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A survey of corneal changes caused by daily wear silicone hydrogel contact lenses

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Purpose: The examination of the effects of second generation lotrafilcon B silicone hydrogel (SiH) lenses on the cornea when worn for three years of daily wear. **Material and Methods:** 55 healthy patients were divided into two groups: current hydrogel contact lens wearers refitted with lotrafilcon B lenses (Group 1; 28 patients) and neophyte contact lens wearers (Group 2; 27 patients). Each patient's subjective eye comfort was measured with a self-administered questionnaire. The corneas were analyzed using contact specular microscope to measure corneal thickness and the endothelium before the SiH lenses were fitted after four weeks, one month, six months, one year, two years, and three years of lens wear. **Results:** Subjective complaints of patients in Group 1 were reduced; however patients in Group 2 experienced discomfort during the first two to four weeks of use. In Group 1, objective examinations identified a decrease in endothelial cell density. In Group 2, the endothelial cell density increased slightly in the first two years but decreased after three years. The results indicate that lotrafilcon B slows down the deleterious effects of contact lenses. The coefficient of variation significantly decreased after six months in Group 1 (0.47 vs 0.44; $p = 0.049$), whereas, in Group 2, the hexagonal cells improved significantly after one month (27.78 vs 28.25; $p = 0.025$). **Conclusion:** Based on the subjects involved and the period of time under examination, it can be concluded that high-Dk SiH lenses support the physiological metabolism and functions of the cornea by improving oxygen provision.

Keywords: Contact lens; corneal endothelium; silicone hydrogels; specular microscopy; cell density.

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1. Introduction

For a healthy cornea, oxygen is required. A cornea can be affected by the presence of a contact lens. Unfortunately, long-term contact lens usage can impair the anterior segment of the eye. This is because the environmental oxygen used by the cornea's metabolism is, to some extent, blocked by the barrier of the lens. Hypoxia appears to take place at all corneal levels.[1,2]

Oxygen passes through a contact lens by diffusion. The International Organization for Standardization (ISO) standard measure of the oxygen permeability of a lens material (at a uniform, standardized thickness) is called Dk. Dk has the unit of 10^{-11} (cm^2/s) × [ml O_2/(ml × hPa) or (cm/sec) × (ml O_2/ml × mmHg)]. The actual oxygen transmissibility of the lens is called Dk/t. This measurement takes into account of the central thickness (t) of a −3.00 D lens (ISO standard) or the t at any other place of the lens. Dk/t has the unit of 10^{-9} (cm/s) × [ml O_2)/(ml × hPa)] or (cm/sec) × (ml O_2/ml × mmHg).[2,3]

A transmissibility graph shows the Dk/t values across the entirety of any given lens and describes the distribution of maximum and minimum oxygen transmissibility (power, base curve).

In silicone hydrogel (SiH) contact lenses, silicone rubber is combined with conventional hydrogel monomers. The silicone component of these lens materials provides extremely high oxygen permeability. The hydrogel component facilitates flexibility, wettability and fluid transport. This aids lens movement. Their oxygen transmissibility (Dk/t) is high because silicone is a better oxygen transmitter than water. These properties may improve the comfort of wearing contact lenses. However, a disadvantage of these lenses is the higher rigidity moduli, due to the high silicone content. First generation SiH contact lenses (lotrafilcon A, balafilcon A) have a lower water content and higher rigidity moduli, when compared with second generation SiH contact lenses (lotrafilcon B, senofilcon A, galyfilcon A, lotrafilcon B). Second generation SiH contact lenses are more comfortable, even though their oxygen permeability is lower than that of first generation SiH contact lenses. This is because they have increased water content and reduced moduli.[4]

In this prospective nonrandomized study, we investigated the effects of contact lens wear on the cornea and the corneal endothelium in subjects who were wearing second generation SiH lotrafilcon B (Air Optix, 33% H_2O, 8.6 mm BC, 14.2 mm diameter, CIBA Vision Corporation, Duluth, GA, USA). These subjects used soft contact lenses on a daily wear schedule.

2. Material and Methods

2.1. *Subjects*

In this study, we enrolled 55 people (110 eyes). The subjects were divided into two groups. To Group 1, we assigned 56 eyes of 28 subjects. These were habitual, nonsilicone hydrogel soft contact lens wearers (one male and 27 females with a mean age 25 ± 7.1 years), with a mean contact lens wear time of 5.93 ± 6.02 years (minimum: two years, maximum: 31 years). The reason for refitting these subjects with more modern contact lenses was to preserve the physiological status of the eye. In Group 2, 27 neophytes (three male and 24 females with a mean age 20 ± 2.15 years) had never worn contact lenses before they were fitted with lotrafilcon B lenses. The subjects were examined before being fitted with the SiH lens. They were then examined at two weeks, four weeks, three months, six months after their fitting and six-monthly thereafter. At every visit, we recorded visual acuity by Snellen chart. This was defined by clinical measurements and biomicroscopic examination results (lens centration and movement, morphological alterations of contact lens, anterior segment of the eye and corneal staining). Only the subjects who appeared at all their examinations and had appraisable data were included in our study analysis. For the publication of this paper, we obtained written informed consent from all of the subjects. The protocol used in this study was in full compliance with good clinical practices, the Declaration of Helsinki (1996) and the guidelines of the Medical and Health Science Center of the University of Debrecen.

3. Subjective and Objective Evaluation Methods

With the help of self-administrated questionnaires (yes or no choices), we collected the subjective experiences of the subjects. We created the response format applying several similar configurations.

Inquiries included: uncomfortable sensation at the end of the day, itchy or irritating sensation, dryness, redness, inability to wear contact lenses for an entire day, blurred vision and fluctuating visual acuity with the subjects' old lenses and with their new lotrafilcon B lenses. The questionnaires were filled in before fitting the SiH lenses and four weeks later. The endothelium cell density was measured with an EM 1100 (Tomey, Tennenlohe, Germany) contact specular microscope. The examinations were performed at scheduled intervals, with photos taken before the lotrafilcon B lenses were worn and then again at one month, six months, one, two and three years.

Before taking the photo, the cornea was anaesthetized with a drop of local anaesthetic (0.4% oxybuprocain hydrochloride). Six to seven pictures of the central region of each cornea were taken. The three best quality ones (including at least 100 cells) were analyzed using EM 1200, V 1.5.1, Tomey software.

Apart from cell density, the following parameters were determined by specular microscopy: corneal thickness, average endothelium cell size, coefficient of variation of endothelial cells and the percentage of endothelial hexagonal cells. The result obtained via specular microscopy is based on reflection. Thus, it must be considered that the magnification depends on the light path length. Consequently, in thick corneas, cell density will be under-estimated and vice versa. So we corrected the determined cell density. The correction was then calculated using the equation below (given by the Tomey for use):

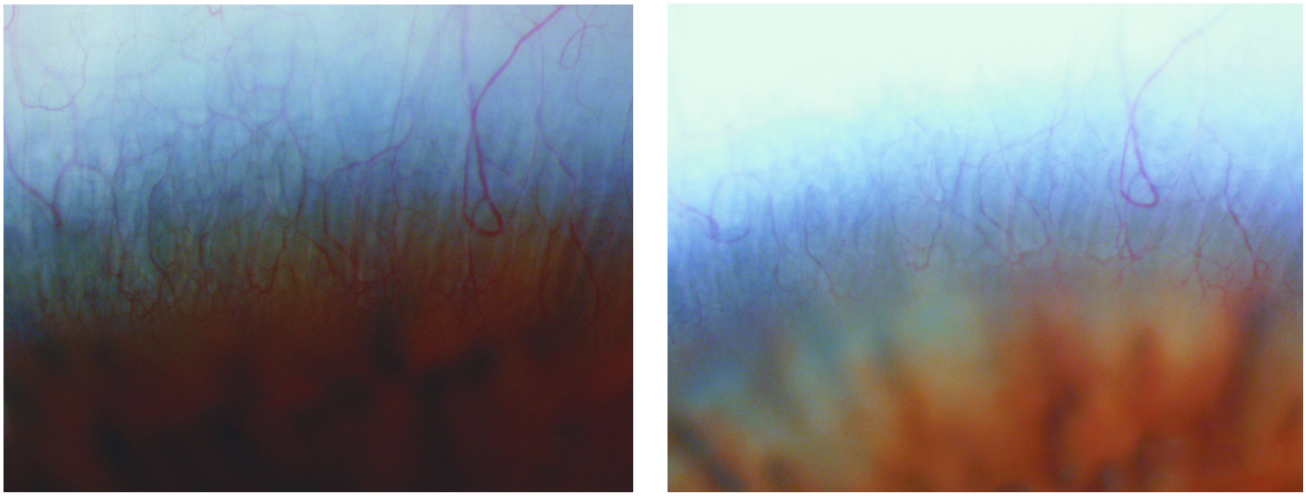
Z (corr) $= Z \times (F/10,566)^2$, where:
Z (corr): corrected cell density;
Z: actual cell density;
F: focus, namely, the thickness of the cornea;
10.566: calibration data from the manufacturer.

4. Statistical Analysis

The data were analyzed using SPSS 9.0 for Windows and were marked with means and standard deviations (SD). Comparisons were made using the Student's t-tests. The correlations between different parameters were assessed using Spearman's correlation coefficient (r). Repeated measures analysis of variances were used to compare each parameter at different time points. Finding with an error probability of less than 0.05 were considered to be statistically significant ($p < 0.05$).

5. Results

In all cases, the distance corrected visual acuity was 20/20. All lenses were well centered with a 1–2 mm lens movement. The anterior segment findings were normal and staining was not more than grade I (Efron Grading Scale). Limbal hyperaemia was reduced in Group 1 but had not developed in Group 2 (Figs. 1(a) and 1(b)).



(a) (b)

Fig. 1. Images at a higher magnification (40× magnification) of limbal hyperaemia in subjects from Group 1 before (1(a)) and 3 months after wearing lotrafilcon B lenses (1(b)).

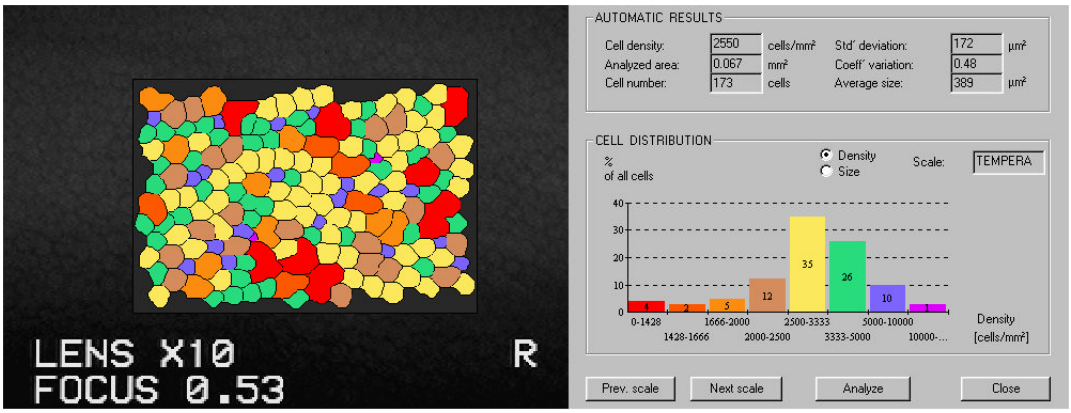


Fig. 2. Specular microscopic analysis of endothelial cell layer performed by Tomey EM 1100 equipment.

Approximately 60% (16/28) of the subjects in Group 1 found their current habitual lenses to be uncomfortable. However, after the subjects were refitted with lotrafilcon B lenses, this percentage decreased to 6% (1/28). Similar results were obtained concerning the self-assessed redness of the eye. Approximately 53% (14/28) of the investigated subjects reported lens awareness and irritation with their previous, habitual lenses. This decreased to 0% after the subjects were refitted with lotrafilcon B lenses. Dryness was a problem for 60% (16/28) of the subjects but, after wearing lotrafilcon B lenses, this completely disappeared (0%). Approximately 53% (14/28) of the investigated subjects said that they could wear lotrafilcon B lenses longer than their habitual lenses. With their previous lenses, approximately 60% (16/28) of the investigated subjects complained of blurred vision. However, none reported this symptom when wearing lotrafilcon B lenses.

Approximately 44% (12/27) of the subjects in Group 2 reported lens awareness and mild irritation in the first two to four weeks but not thereafter. This feeling of discomfort is incredibly common among new lens wearers. It develops at the beginning stages of wearing lenses of all types and decreases after a period of adaptation.

Hypoxia-related complications (microcysts, Descemet's striae, corneal staining) were not discovered by slit lamp examination. However, a decrease in limbal vascularization was observed in Group 1 (Fig. 1(a) shows more dilated limbal vessels than those three months after wearing lotrafilcon B lenses on Fig. 1(b)).

Repeated measures analysis of variances disclosed no statistically significant difference in the measured parameters in either group during the follow up period ($p = 0.06-0.96$).

The change in corneal thicknesses was not statistically significant in either group during the three-year period (Fig. 2). The same was true for endothelial cell density. Nevertheless, we noted an interesting trend in Group 2: cell density slightly decreased in the first month, which was not observed after six months of lens use (Fig. 3).

Cell density decreased in Group 1 by 1.62% after one year, by 0.85% after two years and by 6.43% after three years ($p = 0.25$; 0.26; 0.59). This contrasts the cell density found in Group 2, which increased slightly in the first two years (0.78% after one year and 0.46% after two years) but decreased by 3.7% after three years ($p = 0.28$; 0.06; 0.93). There was a significant difference in the ages of the two groups (the average age was 25.3 years in Group 1 and 19.89 years in Group 2; $p = 0.024$). However, cell densities were not significantly different at baseline (2554.76 cells/mm^2 and 2629.27 cells/mm^2, respectively; $p = 0.17$). Cell size (Fig. 4) and

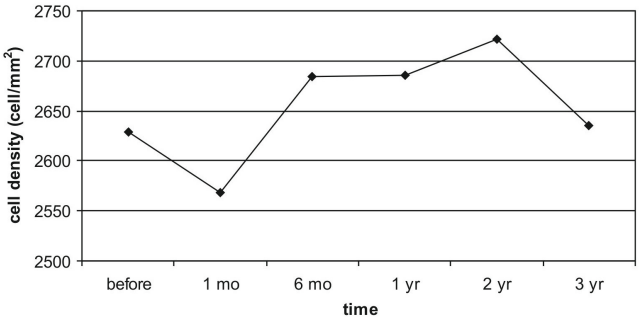


Fig. 3. The fluctuation of cell density in Group 2. The cell density slightly decreased in the first month. However, this phenomenon did not persist after 6 months.

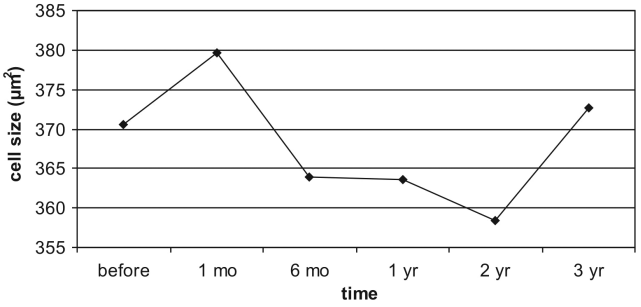


Fig. 4. The fluctuation of cell size in Group 2. Cell size changes are not synchronized with cell density changes because they are reversely interdependent.

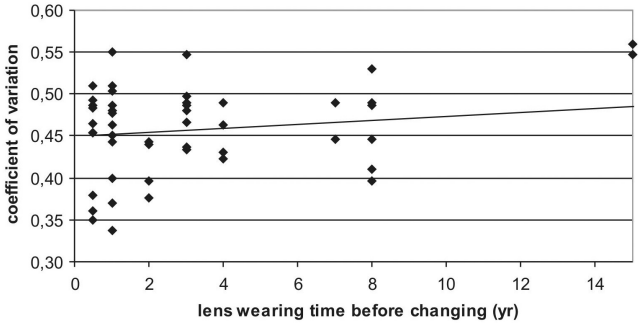


Fig. 6. The correlation between the lens wearing time and the coefficient of variation in Group 1, direct proportion ($r = 0.28$; $p = 0.045$).

cell density are interdependent variables. In a given field, cell density is higher when the cells are smaller and vice versa.

In this study, there was a correlation between the coefficient of variation and the time of lens wear. In Group 1, the coefficient of variation decreased significantly after six months compared to baseline values (the baseline coefficient of variation was 0.47, whereas, after six months, it was 0.44; $p = 0.049$). In Group 2, there was no significant change.

The percentage of hexagonal cells increased significantly after one month in Group 2 (before the lenses were worn, it was 27.78%, whereas, after one month, it was 28.25%; $p = 0.025$). In Group 1, there was no significant change.

In Group 1, we observed and documented the regression of limbal hyperaemia and neovascularization in the subjects during lotrafilcon B lens wear (Figs. 1(a) and 1(b)). Age is known to be inversely proportional to cell density. This outcome was also observed in this study because cell density decreased with the progression of age (but without statistical significant level) ($r = -0.43$; $p = 0.094$; Fig. 5).

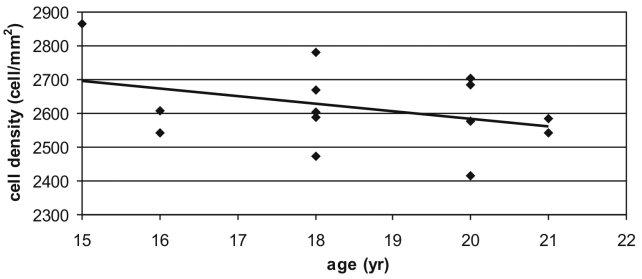


Fig. 5. The correlation between age and cell density in the two groups, inverse proportion ($r = -0.43$; $p = 0.094$).

This study also found that the lens wearing time was directly proportional to the coefficient of variation ($r = 0.28$; $p = 0.045$; Fig. 6).

The first correlation was examined in Group 2 using parameters that were obtained prior to the lenses being worn. This was to eliminate the influence of any previous contact lens usage on cell density. The second correlation was investigated in Group 1 using data that were obtained before the subjects were fitted with lotrafilcon B lenses. The parameters of the corneal physiology in Group 1 and Group 2 are in Tables 1 and 2.

6. Discussion

Our investigation found that wearing lenses with low oxygen permeability (called conventional hydrogel lenses) generated irreversible damage to the corneal endothelium (a comparison of the baseline values of the nonlens wearing vs lens-wearing groups). Furthermore, it showed that not even high Dk/t lotrafilcon B contact lenses were able to stop the consequential increase in cell destruction. The decrease observed in cell density in Group 1 exceeded 0.56%, which is the mean annual decrease that has been reported.[3] The fact that neither of the examined parameters significantly decreased in Group 2 suggests that lotrafilcon B provides the cornea with enough oxygen over the three-year period.

By comparing changes in cell density to age and examining the correlation between the coefficient of variation and lens wearing time, we came to the same conclusions as Sheng and Bullimore. Their research found that age is inversely proportional to cell density and that years of contact lens wear is directly proportional to the coefficient of variation.[5]

The two groups in our study is not age-matched, it is matching at the beginning age of lens wearing. This fact could be a limitation factor and therefore further researches are needed to understand the effects of second generation lotrafilcon B SiH lenses on the cornea.

The coefficient of variation of the endothelial cells is a measure of the diversity in cell size. A lower coefficient of variation is considered to be better because it indicates that the cells are more similar to one another. Healthy eyes are known to possess more similar, regular shapes. The coefficient of variation is lower when, for the same or a slightly smaller mean, the standard deviation becomes smaller (which is likely to be the case for the corneal endothelium). Additionally, it is lower when, for the same or a slightly increased standard deviation, the mean becomes larger or when they both change for the better (for example, a relatively lower standard deviation and a corresponding smaller change in the mean).

The present study investigated the central region of the cornea. This is important because, according to Amann *et al.* the cornea has a larger endothelial cell density in the paracentral and peripheral regions, in comparison to that in the central region.[6] However, this difference cannot be seen in contact lens wearers. This suggests that contact lens wear may cause a mild redistribution of the endothelial cells from the center to the periphery of the cornea.[7]

Only a few published studies have examined lotrafilcon B contact lenses.[8,9] Our results support the outcomes of these papers. The daily wear of lotrafilcon B lenses improved corneal signs and health (conjunctival and limbal redness, corneal neovascularization, corneal oedema, corneal and conjunctival staining, etc.) and subjects' symptoms (uncomfortable lens wear, redness, dryness, irritation, blurred vision, etc.). The half of the subjects in Group 2 had mild irritation in the first two to four weeks but not thereafter. This feeling of discomfort is incredibly common among new lens wearers. It develops at the beginning stages of wearing lenses of all types and decreases after a period of adaptation.[10]

Additionally, it provided excellent vision and comfort. Subjects preferred these new lenses over their habitual lenses.

Silicone hydrogel contact lenses provided enough oxygen for the cornea. Thus, they protect the cornea from the hypoxia caused changes.[11–14] Furthermore, Santos *et al.* have proven that SiH contact lenses are generally less susceptible to microbial adhesion, in comparison to conventional hydrogels. This feature facilitates better lens resistance to bacteria.[15] According to a study by Lira *et al.* SiH contact lenses are less susceptible to damage over time, resulting in sustained biocompatibility for longer periods of time. This contributes to the clinical success of this type of lens.[16]

The Gothenburg study has demonstrated that prolonged wearing of low Dk/t contact lenses disturbs the metabolism of the epithelium, decreases the oxygen absorption of the eye and thin the epithelium.[17] Jalbert *et al.* have recently shown that this effect can be significantly reduced via the use of SiH contact lenses.[18]

Dumbleton *et al.* refitted successful soft lens wearers with other high Dk/t SiH contact lenses. They then evaluated the objective and subjective responses of subjects. Their results demonstrate that bulbar and limbal hyperaemia significantly decreased in all quadrants. This was also observed in the subjects of our study. In addition, dryness diminished and the end-of-day comfort improved.[19] Doughty *et al.* experienced improvement in the mean bulbar and limbal redness after six months of SiH lens usage.[11] Consequently, high oxygen availability ensured better comfort for the wearer and in this investigation lotrafilcon B, supports the physiological metabolism and functions of the cornea by improving oxygen provision. Thus, it can be argued that contact lens wear does not provoke corneal damage.

A state of hipoxia is caused by the prolonged wearing of older hydrogel low Dk/t contact lenses.[17,20] Nearly all contact lens wearers report instances when they do not remove their contact lenses before sleeping ("closed-eye contact lens wear"). At such times, tear flow stops between the contact lens and the anterior surface of the cornea, which, in just a few minutes, induces metabolic changes in the micro-environment of the corneal epithelium.[21] After some minutes, both the stroma and the endothelial cells automatically undergo anaerobic glycolysis. The consequence of this is corneal swelling. A short-term disorder of the metabolism does not lead to irreversible deviations in the structure of the cornea. However, prolonged, frequent hypoxia results in secondary morphological changes in the epithelium, stroma and endothelium

Table 1. The results from Group 1: parameters of the corneal physiology (corneal thickness and endothelial morphology).

	Before changing lenses	After one month	After six months	After one year	After two years	After three years
Corneal thickness (μm)	0.53	0.53	0.63	0.53	0.53	0.54
p-value		0.92	0.13	0.62	0.91	0.93
Cell density (cell/mm^2)	2554.76	2542.2	2540.4	2491	2630.4	2515.7
p-value		0.76	0.80	0.25	0.26	0.59
Cell size (μm^2)	383.6	384.13	388.41	383.28	369.47	388.07
p-value		0.92	0.53	0.97	0.13	0.65
Coefficient of variation	0.47	0.45	0.44	0.46	0.43	0.45
p-value		0.12	**0.049**	0.91	0.06	0.46
Hexagonal frequency (%)	28.99	28.29	27.89	27.25	31.44	27.63
p-value		0.51	0.45	0.23	0.16	0.46

Table 2. The results from Group 2: parameters of the corneal physiology (corneal thickness and endothelial morphology).

	Before wearing lenses	After one month	After six months	After one year	After two years	After three years
Corneal thickness (μm)	0.54	0.54	0.55	0.56	0.55	0.57
p-value		0.71	0.62	0.35	0.63	0.16
Cell density (cell/mm^2)	2629.27	2568.9	2684.9	2685.5	2722.2	2635.5
p-value		0.17	0.25	0.28	0.06	0.93
Cell size (μm^2)	370.5	379.71	363.97	363.67	358.33	372.75
p-value		0.12	0.27	0.31	0.06	0.81
Coefficient of variation	0.43	0.44	0.39	0.41	0.40	0.41
p-value		0.85	0.07	0.41	0.19	0.63
Hexagonal frequency (%)	27.78	28.25	23.23	30.67	32.04	29.5
p-value		**0.025**	0.82	0.73	0.56	0.34

that are only minimally reversible. Oxygen deprivation has been associated with the appearance of microcysts in the epithelium, epithelial thinning, slowed mitosis, the loss of hemidesmosomes, reduced epithelial oxygen consumption and an increased superficial cell size in the epithelium. Stromal changes include a chronic loss of glycosaminoglycans and thinning and the endothelium shows signs of increased polymegethism.[22] Furthermore, conjunctival hyperaemia, corneal neovascularization, corneal oedema, corneal staining, myopic shift and a decreased resistance against microbial keratitis develop due to oxygen deprivation.[17,23,24] These effects lead to subjective symptoms, including a decreased or fluctuant visual acuity, blurred vision, seeing a rainbow circle around lights, dryness and lens awareness. Schafer *et al.* examined the stability of dryness symptoms after refitting subjects with high-Dk/t SiH contact lenses. According to their results, during-the-day and end-of-day dryness symptoms significantly improved during the first week after refitting with lotrafilcon B lenses and remained stable for three years. The presence of dryness symptoms after one week was associated with the discontinuation of contact lens wear.[25]

Hypoxia that affects the periphery of the cornea is an even more important problem than hypoxia of the central cornea. This is because the limbus is the only source of epithelial stem cells that ensure unlimited new epithelial cells and fast regeneration after surface damage. Any stem cell deprivation or damage consequently results in recurrent erosion, chronic keratitis or vascularization.[26]

Conflicts of Interest

None of the authors has any potential financial conflict of interest related to this manuscript.

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References

1. E. Papas, "On the relationship between soft contact lens oxygen transmissibility and induced limbal hyperemia," *Exp. Eye Res.* **67**, 125–131 (1998).
2. E. Papas, "The significance of oxygen during contact lens wear," *Cont. Lens Anterior Eye* **37**, 394–404 (2014).
3. S. Mishima, "Clinical investigations on the corneal endothelium-XXXVIII Edward Jackson Memorial Lecture," *Am. J. Ophthalmol.* **93**, 1–29 (1982).
4. G. Iskeleli, Y. Karakoc, A. Ozkok, C. Arici, O. Ozcan, O. Ipcioglu, "Comparison of the effects of first and second generation silicone hydrogel contact lens wear on tear film osmolarity," *Int. J. Ophthalmol.* **18**, 666–70 (2013).
5. H. Sheng, M. A. Bullimore, "Factors affecting corneal endothelial morphology," *Cornea* **26**, 520–525 (2007).
6. J. Amann, G. P. Holley, S. B. Lee, H. F. Edelhauser, "Increased endothelial cell density in the paracentral and peripheral regions of the human cornea," *Am. J. Ophthalmol.* **135**, 584–590 (2003).
7. S. J. Wiffen, D. O. Hodge, W. M. Bourne, "The effect of contact lens wear on the central and peripheral corneal endothelium," *Cornea* **19**, 47–51 (2000).
8. S. M. Dillehay, M. B. Miller, "Performance of Lotrafilcon B silicone hydrogel contact lenses in experienced low-Dk/t daily lens wearers," *Eye Cont. Lens* **33**, 272–277 (2007).
9. R. Chalmers, B. Long, S. Dillehay, C. Begley, "Improving contact-lens related dryness symptoms with silicone hydrogel lenses," *Optom. Vis Sci.* **85**, 778–784 (2008).
10. J. S. Wolffsohn, S. A. Naroo, C. Christie, J. Morris, R. Conway, C. Maldonado-Codina, N. Retalic, C. Purslow, British Universities Committee of Contact Lens Educators (BUCCLE), "History and symptom taking in contact lens fitting and aftercare," *Cont. Lens Ant. Eye* March 25. pii: S1367–0484(15)00040-5. doi: 10.1016/j.clae.2015.03.02. [Epub ahead of print] (2015).
11. P. Bergenske, B. Long, S. Dillehay, J. T. Barr, P. Donshik, G. Secor, J. Yoakum, R. L. Chalmers, "Long-term clinical results: 3 years of up to 30-night continuous wear of lotrafilcon A silicone hydrogel and daily wear of low-Dk/t hydrogel lenses," *Eye Cont. Lens* **33**, 74–80 (2007).
12. M. J. Doughty, B. M. Aakre, A. E. Ystenaes, E. Svarverud, "Short-term adaptation of the human corneal endothelium to continuous wear of silicone hydrogel (lotrafilcon A) contact lenses after daily hydrogel lens wear," *Optom. Vis. Sci.* **82**, 473–480 (2005).
13. D. Fonn, K. E. MacDonald, D. Richter, N. Pritchard, "The ocular response to extended wear of a high Dk silicone hydrogel contact lens," *Clin. Exp. Optom.* **85**, 176–182 (2002).
14. N. A. Brennan, M. L. Coles, T. L. Comstock, B. Levy, "A 1-year prospective clinical trial of balafilcon a (PureVision) silicone-hydrogel contact lenses used on a 30-day continuous wear schedule," *Ophthalmol.* **109**, 1172–1177 (2002).
15. L. Santos, D. Rodrigues, M. Lira, M. E. Real Oliveira, R. Oliveira, E. Z. Vilar, J. Azeredo, "Bacterial adhesion to worn silicone hydrogel contact lenses," *Optom. Vis. Sci.* **85**, 520–525 (2008).
16. M. Lira, L. Santos, J. Azeredo, E. Yebra-Pimentel, M. E. Real Oliveira, "The effect of lens wear on refractive index of conventional hydrogel and silicone-hydrogel contact lenses: A comparative study," *Cont. Lens Ant. Eye* **31**, 89–94 (2008).
17. B. A. Holden, D. F. Sweeney, A. Vannas, K. T. Nilsson, N. Efron, "Effects of long-term extended contact lens wear on the human cornea," *Invest Ophthalmol. Vis. Sci.* **26**, 1489–1501 (1985).
18. I. Jalbert, D. F. Sweeney, F. Stapleton, "The effect of long-term wear of soft lenses of low and high oxygen transmissibility on the corneal epithelium," *Eye* **23**, 1282–1287 (2009).
19. K. Dumbleton, N. Keir, A. Moezzi, Y. Feng, L. Jones, D. Fonn, "Objective and subjective responses in patients refitted to daily-wear silicone hydrogel contact lenses," *Optom. Vis. Sci.* **83**, 758–768 (2006).
20. M. T. Odenthal, I. M. Gan, J. Oosting, A. Kijlstra, W. H. Beekhuis, "Long-term changes in corneal endothelial morphology after discontinuation of low gas-permeable contact lens wear," *Cornea* **24**, 32–38 (2005).
21. J. J. Nichols, P. E. King-Smith, "The effect of eye closure on the post-lens tear film thickness during silicone hydrogel contact lens wear," *Cornea* **22**, 539–544 (2003).

22. D. F. Sweeney, "Clinical signs of hypoxia with high-Dk soft lens extended wear: Is the cornea convinced?," *Eye Cont. Lens* **29**, S22–S25; discussion S6–S9, S192–S194 (2003).
23. C. G. Connor, M. E. Zagrod, "Contact lens-induced corneal endothelial polymegathism: Functional significance and possible mechanisms," *Am. J. Optomol. Physiol. Opt.* **63**, 539–544 (1986).
24. F. Stapleton, L. Keay, K. Edwards, T. Naduvilath, J. K. Dart, G. Brian, B. A. Holden, "The incidence of contact lens-related microbial keratitis in Australia," *Ophthalmol.* **115**, 1655–1662 (2008).
25. J. Schafer, G. L. Mitchell, R. L. Chalmers, B. Long, S. Dillehay, J. Barr, P. Bergenske, P. Donshik, G. Secor, J. Yoakum, "The stability of dryness symptoms after refitting with silicone hydrogel contact lenses over 3 years," *Eye Cont. Lens* **33**, 247–252 (2007).
26. F. Stapleton, S. Stretton, E. Papas, C. Skotnitsky, D. F. Sweeney, "Silicone hydrogel contact lenses and the ocular surface," *Ocul. Surf.* **4**, 24–43 (2006).