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Corneo-scleral limbal changes following short-term soft contact lens wear

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A R T I C L E I N F O

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A B S T R A C T

Purpose: To assess whether short-term soft contact lens wear alters the anterior eye surface.

Methods: Twenty-two neophyte subjects wore soft contact lenses for a period of five hours. Topography based corneo-scleral limbal radius estimates were derived from height measurements acquired with a corneo-scleral profilometer. Additionally, central corneal thickness (CCT), anterior chamber depth (ACD), corneal curvature radius (R) and white-to-white (WTW) diameter were acquired with an OCT-assisted biometer. Measurements were obtained without lens wear (baseline), immediately after lens removal following five hours of wear and three hours after lens removal.

Results: Short-term soft contact lens wear significantly modifies corneo-scleral limbal radius (mean ± SD: 130 ± 74 μm, $p < < 0.001$) and the changes are repeatable. In contrast, the WTW diameter and R were not modified. ACD and CCT were significantly affected but no significant correlations were found between the increment of the limbal radius and the decrease in ACD and CCT. Limbal radius increment was reversed three hours after lens removal for 68% of the subjects but the time course of this reversal was not uniform.

Conclusions: It is possible to accurately quantify limbal radius changes as a consequence of soft contact lens wear. The increment in the limbal diameter could reach over 0.5 mm but that alteration does not correspond to changes in WTW diameter and it was not observable to the examiner using a slit lamp. Assessing topographical limbus after contact lens wear could be a tool to optimize the selection of the contact lens, from the perspective of anterior eye surface changes.

1. Introduction

Contact lenses are widely used as an effective form of visual correction. An estimated 125 million people wear contact lenses worldwide [1], with approximately 90% being soft contact lens wearers [2].

Many studies have shown the importance of having the fit of the lens optimized in relation to comfort, vision quality and corneal health [3,4]. The interaction of the contact lens with the surface of the eye, which goes beyond the mechanics involved in lens fit, has a decisive role in assuring the safety of the contact lens wear [5].

The anterior corneal changes occurring with different types of soft contact lenses have been well documented, particularly in the case of poorly fitted lenses. These include corneal surface irregularity [6], corneal swelling and isolated cases of corneal warpage [7,8]. In contrast, topographical changes occurring at limbal and scleral regions have gained less attention, due to limitations in technology. Videokeratoscopes or Scheimpflug cameras have been traditionally used for studying the induced changes on the cornea after soft contact lens wear [6,7]. The main limitation of these techniques is that their range of measurement is restricted to the cornea to a diameter of about 8 to 11 mm. Although information on corneal topography alone suffices for success fitting of scleral contact lenses [9], for the majority of soft contact lenses, there is little correlation between corneal topography parameters and the best-fitting soft contact lens [10].

The corneo-scleral region influences the soft contact lens fitting and its dynamics [11], while, at the same time, the lens midperipheral shape as well as its edge design influences the corneo-scleral topography [12]. This interaction causes larger topographical changes in the corneo-scleral region compared to the corneal region, as shown using optical coherence tomography (OCT), after short term contact lens wear [13,14]. Studying the potential changes induced by soft contact lens wear on limbal radius, as the structure that connects the cornea and the sclera, could lead us to a better understanding of the interaction of the lens with the eye and subsequently improve the fitting. Besides, recently corneo-scleral profilometry has been proven to be an accurate technique to measure the three dimensional surface of the anterior eye in a non-contact way [15].

The purpose of this study was to characterise how the anterior eye surface changes after short term soft contact lens wear by measuring

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changes in corneo-scleral limbal radius and to relate that parameter to other biometric characteristics of the anterior eye such as: anterior chamber depth (ACD), the central corneal thickness (CCT), radius of corneal curvature (R) and the white-to-white (WTW) diameter.

2. Methods

Participants in this study included twenty-two young, healthy adult subjects (16 females, 6 males) aged 25 ± 5.5 years old (mean ± SD). The study was approved by the Wroclaw Medical University Research Ethics Committee and adhered to the tenets of the Declaration of Helsinki. All subjects gave written informed consent to participate after the nature and possible consequences of the study were explained. Prior to commencement of the study, all subjects were screened to exclude those with any contraindications to contact lens wear (i.e., significant tear film or anterior segment abnormalities). All the participants were contact lens neophytes. Participants had no prior history of eye injury, surgery or current use of topical ocular medications.

All subjects were imaged using a corneo-scleral profilometer (Eye Surface Profiler (ESP), Eaglet Eye BV, Netherlands), a recently developed height profilometer with the potential to measure the corneo-scleral topography far beyond the limbus. Biometric measurements were acquired using an OCT assisted biometer (IOLMaster 700, Carl Zeiss Meditec AG, Germany). To determine surface heights, algorithms used in ESP achieve similar levels of accuracy to those reached in keratoscopy based instruments such as Placido disk videokeratoscopes [15]. Also, the IOL Master 700 has been reported to be in excellent agreement with its predecessors but with smaller failure rate [16]. Accurate measurements of anterior eye surface using ESP require instillation of fluorescein with a more viscous solution than saline [15]. The BioGlo (HUB Pharmaceuticals) ophthalmic strips were used to gently touch the upper temporal ocular surface. They were impregnated with 1 mg of fluorescein sodium ophthalmic moisten with one drop of an eye lubricant (HYLO-Parin, 1 mg/ml of sodium hyaluronate). After acquiring ESP measurements the eye was rinsed with saline before continuing the procedure.

The study consisted of three parts (P1 to P3) and two cases (C1 and C2) that are summarised in Table 1. P1, P2 and P3 constitute the main part of the study, while C1 and C2 are two cases showing examples of dynamics of limbal radius occurred after contact lens wear and the effect of different contact lens design and material on limbal radius, respectively.

Six types of commercially available daily contact lenses (−0.5 D power) were considered. They were four silicone hydrogel and two hydrogel lenses (for more details, see Table 2). In the part P1 of the study one type of lens was selected at random to conduct the study on the whole group of 22 recruited subjects (stenfilcon A; Dk/t = 100; 54% water; d = 14.20 mm; BC = 8.40 mm) while, in the case C2 of the study, all six lenses designs were used by two subjects with similar limbus size, but who experienced different limbal radius increment after wearing the same type of randomly chosen contact lens in P1. Case C2 of the experiment was conducted in six different days separated by at least a seven-day washout period. Lens fit was assessed after 30 min of lens wear [17,18]. The assessment included corneal coverage, lens centration, edge alignment in primary gaze, lag, push-up and post blink movement. Other observations including air bubbles and debris trapped under the lens were also assessed by an experienced optometrist. Overall fit evaluation was graded as either acceptable or unacceptable, depending on the investigator's assessment of the lens fit. The health of the eye was assessed post measurements. Fluorescein corneal staining was graded according to the National Eye Institute (NEI) grading scale [19].

The part P1 of the study was conducted over three sessions on the same day. Each session included six measurements with ESP and one measurement with IOLMaster700 (internally the device acquires and averages several measurements in each acquisition). Contact lenses of the same type were fitted in both eyes. The left eye was later randomly chosen for analysis. Subjects were instructed to open their eyes wide prior the measurements with ESP to insure full coverage of the corneo-scleral area.

Baseline measurements were conducted in the morning with a minimum of two hours after awakening in order to control the influence of diurnal variation [20] and before contact lenses insertion (0 h, session 1, baseline measurements (MB)). Measurements were also acquired immediately post lens removal following 5 h of wear (session 2, M5) and 3 h after lens removal (i.e., 8 h after initial lens insertion) (session 3, M8). Participants were continuing their normal daily activities between the measurement sessions that constituted office/computer work.

A subgroup of 9 subjects, who had participated in part P1 and who volunteered to participate in the part P2 of the study, were asked to repeat the procedure on a different day, but without wearing contact lenses to assess the diurnal changes in the anterior eye surface. During that second day, subjects were also measured in three sessions at the same time as they had been measured on the first day, with both ESP and IOLMaster700.

To assess the repeatability of the observed effects in limbal radius after soft contact lens wear, five subjects were randomly selected from the P2 subgroup to repeat the measurements conducted in the part P1 of the study on two different days separated by a minimum of seven days apart (P3, see Table 1). The same type of soft contact lens as in P1 was worn in P3. Additionally, to estimate the temporal dynamics of corneo-scleral region after a short term soft contact lens wear, two volunteer subjects, who participated in P1 and P2, were asked to return for a third day measurements (C1, see Table 1). Data was acquired exclusively using ESP. Once more, the baseline measurements were obtained in the morning before contact lens insertion, and immediately after 5 h of contact lens wear, 5 min after removal, in 10 min intervals

Table 1
Different parts of the study and brief explanation of each of them.

Part of the study	Number of participating subjects	Short description	Main aim
P1	22	Subjects wore 1 lens design (randomly selected) for 5 h	To characterise how limbal radius changes after soft contact lens wear
P2	9	Control investigation. Subjects were measured in the same time slots than those in P1 but they did not wear contact lenses	To discard diurnal changes in limbal radius
P3	5	Subjects repeated P1	To assess the repeatability of the observed effects in limbal radius after soft contact lens wear
C1	2	Subjects repeated P1 but additional measurements after contact lens removal were acquired	To estimate the temporal dynamics of limbal radius after contact lens wear
C2	2	Subjects wore all 6 designs of contact lenses for 5 h	To ascertain whether the observed limbal radius increment was the same independently of the design worn.

Table 2
Comparison on the effect of wearing different types of spherical soft contact lenses (−0.5D) on limbal radius increment. Two subjects (Subject 1 (S1), female, 28 years-old and Subject 2 (S2), male, 25 years-old) wore different contact lenses on their left eye on six different days. MB, M5, M8 are expressed as the mean limbal radius value for both subjects together. The variation is expressed in mm and is one standard deviation from the mean value calculated from 2 subjects and 6 ESP measurements each.

	MB: Baseline limbal radius (mm)	M5: Limbal radius after 5 h of soft contact lens wear (mm)	M8: Limbal radius after 3 h of soft contact lens removal (mm)	Average increment between MB & M5 (μm)
Stenfilcon A, SiHy (Dk/t = 100, 54% water, d = 14.20 mm, BC = 8.40 mm, round edge)	6.03 ± 0.04	6.21 ± 0.05	6.02 ± 0.04	S1: 140 S2: 210
Delefilcon A, SiHy (Dk/t = 156, 33% water, d = 14.10 mm, BC = 8.50 mm, chisel edge)	6.04 ± 0.02	6.26 ± 0.07	6.03 ± 0.02	S1: 140 S2: 270
Narafilcon A, SiHy (Dk/t = 118, 46% water, d = 14.20 mm, BC = 8.50 mm, knife edge)	6.05 ± 0.03	6.12 ± 0.06	6.03 ± 0.02	S1: 20 S2: 130
Somofilcon A, SiHy (Dk/t = 86, 56% water, d = 14.10 mm, BC = 8.60 mm, round edge)	6.05 ± 0.02	6.17 ± 0.06	6.05 ± 0.05	S1: 70 S2: 160
Omafilcon A, Hy (Dk/t = 28, 60% water, d = 14.20 mm, BC = 8.70 mm, round edge)	6.05 ± 0.03	6.25 ± 0.06	6.05 ± 0.02	S1: 180 S2: 190
Nelfilcon A, Hy (Dk/t = 26, 69% water, d = 14.00 mm, BC = 8.70 mm, chisel edge)	6.04 ± 0.02	6.15 ± 0.06	6.04 ± 0.03	S1: 30 S2: 200

during the first hour, and in 30 min intervals from the first hour after contact lens removal till 4.5 h after lens removal.

Following data acquisition, the raw anterior eye height data (three columns with *X*, *Y*, and *Z* coordinates) was exported from ESP for further analysis. To ensure that the data is not tilted, the realignment was performed by first calculating a geodesic (straight line that joins two points in a given surface) of specific distance from the apex, fitting a 3D plane to the geodesic, and then correcting the data with the estimated tilt. This correction is necessary to ensure the repeatable demarcation of the corneo-scleral region within different measurements. Limbal transition was calculated in 360 semi-meridians, using a custom written algorithm, as the point corresponding to a certain amount of change in the curvature between cornea and sclera [21]. Further, a best-fit-circle was estimated using the points which demarcated the anterior limbus surface in each semi-meridian. The planar radius of this circle was termed the planar corneo-scleral limbal radius, or shortly the *limbal radius*. In addition, biometry parameters (ACD, CCT, R, and WTW diameter) were extracted from IOLMaster 700 and included for statistical analysis.

The statistical analysis was performed using SPSS software for Windows version 23.0 (SPSS Inc., Chicago, Illinois, United States). Normality of all sets of data was not rejected (Shapiro-Wilk test, $p > 0.05$). Furthermore, the ANOVA-repeated-measurements test (adjustment for multiple comparisons: Sidak) was performed to ascertain whether there was a change between sessions, for each of the parameters under analysis. Mauchly's test of sphericity indicated that the assumption of sphericity had not been violated in any of the parameters under analysis.

3. Results

All data reported in this section are given for correctly fitted soft contact lenses that did not induce any noticeable physiological signs in slit lamp examination. In the part P1 of the study, it was found that soft contact lens short-term wear had a statistically significant effect on the limbal radius (Sidak test, $p \ll 0.001$) (Table 3), as well as on the ACD (Sidak test, $p < 0.001$) and CCT (Sidak test, $p = 0.018$), as it shown in Table 4.

The observed increase in the limbal radius was reversed 3 h after contact lens removal for 68% of the participants (15 out of 22). For this subgroup there were no statistically significant differences between MB and M8 (Sidak test, $p = 0.11$). It was assumed that the limbal radius comes back to its original size when it is within the range of ± 20 μm from the baseline measurement. That range was chosen according to the lateral resolution of the instrument. The mean difference between M8 and MB limbal radius was 28 ± 32 μm. Fig. 1 shows the observed increase in limbal radius for the 22 subjects.

It has been observed that short-term soft contact lens wear has an influence not only on limbal radius size but also on limbal shape. Contact lens wear tends to make limbal shape more regular, Fig. 2 shows an example of the observed phenomenon (for having a full coverage of the corneo-scleral area, only in these particular measurements, the subject was asked to open the eye assisted by their fingers).

The limbal radius was measured 3 h after contact lens removal to assess 'how far' it is from its original (baseline) size. Fig. 3 relates to the differences in limbal radius between M8 and MB that describes the recovery in limbal radius to the increment induced in limbal radius (M5 minus M8) that each of the subjects had experienced. A positive statistically significant correlation was found ($R^2 = 0.42$, $p = 0.001$).

To assess the repeatability of the observed effects in limbal radius after the short-term soft contact lenses wear, five randomly selected subjects from part P2 of the study repeated the study (P3, see Table 1). Results are shown in Table 5. Friedman test was used for statistical analysis (0.05 significance level was established). According to the results shown previously in this work, statistical significant difference ($p = 0.039$) was found in limbal size between baseline measurements and, after 5 h of wearing the lenses. However, no statistical significant difference was found between different days ($p = 1.00$) or intra subject ($p = 0.39$). The observed increment in limbal radius after short term contact lens wear is repeatable and the method used for assessing it is consistent.

Fig. 4 shows an example of how the time course affects limbal radius after contact lens removal for two volunteer subjectswho had similar limbal radius increment upon examination (C1, see Table 1). Subject 1 had an increment on the limbal radius of 150 μm while subject 2 had 146 μm. It is noticeable that after 1 h subject 2 had reached the limbus size baseline level, whilst subject 1 took longer (between 60 and 90 min to return to initial state). Please note that subject 1 and subject 2 from Fig 4 do not correspond to data from Table 2 or Table 5. These all are independent experiments and different subjects

Further, correlations were made between the biometrical parameters (limbal radius, R, ACD, CCT and WTW diameter) and the amount of limbal radius increment after contact lens wear. Regarding limbal radius a moderate negative correlation with limbal radius

Table 3
Limbal radius comparison intra session under the influence of wearing soft contact lens during 5 h period (P1, first column) and without wearing contact lenses (P2, second column). In both cases baseline measurements were acquired in the early morning (MB); and in P1 immediately after contact lens removal (M5) and three hours after removal (M8); in the same time interval measurements data was acquired in P2, this is, 5 h after the morning baseline measurements (M5) and 3 h after MB (M8). Data was obtained with ESP and processed with a custom made algorithm. [21] The variation is expressed in mm and is one standard deviation from the group mean value calculated from each subject mean measurements.

		Limbal radius under the influence of 5 h soft contact lens wear (P1) (22 subjects)	Diurnal changes in limbal radius − no contact lens wear (P2) (9 subjects)
Mean ± SD (mm)	MB	6.12 ± 0.19	6.14 ± 0.15
	M5	6.25 ± 0.16	6.14 ± 0.15
	M8	6.15 ± 0.19	6.14 ± 0.17
Testing the difference in limbal radius between sessions	MB vs M5	$\boldsymbol{p \ll 0.001}$	$p = 1.00$
	MB vs M8	$\boldsymbol{p = 0.002}$	$p = 1.00$
	M5 vs M8	$\boldsymbol{p \ll 0.001}$	$p = 0.99$
F-test statistics		F(2,42) = 28.00	F(2,16) = 0.17
Average increment (μm) (between MB & M5)		130 ± 74	−1 ± 16
Maximum absolute change (μm) (between MB & M5)		280	20
Minimum absolute change (μm) (between MB & M5)		20	0

Numbers in bold indicates statistically significant difference.

increment ($R^2 = 0.29$, $p = 0.005$) was found. Similarly, a moderate positive correlation ($R^2 = 0.26$, $p = 0.008$) between corneal radius and limbal radius increment was found (see Fig. 5). No significant correlations were found between the amount of limbal radius increment and the ACD ($R^2 = 0.082$, $p = 0.090$), CCT ($R^2 = 0.003$, $p = 0.40$) or WTW diameter ($R^2 = 0.023$, $p = 0.25$).

It was also of interest to ascertain whether the observed limbal radius increment was common independently of the type of soft contact lenses worn (C2, see Table 1). For that, two selected subjects with similar limbus size (6.05 ± 0.04 mm (mean ± SD)), but who experienced different limbal radius increment after wearing the same type of contact lenses in P1 (Subject 1 (S1): 140 μm limbal radius increment; Subject 2 (S2): 210 μm limbal radius increment), repeated the experience using different kinds of contact lenses on separate days. The experiment was always conducted in the same time slots. The results are shown in Table 2.

Statistical power post-hoc estimation was made. The analysis was conducted for 90% power at the 5% alpha level. For a sample size of 22 subjects, differences in limbal radius of 120 μm could be differentiated.

4. Discussion

The long term soft contact lens effect on anterior surface of the eye e.g. the corneal shape, epithelial thickness and cells size has been well studied [22–26]. In this study, it was found that a relatively short term of soft contact lens wear modifies the shape of the anterior eye surface. Limbal radius increment was found to be the most noticeable effect. This increment amounted, on average, to 130 ± 74 μm (Sidak test, $p \ll 0.001$), implying a 2.2 ± 1.3 % change from its original (baseline) size. This amount is in agreement to changes observed in other peripheral parameters of the anterior eye after one day of soft contact lens wear [13].

The interaction of contact lenses with the cornea and the influence they have on the physiological processes of corneal tissue have been intensively studied. The physical presence on eye of any type of a contact lens is not neutral for ocular health. Even lenses with high Dk/t values induce some level of oedema by restricting corneal oxygen availability and creating a hypoxic environment at the anterior corneal surface [27]. Corneal hypoxia, with corresponding hypercapnia, could be a consequence of contact lens wear, leading to decrease of the immune resistance of the cornea, particularly in the case of extended wear [28]. It has been suggested that daily-wear soft contact lenses should have a Dk/t of 20–34 to avoid inducing corneal oedema [29,30]. All soft contact lenses used during this study met this requirement. However, the studies on the minimum requirement of soft lenses for gas permeability were focused only on corneal tissue and the Dk/t value that is included in lens data sheets published in trade magazines is for the center of the lens of power −3.00 D. Different reaction and corneal

Table 4
ACD, CCT, WTW and R comparison intra session under the influence of wearing soft contact lens during 5 h period (first block) and without wearing contact lenses (second block). In all cases baseline measurements were acquired in the early morning (MB); and on P1 immediately after contact lens removal (M5) and three hours after removal (M8); on the same time interval measurements were acquired on P2, this is, 5 h after the morning baseline measurements (M5) and 3 h after M5 (M8). Data was obtained with IOLMaster700. The variation is expressed in mm (CCT in μm) and is one standard deviation from the group mean value calculated from each subject's mean measurements.

		Influence of 5 h soft contact lens wear (P1) (22 subjects)				Diurnal changes − no contact lens wear (P2) (9 subjects)			
		ACD (mm)	CCT (μm)	WTW (mm)	R (mm)	ACD (mm)	CCT (μm)	WTW (mm)	R (mm)
Mean ± SD	MB	3.54 ± 0.34	550 ± 25	12.1 ± 0.34	7.79 ± 0.33	3.61 ± 0.32	530 ± 12	12.1 ± 0.44	7.65 ± 0.13
	M5	3.52 ± 0.35	547 ± 27	12.1 ± 0.35	7.76 ± 0.26	3.61 ± 0.33	527 ± 15	12.1 ± 0.47	7.65 ± 0.13
	M8	3.55 ± 0.36	549 ± 26	12.1 ± 0.36	7.75 ± 0.25	3.61 ± 0.33	526 ± 15	12.1 ± 0.45	7.64 ± 0.13
Testing the difference between sessions	MB vs M5	$p < 0.001$	$\boldsymbol{p = 0.018}$	$p = 1.00$	$p = 0.63$	$p = 0.68$	$p = 0.29$	$p = 0.94$	$p = 0.88$
	MB vs M8	$p = 0.81$	$p = 0.86$	$p = 0.86$	$p = 0.45$	$p = 0.93$	$p = 0.064$	$p = 0.94$	$p = 0.15$
	M5 vs M8	$\boldsymbol{p < 0.001}$	$p = 0.057$	$p = 0.89$	$p = 0.35$	$p = 0.96$	$p = 0.76$	$p = 1.00$	$p = 0.48$
F-test statistics		F(2,42) = 13.00	F(2,42) = 4.90	F(2,42) = 0.31	F(2,42) = 1.60	F(2,16) = 0.19	F(2,16) = 3.80	F(2,16) = 0.23	F(2,16) = 1.70
Average increment (between MB & M5)		−0.03 ± 0.02	−3 ± 5	0.0 ± 0.1	0.00 ± 0.02	−0.01 ± 0.02	−4 ± 3	0.0 ± 0.1	−0.01 ± 0.03
Maximum absolute change (between MB & M5)		0.07	10	0.2	0.05	0.04	10	0.1	0.05
Minimum absolute change (between MB & M5)		0.00	1	0.0	0.00	0.01	0	0.0	0.01

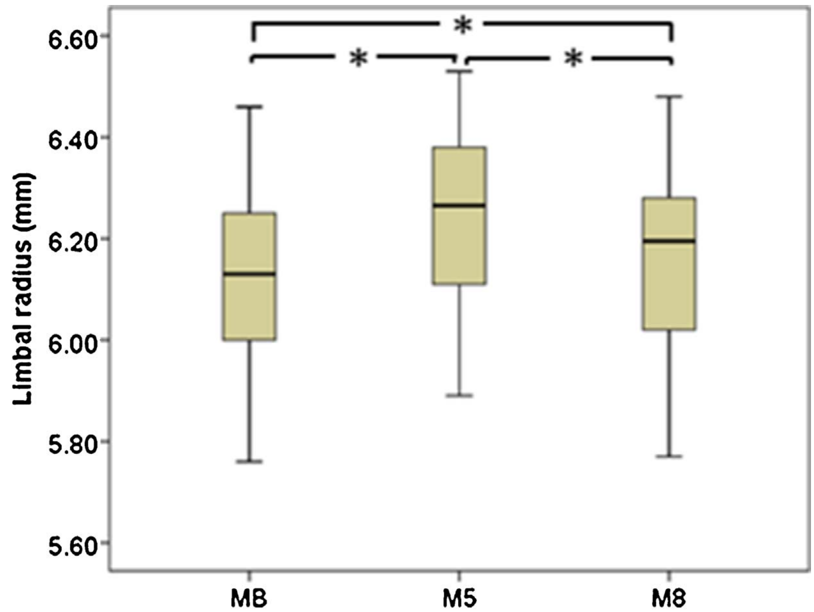

Fig. 1. The boxplot illustrates the changes in limbal radius for the 22 subjects who participated in the experiment, within the three sessions: before contact lens wear (MB), immediately after contact lens removal (M5) and 3 h after contact lens removal (M8). Asterisks denote statistically significant difference between sessions. For details see text.

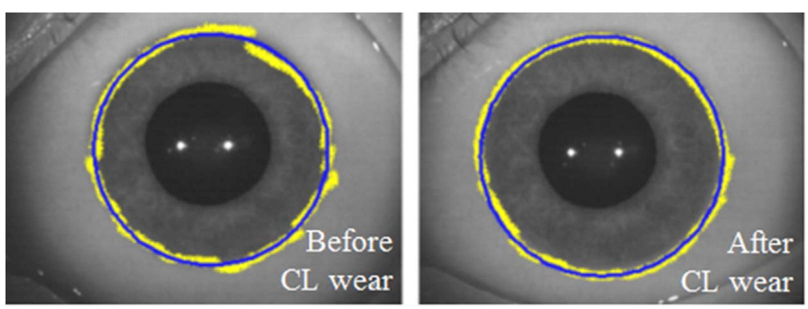

Fig. 2. Limbus demarcation points (denoted by yellow overlapping circles), calculated using [21], and the corresponding circular fit (blue line) for a subject (male, 25 years-old) before contact lens (CL) wear and immediately after contact lens removal.

response to soft contact lens wear depending on the distance from its center could be expected because soft contact lens thickness is not uniform, particularly for lenses of higher power [26,31].

A recent OCT based study from Read et al. [32], has shown that scleral thickness is affected by diurnal variation and amounts on averagely 21 ± 8 µm. This change is more noticeable immediately after awaking. Their result suggests that the sclera has a similar swelling behaviour as the cornea due to the limited access of oxygen when the eye is closed. It further suggests that contact lens wear might cause scleral thickening due to the limitation in oxygen and this could be directly related to the observed increment in limbal radius.

In another study of corneo-scleral morphology after soft contact lens

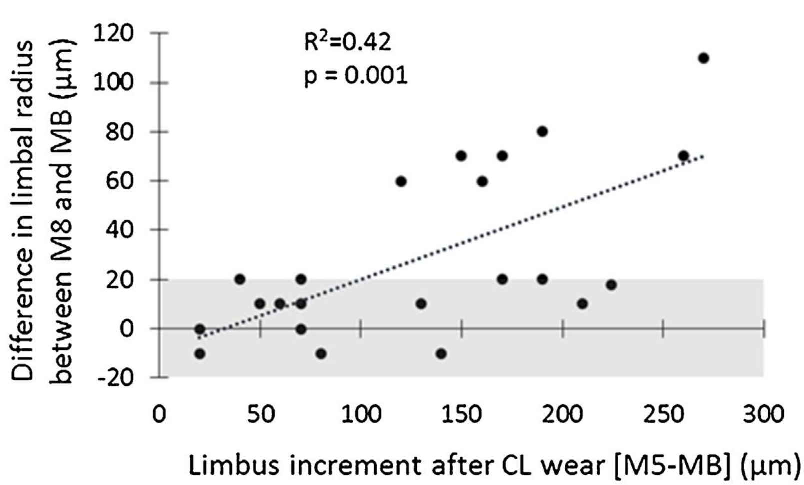

Fig. 3. Relationship between M8-MB (difference in limbal radius between 3 h after contact lens removal (M8) and baseline measurement (MB)) and the magnitude of limbal radius increment examined for the 22 subjects. The points within the grey area (± 20 µm, the lateral resolution of the instrument) are considered to have reversed the limbal radius increment after 3 h of contact lens removal.

Table 5
Intra subject repeatability of limbal radius increment under the same conditions (same contact lens, same time of wear).

		Baseline limbal radius (mm)	Limbal radius after 5 h of soft contact lens wear (mm)
Subject 1	Day 1	6.00 ± 0.06	6.21 ± 0.03
	Day 2	6.00 ± 0.04	6.21 ± 0.03
Subject 2	Day 1	6.03 ± 0.04	6.11 ± 0.01
	Day 2	5.99 ± 0.06	6.11 ± 0.06
Subject 3	Day 1	6.03 ± 0.01	6.17 ± 0.05
	Day 2	6.06 ± 0.03	6.14 ± 0.01
Subject 4	Day 1	6.03 ± 0.02	6.19 ± 0.02
	Day 2	6.00 ± 0.04	6.21 ± 0.01
Subject 5	Day 1	5.79 ± 0.02	6.14 ± 0.02
	Day 2	5.82 ± 0.02	6.14 ± 0.02

wear, also performed with OCT technology [13], it was shown that the changes in thickness of the tissue were more noticeable in corneo-scleral region than in the corneal region. In addition, corneal oedema development found to be highly subject dependent [33,34]. Results showed intersubject variability in limbal radius increment but at a lower range of change (i.e., 1 % to 3 %) than those reported in 1983 by Sarver et al. [33] for the oedema response (3.7% to 12.2%). However, in this study modern daily disposable lenses were used, superior in oxygen permeability than those lenses available several decades ago. The observed limbal radius increment was not fully reversed in all participants 3 h after contact lens removal (Sidak test, $p = 0.001$). The results suggest that if the increment in limbal radius is smaller than around 100 µm it is more likely that the return to limbal radius baseline size occurs within 3 h. Contrarily, if the increment in limbal radius is large, it takes longer to reverse the effect of contact lens wear (see Fig. 3). However, there is not a clear relationship between the limbal radius increment that a subject has and the time it takes to reverse the effect, Fig. 4 is an example. Two different subjects had the same limbal radius increment but it took different time for each of them to return to their natural (baseline) limbal radius. The limbal radius increment may be a result from pressure induced in the corneo-scleral region by the contact lens edge. Para-limbal indentation is considered an indicator of a tight-fitting soft contact lens; however, the contact lenses fit in this study were not considered tight. Blinking is another factor that may increase the pressure that the lens has on the eye surface. The friction associated with natural lens movement, the stiffness of the material, and the pressure from the eyelids [35] are commonly associated with staining observed after contact lens removal [4,36]. It should be noted, however, that no substantial staining (NEI score of 1 or less) was observed in subjects participating in this study.

A moderate significant negative correlation ($R^2 = 0.29$, $p = 0.005$) was found between the magnitude of limbal radius increment and the original size (baseline) of the limbal radius. It seems likely that the larger the limbus, the smaller the limbal increment. Similarly, a moderate significant correlation ($R^2 = 0.26$, $p = 0.008$) was found between the magnitude of limbal radius increment and the original size (baseline) of the corneal radius. The result suggests that the larger the corneal radius, the larger the limbal radius increment. All 22 subjects were fit with the same contact lens (BC = 8.40 mm, d = 14.20 mm), but their corneal radius varied from 7.4 mm to 8.4 mm. However, this did not compromise the validity of the fit, in all cases assessed by an experienced optometrist. Due to the relatively small sample size used in this study, the results of correlating limbal radius with the limbal radius increment after contact lens wear should be viewed with some caution. Factors that could contribute to the correlations include eyelid pressure, lens flexure, position of the lens edge on corneo-scleral region, and other biomechanical properties of the lens.

Baseline ACD measurements from ocular biometry were in agreement with those reported earlier [37]. Results here presented shown that ACD is affected by short term soft contact lens wear (mean ± SD: −27 ± 22 µm, $p < 0.001$), however no correlation was found between the ACD decrease and the increment of limbal radius ($R^2 = 0.082$, $p = 0.09$). Similarly, no statistically significant changes in WTW diameter measurements were found after contact lens removal. This is in accordance with previous reports [11,21,38], showing that the topographical corneo-scleral limbus does not necessarily coincide with the maximum rate of change in colour from the iris to sclera that is observable with en-face imaging when estimating WTW diameter. Regarding the CCT, a subtle thinning was found after contact lens wear most likely as consequence of the compression of the tissue. The magnitude of corneal swelling induced by short term contact lens wear is known to be minimal, sometimes even smaller than the natural diurnal thinning of the cornea over the same period of time [8,39,40]. In accordance with these studies, even though statistically significant difference in CCT (paired t-test, $p = 0.006$) was found between MB and M5 for the main group of 22 subjects and the subgroup of 9 subjects, the measured diurnal differences in the subgroup of 9 subjects (M8-MB session in P2 measurements) (mean ± SD: −3.8 ± 3.4 µm, $p = 0.064$) were of the same magnitude as those achieved for the main group after contact lens wear (mean ± SD: −3.0 ± 4.5 µm, $p = 0.018$).

In case C2 of this study that has a pilot character, it was further investigated the effect of different contact lenses under the same

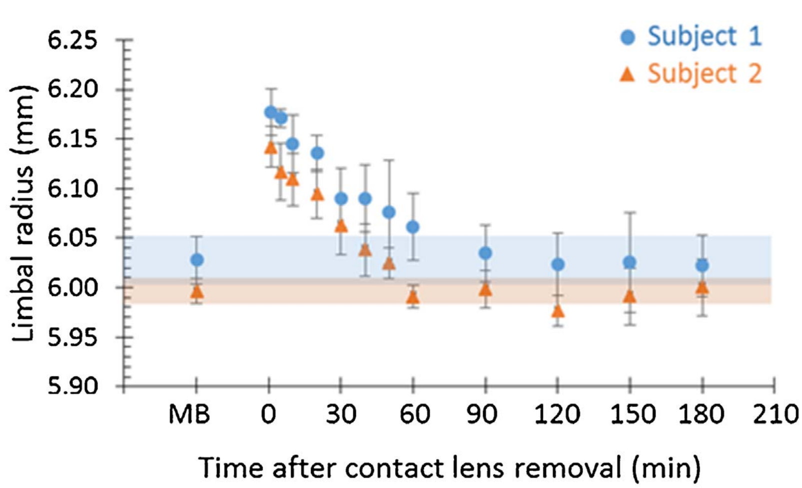

Fig. 4. Time dependency in limbal radius after contact lens removal. Two subjects participated in case C1 of the study. Error bars are calculated as one standard deviation from the mean value of six measurements acquired in the same time slot (those six measurements were acquired in less than 30 s). Coloured areas indicate the variation (one standard deviation from the mean) of the baseline limbal radius for each of the participants. The blue colour (male, 25 years-old), has a 6.02 ± 0.02 mm limbal radius prior lens insertion. The orange colour (female, 27 years-old) has a 5.99 ± 0.01 limbal radius prior lens insertion.

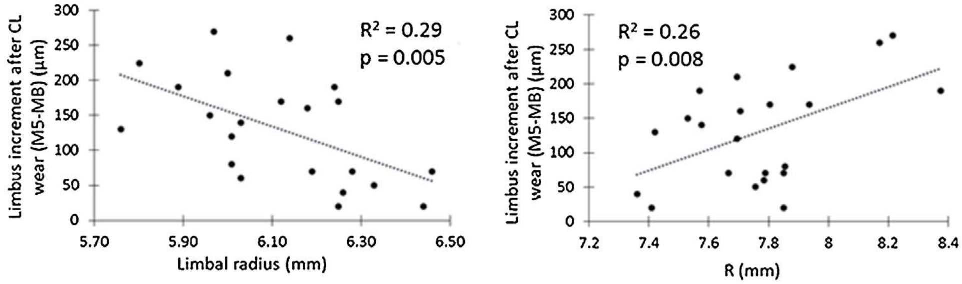

Fig. 5. Relationship between limbal radius increment after contact lens removal (M5) and morning baseline measurement (MB), and the original (baseline) size of their limbus (left) and radius of corneal curvature (right).

conditions using a pair of selected subjects (denoted as S1 and S2, see methodology section). The results showed no clear relationship between the characteristics of the contact lens and the limbal radius increment induced. This indicates subjective differences related to contact lens material and design. Even though the fit was always assessed as adequate by an experienced optometrist, in some particular cases the fit was on the tight or loose side. No association was found between the increment in limbal radius measured and the assessment of the fit. After averaging the limbal radius increment post wearing six different types of contact lenses, a smaller but with larger variability increment in limbal radius for subject S1 was obtained (mean ± SD: 97 ± 60 μm). The opposite was true for subject S2 (mean ± SD: 193 ± 43 μm). This indicates that subject S1 only had a substantial limbal radius increment wearing certain type of contact lenses, whilst subject S2 had a substantial limbal radius increment independent of the contact lens worn. It is worth noticing that the range of limbal radius increment obtained with different lenses (minimum limbal radius increment: 20 μm; maximum limbal radius increment: 270 μm, see Table 5) coincides to that found for a single lens for the entire group of subjects (see Table 1). Data distribution was Gaussian and the range [−15, 275] μm indicates the 95% confidence interval level. This suggests that the range of limbal radius increment found in this study do not contain outliers and may correspond to a standard increment range after soft contact lens wear. That range was found to be independent of the type of the contact lens worn and the personal characteristics of the wearer. The case C2 of the study indicates that different designs of contact lenses affect the limbal radius of a particular subject in a different manner. Hence, estimates of the limbal radius may help better assessing the suitability of a given contact lens.

The study has some limitations. Firstly, all participants were neophytes who could be affected by contact lens wear in a different way than the regular wearers. Whether the changes in limbal radius reported are such in experienced contact lens wearers is yet to be determined. Secondly, only lenses of −0.5 D power were considered. Some differences could be anticipated with higher power contact lenses. However, it was reported that even for lenses of high power (−10.0 D or +6.0 D) differences in CCT were not of clinical significance [41]. Furthermore, all considered contact lenses were daily soft contact lenses. However, long-term wear contact lenses are also popular among users. Also mini-scleral contact lenses are recently gaining interest [42]. Further work is needed to study how such types of contact lenses might affect the surface of the eye.

In summary, a wealth of information is already obtained from this study. Statistically significant differences in the parameters of the anterior eye associated with soft contact lens wear were observed. It has been demonstrated that it is possible to measure and accurately quantify limbal radius changes as a consequence of soft contact lens wear. This was enabled with the new technology, corneo-scleral profilometry, utilized in this study. It is expected that other imaging modalities, such as high resolution OCT, could also provide such information.

In the present study, limbal radius increment was found for all, except for two, participants. For those two subjects the limbal radius increment of 20 μm was at the resolution limit of the instrument. This shows the procedure of the study to be an accurate and precise indicator of anterior eye surface changes after contact lens wear. This study has clinical relevance because, in some cases, more than 0.5 mm increment in limbal diameter was found after short term soft contact lens wear and that change was unavailable to the examiner using a slit lamp. In addition, the results show a high subject dependency regarding limbal radius increment after contact lens wear, remarking the importance of the lens-subject biocompatibility. Measuring limbal changes after contact lens wear could be used as an easy and effective tool for the clinician to optimize the selection of the contact lens, from the perspective of anterior eye surface changes, for each particular patient.

It would be of interest to further investigate if the reported changes in limbal radius reverse with lens use, as a consequence of the adaptation of the subjects to lens wear. It could also happen that the limbal radius change was permanent as a consequence of contact lens wear, in which case it would be of interest to ascertain whether the limbal radius change is constant (same magnitude) or if it could progress further. Future work is needed to better understand and explore the consequences of soft contact lens wear on the corneo-scleral surface of the eye.

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