EXTENDED REPORT

Legeais BioKpro III keratoprosthesis implantation: long term results in seven patients

E J Hollick, S L Watson, J K G Dart, P J Luthert, B D S Allan

Br J Ophthalmol 2006;90:1146–1151. doi: 10.1136/bjo.2006.092510

See end of article for authors' affiliations

Correspondence to:
Emma J Hollick,
Department of
Ophthalmology, King's
College Hospital, Denmark
Hill, London SE5 9RS, UK;
emma.hollick@kingsch.
nhs.uk

Accepted for publication
4 May 2006

Aims: The long term results of the Legeais BioKpro III keratoprosthesis are presented for seven patients with severe corneal scarring.

Methods: The study took place at Moorfields Eye Hospital, London. Patients had either end stage ocular surface disease or corneal opacification after multiple failed graft surgery, with the potential for significant visual improvement. After insertion the device was covered with a conjunctival flap or buccal mucous membrane graft, which was later opened to expose the optic. The outcome measures were vision, complications, and retention of the device.

Results: The BioKpro III was inserted into seven patients with severe corneal scarring: ocular cicatricial pemphigoid, measles keratitis, thermal injury, Stevens-Johnson syndrome, aniridia, chemical injury, and congenital rubella. The follow up was 18–48 months. The keratoprosthesis failed in six, because of extrusion occurring 2–28 months postoperatively. Retroprosthetic membranes occurred in three patients, and endophthalmitis in one. Vision improved from hand movements to 6/12 in the only patient who retained the KPro; however he was troubled by mucus accumulation on the optic.

Conclusions: The one success has been in a patient with thermal burns. The remaining results have been poor, with the KPro extruding in six of the seven patients.

The visual rehabilitation of patients with corneal blindness continues to be a challenging and, at times, unrewarding process for both the patients and their ophthalmologists. Corneal opacification is the second commonest cause of world blindness affecting an estimated 10 million people.¹ The prognosis for successful visual rehabilitation with conventional corneal grafting in patients who have corneal scarring and neovascularisation is usually poor.² Exciting progress is currently being made in the development of tissue engineered alternatives to cadaveric corneal donor material.³ But, as with conventional allograft material, collagen based constructs may fail to sustain a normal corneal epithelium or stromal tissue clarity in a hostile ocular surface environment. For the present, the only alternative to keratoplasty in corneal blindness is a synthetic keratoprosthesis (KPro).^{4–5}

While the initial recovery of vision after KPro surgery may be good, most KPros fail because of poor interaction between the artificial implant and the host cornea.⁵ This may be associated with extrusion, endophthalmitis, or retroprosthetic membrane formation. Mechanical failure of the device can also lead to a poor outcome. The emergence of biocompatible materials that support colonisation by host keratocytes has shown that it is possible to integrate alloplastic materials into the recipient cornea.^{6–9} However tissue breakdown with stromal melting and aqueous leakage still occur.

Two fully synthetic KPros are currently available commercially in the United Kingdom: the Legeais BioKpro III (FCI Ophthalmics, Marshfield Hills, MA, USA) and the AlphaCor (Argus Biomedical, Perth, Australia). At the time we commenced this short clinical series, the Legeais BioKpro III was the only CE marked device available for implantation in the United Kingdom. We chose this design as an alternative to the osteo-odontokeratoprosthesis (OOKP), which involves more complex surgery¹⁰; and to the Dohlman KPro, a non-integrated design, which has had poor results in patients with ocular cicatricial pemphigoid (OCP) and Stevens-Johnson syndrome (SJS).^{11–12}

The BioKpro I was developed by J-M Legeais after experimental work suggested that microporous biocompatible polymers promote colonisation by host corneal cells, thereby potentially providing better KPro fixation.¹³ Several preliminary studies in the rabbit showed that an expanded poly(tetrafluoroethylene) (ePTFE), with a regular fibril arrangement (Impra), a thickness of 200 µm and a pore size of 50 µm resulted in resolution of inflammation and complete infiltration by keratocytes with collagen production with the same protein-collagen ratio and similar distribution of collagen types as control corneas.¹⁴

The BioKpro I consisted of four pieces: a 9 mm diameter skirt of opaque fluorocarbon poly(tetrafluoroethylene) (PTFE), with 80 µm pores; a 4 mm diameter, 2.67 mm long poly(methylmethacrylate) (PMMA) optic; a 5 mm diameter PMMA fixation clip, and a 5 mm diameter PMMA sealing ring. The haptic was inserted into a lamellar pocket in the host cornea, and the optic was positioned through a hole trephined in the central cornea. The 4–28 month follow up results of 24 patients implanted with this device showed that 17 patients (71%) had visual acuity improvements.¹⁵ Five anatomical failures occurred (21%) in the first 6 months (three extrusions, one dislocation of the optic, and one endophthalmitis). Five patients developed retroprosthetic membranes (RPM), which were successfully removed in four. A recent report has described the longer term results with the Legeais BioKpro I in 11 patients with follow up of up to 5 years (range 8–60 months).¹⁶ Unfortunately the outcome in all but two of the 11 patients was very disappointing. There were five cases of endophthalmitis, eight melts with partial

Abbreviations: BMG, buccal mucosal graft; ePTFE, expanded poly(tetrafluoroethylene); HM, hand movement; IOP, intraocular pressure; KPro, keratoprosthesis; OCP, ocular cicatricial pemphigoid; OOKP, osteo-odontokeratoprosthesis; PDMS, poly(dimethylsiloxane); PHEMA, poly(2-hydroxyethyl methacrylate); PL, perception of light; PMMA, poly(methylmethacrylate); PTFE, poly(tetrafluoroethylene); PVP, poly(vinylpyrrolidone); RPM, retroprosthetic membranes; SJS, Stevens-Johnson syndrome

KPro dislocation, four extrusions, three retinal detachments, and two cases of phthisis. RPMs developed in 10 cases. At the last visit five eyes were blind, and only one showed a slight improvement in vision. Six eyes showed an improvement in vision before having significant complications, and the functional performance period was limited to a mean of 22 months.

There were a number of functional limitations of this first generation BioKpro I. The rigid PMMA optic precluded intraocular pressure (IOP) measurements and did not integrate with the corneal stroma. The optic size did not permit visualisation of the peripheral retina. Cataract extraction was necessary as the posterior face of the optic would have been in contact with the anterior surface of the crystalline lens. The mechanical clips holding the optic to the rim were too weak for long term implant stability and safety.

The BioKpro II developed by Legeais in an attempt to circumvent some of the limitations of the first generation multipiece KPro. The BioKpro II was available from France Chirurgie Industries (FCI) SA, Paris, France as the BioKPro sil. The optic size was increased from 4 mm to 7 mm, and its thickness decreased from 2.37 mm to 0.55 mm. The device consisted of two components: a 500 µm thick optic of soft poly(dimethylsiloxane) (PDMS) coated with poly(vinylpyrrolidone) (PVP) and an 11 mm diameter disc of opaque fluorocarbon PTFE haptic (skirt). The skirt has a thickness of 250 µm and a pore size of 80 µm. The new optic was made of a more distensible copolymer, and the anterior and posterior curvatures of the optic gave the device an aspheric quality similar to that of the human cornea. The optic was chemically fused to the skirt by interpenetration of the PDMS into the PTFE to make a one piece KPro. Hydrophilisation of the PTFE copolymer aided colonisation of the supporting rim by fibroblasts with the objective of increasing the adherence to the surrounding host tissue. Phacoemulsification or pars plana vitrectomy could theoretically be performed with the device in place months or years after implantation.

The 6 month results of the first 13 cases implanted with the BioKpro II showed that 11 (84%) were stable and seven (53%) had an improvement in vision.⁶ Five cases failed (38.5%), with two extrusions, two RPMs, and one case of endophthalmitis. These results were similar to those with the first generation BioKpro I multipiece device. The extrusions were thought by Legeais *et al*⁶ to be caused by premature retraction of the buccal mucous membrane graft, which is placed over the surface of the device for 2 months to allow

epithelialisation of the device. The authors thought that a healthy epithelium must form over the bare optic and haptic junction to ensure the long term stability of the device, to avoid the underlying stoma being exposed to the deleterious effects of enzymes produced by the neighbouring traumatised epithelial cells, tear film and inflammatory cells, leading to melting.

The Legeais BioKpro III device (fig 1) consists of two components: a 500 µm thick central silicone optic and a disc of opaque fluorocarbon PTFE porous surround. This skirt has a thickness of 250 µm and a pore size of 80 µm. The skirt and the optic are chemically bonded in the same way as the BioKpro II, but the optic is smaller (diameter 5 mm) and the skirt is larger (diameter 10 mm). In this paper we present the long term results of seven patients in which the Legeais BioKpro III was implanted. These are the first published results for this device.

METHODS

Patient details

Inclusion criteria for the study were the potential for clinically significant visual improvement, age older than 20 years, corneal opacification with less than 50% chance of graft survival at 5 years, in association with multiple (more than two) failed corneal graft surgery, or four quadrants of deep corneal neovascularisation, or end stage ocular surface disease (OCP, SJS, chemical or thermal injury, severe dry eyes, atopic keratoconjunctivitis, atopic keratoconjunctivitis, silicone oil, neurotrophic keratopathy). Exclusion criteria were active inflammation, uncontrolled raised IOP, ultrasound evidence of significant posterior segment pathology, and inability to give informed consent. Taped patient information was prepared to assist with informed consent before entry into the study. Ethical approval for the study was granted by the Moorfields Eye Hospital NHS Trust research ethics committee.

Surgical technique

Stage I, device implantation

All keratoprotheses were implanted under general anaesthetic. Coating of the haptic portion of the device with autologous blood was performed according to manufacturer's instructions. Exposure of the ocular surface was assisted by 4/0 silk lid retraction sutures where necessary. The ocular surface tissues were recessed to expose subjacent stroma back to the muscle insertions, with cautery to obtain haemostasis. Then in patients with a mobile conjunctiva, a Gunderson conjunctival flap was prepared. Where the conjunctiva was inadequate for flap formation, a buccal mucous membrane graft was prepared before preparation of the ocular surface using standard techniques. In cases where the limbus could not be identified accurately the corneal centre was then marked using cold light retroillumination. A 5 mm partial thickness trephination was followed by mid-depth lamellar dissection into the corneal periphery to accommodate the KPro skirt. Two equidistant radial incisions in the superficial lamella were then performed to assist intralamellar placement of the KPro skirt. A paracentesis was made, before a 4 mm diameter full thickness trephination to clear the optical pathway.

Extracapsular cataract extraction or ocutome clearance of lens/iris remnants from the visual axis was performed at this stage with relieving incisions in the posterior corneal lamella where required. After closure of any posterior relieving incisions with 10/0 nylon, the KPro was inserted and the radial incisions in the anterior corneal lamella were closed, also with 10/0 nylon. Conjunctiva or buccal mucous membrane was then secured over the device with 8/0 Vicryl.

Figure 1 The Legeais BioKpro III held in forceps before implantation. The device consists of a central 5 mm clear silicone optic chemically bonded to a 10 mm opaque fluorocarbon PTFE porous skirt.

Table 1 Patient characteristics and treatment

	Patient						
	1	2	3	4	5	6	7
Sex/age	F/82	M/84	M/54	F/20	F/66	M/32	M/38
Diagnosis	OCP	Childhood infective keratitis	Molten metal injury	SJS	Aniridia, microcornea	Chemical injury	Congenital rubella
BSCVA preop	HM	HM	HM	HM	HM	PL	HM
BSCVA postop	HM	HM	6/12	HM	HM	HM	HM
Significant subjective visual gain at any stage	None	None	Yes	Yes	None	None	Yes
Co-pathology influencing visual outcome	None	Amblyopia	None	Amblyopia	Optic atrophy	None	Congenital glaucoma; amblyopia
Final BSCVA (after device removal)	PL	HM	6/12	NPL	PL	HM	HM
Follow up post stage II (months)	35	38	48	38	25	Device extruded before stage II	19
Reason for failure	Extrusion	Extrusion	N/A	Extrusion	Extrusion	Extrusion	Extrusion
Failure time (months)	7	13	N/A	28	16	2	6
RPM	+	+	—	+	—	+	—
Mucous membrane contraction with haptic exposure	+	+	—	—	+	+	+
Other complications		Contraction of conjunctiva over optic	Optic spoilation	Endophthalmitis	Entropion		Contraction of conjunctiva over optic
Further interventions before failure (device removal/PK)	Excision of RPM + BMMG revision	Expansion of flap opening over optic; YAG to RPM	BMMG revision	Vitreous tap/intraocular antibiotics	Entropion correction	None	Repeat stage II; lamellar corneal graft and repeat conjunctival flap; second repeat stage II
Comments		Uncertain preoperative history; corneal infection may have been congenital	Device well integrated but vision has deteriorated secondary to recurrent optic spoilation	Operated eye is now phthisical	Optic atrophy diagnosed after stage II	Lost to follow up between stage I and extrusion before stage II	

BCVA, best corrected visual acuity; OCP, ocular cicatricial pemphigoid; HM, hand movement; NPL, no perception of light; PL, perception of light; RPM, retroprosthetic membrane.

Stage II, optic exposure

Optic exposure was performed after a minimum of 3 months under either local or general anaesthetic. A gentian violet marker was used to define a 4 mm diameter opening in the mucous membrane covering the optic portion of the device. Cold light retroillumination was used where necessary to aid

visualisation of the KPro optic beneath the flap. Curved Vannas scissors were then used to excise the conjunctiva over the marked 4 mm diameter central zone.

Figure 2 Our only successful case with the KPro in situ 3 years after surgery. Surface spoilation can be seen on the optic that reduces the patient's vision and requires regular cleaning.

Figure 3 Early exposure of the KPro skirt. The figure shows a KPro with a white arc of exposed and infiltrated skirt material. A retroprosthetic membrane (RPM) can also be seen through the optic. A clear area can be seen in the RPM where it has been partially treated by the YAG laser.

Figure 4 End stage extrusion of the KPro device. The eye is very inflamed with exposure of the skirt over 360 degrees around the optic. Melting of tissues has led to extrusion of the device with exposure of the edge of the skirt between 12 o'clock and 2 o'clock.

Postoperative medication

In line with previous publications on the Legeais KPro, topical steroids were not used postoperatively. After stage I implantation, systemic antibiotics (ciprofloxacin 750 mg twice daily orally) were used for 5 days. Topical antibiotics (ofloxacin or chloramphenicol) were administered four times daily until the epithelium was healed and all Vicryl sutures were out. Systemic doxycycline 100 mg daily was used until 1 month after stage II. Postoperative immunosuppression (cyclophosphamide) was given to only one patient (patient 6), with sulphapyridine being continued in the patient with OCP as prophylaxis against disease reactivation.

Outcome measures

The following outcome measures were recorded at 6 monthly intervals after surgery: Snellen acuity, intraocular pressure (recorded using a TonoPen (Mentor, Norwell, MA, USA), presence/absence of a RPM or tissue breakdown over the KPro haptic, additional surgical interventions, and time (months) to device failure.

Figure 5 Explantation of an extruded KPro. The conjunctival flap has been recessed to expose the anterior surface of the skirt. There is a sharp demarcation line between the grey well integrated portion of the skirt and the white portion which has been infiltrated and has not integrated.

RESULTS

The original cause for the corneal scarring was different for each patient and included OCP, measles keratitis, molten metal injury, SJS, aniridia with microcornea, chemical injury, and congenital rubella (table 1). There were three female and four male patients. The average age at the time of keratoprosthesis surgery was 53.7 years (range 20–84). Six patients had hand movement (HM) vision in the eye, and one perception of light (PL). The vision was the same or worse in the fellow eye. All patients had between 1 year and 80 years of visual disability with an average of 32 years. One of the patients had undergone no previous ocular surgery, and one had had just lid surgery. The other five had had a combination of previous operations including cataract surgery in three, penetrating corneal grafting in two, lamellar corneal grafting in one, amniotic membrane grafting in one, and multiple glaucoma procedures had been performed in the one patient with a history of glaucoma. All patients had four quadrants of corneal vascularisation and none had active inflammation.

The first stage surgery also included cataract extraction in the four phakic patients, lamellar grafting in patient 6, and insertion of a Baerveldt drainage device in patient 7. The keratoprosthesis was covered by a buccal mucosal graft (BMG) in three cases (patients 1, 3, and 6), and a conjunctival flap in the other four patients.

All patients had 18 months or more of follow up, except one man (patient 6), who was referred from Greece for his surgery; this patient's KPro extruded at 2 months (before the second stage), and he returned to Greece after 4 months to continue his follow up. The maximum and mean follow up were 48 months and 33.8 months, respectively.

Only one patient retained the KPro (follow up 48 months); the vision in this eye improved from HM to 6/12. This patient though was troubled by mucus accumulation on the optic of the KPro which reduced his vision and necessitated monthly follow up to clean the mucus debris from the optic surface (fig 2).

The keratoprosthesis failed in six of the seven patients, because of extrusion of part of the haptic in five and complete extrusion of the KPro in one (figs 3–5). This extrusion occurred between 2 months and 28 months postoperatively. Other complications seen were an RPM in three patients, requiring surgical excision at 4 months in patient 1, and YAG treatment at 7 months in patient 2 and 2 years in patient 5. Patient 4 had endophthalmitis in association with aqueous leakage 1 year postoperatively.

In addition to the two stages of the KPro procedure, all patients required between one and three further surgical procedures such as revision of the BMG, treatment of RPMs, enlargement of the conjunctival opening, or reversal of the procedure (using a lamellar corneal graft with conjunctival flap or BMG).

Pathology

Typical macroscopic findings at device explantation were a grey, well integrated haptic area and a white, poorly integrated portion (fig 5). In the area of successful integration microscopy revealed fibrous integration with little inflammatory tissue (left hand side). In the white poorly integrated portion microscopy showed a chronic inflammatory infiltrate (on the right). This poorly integrated portion is shown under higher magnification in figure 7 with lymphocytes, macrophages, and giant cells in the chronic inflammatory infiltrate.

DISCUSSION

Our experience with the Legeais BioKPro III has been disappointing, with only one of seven patients retaining the

Figure 6 Photomicrograph showing a well integrated portion of the KPro skirt (left) and a poorly integrated portion (right) containing a chronic inflammatory infiltrate and less collagen within the interstices (haematoxylin and eosin, $\times 20$ objective).

Figure 7 Higher magnification view of a poorly integrated section of the KPro skirt showing the lymphocyte rich chronic inflammatory infiltrate (haematoxylin and eosin, $\times 40$ objective).

device (fig 2). This patient requires monthly cleaning of the KPro optic to remove mucous debris that affects vision when present.

The failure of a KPro device to integrate well into the tissues is a major complication and extrusion, associated with RPM formation in two, was the cause of failure in six of our patients (figs 3–5). Endophthalmitis is a much feared complication, which occurred in one patient in our series. The amount of time and effort invested by patients was very significant, with all of them undergoing between three and five operations aimed at trying to maintain the KPro, deal with the complications, or finally reverse the procedure. This may be an acceptable price to pay for a temporary improvement in vision, but is questionable in the face of such disappointing results. We no longer implant this device.

Published results from clinical series of patients implanted with the Legeais BioKPro I and II suggest that up to 40% of these devices fail within 1 year of implantation,^{6,13} with over 60% failing with longer follow up.¹⁶ This occurs because of retraction of the surface tissues over the haptic element of the device, RPM formation, infection, or aqueous leakage necessitating device removal or revision of implantation.

Our results for the Legeais BioKPro III are no better, possibly as this device incorporates the same skirt material as earlier embodiments. Pathology of the extruded KPros demonstrated the lack of integration of this KPro and the presence of chronic inflammation (figs 6 and 7). The stimulation of chronic inflammation and inadequate colonisation of the material by host tissue was the likely cause of failure of the device to integrate. In vitro data from our group have shown that although cells adhere to ePTFE, cell viability is poor compared to hydroxyapatite,¹⁷ and a poor initial cell adhesion environment in the skirt element of KPros may reduce subsequent tissue integration and increase device failure rates.

We immersed the device in autologous blood before implantation according to manufacturer's instructions, a technique derived from PTFE vascular grafts, to precoat with fibrin fibronectin and other adhesion molecules to encourage colonisation of the skirt with cells.^{6,18} We did not use postoperative steroids as advised by Legeais, to avoid possible inhibition of fibroblast activity.¹⁵ Medroxyprogesterone has been thought to be less associated with melting in keratoprosthesis patients¹⁹; however, this was not available to us at the time of the surgery.

Direct comparison between our results and those from other KPros is difficult because inclusion criteria vary between case series, and much shorter follow up is usually reported. Other KPros under investigation include the AlphaCor artificial cornea, the Dohlman-Doane KPro, and the osteo-odonto KPro. Problems with poor tissue integration may be equally common with the AlphaCor device. The AlphaCor artificial corneas are made entirely from the hydrophilic polymer poly(2-hydroxyethyl methacrylate) or PHEMA, and consist of a central transparent optic fused to a peripheral porous skirt that is chemically identical yet higher in water content. In a series of 40 implanted eyes followed for up to 36 months, the overall rate of surgical revision for complications associated with poor tissue integration was 30%.⁷ These cases were a selected group comprising mainly patients with a normal ocular surface, and included 14 patients who had not yet completed stage II of the implantation process in which the surface tissues are opened over the device optic. Most tissue integration problems are not clinically evident until after this surgical stage. The AlphaCor is unsuitable for patients without a moist ocular surface, and this excludes many of the patients most in need of a KPro. Both the AlphaCor and Legeais devices are implanted into lamellar pockets in the cornea; however, the anterior lamellar is left intact in the AlphaCor technique until stage II, whereas the anterior lamellar is opened centrally and covered with conjunctiva or mucous membrane in the Legeais technique. Breakdown of the conjunctiva over the optic was not a problem in our series and we can see no particular benefit of the AlphaCor technique.

The OOKP is a much better option in this type of patient with dry eyes, severe scarring, and no chance of graft survival. This KPro consists of an annular wafer of alveolar tooth glued to a central PMMA optic. As the OOKP is pre-implanted in the cheek it is the only KPro in which the skirt is already colonised with autologous fibroblasts at the time of implantation into the eye. The OOKP has been implanted since the 1960s with continuing relative success. In particular, the device failure rate in association with poor tissue integration for this KPro would appear to be significantly less than that for fully synthetic devices. Only five of 85 (5.9%) patients implanted with the OOKP and followed for up to 16 years had clinical problems with tissue integration.¹⁰ A recent report of 181 patients with OOKPs using a modified technique and a median follow up of 12 years showed impressive anatomical and functional results, with a

cumulative probability of retaining the device of more than 90% at 8 years, and greater than 80% more than 18 years after surgery.²⁰ Survival analysis estimated that 18 years after surgery the probability of retaining best postoperative visual acuity was 56%. Indications for implantation in these series included severe ocular surface disease secondary to OCP, SJS, and previous chemical injury.

The Dohlmann-Doane KPro consists of a collar button of PMMA. The anterior plate has a stem which pierces a donor corneal button, and a back plate. The carrier graft is sutured into place like a penetrating keratoplasty. In a series of 11 patients followed up over 3 years, RPMs occurred in five, nine retained their KPro, six with a significant improvement in vision.¹¹ Subsequent vitreoretinal procedures were required in 22 eyes of 110 patients who received this KPro (six for RPMs, 13 for retinal detachments, and five for vitreous opacities).²¹ In a report of 63 eyes with the Dohlman-Doane KPro with between 21 months and 101 months of follow up, 49% of patients required between one to eight revisions to repair areas of tissue melting.¹² Permanent removal of the KPro was performed in 16%, and the KPro was replaced in 10%. Endophthalmitis occurred in 8%, RPM in 37%, glaucoma in 46% (despite glaucoma shunt insertion in 72% at the time of the initial surgery), and retinal detachment in 19%. Eleven patients (17.5%) lost vision to no perception of light postoperatively. In a recent report on 25 patients with the Dohlman-Doane KPro and 2–22 months of follow up, all KPros were retained, however only patients with relatively good prognoses were included, with SJS and OCP patients excluded.²² There were two cases of loss of vision, and three RPMs.

Indications for KPro implantation are currently restricted to bilateral corneal opacity where penetrating keratoplasty with stem cell grafting and immunosuppression are impossible or have failed. It is currently a last ditch procedure but the indications would widen if KPro were improved. The ideal KPro would be biocolonisable—supporting a stable multilayered epithelium; biointegratable—forming a stable bond with the surrounding tissues; and bioinert—not stimulating ongoing inflammation in the anterior chamber and surrounding tissues. The Legeais BioKpro III unfortunately does not achieve these goals, and our results were disappointing, with only one of the seven devices being retained at the most recent follow up. The problems of extrusion, retroprosthetic membranes, and endophthalmitis continue to blight the success of this device, and alternative technology and materials are required in the future.

Authors' affiliations

E J Hollick, King's College Hospital, Denmark Hill, London SE5 9RS, UK
S L Watson, J K G Dart, P J Luthert, B D S Allan, Moorfields Eye Hospital, City Road, London EC1V 2PD, UK
P J Luthert, Institute of Ophthalmology, University College London, 11–43 Bath Street, London EC1V 9EL, UK

SLW is supported by a Health Professional Research Fellowship from the National Health and Research Council, Australia

Financial/proprietary interest: The authors have no commercial or proprietary interest in the Legeais BioKpro device. Likewise, they have no financial interest and do not receive payment as consultant, reviewer, or evaluator.

REFERENCES

- 1 **World Health Organization**. *The World Health Report 1998: life in the 21st century*. Geneva: WHO, 1998:47.
- 2 **Williams KA**, Roder D, Esterman A, *et al*. Factors predictive of corneal graft survival: report from the Australian Corneal Graft Registry. *Ophthalmology* 1992;**99**:403–14.
- 3 **Li Fengfu, Carlsson D, Lohmann C**, *et al*. Cellular and nerve regeneration within a biosynthetic extracellular matrix for corneal transplantation. *Proc Nat Acad Sci*, 2003; www.pnas.org/cgi/doi/10.1073/pnas.2536767100.
- 4 **Allan BDS**. Artificial corneas. *BMJ* 1999;**318**:821–2.
- 5 **Hicks CR**, Fitton HF, Chirila TV, *et al*. Keratoprostheses: advancing toward a true artificial cornea. *Surv Ophthalmol* 1997;**42**:175–89.
- 6 **Legeais J-M**, Renard G. A second generation of artificial cornea (Biokpro II). *Biomaterials* 1998;**19**:1517–22.
- 7 **Hicks CR**, Crawford GJ, Lou X, *et al*. Corneal replacement using a synthetic hydrogel cornea Alphacor device preliminary outcomes and complications. *Eye* 2003;**17**:385–92.
- 8 **Chirila TV**, Constable UJ, Crawford GJ, *et al*. Poly (2-hydroxyethyl methacrylate) sponges as implant materials: in vivo and in vitro evaluation of cellular invasion. *Biomaterials* 1993;**14**:26–38.
- 9 **Legeais J-M**, Rossi G, Renard G, *et al*. A new fluorocarbon for keratoprosthesis. *Cornea* 1992;**11**:538–45.
- 10 **Marchi V**, Riici R, Pecorella I, *et al*. Osteo-odonto-keratoprosthesis. Description of the surgical technique with results in 85 patients. *Cornea* 1992;**13**:125–30.
- 11 **Dohlman CH**, Doane MG. Some factors influencing outcome after keratoprosthesis surgery. *Cornea* 1994;**13**:214–18.
- 12 **Yaghouti F**, Nouri M, Abda JC, *et al*. Keratoprosthesis: preoperative prognostic categories. *Cornea* 2001;**20**:19–23.
- 13 **Legeais J-M**, Renard G, Parel J-M, *et al*. Expanded fluorocarbon polymer for keratoprosthesis: cellular ingrowth and transparency. *Exp Eye Res* 1994;**58**:41–51.
- 14 **Legeais J-M**, Renard G, Parel J-M, *et al*. Effects of pore diameter on corneal ingression patterns in expanded polytetrafluoroethylene (abstract). *Invest Ophthalmol Vis Sci* 1992;**33**(Suppl):992.
- 15 **Legeais J-M**, Renard G, Parel J-M, *et al*. Keratoprosthesis with biocolonisable microporous fluorocarbon haptic. *Arch Ophthalmol* 1995;**113**:757–63.
- 16 **Alio JL**, Mulet ME, Haroun H, *et al*. Five year follow up of biocolonisable microporous fluorocarbon haptic (BIOKOP) keratoprosthesis implantation in patients with high risk of corneal graft failure. *Br J Ophthalmol* 2004;**88**:1585–9.
- 17 **Anitua E**, Andia I, Ardanza B, *et al*. Autologous platelets as a source of proteins for healing and tissue regeneration. *Thromb Haemost* 2004;**91**:4–15.
- 18 **Mehra JS**, Futter CE, Sanderman SR, *et al*. Hydroxyapatite promotes superior keratocyte adhesion and proliferation in comparison with current keratoprosthesis skirt materials. *Br J Ophthalmol* 2005;**89**:1356–62.
- 19 **Hicks CR**, Crawford GJ. Melting after keratoprosthesis implantation: the effects of medroxyprogesterone. *Cornea* 2003;**22**:497–500.
- 20 **Fancinelli G**, Falsini B, Taloni M, *et al*. Modified osteo-odonto-keratoprosthesis for the treatment of corneal blindness. Long-term anatomical and functional outcomes in 181 cases. *Arch Ophthalmol* 2005;**123**:1319–29.
- 21 **Khan RS**, Dohlmann CH, D'Amico DJ. Management of vitreoretinal complications in eyes with permanent keratoprosthesis. *Arch Ophthalmol* 2002;**120**:559–66.
- 22 **Aquavella JV**, Qian Y, McCormick GJ, *et al*. Keratoprosthesis: the Dohlman-Doane device. *Am J Ophthalmol* 2005;**140**:1032–8.