

Role of the Water Gradient Structure in Inhibiting Thin Aqueous Layer Break in Silicone Hydrogel-Soft Contact Lens

Hisataka Fujimoto¹, Shintaro Ochi², Tsutomu Yamashita³, Yasushi Inoue², and Junichi Kiryu¹

¹ Department of Ophthalmology, Kawasaki Medical School, Kurashiki, Okayama, Japan

² Inoue Eye Clinic, Tamano, Okayama, Japan

³ Kawasaki University of Medical Welfare, Kurashiki, Okayama, Japan

Correspondence: Hisataka Fujimoto, Department of Ophthalmology, Kawasaki Medical School, 577 Matsushima, Kurashiki, 701-0192 Okayama, Japan. e-mail: fujimoto-h@med.kawasaki-m.ac.jp

Received: June 7, 2021

Accepted: August 10, 2021

Published: September 2, 2021

Keywords: water gradient, structure; silicone hydrogel-soft contact lens; thin aqueous layer break; tear film; contact lenses

Citation: Fujimoto H, Ochi S, Yamashita T, Inoue Y, Kiryu J. Role of the water gradient structure in inhibiting thin aqueous layer break in silicone hydrogel-soft contact lens. *Transl Vis Sci Technol.* 2021;10(11):5. <https://doi.org/10.1167/tvst.10.11.5>

Purpose: Soft contact lenses (SCLs) are effective for refractive error correction, but prolonged wear triggers discomfort and discontinuation. This study investigates whether water gradient technology of delefilcon A-based SCLs improve tear film dynamics.

Methods: This retrospective observational study included 50 asymptomatic delefilcon A or narafilcon A users. Data on thin aqueous layer break (TALB; %), noninvasive tear break-up time (NIBUT), tear meniscus height (TMH; mm), subjective dryness, and higher-order aberrations (HOAs) were collected. Measurements of the bare eye, the SCL-worn eye after 15 minutes (visit 1 [v1]) and 30 ± 5 days after v1 after SCL was worn for ≥5 hours (visit 2 [v2]) were recorded.

Results: TALB was significantly reduced in the delefilcon A group compared to the narafilcon A group (33.3% vs. 85.5% at v1; $P < 0.0001$ and 31.7% vs. 80.4% at v2; $P < 0.0001$). The NIBUT was also significantly higher in the former (4.2 ± 2.1 seconds vs. 2.9 ± 1.5 at v1; $P < 0.01$ and 4.1 ± 2.3 seconds vs. 2.7 ± 1.6 seconds at v2; $P < 0.01$) across both visits. The TMH was significantly reduced in the former in both v1 and v2. The total ocular HOAs were significantly lower in the former at v1 ($P < 0.001$) and v2 ($P < 0.05$) compared to the bare eye.

Conclusions: The water gradient technology of delefilcon A reduces TALB and increases NIBUT.

Translational Relevance: The use of water gradient technology improves tear film dynamics and alleviate pathological break-up pattern, improving lens performance.

Introduction

Advances in the field of corneal physiology have extensively improved the material, design, and production of soft contact lenses (SCLs), making them one of the safest and most sought after and effective interventions for refractive error correction.¹ However, continuous and extended SCL wear has been associated with side effects and undue stress to the corneal physiology mainly due to oxygen shortage,² corneal neovascularization,³ and endothelial damage.¹

Silicone hydrogel (SH) SCLs were developed about 2 decades ago to counter the caveats associated with

SCLs and conventional hydrogel lenses.^{4,5} The interaction of the mobile silicon-oxygen bonds imparts distinct surface and mechanical properties to the SHs, enhancing oxygen permeability, reducing protein deposition and modest frictional interaction, and causing increased lipid and elastic response.⁶ Studies have also established that SH lenses reduce the level of limbal redness,⁷ alleviate contact lens-associated keratitis,⁸ and enhance the supply of oxygen to the ocular surface over their conventional hydrogel counterparts.⁹ Despite these advantages, symptoms associated with contact lens discomfort (CLD) persist.¹⁰ SCLs (both conventional and SH) wear alters the lipid layer by reducing the pre-lens lipid layer thickness; increasing

tear evaporation rate; reducing tear break-up time; and altering the concentration of cholesterol esters, wax esters, and phospholipids.¹¹

The tear film kinetics of SCL are governed by features such as a shorter break-up time, decreased contact lens surface coverage by the tear film during the overall interblink period, and greater contact lens surface exposure to the atmosphere at the time of the blink.¹² The two key factors that cause CLD were reported to be the contact lens material and environment.¹⁰ Specifically, the factors associated with the lens material include lubricity and water content.

Dailies Total1 (DT1; delefilcon A) was developed as a water gradient SH-SCL whose lens surface has distinct properties designed to minimize surface problems associated with the SH-SCLs. It has a core silicone hydrogel material comprising 33% water that can transit to the outer surface layer with 80% water. The surface has a low compression modulus and a unique water gradient technology that ensures that the surface is lubricated along with continual high oxygen transmission.¹³ The present study investigates whether the water gradient structure of SH-SCL, delefilcon A, contributes to improving the tear film dynamics including break-up patterns, noninvasive tear break-up times (NIBUT), tear meniscus height (TMH), and other end points such as higher-order aberrations (HOAs), subjective dryness, and SCL thickness, compared to the conventional SH-SCLs, narafilcon A.

Materials and Methods

Study Design

This retrospective observational study included 50 regular SH-SCL asymptomatic users. The study was approved by the institutional review board of Kawasaki Medical School Hospital (approval number 3403). Informed consent was obtained from all the study participants, and the study adhered to the tenets of the Declaration of Helsinki and was performed according to Good Clinical Practice (GCP). The study end points were evaluated by the researchers in a masked manner. The identity of the sponsor of the study (Alcon) was masked to the assessors until the completion of the study. This study did not involve patients or the public in its design, participant recruitment, or conduct.

Data Collection

The study observation period was defined as the date from which the patient started receiving care at

the study site until the last data point was measured and was between May 1, 2019, and February 29, 2020. To ensure uniform data collection, assessment, and compliance with GCP, onsite training was conducted. The patient data records were selected based on the study inclusion and exclusion criteria and the patients receiving care between May 1, 2019, and February 29, 2020, were included in the study. To minimize bias, the eligible patients were enrolled in one of the two study groups (delefilcon A and narafilcon A) allotted in a consecutive series. Delefilcon A lenses are SH-SCLs with a water gradient structure and high lubricity surface.^{14,15} The core has a low water content of 33%, similar to other conventional SH-SCLs.¹⁶ To compare delefilcon A with conventional SH-SCLs, we chose narafilcon A as the control lens, because its core also has a low water content of 46%.¹⁷ Both are daily disposable SH-SCLs.¹⁸ The water content of narafilcon A is constant throughout the lens, whereas water gradient technology of delefilcon A creates a low water content core with a high water content surface.¹⁷ Numerous previous studies of delefilcon A have also compared it with narafilcon A.^{19–22}

The background data included age, gender, power (diopter), Schirmer's test (mm), central corneal thickness (CCT; μm), ophthalmic solution use, and the following data elements measured on the bare eye, namely TALB (%), NIBUT (seconds) by the tear interferometer DR-1 α (Kowa, Tokyo, Japan), and video-corneal topographer Keratograph 5M (Oculus, Wetzlar, Germany), TMH (mm), subjective dryness estimated by the visual analog scale (VAS; minimum 0 and maximum 100), and ocular HOA. The post-baseline data were categorized as visit-1 (v1) and visit-2 (v2) for each patient based on the chronology of availability. For data based on the qualification tests, bare eye measurements, the time that SCLs were worn to the hospital, removed, and washed-out was set as ≥ 30 minutes. Data were collected for clinical v1 after tests and observation parameters were measured post-SCL wearing for 15 minutes. For clinical v2, data from tests and observation parameters measured after wearing SCLs for ≥ 5 hours, after 30 ± 5 days of wearing SCLs following v1, were collected. Between v1 and v2, SCLs were used 5 to 12 hours per day, and 5 to 7 days per week. Room temperature and humidity was maintained at 23 to 25°C and 30 to 40%.

Using the tear interferometer DR-1 α (Kowa, Tokyo, Japan), the break up pattern with SCLs was classified into six patterns consist of area break (AB), line break (LB), thin aqueous layer break (TALB), spot break (SB), dimple break (DB), and random break (RB), as previously reported by Yokoi et al.^{23,24} For these break-up pattern, the three videos captured using the

DR-1 α were judged in a masked manner. A total of nine judgments comprising three videos by three researchers per one eye were used, and the majority of the break-up patterns were adopted. From the previous reports,^{23–25} AB is observed when there is no aqueous tear on the SCL surface; LB, when streak line shape near the lower SCL because of aqueous tear deficient and suction effect on the aqueous tear from the lower tear meniscus; TALB, when colorful interference fringes immediately after eye opening when there is no lipid layer on the SCL surface due to thin aqueous tear; SB, when the wettability of the SCL surface is decreased and observed spot shape; DB, when streak line shape around the central SCL because of impaired wettability of the SCL surface; and RB, after the complete establishment of tear film and the result of evaporation of aqueous tear. For instance, AB, LB, and TALB were defined as aqueous deficient types. SB and DB were defined as decreased wettability types. RB was defined as increased evaporation type.

For the NIBUT, the three videos captured using the tear interferometer DR-1 α were analyzed in a masked manner, and the three break-up times were averaged.

TMH, CCT, and SCL thickness were obtained using anterior segment optical coherence tomography (AS-OCT) CASIA 2 (Tomey Corporation, Nagoya, Japan). The analysis software (Tomey Corporation) identified and digitized the anterior corneal or SCL surfaces and posterior corneal surfaces as well as tear meniscus areas. All of the digitization were confirmed by researches in a masked manner. For TMH and CCT, the three measurement values were averaged. SCL thickness were calculated as CCT wearing SCL – CCT without SCL.

Ocular HOAs measured were total HOA, coma, trefoil, spherical, tetrafoil, and second order astigmatism aberrations through a 6 mm pupil using a Shack—Hartmann wavefront sensor in the KR-1W Wavefront Analyzer (TOPCON, Tokyo, Japan). The HOA values (RMS; in μm) measured every 1 to 10 seconds after each blink were averaged.

All the data from the measurements done on bilateral eyes were collected.

Study Participants and Visits

Participants

A retrospective review of the clinical records (including video records), of 50 SH-SCL users was conducted for the potential participants who were able to achieve a clinically acceptable fit with each of the study lenses. Asymptomatic participants who were ≥ 20 years of age with far corrected vision of ≥ 0.8 in both eyes, those wearing contact lenses at least 5 days

a week for greater than 5 hours a day, and regular users of Dailies Total 1 (DT1); Alcon (delefilcon A) or 1-Day Acuvue TruEye (TE); Johnson & Johnson Vision (narafilecon A) lenses were included from one site (Inoue eye clinic) in Japan.

Contact lens wearers without active ocular surface disorders, such as epithelial disorders, infections, conjunctivitis, ocular inflammatory disease, and nasolacrimal duct obstruction were selected. As an exception, those with a dry eye with a short break-up time were included in the study because such symptoms are often evident in contact lens users and hold clinical significance capable of being targeted effectively with delefilcon A. Those individuals with a history of ocular surface surgery or those who were considered unsuitable by the principal investigator were excluded from the study. To minimize the intervention in this retrospective study, subjects were enrolled as delefilcon A or narafilecon A habitual users. The 50 SH-SCL users consisted of a consecutive series of 25 delefilcon A habitual users and 25 narafilecon A habitual users who met the above criteria.

Statistical Analysis

The study was designed to assess the difference between delefilcon A and narafilecon A groups in terms of tear film dynamics. The sample size was planned for examining the null hypothesis of no difference between the two groups (delefilcon A/narafilecon A) with the specified probability. The data distributions were assessed for normality using the Shapiro-Wilk test. Following the assumption that all the data on the outcomes of interest followed a parametric distribution, the two-sample independent *t*-test was used to analyze the data, except for the male/female ratio, ophthalmic solution use ratio, and TALB ratio. Additionally, the paired *t*-test with Bonferroni correction were performed to compare the HOAs among bare eyes, v1, and v2. For the male/female ratio, ophthalmic solution use, and TALB ratio, Pearson's chi-squared test was used. All the statistical analyses were performed using the SPSS version 25.0 (IBM Corp. Released 2017; IBM SPSS Statistics for Windows, Version 25.0; Armonk, NY: IBM Corp. USA).

Results

Enrollment

In this study, a total of 50 patient records were reviewed and 100 eyes of 50 regular SH-SCL users were enrolled into 2 groups. These were 25 regular users

(50 eyes) of delefilcon A-based DT1, and 29 regular users (58 eyes) of narafilecon A-based TE. In the 29 narafilecon A participants, 4 participants (8 eyes) also used delefilcon A and were included in the delefilcon A group. For those 4 participants that used both lenses, the v1 and v2 measurements were recorded for an additional day after 60 days, compared to the measurements for the individuals using only either delefilcon A and narafilecon A.

The study of three patients who never appeared for the v2 was discontinued after v1. The three patients included two participants from the delefilcon A group and one participant from the narafilecon A group. There were no reports of discontinuation due to adverse events.

Demographics

The study comprised a total of 10 male subjects and 40 female subjects with an average age of 34.59 ± 9.95 years and 32.47 ± 8.66 years for the delefilcon A and narafilecon A groups, respectively. There were no significant differences between the study groups in the baseline parameters (Table 1), and studied parameters in bare eye (Table 2). No ophthalmic solution was used other than artificial tears or anti-allergic eye drops.

Abnormal Break-Up Patterns: Thin Aqueous Layer Break

Among the abnormal break-up patterns assessed at v1 and v2, there was a significantly lower rate of TALB in the delefilcon A compared to the narafilecon A ($P < 0.0001$; Fig. 1, Supplementary Video 1). At v1 after 15 minutes of SCL wear, the TALB was 33.3% and 88.5% in the delefilcon A group and narafilecon A

group, respectively. At v2 after ≥ 5 hours of SCL wear, the TALB was 31.7% and 80.4% in the delefilcon A group and narafilecon A group, respectively.

NIBUT

There was a significant difference in NIBUT measured with DR-1 α , between the two study groups. At v1, the mean NIBUT in the delefilcon A group and narafilecon A group was 4.2 ± 2.2 seconds and 3.0 ± 1.6 seconds, respectively. At v2, the mean NIBUT in the delefilcon A group and narafilecon A group was 4.1 ± 2.4 seconds and 2.7 ± 1.6 seconds, respectively.

The NIBUT was significantly higher in the delefilcon A group than in the narafilecon A group ($P = 0.0016$ at v1, and $P = 0.0017$ at v2; Table 2, Fig. 2). The NIBUTs measured with the Keratograph 5M while wearing the SCLs showed no significant difference across groups.

TMH

At baseline, when measured on a bare eye, the mean TMH was 0.27 ± 0.07 mm and 0.25 ± 0.07 mm in the delefilcon A and narafilecon A groups, respectively. After SCL wear at v1 and v2, there was a decrease in TMH in both delefilcon A and narafilecon A groups. TMH was found to be significantly lower in the delefilcon A group at both v1 and v2 than in the narafilecon A group ($P = 0.002$ and $P = 0.019$, respectively; Fig. 3).

Subjective Dryness

The mean subjective dryness score measured on the bare eye through a VAS was 49.6 ± 23.1 and 53.8 ± 23.1

Table 1. Comparison of the Background Data Between the Two SH-SCLs

	Narafilecon A (in Narafilecon A) Average \pm SD	Delefilcon A (in Delefilcon A) Average \pm SD	P Value Delefilcon A vs. Narafilecon A
CCT (μ m)	533.7 ± 32.2	530.7 ± 31.2	0.32
Power (diopter)	-3.71 ± 1.47	-3.30 ± 1.50	0.17
Schilmer' test (mm)	20.7 ± 2.8	17.5 ± 0.9	0.20
Age (years)	32.47 ± 8.66	34.59 ± 9.95	0.42
Female ratio	0.83	0.70	0.28 ^a
Artificial tears use	20.7% (6/29)	40.0% (10/25)	0.12 ^a
Anti-allergic use	3.5% (1/29)	12.0% (3/25)	0.23 ^a

The data are expressed as mean \pm standard deviation.

^aP values were calculated using two-sample independent *t*-test in all instances except for Female ratio and ophthalmic solution use ratio where the Pearson chi-squared test was used.

CCT, central corneal thickness; SD, standard deviation; SH-SCL, silicone hydrogel-soft contact lens.

Table 2. Comparison of the End Points Between the Two SH-SCLs

	Narafilcon A (in Narafilcon A) (Average ± SD)	Delefilcon A (in Delefilcon A) (Average ± SD)	P Value Delefilcon A vs. Narafilcon A
Bare eye:			
NIBUT (DR-1α) (in seconds)	6.9 ± 2.9	6.7 ± 3.2	0.71
TMH (mm)	0.25 ± 0.07	0.27 ± 0.07	0.20
Subjective dryness (VAS score)	53.8 ± 23.1	49.6 ± 23.1	0.36
NIBUT (in seconds) (Keratograph 5M)	7.3 ± 3.1	7.6 ± 3.6	0.60
TALB (%)	0	0	1 ^a
HOA (RMS; in μm)	0.39 ± 0.13	0.39 ± 0.18	0.95
Visit 1 (v1):			
NIBUT (DR-1α) (in seconds)	3.0 ± 1.6	4.2 ± 2.2	0.0016
TMH (mm)	0.24 ± 0.07	0.19 ± 0.06	0.002
Subjective dryness (VAS score)	16.4 ± 16.4	19.6 ± 18.6	0.37
NIBUT (in seconds) (Keratograph 5M)	6.3 ± 2.9	7.1 ± 2.7	0.13
TALB (%)	88.5	33.3	<0.0001 ^a
SCL thickness (μm)	94.1 ± 6.7	106.4 ± 11.5	<0.0001
HOA (RMS; in μm)	0.40 ± 0.16	0.34 ± 0.15	0.18
Visit 2 (v2):			
NIBUT (in seconds) (DR-1α)	2.7 ± 1.6	4.1 ± 2.4	0.0017
TMH (mm)	0.22 ± 0.08	0.18 ± 0.05	0.019
Subjective dryness (VAS score)	26.7 ± 21.6	23.0 ± 17.0	0.35
NIBUT (in seconds) (Keratograph 5M)	6.8 ± 3.6	6.3 ± 2.7	0.49
TALB (%)	80.4	31.7	<0.0001 ^a
SCL thickness (μm)	93.5 ± 7.0	103.0 ± 8.8	<0.0001
SCL thickness ratio (v2/v1)	0.994 ± 0.082	0.977 ± 0.077	0.28
HOA (RMS; in μm)	0.40 ± 0.14	0.35 ± 0.13	0.14
CLDEQ-8 questionnaire score in v2:			
1-a discomfort: frequency	1.15 ± 0.81	1.14 ± 0.84	0.98
1-b discomfort: severity	1.33 ± 1.23	1.43 ± 1.31	0.72
2-a dryness: frequency	1.30 ± 0.60	1.24 ± 0.93	0.73
2-b dryness: severity	1.48 ± 1.08	1.71 ± 1.37	0.37
3-a blurry vision: frequency	0.85 ± 0.90	0.76 ± 0.62	0.56
3-b blurry vision: severity	0.81 ± 0.99	0.95 ± 1.10	0.53
4 The need for closing eyes	0.52 ± 0.79	0.81 ± 0.92	0.11
5 The need for removing the lenses	1.44 ± 1.00	1.33 ± 1.22	0.63

The data are expressed as mean ± standard deviation.

^aP values were calculated using two-sample independent t-test in all instances except for TALB (%) where the Pearson chi-squared test was used. Compared with narafilcon A, there were significant changes in TALB, NIBUT, TMH in delefilcon A.

CLDEQ-8, contact lens dry eye questionnaire-8; HOA, higher-order aberration; NIBUT, non-invasive tear break-up time; SD, standard deviation; SH-SCL, silicone hydrogel-soft contact lens; TALB, thin aqueous layer break; TMH, tear meniscus height; VAS, subjective dryness estimated by the visual analog scale.

in the delefilcon A and narafilcon A groups, respectively.

At v1 and v2, there was a decrease in subjective dryness scores in the delefilcon A group (19.6 ± 18.6 and 23.0 ± 17.0, respectively) and in the narafilcon A group (16.4 ± 16.4 and 26.7 ± 21.6) from the baseline.

No significant difference in the VAS scores on subjective dryness was observed between the delefilcon A and narafilcon A groups across both visits. No differences were observed between the study groups when the CLDEQ-8 questionnaire was administered at v2.

Total Ocular HOAs

When measured one second after eye blink on the bare eye, the total ocular HOAs (RMS; in μm) in the delefilcon A group were 0.39 ± 0.18 at baseline and significantly decreased to 0.34 ± 0.15 at v1 and to 0.35 ± 0.13 at v2 ($P = 0.0003$ at v1 and $P = 0.038$ at v2). In the narafilcon, A group, the bare eye HOAs were 0.39 ± 0.13, and there was no significant difference observed in HOAs at visits v1 and v2 compared to the bare eye (Fig. 4, Table 3). The total ocular HOAs, 2 seconds after the blink did not significantly ($P \geq 0.05$) differ from

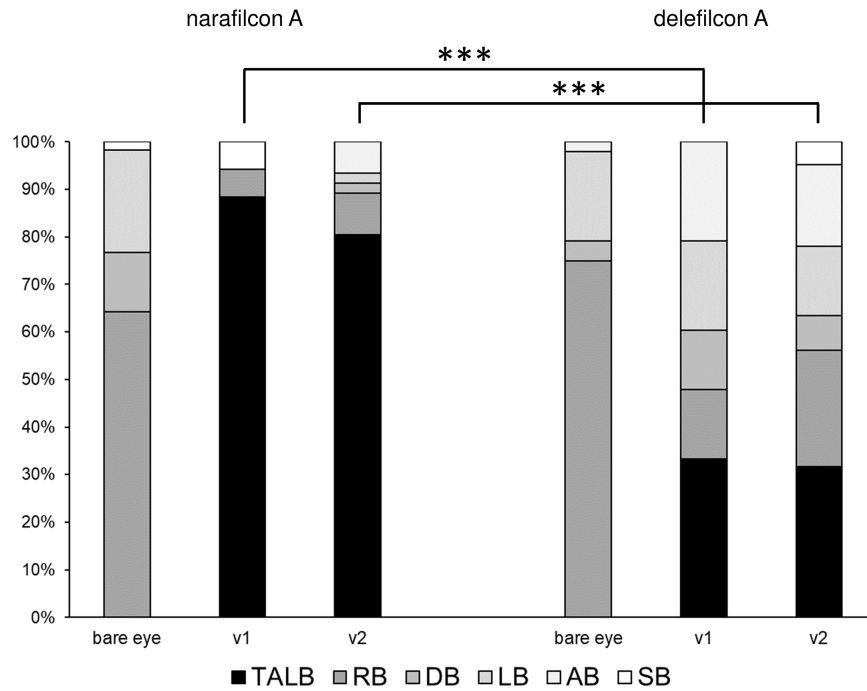


Figure 1. Comparison of break-up patterns between study groups at visit 1 and visit 2. Abnormal break-up pattern TALB was significantly suppressed in the SH-SCL (delefilcon A) equipped with a water gradient structure. *** $P < 0.0001$, Pearson’s chi-square test. TALB, thin aqueous layer break; RB, random break; DB, dimple break; LB, line break; AB, area break; SB, spot break; v1, visit 1; v2, visit 2.

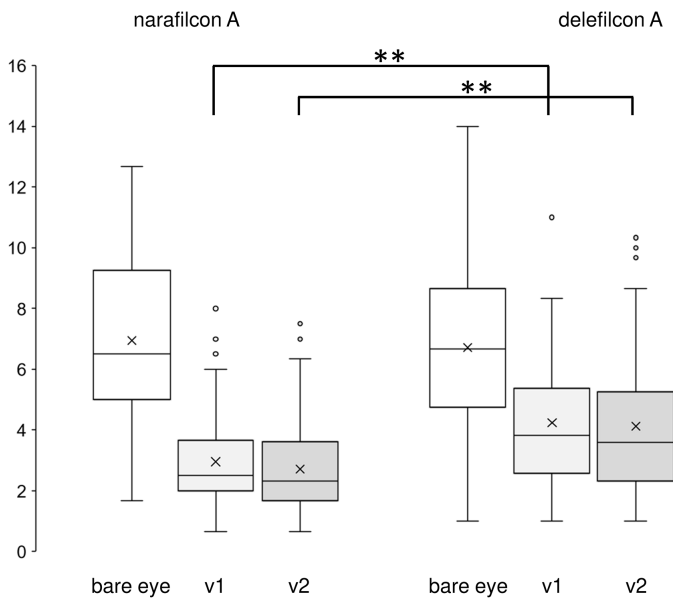


Figure 2. Comparison of NIBUT measured by DR-1α. The amount of NIBUT (in seconds) shortening was significantly inhibited with delefilcon A as compared to narafilcon A. The horizontal lines in the box and whisker plots represent the median values, and the bottom and top of the boxes represent the lower and upper quartiles, respectively. The x represents the mean and the bars represent the minimum and maximum values within 1.5 times the lower and upper quartiles. ** $P < 0.01$, t -test, the two-sample independent t -test.

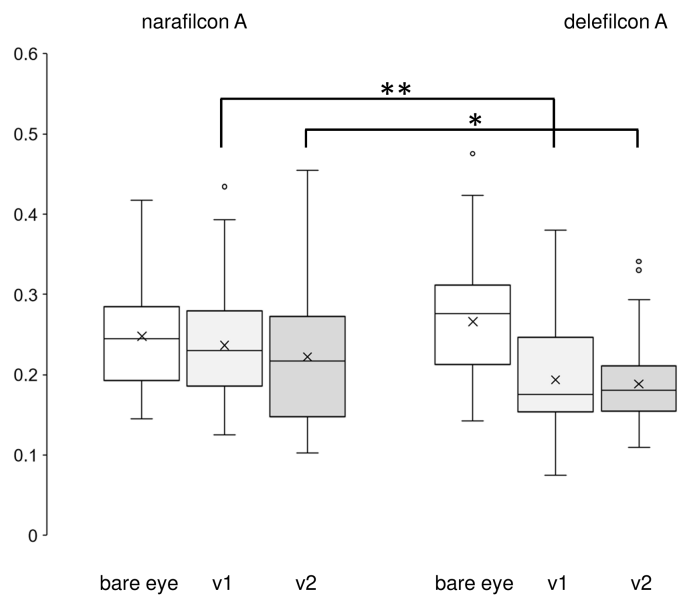


Figure 3. Comparison of TMH measured across study groups and visits. The tear meniscus height (TMH; in mm) was lower with delefilcon A in both visit 1 (v1) and visit 2 (v2). The horizontal lines in the box and whisker plots represent the median values, and the bottom and top of the boxes represent the lower and upper quartiles, respectively. The x represents the mean and the bars represent the minimum and maximum values within 1.5 times the lower and upper quartiles. ** $P < 0.01$, * $P < 0.05$, the two-sample independent t -test.

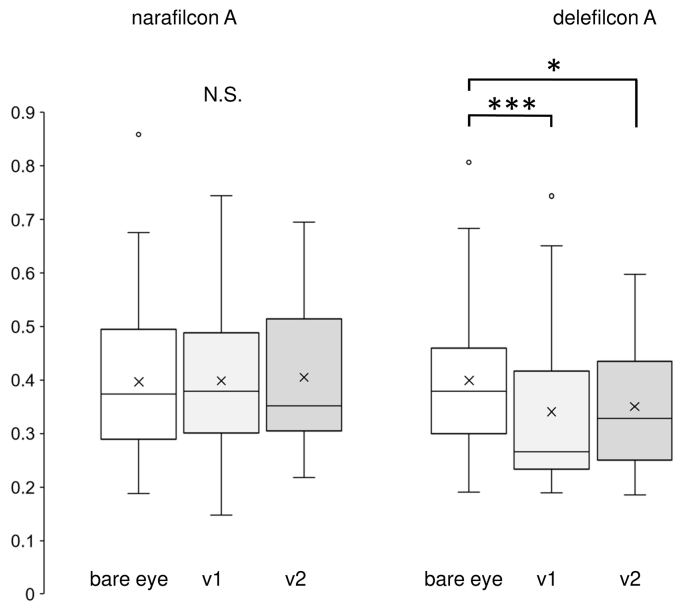


Figure 4. Total ocular HOAs across study visits, 1 second after eye blink. In delefilecon A, the total ocular HOAs (RMS; in μm) in visit 1 (v1) and visit 2 (v2) is superior to bare eye. The horizontal lines in the box and whisker plots represent the median values, and the bottom and top of the boxes represent the lower and upper quartiles, respectively. The x represents the mean and the bars represent the minimum and maximum values within 1.5 times the lower and upper quartiles. *** $P < 0.001$, * $P < 0.05$, paired t -test with Bonferroni correction. HOAs, higher-order aberrations.

those at the bare eye in both delefilecon A and narafilecon A groups.

SCL Thickness

The SCL thickness measured at v1 was $106.4 \pm 11.5 \mu\text{m}$ and $94.1 \pm 6.7 \mu\text{m}$ in the delefilecon A and narafilecon A groups, respectively. At v2, the delefilecon A and narafilecon A groups had an SCL thickness of $103.0 \pm 8.8 \mu\text{m}$ and $93.5 \pm 7.0 \mu\text{m}$, respectively. There was no significant difference in the rate of decay from v1 to v2, between both study groups.

Discussion

This study assessed whether the water gradient structure of the SH-SCL, delefilecon A, has an impact on tear film dynamics, including break-up patterns, NIBUT, and TMH measured for the bare eye and while wearing SCL. It also assessed the impact on ocular HOAs, subjective dryness, and SCL thickness. Overall, the SH-SCL delefilecon A lenses with a water gradient structure showed a significantly lower TALB compared to the conventional SH-SCL narafilecon A. The tear break-up times as measured by interferometry

were significantly increased in the SH-SCL delefilecon A lens wearers compared to the SCL narafilecon A lens wearers. However, the TMH, which is a measure of the tear volume was significantly lowered in delefilecon A wearers compared to narafilecon A lens wearers.

Prolonged soft contact lens usage often produces dry eye syndrome that results in discomfort that eventually lead to the discontinuation of use.^{26–28} SCL use often induces reversible changes in the corneal and conjunctival sensitivity and inflammation producing dry eye.^{29–32} The dry eye syndrome arises either due to inadequate tear film secretion or excessive water loss from the tear film by evaporation. According to the National Eye Institute and Industry Workshop, contact lens-associated dry eye occurs due to the evaporative loss of tears^{33,34} that reduces the break up time (BUT).

Tear film dynamics and break-up patterns like TALB were initially proposed by Yokoi and Georgiev,^{23,25} as one of the major mechanisms of diagnosis and pathogenesis of dry eye. TALB is known to occur immediately after eye-opening when there is no lipid layer on the SCL surface due to a thin aqueous layer tear, and rarely observed in bare eye.²⁴ In our study, we found a significant decrease in TALB among the SH-SCL delefilecon A lens wearers compared to the SCL narafilecon A lens wearers. The conventional SH SCLs (narafilecon A) has a low water content of 30% to 40% in all the layers such that the SCL surface is water-repellent, and tears evaporate immediately and easily from the surface. In our results, almost all break-up patterns were TALB among conventional SH-SCL wears in both v1 and v2 (Supplementary Video 1). On the contrary, delefilecon A exploits the innovative water gradient technology to provide surface lubrication (or wettability), which reduces the TALB of the surface of the lens and retains the wettability of the surface.

Previous studies have reported that the delefilecon A lens has prolonged wettability¹⁹ and a longer NIBUT (13.4 seconds) compared to narafilecon A (12.3 seconds; $P < 0.001$).²¹ Another study by Guillon et al.³⁵ showed that the mean NIBUT of delefilecon A was longer (9.2 seconds) than that of narafilecon A (5.1 seconds, $P = 0.006$). The recent study by Itokawa et al.²⁴ showed that the NIBUT measured by Keratograph 5M did not correlate to that measured by DR-1 α in the eyes with SCL and proposed the possibilities that Keratograph 5M frequently captures the tear dynamics in the posterior but not the anterior surface of SCL, resulting in inaccurate NIBUT values. In our measurements, Keratograph 5M was unstable as reported by Itokawa et al.; thus, we used DR-1 α measurements for the NIBUT analysis. The results of NIBUT measured in the current study also showed similar results. The mean

Table 3. Comparison of HOAs Between the Two SH-SCLs Across Study Visits, 1 Second After Eye Blink

HOA (RMS; in μm)	Narafilcon A (in Narafilcon A) (Average \pm SD)	Delefilcon A (in Delefilcon A) (Average \pm SD)	<i>P</i> Value Delefilcon A vs. Narafilcon A		
Bare eye:					
Total	0.39 \pm 0.13	0.39 \pm 0.18	0.95		
Third					
Coma	0.20 \pm 0.11	0.19 \pm 0.10	0.73		
Trefoil	0.18 \pm 0.11	0.15 \pm 0.08	0.14		
Fourth					
Spherical	0.14 \pm 0.09	0.18 \pm 0.10	0.10		
Tetrafoil	0.07 \pm 0.04	0.08 \pm 0.04	0.49		
Second astigmatism	0.09 \pm 0.07	0.07 \pm 0.05	0.30		
HOA (RMS; in μm)	Narafilcon A (in Narafilcon A) (Average \pm SD)	<i>P</i> Value vs. Bare Eye	Delefilcon A (in Delefilcon A) (Average \pm SD)	<i>P</i> Value vs. Bare Eye	<i>P</i> Value Delefilcon A vs. Narafilcon A
Visit 1 (v1):					
Total	0.40 \pm 0.16	0.66	0.34 \pm 0.15	0.0003	0.18
Third					
Coma	0.18 \pm 0.08	0.11	0.17 \pm 0.09	0.06	0.60
Trefoil	0.20 \pm 0.12	0.69	0.12 \pm 0.07	0.0041	0.005
Fourth					
Spherical	0.11 \pm 0.09	0.34	0.11 \pm 0.09	<0.0001	0.036
Tetrafoil	0.11 \pm 0.10	0.13	0.08 \pm 0.04	0.93	0.21
Second astigmatism	0.10 \pm 0.05	0.58	0.09 \pm 0.06	0.99	0.33
Visit 2 (v2):					
Total	0.40 \pm 0.14	0.73	0.35 \pm 0.13	0.038	0.14
Third					
Coma	0.19 \pm 0.10	0.66	0.19 \pm 0.11	0.41	0.91
Trefoil	0.20 \pm 0.10	0.12	0.14 \pm 0.09	0.017	0.023
Fourth					
Spherical	0.12 \pm 0.08	0.028	0.12 \pm 0.08	0.0008	0.90
Tetrafoil	0.10 \pm 0.06	0.014	0.09 \pm 0.07	0.82	0.88
Second astigmatism	0.09 \pm 0.04	0.39	0.10 \pm 0.06	0.08	0.95

The data are expressed as mean \pm standard deviation. *P* values were calculated using two-sample independent t-test to compare between the two SH-SCL groups. *P* values were calculated using the paired *t*-test with Bonferroni correction to compare the HOAs among bare eye, v1, and v2.

HOA, higher-order aberration; SD, standard deviation; SH-SCL, silicone hydrogel-soft contact lens.

break-up time in the delefilcon A lens wearers at visits v1 and v2 were 4.2 seconds and 4.1 seconds, respectively, whereas the mean break-up time in the narafilcon A group was about 3.0 seconds and 2.7 seconds at visits v1 and v2, respectively. The differences were statistically significant. In our results, NIBUTs were relatively shorter than the previous reports. This may be because we included the patients with a dry eye with a short break-up time, which is clinically important in SCL users including delefilcon A.

The TMH evaluates the tear volume, and a low tear meniscus height correlate to dry eye. Previous studies have established that in dry eye syndrome, discomforts arise due to the reduction in the tear meniscus.^{36,37} A study by Wolffsohn et al.²¹ had demonstrated that

TMH of delefilcon A was greater (0.35 mm) than that of narafilcon A (0.32 mm; *P* = 0.016). However, in the current study, the TMH was found to be significantly lower with delefilcon A in both v1 and v2 compared to that with narafilcon A. This shortening of TMH could be attributed to the thin high-water content film that absorbs the tears in eyes with relatively short NIBUT in our study.

Measurement of the higher-order aberrations represents the quality of vision. A previous study by Mico et al.¹⁷ has shown that delefilcon A demonstrates a lower level of aberrations compared to other lenses. In the current study, the total ocular HOAs were significantly lower in the delefilcon A group at v1 and v2 compared to the bare eye, 1 second after eye blink. No such

significance was observed in the narafilecon A group. Thus, lower HOAs in the delefilecon A group could result in a higher quality of vision compared to that of the bare eye. This may be because the delefilecon A surface is optically smooth due to the tear rich environment shortly after an eye blink compared to narafilecon A, which have relatively water repellent surface and frequently accompany TALB. The reduction of HOAs was not observed after 2 seconds after the eye blink. The NIBUT was 4.2 ± 2.2 seconds at v1 and 4.1 ± 2.4 seconds at v2 in delefilecon A. After 2 seconds after the eye blink, the tear film on the delefilecon A may be disturbed if not broken up. In HOAs, a decrease in trefoil aberration by delefilecon A use was observed at both v1 and v2, likely one of the reasons for the reduction in total HOAs. In addition, spherical aberration decrease was observed in delefilecon A eyes in v1 and v2, and narafilecon A eyes in v2, which may also contribute to the total HOA decrease, considering the previous report that SH-SCL use affects spherical aberration.³⁸

For assessing the subjective dryness experienced by the participants, the contact lens dry eye questionnaire (the CLDEQ-8) was used.³⁹ Chalmers et al.²⁷ previously reported the use of the CLDEQ-8 questionnaire. In this study, there was no difference in the subjective dryness between SCLs with (delefilecon A) or without (narafilecon A) the water gradient structure. The absence of any changes in the subjective dryness score using the VAS could be either because this study was a parallel-design study, with few comparisons made with respect to SCL-worn by the same subject, or that this study was conducted on normal subjects; hence, there might have been no evident differences in the subjective symptoms.

Delefilecon A constitutes the daily disposable water gradient contact lenses marketed as DAILIES TOTAL1 (by Alcon Laboratories, Inc., Fort Worth, TX, USA). They possess the characteristics of both conventional hydrogel and SH lenses. The delefilecon A lenses have a SH core with a water content of $33\% \pm 2\%$ and a surface water content of 84.6% .¹³ They have a total surface thickness of $5.9 \pm 0.8 \mu\text{m}$, including a 1 to 2 μm transition zone and 4 to 5 μm outer surface layer with a lower compression modulus and a significant modulus gradient in the zone of transition.¹³ These features result in a water gradient that transitions from the lower water content core to the higher water content outermost hydrophilic gel layer, which provides high oxygen transmissibility and high tensile modulus to these lenses compared to their conventional SH counterpart, narafilecon A, which has only 46% water content. Therefore, the water gradient structure might have contributed to a reduction of

TALB and an increase in NIBUT among the delefilecon A lens users.

This was a retrospective and an observational study. Therefore, no randomization was done. To minimize the bias, the break-up patterns and NIBUT were assessed by the researchers under masked conditions. In addition, a consecutive series of individuals were included in both delefilecon A and narafilecon A groups with characteristics that matched the inclusion criteria to negate the chance of bias. In this study, artificial tears or anti-allergic ophthalmic solutions were used in some patients, which could impact the results on tear dynamics; however, the distribution of participants did not differ between the delefilecon A and narafilecon A groups.

Conclusion

In conclusion, the tear film dynamics, including break-up patterns and break-up times, are significantly influenced by the water gradient structure of the delefilecon A lens. Thus, the usage of the delefilecon A lens can alleviate the abnormal break-up pattern among the lens wearers and improve lens performance.

Acknowledgments

The authors thank H. Kamao, Y. Ieki, K. Tomita, A. Masuda, Y. Mito, and Y. Setoguchi for the discussions, advice, and criticism that greatly benefited this project.

Funded in part by an unrestricted investigator-initiated grant from Alcon Japan Ltd (Grant Number: 42166553). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Approved by the institutional review board of Kawasaki Medical School Hospital (approval number 3403). Informed consent was obtained from all study participants, and the study adhered to the tenets of the Declaration of Helsinki.

Disclosure: **H. Fujimoto**, Alcon (F), Otsuka (F), Kowa (F, P), Santen (F), Novartis (F); **S. Ochi**, Santen (F); **T. Yamashita**, Alcon (F); **Y. Inoue**, Santen (F); **J. Kiryu**, (F), Kowa (F), Alcon (F), Novartis: (F), Otsuka (F)

References

- Inoue T, Maeda N, Young LS, et al. Epithelial pigment slide in contact lens wearers: a possible marker for contact lens-associated stress on the corneal epithelium. *Am J Ophthalmol*. 2001;131(4):431–437.
- Chan WK, Weissman BA. Corneal pannus associated with contact lens wear. *Am J Ophthalmol*. 1996;121(5):540–546.
- Holden BA, Mertz GW. Critical oxygen levels to avoid corneal edema for daily and extended wear contact lenses. *Invest Ophthalmol Vis Sci*. 1984;25(10):1161–1167.
- Dumbleton KA, Woods CA, Jones LW, Fonn D. Comfort and adaptation to silicone hydrogel lenses for daily wear. *Eye Contact Lens*. 2008;34(4):215–223.
- Dumbleton K, Woods CA, Jones LW, Fonn D. The impact of contemporary contact lenses on contact lens discontinuation. *Eye Contact Lens*. 2013;39(1):93–99.
- Chirila TV. An introduction to ophthalmic biomaterials and their application through tissue engineering and regenerative medicine. *Biomater Regenerat Med Ophthalmol*. Cambridge, England, UK: Woodhead Publishing; 2010:1–13.
- Fonn DP, Situ P, Simpson T. Hydrogel lens dehydration and subjective comfort and dryness ratings in symptomatic and asymptomatic contact lens wearers. *Optom Vis Sci*. 1999;76(10):700–704.
- Efron N, Morgan PB. Rethinking contact lens-associated keratitis. *Clin Exp Optom*. 2006;89(5):280–298.
- Maldonado-Codina C, Morgan PB, Schnider CM, Efron N. Short-term physiologic response in neophyte subjects fitted with hydrogel and silicone hydrogel contact lenses. *Optom Vis Sci*. 2004;81(12):911–921.
- Nichols JJ, Jones L, Nelson JD, Stapleton F, Sullivan DA, Willcox MD. The TFOS international workshop on contact lens discomfort: introduction. *Invest Ophthalmol Vis Sci*. 2013;54(11):TFOS1–TFOS6.
- Rohit A, Willcox M, Stapleton F. Tear lipid layer and contact lens comfort: a review. *Eye Contact Lens*. 2013;39(3):247–253.
- Guillon M, Dumbleton K, Theodoratos P, et al. Association between contact lens discomfort and pre-lens tear film kinetics. *Optom Vis Sci*. 2016;93(8):881–891.
- Pruitt J, Qiu Y, Thekveli S, Hart R. Surface characterization of a water gradient silicone hydrogel contact lens (delefilcon A). *Invest Ophthalmol Vis Sci*. 2012;53(14):6107.
- Tighe BJ. A decade of silicone hydrogel development: surface properties, mechanical properties, and ocular compatibility. *Eye Contact Lens*. 2013;39(1):4–12.
- Dunn AC, Urueña JM, Huo Y, et al. Lubricity of Surface Hydrogel Layers. *Tribol Lett*. 2013;49:371–378.
- Belda-Salmerón L, Ferrer-Blasco T, Albarrán-Diego C, Madrid-Costa D, Montés-Micó R. Diurnal variations in visual performance for disposable contact lenses. *Optom Vis Sci*. 2013;90(7):682–690.
- Montés-Micó R, Belda-Salmerón L, Ferrer-Blasco T, Albarrán-Diego C, García-Lázaro S. On-eye optical quality of daily disposable contact lenses for different wearing times. *Ophthalmic Physiol Opt*. 2013;33(5):581–591.
- Varikooty J, Keir N, Richter D, Jones LW, Woods C, Fonn D. Comfort response of three silicone hydrogel daily disposable contact lenses. *Optom Vis Sci*. 2013;90(9):945–953.
- Varikooty J, Schulze MM, Dumbleton K, et al. Clinical performance of three silicone hydrogel daily disposable lenses. *Optom Vis Sci*. 2015;92(3):301–311.
- Dursch TJ, Liu DE, Oh Y, Radke CJ. Fluorescent solute-partitioning characterization of layered soft contact lenses. *Acta Biomater*. 2015;15:48–54.
- Wolffsohn JS, Mroczkowska S, Hunt OA, Bilkhu P, Drew T, Sheppard A. Crossover evaluation of silicone hydrogel daily disposable contact lenses. *Optom Vis Sci*. 2015;92(11):1063–1068.
- Rex J, Knowles T, Zhao X, Lemp J, Maissa C, Perry SS. Elemental Composition at Silicone Hydrogel Contact Lens Surfaces. *Eye Contact Lens*. 2018;44(Suppl 2):S221–S226.
- Yokoi N, Sakai R, Georgiev GA, Kato H, Sotozono C, Kinoshita S. Impact of soft contact lens wear on tear film breakup patterns, meniscus tear volume, and tear film stability. *Invest Ophthalmol Vis Sci*. 2018;59:E–Abstract 1751.
- Itokawa T, Suzuki T, Iwashita H, Hori Y. Comparison and evaluation of pre-lens tear film stability by different noninvasive in vivo methods. *Clin Ophthalmol*. (Auckland, NZ). 2020;14:4459.
- Yokoi N, Georgiev GA. Tear-film-oriented diagnosis for dry eye. *Jpn J Ophthalmol*. 2019;63(2):127–136.
- Young G, Veys J, Pritchard N, Coleman S. A multi-center study of lapsed contact lens wearers. *Ophthalmic Physiol Opt*. 2002;22(6):516–527.

27. Chalmers RL, Begley CG. Dryness symptoms among an unselected clinical population with and without contact lens wear. *Cont Lens Anterior Eye*. 2006;29(1):25–30.
28. Richdale K, Sinnott LT, Skadahl E, Nichols JJ. Frequency of and factors associated with contact lens dissatisfaction and discontinuation. *Cornea*. 2007;26(2):168–174.
29. Schultz CL, Kunert KS. Interleukin-6 levels in tears of contact lens wearers. *J Interferon Cytokine Res*. 2000;20(3):309–310.
30. Liu H, Begley C, Chen M, et al. A link between tear instability and hyperosmolarity in dry eye. *Invest Ophthalmol Vis Sci*. 2009;50(8):3671–3679.
31. 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. *Invest Ophthalmol Vis Sci*. 2010;51(12):6111–6117.
32. Dogru M, Ward SK, Wakamatsu T, et al. The effects of 2-week senofilcon—a silicone hydrogel contact lens daily wear on tear functions and ocular surface health status. *Cont Lens Anterior Eye*. 2011;34(2):77–82.
33. Pflugfelder SC, Solomon A, Stern ME. The diagnosis and management of dry eye: a twenty-five-year review. *Cornea*. 2000;19(5):644–649.
34. Lemp A. Report of the National Eye Institute/Industry workshop on clinical trials in dry eyes. *Eye Contact Lens*. 1995;21(4):221–232.
35. Guillon M, Patel T, Patel K, Gupta R, Maissa CA. Quantification of contact lens wettability after prolonged visual device use under low humidity conditions. *Cont Lens Anterior Eye*. 2019;42(4):386–391.
36. Del Águila-Carrasco AJ, Ferrer-Blasco T, García-Lázaro S, Esteve-Taboada JJ, Montés-Micó R. Assessment of corneal thickness and tear meniscus during contact-lens wear. *Cont Lens Anterior Eye*. 2015;38(3):185–193.
37. Potvin R, Makari S, Rapuano CJ. Tear film osmolarity and dry eye disease: a review of the literature. *Clinical Ophthalmology* (Auckland, NZ). 2015;9:2039.
38. Awwad ST, Sanchez P, Sanchez A, McCulley JP, Cavanaugh HD. A preliminary in vivo assessment of higher-order aberrations induced by a silicone hydrogel monofocal contact lens. *Eye Contact Lens*. 2008;34(1):2–5.
39. Begley CG, Chalmers RL, Mitchell GL, et al. Characterization of ocular surface symptoms from optometric practices in North America. *Cornea*. 2001;20(6):610–618.

Supplementary Materials

Supplementary Video 1. Representative tear interferometer movie using the DR-1 α in an eye with narafilcon A silicone hydrogel-soft contact lens. The thin aqueous layer break (TALB) was observed. The colorful interference fringes shortly after eye opening and thin aqueous tear gradually evaporate.