Original Research

Improving the practicality and safety of artificial corneas: Pre-assembly and gamma-rays sterilization of the Boston Keratoprosthesis

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ABSTRACT

Purpose: To make the Boston keratoprosthesis (B-KPro), together with its carrier corneal graft, more easily procured, transported and stored, as well as less expensive, easier for the surgeon to implant and safer for the patient, it is proposed that the B-KPro-graft combination be pre-assembled by an expert technician, followed by sterilization with gamma ray irradiation (GI) allowing long-term storage at room temperature. For this to be possible, it must be shown that the B-KPro itself (not only the graft) remains unharmed by the irradiation.

Methods: Polymethyl methacrylate (PMMA) discs and B-KPros were submitted to either ethylene oxide sterilization or different doses of GI. Cell biocompatibility, mechanical strength and optical quality were evaluated. The feasibility of assembling the B-KPro to a corneal graft, and gamma-radiate afterwards, was also assessed.

Results: There were no differences in cell biocompatibility between the samples. The optical evaluation showed high levels of transparency for all the groups. The absorbance of ultraviolet was higher for the groups treated with GI. The mechanical evaluation by nanoindentation showed no alterations of the PMMA discs after GI. The flexure test revealed a similar mechanical behavior. Technically, pre-assembly and GI of the B-KPro revealed no problems.

Conclusions: Sterilization of B-KPro using GI has no detrimental influence on the device. The pre-assembly of B-KPro to a donor cornea, followed by gamma sterilization, emerges as an efficient and safe procedure.

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1. Introduction

An artificial cornea is increasingly resorted to as a rescue procedure in cases of corneal transplant failure, or in severe corneal diseases that have poor prognosis for standard treatment. One such device is the Boston keratoprosthesis (B-KPro), which has by now been implanted in over 13,000 human eyes, worldwide [1]. The B-KPro is a double-plated device, made of transparent polymethyl methacrylate (PMMA), which usually requires a fresh corneal transplant as a carrier. The assembly is presently performed by the surgeon at the beginning of the surgical procedure and the combination is then implanted into the patient's eye like a standard corneal transplant [2].

B-KPro is a well-established procedure for repeated corneal graft failure [3], showing higher probability of maintaining visual improvement compared to repeat donor penetrating keratoplasties, without greater risk of postoperative glaucoma [4]. Moreover, B-KPro is also an accepted treatment in patients with limbal stem cell deficiency, mainly derived from chemical or thermal injuries, aniridia or autoimmune diseases [5–8]. The retention rates vary from series to series, from 67% at 7 years [9] to 95% at 8 years [10]. The postoperative corrected distance

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more than 40 years [11], and it has been employed for ophthalmological use for years. EtO has been also used for sterilization of tissues and organs. In most of the cases, due to the high incidence of corneal blindness, the lack of donor corneas, eye banks and readiness for corneal transplantation therefore hinders the use of the device and the adequate treatment to the patient. Moreover, the assembly of the B-KPro into a fresh graft in the operating room by the surgeon is not only time-consuming but can occasionally result in inadvertent decentration of the device in the donor cornea. A cornea and B-KPro preassembled, and preserved at room temperature (“off-the-shelf”), would likely facilitate safe use of the device [12].

A change of sterilization technique from the present ethylene oxide (EtO) to gamma radiation promises to open up new possibilities. EtO has been widely used for sterilization of medical devices. However, it has several important disadvantages: the cost, lengthy sterilization cycle, potential toxicity and risks of handling an explosive and flammable gas [13]. EtO has been also used for sterilization of tissues and organs. Nonetheless, it has not been generally adopted because of its limited capacity to penetrate through dense tissues [14]. In order to avoid those inconveniences, other methods of sterilization are replacing EtO, such as gamma irradiation (we will use “gamma” as an abbreviation of ‘gamma-rays’). Gamma sterilization has been widely used in industry for more than 40 years [15], and it has been employed for ophthalmological devices and also, more recently, for donor corneas [16–22]. Such corneas have been successfully used as carrier for B-KPro as well [23,24].

Gamma irradiation should also allow a simplified pre-assembly technique of the B-KPro to a donor cornea in an eye bank or central facility, allowing subsequent storage and transport at room temperature, as well as freeing the surgeon from assembly in the operating room. Thus, a skilled technician should be able to assemble the B-KPro into the carrier corneal graft in-house, and then transfer the combination to a storage vial for sterilization with gamma irradiation. The resulting combination should then be ready for long-time storage at ambient temperature, and be easily transported to anywhere in the world, including those countries where donor corneas are scarce. However, it has to be shown that sterilization by gamma irradiation will not damage the B-KPro and its interface with the graft. This is the purpose of the present study.

2. Methods

2.1. Sterilization methods

All the sterilized samples used in this work were treated with ethylene oxide or gamma irradiation. Afterwards, the samples were stored at room temperature until further processing.

EtO sterilization was performed in Steris Isomedix Services facility (Spartanburg, SC) with sterility assurance level of 10⁻⁶ overkill approach in accordance with ANSI/AAMI/ISO 11135 Standard. EtO concentration of 607 mg/L was used for 3 h at 51.7 °C, followed by aeration for 72 h at 40–54 °C. These samples were individually packaged with double packaging using Wipak Steriking self-seal sterilization pouches (Wipak; Nas-tola, Finland).

Gamma rays irradiation was performed using a cobalt-60 source (MDS Nordion Gammacell 220E irradiator, at MIT’s Department of Biological Engineering; Cambridge, MA). The samples were individually packaged in sealed 25 ml-tubes placed centrally in the irradiator chamber and delivered a dose of 10, 25 or 50 kGy of gamma irradiation at room temperature. The dose was calculated according to cobalt-60 source decay calculation.

2.2. Optical evaluation

15 mm-diameter polished discs (0.5 mm thickness) of medical grade PMMA (Rod number 2, PolyOne; Littleton, MA) were exposed to different doses of gamma irradiation (10, 25 and 50 kGy), independently (n = 3 each; n: number of samples). A control group was established with discs that were not gamma irradiated. The spectral transmission measurements were made using an UV-Visible spectrophotometer (Evolution 220, Thermo Fisher Scientific; Waltham, MA) between 200 and 800 nm (slit width 2 nm) one day after finishing the respective sterilization process. 3 measurements were made for each disc in different areas of the disc. Data from the different measurements on each disc were averaged over 5 nm-intervals, and then those 3 spectra (one spectrum per disc) were averaged to provide the final spectrum of each group. Changes in daylight transmission through the PMMA discs were quantified by the color coordinates in the CIE (Commission Internationale de l’Eclairage) color space, the dominant wavelength, and the saturation [25]. For ‘daylight’ we used the CIE D65 illuminant that simulates direct sunlight and the light diffused by the sky.

Additionally, the spectral transmission of individual B-KPros before and after gamma irradiation was assessed using an UV-Visible spectrophotometer (SpectraMax Plus 384; Molecular Devices; Sunnyvale, CA). The B-KPros were placed in a quartz 96-well microplate and their spectral transmittance values were measured before and after gamma irradiation with 25 kGy, at different time points up to 3 months after irradiation. The transmittance data was recorded at 1 nm wavelength increments from 250 to 850 nm. Experiments were quadruplicate and transmittance of the samples was corrected with corresponding blank wells of the microplate. The mean percentage of transmittance for each group was calculated and plotted as a function of wavelength for each time point.

A transparency-resolution evaluation of the B-KPro was performed before and after gamma irradiation with 25 kGy, using an optical bench following our previously described method [26]. Non-gamma and gamma irradiated B-KPros (n = 3 each) were independently held in a diaphragm in front of a microscope, which was placed 304.8 cm (10 feet) away from an illuminated 1951 US Air Force resolution bar chart (Edmund Industrial Optics, Barrington, NJ). Three blind independent observers looked to the bar chart through the microscope focused on the B-KPro in order to determine the smallest recognizable 3-bar element of the chart. The limiting resolution was obtained using an automatic calculator (facilitated by Edmund Industrial Optics website) that determines resolution in terms of line pairs per millimeter based on the relationship between group number and element number of the chart, following this equation: Resolution (Line-pair/mm) = 2(Group + (Element-1)/6). The theoretical visual acuity was obtained after converting the element numbers of the resolution chart into their corresponding optotypes. The conversion was made applying to the different elements of the resolution chart the rules that define Snellen optotypes based on distance and angle of the optotype bars. Thus, Element Number 2 in Group Number –1 would correspond to a visual acuity of 20/20 at 10 feet. The independent values obtained from the observers were averaged to define a limiting resolution and a theoretical visual acuity for each analyzed B-KPro. Representative images of the different samples attaching a digital camera with a 21x macro lens to the microscope were taken.

2.3. Mechanical evaluation

Nano-indentation was used to determine the hardness (H) and indentation modulus (M) of 15 mm-diameter PMMA discs (Rod number 2, PolyOne) exposed to either EtO sterilization, or different doses of gamma irradiation (10, 25 and 50 kGy), independently (n = 3 each). A control group was established with discs that were not gamma irradiated or EtO treated. Each PMMA disc was first polished with a sequence of SiC papers of decreasing abrasiveness before being fixed on a metallic stub (25 mm x 25 mm x 6 mm) with cyanoacrylate glue. The samples were placed in a chamber of controlled climate (20 °C, 20% RH) for...
indentation. The nano-indentet test fixture (UNHT, Anton Paar; Graz, Austria) consists of a three-sided pyramid-like Berkovich diamond tip coupled to an active spherical reference located at 3 mm from the Berkovich tip. The reference sits on the sample surface and makes it possible to measure the mechanical properties of the sample without any thermal drift. The sample was indented over a square grid of 8 x 8 = 64 indents, separated by 10 μm. Each indent was performed in a force-controlled mode to a maximum indentation depth of 300 nm, which corresponds to a typical load of approx. 0.6 mN to 0.8 mN, depending on the mechanical properties of the sample. The force was increased linearly at a rate of 10 mN/min until the desired depth of 300 nm was reached, then maintained constant at the corresponding value for 10 s, before being ramped back down to zero at the same rate. The indentation modulus and the hardness were computed from the raw curves following the method of Oliver and Pharr [27,28].

Flexural strength and brittleness measurements were performed to evaluate the mechanical properties of the B-KPro before and after gamma irradiation. The measurements were obtained applying a 3-points bending test using a tripod, which was designed to hold the B-KPro in place, restricting the X,Y plane movements while allowing only Z-direction travel. The tripod was fabricated using a computer numerical control machine. Then, non-gamma and 25 kGy gamma irradiated B-KPros were placed on the tripod and subjected to compression force applied by a tensile compression force tester (Mark-10 ESM 303; Copiague, NY), equipped with MESUR Gauge Plus software and a load cell of 50 N capacity at crosshead speed of 0.5 mm/min. The ultimate flexural strength of the B-KPro (n = 10 per group) was recorded as the maximum force measured in the load/displacement curve (rupture of material). Further, the slope of the force/displacement curve was evaluated for the modulus of the B-KPros.

2.4. Cell biocompatibility

2.4.1. Presto blue assay

The influence of different sterilized treated PMMA on the viability of cultivated corneal cells was measured by PrestoBlue assay according to standard protocol. 15 mm-diameter PMMA discs were submitted to either EtO sterilization or 25 kGy of gamma irradiation (n = 4 each). Green fluorescence protein tagged (GFP) human corneal epithelial cells (GFP-HCEC) [29] were used for this study; kindly donated by Professor May Griffith. GFP-HCEC were cultured with keratinocyte serum-free medium (KSFM) supplemented with 50 μg/ml bovine pituitary extract and 5 ng/ml epidermal growth factor (EGF) (Gibco; California, USA).

Primary human corneal fibroblasts (HCF) were also used for a cell viability study. Cells were isolated from donated human corneoscleral rims discarded after penetrating keratoplasties performed at the Massachusetts Eye and Ear Infirmary, Massachusetts, USA. Corneal tissue was separated from the corneoscleral limbus and sclera. The corneal pieces were cultured using an explant technique with EMEM media (ATCC; Virginia, USA) supplemented with 10% fetal bovine serum (Gibco; California, USA) to generate corneal fibroblasts [30]. HCF were allowed to migrate from the tissue and expand over the period of several weeks. HCF were utilized between passages 4 and 7.

The PrestoBlue study was performed in 6-well cell culture inserts (Coster; Maine, USA) with each cell type. Gamma irradiated and ethylene oxide treated PMMA discs were placed on the membrane of the insert. 30,000 cells (GFP-HCEC or HCF) were seeded on the bottom surface of the insert plate. Once a monolayer cell culture was obtained, cells were incubated in Dulbecco's modiﬁed medium (DMEM)/F-12 (Sigma-Aldrich; St. Louis, MO) supplemented with 10% newborn calf serum (Thermo Scientific; Rockford, IL) and 10 ng/ml EGF (Life Technologies) for 7 days to promote stratification and differentiation. Cells cultured on the bottom surface of wells of empty 6-well cell culture inserts were used as control. For the dye penetration assay, cells were rinsed with PBS and incubated for 5 min with a 0.1% solution of rose bengal. Afterwards, the dye was aspirated and the cells washed with PBS. The extent of dye penetration in cell culture was assessed using an inverted microscope (Nikon Eclipse TS100). Representative pictures of each sample were taken with a SPOT Insight Fire Wire Camera (Diagnostic Instruments, Inc.; Sterling Heights, MI) and analyzed with ImageJ applying the methodology previously described by Argueso et al. [31].

2.5. Stability of the assembly

To evaluate the stability of the preassembled B-KPro after gamma irradiation, a B-KPro Type 1 (PMMA backplate, with locking ring) was assembled to a human donor cornea previously trephined with a 3 mm punch. Afterwards, the combination was placed into a vial with 5% dextran and gamma-irradiated with 25 kGy, and followed with Anterior Segment Optical Coherence Tomography (AS-OCT) (OCT Spectralis; Heidelberg Engineering Inc.; Franklin, MA) for 6 months in order to assess any alteration of the tissue carrier or the interface between the carrier and the B-KPro.

2.6. Statistical analyses

Multiple groups were compared using one-way ANOVA, including Tukey's multiple comparison test. Statistical analyses for comparison of two groups were carried out using Mann-Whitney U test. All data are
shown as mean ± standard deviation. In all tests, p-values less than 0.05 were considered statistically significant.

3. Results

3.1. Optical evaluation

The optical evaluation of PMMA discs showed high levels of optical transmission (>80%) in the visible spectrum (between 400 and 800 nm) for the control (designation PMMA), 10 and 25 kGy groups (Fig. 1a). A slight drop on transmission on those wavelengths is seen in the 50 kGy group. Changes in transmission are particularly pronounced in the ultraviolet spectrum (below 400 nm), indicating an improved UV absorption of the material as a result of gamma irradiation. The transmission assay also showed a high transmission of the visible light for all the groups except for a decrease in the transmission of the blue light through irradiated B-KPros, which gradually disappears with time after the irradiation.

The optical transmission of B-KPro before and after gamma irradiation was similar (>85%) at the time points tested for the visible wavelengths between 500 and 800 nm (Fig. 1c). However, the blue band with wavelength range from 400 to 499 nm exhibited a reduction in light transmission in the gamma irradiated groups (Fig. 1d), like for the discs. Such blue light absorption contributes to the pale yellow appearance of the B-KPros after gamma irradiation (Fig. 1b), which gradually diminished over time. These changes resulted in small changes in the color characteristics of light transmitted by the B-KPro (Table 2). Therefore, the gamma irradiated PMMA will not significantly affect the patient's

<table>
<thead>
<tr>
<th>Color</th>
<th>Dominant Wavelength (nm)</th>
<th>Saturation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMMA Control</td>
<td>489.8</td>
<td>6.5</td>
</tr>
<tr>
<td>After Gamma 10 kGy</td>
<td>490.0</td>
<td>6.6</td>
</tr>
<tr>
<td>After Gamma 25 kGy</td>
<td>491.1</td>
<td>6.0</td>
</tr>
<tr>
<td>After Gamma 50 kGy</td>
<td>493.8</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Table 1: Color characteristics of white light transmitted by PMMA discs before (control) and after different doses of gamma irradiation.

a D65: Standard Daylight Spectral Distribution (direct sunlight and diffused skylight).

b Coordinates in the CIE 1931 color space derived from the spectral distribution of the transmitted light by the PMMA discs.

c Wavelength of monochromatic light that evokes an identical perception of hue.

d Measure of the colorfulness or purity of the perceived hue.
Table 2  
Color characteristics of white light transmitted by B-KPros before (control) and at different time point after gamma irradiation with 25 kGy.

<table>
<thead>
<tr>
<th>Color Dominant</th>
<th>Saturation</th>
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<tr>
<td>Coordinates</td>
<td>Wavelength</td>
</tr>
<tr>
<td>X</td>
<td>Y</td>
</tr>
<tr>
<td>D65&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.313</td>
</tr>
<tr>
<td>B-KPro Control</td>
<td>0.314</td>
</tr>
<tr>
<td>After 1 day</td>
<td>0.324</td>
</tr>
<tr>
<td>After 15 days</td>
<td>0.324</td>
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<tr>
<td>After 90 days</td>
<td>0.324</td>
</tr>
</tbody>
</table>

<sup>a</sup> D65: Standard Daylight Spectral Distribution (direct sunlight and diffused skylight).
<sup>b</sup> Coordinates in the CIE 1931 color space derived from the spectral distribution of the transmitted light by the B-KPro.
<sup>c</sup> Wavelength of monochromatic light that evokes an identical perception of hue.
<sup>d</sup> Measure of the colorfulness or purity of the perceived hue.

The transparency-resolution evaluation was performed using an optical bench, composed by a microscope (1), a diaphragm that hold the B-KPro (2) and a resolution chart (3). Representative images of the chart were taken through gamma (b) and non-gamma irradiated (c) B-KPros. The resolution assessment revealed no significant differences between the non-gamma and the gamma irradiated B-KPros (p > 0.05). Three independent observers achieved the same visual acuity (VA) looking to the chart through non-gamma or gamma irradiated B-KPros (p > 0.05). n.s., non-significant.

3.3. Cell biocompatibility

We next evaluated the effect of gamma-radiated PMMA in GFP-HCEC and HCF to determine if cells under indirect contact with gamma-radiated or ethylene oxide treated PMMA can proliferate and properly differentiate. PrestoBlue analysis (Fig. 4a) showed no significant differences among the groups after 1 day in culture. However, after 4 and 7 days in culture, HCEC and HCF viability was significantly higher in the absence of PMMA (control group), compared to those groups where gamma-radiated or EtO sterilized PMMA were present. For GFP-HCEC, significant differences were found between gamma and EtO sterilization methods only after 7 days in contact, with a higher number of cells in the gamma irradiated group. For HCF, the EtO group showed a statistically significantly better cell survival rate after 4 days in culture compared to the gamma irradiated group. However, after 7 days in culture, there were no significant differences between groups.

Fluorescence studies revealed confluent cultures of HCEC and HCF on top of the tissue culture plate after 10 days under culture in indirect contact with the treated PMMA, with no significant differences compared to the control (Fig. 4b). Each group exhibited a characteristic cell morphology, without differences between the treated PMMA samples and the control. The Live-Dead assay revealed no significant difference in the viability of HCF cultured in indirect contact with EtO treated or gamma-radiated PMMA.

In the Rose Bengal assay, treated PMMA samples and the control showed a normal pattern of corneal epithelial cell stratification, with multiple non-stained areas where the differentiated surface epithelial cells exclude the dye (Fig. 4b). No statistically significant differences were observed between groups (Fig. 4c).

Fig. 2. a) The transparency-resolution evaluation was performed using an optical bench, composed by a microscope (1), a diaphragm that hold the B-KPro (2) and a resolution chart (3). b and c) Representative images of the chart were taken through gamma (b) and non-gamma irradiated (c) B-KPros. The resolution assessment revealed no significant differences between the non-gamma and the gamma irradiated B-KPros (p > 0.05). n.s., non-significant.
3.4. Stability of the assembly

A preassembled B-KPro in a human donor cornea, placed in a vial and then gamma irradiated, is shown in Fig. 5a. At 6 months after gamma-sterilization, AS-OCT showed a normal assembled device, without retraction or swelling for the corneal tissue (Fig. 5b).

4. Discussion

The present study demonstrates that 25 kGy of gamma rays irradiation may be suitable for sterilization of a preassembled B-KPro in combination with a corneal graft. The optical and mechanical evaluations, cell biocompatibility assays, and observed stability of the device-graft combination suggested that a preassembled device will function as well as the presently used ethylene oxide-sterilized (FDA approved) B-KPro. Transmission of visible light through an untreated B-KPro is reduced only slightly (<20%) and the difference between the samples from the various sterilization techniques likely has no clinical significance. A mild yellowing effect was observed, as with most acrylics exposed to gamma irradiation. This effect is temporary and it is directly associated with the dosage used, as previously described [37,38]. Some techniques previously described have the potential to substantially reduce recovery time [38]. Moreover, gamma irradiated samples showed a protective effect against photochemical damage by blocking blue light and the UV, in agreement with previous studies [39]. This effect was higher than the protection already described for non-irradiated B-KPros [40]. Transparency and resolution (image formation) are arguably the most important aspects of the optical evaluation, and gamma irradiation appeared to have no deleterious effect as compared to EtO-sterilized device. The minimal reduction of resolution recorded in non-gamma as well as gamma irradiated B-KPros may be due to surface irregularities from machining and polishing, but does not prevent normal visual acuity (20/20) in three healthy observers, as described in this work, and in clinical use with non-gamma irradiated B-KPros [41,42]. It has been suggested that gamma irradiation can be associated with degradation and an increase of fragility of some polymers [43–46]. Loss of structural integrity could be caused by structural modifications related to polymer chain scission [47] and changes in molecular weight and molecular size distribution, which might then lead to alterations of the optical properties of the material [45]. However in our study, there were no significant differences between the mechanical behavior of non-gamma and gamma irradiated B-KPros in terms of hardness and fragility. Also structural modifications or optical impairments were not seen after gamma irradiation. These data were in agreement with previous reports that demonstrated that PMMA is not mechanically affected by the irradiation treatment, with only insignificant differences in the density of its backbone structure [37,45]. Some researchers even noticed that gamma irradiation can improve the mechanical stability, which can originate from introduction of crosslinking bridges in the polymer network [46].
PMMA has been always considered a biocompatible material, and is used not only for ophthalmic devices but also in orthopedics. However, while the polymer is biologically inert, PMMA monomers and polymerization reaction intermediates can induce an immune reaction in the host [46]. PMMA radicals can also be generated after irradiation [45]. However, in our study, corneal cells under indirect contact with gamma-radiated or ethylene oxide treated PMMA were able to properly grow and proliferate, showing no significant differences between groups. In this regard, previous researchers suggest that high doses of gamma irradiation might lead to better cellular response because of decreasing eluates from polymerized PMMA [48].

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Fig. 4. Cultured corneal cells can proliferate and properly differentiate under indirect contact with gamma irradiated (25 kGy) or EtO treated samples. a) PrestoBlue assay showed that the viability of HCEC and HCF was not superior in the EtO group compared to 25 kGy. b) Fluorescence-based studies (first two rows) revealed confluent cultures of HCEC and HCF after 10 days of culture in indirect contact with the treated PMMA, not observing differences compared to the control (CTRL) (Scale bars: 1000 μm). Rose Bengal (RB) assay showed a normal pattern of stratification of the corneal epithelial cells, exhibiting multiple non-stained areas where the stratified epithelial barrier function excludes the dye. c) The quantification of the stratified area observed in the RB assay using ImageJ revealed no significant differences among EtO-treated or gamma irradiated PMMA discs and the control. *p < 0.05; **p < 0.01; ****p < 0.0001; ns, non-significant; Px, pixel.

Fig. 5. The final product after assembling the B-KPro into a corneal graft and storing it in a vial with 5% dextran solution where it is stable for at least 6 months. a) Photo of the glass vial with storage solution and the pre-assembled B-KPro-allograft combination (white dotted square), subjected to 25 kGy of gamma irradiation. The process of preassembling the human donor cornea (1) with the device (2), and gamma irradiate afterwards, showed no complication in terms of handling and sterilizing. Pictures on the right are magnified photos of the B-KPro-allograft combination from different angles. b) After 6 months of performing the gamma-sterilization treatment, the AS-OCT revealed that the corneal tissue (1) had not significantly receded from the B-KPro (2). Line of reflection of the glass vial (3).
Fig. 6. Possible flow-chart for more practical implantation of artificial corneas.

In conclusion, sterilization of the B-KPro using gamma irradiation has no detectable influence on the biocompatibility, mechanical or optical properties of the device. With the proposed pre-assembled, gamma irradiated, graft-B-KPro combination, implantation of a B-KPro should be simplified. Thus, the theoretical main advantages of a preassembled B-KPro would include off-the-shelf use with easier access to the device in locations where corneal tissue is sparse or frankly unavailable, and a standard centration without concern for intraoperative errors by the surgeon. Such a development should be particularly welcome in the non-industrialized world, which may lack eye banks, rapid transportation systems and financial resources in general. Further improvements may come in the form of less expensive carrier donor material. In this regard, modified xenografts or laboratory-made constructs might require less testing for infectious agents, and further reduce overall cost [12] (Fig. 6). In combination with potential reductions in manufacturing costs, the total expense for B-KPro surgery could become more affordable. Thus, pre-assembly of the B-KPro in a donor cornea, followed by sterilization with gamma irradiation, allowing long-term storage at ambient temperature, portends a potentially more efficient and safer procedure to treat corneal blindness not otherwise amenable to corneal transplantation.

Conflicts of interest

Miguel Gonzalez-Andrades, Roholah Sharifi, Mohammad-Mirazul Islam, Eleftherios I. Paschalis, Larisa Gelfand, Andrea Cruzat, James Chodosh, Francois Delori and Claes H. Dohlman are, or were in the past, full-time employees of Massachusetts Eye and Ear Infirmary, Boston - the manufacturer of the Boston Keratoprosthesis.

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