Prosthetic Replacement of the Ocular Surface Ecosystem for Limbal Stem Cell Deficiency: A Case Series

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Objectives: To assess outcomes of limbal stem cell deficiency (LSCD) in patients treated with Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE).

Methods: Retrospective case series. Patients with LSCD who received PROSE treatment were included. Data including best-corrected visual acuity (BCVA) and LSCD staging before and after PROSE dispensing were collected to characterize each case.

Results: Five eyes of four patients were included. All patients were female, with an age range of 21 to 80 years. Each patient received a PROSE device with diameters ranging from 16 to 18.5 mm. Follow-up ranged from 11 to 29 months. Tolerated wear times ranged from 3.5 to 10 hr daily. Four eyes showed improved BCVA and unchanged LSCD staging as per the global consensus after PROSE treatment. Three of these eyes had stage 3 and one had stage 1C LSCD at diagnosis. The fifth eye had worse BCVA and recurrence of stage 3 LSCD post–living-related conjunctival limbal allograft transplant despite PROSE treatment.

Conclusions: Prosthetic Replacement of the Ocular Surface Ecosystem may be a viable treatment for LSCD, including severe cases, because it can provide symptom relief and improve vision. Its customizability, as demonstrated in this study, is beneficial for troubleshooting issues with fitting. Future studies are needed to further assess PROSE as treatment for LSCD.

Key Words: Contact lens—Limbal stem cell deficiency—Ocular surface disease—Prosthetic Replacement of the Ocular Surface Ecosystem.

(*Eye & Contact Lens* 2022;48: 493–496)

Limbal stem cell deficiency (LSCD) is an ocular surface disease that occurs because of loss or improper functioning of limbal stem cells (LSCs), resulting in the inability to maintain the corneal epithelium. It has many causes, including chemical and thermal injury, contact lens wear, Stevens–Johnson syndrome (SJS)/toxic epidermal necrolysis spectrum disease, and graft-vs-host disease, but may be idiopathic in some cases.[1] This disease begins with the corneal epithelium becoming hazy and irregular, but it may progress to persistent epithelial defects, scarring, ulceration, and perforation. Patients tend to have symptoms, such as decreased vision, irritation, and photophobia. The management of LSCD includes medications, such as topical corticosteroids and autologous serum tears or surgical options, such as amniotic membrane grafting and ocular surface reconstruction.[2]

Scleral lenses have also been used to treat LSCD.[3] Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE) (BostonSight, Needham Heights, MA) is a customizable, rigid, fluid-ventilated, gas-permeable therapeutic scleral contact lens that vaults the cornea and limbus. It can be used to treat patients with distorted corneal surfaces and ocular surface diseases and was approved by the US Food and Drug Administration in 1994.[4] Specifically, in LSCD, PROSE may improve symptoms by protecting the LSCs while neutralizing irregular corneal astigmatism.[5] Few studies have reported on the use of PROSE to treat LSCD.[5–7] This study reports on a series of patients with LSCD who underwent PROSE treatment based on outcomes, such as visual acuity (VA) and staging according to the global consensus published in 2019 by the LSC working and writing groups of the Cornea Society.[1]

METHODS

This study was carried out with approval from the University of Toronto Research Ethics Board (Research Information System Human Protocol #37130) and in accordance with the Declaration of Helsinki. Informed consent for the research was obtained from the patients.

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M. Mimouni: Lapidot Medical, EyeYon Medical. Recipient of Fellowship Grant from The American Physicians Fellowship for Medicine in Israel (APF). S. Ramdass: previously received honoraria from Bausch & Lomb, Synergeyes, BostonSight, and Pentavision LLC. J. Liao: previously received honoraria from Santen Medical, Coopervision, and BostonSight. C. C. Chan: previously received honoraria from Alcon, Allergan, Bausch & Lomb, Santen, Shire, Tearlab, Johnson and Johnson, and Zeiss. A. R. Slomovic: consultant for Alcon, Novartis, Bausch & Lomb, Santen, Shire, and Acqueous. On advisory board for Allergan and Labtician/Thea. Provided research assistance to AMO. The remaining authors have no funding or conflicts of interest to disclose.

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.eyeandcontactlensjournal.com).

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Accepted June 24, 2022.

DOI: 10.1097/ICL.0000000000000928

Study Population

The medical records of 78 patients who had all of their PROSE fitting appointments and received a PROSE device at the Kensington Eye Institute (KEI) PROSE clinic (Toronto, ON, Canada) were retrospectively reviewed. Inclusion criteria were the following: (1) diagnosis of LSCD, (2) dispense of a PROSE device with parameters customized to their eye, (3) availability of best-corrected visual acuity (BCVA) data before and after PROSE dispense, and (4) availability of LSCD staging data as per the Cornea Society global consensus before and after PROSE dispense. Table 1 summarizes the Cornea Society global consensus LSCD staging based on clinical presentation. Five eyes of four patients met the inclusion criteria for this case series.

Clinical Assessment

All patients were referred by their cornea specialist (C.C.C. and A.R.S.) to the KEI PROSE clinic for fitting with conventional scleral lenses or PROSE after failing other treatments. Each patient completed an intake form to report their symptoms, medical and ocular history, and previous lens modalities attempted. Patients were assessed by an optometrist (S.R., J.L.) who received PROSE Fellowship training at BostonSight (Needham Heights, MA). Patients were fitted with PROSE devices from a fitting set that were customized as needed. The device was dispensed to the patient once satisfactory fit, comfort, vision, and patient education regarding handling were achieved. An important aspect of a satisfactory fit was ensuring that the PROSE device cleared the limbus to prevent stress on the LSCs, which was assessed by slitlamp examination, anterior segment optical coherence tomography in the four major meridians, and sodium fluorescein application postlens removal. Patients were followed by the KEI PROSE clinic to manage PROSE wear and by their cornea specialist to monitor LSCD progression.

RESULTS

Table 2 provides a summary of each of the cases described below.

CASE 1

A 43-year-old woman with bilateral LSCD secondary to SJS from sulfa antibiotics at age 12 years was referred to the PROSE clinic. She had stage 3 LSCD in both eyes (OU). She was thought to be a good candidate for PROSE given the degree of keratinization of her conjunctiva and lids alongside extensive LSCD.

TABLE 1. *Limbal Stem Cell Deficiency Staging (Cornea Society Global Consensus)*

Stage	A	B	C
I Normal corneal epithelium within the central 5 mm zone of the cornea	<50% of limbal involvement	≥50% but <100% of limbal involvement	100% of limbal involvement
II The central 5 mm zone of the cornea is affected	<50% of limbal involvement	≥50% but <100% of limbal involvement	
III The entire corneal surface is affected			

She reported pain, blurry vision, and photophobia on presentation. Her BCVA was Snellen 20/30 in the right eye (OD) and 20/40 in the left eye (OS) with spectacles. Her dispensed PROSE devices had a diameter of 18.5 mm. She had adequate corneal clearance OU with a central clearance of 360 μm OD and 400 μm OS. At 29 months of follow-up, her BCVA was 20/25 OD and 20/25 OS. She remained stage 3 LSCD OU. She was able to wear PROSE for at least 10 hr per day with only mild discomfort OD, where she reported being able to feel the edge of the lens. Updated PROSE devices with a slight haptic modification were ordered to correct for this.

CASE 2

An 80-year-old woman with bilateral LSCD and marked Terrien's marginal degeneration was referred to the PROSE clinic. She had stage 1C LSCD OU.

She reported pain, blurry vision, redness, tearing, and photophobia on presentation. Her BCVA was 20/100 OD and 20/150 OS with spectacles. Slitlamp examination showed a hazy central cornea along with 360 degrees of vascularization around the peripheral cornea extending 5 mm into the cornea OU.

At the initial fitting, she achieved OD VA 20/150 and OS VA 20/40. She had poor wetting with the lens OD. In addition, she was advised to discontinue PROSE wear OS as a result of an upcoming LSC transplant because her LSCD was worsening.

Her OD PROSE device was reduced to a diameter of 16.5 mm because she struggled to insert a larger lens as a result of her smaller lid apertures. Her BCVA was 20/70, and she had no signs of edema. She remained stage 1C LSCD. She was able to wear PROSE for up to 6 hr per day at 11-month follow-up.

CASE 3

A 21-year-old woman with LSCD OD was referred to the PROSE clinic. She underwent living-related conjunctival limbal allograft (LR-CLAL) transplant as a result of aniridia from PAX6 mutation a year before her referral. She did not have any evidence of LSCD on examination during the first consult for PROSE.

Despite her transplant, she continued to report blurry vision, tearing, and frequent headaches. Her VA was 20/150 on presentation. At 2 months of follow-up, she was able to achieve BCVA 20/80 but had diffuse ocular hyperemia with the lens. Her PROSE device had a diameter of 17.5 mm. After haptic adjustment to improve device centration and prevent bubbles from entering the reservoir, she achieved 12 hr of daily wear time with a BCVA of 20/150. The ocular hyperemia resolved, but there was temporal and nasal impingement of the lens edge caused by conjunctival cysts, requiring further adjustments and addition of radial channels on the PROSE device to alleviate discomfort. At 6 months of follow-up, she had a hazy cornea with neovascularization. She was able to wear PROSE for 9 hr daily and had a BCVA of 20/200. At 12 months of follow-up, her BCVA was 20/320, and she was diagnosed with recurrence of stage 3 LSCD. She was only able to wear her PROSE device for 3.5 hr before needing to remove it for cleaning because of fogginess. The details regarding the specific adjustments and timing of changes are included as Supplemental Digital Content, http://links.lww.com/ICL/A224.

TABLE 2. *Summary of Cases*

Case	Eye	Ocular History	Previously Failed Lenses	Topical Treatments	Pre-PROSE VA (Snellen)	Post-PROSE VA (Snellen)	Pre-PROSE LSCD Stage (Global Consensus)	Post-PROSE LSCD Stage (Global Consensus)	Daily Wear Time (hr)	Follow-up Length (mo)	Number of Devices Cut Before Finalization
1	OD	Trichiasis	GP, scleral	Lubricants, steroids, autologous serum (30%)	20/30	20/25	3	3	10	29	5
1	OS	Trichiasis	GP, scleral	Lubricants, steroids, autologous serum (30%)	20/40	20/25	3	3	10	29	5
2	OD	DALK, cataract surgery	GP, piggyback, scleral	Lubricants	20/100	20/70	1C	1C	6	11	4
3	OD	LR-CLAL	None	Steroids	20/150	20/320	None (post-LR-CLAL)	3	3.5	12	4
4	OD	Trichiasis	None	Lubricants	20/400	20/100	3	3	8	21	6

DALK, deep anterior lamellar keratoplasty; GP, gas permeable; PROSE, Prosthetic Replacement of the Ocular Surface Ecosystem; VA, visual acuity; LSCD, limbal stem cell deficiency; LR-CLAL, living-related conjunctival limbal allograft.

CASE 4

A 48-year-old woman with stage 3 LSCD OD secondary to SJS diagnosed at age 18 years was referred to the PROSE clinic. She reported pain, grittiness, blurry and fluctuating vision, diplopia, redness, discharge and tearing, photophobia, and frequent headaches on presentation. Her VA was 20/400. Slitlamp examination showed keratinization of the conjunctiva and 360 degrees of neovascularization at the cornea along with scarring superiorly at the midperiphery. She required several teaching sessions before she was comfortable with PROSE application and removal. Her dispensed PROSE device had a diameter of 16 mm. She had adequate clearance with a central clearance of approximately 400 μm (Fig. 1). Additionally, there was debris noted in the lens reservoir which required management by removing the lens periodically throughout the day to clean it and reinsert with fresh preservative-free saline and/or using a more viscous solution in the bowl with lens application.

At 21 months of follow-up, her BCVA was 20/100, her daily wear time was 8 hr, and she remained stage 3 LSCD. She had discomfort secondary to poor surface wetting, so a replacement lens with Hydra-PEG coating (Tangible Science, Redwood City, CA), which is a 90% water polyethylene glycol–based polymer mixture designed to improve lens surface wettability by creating a wetting surface on the lens material, was ordered.

DISCUSSION

Based on this case series, PROSE may be a viable treatment for most patients with LSCD, including severe cases, to provide symptom relief and improve VA. Every patient reported symptoms in addition to poor vision on presentation, and all cases had these symptoms resolved with PROSE treatment. Three patients had considerable improvement in their VA despite variability in their baseline BCVA and LSCD stage. The one patient who had worsened vision after PROSE had a recurrence of LSCD after LR-CLAL. She likely had worse vision at her most recent follow-up because PROSE was unable to prevent her increased corneal opacification, which is a limitation of this treatment. Previous studies have reported favorable vision outcomes in patients with LSCD who received PROSE treatment, but those studies either had mostly less severe cases or did not stage their cases as per the Cornea Society global consensus.[5,6] Treatment with PROSE can improve vision in these patients because ocular surface irregularities are masked by the fluid reservoir created between the lens and the cornea as well as the "new" ocular surface of the PROSE device. Thus, PROSE may spare patients with severe LSCD from requiring medical or surgical management.

This case series provides some insight into the influence of PROSE treatment on LSCD severity. In addition, unlike previous studies, this study explicitly addresses some possible issues and

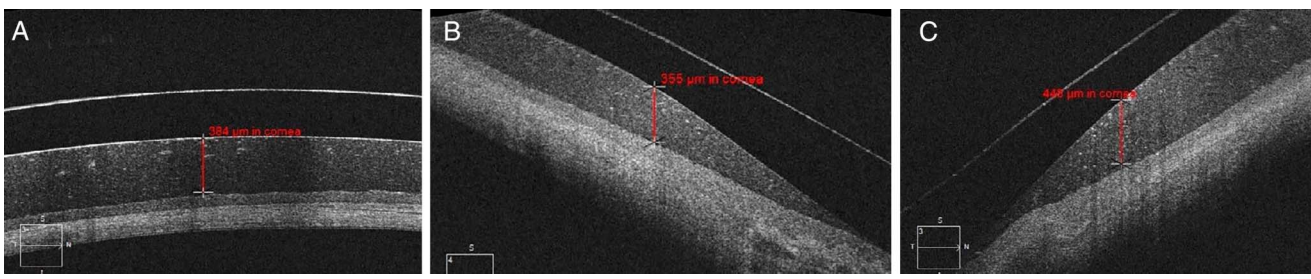

FIG. 1. An example of a PROSE device with adequate clearance of approximately 400 μm over the central cornea. (A) PROSE lens vault over the peripheral nasal (B) and temporal (C) cornea, with adequate clearance on both sides. Note the thin apical cornea in (A) with a reservoir that is opacified in a heterogenous fashion due to debris in the tear film. This would require further management to mitigate its effects on vision.

adjustment techniques with PROSE fitting in LSCD patients. The PROSE device may help to rehabilitate LSCs by protecting them from mechanical trauma because of the eyelids.[3] It has also been hypothesized that PROSE is beneficial in LSCD treatment because it may protect the limbal niche, which is important for proper functioning of LSCs, by limiting dryness and inflammation.[5] This is achieved in PROSE treatment using the customizability of the device because each eye receives a lens that vaults the limbus and completely covers the ocular surface in saline to maintain hydration and health of the limbal niche and LSCs.[5] This custom-fit ability was demonstrated in this case series, where each patient received PROSE devices with differing diameters ranging from 16 to 18.5 mm based on their individual eye. Unfortunately, information regarding the deficiencies of previous treatment modalities, such as conventional scleral lenses in cases 1 and 2, was unavailable. Consequently, it is only possible to speculate on the benefits of PROSE compared with other treatments. Potential advantages of PROSE in these cases may have included a wide range of diameters because PROSE can range from 13 to 23 mm and the ability to use unique Design to Fit software capabilities to precisely modify PROSE at specific points in various meridians at a micron level to better contour the sclera. Challenges with PROSE include edge awareness limiting wear time, issues with fogging requiring removal to clean the lens, and limbal hypoxia from the lens covering the entire surface potentially being detrimental to LSCs and thus contributing to worsening of disease.[8]

Previously, PROSE has been reported to contribute to reversal of LSCD.[9] Reversal of LSCD staging was not seen in this case series. In this study, one eye at stage 1C remained stable with 11 months of follow-up, whereas the other progressed to stage 3 within 12 months. Three of the eyes presented at stage 3 and remained at stage 3 throughout follow-up periods up to 29 months. Therefore, PROSE treatment may contribute to stability of LSCD in some cases but does not prevent progression.

An important factor in assessing the viability of PROSE treatment is its tolerability. The device was well-tolerated by most patients in this case series with daily wear times of 6, 8, and 10 hr. This is consistent with a previous study assessing PROSE in LSCD.[5] The patient with progression of LSCD peaked at a daily wear time of 12 hr but was only able to wear her device for 3.5 hr per day at most recent follow-up. It is likely that her disease progression resulted in changes to her ocular surface and possible that further customization at future appointments may have helped her achieve a higher daily wear time. This demonstrates the importance of regular follow-up to assess for any necessary changes to the PROSE device because the patient's ocular surface may change owing to disease progression.

This study has several limitations. First, the small sample size makes it difficult to draw firm conclusions regarding the findings. In addition, as a retrospective noncomparative study, there was no assessment of the outcomes of alternative treatments in a similar cohort of patients. Also, impression cytology was not obtained. Furthermore, most eyes already had stage 3 LSCD at presentation, limiting in-depth assessment of whether PROSE can limit disease progression. Finally, variation in underlying etiology for LSCD and ocular comorbidities between patients may have confounded the findings.

This case series has multiple strengths. To begin, the inclusion of patients with more severe LSCD compared with previous studies contributes to an understanding of the feasibility of PROSE in advanced disease. In addition, using the most recent global consensus staging system provides clinically relevant information regarding LSCD severity.[1] Finally, details regarding the customizations made during the fitting process provide practitioners with insight into troubleshooting the PROSE device.

In conclusion, this case series demonstrates that PROSE may be considered as a viable treatment option for patients with LSCD. The high degree of customizability of PROSE is a significant benefit in LSCD treatment. Large prospective studies, including patients in earlier stages of LSCD, are needed to further assess the benefits of PROSE treatment in these patients. Furthermore, it is important for future studies to compare patients treated with PROSE with those who do not undergo PROSE treatment or undergo an alternative treatment option for LSCD.

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