International Results with the Boston Type I Keratoprosthesis

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Purpose: To determine the indications and outcomes of Boston type 1 keratoprosthesis (Massachusetts Eye and Ear Infirmary, Boston, MA) surgery performed outside of North America and to compare them with those obtained in the United States by the surgeon who trained the international surgeons.

Design: Retrospective review of consecutive clinical case series.

Participants: One hundred ninety-four patients (223 keratoprosthesis procedures performed in 205 eyes) who received Boston type 1 keratoprosthesis at 11 ophthalmology centers in Armenia, India, Indonesia, Nepal, Philippines, Russia, and Saudi Arabia between May 1, 2006, and July 1, 2011 (international series), and at the Jules Stein Eye Institute between May 1, 2004, and July 1, 2011 (University of California, Los Angeles [UCLA] series).

Methods: Data were collected for each procedure regarding the preoperative characteristics of each eye, the surgical procedure(s) performed, and the postoperative outcomes. Statistical analysis was performed to identify significant differences between the international and UCLA series in terms of retention and complications.

Main Outcome Measures: Interval visual acuities, keratoprosthesis retention, and significant postoperative complications.

Results: In the international series, 113 Boston type I keratoprostheses were implanted in 107 eyes of 100 patients. The most common indication for surgery was corneal graft failure (n = 50; 44%) followed by chemical injury (n = 30; 27%). Although only 2% of eyes had a preoperative corrected distance visual acuity (CDVA) of 20/20 to 20/200, 70%, 68%, and 59% of eyes had a postoperative CDVA of 20/20 to 20/200 at 6 months, 1 year, and 2 years after surgery, respectively. Ninety-one of the 113 keratoprostheses implanted (80.5%) were retained at a mean follow-up of 14.2 months, for a retention failure rate of 22 per 134.6 eye-years (0.163/eye-year). The most common postoperative complications were retroprosthetic membrane formation (27%) and sterile corneal necrosis (18%). The only postoperative complication that was more common in the international series than in the UCLA series was infectious endophthalmitis, which developed in 9% of eyes.

Conclusions: Boston keratoprosthesis is a viable means of managing repeat graft failure and ocular chemical injury outside of North America, with similar visual acuity outcomes, retention rates, and incidence rates of postoperative complications to those obtained by North American surgeons.

Financial Disclosure(s): The author(s) have no proprietary or commercial interest in any materials discussed in this article. *Ophthalmology 2012;119:1530–1538 © 2012 by the American Academy of Ophthalmology.*

Boston type I keratoprosthesis is the most commonly implanted keratoprosthesis worldwide, with more than 6000 devices implanted to date (*Boston Kpro News*, Fall 2011, no. 8; available at www.masseyeandear.org; accessed January 21, 2012). Approximately 4300 of these procedures have been performed in the United States, whereas 1900 have been performed in approximately 50 countries around the world (Larisa Gelfand, personal communication, October 18, 2011). Although several large single-surgeon, single-center, and multicenter series have been published establishing the indications for and outcomes of Boston keratoprosthesis implantation, all have been published by North American surgeons. A review of the peer-reviewed literature in PubMed (search term, *Boston keratoprosthesis*; accessed October 9, 2011) revealed that the outcomes of Boston keratoprosthesis implantation have been reported in only 32 eyes outside of North America.[1–7] Only 1 of the 8 reports that were identified was a consecutive case series, whereas each of the other reports addressed a specific indication for keratoprosthesis implantation or postoperative complication in a series of 8 or fewer patients. Therefore, essentially nothing is known about the indications for and outcomes of Boston keratoprosthesis surgery outside of North America.

Since 2006, one of the authors (A.J.A.) has traveled to major ophthalmology institutes in 7 different countries to train experienced corneal surgeons in performing Boston keratoprosthesis surgery. Although significant variability

ISSN 0161-6420/12/$–see front matter
doi:10.1016/j.ophtha.2012.02.015

exists between these institutions in terms of climate, geography, causes of corneal opacification, and availability of donor corneal tissue, the indications for surgery, the surgical technique, and the postoperative management that were taught at each were the same as those of the training keratoprosthesis surgeon. The collection of data regarding the indications for and outcomes of more than 100 keratoprosthesis surgeries performed by these experienced corneal surgeons provides invaluable data regarding the feasibility of performing Boston keratoprosthesis surgery in developing and developed countries outside of North America. In addition, a comparison of these procedures with more than 100 procedures performed by the training surgeon at the University of California, Los Angeles (UCLA), provides an opportunity to compare outcomes directly within and outside the United States.

Patients and Methods

After study approval was granted by the institutional review board at UCLA (study nos.: 04-11-058-[01-13], 11-001336), informed consent for the collection and analysis of preoperative and postoperative data from the patient record was obtained from each patient who underwent implantation of a Boston type I keratoprosthesis by one of the authors (A.J.A.) at the Jules Stein Eye Institute between May 1, 2004, and July 1, 2011. Data collection was performed in a manner compliant with the Health Insurance Portability and Accountability Act, and the described research adhered to the tenets of the Declaration of Helsinki. After study approval was granted by the institutional review board at UCLA (study no.: 11-000983), deidentified data were collected from each of the surgeons outside of North America who had been trained to perform keratoprosthesis surgery by one of the authors (A.J.A.).

Preoperative Evaluation

To determine candidacy for keratoprosthesis surgery, a complete ocular history was obtained and a complete ocular examination, including indicated diagnostic testing, was performed for each patient. Additional information was requested of the referring physician or other ophthalmologists involved in the patient's care when this information was deemed relevant to the decision of whether to perform keratoprosthesis implantation and whether additional procedures should be performed either before or at the time of keratoprosthesis implantation. The criteria used to determine candidacy for keratoprosthesis surgery, which have been published previously and are summarized in The Boston Keratoprosthesis International Protocol (The Boston Keratoprosthesis International Protocol, version 2, 2009; available at www.masseyeandear.org; accessed January 21, 2012), were the same outside the United States as they were at UCLA.[8]

Surgical Technique and Postoperative Management

The surgical technique that was used in each country outside of the United States was the same as that of one of the authors (A.J.A.), with minor differences based on each individual surgeon's preferences. All patients were maintained on topical antibiotic prophylaxis after surgery, and most patients were maintained in a bandage soft contact lens indefinitely, unless either contact lens placement or exchange was not possible because of anatomic factors such as the presence of symblepharons or an extensive tarsorrhaphy. In most cases, the bandage soft contact lens was exchanged once monthly by the patient, a family member, or a local eye care provider.

Data Collection and Analysis

Each patient's chart was reviewed and data were collected regarding ocular history, indication for keratoprosthesis implantation, intraoperative information regarding procedures that were performed, and postoperative outcomes, including the development of complications and need for subsequent surgical procedures. Corrected distance visual acuity (CDVA) was recorded at intervals of 6 months (±2 months), 12 months (±2 months), and each year (±2 months) thereafter after surgery. In cases in which a repeat keratoprosthesis was performed, all complications that developed after the first and second keratoprosthesis procedures were documented. In addition, postoperative visual acuities were recorded after the initial, the second, and the third keratoprosthesis procedures for as long as the keratoprostheses remained in place. For repeat keratoprosthesis procedures, visual acuities were recorded in terms of time after the most recent keratoprosthesis implantation, not from implantation of the initial keratoprosthesis. The keratoprosthesis retention failure rate was expressed in terms of the number of implanted keratoprostheses that were removed per eye-years, which was calculated as the cumulative number of years that all keratoprostheses were retained. In eyes in which the keratoprosthesis was removed, the time that it remained in place before removal was included in the cumulative total, as was the time that a replacement keratoprosthesis remained in place, if performed.

Collected data were entered onto a Microsoft Excel spreadsheet (Microsoft, Redmond, WA) for compilation and subsequent analysis. Statistical analysis was performed using SAS software version 9.1 (SAS, Inc., Cary, NC), with P values less than 0.05 considered to be statistically significant. The differences between the international and the UCLA keratoprosthesis series in terms of patient demographics, indications for keratoprosthesis surgery, comorbid ocular conditions, and the percentage of eyes experiencing postoperative complications and requiring postoperative procedures were compared using Fisher exact tests. The difference in the number of corneal transplants performed before keratoprosthesis implantation was compared using the Wilcoxon rank-sum test. A Kaplan-Meier survival analysis was used to evaluate keratoprosthesis retention rates in each series and the differences in the retention rates were compared using the log-rank test.

Results

Demographic Features

A total of 113 Boston type 1 keratoprostheses were implanted in 107 eyes of 100 patients in 7 different countries (Fig 1). Most of the surgeries (59%; 67/113) were performed at 1 of 5 different centers in India. When compared with the UCLA series (110 procedures in 98 eyes of 94 patients), a significantly higher percentage of the patients were male (70% vs. 50%; $P = 0.018$) and were significantly younger (mean, 46 years vs. 63 years; $P = 0.018$; Table 1). The most common indication for keratoprosthesis implantation was failed corneal transplant (44%), although the percentage was significantly lower than that in the UCLA series (64%; $P = 0.005$). The second most common indication was chemical injury (27%), which was significantly higher than the percentage in the UCLA series (7%; $P = 0.0001$; Table 1). Preoperative CDVA ranged from 20/100 to light perception, with vision of counting fingers or worse in 97% of eyes. The mean follow-up after keratoprosthesis implantation (measured after the

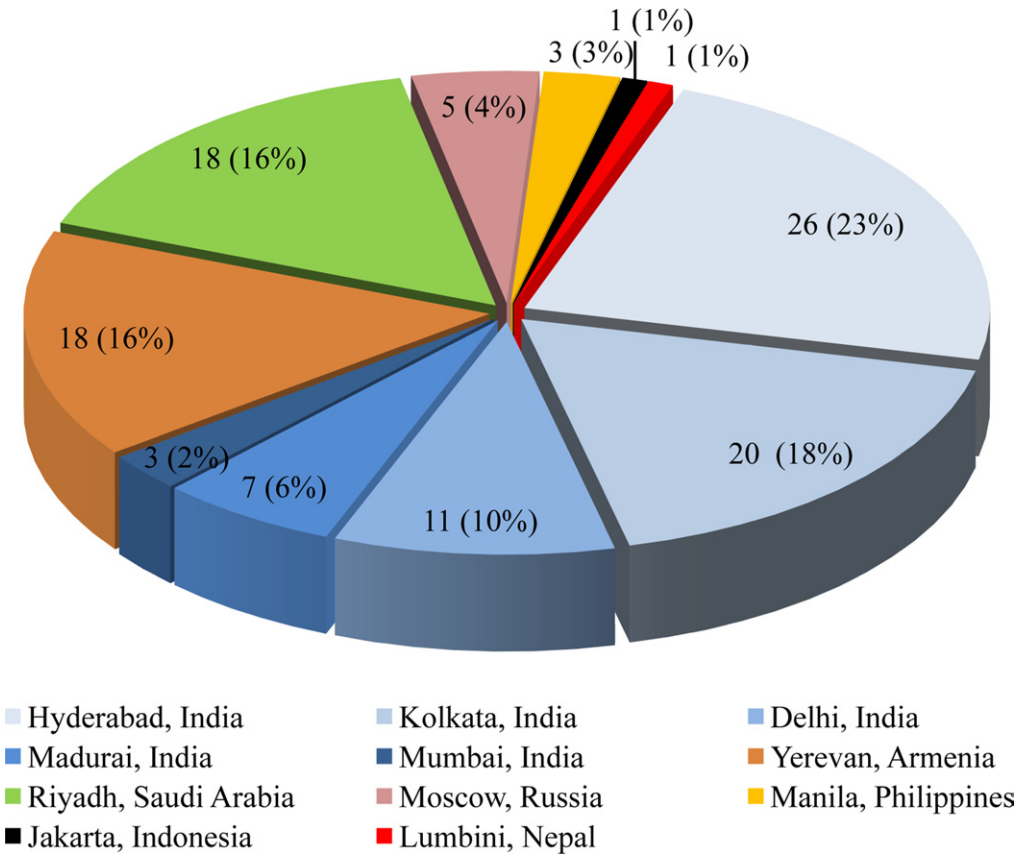

Figure 1. Locations of Boston type I keratoprosthesis procedures performed outside of the United States.

last keratoprosthesis implantation for patients requiring replacement of the keratoprosthesis) was 14.2 months (range, <1.0–48 months).

Comorbid Ocular Conditions and Previous Ocular Surgeries

Glaucoma was the most common comorbid ocular condition present before keratoprosthesis implantation, diagnosed in 43 of 107 eyes (40%; Table 1). However, this percentage is significantly less than the 78% of eyes in the UCLA series diagnosed with preexisting glaucoma (76/98 eyes; $P<0.0001$). Similarly, the percentage of glaucomatous eyes that had undergone trabeculectomy, tube shunt placement, or both before keratoprosthesis implantation (20/107 eyes; 19%) was significantly lower than in the UCLA series (58/98 eyes; 59%; $P<0.0001$).

Although the Boston keratoprosthesis traditionally is considered for patients with a history of repeat corneal transplant failure, a prior corneal transplant had not been performed previously in approximately one third (31%) of eyes, and no or only 1 prior corneal transplant had been performed in approximately two thirds (67%) of eyes (compared with 33% in the UCLA series).

Operative Procedures

Of the 113 keratoprostheses implanted in the international series, 43 (38%) were pseudophakic and 70 (62%) were aphakic. The procedures most commonly performed in conjunction with keratoprosthesis implantation were cataract extraction (45/113; 39.8%), anterior vitrectomy (16/113; 14.2%), tube shunt implantation (13/113; 11.5%), and intraocular lens removal (8/113; 7.1%). No significant intraoperative complications occurred in this series.

A contact lens was placed on the operative eye at the completion of 97% (110/112) of the procedures that were performed (information was not available regarding contact lens placement after 1 procedure). Although the type of contact lens used was not specified for 24 procedures; for those for which it was, a Kontur contact lens (Kontur Kontact Lens Co., Hercules, CA), which is supplied with the Boston keratoprosthesis, was used for 82 of the 86 procedures (95.3%). A silicone hydrogel contact lens was placed after the other 4 procedures. A bandage soft contact lens was not placed after 2 procedures.

Postoperative Outcomes

Visual Acuity. Although only 2% of eyes in the international series had a preoperative CDVA of 20/200 or better, 70%, 68%, and 59% of eyes had a CDVA of 20/200 or better 6 months, 1 year, and 2 years, respectively, after keratoprosthesis implantation (Table 2). More than 50% of eyes demonstrated a CDVA of 20/20 to 20/100 at 6 months, 1 year, and 2 years after surgery, and 29% of eyes had a CDVA of 20/20 to 20/50 at each of these time points. When the visual outcomes in the international series are compared with those in the UCLA series, it can be seen that the percentages of eyes that had CDVAs of 20/20 to 20/50, 20/20 to 20/100, and 20/20 to 20/200 at 6 months, 1 year, and 2 years after surgery are very similar (Table 2). The small number of eyes in the international series with CDVA recorded more than 2 years after keratoprosthesis surgery prevents a comparison with the visual outcomes

Table 1. Preoperative Characteristics of Patients Undergoing Boston Keratoprosthesis Implantation

	International	University of California, Los Angeles	*P* Value*
No. of procedures	113	110	
No. of eyes	107	98	
No. of patients	100	94	
Gender (female; male)	30; 70	44; 50	0.018
Mean age (range), yrs	46 (4–86)	63 (15–95)	
Follow-up (mos)			
Mean	14.2	24.1	
Median	12.2	20.4	
Standard deviation	11.5	19.5	
Range	0–48	0–84	
Indication for keratoprosthesis			
Failed corneal transplant	50 (44%)	70 (64%)	0.005
Chemical injury	30 (27%)	8 (7%)	0.0001
Stevens-Johnson syndrome	9 (8%)	6 (5%)	0.59
Repeat keratoprosthesis	6 (5%)	13 (12%)	0.096
Mucus membrane pemphigoid	6 (5%)	0	0.029
Thermal injury	3 (3%)	0	0.25
Herpetic keratitis	3 (3%)	0	0.25
Infectious keratitis	2 (2%)	0	0.50
Limbal stem cell deficiency	2 (2%)	6 (5%)	0.17
Corneal vascularization	1 (1%)	1 (1%)	1.00
Aniridia	1 (1%)	4 (4%)	0.21
AKC	0	2 (2%)	0.24
Glaucoma	43 (40%)	76 (78%)	<0.0001
Previous glaucoma surgery	20 (19%)	58 (59%)	<0.0001
Previous corneal transplant(s)			<0.0001†
None	33 (31%)	16 (16%)	
1	38 (36%)	17 (17%)	
2	20 (19%)	31 (32%)	
3	12 (11%)	18 (18%)	
4 or more	3 (3%)	16 (16%)	
Unknown	1 (1%)	0	

AKC = atopic keratoconjunctivitis.
*Fisher exact test.
†Comparing 1 or fewer to 2 or more.

at these time points with those in the UCLA series. However, an increasing trend was observed in the international series in the percentage of eyes returning to the level of light perception after surgery. Although 50% of patients in the international series demonstrated a preoperative CDVA of light perception, this percentage decreased to 13% at 6 months after surgery, then increased at each subsequent follow-up point, eclipsing the preoperative percentage at 3 years, when 6 of 10 eyes (60%) had a CDVA of light perception. In 82.2% (74/90) of the eyes in the international series in which the keratoprosthesis was retained at the final follow-up visit, the final postoperative CDVA was better than the preoperative CDVA, and in 13.3% (12/90) of eyes, the preoperative and postoperative CDVAs were the same. In 4 eyes (4.4%), the final postoperative CDVA was worse than the preoperative CDVA (counting fingers to light perception; counting fingers, hand movements, and light perception to no light perception).

Complications. The most common postoperative complications in the international series were retroprosthetic membrane formation (26.7% of eyes), sterile corneal stromal necrosis (17.8% of eyes), and elevated intraocular pressure (13.9%; Table 3). Correspondingly, 3 of the 4 most commonly performed procedures after keratoprosthesis implantation were yttrium–aluminum–garnet laser membranotomy (9.9% of eyes), keratoprosthesis replacement (20.8% of eyes), and glaucoma surgery (8.9% of eyes). The diagnosis of a retroprosthetic membrane was made based on the development of a vascular or avascular membrane on the posterior surface of the keratoprosthesis optic, and an yttrium–aluminum–garnet laser or surgical membranotomy was performed when the membrane was considered visually significant. The development of a corneal infiltrate presumed to represent an infectious keratitis was observed in 12 eyes (11.9%). Each of the infiltrates was cultured, with bacterial growth identified in 4, fungal growth in 2, and both bacterial and fungal growth in 1. Several of the most common postoperative complications developed in a significantly lower percentage of eyes in the international series than in the UCLA series: retroprosthetic membrane formation, persistent corneal epithelial defect formation, and retinal detachment (includes retinal detachments that were observed or suspected to be present before keratoprosthesis surgery as well; Table 3).

Infectious endophthalmitis was the only complication that developed in a significantly higher percentage of eyes in the international series (8.9%; 9/101) than in the UCLA series (1.1%; 1/94; $P = 0.019$), developing at an average of 5.9 months after surgery (range, 0.8–11.3 months). Keratoprostheses were removed at the time that endophthalmitis was diagnosed in 5 of the 9 eyes, and vitreous taps were performed in 4 eyes, including 3 of the 4 in which the keratoprosthesis was retained. Cultures of the intraocular contents were collected for 5 of the eyes diagnosed with endophthalmitis: 2 demonstrated growth of *Candida* species, whereas the other 3 cultures did not demonstrate the growth of any organisms. Two of the cases of endophthalmitis were associated with corneal infiltrates, one of which was a *Candida* endophthalmitis that was associated with a corneal ulcer that also demonstrated positive culture results for *Candida* species. At the time that fungal keratitis (2.7 months after surgery), endophthalmitis (2.9 months after surgery), or both (4.6 months after surgery) were diagnosed, each of the 3 eyes was maintained on topical moxifloxacin, vancomycin, and a Kontur contact lens, but none had received prophylactic antifungal therapy.

Retention. Of the 113 keratoprostheses that were implanted in 107 eyes, 22 were removed from 20 eyes of 19 patients, with the time from implantation to removal averaging 6.43 months (range, 0.8–15.7 months). Eight of the 22 keratoprostheses that were removed were placed for the management of graft failure, whereas 7 were removed from eyes with a history of prior chemical injury. In 6 of the 20 eyes from which keratoprostheses were removed, another Boston type I keratoprosthesis was placed. The retention of 80.5% of implanted keratoprostheses at the final follow-up, with a mean follow-up of 14.2 months (range, 0.03–48.1 months) and a cumulative 133.4 years of follow-up, corresponds to a retention failure rate of 0.165/eye-year (Table 4). Although the number of retention failures (n = 22) and the percentage of implanted keratoprostheses retained at final follow-up (80%) was the same in the international and UCLA series, the longer mean follow-up in the UCLA series resulted in a lower retention failure rate of 0.100/eye-year in the UCLA series. Although the cumulative proportion of keratoprostheses retained was higher in the UCLA series than in the international series 1 year after surgery (91.7% vs. 79.2%), the difference between the 2 series was minimal 2 years after surgery (78.4% vs. 74.6%) and essentially was the same 3 years after surgery (74.5% vs. 74.6%; Fig 2 and Table 5). To determine whether the difference in the retention failure rate between the 2 series was associated with the significant difference in the percentage of eyes for which the indication for surgery was graft failure and chemical injury, the retention failure rate was determined for both indications. Although 8 retention failures in both the international and UCLA series occurred in eyes for which graft failure

Table 2. Preoperative and Postoperative Visual Acuities at Specific Follow-up Time Points

	Baseline	6 Months	1 Year	2 Years	3 Years	4 Years	5 Years
No. of eyes							
UCLA	98	91	77	47	31	16	7
International	107	87	65	34	10	4	1
20/20–20/50							
UCLA	0	27 (30%)	26 (34%)	16 (34%)	12 (39%)	6 (38%)	3 (43%)
International	0	25 (29%)	19 (29%)	10 (29%)	1 (10%)	1 (25%)	0
20/60–20/100							
UCLA	0	27 (30%)	16 (21%)	6 (13%)	2 (7%)	2 (13%)	2 (28%)
International	1 (1%)	20 (23%)	14 (22%)	8 (24%)	2 (20%)	0	0
20/200							
UCLA	6 (6%)	8 (9%)	6 (8%)	6 (13%)	5 (16%)	4 (25%)	0
International	1 (1%)	16 (18%)	11 (17%)	2 (6%)	0	0	0
20/400							
UCLA	5 (5%)	4 (4%)	2 (3%)	1 (2%)	0	1 (6%)	0
International	1 (1%)	4 (5%)	2 (3%)	2 (6%)	0	0	0
CF							
UCLA	40 (41%)	15 (17%)	13 (17%)	6 (13%)	3 (10%)	2 (13%)	0
International	33 (31%)	8 (9%)	4 (6%)	2 (6%)	1 (10%)	0	0
HM							
UCLA	38 (39%)	6 (7%)	8 (10%)	10 (21%)	5 (16%)	0	1 (14%)
International	18 (17%)	1 (1%)	2 (3%)	2 (6%)	0	0	0
LP							
UCLA	9 (9%)	3 (3%)	4 (5%)	1 (2%)	3 (10%)	1 (6%)	1 (14%)
International	53 (50%)	11 (13%)	11 (17%)	7 (21%)	6 (60%)	3 (75%)	1 (100%)
NLP							
UCLA	0	1 (1%)	2 (3%)	1 (2%)	1 (3%)	0	0
International	0	2 (2%)	2 (3%)	1 (3%)	0	0	0

CF = counting fingers; HM = hand movements; LP = light perception; NLP = no light perception; UCLA = University of California, Los Angeles.

was the indication for surgery, the longer follow-up in the UCLA series led to a lower retention failure rate compared with the international series (0.054/eye-year vs. 0.129/eye-year; $P = 0.08$), although the difference was not statistically significant (Table 4). In addition, although a marked difference also was observed between the 2 series in the retention failure rate in eyes with a history of chemical injury (0.187/eye-year in the international series and 0.048/eye-year in the UCLA series), the difference was not statistically significant ($P = 0.47$).

Discussion

This article reports the indications for surgery, the incidence of postoperative complications, the keratoprosthesis retention failure rate, and visual outcomes up to 5 years after implantation of the Boston keratoprosthesis in patients from 7 countries outside of North America. The comparison of these 113 procedures with 110 procedures performed by the surgeon who traveled to each of these countries to train experienced corneal surgeons to implant the Boston type I keratoprosthesis represents the largest multicenter series reported to date, and the first series of more than a dozen patients outside of North America. Although corneal transplant failure was the most common indication for keratoprosthesis implantation in both series, it was a significantly less common indication in the international series compared with the UCLA series. Conversely, chemical injury was a significantly more common indication for surgery in the international series, a fact that must be kept in mind when evaluating the outcomes of keratoprosthesis implantation in the international series, because previous chemical injury has been shown to be associated with an increased retention failure rate and incidence of postoperative complications.[9] It was interesting to observe the significant differences between the 2 series in terms of the percentage of eyes with a history of glaucoma, glaucoma surgery, and number of prior corneal transplants (1 or fewer compared with 2 or more). Although it may be assumed that the lower incidence of glaucoma in the international series would be associated with a lower incidence of elevated intraocular pressure after surgery, the difference in the percentage of eyes between the 2 series in which elevated intraocular pressure developed after surgery was not significantly different. In addition, although the authors previously demonstrated better visual outcomes in eyes with fewer corneal procedures before keratoprosthesis implantation, the significantly greater percentage of eyes in the international series with a history of fewer than 2 previous corneal transplants was not associated with superior visual outcomes.[10]

That a similar percentage of eyes in both series obtained and maintained CDVA of 20/20 to 20/200 up to 2 years after surgery confirms the efficacy of the Boston keratoprosthesis in restoring and maintaining vision in most recipients. The observation that the percentage of eyes that regain vision of 20/20 to 20/100 after surgery remains constant up to 2 years after surgery indicates that the postoperative

Table 3. Postoperative Complications and Secondary Surgical Procedures

	International	University of California, Los Angeles	*P* Value*
No. of eyes with >1 mo of follow-up	101	94	
Retroprosthetic membrane	26.7% (27)	48.9% (46)	0.002
YAG laser membranotomy	9.9% (10)	34.0% (32)	<0.0001
Surgical membranectomy	4.0% (4)	7.4% (7)	0.36
Sterile corneal stromal necrosis	17.8% (18)	16.0% (15)	0.85
Keratoprosthesis replacement	20.8% (21)	18.1% (17)	0.72
Elevated IOP (>25 mmHg)	13.9% (14)	20.2% (19)	0.26
Glaucoma surgery	8.9% (9)	6.4% (6)	0.60
Corneal infiltrate	11.9% (12)	9.6% (9)	0.65
Persistent epithelial defect	9.9% (10)	36.2% (34)	<0.0001
Tarsorrhaphy	12.9% (13)	21.3% (20)	0.13
Infectious endophthalmitis	8.9% (9)	1.1% (1)	0.019
Vitreous tap and injections	6.9% (7)	11.7% (11)	0.32
Retinal detachment	5.0% (5)	16.0% (15)	0.017
Repair of retinal detachment	2.0% (2)	9.6% (9)	0.029
Sterile vitreitis	4.0% (4)	10.6% (10)	0.096
CME	3.0% (3)	9.6% (9)	0.074
Intravitreal injection	1.0% (1)	5.3% (5)	0.11

CME = cystoid macular edema; IOP = intraocular pressure; YAG = yttrium–aluminum–garnet.
*Fisher exact test.

development of complications associated with loss of vision, such as retroprosthetic membrane formation, glaucoma, retinal detachment, sterile vitreitis, and cystoid macular edema, do not result in loss of vision in a significant percentage of eyes. As this study demonstrates, for the 84% of eyes in which the keratoprosthesis was retained at the final follow-up visit, the final postoperative CDVA was worse than the preoperative CDVA in fewer than 5% of eyes. However, the increasing percentage of eyes at each postoperative time point that returned to the preoperative level of light perception vision indicates that continued monitoring of postoperative visual outcomes is indicated. Given the small number of eyes in the international series with follow-up of more than 2 years, it could not be determined whether the percentage of eyes that return to light perception vision will continue to increase with increased length of postoperative follow-up.

It was encouraging that endophthalmitis was the only postoperative complication that developed in a significantly higher percentage of eyes in the international series than in the UCLA series. Although the 8.9% of eyes in which endophthalmitis developed was significantly higher than the 1% (1/98 eyes) in the UCLA series and the multicenter Boston type I keratoprosthesis study (0%; 0/136 eyes),[11] it is lower than the percentage reported in 2 other single-center series from the United States (11.4% [4/35 eyes]; 12.5% [5/40 eyes]).[12,13] However, the differential length of follow-up between these series and the reporting of complications in terms of percentage of eyes rather than as rates (which takes length of follow-up into account) prevents a direct comparison of the risk of endophthalmitis and other postoperative complications within and outside of North America. Even if all authors reported complications as rates in terms of eye-years, the fact that the risk of developing each complication is not constant over time, as has been demonstrated previously,[8] indicates that even controlling for different lengths of follow-up between series may not allow an unbiased comparison of the incidence of postoperative complications between various centers or countries. In addition, although significant postoperative complications such as endophthalmitis and stromal necrosis with corneal perforation may be assumed to be recognized and reported uniformly, less significant complications, such as persistent corneal epithelial defect formation and cystoid macular edema, may be underrecognized and therefore underreported. A clinician who does not have ready access to diagnostic imaging methods, such as optical coherence tomography (OCT) to diagnose cystoid macular edema or B-scan ultrasonography to diagnose a retinal detachment, or who does not remove the contact lens during each postoperative visit to evaluate for the presence of a corneal epithelial defect will not report these complications as frequently as one who does. This may explain the significantly greater percentage of eyes in the UCLA series that were diagnosed with each of these postoperative complications. Given the significantly increased risk of developing infectious keratitis, stromal necrosis, or both in the setting of a persistent corneal epithelial defect after keratoprosthesis surgery,[10] all keratoprosthesis surgeons are encouraged to evaluate for and aggressively manage persistent corneal epithelial defects. In addition, because intraocular cultures were collected from only 5 of the 9 eyes in the international series in which infectious endophthalmitis developed, all keratoprosthesis surgeons are strongly encouraged to obtain aqueous or vitreous aspirates, or both, when a presumptive clinical diagnosis of either sterile or infectious endophthalmitis is made. Only when the pathogenic organisms are identified can evidenced-based decisions be made regarding whether a surgeon's preferred postoperative prophylactic antimicrobial regimen is appropriate.

Table 4. Keratoprosthesis Retention Failure Rate

	International	University of California, Los Angeles	*P* Value
Percentage of keratoprostheses retained	91 of 113 (80.5%)	88 of 110 (80.0%)	
Mean follow-up (mos)	14.2	24.1	
Retention failure rate			
All eyes	22 per 133.4 eye-years, 0.165/eye-year	22 per 220.9 eye-years, 0.100/eye-year	0.24
Graft failure	8 per 62.1 eye-years, 0.129/eye-year	8 per 148.1 eye-years, 0.054/eye-year	0.08
Chemical injury	7 per 37.5 eye-years, 0.187/eye-year	1 per 20.9 eye-years, 0.048/eye-year	0.47

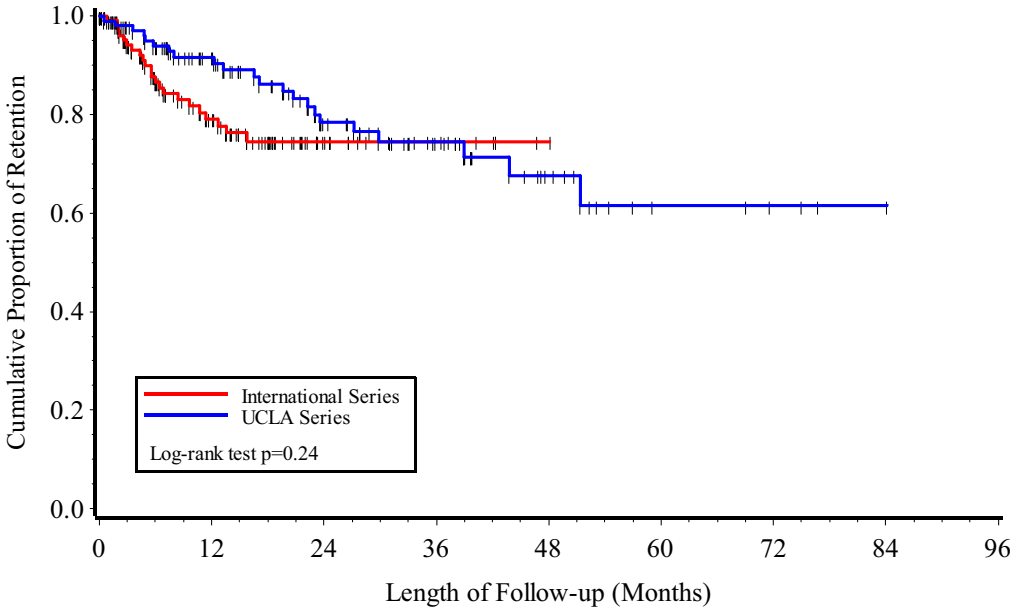

Figure 2. Kaplan-Meier survival curves demonstrating cumulative percentage of keratoprostheses retained up to 48 months in the international series and 84 months in the University of California, Los Angeles (UCLA) series.

Although the percentage of keratoprostheses retained at the last follow-up visit in the international and UCLA series was the same, the keratoprosthesis retention failure rate in the international series was higher than that in the UCLA series. The difference in the retention failure rate between the 2 series cannot be attributed to the significantly higher percentage of eyes in the international series with a history of chemical injury compared with the UCLA series, because a higher retention failure rate for both repeat graft failure and chemical injury in the international series was shown. The lower incidence of retention failure in the UCLA series may be the result of a number of factors, including earlier diagnosis and management of persistent corneal epithelial defects and greater patient adherence to the prescribed medication and contact lens regimen. Because it is difficult to determine patient compliance with the prescribed topical medications accurately, critical evaluation for an association between medication noncompliance and retention failure was not possible. Although compliance with postoperative follow-up visits may be determined more easily than compliance with prescribed medication regimens, the shorter length of follow-up for eyes in which the keratoprosthesis was removed and the greater the chance of missing an appointment with increasing length of follow-up complicates attempts to evaluate for an association between missing appointments and keratoprosthesis retention failure. However, of the 22 keratoprosthesis retention failures in each series, only 1 in the UCLA series and none in the international series occurred in a patient who missed a 1-month, 6-month, or annual follow-up examination. Thus, noncompliance with follow-up examinations does not seem to be a risk factor for keratoprosthesis retention failure. In addition, although data were collected regarding whether a contact lens was in place at each follow-up visit, an ob-

Table 5. Annual Number of Keratoprosthesis Cases at Risk and Cumulative Proportion of Retention in the International and University of California, Los Angeles Series

	International		University of California, Los Angeles	
Follow-up (mos)	*No. of Cases at Risk*	*Cumulative Proportion of Retention**	*No. of Cases at Risk*	*Cumulative Proportion of Retention**
0	113	100%	110	100%
12	58	79.2% (69.2%–86.3%)	74	91.7% (84.1%–95.8%)
24	18	74.6% (63.8%–82.7%)	45	78.4% (67.2%–86.2%)
36	8	74.6% (63.8%–82.7%)	29	74.5% (62.3%–83.2%)
48	1	74.6% (63.8%–82.7%)	14	67.7% (52.8%–78.8%)
60	0	—	5	61.6% (43.0%–75.7%)
72	0	—	3	61.6% (43.0%–75.7%)
84	0	—	1	61.6% (43.0%–75.7%)

— = indicates no data.
*95% confidence interval shown in parentheses.

served association between failure to wear a contact lens and keratoprosthesis retention failure is not necessarily indicative of a causal relationship between the two. As has been pointed out previously, conditions associated with an impaired ability to maintain a contact lens, such as forniceal foreshortening and symblepharon formation, are associated with chronic cicatrizing conditions (including Stevens-Johnson syndrome and mucus membrane pemphigoid) that are known to be associated with an increased retention failure rate.[10]

Based on the visual acuity, postoperative complications, and retention data presented, the Boston keratoprosthesis is an effective means of improving vision in most selected patients who are considered poor candidates for either initial or repeat traditional corneal transplantation, both within and outside of the United States. The series of 113 Boston keratoprosthesis procedures performed in 7 countries represents approximately 6% of all keratoprosthesis procedures performed outside of the United States and thus may be considered a reliable representation of the expected outcomes of keratoprosthesis surgery outside of North America. It is important to emphasize that the surgeries were performed by experienced corneal surgeons in major ophthalmology centers after receiving formal didactic instruction in patient selection, surgical technique, and management of postoperative complications as part of a keratoprosthesis training course. In addition, by virtue of their practicing in major ophthalmology centers, these corneal surgeons also had ready access to the expertise and assistance of glaucoma, retina, and oculoplastics specialists, whose involvement in the management of keratoprosthesis patients is essential to optimizing patient outcomes. Thus, the authors strongly encourage experienced corneal surgeons throughout the world who are interested in beginning a keratoprosthesis program to attend one of the formal instruction courses on the Boston keratoprosthesis that are held at many of the international ophthalmology meetings. In addition, interested surgeons are recommended to arrange either to observe an experienced keratoprosthesis surgeon perform surgery or to have an experienced keratoprosthesis surgeon assist them with their initial keratoprosthesis procedure(s). All keratoprosthesis surgeons also are strongly encouraged to monitor the results of the keratoprosthesis surgeries that they perform and to consider submitting deidentified data regarding their outcomes to a centralized, web-based database such as the KPro Study Group keratoprosthesis database. Such ongoing monitoring of outcomes data is essential to permit keratoprosthesis surgeons to be able to make evidence-based decisions regarding patient selection, surgical technique, management of comorbid conditions, and prevention and management of postoperative complications. Although this report provides initial evidence that Boston keratoprosthesis is a viable means of restoring functional vision to most recipients outside of North America, larger numbers of patients and longer follow-up are needed to develop customized management regimens for each locale based on the varied indications for surgery and the regional, cultural, environmental, and economic factors that may influence postoperative outcomes.[14]

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Footnotes and Financial Disclosures

Originally received: December 19, 2011.
Final revision: January 23, 2012.
Accepted: February 8, 2012.
Available online: April 19, 2012. Manuscript no. 2011-1815.

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Financial Disclosure(s):
The author(s) have no proprietary or commercial interest in any materials discussed in this article.

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