Boston Scleral Lens Prosthetic Device for Treatment of Severe Dry Eye in Chronic Graft-Versus-Host Disease

Deborah S. Jacobs, MD,† and Perry Rosenthal, MD*†*

Purpose: To determine if the Boston Scleral Lens Prosthetic Device (BSLPD) reduces symptoms and improves quality of life in patients with severe dry eye from chronic graft-versus-host disease (cGvHD).

Methods: This is a noncomparative interventional case series reporting 33 consecutive patients with severe dry eye from cGvHD, unresponsive to conventional therapy, who were fitted with the BSLPD. A patient survey was undertaken after lenses were dispensed and worn regarding the effect of scleral lens wear on their symptoms, quality of life, and activities of daily living. The patient population was characterized from a retrospective chart review. Survey data were tabulated.

Results: BSLPD wear resulted in improvement in pain, photophobia, and general quality of life in nearly all patients, with more than half reporting the highest improvement level for pain (52%) and photophobia (63%), and more than two thirds (73%) reporting the highest improvement level for quality of life. There was improvement in reading and driving in >90% of those who reported previous compromise, with >60% reporting the highest improvement level for each of these activities.

Conclusions: The BSLPD mitigates symptoms and improves quality of life in patients with severe dry eye from cGHvD.

Key Words: scleral lens, contact lens, dry eye syndrome, graft-versus-host disease

(*Cornea* 2007;26:1195–1199)

Management of severe dry eye associated with chronic graft-versus-host disease (cGvHD) after allogeneic bone marrow or hematopoietic stem cell transplantation can be challenging to patients and their physicians. The ocular surface disease of these patients is made up of dry eye syndrome and keratoconjunctival inflammation. Ocular therapy is multimodal, involving topical lubricants, punctal occlusion, topical steroids, and topical immunomodulators, as well as adjustment of systemic steroids and immunomodulators.[1] Conjunctival involvement occurs in 11.1% of patients with cGvHD.[2] Alternatively, ocular manifestation of cGvHD may appear independent and even in the absence of systemic manifestations of the disease in marrow and stem cell recipients.[1] Despite attentive ophthalmologic care, many patients continue to experience significant morbidity from disabling pain and photophobia from surface-related reduction in visual acuity and from sight-threatening corneal ulceration.[1,2]

The Boston Scleral Lens Prosthetic Device (BSLPD) was initially developed to mask cornea first surface irregular astigmatism in eyes that were intolerant of corneal contact lenses. Clinical indications were extended to eyes with severe dry eye or ocular surface disease that might otherwise require tarsorrhaphy and/or high-risk corneal transplantation.

The BSLPD is a custom-designed, rigid gas-permeable optical lens that vaults the cornea and limbus and rests entirely on the sclera. It was Food and Drug Administration (FDA) approved in 1994 for the management of corneal disorders. The space created by the vault of the BSLPD is occupied by artificial tears placed in the lens reservoir at the time of insertion (Fig. 1). This expanded precorneal tear film eliminates desiccation of the ocular surface during lens wear. The rigidity and stability of the BSLPD eliminate shear forces generated by the lids during blinking. In summary, BSLPD creates a liquid bandage and modifies the environment at the corneal surface. The BSLPD is well tolerated when worn on a daily-wear basis as an ocular surface prosthesis in the treatment of severe ocular surface disease.[4] The device has been shown to support healing of persistent epithelial defects when worn on an extended-wear schedule.[5]

The use of fluid-ventilated gas-permeable scleral lenses in the management of ocular surface disease is well established.[6–11] The BSLPD incorporates several design features that distinguish it from other scleral lenses. Each BSLPD is custom designed by using proprietary computer-assisted design and manufacture (CAD-CAM) software that drives the manufacturing lathe. The design software is based on spline functions (US patent 5,452,031; Contact Lens and a Method for manufacturing contact lens) that create the junctionless surface shapes needed for minimizing scleral compression from the bearing surface of the haptic, compression that causes wearing discomfort, and increases tendency toward potentially

Received for publication March 29, 2007; revision received July 15, 2007; accepted July 18, 2007.

From the *Boston Foundation for Sight, Needham, MA; and the †Harvard Medical School, Boston, MA.

Supported by the non-profit 501(c)3 Boston Foundation for Sight, Needham, MA.

The authors are salaried employees of the Boston Foundation for Sight, Needham, MA. Their salaries are fixed, with no productivity incentive, and are determined by the compensation committee of the Foundation's independent board of directors. Neither author has financial or proprietary interest in the Boston Scleral Lens Prosthetic Device.

Reprints: Deborah S. Jacobs, Boston Foundation for Sight, 464 Hillside Avenue, Suite 205, Needham, MA 02494 (e-mail: djacobs@bostonsight.org).

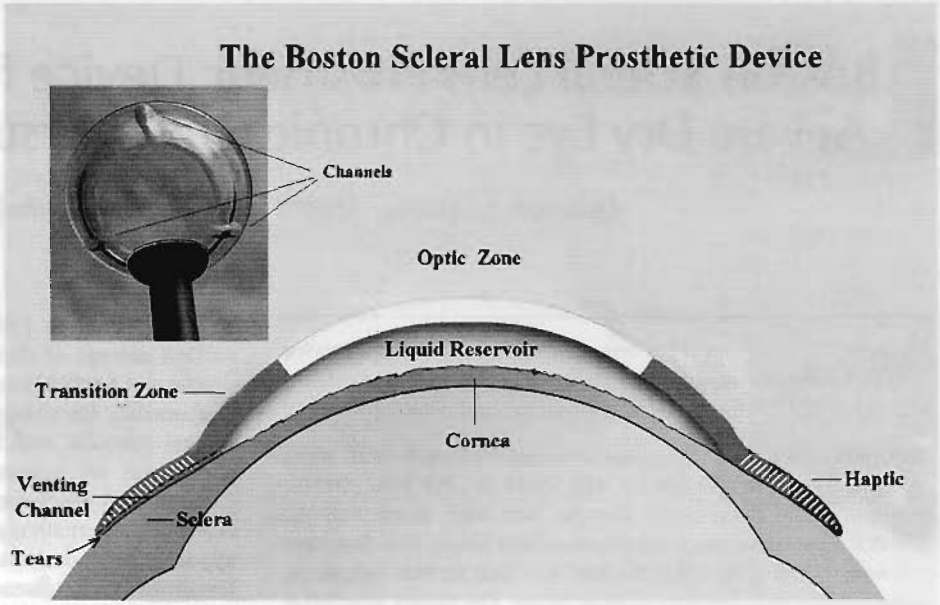

FIGURE 1. The BSLPD is an FDA-approved, custom-designed, rigid gas-permeable optical lens that vaults the cornea and limbus and rests entirely on the sclera. The bearing surface (haptic) of this scleral lens incorporates radial channels. These channels facilitate flow between tears external to the lens and fluid in the lens reservoir. This fluid-ventilated design prevents lens suction. The BSLPD immerses the cornea in a reservoir of oxygenated artificial tears. This figure is a schematic cross-sectional drawing of the BSLPD. The inset at the top left is a surface photograph of BSLPD revealing the radial channels.

dangerous lens suction. This spline-based software also allows control of the vault of the lens with high precision and predictability, independent of the base curve radius. Finally, this software also allows specification and creation of radial channels of ~200-μm depth in the bearing surface of the haptic when necessary to facilitate the aspiration of outside tears into the fluid reservoir when necessary to prevent lens suction. This degree of design customization facilitates the maintenance of its expanded, oxygenated precorneal tear film, with no corneal touch and virtually no lens movement—all of which are critical to the effectiveness of this device in eyes with severe ocular surface disease. (More detailed descriptions of the special design features of the BLSPD are available on our Web site: http://www.bostonsight.org.)

Patients with ocular manifestations of cGvHD are typically referred for BSLPD fitting by their treating ophthalmologists or oncologists after failure of conventional therapy. In 2004, we noted a steep increase in the number of patients with this condition referred to us compared with the prior year and undertook this study to better understand the role of the BSLPD in this subpopulation. We report results in our first 33 patients who were fitted with this lens as treatment for severe dry eye in cGvHD.

MATERIALS AND METHODS

All patients fitted with the BSLPD provided informed consent regarding the risks and benefits of wearing this device. The work conducted is HIPAA compliant.

The BSLPD is fabricated from either of 2 high gas-permeable fluorosilicone-acrylate polymers (dk 85 or 127 × 10^{-11} cm^2 ml O_2/s mL mm Hg [ISO/Fatt]) by using internally developed CAD-CAM design/lathe technology to customize the bearing surface of the haptic and vaulting optic and to create venting channels when necessary. Diameters ranged from 15 to 23 mm. The vaulted optic zone avoids all contact with the cornea. Adequacy of fit is determined by direct assessment of corneal clearance with the slit beam and inspection of the vascular compression patterns under the haptic-bearing surface. The fitting process includes evaluation of fit, ventilation, and subjective tolerance after 1, 3–4, and 6–8 hours of lens wear. Once the initial fitting process is completed, patients typically return for fit checks at intervals of 1 and 6 months or as problems arise. Most return yearly for reevaluation of fit.

A list of consecutive patients with cGvHD who were fitted with the BSLPD between December 2002 and February 2005 (n = 33) was extracted from our patient database. These patients were mailed a survey form (Appendix 1) between November 2004 and February 2005 regarding their symptoms in the worse eye, quality of life, and activities of daily living after being fitted with the BSLPD. If there was no reply, the survey was conducted by telephone. A survey response was obtained from every patient. The patient population was characterized in more detail by retrospective database and chart review. The survey responses were tabulated. Medical records and survey responses were reviewed for complications of contact lens wear.

RESULTS

The age and sex distribution of the 33 patients fitted with the BSLPD is presented in Table 1. All patients had been treated previously with various conventional therapies including punctal occlusion, topical cyclosporine, topical and systemic steroids, and partial tarsorrhaphy, as described in Table 1. The period of daily lens wear (range, 1 week to 24 months) at the time of the completion of the survey is also described in Table 1. This period was defined as the interval between dispense date and survey date. Lenses were dispensed after the initial fitting and training, which sometimes can be both prolonged and delayed by medical or logistical reasons.

TABLE 1. Patient Characteristics

Sex	n		
M	17		
F	16		
Age (y)	n		
20–29	3		
30–39	6		
40–49	6		
50–59	13		
60–69	4		
70–79	1		
Previous therapy	Yes	No	Indeterminate
Punctal occlusion	26	3	4
Restasis	25		8
Topical steroid	11	—	22
Systemic steroid	21	—	12
Partial tarsorrhaphy	3	30	—
Period of daily lens wear	n		
1–4 wk	5		
1 to <3 mo	6		
3 mo to <1 y	16		
1 to <2 y	5		
>2 y	1		

Nearly all patients (97%) reported reduction in eye pain in the worse eye, with more than half (52%) choosing the highest category of reduction in pain offered (Table 2). Ninety-four percent of patients reported improvement in photophobia in the worse eye, with 63% reporting the highest level of improvement or total resolution of this symptom (Table 2).

Patients were also surveyed regarding the performance of activities of daily living and their general quality of life. All patients responded to the question regarding quality of life, with 97% reporting improvement and more than two thirds (73%) selecting the highest level of improvement (Table 3). Of those who reported on driving, 92% (22/24) had improvement after treatment with the lens, with more than half of reporters (63%) reporting the highest level of improvement. Of those who reported on reading, 93% (26/28) reported improvement, with 61% reporting the highest level of improvement (Table 3).

None of the 33 patients developed infectious keratitis during the survey period, as ascertained by chart and survey review. One patient, who had a failing, nonepithelializing graft at the time of fitting, eventually developed diffuse corneal neovascularization of multiple possible etiologies. Two other patients had notation of a sector of increased peripheral superficial corneal neovascularization in the setting of additional predisposing factors.

At the time of the follow-up survey, 2 of 33 patients were not wearing their lenses on a regular daily-wear basis. One had discontinued regular wear because the lenses offered no improvement, and another had discontinued lens wear because of gradual improvement in eye symptoms over the prior 4 months. These patients responded to the survey from their experience with lens wear.

DISCUSSION

Patients suffering from ocular cGvHD present a challenge to their oncologists and ophthalmologists. Some patients with severe dry eye from cGvHD progress to sight-threatening corneal surface breakdown, ulceration, and melting, despite intensive and attentive care. Although avoiding these complications may be considered successful treatment, many patients who do not suffer ulceration are nevertheless disabled by pain and photophobia that persist despite conventional therapy with lubricants, punctal occlusion, and topical and systemic immunosuppression.

TABLE 2. Results: Symptoms

Eye pain	n = 33
Same	1
Slightly reduced	1
Slightly to moderately reduced	0
Moderately reduced	4
Moderately to greatly reduced	10
Greatly reduced	17 (17/33 = 52%)
Photophobia	n = 32
None at baseline	1
No answer	1
No improvement	1
Slight improvement	4
Mild improvement	2
Moderate improvement	4
Great improvement	18
Resolved	2
Great improvement or resolved	20/32 (63%)

TABLE 3. Results: Quality of Life and Activities of Daily Living

Quality of life	n = 33
Unchanged	1
Slight improvement	2
Moderate improvement	6
Great improvement	24 (24/33 = 73%)
Driving	n = 24
Did not report on activity	9
No improvement	2
Slight improvement	2
Moderate improvement	5
Outstanding improvement	15 (15/24 = 63%)
Reading	n = 28
Did not report on activity	5
No improvement	2
Slight improvement	1
Moderate improvement	8
Outstanding improvement	17 (17/28 = 61%)

Ophthalmologists may be reluctant to recommend any sort of contact lens in patients with cGvHD precisely because the eyes are dry and tend toward corneal epithelial breakdown and because many of these patients are immunosuppressed. It is counterintuitive that wearing a large hard, plastic device on the surface of a painful, photophobic eye would be beneficial unless one appreciates that the BSLPD creates an expanded precorneal tear film.

The initial goal in fitting patients with cGvHD with the BSLPD was to improve and maintain the integrity of the ocular surface. Bandage soft contact lenses have a therapeutic role in the relief of symptoms from ocular surface disease, such as recurrent erosion and in traumatic corneal abrasions.[12,13] What was unexpected was the immediate and striking relief of pain and photophobia that the patients reported after insertion of the initial trial BSLPD, even in the absence of a frank epithelial defect. Moreover, as patients returned for follow-up examinations during the fitting process, they reported marked improvement in their activities of daily living. It was for this reason that we decided to survey patients after dispensing optimally fitted devices.

We report that the BSLPD shows a striking benefit in the treatment of pain and photophobia symptoms and in improvement of quality of life. That these patients persevere in mastering the challenging insertion and removal process is a testament to the overriding subjective benefits of the BSLPD. More than 90% of this cohort found enough benefit to persist in BSLPD wear (we report 2 wearing failures among 33 patients fitted), showing the feasibility of this treatment option.

Many patients with ocular cGvHD are like other patients with dry eye whose ocular symptoms can be disproportionate to their clinical signs.[14] Severity of symptoms was the principal criterion for fitting these patients, even in the absence of clinical signs. This study was designed to assess the effect of this device on these symptoms. Study and analysis of the therapeutic effect of the BSLPD on the clinical signs of cGvHD was beyond the scope of this study.

Our findings may be subject to potential sources of bias from our survey approach and our instrument. Retrospective surveys such as ours may be subject to recall bias. Our high rate of success and low rate of wearing failures may reflect selection bias because our study design tracked only patients fitted with the lens and not those who were determined not to be candidates at time of consultation, those who decided not to pursue lens fitting despite being candidates, and those who were fitting failures. Furthermore, we have no control group for comparison.

Also, our patient population, most of whom were referred after exhausting conventional treatment regimens elsewhere, may be enriched by those whose ocular cGvHD is particularly symptomatic or by those who are inclined to perceive benefit from this intervention that they may have traveled great distance to receive. A larger treatment effect may be seen in this group than in other ocular surface disease populations. Some of these factors may be eliminated as the BSLPD becomes more universally available. We have satellite fitting centers currently in development at tertiary eye care facilities, domestically and abroad at the Doheny Eye Institute in Los Angeles, the Cullen Eye Institute in Houston, and in India and Japan.

In our ongoing work, we are surveying all ocular surface disease patients prospectively, before lens fitting, and again after a fixed interval, by using a validated survey instrument, the VFQ-25.[15] We hope to use this more complete dataset, which will include analysis of early dropouts, to understand which patient groups are most likely to benefit from our lens.

The physiologic mechanism through which the BSLPD relieves pain and photophobia remains to be shown. Dysfunctional tear syndromes characterized by the pain and photophobia, including cGvHD, probably share pathologic neurogenic and immunologic mechanisms.[16,17] There is evidence in animal models that environmental stressors such as hyperosmolarity[18] and desiccation[19,20] can induce an inflammatory response and contribute to apical corneal barrier disruption.[21] The BSLPD creates an expanded precorneal tear film or "liquid bandage" that modifies the environment at the corneal surface. It is plausible that the BSLPD reduces hyperosmolarity, desiccation, and shear forces from the lids. This reduction in local insult modifies normal and, for cGvHD, pathologic neurogenic and immunologic responses at the ocular surface. This modification of responses may account for the mitigation of symptoms and the improved quality of life that we report in this group of patients.

REFERENCES

1. Balaram M, Rashid S, Dana R. Chronic ocular surface disease after allogeneic bone marrow transplantation. *Ocul Surf.* 2005;3:203–211.
2. Jabs DA, Wingard J, Green WR, et al. The eye in bone marrow transplantation *Arch Ophthalmol.* 1989;107:1343–1348.
3. Ogawa Y, Okamoto S, Wakui M, et al. Dry eye after haematopoietic stem cell transplantation. *Br J Ophthalmol* 1999;83:1125–1130.
4. Rosenthal P, Croteau A. Fluid-ventilated gas-permeable scleral contact lens is an effective option for managing severe ocular surface disease and many corneal disorders that would otherwise require penetrating keratoplasty *Eye Contact Lens.* 2005;31:130–135.
5. Rosenthal P, Cotter JM, Baum J. Treatment of persistent corneal epithelial defect with extended wear of a fluid-ventilated gas-permeable scleral contact lens. *Am J Ophthalmol.* 2000;130:33–41.
6. Kok JHC, Visser R. Treatment of ocular surface disorders and dry eyes with high gas-permeable scleral lenses. *Cornea.* 1992;11:518–522.
7. Tan DTH, Pullum KW, Buckley RJ. Medical application of scleral contact lenses: 1. A retrospective analysis of 343 cases. *Cornea.* 1995; 14:121–129.
8. Tan DTH, Pullum KW, Buckley RJ. Medical application of scleral contact lenses: 2. Gas-permeable scleral contact lenses. *Cornea.* 1995;14: 130–137.
9. Segal O, Barkana Y, Hourovitz D, et al. Scleral contact lenses may help where other modalities fail. *Cornea.* 2003;22:308–310.
10. Pullum KW, Whiting MA, Buckley RJ. Scleral contact lenses, the expanding role. *Cornea.* 2005;24:269–277.
11. Pullum K, Buckley R. Therapeutic and ocular surface indications for scleral contact lenses. *Ocul Surf.* 2007;5:40–48.
12. McDermott ML, Chandler JW. Therpeutic uses of contact lenses. *Surv Ophthalmol.* 1989;33:381–394.
13. Donnenfeld ED, Selkin BA, Perry HD, et al. Controlled evaluation of a bandage contact lens and a topical nonsteroidal anti-inflammatory drug in treating traumatic corneal abrasions. *Ophthalmology.* 1995;102: 979–984
14. Nichols KK, Nichols JJ, Mitchell GL. The lack of association between signs and symptoms in patients with dry eye disease *Cornea.* 2004; 23:762–770.
15. Mangione CM, Lee PP, Gutierrez PR, et al. Development of the 25-item National Eye Institute Vision Function Questionnaire. *Arch Ophthalmol.* 2001;119:1050–1058.

16. Stern ME, Beuerman RW, Fox RI, et al. The pathology of dry eye: the interaction between the ocular surface and lacrimal glands. *Cornea*. 1998; 17:584–589.
17. Gipson IK, Argüeso P, Beuerman R, et al. Research in dry eye: report of the Research Subcommittee of the International Dry Eye Workshop (2007). *Ocul Surf*. 2007;5:179–193.
18. Luo L, Li DQ, Corrales RM, et al. Hyperosmolar saline is a proinflammatory stress on the mouse ocular surface. *Eye Contact Lens*. 2005; 31:186–193.
19. Neiderkorn JY, Stern ME, Pflugfelder SC, et al. Desiccating stress induces T cell-mediated Sjogren's syndrome–like lacrimal keratoconjunctivitis. *J Immunol*. 2006;176:3950–3957.
20. Barabino S, Shen LL, Chen L, et al. The controlled-environment chamber: a new mouse model of dry eye. *Invest Ophthalmol Vis Sci*. 2005;46: 2766–2771.
21. DePaiva CS, Corrales RM, Villareal AL, et al. Apical corneal barrier disruption in experimental murine dry eye is abrogated by methylprednisolone and doxycycline. *Invest Ophthalmol Vis Sci*. 2006;47:2847–2856.