



TECHNICAL NOTE

The Boston keratoprosthesis provides a wide depth of focus

Rony R. Sayegh^{1,2}, Claes H. Dohlman², Scott H. Greenstein² and Eli Peli²

¹University Hospitals Eye Institute, University Hospitals Case Medical Center, Case Western Reserve University School of Medicine, Cleveland, USA, and ²Schepens Eye Research Institute, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, USA

Citation information: Sayegh RR, Dohlman CH, Greenstein SH & Peli E. The Boston keratoprosthesis provides a wide depth of focus. *Ophthalmic Physiol Opt* 2015; **35**: 39–44. doi: 10.1111/opo.12181

Keywords: depth of focus, keratoprosthesis, optics, refraction, through-focus

Correspondence: Eli Peli
E-mail address: eli_peli@meei.harvard.edu

Received: 24 September 2014; Accepted: 3 November 2014; Published Online: 25 November 2014

Abstract

Purpose: To measure the through-focus curve for eyes implanted with a type 1 Boston keratoprosthesis (KPro) and compare it to that of pseudophakic controls with fixed pupil sizes. The results should assist in evaluating postoperative visual quality after surgery. They should also help to determine the necessary KPro inventories in terms of refractive power steps.

Methods: Autorefractometry and manifest refraction were performed on all eyes. The monocular through-focus acuity curve was plotted in reference to the best-corrected visual acuity by spectacle plane defocus ranging from +5.00 to –5.00 dioptres in 0.50 dioptre increments. These measurements were obtained on KPro-implanted eyes, pseudophakic eyes as controls, and on the same control eyes after fixing the pupil diameter to 3 and 2 mm using black painted iris contact lenses.

Results: Ten KPro eyes and five control eyes were included. Good agreement was noted between the subjective refractions and autorefractometry in KPro eyes. The average through-focus curve for the control eyes was significantly steeper than that of the KPro curve, but became comparable after fixing the control pupil to 2 and 3 mm.

Conclusion: The KPro's wide depth-of-focus makes the visual acuity less dependent on an exact refractive correction at distance and explains the 'pseudoaccommodation' experienced by these patients. This is primarily due to the small pupil diameter of the KPro. The current manufacturing steps in 0.50 dioptre increments appears to be sufficient.

Introduction

Depth-of-focus is a clinically important concept that affects the tolerance for error in refractive correction needed for best-corrected acuity. It reflects the minimal amount of defocus and blur that can be detected by an eye.¹ In some pseudophakic patients with a monofocal intraocular lens, it has been shown to be responsible for the ability to enjoy satisfactory visual acuity at both near and distance, or 'pseudoaccommodation'.² Multiple factors have been found to influence the depth-of-focus of the eye.³ An increased depth-of-focus has been observed with a smaller pupil, poorer visual acuity, increased age, higher myopic refraction, increased corneal aberrations, and increased retinal eccentricity.⁴ Aperture size is the main

factor influencing the depth-of-focus of optical systems, including the human eye. Under fixed test chart luminance, the optimal Snellen acuity is achieved with a 3 mm pupil. Smaller pupils would result in diffraction limiting the visual acuity. Conversely, higher order aberrations and retinal factors predominate in limiting visual acuity in pupils larger than 3 mm.⁵

Several methods by which depth-of-focus can be measured have been proposed.⁶ The most clinically relevant method consists of measuring the visual acuity as a function of out-of-focus blurring. This is achieved by blurring the image of a target (checkerboards, gratings, etc.) with the addition of spectacle plane lenses. The use of a Snellen chart as a target has been recognised as a valid alternative that more closely mimics routine clinical testing,

although the process involved in the recognition of the blurred individual letters with differing spatial frequency spectra may be more complex than simpler targets.⁵ We use this method to measure the through-focus curve for eyes implanted with a type 1 Boston keratoprosthesis (KPro).

The Boston keratoprosthesis has been recognised as a viable alternative to penetrating keratoplasty in the treatment of select patients with corneal pathology.⁷ It consists of two plates that are joined by a PMMA cylindrical stem and assembled around a corneal graft that is sutured in place in a similar fashion to a regular corneal transplant.⁸ Its main optical element, constitutes a plano-convex lens which is optically limited to 3.0 mm in diameter by the stem and has a total length of about 3.0 mm, depending on the curvature of the anterior refractive surface.⁹ The optical portion remains clear when the surrounding graft opacifies, acting as a fixed-diameter aperture into the eye.

The power of the KPro is chosen based on the eye's axial length, typically aiming for a plano refraction. Any residual postoperative refractive error is corrected either with the protective bandage soft contact lens or with spectacles. However, many of our patients function very well without additional correction and we observed a limited effect of refractive error (or its correction) on visual acuity in KPro patients.¹⁰ Measuring the through-focus curve should help determine the extent of pseudoaccommodation experienced by these patients and inform the precision of refractive correction that needs to be used.

Methods

The study was conducted in accordance with the tenets of the Declaration of Helsinki. It was approved by the Institutional Review Board of the Massachusetts Eye and Ear Infirmary, and informed consent was obtained from all participants.

Patients and lenses

Patients with eyes implanted with a type 1 KPro and with a best-corrected visual acuity (BCVA) of 0.50 logMAR (Snellen 6/18 or 20/60) or better were selected. All eyes had been operated by the same surgeon (CHD) at least 2 years prior. The control group consisted of pseudophakic eyes with a BCVA of 0.00 logMAR (Snellen 6/6 or 20/20) or better. Uneventful cataract extraction was performed on these patients by the same surgeon (SHG) at least 6 months prior, and a monofocal Acrysof SN60WF intraocular lens (Alcon Laboratories, Inc., www.alcon.com) was placed in the capsular bag. Slit-lamp and fundus examination was performed on all eyes, and eyes with macular pathology or with corneal pathology were excluded.

The pupillary diameter was estimated using the pupil gauge on a Rosenbaum pocket vision screener (Graham-Field Health Products, Atlanta, www.grahamfield.com). Control of the pupil size in the pseudophakic eyes was achieved with the use of a black iris-painted soft contact lenses (Kontur lens; Kontur Kontakt Lens Co., Hercules, CA www.kontur55.com) with plano optical power and a

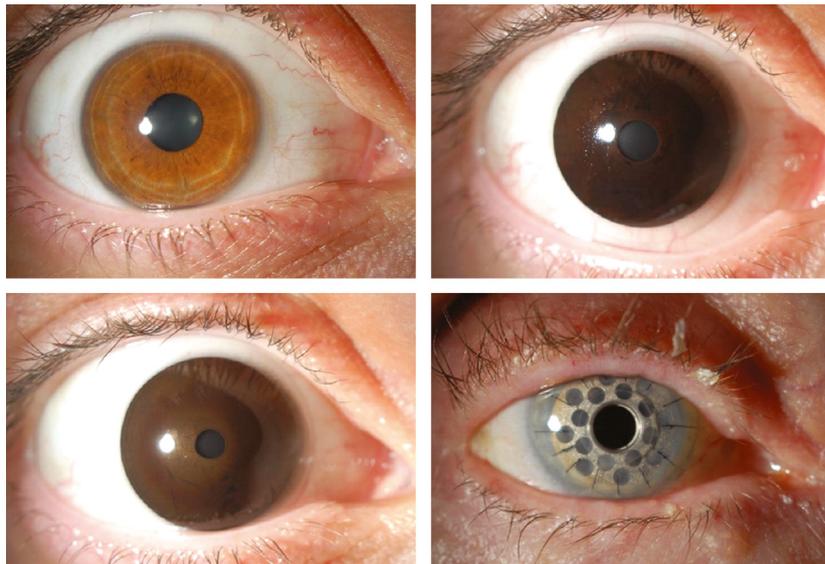


Figure 1. Slit-lamp photos illustrating the different pupils of eyes included in the study. *Top left*, undilated eye. *Top right*, same eye after placement of a Kontur soft contact lens, 15 mm in diameter with a 13 mm in diameter opaque zone and a central 3 mm clear pupillary opening. *Bottom left*, same eye with a similar contact lens with a 2 mm central pupil. *Bottom right*, eye implanted with a Boston keratoprosthesis type 1, with a fixed 3 mm anterior pupil.

fixed central clear pupil of 2.0 and 3.0 mm were used.^{11, 12} These pupil sizes were chosen to correspond to the size of the opening of the optic of the KPro. The lenses used were 15.0 mm in diameter, with the opaque zone spanning 13 mm in diameter. A choice of base curves of 8.30, 8.60, and 8.90 mm was made available for use. (Figure 1).

Each control eye was dilated by instilling two drops of cyclopentolate 1%, 5 min apart. After a minimum of 30 min, the iris-painted soft contact lens was placed on the cornea and allowed to settle for 10 min. The appropriate base curve of the contact lens was chosen based on the automated corneal keratometry measurement, and examination with a slit-lamp was then performed to insure good fit, centration, and a movement of approximately 1 mm following blinks. The choice of which pupil size to start with was counterbalanced. Prior to testing the KPro eyes, the habitually used bandage clear contact lens (Kontur lens) was cleaned and/or replaced if needed.

Measurements

Autorefractometry was attempted on all eyes using the Nidek ARK-530A (Nidek, www.nidek.com). Distance BCVA was obtained monocularly for all KPro eyes, control eyes, and control eyes fitted with the opaque iris-contact lenses. The same computerised video Snellen letter chart (M&S Technologies, www.mstech-eyes.com) at 20 feet (6 m) was used for all patients, with five random single-letters of the same size presented successively to the patient.¹³ The chart luminance contrast was measured by a digital light meter and the Weber contrast was found to be -0.99 . Subjective refraction was performed using a trial frame with the previous clinic visit's manifest refraction used as starting point. Refraction was refined with the addition of lenses in 0.50 D sphere then 0.25 D increments until no improvement in visual acuity was achieved. Determination of cylinder and its axis followed by refinement of the sphere was then performed in the usual way.¹⁴ Care was taken to avoid over-correction by 'fogging' with additional plus sphere until vision blurs, then unfogging until best acuity is just reached.

The monocular through-focus curve was plotted in reference to the BCVA by spectacle defocus ranging from +5.00 D to -5.00 D from the manifest refraction values, in 0.50 D increments. Eyes were initially defocused to +5.00 D or -5.00 D at random, and visual acuity was recorded. The spherical power was gradually decreased in 0.50 D steps until the original manifest refraction values were reached. Defocus to 5.00 D of the opposite sign was then performed, and again the power was decreased in 0.50 D steps back to the original manifest refraction value. At each defocus point, the distance visual acuity was recorded as the smallest sequence of five letters

correctly identified, in addition to the number out of five next-in-size letters correctly identified. All visual acuity values were converted into logarithm of the minimum angle of resolution (LogMAR) for analyses.¹⁵ The use of random letter sequences and randomisation of the starting sequence (whether positive or negative powered lenses are used first) has been shown to improve the accuracy of the obtained through-focus curve.¹⁶

Statistical analysis

Data analysis was performed using STATA statistical software (StataCorp LP, www.stata.com). A paired-sample *t*-test was used to evaluate the symmetry of the through-focus curves along the *y*-axis for each condition. Analysis of variance (ANOVA) testing was performed to compare through-focus curve slopes between groups. Multivariate regression analysis was performed to look for a correlation between the depth-of-focus of the KPro eyes and the various factors known to influence the depth-of-focus. Differences were considered statistically significant when the *p*-value was less than 0.05.

Results

Ten KPro-implanted eyes of nine patients were included. Patients' mean age was 67 years (range: 44–96 years) and five were female. Seven were right eyes. Seven eyes had a clear Kontur soft contact lens in, and three eyes had a hybrid lens (SynergEyes, Inc., Carlsbad, CA www.synergeyes.com). The indication for the KPro surgery in all patients was recurrent graft failure for various reasons including atopy, herpes simplex keratitis and chronic exposure keratopathy. Two patients were monocular with absolute glaucoma in the contralateral eye. Five of the tested eyes had glaucoma which was controlled either with drops and/or an Ahmed shunt. Testing was performed at a scheduled follow-up clinic visit, on average 4 years after KPro surgery (range 2–7 years). Average BCVA was 0.24 logMAR (Snellen 6/11 or 20/35; range 6/6–6/15⁻² or 20/20–20/50⁻²) in all eyes, with a spherical equivalent correction ranging from -4.00 to $+2.25$ D. A maximal cylinder of 1.50 D was measured by the autorefractor and manifest refraction for one eye, six of the 10 eyes had no cylindrical error, as expected.

Five pseudophakic eyes were included in the control group. The mean age was 66 years (range: 58–77 years) and two were female. Two were right eyes, with the tested side randomly chosen in bilateral pseudophakic patients. The average undilated pupil size was 3.5 mm. Testing was performed on average 2 years after cataract extraction surgery (range 10 months–3 years). BCVA was 0.0 logMAR (Snellen 6/6 or 20/20) or better in all eyes, with a spherical

equivalent best correction ranging from -2.00 D to $+0.25$ D. Cylinder was measured in three control eyes and was 1.50 D or less. There was no statistical difference in BCVA between the control eyes with and without the 2 mm artificial-iris contact lens, nor between the 2 and the 3 mm artificial-iris contact lenses. The 3 -mm artificial-iris contact lens resulted in an average acuity drop of three letters compared to no contact lens which was found to be statistically significant, but is meaningless clinically.

Autorefractometry was possible in six out of the 10 KPro eyes. There was good concordance between the sphere measured with autorefractometry and that obtained with manifest subjective refraction [only in eye (#3) was the difference greater than 0.50 D sphere]. The autorefractor measured cylinder of 0.75 D or above in all six eyes, while only three of these demonstrated any cylinder on manifest refraction (Table 1). The concordance between the autorefractor and manifest measurements was higher in the pseudophakic control group (data not shown).

Figure 2 compares the through focus curve average over the KPro eyes to that of controls measured through a natural pupil, as well as with the 3 and 2 mm pupil contact lenses following cycloplegia. The average KPro curve is the flattest indicating lesser drop in vision with increasing defocus and thus reflecting a higher tolerance to induced blur (greater depth of focus). In the control group, the use of the iris-painted contact lenses resulted in a flattening (a decreased slope) of the through-focus curves.

A paired t -test was performed to evaluate the symmetry of the slopes for the various through-focus curves conditions. No significant difference was found between positive and negative defocus curve slopes ($t = 1.09$, $dF = 24$, $p = 0.29$), and hence averaging the two slopes for each subject is appropriate and provides a better representation of each eye's tolerance to blur. This average was therefore used for the remaining analyses.

Using the univariate ANOVA, a comparison of the slopes between the various groups/conditions was performed and

a main effect of condition was found, $F(3,25) = 17.87$, $p < 0.001$. In *post hoc* analyses the slope of the KPro group curve differed significantly from that of the control group with the natural pupil ($p < 0.001$) and the 3 mm pupil ($p = 0.018$, Tamhane *post-hoc* tests). A significant difference was also found between the control group with natural pupil and both with the 2 mm pupil ($p = 0.03$) and the 3 mm pupil ($p = 0.009$) groups. No significant difference was found between the KPro group and the 2 mm pupil ($p = 0.3$) control group.

It took an average error of about 3.0 D in refraction to drop the visual acuity of the eyes implanted with a KPro by three lines. In comparison, only an average of 2.2 D was required for the same effect for a pseudophakic eyes with the 2 and 3 mm pupil, and a mere 0.9 D for the same aver-

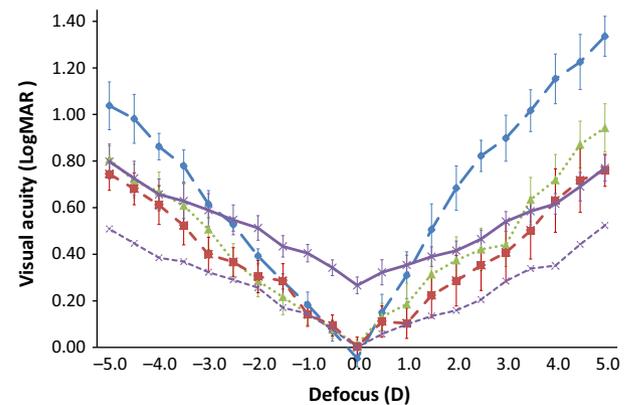


Figure 2. Average through-focus curves for the pseudophakic control eyes (diamonds), the same eyes after fixing the pupil size to 3.0 mm with the iris-painted Kontur contact lenses (triangles), and the same eyes after fixing the pupil size to 2.0 mm with the iris-painted Kontur contact lenses (squares). The average through-focus curve for the Boston type 1 keratoprosthesis is also represented here (crosses). This same curve is reproduced after shifting it down to the zero LogMAR point on the y-axis (dashed line with crosses) to allow for easier visual comparison of the slopes of the various curves.

Table 1. Demographics and refractions of patients with an eye implanted with a Boston keratoprosthesis type 1

KPro Eye	Age	Sex	Eye	Autorefractometry	Manifest refraction	BCVA
1	44	M	OS	Unable	$-0.50 -1.00 \times 180$	$20/30^{-2}$
2	44	M	OD	$+0.50 -1.50 \times 154$	$+1.00 -1.50 \times 145$	$20/40^{-2}$
3	65	M	OD	$-4.50 -0.75 \times 006$	-2.00	$20/30^{-2}$
4	74	F	OD	Unable	-0.75	$20/50^{-2}$
5	87	M	OD	$-1.50 -1.25 \times 134$	$-1.00 -1.00 \times 180$	$20/30^{+2}$
6	40	M	OS	Plano -1.00×180	Plano -0.75×180	$20/25^{+1}$
7	96	M	OD	$+2.25 -1.00 \times 158$	$+2.25$	$20/40^{-2}$
8	64	F	OD	$-4.25 -2.50 \times 163$	-4.00	$20/50$
9	59	F	OS	Unable	-1.00	$20/30^{-2}$
10	71	F	OD	Unable	-3.00	$20/40^{+1}$

M, male; F, female; OD, right eye; OS, left eye; BCVA, Snellen best-corrected visual acuity.

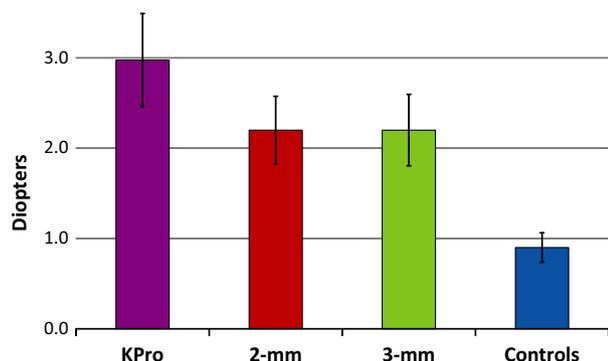


Figure 3. Comparison of the average amount of dioptic defocus needed to drop the eye's visual acuity by three lines. This reflects the increased tolerance to blur associated with an increased depth-of-focus.

age drop in acuity for the control pseudophakic eye with natural pupils (average 3.5 mm) (Figure 3).

Multivariate regression analysis was performed to look for a correlation between the slope of the through the focus curve of KPro-implanted eyes, and the previously established influencing parameters, namely BCVA, age, spherical equivalent, and astigmatism (reflecting retinal eccentricity). No significant correlation was found for any of these factors. The same analysis was also performed for the control group with no contact lens limiting the pupil size, and no correlation was found for this group either. Only group effect was significant and BCVA was the closest to being correlated with the slope significantly. Within the KPro group, BCVA was associated with slope (Pearson correlation, $r = -0.56$, KPro eyes with worse visual acuity have flatter slopes), but the effect did not reach significance ($p = 0.096$). Looking at the curves in Figure 2, the prominent difference in baseline BCVA between KPro eyes and all other controls becomes less prominent at high levels of defocus. As high defocus becomes the controlling variable, the effect of BCVA becomes less significant.

Discussion

Compared to the pseudophakic eyes, the eyes implanted with a Boston KPro show a significantly wider depth-of-focus. This 'pseudoaccommodation' confirms our previous observations that many patients are able to have good functional vision both at distance and near without the need for glasses. Furthermore, good visual acuity in these patients is less critically dependent on an exact refractive correction.¹⁰

This wide depth-of-focus is primarily due to the small pupil inherent to the KPro. Small pupils, natural or artificial, improve vision mainly by reducing the blur circle formed on the retina by each point light source by restriction the angular span of the beam of light entering the eye.

Small pupils also improve retinal imaging by blocking corneal peripheral aberration, or in our case, the KPro spherical aberrations. These effects increase the depth of focus, as a larger dioptic error is required with a small pupil to achieve the same blurring effect. The average through-focus curve of the KPro eyes in this study became comparable to that of pseudophakic control eyes once we reduced the size of the pupil in the control group to a comparable 2 mm using the iris-painted contact lens.

While BCVA,¹⁷ spherical equivalent,¹⁸ astigmatism,¹⁹ and age²⁰ were reported to affect the slope of the through-focus curve, none of these factors were found to have a statistically significant impact on the depth of focus of neither the KPro eyes nor the control eyes. This may be due to our small sample size. A small sample size is an inherent limitation with the population under study, which is limited to patients with severe anterior segment pathology requiring KPro implantation, yet with minimal associated other ocular abnormalities and with good BCVA arbitrarily chosen as 0.50 logMAR (Snellen 6/18 or 20/60) or better. Holding all other factors constant, BCVA was the closest factor to significance in this analysis. That correlation has previously been proven in the human eye¹⁷ and may account for the tendency of the KPro curve to remain flatter than all control curves (Figure 3). The KPro eyes had an average baseline BCVA of 0.24 logMAR (Snellen 6/11 or 20/35), compared to an average -0.02 logMAR (Snellen 6/6⁺¹ or 20/20⁺¹) for all controls combined, with and without the iris-painted contact lenses. The poorer visual acuity in the KPro group can be due to causes such as glare and decreased contrast sensitivity,¹⁰ altered tear film dynamics and retroprosthesis membranes, or from neuroretinal causes such as glaucoma and maculopathy.

Our non-dilated controls had a flatter slope of the through-focus curve and thus a wider depth-of-focus in the negative range, although the effect was not significant. This is likely a consequence of induced pupillary miosis from the stimulation of the near triad with the use of negative lenses.²¹ As expected, this effect is lost after fixing the pupil size in our controls with the iris contact lens and is absent in our KPro eyes.

Autorefractometry seems to be a useful adjunct in refracting KPro patients, when possible, suggesting that autorefractometry may be a useful as a starting point for refracting KPro patients. It is interesting that cylindrical refractive error was measured in some patients despite the anterior curvature of the KPro being spherical. This may suggest possible tilting of the KPro. Indeed, such a tilt has recently been observed with anterior segment optical coherence tomography.²² With the high power of the KPro, a small tilt may cause the induction of measurable cylinder.

In summary, our findings support the current manufacturing specification of the device in 0.50 D incre-

ments, rather than the previous 0.10 D power increments requirements. This appears to be sufficient, since an error of a 0.50 D magnitude would result in the mere loss of two to three letters off the Snellen chart without correction. Spectacles, however, remain of importance in this frequently monocular patient population, in which protective eyewear is important. One may argue that leaving a larger residual refractive error may be desirable, as it will provide a notable difference to patients and therefore encourage them to wear spectacles. This also supports the recent development of a low cost KPro (the 'Lucia' KPro) with a single refractive error that can be stocked and shipped in bulk.

Acknowledgements

The study was supported in part by the Keratoprosthesis Fund, Massachusetts Eye and Ear Infirmary and by NIH grant # R01EY12890 (EP). We thank P. Matthew Bronstad PhD for statistical help.

Disclosure

All authors were full-time academic employees of Massachusetts Eye and Ear Infirmary (MEEI), the manufacturer of the Boston Keratoprosthesis. The MEEI is a not-for-profit organization and the authors have no commercial interest in any of the material discussed in the paper.

References

- Campbell FW & Weir JB. The depth of focus of the human eye. *J Physiol* 1953; 120: 59P–60P.
- Tucker J & Rabie EP. Depth-of-focus of the pseudophakic eye. *Br J Physiol Opt* 1980; 34: 12–21.
- Wang B & Ciuffreda KJ. Depth-of-focus of the human eye: theory and clinical implications. *Surv Ophthalmol* 2006; 51: 75–85.
- Atchison DA, Charman WN & Woods RL. Subjective depth-of-focus of the eye. *Optom Vis Sci* 1997; 74: 511–520.
- Tucker J & Charman WN. The depth-of-focus of the human eye for Snellen letters. *Am J Optom Physiol Opt* 1975; 52: 3–21.
- Ogle KN & Schwartz JT. Depth of focus of the human eye. *J Opt Soc Am* 1959; 49: 273–280.
- Traish AS & Chodosh J. Expanding application of the Boston type I keratoprosthesis due to advances in design and improved post-operative therapeutic strategies. *Semin Ophthalmol* 2010; 25: 239–243.
- Dohlman CH, Harissi-Dagher M, Khan BF et al. Introduction to the use of the Boston keratoprosthesis. *Expert Rev Ophthalmol* 2006; 1: 41–48.
- Dohlman CH, Harissi-Dagher M & Graney J. The Boston keratoprosthesis: a new threadless design. *Digit J Ophthalmol* 2007; 13.
- Sayegh RR, Avena DL, Vargas-Martin F et al. Optical functional properties of the Boston Keratoprosthesis. *Invest Ophthalmol Vis Sci* 2010; 51: 857–863.
- Elder MJ, Murphy C & Sanderson GF. Apparent accommodation and depth of field in pseudophakia. *J Cataract Refract Surg* 1996; 22: 615–619.
- Garcia-Lazaro S, Ferrer-Blasco T, Radhakrishnan H et al. Visual function through 4 contact lens-based pinhole systems for presbyopia. *J Cataract Refract Surg* 2012; 38: 858–865.
- Bailey IL & Lovie JE. New design principles for visual acuity letter charts. *Am J Optom Physiol Opt* 1976; 53: 740–745.
- Guyton LG, West CE, Miller JM & Wisnicki HJ. *Ophthalmic Optics and Clinical Refraction*. 2nd ed. Prism Press: Baltimore, MD, 1999.
- Holladay JT. Visual acuity measurements. *J Cataract Refract Surg* 2004; 30: 287–290.
- Gupta N, Wolffsohn JS & Naroo SA. Optimizing measurement of subjective amplitude of accommodation with defocus curves. *J Cataract Refract Surg* 2008; 34: 1329–1338.
- Green DG, Powers MK & Banks MS. Depth of focus, eye size and visual acuity. *Vision Res* 1980; 20: 827–835.
- Rosenfield M & Abraham-Cohen JA. Blur sensitivity in myopes. *Optom Vis Sci* 1999; 76: 303–307.
- Sawusch MR & Guyton DL. Optimal astigmatism to enhance depth of focus after cataract surgery. *Ophthalmology* 1991; 98: 1025–1029.
- Mordi JA & Ciuffreda KJ. Static aspects of accommodation: age and presbyopia. *Vision Res* 1998; 38: 1643–1653.
- Pieh S, Kellner C, Hanselmayer G et al. Comparison of visual acuities at different distances and defocus curves. *J Cataract Refract Surg* 2002; 28: 1964–1967.
- Fernandez AG, Radcliffe NM, Sippel KC et al. Boston type I keratoprosthesis-donor cornea interface evaluated by high-definition spectral-domain anterior segment optical coherence tomography. *Clin Ophthalmol* 2012; 6: 1355–1359.