keratograph 5M: Noninvasive tear breakup time measurements were carried out three times, with an interval of a minimum of 2 minutes between each measurement, in order to ensure that the tear film stabilized again after each measurement.

**TABLE 1.** Mean ± SD of background statistics

	Asymptomatic (group A)	Symptomatic (group B)
No. of subjects	20	20
Age	28.6 ± 8.5 y	27.2 ± 6.4 y
Female + male	13 + 7	14 + 6
CL wear history	11.1 ± 6.7 y	9.5 ± 6.1 y
CLDEQ-8 score	4.3 ± 2.3	19.4 ± 4.2
Average screen time/day	6.8 ± 2.5 h	7.3 ± 2.7 h

CL = contact lens; CLDEQ-8, 8-item Contact Lens Discomfort Questionnaire; SD = standard deviation.

- Ocular thermography: The participant's eye was placed at a fixed distance of 17 cm between the forehead and the thermal camera lens. The camera was turned on 1 hour before starting the experiment (adequate time for camera adaptation to room environment). All participants had adapted to the experimental room at least 15 minutes. In the experiment room, there was no direct exposure to sunlight, incandescent light sources, or wind current. Thermography was recorded (1) during 30 s of natural blinking and (2) for the duration of one blink, whereby the participant kept the eye open for 10 s.

### Statistical analysis

The data were tested for normality with Shapiro-Wilk test and Q-Q plots. Repeated-measures analysis of variance was applied with  $\alpha = 0.05$  and with factor time (V1 and V2) and group (group A, asymptomatic contact lens wearers; group B, symptomatic contact lens wearers). Post hoc two-tailed unpaired *t* tests (or equivalent non-parametric Mann-Whitney tests) were applied to test for differences in variables between the groups at different time points. In addition, linear models were applied with OSDI (OSDI score) as the dependent variable at baseline, with contact lens *in situ* and immediately after contact lens removal. Correlations between variables were explored with Pearson tests (or equivalent nonparametric Spearman tests). The R (version 4.2.1, R Core Team, Vienna, Austria) was used for the statistical analysis.

**TABLE 2.** Descriptive statistics for clinical measurements

	Group asymptomatic		Group symptomatic	
	Mean (SD)	Median (range)	Mean (SD)	Median (range)
OSDI				
Visit 1	6.95 *(8.9)	3.35 (0–30.56)	22.02 *(13.2)	18.75 (2.1–60.4)
Visit 2: baseline	3.55* (4.8)	2.09 (0–16.7)	14.3* (15.1)	9.75 (0–62.5)
Hyperemia				
Visit 1: after CL removal	38.46 (4.2)	36.4 (34.54–50.07)	37.43 (2.4)	36.83 (34.97–46.26)
Visit 2: baseline	36.68 (1.7)	36.4 (34.56–41.52)	36.54 (1.1)	36.6 (34.38–39.11)
NIK BUT				
Visit 1: with CL <i>in situ</i>	11.29 (6.3)	9.78 (3.76–21.8)	10.67 (6.4)	7.39 (3.5–24.5)
Visit 1: after CL removal	14.32 (7.1)	13.41 (3.57–24.89)	12.57 (6.9)	9.05 (4.33–24.92)
Visit 2: baseline	16.89 (7.4)	17.53 (5.93–24.92)	15.73 (7.6)	18.92 (4.01–24.92)
Corneal staining				
Visit 1: after CL removal	121.25 (28.5)	62.5 (0–450)	97.5 (104.4)	50 (0–350)
Visit 2: baseline	77.5 (92.4)	50 (0–300)	68.75 (92.1)	50 (0–350)

\*Significant difference. CL = contact lens; NIK BUT = non-invasive tear break-up time; OSDI = Ocular Surface Disease Index; SD = standard deviation.

All corneal temperature data were preprocessed; i.e., the masks were manually annotated and exported, the blink information was automatically extracted, and the blink information was debugged and cleaned from noisy measurements, undetected blinks, falsely detected blinks, and measurement errors.

### RESULTS

Forty participants completed the study (n = 20 per group), of which 27 were female. Table 1 shows the mean ± standard deviation for age, gender distribution, contact lens discomfort (CLDEQ-8) score, and computer screen time for the participants of the study.

Twenty-seven participants wore silicone hydrogel and 13 hydrogel contact lenses: nine hydrogel contact lens wearers were in the symptomatic group B, and four hydrogel contact lens wearers were in the asymptomatic group A. Average ambient temperature during visit 1 was 22.6 ± 0.6°C, and during visit 2, it was 22.7 ± 0.8°C. Average humidity during visit 1 was 27.2 ± 6.7%, and during visit 2, it was 27.4 ± 6.5%.

### Differences between the symptomatic and asymptomatic group

Table 2 shows the descriptive statistics of clinical parameters for the symptomatic and asymptomatic groups at different visit time points.

Table 3 shows the descriptive statistics for thermal cooling rate for the symptomatic and asymptomatic groups. Thermal cooling rate is reported for visit 1 with contact lens *in situ* and immediately after contact lens removal, and for visit 2, at baseline after the washout period. It was computed in the central and lower corneal regions, as well as during natural blinking during 30 s and when the eye was kept open during 10 s. Thermal cooling rate was computed by fitting a linear model to the first 500 milliseconds of thermal graph of the blink cycle. To avoid outlier data and for noise removal, the interquartile range method was used.

The analysis of variance delivered statistically significant differences between the three measurement time points regarding the variables: dry eye symptoms (OSDI, p=0.0011), tear breakup time (NIK BUT, p=0.0002), and cooling rates for the central cornea during 30 s (p=0.0014), as well as for the lower cornea during 30 s (p=0.0016). For overall group differences, it showed statistically significant differences for dry eye symptoms (OSDI, p=0.0002)

**TABLE 3.** Descriptive statistics for cooling rate in the central corneal and lower corneal regions

	Group asymptomatic		Group symptomatic	
	Mean (SD) (°C/s)	Median (range) (°C/s)	Mean (SD) (°C/s)	Median (range) (°C/s)
Cooling rate in CC, 30 s				
Visit 1: with CL <i>in situ</i>	-0.38 (0.2)	-0.38 (-0.93 to -0.06)	-0.46 (0.3)	-0.35 (-1.09 to -0.02)
Visit 1: after CL removal	-0.22* (0.2)	-0.15 (-0.56 to -0.05)	-0.35* (0.2)	-0.29 (-0.9 to -0.06)
Visit 2: baseline	-0.28 (0.3)	-0.17 (-1.01 to -0.06)	-0.36 (0.2)	-0.37 (-0.81 to -0.03)
Cooling rate in CC, 10 s				
Visit 1: with CL <i>in situ</i>	-0.58 (0.5)	-0.32 (-1.44 to -0.05)	-0.71 (0.3)	-0.71 (-1.49 to -0.13)
Visit 1: after CL removal	-0.56 (0.3)	-0.43 (-1.26 to -0.2)	-0.50 (0.3)	-0.58 (-1.09 to -0.08)
Visit 2: baseline	-0.41 (0.3)	-0.31 (-1.17 to -0.04)	-0.58 (0.4)	-0.51 (-1.43 to -0.13)
Cooling rate in LC, 30 s				
Visit 1: with CL <i>in situ</i>	-0.31 (0.2)	-0.26 (-0.79 to -0.04)	-0.32 (0.2)	-0.27 (-0.72 to -0.09)
Visit 1: after CL removal	-0.17 (0.1)	-0.14 (-0.39 to -0.03)	-0.25 (0.2)	-0.16 (-0.75 to -0.08)
Visit 2: baseline	-0.2 (0.2)	-0.15 (-0.72 to -0.04)	-0.28 (0.3)	-0.14 (-0.8 to -0.04)
Cooling rate in LC, 10 s				
Visit 1: with CL <i>in situ</i>	-0.26* (0.2)	-0.21 (-0.72 to -0.06)	-0.49* (0.3)	-0.41 (-1.23 to -0.11)
Visit 1: after CL removal	-0.26 (0.2)	-0.15 (-0.99 to -0.07)	-0.36 (0.3)	-0.2 (-0.94 to -0.07)
Visit 2: baseline	-0.2 (0.1)	-0.21 (-0.39 to -0.04)	-0.37 (0.3)	-0.23 (-0.96 to -0.08)

\*Significant difference. CC = central cornea; CL = contact lens; LC = lower cornea; SD = standard deviation.

and cooling rate in the lower cornea region for the 10-s measurement ( $p=0.016$ ).

The score for dry eye symptoms (OSDI) was significantly higher in the symptomatic group during contact lens wear ( $p<0.001$ ) and at baseline ( $p=0.001$ ). Fig. 3 illustrates the differences in dry eye symptoms within groups.

No significant differences were found between symptomatic and asymptomatic groups for hyperemia, noninvasive tear film breakup time, and corneal staining at either visit.

Cooling rate was consistently higher in the symptomatic group (negative values), reaching statistical significance in the lower corneal region during the 10-s measurement with the contact lens *in situ* ( $p=0.013$ ) and in the central corneal region with the 30-s measurement duration immediately after contact lens removal ( $p=0.045$ ). The highest cooling rate was noted in the symptomatic group in the central corneal region with the 10-s duration with the contact lens *in situ* ( $-0.71^{\circ}\text{C/s}$ , Table 3). Fig. 4 shows the differences of thermal cooling rate between the asymptomatic and symptomatic group for the 10-s measurement duration in the lower part of the cornea at different visit time points.

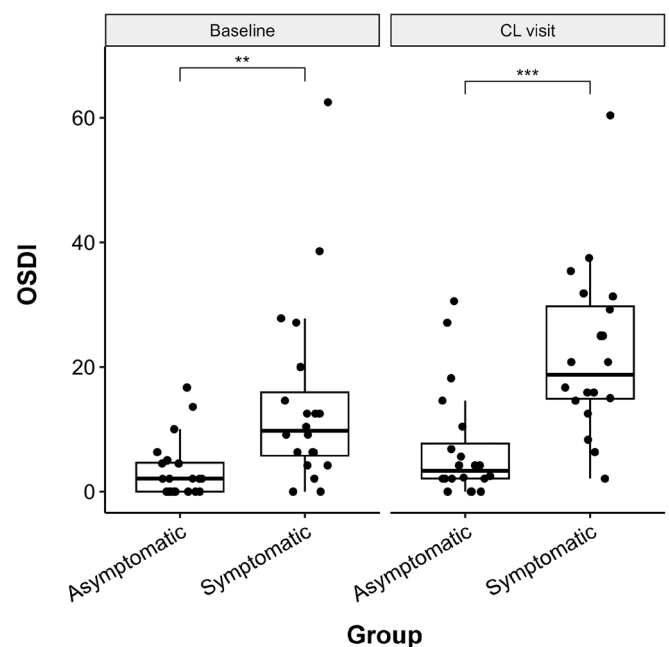
### Correlations between thermal cooling rate and clinical tests

Correlations were computed for the baseline visit, with the contact lens *in situ* and immediately after contact lens removal. The significant correlations between clinical tests and thermal cooling rate are reported in Table 4.

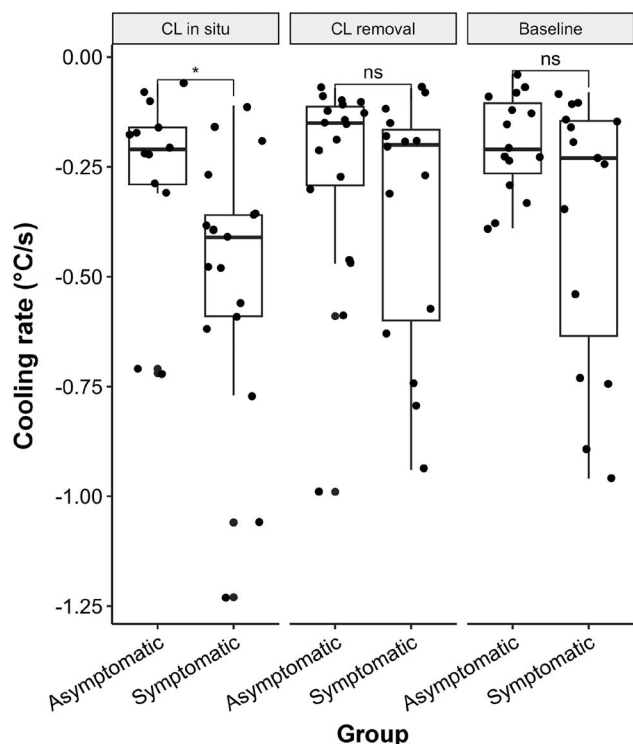
At baseline, dry eye symptoms (OSDI) score as well as noninvasive tear breakup time correlated moderately with thermal cooling rates in the central cornea with both (10 and 30 s) measurement durations in the symptomatic group (Table 4). In the asymptomatic group, only the cooling rate in the lower cornea with the 10-s duration correlated with dry eye symptoms (OSDI) to a statistically significant degree at baseline. Moreover, the dry eye symptom scores (OSDI) significantly correlated with the contact lens discomfort score in the asymptomatic group. In the symptomatic group, the dry eye symptoms score (OSDI) correlated well with noninvasive tear film breakup time. Cooling rate in the lower cornea

(30-s duration) correlated moderately with hyperemia in the symptomatic group at baseline.

During visit 1 (after contact lens removal), only the cooling rate in the central cornea with 10-s duration correlated with dry eye symptoms (OSDI). None of the cooling rates computed for the asymptomatic group after contact lens removal during visit 1 correlated with noninvasive tear film breakup time. Corneal staining correlated moderately with various cooling rate measurements in the asymptomatic group after contact lens removal.



**FIGURE 3.** Dry eye symptoms score (OSDI) differences within groups. OSDI = Ocular Surface Disease Index.



**FIGURE 4.** Group differences in different visits for LC, 10-s measurement. LC = lower cornea; CL = contact lens.

With the contact *in situ* and in the asymptomatic group, non-invasive tear film breakup time correlated with cooling rate in the lower cornea (10-s duration). Hyperemia also correlated with cooling rate in the central cornea (10-s duration). Corneal staining correlated moderately with the thermal cooling rate with duration of 30-s measurements in the asymptomatic group as well.

At baseline, the generalized least square model was applied for prediction of OSDI as response variable. Cooling rate in the central corneal region for the 10-s duration ( $p < 0.0001$ ) and NIKBUT ( $p < 0.0001$ ) was identified as statistically significant predictor variables for OSDI. Eq. 1 shows the computed coefficients of the linear model.

$$\text{OSDI} = -11.01 \times \text{cooling rate} - 0.23 \times \text{NIK BUT} + 5.88 \quad (1)$$

The variance influence factor of thermal cooling rate (variance influence factor, 1.02) and tear breakup time (variance influence factor, 1.02) was computed, and no multicollinearity was observed between the predictor variables. Model residuals were also normally distributed (Q-Q plot and Shapiro-Wilk test) and had constant variance throughout predicted values. The computed  $R^2$  was 0.28, and the adjusted  $R^2$  was 0.24.

## DISCUSSION

This study aimed to identify relevance of thermography parameters with clinical tests that may have an impact on discomfort and dry eye symptoms during contact lens wear. For the purpose of this study, a symptomatic group and an asymptomatic group of contact lens wearers were recruited, whereby the groups were clearly separated with regard to symptom severity, according to the contact lens discomfort score (CLDEQ-8). Contact lens-related factors (such as material, water content, lens design, wear modality, and replacement schedule) were not taken into account.

The participants in this study wore daily, 2-weekly, or monthly disposable contact lenses, and a majority of them wore silicone hydrogels (27 participants with silicone hydrogels and 13 with hydrogels). Interestingly, of the 13 hydrogel lens wearers, 9 were in the symptomatic group. Dry eye symptoms have been reported to occur more frequently in hydrogel compared with silicone hydrogel contact lens wearers.<sup>9</sup> Two other retrospective studies, however, did not observe any difference.<sup>30,31</sup> Patient-related factors were mostly controlled, as gender and age were matched in the same group. Patients with concurrent ocular surface conditions were excluded from participation, and only one ethnicity (Caucasians) was represented.

**TABLE 4.** Significant correlations between clinical tests, symptoms, and thermal cooling rate

Parameter 1	Parameter 2	r	p	Group	Visit
Cooling rate in CC, 30 s	OSDI	-0.5	0.03	Symptomatic	Baseline
Cooling rate in CC, 10 s	OSDI	-0.63	0.005	Symptomatic	Baseline
Cooling rate in LC, 10 s	OSDI	-0.53	0.03	Asymptomatic	Baseline
Cooling rate in CC, 30 s	NIK BUT	0.6	0.005	Symptomatic	Baseline
Cooling rate in CC, 10 s	NIK BUT	0.55	0.02	Symptomatic	Baseline
Cooling rate in LC, 30 s	Hyperemia	-0.47	0.04	Symptomatic	Baseline
CLDEQ-8	OSDI	0.56	0.01	Asymptomatic	Baseline
NIK BUT	OSDI	-0.77	<0.001	Symptomatic	Baseline
Cooling rate in CC, 10 s	OSDI	-0.57	0.04	Asymptomatic	After CL removal
Cooling rate in CC, 30 s	Corneal staining	0.59	0.006	Asymptomatic	After CL removal
Cooling rate in LC, 30 s	Corneal staining	0.6	0.005	Asymptomatic	After CL removal
Cooling rate in LC, 10 s	Corneal staining	0.59	0.01	Asymptomatic	After CL removal
Cooling rate in CC, 30 s	Corneal staining	0.54	0.02	Asymptomatic	CL <i>in situ</i>
Cooling rate in LC, 30 s	Corneal staining	0.53	0.02	Asymptomatic	CL <i>in situ</i>
Cooling rate in LC, 10 s	NIK BUT	0.6	0.008	Asymptomatic	CL <i>in situ</i>
Cooling rate in CC, 10 s	Hyperemia	-0.62	0.01	Asymptomatic	CL <i>in situ</i>

CC = central cornea; CL = contact lens; CLDEQ-8, 8-item Contact Lens Discomfort Questionnaire; LC = lower cornea; NIKBUT = non-invasive tear break-up time; OSDI = Ocular Surface Disease Index.

Prolonged work in front of a computer screen is considered to represent an important environmental factor for contact lens discomfort.<sup>32</sup> Both groups reported high levels of daily screen use in this study, which was only slightly higher in the symptomatic group than in the asymptomatic group. It could therefore be considered to have similar effects on the two groups in this study.

Dry eye symptomatology (OSDI) was significantly higher in the symptomatic than in the asymptomatic group during both visits. The more pronounced dry eye symptoms in symptomatic contact lens wearers at baseline group may therefore predispose them to developing contact lens discomfort—this hypothesis is supported by the high inverse correlation between the OSDI score and tear film stability, i.e., noninvasive tear breakup time, found in our study. However, a longer washout period than the 14 days applied in this study would be required to confirm this hypothesis. Dry eye symptoms (OSDI) at baseline correlated with the contact lens discomfort (CLDEQ-8) score in the asymptomatic group as well. It indicates that, although OSDI is not particularly targeted for contact lens discomfort, its results align with those from the contact lens discomfort score (CLDEQ-8). Our findings are in accordance with the results of Pastor-Zaplana et al. that showed the significance of dry eye symptoms score (OSDI) for identifying symptomatic contact lens wearers from asymptomatic ones.<sup>33</sup>

Impaired contact lens wettability affects contact lens discomfort. A shorter pre-lens noninvasive tear breakup time was previously observed in symptomatic contact lens wearers.<sup>5,34</sup> Reduced tear film stability, i.e., shorter noninvasive<sup>34,35</sup> and invasive tear film breakup time,<sup>36,37</sup> higher tear film evaporation rate, and thinner lipid layer thickness,<sup>38</sup> were observed in contact lens discomfort. In cases of contact lens dropout, a shorter invasive tear film breakup time was shown, compared with matched controls.<sup>39</sup> However, other studies failed to establish an association between tear film stability and contact lens discomfort<sup>40</sup> or when comparing dropouts to successful contact lens wearers.<sup>41</sup> In this study, noninvasive tear film breakup time did not show significant differences between the symptomatic and asymptomatic group, neither at baseline nor during the contact lens visit. This may be explained by the high inherent variability in tear film breakup time measurement in the relatively small sample size in this study. However, it significantly (negatively) correlated with dry eye symptoms (OSDI) in the symptomatic group at the baseline; i.e., patients suffering from dry eye symptoms during contact lens wear are more likely to have a shorter tear film breakup time at baseline. This indicates that tear film stability may have predictive value for the likelihood of contact lens discomfort.

Regarding the thermal cooling rate, the relationship between decrease of ocular surface temperature and tear film instability has been well established.<sup>17–21</sup> This relationship was also observed in contact lens wearers<sup>11</sup> as well. However, the link between ocular thermography and contact lens discomfort is not yet established, as very little research has been carried out in this field.<sup>22</sup>

Kim et al. observed higher rates of evaporation (measured by *in vivo* evaporimeter) as well as faster thermal cooling rates in a symptomatic group of contact lens wearers; however, this did not reach statistical significance.<sup>22</sup> They reported ocular surface cooling rate as °C/s during full blink cycles, whereas, in this study, the thermal cooling rate was computed during the initial phase of the cooling cycle (first 500 milliseconds).

In this study, thermal cooling rate was consistently higher in the symptomatic group, reaching statistical significance in the lower corneal region during the 10-s measurement and in the central corneal region during the 30-s measurement duration, focusing on the first phase of cooling in the blink cycle (first 500 milliseconds). This observation suggests the idea of multiphase analysis of thermal cooling rate,

looking into different time intervals during the blink cycle.<sup>42</sup> Looking at the lower cornea as well as central cornea could also provide more information for differentiation between the groups.

In addition, moderate correlations were observed between the cooling rate in the central cornea for both measurement durations (10 and 30 s) and dry eye symptoms (OSDI score) in the symptomatic group. Li et al. could not find an association between dry eye symptoms score (OSDI) and thermal cooling rate. This discrepancy could be explained due to smaller sample size and cohort of healthy non-contact lens wearers in their study. However, they showed a border line significance between dry eye symptoms and the regression curves of tear breakup time on ocular surface temperature.<sup>16</sup>

Thermal cooling rate also correlated with noninvasive tear film breakup time at baseline in the symptomatic group. This finding suggests that a less stable tear film corresponded to higher cooling rate in the center of the cornea. These results are consistent with the finding of Itokawa et al.<sup>11</sup> and Li et al.<sup>16</sup> Itokawa et al. showed that temperature difference correlated with noninvasive tear film breakup time both with and without contact lens wear.<sup>11</sup> Li et al. also showed significant correlation between cooling rate and tear breakup time in the cohort of noncontact lens wearers.<sup>16</sup>

Thermal cooling rate and noninvasive tear film breakup time were identified as statistically significant predictor variables for the development of contact lens-induced dry eye. However, given that dry eye symptoms are multifactorial, the predictor variables identified in this study cannot fully explain the variance in the scores for dry eye symptoms (OSDI).

In this study, hyperemia did not show any significant difference between symptomatic and asymptomatic group. However, it significantly correlated with thermal cooling rate in the lower region at baseline in the symptomatic group. This result is in accordance with the work of McMonnies that shows the relationship of hyperemia and the evaporation rate.<sup>43</sup>

Inferior corneal staining has been associated with impaired contact lens comfort<sup>44</sup> and has been proposed to contribute to contact lens-induced dry eye,<sup>45</sup> due to incomplete blinking during lens wear. However, even with dry eye symptoms, it has not been reported to occur frequently.<sup>46</sup> In this study, total corneal staining (averaged for all zones of ocular surface) was measured, and no significant correlation was shown with thermal cooling rate at baseline. However, immediately after contact lens removal, the corneal staining score significantly correlated with thermal cooling rate in the central and lower corneal regions during the 30-s measurement and in the lower cornea during the 10-s measurement. This correlation was observed in the asymptomatic group only.

This preliminary study focused on analysis of the first phase of cooling cycle over the ocular surface. For future work, a more comprehensive model will be developed and applied to better analyze the entire cooling process between blinks. Furthermore, it is envisaged to investigate the relationship of blink frequency and thermal cooling rate. This will, however, require an additional recording of blinking behavior over a longer period in a more natural setting than during thermography measurement with the patient's head placed on a chin rest. Finally, a larger-scale study will help to augment the clinical validity of the findings of this current study.

## CONCLUSIONS

This study showed that ocular thermography and dry eye symptomatology are related in the cohort of symptomatic and asymptomatic contact lens wearers, as thermal cooling rate increased with ocular dryness and discomfort in symptomatic habitual contact lens wearers. Noninvasive tear film breakup time and thermal cooling rate were identified as significant predictor variables for contact lens-induced dry eye. The automated blink detection algorithm helped to accurately identify the blinks and the onset

of the blink cycle. These findings may suggest potential for the additional application of ocular thermography in the evaluation of contact lens discomfort. The automated, noninvasive, noncontact, and quantitative nature of ocular thermography may suggest it as a viable method to indirectly measure evaporation rate, assisting screening for the diagnosis of dry eye symptoms and, consequently, discomfort in contact lens wear.

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