



## Corneal sensitivity in new silicone hydrogel contact lens wearers

Marion Seghetti <sup>a,\*</sup>, Daniela S. Nosch <sup>b,c,\*</sup> , Julie Albon <sup>d,e</sup>

<sup>a</sup> Optique Messerli SA Optometry Centre, Route des Pralettes 1, 1723 Marly, Switzerland

<sup>b</sup> Institute of Optometry, University of Applied Sciences and Arts Northwestern Switzerland (FHNW), 4600 Olten, Switzerland

<sup>c</sup> ELZA Institute AG, Bahnhofplatz 15, 8001 Zurich, Switzerland

<sup>d</sup> School of Optometry & Vision Sciences, Cardiff University, Cardiff CF24 4HQ, United Kingdom

<sup>e</sup> Viva Scientia Bioimaging Laboratories, Cardiff University, Cardiff CF24 4HQ, United Kingdom



### ARTICLE INFO

#### Keywords:

Cornea  
Ocular surface sensation  
Corneal sensitivity measurement  
Liquid jet aesthesiometry  
Silicone hydrogel contact lens  
New contact lens wearers

### ABSTRACT

**Purpose:** To explore the influence of silicone-hydrogel contact lens (CL) neophyte wear on corneal sensitivity and its correlation with CL comfort.

**Methods:** In this prospective longitudinal clinical study 42 participants new to CL wear were recruited for three visits over a period of six weeks with Visit 2 being  $7 \pm 2$  days after Visit 1, and Visit 3 being six weeks  $\pm 2$  days after Visit 1. Corneal sensitivity was measured in the right eye at each visit, using the Swiss Liquid Jet Aesthesiometer for Corneal Sensitivity (SLACS). Participants completed the Contact Lens Dry Eye Questionnaire (CLDEQ-8©) during the second and third visits to assess CL comfort.

**Results:** 38 participants (mean age:  $26.55 \pm 5.7$  years; 26 females and 12 males aged:  $25.23 \pm 5.3$  years and  $29.42 \pm 5.8$  years respectively) completed the study. No significant difference in the corneal sensory threshold was noted between the three visits ( $p = 0.175$ ,  $\eta^2 = 0.044$ , ANOVA repeated measures). However, a difference in corneal sensory threshold between visit was dependent on gender (visit\*gender  $p = 0.004$ ,  $\eta^2 = 0.214$ ); with a decreasing trend in corneal sensitivity observed in females compared to an increasing trend in males. No significant correlations were obtained between corneal sensitivity and CL comfort after one week (Spearman correlation coefficient  $r = -0.138$ ,  $p = 0.409$ ) or six weeks (Spearman correlation coefficient  $r = -0.073$ ,  $p = 0.662$ ).

**Conclusions:** The adaptation of silicone hydrogel CLs to new wearers did not cause any change in corneal sensitivity during the first six weeks of CL wear. However, the effect of gender and its influence on corneal sensitivity requires further investigation.

### 1. Introduction

Corneal sensitivity is essential for maintaining ocular health of the anterior segment due to its influence on processes such as healing and renewal of the corneal epithelium,[1,2] blinking mechanisms,[3,4] tear film production,[5–7] as well as detection of noxious agents and foreign bodies.[8,9].

A decrease in corneal sensitivity has several consequences for ocular health including impaired detection of certain stimuli such as foreign bodies or harmful substances;[9] altered blinking or tear film production;[10]. Additionally, impaired sensory pathways may lead to various diseases such as dry eye disease,[11] neuropathic pain [12] and / or herpes keratitis.[13] The release of neurochemicals, important role in

maintaining the health and healing of the ocular surface, may also be compromised.[2].

Contact lens wear naturally interacts with the ocular surface and can affect corneal sensitivity. It has been postulated that the following mechanisms cause a decrease in the sensitivity of the ocular surface when wearing contact lenses (CLs): Metabolic impairment of the cornea due to hypoxia (reduced oxygen supply),[14–18] sensory adaptation to mechanical irritation[19,20] and corneal acidosis.[21] Metabolic impairment due to hypoxia may be caused by an impairment in the production of the neurotransmitter acetylcholine, which has a higher concentration in the corneal epithelium than in other areas of the body. [22] It is therefore assumed that acetylcholine plays an important role in ionic transport (sodium chloride) in the cornea, which in turn has an

\* Corresponding authors at: FHNW University of Applied Sciences and Arts Northwestern Switzerland, School of Engineering, Institute of Optometry, Riggensbachstrasse 16, 4600 Olten, Switzerland (D.S. Nosch).

E-mail addresses: [msegheotti@optiquemesserli.ch](mailto:msegheotti@optiquemesserli.ch) (M. Seghetti), [daniela.nosch@fhnw.ch](mailto:daniela.nosch@fhnw.ch) (D.S. Nosch).

influence on the generation of nerve impulses.<sup>[23]</sup> A sensory adaptation to mechanical stimulation is plausible due to the altered and reversible arrangement of the nerves in the epithelial subbasal nerve plexus during the orthokeratology CL wear.<sup>[24]</sup> Small changes in the pH value significantly alter nerve activity,<sup>[21]</sup> a reduction in pH occurs as a result of hypercapnia (accumulation of carbon dioxide). Sensitisation of the corneal nerves, on the other hand, is thought to be the result of hyperosmolarity and/or inflammatory mediators during CL wear.<sup>[25,26]</sup>

In many clinical studies, the Cochet Bonnet aesthesiometer (CBA) was used. Limitations of the CBA include that: it is invasive and presents a risk of epithelial abrasion, imprecision and difficulty in positioning; its stimulus range is limited, as well as non-linear, especially in the upper sensitivity range, which means that corneal sensitivity is underestimated and slight sensitivity changes cannot be detected. Additionally CBA; measurement reliability is inconsistent, because the nylon filament is influenced by ambient humidity in the way it bends.<sup>[27–30]</sup>

To overcome these drawbacks and to allow a more detailed evaluation of nerve receptors in the epithelial subbasal nerve plexus that is responsible for ocular sensitivity, several prototypes of no-contact aesthesiometers have been developed and used in clinical studies.<sup>[25,31–37]</sup> Non-Contact air jet aesthesiometers work with different stimuli such as compressed air or CO<sub>2</sub>.<sup>[25,31,32,34,38,39]</sup> Air jet warping the cornea with a temperature adapted to the ocular surface supposedly produce a purely mechanical stimulation,<sup>[28,31,35]</sup> activating mechano- and polymodal nociceptors. However, the air jet stimulus also appears to cause a cold sensation<sup>[31]</sup> and a decrease in ocular surface temperature<sup>[40]</sup> indicating cold thermoreceptor activation subsequent to tear evaporation. Using an air jet also has the disadvantage of potentially dispersing after contact with the central cornea, thereby contacting with a larger surface and potentially activating more receptors than desired.<sup>[41]</sup> To remedy the disadvantages linked to the air jet, liquid jet aesthesiometers employing isotonic saline have been developed, with the aim of producing a mechanical stimulation that does not activate the thermal receptors.<sup>[36,42]</sup> A recent study has demonstrated that the Swiss Liquid Jet Aesthesiometer for Corneal Sensitivity (SLACS) has very little variability in the mass and velocity of the liquid jet for the pressure range necessary to measure corneal sensitivity. In addition, the aesthesiometer allows reproducible measurement on a precise surface of the cornea<sup>[36]</sup> with appropriate repeatability.<sup>[37]</sup>

Studies using the CBA observed a clear but reversible decrease in corneal sensitivity when wearing oxygen-impermeable polymethyl methacrylate (PMMA) CLs,<sup>[15,43–48]</sup> but only a slight effect or no effect at all during daily rigid gas permeable (RGP) CL wear.<sup>[15,16,21,47–49]</sup> Even with SLACS, no difference was found between RGP CL wearers and silicone hydrogel (SH) CL wearers and a control group.<sup>[49]</sup> In addition, corneal sensitivity recovered when switching from PMMA to RGP CLs.<sup>[15]</sup> When wearing RGP CLs, only a very slight or no decrease in sensitivity was observed compared to a control group or a soft CL group.<sup>[15,20,21,47,49]</sup>

The results to date for soft CL wear are more complicated: the studies conducted with CBA agree that corneal sensitivity decreases with hydrogel CLs with a low Dk value (= low oxygen permeability),<sup>[14,17,50]</sup> but not or only to a small extent with SH-CLs with a high Dk value (= high oxygen permeability).<sup>[20,26]</sup> Studies with air jet aesthesiometry and SLACS observed no or only very minor effects in hydrogel and SH-CL wearers with a low or high Dk value.<sup>[20,25,26,49,51]</sup> Interestingly, however, in a study with SLACS (but not with CB), a slight sensitisation of the cornea was observed in SH-CL with overnight wear after one week compared to baseline.<sup>58</sup> This increased nerve activity could be an expression of a subclinical inflammatory reaction or indicate a certain biochemical stress.

The decrease in corneal sensitivity following oxygen impermeable PMMA and low Dk hydrogel CLs supports the hypothesis that hypoxia represents the most probably cause for a decrease in corneal sensitivity during CL wear.

Murphy et al. proposed that corneal sensitivity stabilizes during the first months of CL wear when using soft or rigid gas permeable (RGP) CLs.<sup>[16]</sup> This was confirmed by Kocabeyoglu et al. who found no significant differences in corneal sensitivity following six months of silicone hydrogel CL wear.<sup>[52]</sup>

The hypothesis of the present study was that corneal sensitivity may vary during the first few weeks of CL wear during the adaptation period and that the use of a non-contact liquid jet aesthesiometer may detect finer variations than with the CBA. In addition, the correlation between corneal sensitivity and CL comfort was explored.

A recent study using SLACS already concluded that there were no differences in corneal sensitivity between silicone hydrogel, RGP CL, and non-CL wearers.<sup>[49]</sup> Moreover, they did not observe any correlations between corneal sensitivity, CL comfort and wearing time. However, these participants were long-term wearers and no comparison to baseline before CL wear was carried out. In addition, they potentially had better comfort than new CL wearers. In contrast to the previous cross-sectional study using SLACS, this study represents a longitudinal within participant comparison with a baseline and additional measurements during the adaptation period.

The overall aim of the study was to determine the effect of daily silicone hydrogel CL wear on corneal sensitivity in neophyte wearers. The secondary objective was to explore the correlation between corneal sensitivity and CL comfort.

## 2. Methods

This was a prospective longitudinal within-participant comparison study and was approved by the Swiss ethics commission (2022-D0124) and complied with the tenets of the Declaration of Helsinki. 51 volunteers new to CL wear were recruited by email from the Optique Messerli Optometry Centre in Switzerland and by an advertisement at the University of Fribourg. Inclusion criteria were good general and ocular health, with an Ocular Surface Disease Index (OSDI) <= 13 (OSDI©1995, AbbVie) and within the age range of 18–38 years, as age has been shown to have an effect on corneal sensitivity.<sup>[53–57]</sup> and CL comfort has been observed to change after the age of 45.<sup>[58]</sup> The central corneal radius was between 7.4 mm and 8.0 mm. Participants with a corneal radius of >8.0 or <7.4 mm were eligible if their corneal diameter was greater or smaller than 12.0 mm, respectively. Total astigmatism did not exceed 1.25 DC. Participants were neophytes to CL wear and those that expressed an interest in CL wear, to ensure that they were motivated, reducing the risk of dropouts during the course of the study.

In order to allow an analysis of changes in corneal sensitivity in participants during the first six weeks following a new CL fitting, a prospective longitudinal comparison within participants was chosen as the clinical investigative design. All measurements undertaken were part of standard CL fitting procedures in optometric practice.

### 2.1. Measurement procedures

All participants invited to take part in the study received a detailed information sheet explaining the nature and measurement procedures of the clinical study, before giving signed consent. All corneal sensitivity measurements were carried out on the right eye during all visits and at least four hours after awakening and approximately at the same time of the day, to avoid any possible diurnal bias on ocular surface sensitivity.<sup>[59,60]</sup> Participants were seen during three visits over a period of six weeks.

During the first session, the participant signed the consent form. Then, the inclusion and exclusion criteria were assessed by collecting the following information: general and ocular health, frequency of past and future CL use, the OSDI© questionnaire result and the measurement of corneal shape by corneal topography (Oculus M5 Keratograph, Oculus GmbH, Wetzel, Germany). Glasses were measured using a focimeter and a subjective refraction was performed.

At baseline, slit lamp microscopy with white light and blue light (with use of fluorescein) and corneal sensitivity measurement were performed. The same monthly CL (Biofinity®spheric and toric: Comfilcon A, CooperVision) was placed on the participants' eyes and the CL fit was evaluated according to the guidelines by Wolffsohn et al.[61] Toric CLs were fitted if an astigmatism of at least 0.75 D was found. CL handling and cleaning instructions with hydrogen peroxide (AOSept® Plus (Alcon)) were given.

Subsequently, the participants gradually increased CL wearing time to a minimum of eight hours during at least five days.

The second visit took place  $7 \pm 2$  days after visit 1 and participants arrived wearing their CLs for a minimum of four hours. The CL fit was again evaluated using slit lamp microscopy and CL comfort was evaluated with the CLDEQ-8© questionnaire.[62] Upon removal of the CLs, the anterior segment was examined and measurement of corneal sensitivity with SLACS was repeated. A new CL pair was handed to the participants, and they were instructed to replace the first pair after one month of wear.

The third visit took place six weeks after the first visit, during which period the participants wore their CLs for at least eight hours per day and a minimum of five days per week. The same measurements were repeated as during Visit 2 (including CL comfort evaluation).

## 2.2. Corneal sensitivity measurement with SLACS

Measurement procedures with the prototype SLACS (developed by the engineering department of FHNW University of Applied Sciences and Arts Northwestern Switzerland), shown in Figs. 1 and 2, were carried out adhering to the previously published protocol.[36,37,49,57].

Briefly, the measurements were carried out as follows: The liquid (Bausch & Lomb balanced 0.9% salt solution) jet valve was positioned at a distance of 15 mm from the center of the participants' corneas (Figs. 1 and 2). High speed recording of the liquid jet stimulus showed that the

stimulus arrives at the central corneal region of approximately 2 mm in diameter for a pressure of 400 mbar, representing a stimulus strength at a typical sensitivity threshold. Ocular Surface temperature (OST) was monitored with a thermal camera FLIR-T420s (Teledyne FLIR, Wilsonville OR, USA) and the liquid jet stimulus was set approximately  $+1.7^\circ\text{C}$  above the OST, using a stimulus duration of 40 ms. Ambient temperature and humidity were controlled ( $22^\circ \pm 0.8^\circ\text{C}$  and  $42.2 \pm 2\%$  respectively) to ensure good repeatability of measurements. Detection threshold measurements were examiner-independent, i.e. determined by an implemented software algorithm: Stimulus intensities were randomly presented within upper and lower intensity limits, which became narrower during the testing procedure, dependent on the participant's answers. The standard deviation for the final threshold was set at 0.8 dB, i.e. the threshold was found when 50 % of answers of the last six stimulus presented intensities within this standard deviation were positive.

## 2.3. Statistical analysis

For statistical analysis, all SLACS measurements were transformed to a logarithmic scale and the outcome of the transformation formula was called "dB" as previously published.[36,37,49,57].

A power calculation using *G\*Power* was performed for the post hoc Wilcoxon paired signed-rank tests before the start of the study.[63] With an effect size *d* of 0.48, and  $\alpha$  of 0.05 and a power of 0.8, based on previously published data for corneal sensory threshold ( $H_0: m_1 = 26.5$  dB;  $H_1: m_2 = 25.3$  dB;  $SD = 2.5$ ), a sample size of  $n = 38$  was obtained. [64] To compensate for possible dropouts, an additional four participants were recruited for a sample size of  $n = 42$ .

Statistical analysis was carried out using *SPSS* 27 (IBM PSS). Normality, skewness and kurtosis of the data distribution were evaluated. A repeated measures ANOVA was carried out, to test for differences in corneal sensory threshold between visits. The Mauchly test was

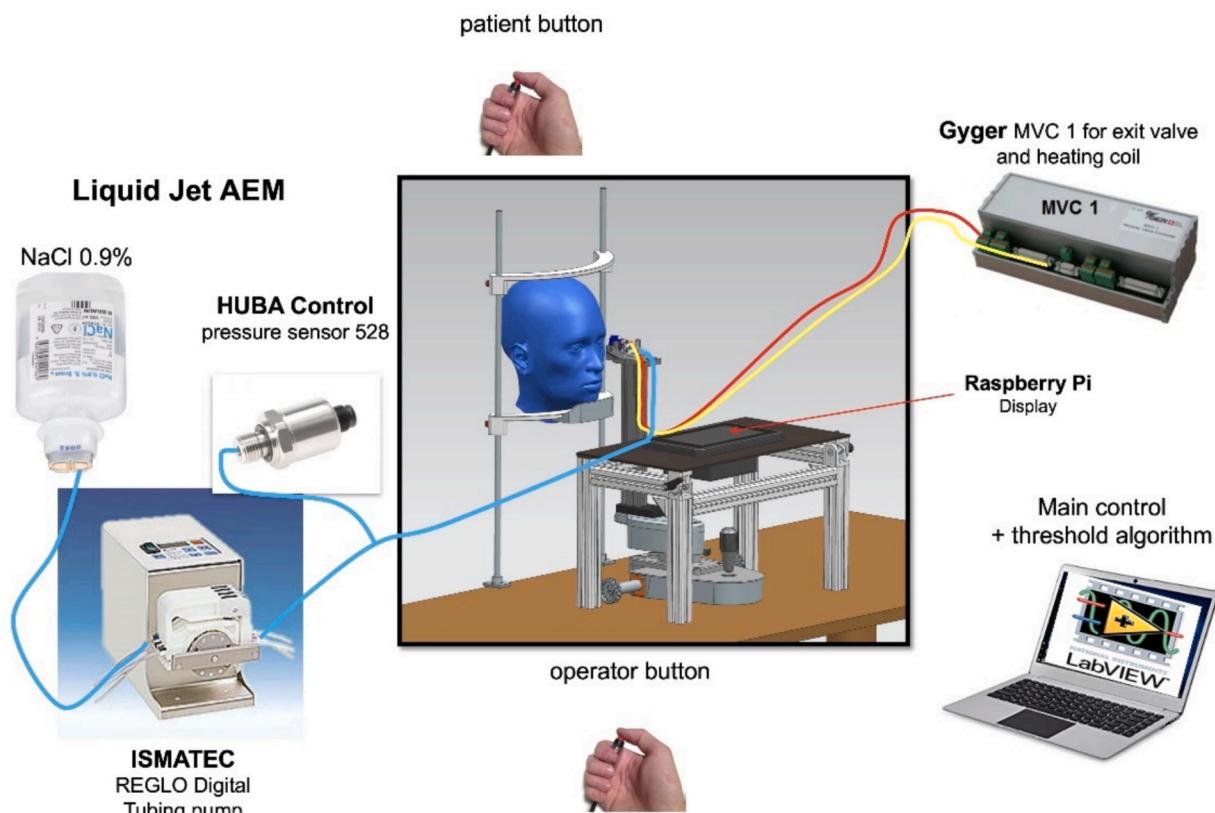


Fig. 1. Diagram of the entire prototype Swiss Liquid Jet Aesthesiometer for Corneal Sensitivity (SLACS).[36].

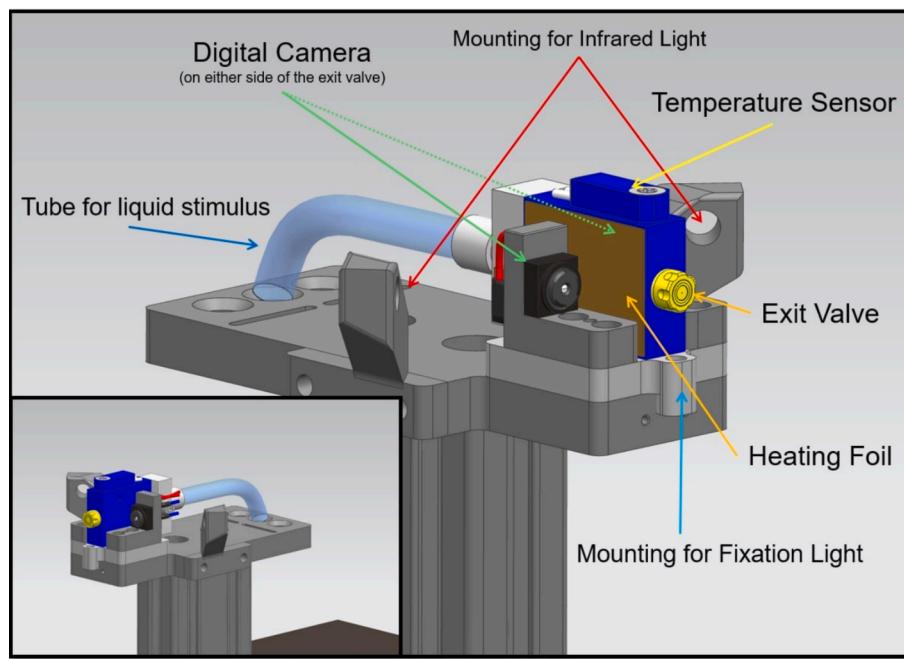


Fig. 2. Diagram of the prototype head Swiss Liquid Jet Aesthesiometer for Corneal Sensitivity (SLACS). [36].

used to evaluate the variances of the differences such that if  $p > 0.05$ , sphericity was assumed. ANCOVA repeated measures were applied to test the influence of covariants such as age and gender. The level of significance was defined with an alpha of 0.05.

To explore the correlation between the CLDEQ-8© score and the change in corneal sensory threshold, the Pearson or non-parametric Spearman test were applied, depending on normality and linearity of the data.

### 3. Results

A total of 42 participants completed the study. Four participants were removed from the statistical analysis; three due to a misunderstanding of instructions that lead to abnormally high corneal sensitivity thresholds at Visit 1. In the fourth, unrealistically low thresholds were obtained during Visits 2 and 3, due to stress-induced clicking (without feeling the stimulus) during the measurement.

Consequently, 38 participants were retained for statistical analysis (see Tables 1 and 2). The corneal sensory threshold difference between the genders at baseline (Visit 1) was not statistically different ( $p = 0.144$ , Independent sample T test). However, a trend for lower corneal sensory thresholds (i.e. higher corneal sensitivity) was observed in females.

#### 3.1. Differences in corneal sensitivity between visits, gender and age

No statistically significant difference in corneal sensitivity was obtained between the three visits ( $p = 0.175$ ,  $\eta^2 = 0.044$ , ANOVA repeated measures), although a trend for lower corneal sensory thresholds, i.e. higher corneal sensitivity, was observed for Visit 3

(Fig. 3).

The interaction visit\*gender was statistically significant ( $p = 0.004$ ,  $\eta^2 = 0.214$ ), i.e. differences in corneal sensory thresholds between visits were dependent on gender. A trend for an increase in corneal sensory thresholds in males and a decrease in females during the course of the study was observed, indicating a lower and higher corneal sensitivity, respectively (Figs. 4 and 5). However, no overall statistical difference was obtained between males or females during the three visits (main effect of gender,  $p = 0.219$ ,  $\eta^2 = 0.043$ ).

Age did not significantly influence corneal sensitivity differences in this study (for visit\*age,  $p = 0.163$ ,  $\eta^2 = 0.051$ ; ANCOVA repeated measures with covariant age).

#### 3.2. Correlation between contact lenses comfort and corneal sensitivity

No significant correlations between corneal sensory threshold and CL comfort (CLDEQ-8©) were observed (Visit 2:  $r = -0.138$ ,  $p = 0.409$ ; Visit 3:  $r = -0.073$ ,  $p = 0.662$ ; Spearman test) (Tables 2).

### 4. Discussion

Whilst there is some clinical evidence that corneal sensitivity decreases reversibly with daily hydrogel CL wear of low oxygen transmissibility,[14,17,51] the majority of studies show no or minor effects on corneal sensitivity with modern hydrogel and silicone hydrogel CLs. [20,25,49,51]

This is the first study to explore the association between corneal sensitivity and daily silicone hydrogel CL wear in neophyte wearers using SLACS and assessment of CL comfort during the CL adaptation

Table 1

Descriptive data for participants and CL corrections.

Numbers of participants		38		
Female: Male		26: 12		
Age (Years)		26.55 $\pm$ 5.7		
CL correction	Right eye	Females	Males	p-value
	Left eye	25.23 $\pm$ 5.3	29.42 $\pm$ 5.8	0.035
		Cyl (D): $-1.00 \pm 0.26$ (n = 18)		
		Cyl (D): $-0.88 \pm 0.22$ (n = 20)		

**Table 2**  
Summary of descriptive data during each visit.

	Visit 1 (mean $\pm$ SD)	Visit 2 (mean $\pm$ SD)	Visit 3 (mean $\pm$ SD)
Contact Lenses wearing time duration before visit (hours)	–	7.7 $\pm$ 1.7 Females 7.9 $\pm$ 1.8 Males 7.4 $\pm$ 1.5	7.7 $\pm$ 1.5 Females 7.6 $\pm$ 1.5 Males 8.0 $\pm$ 1.6
Screening time before visit (hours)	–	3.2 $\pm$ 2.6 Females 3.5 $\pm$ 2.7 Males 2.6 $\pm$ 2.4	2.4 $\pm$ 2.7 Females 2.3 $\pm$ 2.7 Males 2.5 $\pm$ 2.8
Corneal sensory threshold (dB)	26.36 $\pm$ 1.09 Females 26.54 $\pm$ 1.09 Males 25.98 $\pm$ 1.05 p-value 0.144	26.38 $\pm$ 1.13 Females 26.29 $\pm$ 1.12 Male 26.55 $\pm$ 1.20	26.01 $\pm$ 1.32 Females 25.62 $\pm$ 1.27 Males 26.84 $\pm$ 1.04
Corneal sensory threshold (mbar)	446 $\pm$ 113 Females 406 $\pm$ 91 Males 464 $\pm$ 119	449 $\pm$ 125 Females 440 $\pm$ 119 Males 469 $\pm$ 141	416 $\pm$ 119 Females 379 $\pm$ 102 Males 496 $\pm$ 117
CLDEQ-8 scoreMedian (IQR)	– 8.5 $\pm$ 9 Females 10 $\pm$ 11 Males 7.5 $\pm$ 7	10 $\pm$ 12 Females 9 $\pm$ 11	11.5 $\pm$ 10
AT (°C)	22 $\pm$ 0.6	21.9 $\pm$ 0.8	22.1 $\pm$ 1
Humidity (%)	42.2 $\pm$ 2.3	42.5 $\pm$ 2.0	42.0 $\pm$ 1.5
SCT (°C)	34.4 $\pm$ 0.5	34.3 $\pm$ 0.5	34.3 $\pm$ 0.5

CLDEQ-8 = Contact Lens Dry Eye Questionnaire. SCT = Surface Corneal Temperature. AT = Ambient Temperature.

period. No significant difference in corneal sensitivity was observed during the first six weeks of CL wear in this study. However, a trend towards a decrease in the corneal sensory threshold (i.e. increase in corneal sensitivity) was noted after six weeks. These findings are in line with previous studies that explored the influence of CL wear in neophyte wearers using the CBA to measure corneal sensitivity: Kocabeyoglu et al. observed no change in corneal sensitivity in new silicone hydrogel CL wearers after a six-month period and 12 h after CL removal,[52] although during this time period a potential change may have occurred. In the present study the measurement was performed immediately upon CL removal, consistent with a study by Stapleton who found no difference in corneal sensitivity after six hours of silicone hydrogel and hydrogel CL wear.[25].

The sensory stimulation caused by each instrument is different [28,40] and can therefore lead to similar but also contradictory results in the same study,[26] making comparisons between instrument measures complex.

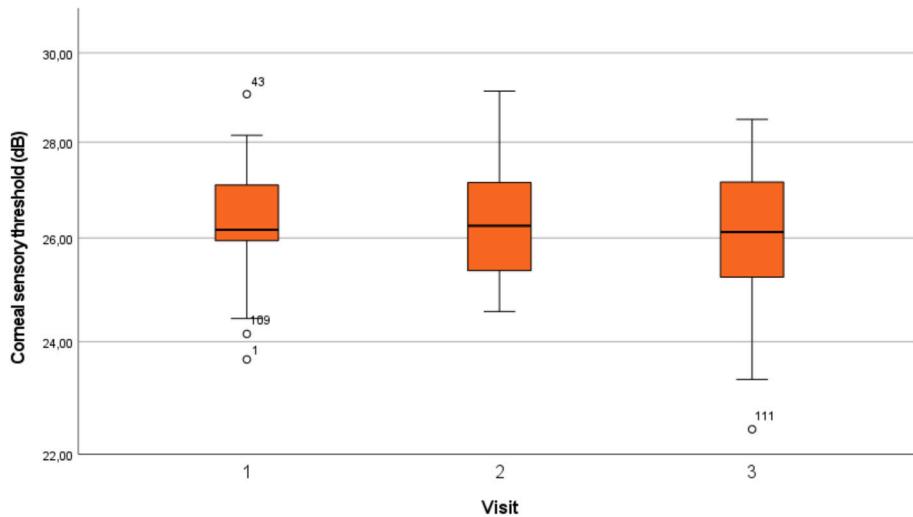
The superficial corneal nerves in the epithelial sub-basal nerve plexus are essential in maintaining the mechanisms of repair and renewal of the epithelium,[4,5] tear film production,[5–7] and blinking,[3,4] as well as the protection of the ocular surface against foreign bodies and harmful substances.[8,9] No or little effect on corneal sensitivity during the adaptation period and prolonged daily CL wear of modern silicone-hydrogel CLs may therefore suggest that these mechanisms are not affected.

Situ et al. and Stapleton et al. observed a trend towards an increased conjunctival sensitivity in silicone hydrogel CL wear,[25,26] an effect described by Situ et al. as transient.[26] In the present study, a trend for increased sensitivity was observed after six weeks. The cause of increased ocular sensitivity has been explained by subclinical inflammation and/or tear imbalances induced by mechanical forces caused by the CL, which would lead to central nociceptive sensitization.[25,26] The mechanical forces of silicone-hydrogel CLs acting on the ocular surface are greater than those of traditional hydrogel CLs due to their higher material modulus and lower elasticity, which may cause complications.[65] The higher modulus of silicone-hydrogel CLs has been put forward to explain the increased sensitivity.[25,26] In this current study, all participants wore the same silicone hydrogel CL brand with a moderate modulus of 0.75 MPa, in contrast to the higher moduli of 1.06 MPa and 1.40 MPa used in the studies by Stapleton and Situ et al.[25,26] Conversely, using the same CL types, as in the latter two studies, over a period of 12 months, Golebiowski et al. showed a reduction in corneal sensitivity when changing from a low modulus CL to a higher modulus. [51] Furthermore, in 20 new wearers with two different CL types (0.69 MPa and 1.06 MPa, proportion of each not detailed), no significant difference was observed after 6 months.[52].

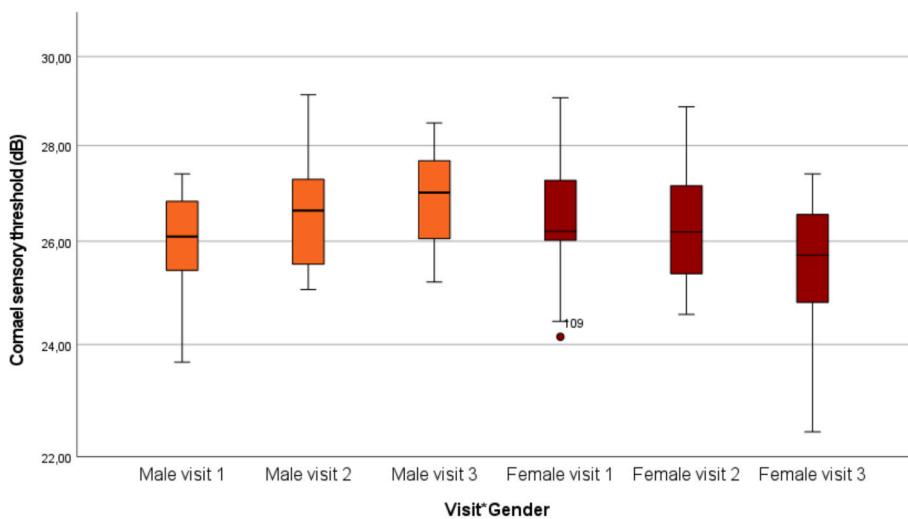
#### 4.1. Effects of gender

Although several studies agree that corneal sensitivity does not significantly differ between genders,[55,57,66] others observed a higher corneal sensitivity in women,[51,67] which was sometimes related to advancing or premenopausal age.[68] Other studies on the contrary, showed lower corneal sensitivity only peripheral cornea in women.[69].

Is there an association between change in corneal sensitivity with CL wear and gender? In this study, an interaction effect with gender was



**Fig. 3.** Boxplots for corneal sensory threshold (dB) for each visit.



**Fig. 4.** Boxplot for corneal sensory threshold for males and females at each visit [dB].

observed. Interestingly, corneal sensitivity showed a tendency to decrease in men and to increase in women with CL wear. As the female-male ratio was not balanced (26 females versus 12 males), it is not possible to draw clear conclusions from this. Velasco et al. showed a significant decrease in corneal sensitivity with a CBA in female hydrogel CL wearers.<sup>[17]</sup> Golebiowski et al. did not find significant corneal sensitivity differences between genders during CL wear, however, for the conjunctiva they observed a higher sensitivity in females using an air jet stimulus.<sup>[51]</sup> In a more recent study applying SLACS and CBA, a significantly higher sensitivity was noted in female silicone hydrogel and RGP CL wearers using SLACS only.<sup>[49]</sup> These results are consistent with the current study results and may suggest that women and men react differently to CL wear at the corneal nerves level.

Underlying reasons are difficult to explain, but hypotheses have been put forward in connection with hormonal changes in the menstrual cycle in women causing more variability in corneal sensitivity.<sup>[68,70,71]</sup> More generally, it seems that the pain threshold and pain sensitivity differ between genders, possibly explaining a greater prevalence of chronic pain disorders in women which has been mentioned to be connected to gonadal hormones potentially influencing the nociceptive system.<sup>[72]</sup> Thus, the functionality at the level of female corneal nociceptors and sensory perception may perhaps differ according to similar mechanisms. Thus, it is probable that the corneal sensory threshold differs between the genders and sensory perception may also be different. Similarly, sensory adaptation to the presence of CLs may also vary. Further research is clearly required.

#### 4.2. Corneal sensitivity related to contact lens comfort

The tear film, already thinned by the presence of the CL, continues to decrease in thickness, blink frequency increases, resulting in eyelid wiper epitheliopathy<sup>[73]</sup> and, due to the increased shear forces during a blink, lid-parallel conjunctival folds may also form.<sup>[74]</sup> In this situation, the polymodal nociceptors and the mechanoreceptors are stimulated, which leads to a sensation of irritation and foreign body sensation. Inadequate sensory adaptation to CLs also causes discomfort.<sup>[75]</sup> Another consequence of these processes is hyperosmolarity, which stimulates the polymodal and cold-sensitive nociceptors, causing a sensation of dryness, burning and cooling. In this context, inflammatory mediators are also released, which in turn sensitise polymodal nerve endings in the cornea and conjunctiva, which also results in irritation and burning.

No correlation between CL comfort (CLDEQ-8©) and corneal sensitivity was observed in this study. This is consistent with a recent inter-

participant study, which also applied SLACS in silicone hydrogel and RGP CL wearers.<sup>[49]</sup> However, in that study the participants were habitual CL wearers and were therefore more likely to present better comfort than in the present study with neophyte CL wearers. A higher corneal sensitivity has been put forward as being an unfavourable factor in CL comfort,<sup>[16]</sup> and this was indeed observed in participants with stronger symptoms of dry eyes at the end of the day in one study.<sup>[76]</sup> Chen and Simpson applied a mechanical air jet stimulus in symptomatic and asymptomatic habitual silicone hydrogel CL wearers, but found no difference in corneal sensitivity between the groups.<sup>[75]</sup> Other studies carried out with cold air jet stimuli reported higher corneal sensitivity levels in symptomatic CL wearers<sup>[77]</sup> and diurnal increases in corneal sensitivity in relation to symptoms.<sup>[78]</sup> In addition, if in fact females respond to CL wear with sensitization of the ocular surface, this may well explain why discomfort and dry eyes are more frequently reported in the female population during CL wear.<sup>[79]</sup> Furthermore, pain thresholds, as well as pain sensitivity, seem to differ depending on gender,<sup>[72]</sup> so possibly the neuronal adaptation also differs and causes different symptomatology between men and women.

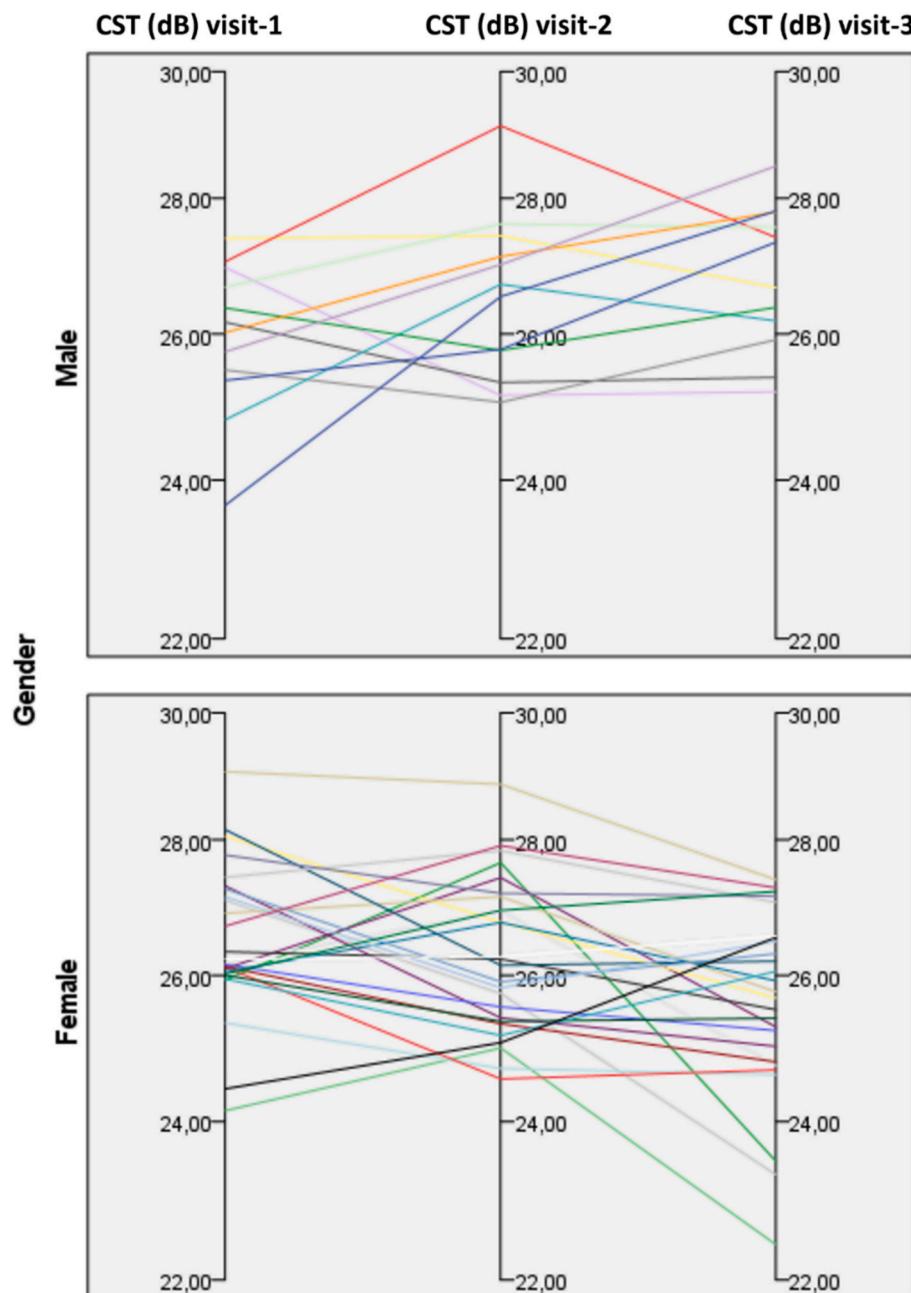
When presenting cold suprathreshold air jet stimuli, symptomatic patients reported higher levels of irritation, although no difference in detection thresholds were noted.<sup>[78]</sup> It has also been hypothesized that symptoms may arise as a consequence of impaired neuronal adaptation.<sup>[76]</sup> If neuronal adaptation plays a role in CL comfort, adding a suprathreshold stimulus may prove beneficial to better evaluate sensory perception, hence providing more information on the mechanisms that lead to the feeling of discomfort. Further research is required to elucidate the association between CL comfort and corneal sensitivity.

This study is not without limitations. Unequal numbers of women and men were recruited, and they were not age matched. However, the larger proportion of women corresponds to the demographic reality of the market where the study takes place as 56 % of women wear CLs in Switzerland.<sup>[80]</sup> A non-CL wearer control group would have additionally strengthened the power of this study, by recording corneal sensitivity longitudinally in non-wearers in parallel, to confirm that the changes in corneal sensitivity were due to CL wear and no other environmental factors.

This study also did not control for hormonal fluctuations in female participants, although they have been postulated to influence tear film quality and possibly corneal sensitivity.<sup>[67,81]</sup>

#### 5. Conclusions

This study did not show any change in corneal sensitivity following



**Fig. 5.** Parallel plots for corneal sensory thresholds during the three visits for all individual participants, separated by gender [dB].

silicone hydrogel CL wear in neophytes during the first six weeks of the adaptation period. This can be considered as reassuring, as it may suggest that good corneal physiology is preserved. However, the effect of gender and its influence on corneal sensitivity requires further investigation. No correlation was noted between corneal sensitivity and CL comfort.

#### Funding

This study was carried out as part of a Master's thesis in Clinical Optometry and did not receive funding from the public, commercial, or not-for-profit sectors. Contact lenses and cleaning solution were provided within the exam room for study measurement by the Optique Messerli Optometry Centre. The Swiss Liquid Jet Aesthesiometer for Corneal Sensitivity device was provided by the Institute of Optometry of FHNW University of Applied Sciences and Arts Northwestern

Switzerland.

#### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### References

- [1] Knyazev GG, Knyazeva GB, Tolochko ZS. Trophic functions of primary sensory neurons: are they really local? *Neuroscience* 1991;42:555–60. [https://doi.org/10.1016/0306-4522\(91\)90397-7](https://doi.org/10.1016/0306-4522(91)90397-7).
- [2] Müller LJ, Marfurt CF, Kruse F, Tervo TMT. Corneal nerves: structure, contents and function. *Exp Eye Res* 2003;76:521–42. [https://doi.org/10.1016/S0014-4835\(03\)00050-2](https://doi.org/10.1016/S0014-4835(03)00050-2).

[3] Doane MG. Blinking and the mechanics of the lacrimal drainage system. *Ophthalmology* 1981;88:844–51. [https://doi.org/10.1016/S0161-6420\(81\)34940-9](https://doi.org/10.1016/S0161-6420(81)34940-9).

[4] Nosch DS, Pult H, Albon J, Purslow C, Murphy PJ. Relationship between corneal sensation, blinking, and tear film quality. *OVS* 2016;93:471–81. <https://doi.org/10.1097/OPX.0000000000000827>.

[5] Jordan A, Baum J. Basic tear flow. *Ophthalmology* 1980;87:920–30. [https://doi.org/10.1016/S0161-6420\(80\)35143-9](https://doi.org/10.1016/S0161-6420(80)35143-9).

[6] Tsubota K. Tear dynamics and dry eye. *Prog Ret Eye Res* 1998;17:565–96. [https://doi.org/10.1016/S1350-9462\(98\)00004-4](https://doi.org/10.1016/S1350-9462(98)00004-4).

[7] Collins M, Seeto R, Campbell L, Ross M. Blinking and corneal sensitivity. *Acta Ophthalmol* 2009;67:525–31. <https://doi.org/10.1111/j.1755-3768.1989.tb04103.x>.

[8] Acosta MC, Peral A, Luna C, Pintor J, Belmonte C, Gallar J. Tear secretion induced by selective stimulation of corneal and conjunctival sensory nerve fibers. *IOVS* 2004;45:2333. <https://doi.org/10.1167/iovs.03-1366>.

[9] Belmonte C, Carmen Acosta M, Gallar J. Neural basis of sensation in intact and injured corneas. *Exp Eye Res* 2004;78:513–25. <https://doi.org/10.1016/j.exer.2003.09.023>.

[10] Rahman EZ, Lam PK, Chu C-K, Moore Q, Pflugfelder SC. Corneal sensitivity in tear dysfunction and its correlation with clinical parameters and blink rate. *Am J Ophthalmol* 2015;160:858–866.e5. <https://doi.org/10.1016/j.ajo.2015.08.005>.

[11] Bourcier T, Acosta MC, Borderie V, Borrás F, Gallar J, Bury T, Laroche L, Belmonte C. Decreased corneal sensitivity in patients with dry eye. *IOVS* 2005;46:2341. doi: 10.1167/iovs.04-1426.

[12] Dua HS, Said DG, Messmer EM, Rolando M, Benitez-del-Castillo JM, Hossain PN, et al. Neurotrophic keratopathy. *Prog Ret Eye Res* 2018;66:107–31. <https://doi.org/10.1016/j.preteyeres.2018.04.003>.

[13] Hamrah P, Cruzat A, Dastjerdi MH, Zheng L, Shahatit BM, Bayhan HA, et al. Corneal sensation and subbasal nerve alterations in patients with herpes simplex keratitis. *Ophthalmology* 2010;117:1930–6. <https://doi.org/10.1016/j.ophtha.2010.07.010>.

[14] Millodot M. Effect of soft lenses on corneal sensitivity. *Acta Ophthalmol* 1974;52: 603–8. <https://doi.org/10.1111/j.1755-3768.1974.tb01096.x>.

[15] Bergenske PD, Polse KA. The effect of rigid gas permeable lenses on corneal sensitivity. *J Am Optom Assoc* 1987;58:212–5.

[16] Murphy PJ, Patel S, Marshall J. The effect of long-term, daily contact lens wear on corneal sensitivity. *Cornea* 2001;20:264–9. <https://doi.org/10.1097/00003226-200104000-00006>.

[17] Velasco MJ, Bermúdez FJ, Romero J, Hita E. Variations in corneal sensitivity with hydrogel contact lenses. *Acta Ophthalmol* 1994;72:53–6. <https://doi.org/10.1111/j.1755-3768.1994.tb02737.x>.

[18] Millodot M, O'Leary DJ. Effect of oxygen deprivation on corneal sensitivity. *Acta Ophthalmol* 1980;58:434–9. <https://doi.org/10.1111/j.1755-3768.1980.tb05744.x>.

[19] Polse KA. Etiology of corneal sensitivity changes accompanying contact lens wear. *IOVS* 1978;17:1202–6.

[20] Lum E, Golebiowski B, Gunn R, Babhooja M, Swarbrick H. Corneal sensitivity with contact lenses of different mechanical properties. *OVs* 2013;90:954–60. <https://doi.org/10.1097/OPX.0000000000000016>.

[21] Brennan NA, Bruce AS. Esthesiometry as an indicator of corneal health. *OVs* 1991; 68:699–702. <https://doi.org/10.1097/00006324-199109000-00004>.

[22] Millodot M, O'Leary DJ. Loss of corneal sensitivity with lid closure in humans. *Exp Eye Res* 1979;29:417–21. [https://doi.org/10.1016/0014-4835\(79\)90058-7](https://doi.org/10.1016/0014-4835(79)90058-7).

[23] Pesin SR, Candia OA. Acetylcholine concentration and its role in ionic transport by the corneal epithelium. *IOVS* 1982;22:651–9.

[24] Lum E, Golebiowski B, Swarbrick HA. Mapping the corneal sub-basal nerve plexus in orthokeratology lens wear using in vivo laser scanning confocal microscopy. *IOVS* 2012;53:1803. <https://doi.org/10.1167/iovs.11-8706>.

[25] Stapleton F. Corneal and conjunctival sensitivity to air stimuli. *BJO* 2004;88: 1547–51. <https://doi.org/10.1136/bjo.2004.044024>.

[26] Situ P, Simpson TL, Jones LW, Fonn D. Effects of silicone hydrogel contact lens wear on ocular surface sensitivity to tactile, pneumatic mechanical, and chemical stimulation. *IOVS* 2010;51:6111–7. <https://doi.org/10.1167/iovs.09-4807>.

[27] Murphy PJ, Lawrenceon JG, Patel S, Marshall J. Reliability of the non-contact corneal aesthesiometer and its comparison with the Cochet-Bonnet aesthesiometer. *OPO* 1998;18:532–9. <https://doi.org/10.1046/j.1475-1313.1998.00390.x>.

[28] Golebiowski B, Papas E, Stapleton F. Assessing the sensory function of the ocular surface: Implications of use of a non-contact air jet aesthesiometer versus the Cochet-Bonnet aesthesiometer. *Exp Eye Res* 2011;92:408–13. <https://doi.org/10.1016/j.exer.2011.02.016>.

[29] Chao C, Stapleton F, Badarudin E, Golebiowski B. Ocular surface sensitivity repeatability with Cochet-Bonnet aesthesiometer. *OVs* 2015;92:183–9. <https://doi.org/10.1097/OPX.0000000000000472>.

[30] Lum E, Murphy PJ. Effects of ambient humidity on the Cochet-Bonnet aesthesiometer. *Eye* 2018;32:1644–51. <https://doi.org/10.1038/s41433-018-0150-z>.

[31] Murphy PJ, Patel S, Marshall J. A new non-contact corneal aesthesiometer (NCCA). *OPO* 1996;16:101–7. [https://doi.org/10.1016/0275-5408\(95\)00102-6](https://doi.org/10.1016/0275-5408(95)00102-6).

[32] Belmonte C, Acosta MC, Schmelz M, Gallar J. Measurement of corneal sensitivity to mechanical and chemical stimulation with a CO<sub>2</sub> esthesiometer. *IOVS* 1999;40: 513–9.

[33] Acosta MC, Tan ME, Belmonte C, Gallar J. Sensations evoked by selective mechanical, chemical, and thermal stimulation of the conjunctiva and cornea. *IOVS* 2001;42:2063–7.

[34] Feng Y, Simpson TL. Nociceptive sensation and sensitivity evoked from human cornea and conjunctiva stimulated by CO<sub>2</sub>. *IOVS* 2003;44:529–32. <https://doi.org/10.1167/iovs.02-0003>.

[35] Swanevelder SK, Misra SL, Tyler EF, McGhee CN. Precision, agreement and utility of a contemporary non-contact corneal aesthesiometer. *Clin Exp Opt* 2020;103: 798–803. <https://doi.org/10.1111/cxo.13036>.

[36] Nosch DS, Oscity M, Steigmeier P, Käser E, Loepfe M, Joos RE. Working principle and relevant physical properties of the Swiss Liquid Jet Aesthesiometer for Corneal Sensitivity (SLACS) evaluation. *OPO* 2022;42:609–18. <https://doi.org/10.1111/opo.12962>.

[37] Nosch DS, Käser E, Bracher T, Joos RE. Clinical application of the Swiss Liquid Jet Aesthesiometer for corneal sensitivity measurement. *Clin Exp Opt* 2023;1:9. <https://doi.org/10.1080/08164622.2023.2191782>.

[38] Vega JA, Simpson TL, Fonn D. A noncontact pneumatic esthesiometer for measurement of ocular sensitivity: a preliminary report. *Cornea* 1999;18:675–81. <https://doi.org/10.1097/00003226-199911000-00009>.

[39] Merayo-Lloves J, Gómez Martín C, Lozano-Sanromá J, Renedo LC. Assessment and safety of the new esthesiometer BRILL: Comparison with the Cochet-Bonnet Esthesiometer. *Eur J Ophthalmol* 2024;34:1036–45. <https://doi.org/10.1177/11206721231210754>.

[40] Nosch DS, Pult H, Albon J, Purslow C, Murphy PJ. Does air gas aesthesiometry generate a true mechanical stimulus for corneal sensitivity measurement? *Clin Exp Opt* 2018;101:193–9. <https://doi.org/10.1111/cxo.12603>.

[41] Golebiowski B, Lim M, Papas E, Stapleton F. Understanding the stimulus of an air-jet aesthesiometer: computerised modelling and subjective interpretation. *OPO* 2013;33:104–13. <https://doi.org/10.1111/opo.12025>.

[42] Ehrmann K, Saha M, Falk D. A novel method to stimulate mechanoreceptors and quantify their threshold values. *Biomed Phys Eng Express* 2018;4:025004. <https://doi.org/10.1088/2057-1976/aa9b8d>.

[43] Millodot M. Effect of length of wear of contact lenses on corneal sensitivity. *Acta Ophthalmol* 1976;54:721–30. <https://doi.org/10.1111/j.1755-3768.1976.tb01791.x>.

[44] Millodot M. Does the long term wear of contact lenses produce a loss of corneal sensitivity? *Experientia* 1977;33:1475–6. <https://doi.org/10.1007/BF01918817>.

[45] Millodot M. Effect of long-term wear of hard contact lenses on corneal sensitivity. *Arch Ophthalmol* 1978;96:1225–7. <https://doi.org/10.1001/archoph.1978.03910060059011>.

[46] Millodot M, Henson DB, O'Leary DJ. Measurement of corneal sensitivity and thickness with PMMA and gas-permeable contact lenses. *OVs* 1979;56:628–32.

[47] Douthwaite WA, Connelly AT. The effect of hard and gas permeable contact lenses on refractive error, corneal curvature, thickness and sensitivity. *J Br Contact Lens Assoc* 1986;9:14–20. [https://doi.org/10.1016/S0141-7037\(86\)80009-X](https://doi.org/10.1016/S0141-7037(86)80009-X).

[48] Sanaty M, Temel A. Corneal sensitivity changes in long-term wearing of hard polymethylmethacrylate contact lenses. *Ophthalmologica* 1998;212:328–30. <https://doi.org/10.1159/000027317>.

[49] Nosch DS, Käser E, Christen A, Schinzel J, Joos RE. Corneal sensitivity in silicone hydrogel and rigid gas permeable contact lens wear. *CLAE* 2023;46:101888. <https://doi.org/10.1016/j.clae.2023.101888>.

[50] Larke JR, Hirji NK. Some clinically observed phenomena in extended contact lens wear. *BJO* 1979;63:475–7. <https://doi.org/10.1136/bjo.63.7.475>.

[51] Golebiowski B, Papas EB, Stapleton F. Corneal and Conjunctival Sensory Function: the impact on ocular surface sensitivity of change from low to high oxygen transmissibility contact lenses. *IOVS* 2012;53:1177. <https://doi.org/10.1167/iovs.11-8416>.

[52] Kocabeyoglu S, Colak D, Mocan MC, Irkec M. Sensory adaptation to silicone hydrogel contact lens wear is not associated with alterations in the corneal subbasal nerve plexus. *Cornea* 2019;38:1142–6. <https://doi.org/10.1097/ICO.0000000000002031>.

[53] Millodot M. The influence of age on the sensitivity of the cornea. *IOVS* 1977;16: 240–2.

[54] Millodot M, Owens H. The influence of age on the fragility of the cornea. *Acta Ophthalmol* 1984;62:819–24. <https://doi.org/10.1111/j.1755-3768.1984.tb05810.x>.

[55] Roszkowska AM, Colosi P, Ferreri FMB, Galasso S. Age-related modifications of corneal sensitivity. *Ophthalmologica* 2004;218:350–5. <https://doi.org/10.1159/000079478>.

[56] Mirzajan A, Khezri F, Jafarzadehpur E, Karimian F, Khabazkhoob M. Normal corneal sensitivity and its changes with age in Tehran, Iran: Age-related corneal sensitivity changes. *Clin Exp Optom* 2015;98:54–7. <https://doi.org/10.1111/cxo.12214>.

[57] Nosch DS, Käser E, Bracher T, Joos RE. Age-related changes in corneal sensitivity. *Cornea* 2023;42:1257–62. <https://doi.org/10.1097/ICO.0000000000003183>.

[58] Naduvilath T, Papas EB, Lazon de la Jara P. Demographic factors affect ocular comfort ratings during contact lens wear. *OVs* 2016;93:1004–10. <https://doi.org/10.1097/OPX.0000000000000884>.

[59] Millodot M. Diurnal variation of corneal sensitivity. *BJO* 1972;56:844–7. <https://doi.org/10.1136/bjo.56.11.844>.

[60] du Toit R, Vega JA, Fonn D, Simpson TL. Diurnal variation of corneal sensitivity and thickness. *Cornea* 2003;22:205–9. <https://doi.org/10.1097/00003226-200304000-00004>.

[61] Wolffsohn JS, Dumbleton K, Huntjens B, Kandel H, Koh S, Kunnen CME, et al. BCLA CLEAR - Evidence-based contact lens practice. *CLAE* 2021;44:368–97. <https://doi.org/10.1016/j.clae.2021.02.008>.

[62] Chalmers RL, Begley CG, Moody K, Hickson-Curran SB. Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8) and opinion of contact lens performance. *OVs* 2012; 89:1435–42. <https://doi.org/10.1097/OPX.0b013e318269c90d>.

[63] Faul F, Erdfelder E, Lang A-G, Buchner A. G\*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 2007;39:175–91. <https://doi.org/10.3758/BF03193146>.

[64] Kleinschmidt V, Zimmermann J. Changes in corneal sensitivity in extended wear of silicone hydrogel contact lenses. Bachelor Thesis. Institute of Optometry, FHNW, 2023.

[65] Dumbleton K. Adverse events with silicone hydrogel continuous wear. CLAE 2002; 25:137–46. [https://doi.org/10.1016/S1367-0484\(02\)00009-7](https://doi.org/10.1016/S1367-0484(02)00009-7).

[66] Henderson L, Bond D, Simpson T. The association between eye color and corneal sensitivity measured using a Belmonte Esthesiometer. OVS 2005;82:629–32. <https://doi.org/10.1097/01.opx.0000171817.32551.05>.

[67] Golebiowski B, Papas EB, Stapleton F. Factors affecting corneal and conjunctival sensitivity measurement. OVS 2008;85:E241–6. <https://doi.org/10.1097/OPX.0b013e3181694f96>.

[68] Acosta MC, Alfaro ML, Borrás F, Belmonte C, Gallar J. Influence of age, gender and iris color on mechanical and chemical sensitivity of the cornea and conjunctiva. *Exp Eye Res* 2006;83:932–8. <https://doi.org/10.1016/j.exer.2006.04.018>.

[69] Khezri F, Mirzajani A, Karimian F, Jafarzadehpur E. Is corneal sensitivity sex dependent? *J Ophthalmic Vis Res* 2015;10:102. <https://doi.org/10.4103/2008-322X.163772>.

[70] Draeger J, Schloth W, Wirt H. Interindividual differences of corneal sensitivity Genetic aspects. *Ophthalmic Paediatr Genet* 1985;6:51–5. <https://doi.org/10.3109/13816818509004117>.

[71] Guttridge NM. Changes in ocular and visual variables during the menstrual cycle. *OPO* 1994;14:38–48. <https://doi.org/10.1111/j.1475-1313.1994.tb00555.x>.

[72] Maurer AJ, Lissounov A, Knezevic I, Candido KD, Knezevic NN. Pain and sex hormones: a review of current understanding. *Pain Management* 2016;6:285–96. <https://doi.org/10.2217/pmt-2015-0002>.

[73] Shiraishi A, Yamaguchi M, Ohashi Y. Prevalence of upper- and lower-lid-wiper epitheliopathy in contact lens wearers and non-wearers. *Eye Contact Lens* 2014;40: 220–4. <https://doi.org/10.1097/ICL.0000000000000040>.

[74] Pult H, Purslow C, Murphy PJ. The relationship between clinical signs and dry eye symptoms. *Eye* 2011;25:502–10. <https://doi.org/10.1038/eye.2010.228>.

[75] Chen J, Simpson TL. A Role of corneal mechanical adaptation in contact lens-related dry eye symptoms. *IOVS* 2011;52:1200. <https://doi.org/10.1167/ios.10-5349>.

[76] Martín-Montañez V. End-of-day dryness, corneal sensitivity and blink rate in contact lens wearers. *CLAE* 2015;38:148–51.

[77] Situ P, Simpson T, Begley C. Hypersensitivity to cold stimuli in symptomatic contact lens wearers. OVS 2016;93:909–16. <https://doi.org/10.1097/OPX.0000000000000857>.

[78] Situ P, Simpson TL, Begley CG, Keir N. Role of diurnal variation of corneal sensory processing in contact lens discomfort. *Ocul Surf* 2020;18:770–6. <https://doi.org/10.1016/j.jtos.2020.08.007>.

[79] Dumbleton K, Caffery B, Dogru M, Hickson-Curran S, Kern J, Kojima T, et al. The TFOS International Workshop on Contact Lens Discomfort: Report of the subcommittee on epidemiology. *IOVS* 2013;54:TFOS20. <https://doi.org/10.1167/ios.13-13125>.

[80] Morgan PB, Efron N. Global contact lens prescribing 2000–2020. *Clin Exp Optom* 2022;105:298–312. <https://doi.org/10.1080/08164622.2022.2033604>.

[81] Du Toit R, Situ P, Simpson T, Fonn D. The effects of six months of contact lens wear on the tear film, ocular surfaces, and symptoms of presbyopes. OVS 2001;78: 455–62. doi: 10.1097/00006324-200106000-00020.