A second generation of artificial cornea (Biokpro II)¹

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Abstract

The properties of a new second-generation colonizable artificial cornea were evaluated in humans. The prosthesis consisted of a peripheral rim of a translucent microporous fluorocarbon polymer (expanded polytetrafluoroethylene) fused with the polymer of the central optic. The optic was made of medical-grade polydimethylsiloxane coated with polyvinylpyrrolidone. Its refractive power was 42.2 diopters and it measured 7.0 mm in diameter and 0.55 mm in thickness. The geometry of the optic was tested by high-frequency ultrasound and intraocular pressure and distensibility were measured in an artificial chamber. Prostheses were implanted in one eye of 13 humans. The average follow-up was 6 months (range 3–9 months). Most of the eyes (11/13) were clinically stable after a 7 months follow up. Seven patients had visual acuity improvements. Mean corrected final visual acuity was 20/200 (range, 20/30 to light perception). Five anatomical failures occurred (two extrusions, two retroprosthetic membranes, one endophthalmitis). The new optical core, junction, and surface properties of the polymers offer many advantages, quicker colonization of the supporting skirt, and an optical core with a geometry similar to that of a normal human cornea. Epithelial cells did not migrate over the interface and optical core. It seems that formation of an epithelium over the artificial device is essential for the long-term stability of the implant. (1998 Elsevier Science Ltd. All rights reserved

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1. Introduction

Artificial cornea or Keratoprostheses (Kpro) have been provided for patients with bilateral corneal blindness who are suffering from conditions that preclude successful penetrating keratoplasty, such as immune-mediated cicatricial conjunctivitis, chemical burns, and severely vascularized corneas. While the initial recovery of vision may be good, most Kpros fail because of poor interaction between the artificial implant and host cornea [1–6]. Mechanical disruption of the interface coupled with the use of materials that do not allow tissue growth into the supporting rim have led to an unacceptably high rate of implant extrusion. However, the recent emergence of biocompatible materials [17–29] that permit the colonization of the supporting material by host keratocytes has shown that it is possible to integrate alloplastic material into the recipient cornea. Nevertheless, stromal melting and aqueous leakage still occur. We have shown that a polymer made of expanded polytetrafluoroethylene [21, 25] provides one of the best interfaces for the migration of fibroblasts. The porosity and thickness of the polymer that permits optimal cell colonization have also been studied [21, 25]. The initially white opaque PTFE polymer becomes translucent some weeks after its intralamellar or posterior corneal implantation [25, 27, 28]. The optical properties of the polymer are thought to be modified by the migrating keratocytes, which synthesize collagen fibrils that closely resemble the organization of collagen in the normal corneal stroma [25, 27].

We have carried out a pilot study on human patients using first generation Kpros [29]. These first generation Kpros consisted of an optic made of polymethylmethacrylate (PMMA) that was attached by clips to a supporting skirt of a biocolonizable expanded polytetrafluoroethylene (PTFE). Visual acuity was improved in approximately half the patients after a mean follow-up of three years, but the high rate of implant extrusion precluded long-term maintenance of vision (Fig. 1). These Kpros viewing of the posterior chamber because of the geometry of the PMMA optic. The thickness of the central optic also requires the removal of the crystalline...
lens from all patients. Certain features of the original Kpro have recently been modified. The clips that formed the mechanical junction between the optic and haptic have been replaced by the chemical fusion of a newly designed optic with its supporting colonizable skirt. The rigidity, thickness, and diameter of the optic have now been approximated to those of the human cornea. And lastly, the optic support has been modified to ensure quicker biocolonization. This report describes the results on artificial cornea implanted in 13 human eyes with a follow-up of seven months.

2. Materials and methods

2.1. Prosthesis

The Kpro had two components (Fig. 1) an optical core of soft polydimethylsiloxane (PDMS) copolymer coated with polyvinylpyrrolidone, and a 11.0 mm diameter disc of white opaque, hydrophobic fluorocarbon haptic (PTFE), with a thickness of 250 μm and a pore diameter of 80 μm. The colonization of the peripheral skirt by cells was encouraged by placing the PTFE polymer in 100% ethanol, and then in autologous serum for 1 min. It was rinsed in a balanced salt solution (BSS) for 5 min. This treatment rendered the PTFE polymer translucent and hydrophilic (Fig. 2). Wettability of the hydrophobic PDMS optic was enhanced by treatment with cold plasma in a nitrogen reactor for 2 min at 50 W, after which it was coated with polyvinylpyrrolidone. The refractive index of the polymer was 1.43, resulting in a refractive power of 42.2 diopters. The diameter of the optic was 7.0 mm and its central thickness was 550 μm. The radius of the anterior surface of the optic was 7.70 mm and that of the posterior surface was 6.82 mm, giving it an asphericity similar to that of the normal human cornea. The optic profile was checked by high frequency ultrasound, using an experimental prototype, the Scanning Ultrasound Microscope (prototype, University of Paris VI), to measure the thickness of the optic at 0.5 mm intervals from its center.

A tight seal was produced between the optic and the supporting skirt during manufacture of the Kpro when the liquid PDMS was injected into a mold supported by the solid PTFE skirt. The mold and its support were then heated at 138°C for 1 h in a sealed chamber to ensure penetration of one polymer into the other. The Kpros were sterilized with ethylene oxide, degassed for one month, and individually wrapped in labeled, sterile packages (Fig. 2).

2.2. Clinical studies

All the procedures were performed on 13 humans after written clinical consent. Patients were at least 18 y of age.
Fig. 2. The white opaque peripheral rim is composed of a microporous colonizable expanded polytetrafluoroethylene (PTFE) polymer. It is chemically joined to a transparent, medical grade optical core made of polydimethylsiloxane. The optic is 7.0 mm in diameter and 0.55 mm thick.

(Fig. 3). Phakic or aphakic patients were included. The procedure was performed by one surgeon (JML). Surgery was conducted under an operating microscope. A central 6.0 mm partial-thickness trephination was done with a Francheschetti trephine. The trephination was made smaller than the diameter of the Kpro to ensure that the Kpro fitted tightly. A crescent knife was used for centrifugal lamellar dissection of the peripheral cornea starting at the area of partial trephination. Radial relaxing incisions were made in the cornea at six and 12 o’clock superficial to the lamellar dissection to permit insertion of the prosthesis. The anterior chamber was entered with a super sharp blade and the cornea was excised with curved corneal scissors. The soft, flexible haptic was then placed intrastromally with a smooth spatula, making sure that its edges did not fold peripherally (Fig. 4). Four interrupted 10-0 monofilament nylon sutures were used and the knots buried to close the edges of the superficial cornea at six and 12 o’clock. A limbal peritomy of the conjunctiva was done over 360° using forceps and blunted scissors. The buccal mucosa were then brought over the cornea and sutured along the midline with interrupted 8-0 Vicryl sutures. Gentamicin drops were applied three times a day for fifteen days. Topical corticosteroids were not used. The buccal mucosa was opened two months post-implantation over the central 7.0 mm to allow externalization of the optic. All eyes were examined by a slit-lamp and photographed daily during the first week, weekly for the first month, and then monthly thereafter for a total of six months. Epithelialization of the optic was evaluated after instillation of 2% sterile fluorescein.

3. Results

3.1. Prosthesis

High-frequency ultrasound using the Scanning ultrasound microscope was performed at 0.5 mm intervals from the center of the optical core to the periphery. The optic thickness was 0.550 mm at the center and 0.681 thick at the 7 mm zone. Scanning electron microscopy of the transition zone between the two polymers of the Kpro showed a coarse entanglement of the PTFE and PDMS polymers.

3.2. In vivo studies

Most of the eyes (10/13) were clinically stable at the end of the study (Fig. 3). The PTFE supporting skirt remained translucent immediately after externalization of the optic and throughout the length of the study. Careful slit-lamp examination of the cornea, as tested with fluorescein, showed that the epithelium did not
Fig. 3. Corneal opacification before implantation.

Fig. 4. Second generation of keratoprosthesis. Pre-operative view.
completely cover the optic at any time (0/13). Two retro-
prosthetic membranes or synechiae formed between the
anterior segment structures and the implant during the
observation period.

Fewer than 1/3 of the eyes fitted with a Kpro (3/13)
developed aseptic necrosis at the junction between the
optic and host cornea: necrosis developed 2 months post-
implantation and the prosthesis was extruded shortly
thereafter. The buccal mucosa had retracted prematurely
in all cases of corneal melting, leaving the cornea exposed.

4. Discussion

The initial preliminary results obtained with a first
generation microporous biointegrable Kpro implanted
in 24 human patients between 1991 and 1993 were prom-
ising [29], but ulceration originating at the tissue-to-
implant interface resulted in a number of complications.
These first generation Kpros consisted of a PMMA optic
attached by clips to a colonizable PTFE skirt. Over half
the patients (17/24) showed an improvement in visual
acuity after an average follow-up of 15.7 months (range,
4–28 months). But five Kpros (20.8%) failed due to anato-
mal complications. These included three implant ex-
trusions (12.5%), one optic dislocation (4.2%), and one
bacterial endophthalmitis (4.2%). The mean follow-up
with the Þrst generation Kpros has extended to 36 ± 19
months (range, 7–69 months) in 73 patients since publica-
tion of this study. Improvement in visual acuity was
obtained in 70% of the patients in the pilot study, but
this was reduced to 47% (34/73) at the last follow-up.
The prosthesis was extruded in 13/73 cases (17.7%), retro-
prosthetic membranes formed in 8/73 cases (10.9%),
optic dislocation occurred in 7/73 cases (9.6%), glau-
comatous optic nerve damage occurred in 6/73 cases
(8.2%), endophthalmitis in 4/73 cases (5.5%), and retinal
detachment in 1/73 cases (1.4%).

The original Kpros also had functional limitations.
The rigidity of the PMMA optic did not permit IOP
measurements and the size (4.0 mm diameter and 2.37
mm long) of the optic, while it provided satisfactory
visual fields (better than 100°), precluded visualization of
the peripheral retina (less than 25°). Concomitant cata-
ract extraction was also necessary because the posterior
face of the optic lay against the anterior surface of the
crystalline lens.

The central optic of the artiÞcial device has been re-
modeled and its diameter increased from 4.0 to 7.0 mm,
and its thickness decreased from 2.37 to 0.55 mm (the
thickness of a normal human cornea). The anterior and
posterior curvatures of the optic are now different, giving
it an aspheric quality similar to that of the human cornea.

The new optic is also made of a more distensible
copolymer, polydimethylsiloxane (PDMS) coated with
polyvinylpyrrolidone.

The junction of the prosthesis has also been extensively
modified. The mechanical clips holding the optic to the
supporting structure have been replaced by a melding of
the PTFE and PDMS polymers. Mechanical systems for
holding the optic to the rim, such as clips [29], screws
[1, 3, 6, 7, 8, 10–16] and glues [4, 14] are inherently too
weak for long term implant stability and safety. It was
once thought that polymeric interdigitation could only
be achieved with materials having similar molecular
compositions [23, 24], but heating the PDMS optic
while still in its liquid phase allows polymerization to
occur within the sponge-like solid PTFE rim. The result-
ing crosslinking of dissimilar polymers (PTFE and
PDMS) occurs at the interface and confers greater rigid-
ity at the junction of the prosthesis, which could help
prevent optic dislocation from mild ocular trauma. Fi-
nally, hydrophilisation of the PTFE polymer ensured
a rapid and complete colonization of the supporting rim
by ßbroblasts which firmly adhered to the surrounding
host tissue [30].

In summary, the newly designed quality-controlled
Kpro offers many technological advantages over the
original Kpro, such as: a medical grade optic geomet-
rically similar to a normal human cornea, quicker colo-
nization by ßbroblasts of the supporting haptic, and the
possibility of performing phacoemulsification or pars
plana vitrectomy months or years after implantation. But
the optic and junction are still not yet covered by epi-
thelial cells.

The implants were extruded in 2/13 human eyes prob-
ably because of the premature retraction of the buccal
mucosa, which occurred before the implant was colo-
nized with ßbroblasts. Considerable efforts are being
made to fabricate a biocompatible artiÞcial cornea that
eliminates the need to bury the prosthesis under conjunc-
tiva, lid, or buccal mucosa for a number of months
[23, 24]. We feel that a healthy epithelium must form
over the bare optic and junction to ensure long term
stability of the Kpro. Otherwise, the space between the
optic and rim that is devoid of epithelium will leave the
underlying stroma exposed to the deleterious e¤ects of
collagenases and proteinases produced by neighboring
traumatized epithelial cells, by the tear ßlm, and by
migrating inßammatory cells, leading to ulceration. It is
our belief that the fabrication of a well-tolerated artiÞcial
device will inevitably include some viable tissue bound to
the alloplastic material, as only a ÔhybridÕ artiÞcial cornea
may offer long term visual recovery and stability.

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