

A keratoprosthesis prototype for the dog

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Abstract

Objective To describe the technique for implantation of a novel keratoprosthesis (KP) prototype and evaluate its application for the treatment of corneal blindness in dogs. **Animals studied** Seven dogs, all of them being clinically blind before surgery as a result of severe corneal endothelial disease (5/7) or chronic superficial keratitis (2/7) that were unresponsive to prior therapy.

Procedures A silicone KP was implanted unilaterally, just anterior to Descemet's membrane, after creating a stromal pocket by deep stromal lamellar dissection.

Results Implantation of the KP was accomplished without complication in six of seven operated dogs. In the remaining case, an intra-operative complication (perforation of Descemet's membrane) was associated with extrusion of the KP 8 weeks postoperatively. All operated eyes regained limited vision after surgery. Three to six months after implantation purulent keratitis occurred in all five eyes with endothelial disease, necessitating surgical removal of the KP 6 months postoperatively in 5/7 eyes.

Conclusions This KP prototype shows promise as a treatment for certain blinding corneal diseases. However, changes in the design of this KP, allowing improved stromal integration, will be necessary before its clinical application can be approved.

Key Words: artificial cornea, corneal transplant, dog, keratoplasty, keratoprosthesis, nonpenetrating

INTRODUCTION

Certain pathologic conditions lead to a loss of corneal transparency and may therefore lead to visual disturbance or even blindness. Conventional corneal transplants may be used to treat those conditions in humans and domestic animals by means of penetrating and nonpenetrating keratoplasty. The logistics of obtaining corneal donor tissue are complicated in veterinary ophthalmology, as to date eye banking does not exist for dogs as it does in human ophthalmology. In addition, many conditions are associated with significant corneal stromal vascularisation and infiltration that contribute to graft rejection. Thus, an artificial cornea would seem to represent an ideal solution for many blinding corneal conditions in the dog. In people, the artificial cornea has long been a management focus for those corneal conditions in which fresh transplants are not applicable or are contraindicated such as chronic keratokconjunctivitis sicca and herpetic keratitis. The concept of utilizing an artificial cornea, or keratoprosthesis (KP), originated in the 18th century, when it was first proposed that a piece of glass could be placed into

the cornea in an attempt to restore vision. Several models have been developed in the last few decades.^{1–3}

In human patients, a number of KP designs are currently used for specific indications. The osteo-odonto-keratoprosthesis (OOKP) is advocated for end-stage dry eyes. Its implantation involves a complicated multi-step procedure, with implantation of the artificial optic into the maxilla prior to definitive transplantation to the cornea.⁴

In newborn babies and children the Boston KP or Aquavella KP is advocated. The Boston KP is assembled utilizing a central 3 mm optical cylinder, with a surface plate, which functions as a new aperture and refractive surface. The KP is fixed to a ring of donor corneal stroma surrounding the optical cylinder and fastened by a fenestrated back plate and locking titanium washer. The device can then be implanted into a recipient eye using standard corneal transplant techniques.⁵ This type of prosthesis can also be used in eyes with herpetic keratitis, which are considered high-risk eyes.⁶

The AlphaCor® KP (Argus Biomedical Pty. Ltd., Perth, Australia) is a commercially available one-piece KP,^{7,8} which

has been used in the management of a wide spectrum of blinding corneal diseases.

All of the aforementioned KP designs are intended for use in penetrating keratoplasties. However, the penetrating technique is associated with an increase in the risk of postoperative complications compared to the placement of a deep stromally located, nonpenetrating KP. Infection and stromal melt are severe complications reported in humans following KP placement. To decrease the incidence of complications such as these, the AlphaCor® KP has been implanted entirely intra-stromally in one study.⁹

Taking these reported complications in human patients into consideration, as well as the relatively increased risk of microbial contamination in dogs into account, the nonpenetrating technique was preferred for investigation in this study. Complicated, multi-step procedures, like the OOKP, are generally not realistic for clinical application in dogs. The practical design of the KP prototype employed in this study resembles that of the AlphaCor® KP. The goal of this KP is to restore a clear visual axis in dogs with blinding corneal disease, in which a conventional corneal donor graft might be expected to fail, or could not be applied. The purpose of this study was to evaluate the clinical use of a novel KP prototype in dogs blinded by severe, total corneal opacification.

MATERIAL AND METHODS

Prosthesis

The KP prototype used consists of a silicone optic, with a diameter of 6 mm, surrounded by a 3 mm wide silicone foam ring (Fig. 1).

Patients

Seven dogs received the KP unilaterally (Table 1). All dogs underwent a complete ophthalmic examination including



Figure 1. Keratoprosthesis prototype: silicone optic with a diameter of 6 mm surrounded by a 3 mm wide ring of silicone foam.

Schirmer tear test; slit-lamp biomicroscopic examination; applanation tonometry, and B-mode ocular ultrasonography preoperatively. All dogs included in this trial were judged to be clinically blind prior to surgery. The dogs were unable to navigate an obstacle course, but showed a positive dazzle reflex. Five dogs were diagnosed with bilateral corneal endothelial disease associated with profound corneal edema. Two dogs with chronic superficial keratitis had dense corneal scarring, pigmentation and vascularization. In all dogs, corneal disease had proven refractory to prior intensive medical, surgical and/or radiation therapy. The eye with the more severe clinical signs was selected for the KP implantation in each patient. The dogs were included with the owners' written informed consent.

Surgical procedure

All surgical procedures were carried out by a single surgeon (IA). Figures 2 and 3 provide step-by-step, schematic and

Table 1. Summary of patient data, diagnosis and treatment prior to KP, operated eye and outcome

	Breed	Age (years)	Gender	Diagnosis	Treatment prior to KP	Operated eye	outcome
1	Dalmatian	13	SF	Endothelial disease	Topical	OD	Purulent keratitis 4 mo. pop, extraction of KP 6 mo. pop
2	German Shepherd	6	M	CSK	Keratotomy, topical	OS	KP in place after 12 mo., visual 12 mo. pop
3	Dachshund	13	SF	Endothelial disease	Thermokeratoplasty 6 mo. prior to KP, topical	OD	Intra-operative perforation of Descemet's membrane, KP extrusion 2 mo. pop
4	German Shepherd	10	F	CSK	Multiple lamellar keratectomies, radiotherapy, topical	OD	KP in place after 34 mo., visual 34 mo. pop
5	Dachshund	11	F	Endothelial disease	Topical	OD	Infection 4 mo. pop, extraction of KP 6 mo. pop
6	Dachshund	14	SF	Endothelial disease	Topical	OS	Infection 6 mo. pop, extraction of KP 6 mo. pop
7	Dalmatian	14	SF	Endothelial disease	Topical	OS	Infection 6 mo. pop, extraction of KP 6 mo. pop

F, female; SF, spayed female; M, male; CSK, chronic superficial keratitis; OD, right eye; OS, left eye; pop, postoperatively; mo, months.

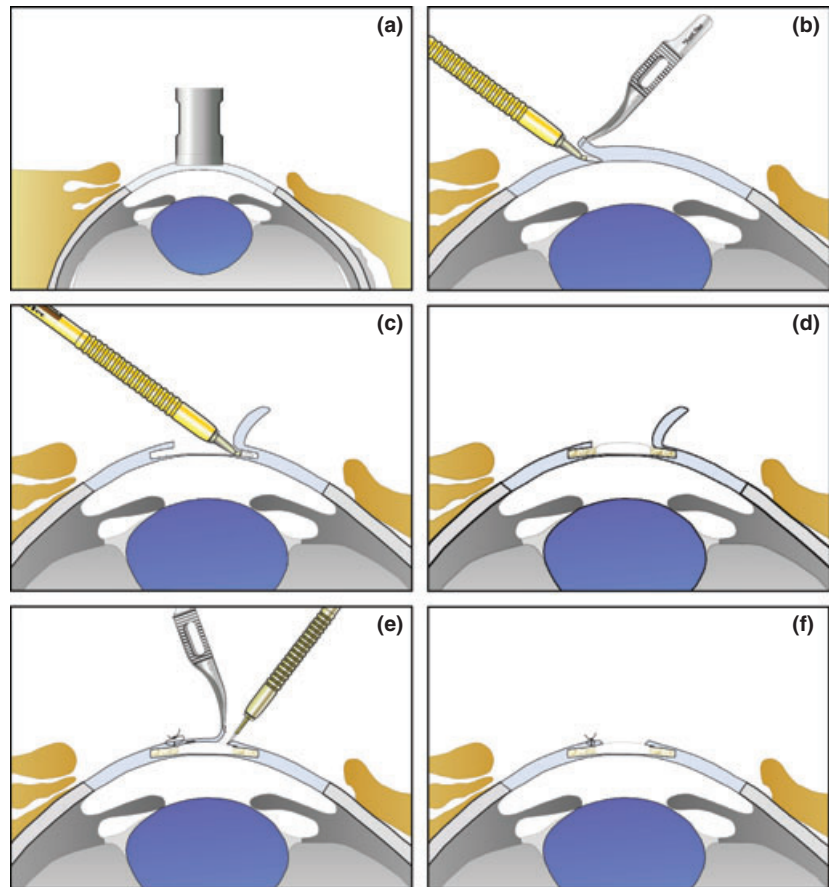


Figure 2. Schematic drawings providing step-by-step illustration of the surgical procedure to implant the keratoprosthesis. (a) A nonpenetrating corneal trephination of 6 mm diameter is performed. (b) Lamellar keratectomy is performed as close as possible to Descemet's membrane creating a corneal flap. (c) A pocket is created within the deep stroma at the margins of the trephined site for 360°. (d) The KP is inserted into the stromal pocket. (e) After suturing the corneal flap in place a small, 3 mm diameter, circular 'window' is created over the center of the KP optic. Note the 45° angulation of the wound edge. (f) Situation at the end of the surgery.

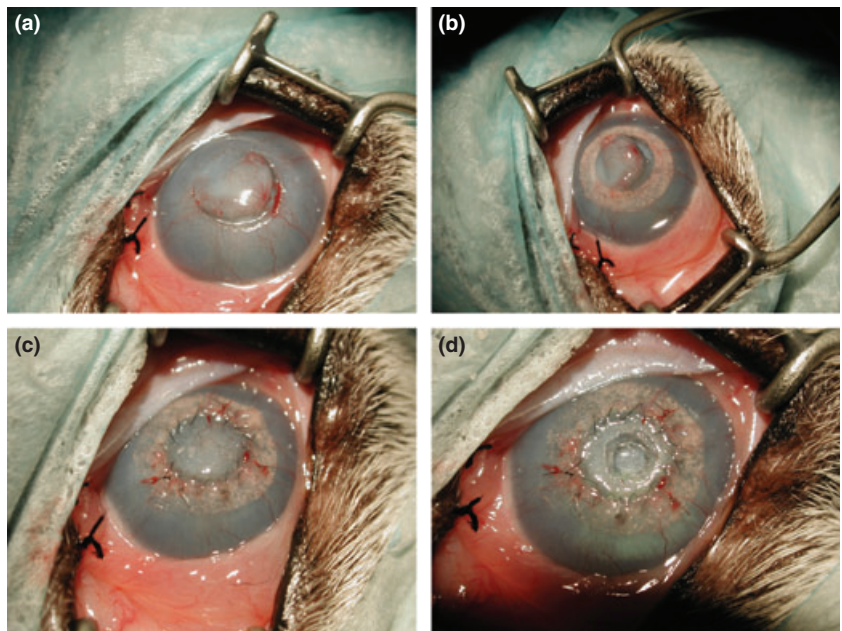


Figure 3. Step-by-step photographic illustration of the surgical procedure to implant the KP in a canine patient. (a) Nonpenetrating corneal trephination and creation of a deep stromal pocket is completed. (b) The KP is inserted into the stromal pocket. (c) The corneal flap is returned to its original position and sutured in place. (d) A 3 mm 'window' is created in the stroma overlying the KP optic at the conclusion of the procedure.

photographic illustrations, respectively, of the surgical procedure.

Under general anesthesia, a nonpenetrating corneal trephination of 6 mm diameter was performed with a corneal trephine. The trephined corneal button was incom-

pletely separated from the stroma. Starting at the margins of the trephined area, lamellar dissection of the peripheral stroma was carried out in a centrifugal fashion, thus creating an approximately 3 mm circumferential 'pocket' within the mid-peripheral stroma. Lamellar dissection was performed

as deeply as possible in the posterior stroma, in immediate proximity to Descemet's membrane. After insertion of the KP into the stromal pocket, the trephined corneal button was relocated to its original position and sutured in place with nonabsorbable suture material (9-0 or 10-0 nylon). Four cardinal stay sutures are placed in each of the four quadrants (at 9, 12, 3 and 6 o'clock) prior to placement of a continuous suture around the circumference of the central, trephined button. Finally, a small, 3 mm diameter, 'window' was created through the corneal stroma over the center of the optic of the prosthesis, using a 15° blade and intentionally creating 45° angulation of the wound edges. A temporary tarsorrhaphy was placed for 14 days postoperatively (5-0 silk).

Postoperative therapy consisted of topical antibiotic eye drops (polymyxin, neomycin, gramicidin) q8h for 2 weeks and oral carprofen, 4.4 mg/kg q24h for 1 week. The topical antibiotics were continued thereafter, q12h for 6 months postoperatively and owners were instructed to avoid taking their dogs to sandy and dusty areas, and to prevent their dogs from entering lakes and swimming. Owners were also shown how to gently clean the surface of the KP with a cotton tip applicator to prevent accumulation of debris that could interfere with vision. Corneal sutures were removed under topical anesthesia 3–4 weeks postoperatively. Ophthalmic examinations were performed 7–10 days after surgery and thereafter every 4–6 weeks. Follow-up times ranged from 8–34 months.

RESULTS

With the exception of one dog (dog 3), no intra-operative complications occurred. In six dogs, the surgery was

uneventful and placement of the KP within the stroma was completed as planned. A fundus reflection could be visualized at the conclusion of the surgical procedure. In these six dogs, the cornea healed without complications (Figs 4 and 5) within 3–4 weeks. All seven dogs were visual after the tarsorrhaphy sutures were removed seven to 10 days postoperatively. Vision was judged subjectively, based on the ability to navigate an obstacle course and to track moving objects.

In one dog (dog 3), Descemet's membrane was perforated during the deep stromal lamellar dissection. Despite this complication, the procedure was continued and a KP was implanted. The KP implanted in this dog was subsequently extruded 8 weeks postoperatively (Fig. 6). Fortunately, concurrent severe keratitis was associated with thickening of the stroma, resulting in rapid restoration of corneal thickness in the area of the KP. While the eye was not lost, vision was severely compromised by stromal scarring.

In the six remaining eyes, that had been successfully implanted with a KP, an increase of corneal stromal vascularization and cellular infiltration was noted during the first 8 weeks after surgery. In the four eyes with endothelial disease, postoperative recovery was uneventful for the first 3 months after KP implantation. However, in these cases, the stromal pocket around the KP started to accumulate a ring of debris, that resisted removal, even with vigorous flushing under topical anesthesia. After 5–6 months, all four remaining eyes with endothelial disease experienced purulent keratitis involving the stromal pocket around the KP (Fig. 7a). Bacterial and fungal cultures were negative in all cases. However, a purulent keratitis developed in all four of these cases, which made extraction of the KP necessary. At the time of surgical extraction of the KP, it was obvious that the silicone foam ring surrounding the KP optic was not

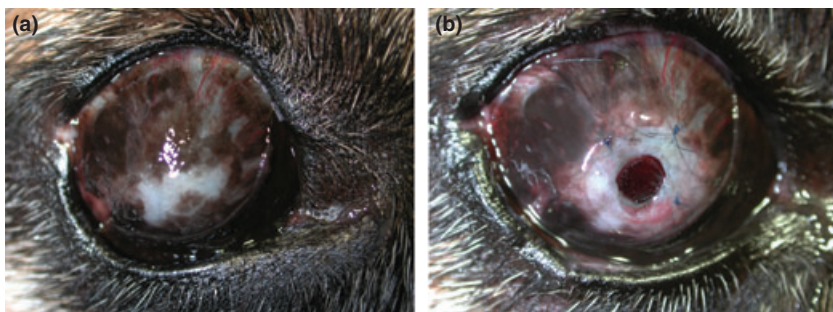


Figure 4. Clinical photographs illustrating the appearance of the left eye of dog 4 (chronic superficial keratitis): (a) pre- and (b) 3 weeks postoperatively.

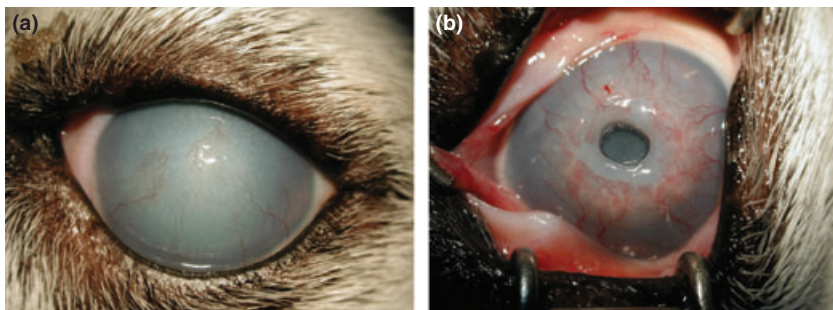
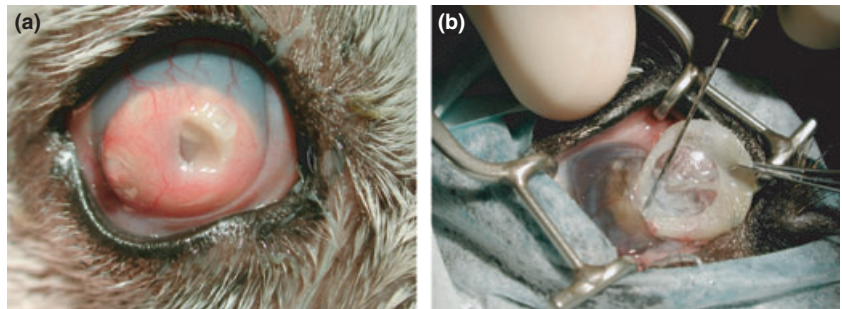


Figure 5. Clinical photographs illustrating the appearance of the right eye of dog 1 (endothelial disease): (a) pre- and (b) postoperatively.



Figure 6. Clinical photographs illustrating the appearance of the right eye of dog 3 (endothelial disease): (a) preoperatively, (b) 4 weeks and (c) 8 weeks postoperatively. The silicone foam ring haptic of the KP was progressively exposed. Note that this dog had previously been treated with a thermokeratoplasty.

Figure 7. (a) Clinical photograph illustrating the appearance of the right eye of dog 1 6 months postoperatively. Note the accumulation of debris around the KP and corneal reaction. (b) Clinical photograph illustrating the appearance of the left eye of dog 6. During surgical removal of the KP for the management of purulent keratitis, 6 months after initial implantation, it is obvious that the KP was not integrated into the stroma but remained within a pocket lined by epithelium.



integrated into the adjacent stroma. Epithelial downgrowth around the KP had formed a true pocket (Fig. 7b). Enucleation was not necessary in any of these eyes, with healing occurring by scarring and neovascularisation of the entire cornea. Vision in these eyes was lost, returning to the preoperative state. Although their dazzle reflexes were positive, all five dogs with pre-existing endothelial disease were ultimately unable to navigate an obstacle course after the KP was surgically removed or extruded.

In the two eyes with chronic superficial keratitis the KP remained in place and appeared to be well-tolerated for the duration of the follow-up periods (12 and 34 months), eliciting little inflammatory response. In contrast to the eyes with endothelial disease, the stromal pocket around the KP in the chronic superficial keratitis (CSK) eyes appeared to conform more tightly to the prosthesis and did not accumulate debris.

DISCUSSION

Due to the lack of eye banking in domestic animals, as well as the logistical problems that limit the availability of fresh donor corneal tissue, synthetic keratoprostheses are an attractive alternative in the management of corneal disease in animals. Moreover, many canine eyes with blinding corneal disorders would be considered high-risk eyes that would not be candidates for a conventional corneal transplantation, due to the extent of stromal vascularization and infiltration that may contribute to graft rejection and corneal opacification.

Stromal implantation of a novel prototype KP was accomplished successfully in six of seven dogs in our case series. In one case, implantation was unsuccessful due to an intraoperative complication and in retrospect, it might be considered that KP implantation should not have been completed in this case. Indications for surgery were severe, blinding chronic superficial keratitis or corneal endothelial disease, that were refractory to other treatments. All dogs were judged to be blind before surgery and all subsequently regained limited vision in the operated eye following KP implantation, as subjectively determined by their ability to negotiate an obstacle course. A similar situation has been reported in human patients, with limited restoration of vision after implantation of the similar AlphaCor® KP. In these human patients, vision remained limited but improved from preoperative light perception only, to around 20/200 following KP implantation.^{8,9}

Among the KP models currently used in human ophthalmology there are complicated models (OOKP, Boston KP) which are implanted in several step procedures (OOKP) as well as the one-piece AlphaCor® KP with a comparably simple implantation technique. Even though the reported follow-up times after implantation of an AlphaCor® KP in human patients are rather short (below 2 years) and the complications described may be severe⁷⁻¹⁰ a similar KP model, the Acrivet KP, was chosen to be evaluated in the dog. The applied surgical procedure to place the KP deep into the stroma is a one-step surgery. It seems to be feasible in dogs compared to other more complicated multi-step procedures like the OOKP used in humans. The major

problem in the described series of dogs was the accumulation of debris and subsequent stromal reaction around the KP despite of continuous topical antibiotic therapy. The stromal inflammation might be avoided by better integration of the haptic into the corneal stroma, which would likely require a change in the texture and topography of the silicone foam and further testing. Interestingly the complication of purulent keratitis did not occur in the two eyes with CSK. Both of these eyes had stromal vascularization and scarring related to chronic inflammation and to prior surgical intervention. Nevertheless, it was apparent that the KP was incorporated by their corneas in a different manner, which did not allow for the accumulation of debris or subsequent infection. Clinically, it appeared that a more intimate contact was established, with perhaps even stromal integration into the foamy KP haptic occurring in the CSK eyes, compared to the eyes with endothelial disease. The eyes with CSK remained visual for 12 and 34 months postoperatively, when they were subsequently lost to follow-up. In the group of dogs with endothelial disease, the KPs remained in place for an average of 6 months. After that time they had to be extracted for uncontrolled purulent keratitis. As these were all clinical patients, and enucleation of blind but pain-free globes was not indicated, histopathological evaluation of the corneal response to KP implantation was not possible in this study.

Stromal melt and deposition of debris on the KP are complications that have been described in relation to KP implantation in human patients.⁷⁻¹⁰ In human patients, other measures like protective hydrophilic bandage lenses, worn over the entire surface of the cornea and covering the KP and its edges have reportedly been effective in eliminating many ocular surface problems common to cornea transplants and KPs. In dogs such adjunctive measures may not be practical in the long term, due to the requirement to strictly maintain contact lens hygiene.

Given the postoperative complications identified in our pilot study, the KP prototype under investigation cannot be recommended for clinical applications in its current form. Considering the visual improvement noted in the dogs in our study, this KP prototype may offer a promising alterna-

tive to corneal transplantation in canine patients following design modifications to enhance its stromal integration.

Although the postoperative complications may be severe and limit the use of currently available devices, KP implantation can play a role in the management of corneal blindness in a selected group of patients with complex ocular diseases who are at high risk for conventional corneal graft failure.

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