Title

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Journal

Contact Lens and Anterior Eye, 46(1)

ISSN

1367-0484

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Publication Date

2023-02-01

DOI

10.1016/j.clae.2021.101528

Peer reviewed

HHS Public Access

Author manuscript

Cont Lens Anterior Eye. Author manuscript; available in PMC 2023 February 01.

Published in final edited form as:

Cont Lens Anterior Eye. 2023 February ; 46(1): 101528. doi:10.1016/j.clae.2021.101528.

Clinical outcomes and complications of fluid-filled scleral lens devices for the management of limbal stem cell deficiency

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Abstract

Aims: To evaluate the clinical and visual outcomes of fluid-filled scleral lens devices (SL) wear in patients with limbal stem cell deficiency (LSCD).

Design: Retrospective consecutive case series.

Methods: 27 eyes with LSCD confirmed by *in* vivo confocal microscopy at the Stein Eye Institute and fitted with SL were included. Correlations between corrected distance visual acuity (CDVA) and LSCD stage determined by clinical grading were performed between baseline (after the SL fit) and the last follow-up (the time of discontinuation of SL wear or the last visit in eyes in which SL were continued). In a subset of patients that had worsened LSCD while using SL, anterior segment optical coherence tomography (AS-OCT) and anterior segment fluorescein angiogram (AS-FA) were performed.

Results: Baseline LSCD grading was stage I in 12 eyes (44.4%), stage 2 in 12 eyes (44.4%), and stage III in 3 eyes (11.1%). At the last follow-up, CDVA was improved in 7 eyes (25.9%), remained stable in 13 eyes (48.1%) and decreased in 7 eyes (25.9%, P=0.16). The LSCD stage was improved in 7 eyes (25.9%), remained stable in 8 eyes (29.6%) and worsened in 12 eyes (44.4%, P=0.10). AS-OCT and AS-FA, performed in 5 eyes, showed limbal compression and delayed fluorescein filling.

Conclusion: SL can improve visual acuity and maintain the ocular surface in the majority of eyes. Worsening of the ocular surface might be a result of limbal hypoxia. Close monitoring of SL fit is necessary in these compromised eyes.

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Keywords

Anterior segment fluorescein angiography; Anterior segment optical coherence tomography; Cornea; In vivo confocal microscopy; Limbal stem cell deficiency; Scleral lens; PROSE lens; EyePrintPRO

INTRODUCTION

Corneal epithelial cells renewal and corneal transparency rely on the normal function of corneal epithelial stem cells located in the limbus, i.e. the junction between the cornea and the sclera.[1] These limbal stem cells (LSCs) are regulated by their surrounding microenvironment, the LSCs niche.[2–4] Dysfunction or destruction of the niche and/or of the LSCs from a variety of etiologies results in limbal stem cell deficiency (LSCD), a disease that can lead to corneal blindness.[5] Medical management of LSCD entails a stepwise approach to improve the ocular surface, including the treatment of any ocular surface comorbidities impairing the function of LSCs [6]. These optimization steps are critical in order to prevent further progression of LSCD and ensure the survival of transplanted LSCs [6].

Scleral lenses are large diameter devices that rest on the sclera, allowing for a full-fluid reservoir over the anterior surface of the cornea, originally developed for visual rehabilitation in keratoconus. Their popularity has increased with the development of more oxygenated materials and customized design, such as the prosthetic replacement of the ocular surface ecosystem (PROSE) lens and the EyePrintPRO. These scleral lens devices (SL) are becoming more widely used with promising visual outcomes [7]. Given their design, which vaults over the cornea and the limbus, they have been proposed as an option for visual rehabilitation of irregular corneal surface, while protecting the ocular surface from microtrauma induced by blinking. The liquid reservoir provides a stable microenvironment in eyes with LSCD and has been used in their medical management [7–11]. However, these studies mainly focus on visual outcome before and after SL treatment. Disease progression and visual outcome have not been investigated during the course of SL treatment using a LSCD grading system [5, 12]. The current study aimed to investigate the visual and clinical outcomes of these fluid-filled SL in a consecutive case series of patients with LSCD.

MATERIALS AND METHODS

This retrospective consecutive case series was approved by the institutional review board at the University of California, Los Angeles (#10–001601). Data collection was compliant with the Health Insurance Portability and Accountability Act and all research adhered to the Declaration of Helsinki.

Participants

Medical records of 167 consecutive patients (267 eyes) referred to the senior author (S.X.D) for evaluation and management of LSCD, at the Stein Eye Institute, University of California, Los Angeles, from 2009 to 2019 were reviewed. All subjects that were successfully fitted with SL (scleral lens, PROSE lens [Boston Foundation for Sight, Needham, MA],

or EyePrintPRO [Advanced Vision Technologies, Lakewood, CO]) were included in the study. Minimum follow-up for inclusion was 6 months. The study flowchart is presented in Supplemental Figure 1. The diagnosis of LSCD was confirmed by in vivo confocal microscopy (IVCM, Heidelberg Retina Tomograph III Rostock cornea Module, Heidelberg Engineering GmBH, Germany), anterior segment optical coherence tomography (AS-OCT, RTVue-100, Optovue, Inc., Fremont, CA) and/or impression cytology [12, 13].

Limbal stem cell deficiency staging

Limbal stem cell deficiency was staged using the system established by the global consensus and our previously published grading system to allow for quantitative analysis: stage I (visual axis not involved, corneal involvement < 50%), stage II (visual axis involved, corneal involvement 50-<100%) or stage III (visual axis involved, total corneal involvement) [5, 12]. (Supplemental Figure 2).

Data collection and analysis

Baseline was defined as the date of the first appointment after the SL fitting. Last follow-up was the time of discontinuation of SL wear when it occurred and the last visit in eyes which SL was continued. Data collected included patient demographics, etiology of LSCD, treatment modalities, slit-lamp findings, LSCD clinical grading/score, and best-corrected distance visual acuity (CDVA) with SL by Snellen chart. When the LSCD score worsened, slit-lamp photography, AS-OCT and anterior segment fluorescein angiogram (AS-FA, Spectralis, Heidelberg Engineering, GmbH, Heidelberg, Germany) were performed on a subset of patients to evaluate limbal perfusion [14].

Fluid-fill scleral lens device fitting

All SL fittings were completed by 3 highly trained providers, fellows of the Scleral Lens Education Society and the American Academy of Optometry. All eyes were fitted with SL (scleral lens, PROSE lens or EyePrintPRO) to vault the cornea, limbus, and land on the conjunctiva, according to the revised definition of SL by the Scleral Lens Education Society (200 μm clearance of the central cornea, 50–75 μm of the limbus) [15, 16]. The median diameter of the SL was 16.8 mm (range 16.0–18.5 mm).

Imaging protocol for subjects with worsened LSCD after SL wear

The imaging protocol was performed on 2 different visits: after 3 h of SL wear, and after 24 h of wear discontinuation. Slit-lamp photographs and AS-OCT were taken in the 4 limbal quadrants. For the AS-FA, a video starting at the time of fluorescein injection, up to 1 minute thereafter was recorded.

Limbal compression was defined as disruption of blood flow and/or as a scleral blanching using slit lamp photography, and a loss of the normal scleral curvature on AS-OCT (Figure 1) [17]. Initial fitting did not present significant limbal compression. However, over the time, settling of the SL could occur, leading to limbal compression (Figure 1). Delayed filling with SL wear was defined as an increase in filling duration of ≥2 s compared with the filling duration without SL wear of the same eye on AS-FA.

Significant change in CDVA was defined as a change from baseline of ≥2 Snellen lines, and classified as improved, stable or worsened. Significant change in the LSCD grading score was defined as a change from the baseline score of ≥2 points.

Statistical analysis

Statistical analyses were performed with R software (www.r-project.org) by a biostatistician (C.H.T). Continuous variables were compared using Wilcoxon signed rank test or the Kruskall-Wallis test [18]. Correlations between CDVA and LSCD clinical score were assessed by Pearson correlation coefficients. The Fisher exact test was used to compare the difference in the percentage of categorical variables. A P value <0.05 was considered significant.

RESULTS

Demographics

Among a cohort of 267 eyes of 167 patients, 35 eyes (13.1%) were referred for SL evaluation during the study period. Four patients (4 eyes) were not interested. Twenty-three patients (31 eyes) underwent the SL fit trial, and 3 patients (4 eyes) withdrew from SL wear because of lack of visual improvement (3 eyes) and epithelial defect (1 eye). Therefore, 20 patients (27 eyes) which achieved final fitting and dispensing of SL were included in the study. The mean final follow-up was 37.1 ± 20.2 months (range 6.8–77.0). Demographics and baseline clinical scores were summarized in Table 1. At baseline, LSCD stage was mild and moderate in 12 eyes (44.4%) each, and severe in 3 eyes (11.1%). A similar staging was obtained using the grading system by the global consensus (Table 2).

Limbal stem cell deficiency management

Ocular comorbidities were common (Table 1). All cases of LSCD were managed following the global consensus guidelines [6].

When an increased LSCD severity was noted after starting SL wear, the duration of SL use was decreased and the fit of the SL was adjusted. If the ocular surface was still impaired after 3 months, the SL was switched to customized variants (PROSE lens or EyePrintPRO) whenever possible, or discontinued. Treatments prior to contact lens fitting included topical corticosteroids in 21 eyes (77.8%), preservative free artificial tears in 16 eyes (59.3%), topical 0.05% cyclosporine in 8 eyes (29.6%), preservative-free autologous serum (50%) in 8 eyes (29.6%), punctal plug placement in 6 eyes (22.2%) and oral doxycycline in 3 patients (15.0%).

Device wear and disease progression

The mean daily time wear was 10.2 ± 4.2 h (median 10.0, range 4.0 – 15.0 h). At the last follow-up, the mean LSCD score (5.8 ± 3.2) was similar to the baseline score (5.3 ± 2.1; P = 0.50). In 7 eyes (25.9%), the LSCD score was improved by an average of 3 points. In 8 eyes (29.6%), the LSCD score was stable at 5 points. In 12 eyes (44.4%), the LSCD score was worsened by an average of 5 points (P = 0.10) after a mean period of 33.9 ± 26.6 months of SL wear (median 42.9; range 5.6 – 63.5 months). The etiology of

LSCD of these 12 eyes were iatrogenic in 5 eyes (41.7%), idiopathic in 3 eyes (25.0%), soft contact-lens wear in 2 eyes, and toxic epidermal necrolysis (TEN) in 2 eyes (16.7% each). Two eyes (16.7%) had a worsening of LSCD prior to the SL wear. The risk of worsening was associated neither with the etiologies ($P = 0.20$) nor with the SL type (6 eyes with PROSE lens, 5 eyes with large diameter scleral lens, 1 eye with EyePrintPRO; $P = 0.15$). Worsening occurred more frequently in moderate and severe stages (Figure 2A, $P = 0.10$). SL wear time was reduced in 7 eyes (58.3%) including 5 eyes that were refitted to loosen the fit and discontinued in 5 eyes. Despite refitting, LSCD progression was noted in 2 eyes, leading to SL discontinuation. In the remaining 3 eyes, the LSCD score remained stable and SL wear was continued. After the SL wear time reduction or discontinuation for 19.6 ± 20.1 months (median 10.7; range, 1.2 – 58.4), the LSCD score improved in 10 eyes and remained stable in 2 eyes.

Visual outcomes with SL treatment

The mean CDVA before the SL fit was significantly worse compared with the baseline CDVA while wearing SL (Figure 2B; $P = 0.02$, r = 0.65). The mean CDVA at last follow-up was comparable with the mean CDVA at baseline ($P = 0.30$, r = 0.20; Figure 2B). The mean CDVA with SL was negatively correlated with the severity of the LSCD at baseline ($P < 0.01$, r = 0.84) and at last follow-up ($P < 0.01$, r = 0.84; Figure 2C). Similar results were found when using the global consensus grading ($P < 0.01$, r = 0.84 at baseline; $P < 0.01$, r = 0.79 at last follow-up). At last follow-up, the CDVA was improved in 7 eyes (25.9%), remained stable in 13 eyes (48.1%) and decreased in 7 eyes (25.9%; $P = 0.16$). Same results were found when using the global consensus grading ($P = 0.30$, r = 0.20).

Subgroup analysis showed that CDVA at last follow up was comparable with that at baseline for all stages of LSCD: mild ($P = 0.67$), moderate and severe stages (all P greater than 0.05; Supplemental Figure 3). Similar visual outcomes were observed when using the global consensus grading.

Among those 12 eyes that had worsened LSCD, the mean CDVA at baseline (0.4 ± 0.3 logMAR) was comparable with the mean CDVA at the time of LSCD progression (0.5 ± 0.4 logMAR; $P = 0.14$) and at last follow-up (0.5 ± 0.3 logMAR; $P = 0.40$). After the SL reduction or discontinuation, CDVA was stable in 5 eyes (41.7%) and worsened in 7 eyes (58.3%).

Anterior segment imaging

Among the 12 eyes (44.4%) that had worsening of LSCD, AS-OCT and AS-FA were performed in 5 eyes of 4 patients. On slit lamp examination and AS-OCT, 3 eyes demonstrated compression of the limbus on 3 quadrants or more, and 2 eyes demonstrated compression of the limbus on 2 quadrants or less. On AS-FA, the perfusion of the limbal vasculature was delayed by 2–5 s in 2 eyes, and more than 5 s (range, 6–20 s) in 3 eyes. In 2 eyes, the compression of the limbus was still visible on AS-OCT more than 24 h after the removal of the SL.

Case presentation

Fig. 3 summarizes the clinical and imaging findings of 3 eyes of 2 patients with worsened LSCD during SL wear. The first case (Fig. 3, top row) is the left eye of a 53 year old female who developed TEN 26 years ago, following a hepatitis B vaccine. She was initially treated at another tertiary center using topical 0.05% cyclosporine, preservative free artificial tears and lubricant ointments, cicatricial entropion repair, epilation of trichiasis, and bilateral oral mucosal graft followed by PROSE lens treatment (diameter 16.0 mm, 15h/day) 6 years prior to her presentation to our institute. At presentation, her baseline CDVA with SL was 20/100 and baseline LSCD severity had a clinical score of 7 points or stage IIB (Fig. 3 top row, left panel). Six months later, her CDVA with SL was 20/125 and her LSCD progressed to 9 points or stage III (Fig. 3 top row, second left panel). AS-OCT showed limbal compression (Fig. 3 top row, middle panel), and AS-FA showed 20 s delay filling at the limbus (Fig. 3 top row, second right panel). Refitting of her PROSE, reduction of the daily wear time to 6–8 h/day and 50% autologous serum drops four times a day were started. Six months later, her LSCD score was improved but still severe (8 points, global consensus: stage III, Fig. 3 top row, right panel) and her CDVA with SL was 20/150.

The second and third cases are the right (Fig. 3, middle row) and left (Fig. 3, bottom row) eye, respectively of a 48 year old female with idiopathic LSCD. The diagnosis of mucous membrane pemphigoid (MMP) was initially suspected 5 years prior when presented at an outside facility and treated with immunomodulating agents for 3 years. Progression of LSCD was noted and she was referred to our center for further management. She had been wearing PROSE lens 12–16 h/day in both eyes for 6 years. Her CDVA with SL was 20/80 OD and 20/30 OS, and her LSCD stage was moderate in the right eye (6 points or stage IIA, Fig. 3 middle row, left panel) and mild in the left eye (4 points or stage IA, Fig. 3 bottom row, left panel). MMP was ruled out clinically based on the absence of severe conjunctival inflammation, cicatricial changes and forniceal foreshortening, and a negative conjunctival biopsy. All immunosuppression therapies were discontinued. She remained stable for 9 months and presented 3 months later with a CDVA with PROSE lens of 20/125 OD and 20/20 OS, her LSCD has progressed in both eyes (10 points or stage III, Fig. 3 middle and bottom row, second left panel). AS-OCT showed limbal compression (Fig. 3 middle and bottom row, middle panel), AS-FA showed 6- and 5-seconds delay, respectively (Fig. 3 middle and bottom row, second right panel). Autologous serum drops, low dose topical corticosteroids and preservative-free artificial tears were started, as well as refitting of the PROSE lenses and decreasing the daily wear to 6–8h/day. The patient was reluctant to decrease her daily wear time. She had refitting of PROSE to loosen the fit. Her CDVA with refitted PROSE lenses 1 year later was stable at 20/125 OD and 20/20 OS, and her LSCD severity remained severe in both eyes (10 points or stage III, Fig. 3 middle and bottom row, right panel).

DISCUSSION

The current study supports the previous finding that SL provides good CDVA and maintains the ocular surface in the majority of eyes with LSCD. However, in a significant number of eyes, LSCD worsened after SL wear despite a stable CDVA with SL. This finding

demonstrates that CDVA with scleral lens is not a sensitive measure for monitoring LSCD progression. The underlying pathology could contribute to the worsening of LSCD. Limbal compression by the SL leading to local hypoxia could be another causative process that further damages the residual LSCs.

The use of SL has been reported with good visual outcomes and is one of the medical management recommended by the global consensus [6–9]. Recently Kim & colleagues described a case series of 31 eyes with LSCD fitted with PROSE [8]. A significant visual improvement was reported in 30 eyes and decreased in 1 eye without significant change in their ocular index score [8]. Ocular index score is designed for grading of dry eye disease and is not precise enough to detect changes in LSCD severity. Therefore, direct comparison between the current study and Kim's study is limited due to the different etiologies and LSCD grading systems.

With SL in particular, limbal hypoxia from the compression of the limbus could be another factor as shown in the current study. In a subset of eyes that had progression of LSCD while using SL, severe limbal compression was detected by AS-OCT, and led to a delay in perfusion as shown on AS-FA. We suspect that the delayed perfusion leads to hypoxia and chronic ischemia of the limbus, which has detrimental effect on LSCs.

While it is commonly accepted that 2.4 clock hours of circumferential limbal bearing can be tolerated during an appropriate fit in eyes without LSCD, the surface and level of compression that can be tolerated in eyes with LSCD remain unknown, but is likely lower [6, 19]. In addition, the distance between the anterior surface of the cornea and the back surface of the SL in the central cornea could be significantly reduced after 4 h of PROSE lens wear, by 68 μm on average [20]. This observation suggests that the SL fit becomes increasingly tighter after hours of wear. All these factors lead to a less favorable outcome in eyes with LSCD than in eyes without LSCD. To address tight fit of SL, modifications of SL landing zone parameters and adding customized posterior venting channels can loosen the fit and decrease limbal bearing [21]. Conjunctival suction is another parameter that can promote limbal compression and reduce fluid-tears exchange in the SL reservoir [22].

Corrected distance visual acuity did not change in eyes with worsening LSCD. Therefore, close monitoring of the severity of LSCD every 3 to 6 months is necessary once SL treatment is started. If LSCD progression is noted, SL-induced damage to the LSCs should be suspected, and evaluation of the SL fit after a few hours of wear should be performed. In addition, evaluating the level of limbal compression and ventilation by AS-OCT after several hours of wear would be informative of the degree of limbal compression by SL [20, 22].

Determining the precise location of the limbus where there are still limbal epithelial cells is critical for an optimal SL fitting [23, 24]. It is challenging in eyes with LSCD, as the anatomy of the limbus can be altered by the presence of corneal neovascularization, scarring, conjunctival remodeling from the filtration blebs, glaucoma drainage devices, repeated surgeries, and chronic conjunctival inflammation [23–25]. IVCM and AS-OCT can determine the locations of the remaining limbal epithelium in these complex eyes [17, 26, 27]. Extra care should be taken to avoid an overly tight fit in these limbal areas. The

SL size should be calculated with regards to the cornea size and horizontal visible iris diameter. Indeed, a small SL landing close to the limbus may also increase the risk of limbal hypoxia. AS-OCT can help designing customized SL and optimize their fitting in a time-efficient manner [28]. Image dewarping and compression of the globe in different gazes could present as compression of the SL. Nevertheless, significant compression to the limbus was confirmed using AS-FA in primary gaze.

There are limitations of our study. The SL size and type are heterogeneous, and it is unclear which technique to loosen the fit, whether the size, shape, or ventilation channels, would achieve better outcomes needs to be further investigated [8, 28]. Moreover, the possible progression of the underlying etiology of LSCD cannot be ruled out as the cause of the LSCD progression. These 2 causative processes of LSCD progression could not be separated completely. Finally, the ocular surface of all the patients was optimized following the global consensus of the management of LSCD [6], including a variety of topical anti-inflammatory medications, accounting for confounding factors of the clinical outcome.

In summary, SL is a good option in the medical management of LSCD to improve visual acuity and maintain ocular surface integrity in a majority of eyes. However, LSCD progression could occur in some patients possibly due to limbal hypoxia secondary to limbal compression by SL. Close monitoring of LSCD progression and adjusting SL fit during SL treatment are easy and simple preventive measures that could reduce the risk of trauma to the LSCs. The current study lays the foundation and provides the rationale of conducting a prospective, multicenter study in the future.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

Gloria Chiu, OD (University of Southern California) provided information on refitting of PROSE on one subject.

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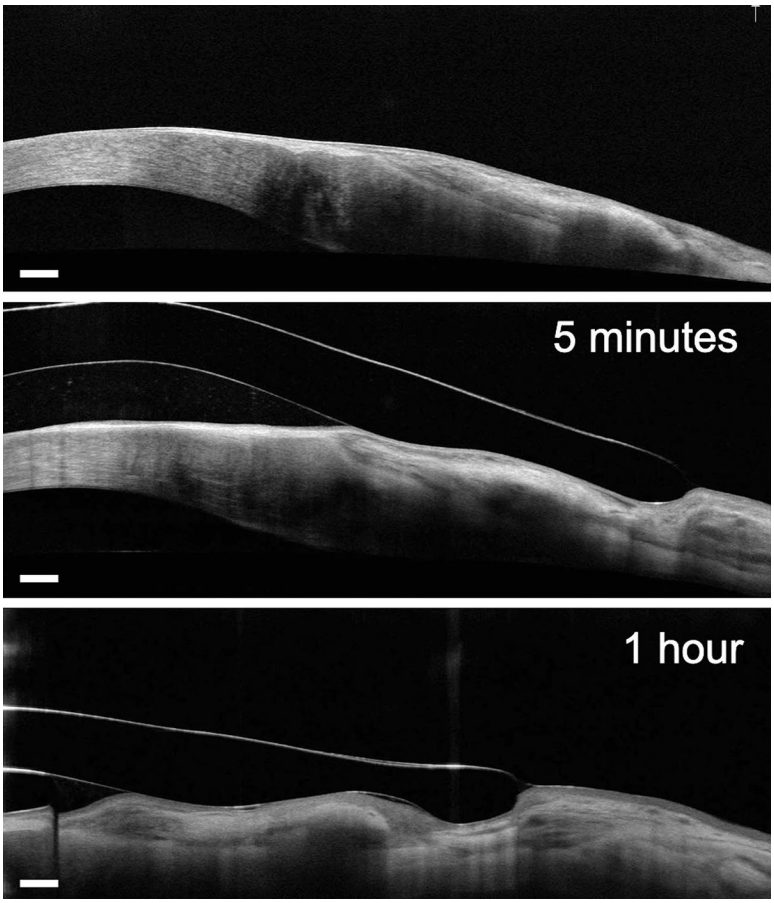

Figure 1.

AS-OCT of progressive limbal compression during SL wear.

Superior panel: limbal curvature without a SL.

Central panel: limbal curvature after 5 minutes of SL wear showing no significant compression of the limbal area.

Bottom panel: limbal curvature after 30 minutes of SL wear showing compression of the limbal area by the SL, not seen at the 5 minutes AS-OCT.

Scale bar indicates 250 μm. AS-OCT: anterior segment optical coherence tomography; SL: fluid-filled scleral lens device.

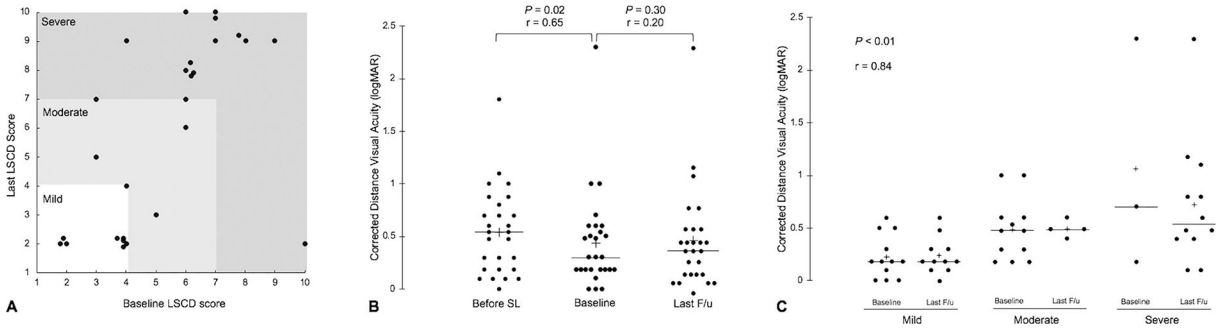

Figure 2.

Clinical and visual outcomes of SL wear

A: Change in LSCD scores among the different stages of severity. Horizontal axis represents the LSCD stage after initial SL fitting. Vertical axis represents the LSCD stage at last follow-up. Twelve patients experienced worsening of LSCD severity during the study period.

B: Changes in the mean CDVA during the study period. CDVA at last follow-up was comparable with CDVA right after initial SL fitting.

C: Changes in the mean CDVA during the study period among the different LSCD stages. CDVA was negatively correlated with the severity of LSCD after initial SL fitting and at last follow-up.

CDVA: corrected distance visual acuity; LSCD: limbal stem cell deficiency; SL: fluid-filled scleral lens device.

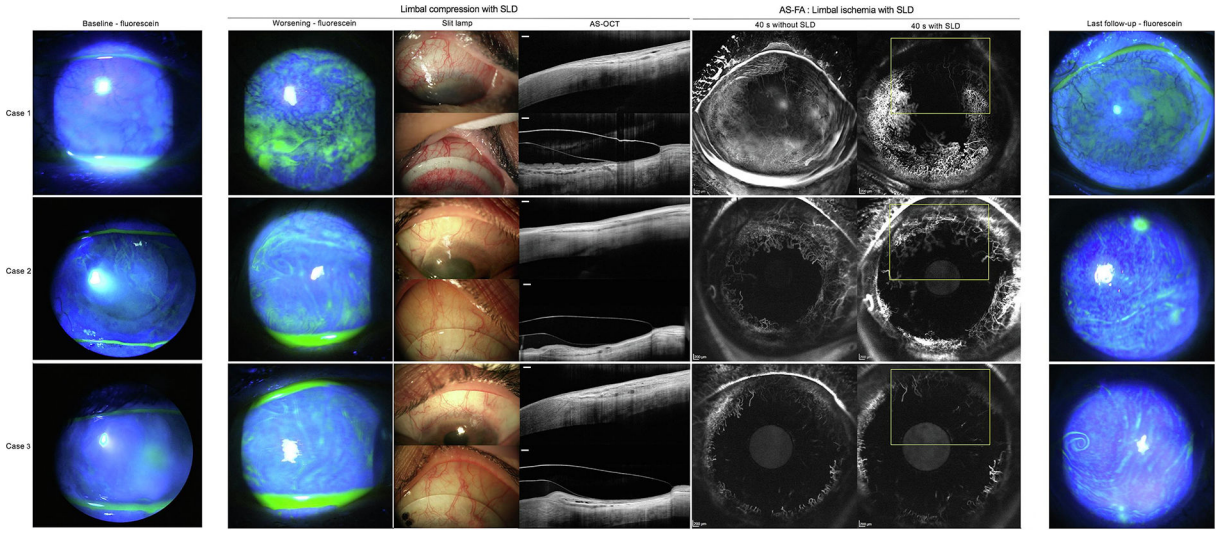

Figure 3.

Anterior segment imaging in 3 eyes presented with worsened LSCD. Fluorescein staining pattern at baseline (left column), at time when LSCD worsened (second left column) and at last follow up (right column). Slit lamp microscopy showed interruption of the blood flow in the limbal area with scleral blanching (left third column). AS-OCT showed compression at the limbus (middle panel). AS-FA showed a delayed fluorescein filling during the SL wear (second right column).

AS-OCT: anterior segment optical coherence tomography; AS-FA: anterior segment fluorescein angiogram; LSCD: limbal stem cell deficiency; SL: fluid-filled scleral lens device.

TABLE 1

Demographics and clinical presentation of study subjects

	n (%)
Total eyes / subjects	27 / 20
Sex, female	12 (60.0)
Age at inclusion, years	
Mean ± SD	56.4 ± 19.8
Median age (range)	60.3 (21.5 – 83.6)
Type of lens	
Scleral lens	8 (29.6)
PROSE lens	12 (44.4)
EyePrintPRO	7 (25.9)
Duration of follow-up,	
Mean ± SD, months	37.1 ± 20.2
Median (range)	32.7 (6.8 – 77.0)
Etiologies of LSCD	
Iatrogenic	12 (44.4)
Previous glaucoma surgeries + antimitotic agent	9 (33.3)
Conjunctival melanoma excision with cryoapplication	2 (7.4)
Other anterior segment surgeries	1 (3.7)
Soft contact lens wear	6 (22.2)
Mucous membrane pemphigoid	4 (14.8)
Idiopathic	3 (11.1)
Toxic epidermal necrolysis	2 (7.4)
Ocular comorbidities, n eyes (%)	
Dry eyes	21 (77.8)
Blepharitis	20 (74.1)
Corneal scar and irregular astigmatism	15 (55.6)
Eyelid malposition	11 (40.7)
Neurotrophic keratopathy	10 (37.0)
Allergic conjunctivitis	8 (29.6)
Previous failed corneal transplants	3 (11.1)
History of herpetic disciform keratitis	2 (7.4)
Baseline LSCD grading	
Mild	12 (44.4)
Mean score ± SD	3.3 ± 0.9
Moderate	12 (44.4)
Mean score ± SD	6.3 ± 0.6
Severe	3 (11.1)
Mean score ± SD	9.0 ± 0.8

LSCD = limbal stem cell deficiency; PROSE = prosthetic replacement of the ocular surface ecosystem, SD= standard deviation.

Table 2.

Individual characteristics and outcomes of the study patients

Eye	Sex	Eiologies	Type of SL	Baseline LSCD score (n points)	Last follow-up LSCD score (n points)	Change in LSCD score	Baseline CDVA (Snellen)	Last with SCL (Snellen)	Change in CDVA
OD	M	Iatrogenic	Scleral lens (Europa)	Moderate (6)	Severe (8)	Worse	20/150	20/300	Worse
OD	M	Iatrogenic	Scleral lens (Europa)	Mild (3)	Moderate (5)	Worse	20/20	20/60	Stable
OS	F	Iatrogenic	Scleral lens (Europa)	Moderate (6)	Severe (8)	Worse	20/100	20/800	Improved
OD	F	CL	Scleral lens (Europa)	Mild (4)	Mild (4)	Stable	20/60	20/40	Improved
OD	F	CL	Scleral lens (SynergEyes)	Mild (2)	Mild (2)	Stable	20/25	20/20	Improved
OS	F	Idiopathic	Scleral lens (SynergEyes)	Moderate (6)	Severe (8)	Worse	20/80	20/300	Stable
OS	F	CL	Scleral lens (SynergEyes)	Mild (2)	Mild (2)	Stable	20/25	20/20	Stable
OD	M	CL	Scleral lens (SynergEyes)	Moderate (7)	Severe (10)	Worse	20/70	20/70	Worse
OD	F	Iatrogenic	PROSE	Mild (3)	Moderate (7)	Worse	20/30	20/60	Worse
OD	F	Iatrogenic	PROSE	Moderate (7)	Severe (9)	Worse	20/70	20/300	Worse
OD	F	Idiopathic	PROSE	Moderate (6)	Severe (10)	Worse	20/100	20/125	Stable
OS	F	Idiopathic	PROSE	Mild (4)	Severe (9)	Worse	20/30	20/40	Stable
OS	M	Iatrogenic	PROSE	Mild (2)	Mild (2)	Stable	20/30	20/30	Improved
OD	F	CL	PROSE	Moderate (6)	Moderate (7)	Stable	20/40	20/50	Worse
OD	F	MMP	PROSE	Mild (4)	Mild (2)	Improved	20/60	20/25	Worse
OS	F	MMP	PROSE	Mild (4)	Mild (2)	Improved	20/40	20/30	Improved
OD	M	MMP	PROSE	Mild (4)	Mild (4)	Improved	20/25	20/25	Stable
OS	M	MMP	PROSE	Mild (4)	Mild (4)	Improved	20/40	20/30	Stable
OD	F	TEN	PROSE	Moderate (7)	Severe (9)	Worse	20/60	20/60	Stable
OS	F	TEN	PROSE	Moderate (7)	Severe (10)	Worse	20/100	20/125	Improved
OD	M	Iatrogenic	EyePrintPRO	Mild (4)	Mild (2)	Improved	20/25	20/30	Improved
OS	M	Iatrogenic	EyePrintPRO	Severe (9)	Severe (9)	Stable	HM	CF	Stable
OD	F	Iatrogenic	EyePrintPRO	Moderate (5)	Mild (2)	Improved	20/250	20/80	Stable
OS	M	Iatrogenic	EyePrintPRO	Severe (10)	Mild (2)	Improved	20/80	20/40	Stable
OS	M	Iatrogenic	EyePrintPRO	Moderate (6)	Moderate (6)	Stable	20/125	20/80	Stable
OD	F	CL	EyePrintPRO	Moderate (6)	Severe (8)	Worse	20/150	20/300	Worse
OS	M	Iatrogenic	EyePrintPRO	Severe (8)	Severe (9)	Stable	20/200	20/300	Stable

CL= contact lens; F= female; LSCD = limbal stem cell deficiency; M= male; MMP= mucous membrane pemphigoid; PROSE = prosthetic replacement of the ocular surface ecosystem; TEN= toxic epidermal necrolysis.