Designing a gas foamed scaffold for keratoprosthesis

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Abstract

Artificial corneas or keratoprosthesis are intended to replace diseased or damaged cornea in the event that vision cannot be restored using donor cornea tissue. A new class of artificial cornea comprising a combination of poly (2-hydroxyethyl methacrylate) and poly (methyl methacrylate) was developed which was fabricated using a gas foaming technique. Referred to as the gas-foamed KPro, it was designed to permit clear vision and secure host biointegration to facilitate long-term stability of the device. In vitro assessments show cell growth into the body of the porous edge or skirt of the gas-foamed KPro. The optically transparent core (i.e., core) of the device demonstrates 85 – 90% of light transmittance in the 500 – 700 nm wavelength range. Mechanical tensile data indicates that the gas-foamed KPro is mechanically stable enough to maintain its structure in the ocular environment and also during implantation. The gas-foamed KPro may provide an alternate option for cornea replacement that minimizes post implantation tissue melting, thereby achieving long-term stability in the ocular environment.

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1. Introduction

A synthetic keratoprosthesis (KPro) or corneal replacement device may benefit patients who are ineligible for donor cornea. While existing synthetic KPros demonstrate a level of utility, they often fail to adequately address one or more of the following vital parameters: long-term host integration, mass transport, tissue epithelialization, or innervation. An inadequate keratoprosthesis design can result in extrusion, necrosis, increased intraocular pressure, or infection [1–3]. Conversely, a well-designed artificial cornea would be mechanically and structurally stable and facilitate long-term biointegration with the host. We recently submitted a patent, US Patent Application 13/284,301, for such an artificial cornea or KPro. The KPro is composed of poly (2-hydroxyethyl methacrylate) (PHEMA) and poly (methyl methacrylate) (PHEMA–PMMA). This study demonstrates that the newly engineered PHEMA–PMMA KPro, referred to as the gas-foamed KPro, is biocompatible, optically transparent, and mechanically strong enough to maintain its structure in the ocular environment.

Typical KPro designs follow a core–skirt model in which an optically transparent core permits vision while a porous skirt allows for tissue ingrowth [1–3]. This is a challenging engineering task because uncontrollable cell growth and debris adsorption on the core should be discouraged to maintain its optical clarity, while the opaque porous skirt (e.g., outer rim of the KPro) is designed to promote tissue ingrowth. When implanted, biointegration achieved through tissue ingrowth into the device is imperative for long-term retention in the patient’s eye. A technique known as gas foaming may benefit KPro designs because the gas foaming of hydrogels is known for generating interconnected pores during polymerization [4]. KPro skirts that permit biointegration may then be created by at least two methodologies. First, an interconnected pore structure can be introduced to a synthetic polymer that has ocular compatibility [1,3]. Second, natural polymers, such as collagen or decellularized animal tissue, can be used as KPro skirts [5,6]. Synthetic polymers, PHEMA and PMMA, allowed us to create a mechanically stable KPro that may benefit patients who are immunologically sensitive to donor cornea or foreign biological material. Synthetic tissue engineering scaffolds also permit a high level of control over mechanical properties, geometry, and biological interaction [7,8]. Both the ocular compatibility and pore interconnectivity of KPro skirts appear to be major determinants of long-term KPro stability.

Clinical outcomes for other core–skirt KPros such as AlphaCor, Seoul Type, and Pintucci indicate that device performance depends on both device design and patient selection. The aforementioned KPros include a core made of either PHEMA or PMMA. Both transparent PHEMA and PMMA cores can permit vision. However, long-term vision restoration depends on KPro retention in the host, and the skirt’s ability to promote tissue ingrowth influences device retention [2,3]. The AlphaCor KPro, a PHEMA-based device which consists of a center optic surrounded by a porous rim or skirt [2], appeared to enhance cell ingrowth following implantation into rabbit cornea [9]. An electron micrograph illustrated the pore structure of the skirt into which cells migrated. However, a...
2005 clinical trial composed of patients with preexisting ocular conditions reported that 8 out of the 14 AlphaCor devices were removed due to corneal tissue melting anterior to the device [10]. Tissue melting could result from inadequate host integration or excessive inflammation [11]. Similar to AlphaCor, the performance of the Seoul Type was influenced by patient selection. The device includes a PMMA optic and a skirt made of polyurethane, polypropylene, or polytetrafluoroethylene [2,12]. SEM images indicate that the skirt of the device has pores of 30 μm or greater that appear to be interconnected. In preclinical trials, fibroblast ingrowth and collagen deposition were observed on devices that use the polypropylene and polyurethane skirts [13], but in clinical trials with patients with preexisting ocular conditions, anatomic retention at 68 months was 67%. Eventually all devices developed corneal melt leading to full exposure of the skirt [2,3]. Increased tissue melting in the Seoul Type KPro compared to AlphaCor suggests that the PHEMA skirt is better tolerated in the cornea than polymers used in the Seoul Type KPro. Like the Seoul Type and AlphaCor KPros, Pintucci triggered complications including corneal melting. Its dacron membrane permitted tissue ingrowth in patients with preexisting ocular conditions, but 2 out of 20 devices extruded. 13 out of 20 patients maintained improved visual acuity for more than 2 years. [14] 50% of patients experienced necrosis of the mucous membrane anterior to the device skirt [1]. A 1996 study reported that 60% Pintucci KPro recipients developed mucous membrane pemphigoid [3], which is an autoimmune disease that can result in vision loss [15]. Clinical data from synthetic KPros show that both materials selection and device design are imperative for long-term host retention. The use of gas foamed PHEMA–PMMA represents a novel approach to create a mechanically and structurally effective artificial cornea that could potentially promote long-term host integration. The biomaterial selection was inspired by the long-term clinical performance of PMMA in the Boston KPro [1], rabbit corneal epithelial cell proliferation on PHEMA–PMMA [16], and the in vivo response to PHEMA–PMMA copolymers in the ocular lens [17]. Since a previous in vivo study indicated that pore interconnectivity in a gas foamed structure facilitates tissue ingrowth throughout the body of the structure [4], pores were introduced to PHEMA–PMMA using a gas foaming technique. This study presents a structural and material design that may permit stable host integration while maintaining a healthy immune response.

2. Methods

2.1. Engineering the gas-foamed KPro

The KPro was fabricated by foaming a PHEMA–PMMA copolymer around a UV polymerized PHEMA cylinder (Fig. 1A). Briefly, to create a transparent PHEMA 70% v/v cylinder that serves as the core, an aqueous solution containing 70% v/v HEMA (Aldrich 477028), 0.1% v/v ethylene glycol dimethacrylate (Aldrich 335681), and 1% w/v Irgacure 2959 (BASF 55047962) was polymerized with UV light (365 nm long wave) for 40 min. For the porous PHEMA–PMMA skirt, HEMA and MMA (Aldrich M55909) monomers were combined with chemical initiators in a solvent consisting of a 1.5 to 1 ratio of deionized water to dimethyformamide (DMF). The monomer solution included 19% v/v MMA, 37% v/v HEMA, 0.014% w/v pentaerythritol tetraacrylate (Aldrich 408263), 0.012% w/v Pluronic PF-127 (Anatrace), 0.027% w/v ammonium persulfate (Sigma), and 0.013% v/v N,N,N′,N′-Tetramethylethylenediamine (Acros Organics). The monomer solution was added to a Chemrus disposable filter funnel. Then, nitrogen gas was pushed through the filter funnel at approximately 10 kPa for 5.5 min to add pores to PHEMA–PMMA. Prior to introducing nitrogen to PHEMA–PMMA, a transparent PHEMA cylinder with a surface modification was added to the filter funnel. To strengthen the bond between the PHEMA core and the porous PHEMA–PMMA skirt, a layer of MMA was added to the PHEMA cylinder using UV polymerization. The MMA surface functionalization process was a modification of a method published by Lee et al. [18] and uses DMF as the solvent in the monomer solution; unlike the Lee et al. protocol, benzyl alcohol and acrylic acid were excluded from the monomer solution. After porous PHEMA–PMMA was added to the transparent PHEMA, the product

![Fig. 1. The gas-foamed KPro was fabricated by foaming a PHEMA–PMMA copolymer around a UV polymerized PHEMA cylinder (A). The transparent core is easy to distinguish from the white porous skirt (B).](image-url)
was cured in 37 °C oven for 20 hours. Prior to cutting the large Gas KPro cylinders into ~0.5 mm disks with a microtome, the cylinders were rinsed in aqueous ethanol solutions in two different concentrations (10% and 20%) and finally hydrated in deionized water. An image of the completed gas-foamed KPro shows a transparent core connected to a porous skirt (Fig. 1B).

2.2. Structural and optical characterization

To observe the pore structure of gas foamed and non-gas foamed PHEMA–PMMA, SEM images of the polymers were generated using a S-3000 N Variable Pressure SEM (Hitachi). Pore size was measured using the Scanco model 50 micro CT system. Micro CT data was acquired with an X-ray tube voltage of 45 kV, current of 133 μA, 0.1 mm aluminum filter, and 1500 ms integration time. Pore size measures were taken using the software included in the Scanco micro CT system; data was obtained by analyzing three scaffold regions of equal volume.

The optical transmittance of transparent PHEMA 70% v/v (n = 8) was measured with a Synergy HT Multi-Mode Microplate Reader (BioTek). Transmittance was measured for three sample groups (n = 8): PHEMA 70% v/v, PHEMA 70% v/v subjected to cell culture conditions, and PHEMA 70% v/v seeded with primary human corneal fibroblasts (HCFs). PHEMA 70% v/v samples were seeded with 1500 HCFs per well in a 96 well plate. After 7 days of cell growth, transmittance was measured. The control samples were non-cell seeded polymers that were subjected to the 7 day cell culture process. Polymer samples were covered in fresh PBS during measurements; therefore, absorbance values for wells that contained PBS were subtracted from the polymer samples’ absorbance values.

2.3. Tensile testing

Hydrated porous PHEMA–PMMA and gas-foamed KPro samples (n = 4) were tested in tension using a custom designed 100LM Test Resources mechanical testing machine (Test Resources Inc., Shakopee MN). Average sample dimensions were approximately 7.0 × 6.0 mm and 3.6 mm depth for porous PHEMA–PMMA. In the tensile testing clamps, the average dimensions of the disk-shaped Gas KPros were 5.6 × 14.2 mm and 1.3 mm depth. Samples were tested at a strain rate of 0.2 mm/s using a calibrated WMC-10 load cell (Test Resources Inc.), which is fatigue-rated for 10 pounds of force in tension and compression. Values taken from the tensile measures included elastic modulus (E), ultimate tensile strength (UTS), and strain at rupture. E is measured in the elastic or linear region of the stress vs. strain plot; E = stress/strain. UTS is the maximum stress response of a material during tensile testing. The strain at rupture is simply the elongation of the sample at the point of rupture. In this study, the elongation was reported as a percentage of the original length of the sample.

2.4. Coating gas-foamed KPros in collagen type I

The gas-foamed KPros were coated with rat tail collagen type I (BD Bioscience) in preparation for in vitro testing. Samples were immersed in a rat tail collagen type I solution (2 mg/ml) with 5 mM N (3-Dimethylaminopropyl)–N′-ethyl-carbodiimide (EDC) and 5 mM N-hydroxysuccinimide (NHS); EDC and NHS were used to crosslink the collagen. After the samples were removed from the solution, collagen type I gelled at 37 °C for 30 min. Monoclonal anti-collagen type I antibody at 1:2000 dilution (Sigma-Aldrich C2456) was used to stain and visualize collagen fibers.

2.5. In vitro assessment

Primary HCFs, passages 8 and 11, were cultured in GIBCO MEM alpha media (Invitrogen) with 10% fetal bovine serum (Atlanta Biologicals) and 1% antibiotic-antimycotic solution (Sigma-Aldrich). 10,000 HCFs were added to the surface of gas-foamed KPros coated with collagen type I, and to the surface of non-gas foamed PHEMA–PMMA. A live-dead cell viability assay (Invitrogen) was used to stain cells at days 4 and 7. The depth of cell growth was estimated using confocal microscopy and MetaMorph Software (Molecular Devices). Ethidium homodimer which stains dead cells also made the polymer surface visible. To quantify the depth of cell growth, cell populations were imaged at 2 distinct locations on the porous structure. For each time point, 5 depth measures were taken from each image (n = 10). The depth of HCF growth was estimated based on the deepest point of cell growth into the structure. Using the side projections, a total of 5 depth measures were taken at ~20 μm intervals from a center vertical line that marked the deepest point of cell growth. Where cells were spaced apart greater than 20 μm on non-porous, non-collagen coated PHEMA–PMMA, measure intervals were increased to measure the near cell or group of cells. The depth measures were taken from a defined polymer edge to the lowest extension of the cell. Alamar Blue assay (Invitrogen) was used to evaluate cell seeding efficiency in porous PHEMA–PMMA with and without collagen coating. A calibration curve was created to convert fluorescent signals from the assay to cells per unit volume. To evaluate cell seeding efficiency on the KPro skirt, ~33,000 HCFs were added to the surface of porous PHEMA–PMMA or collagen-coated porous PHEMA–PMMA. Polymer structures were cut to cover the cell culture well (1.9 cm² area). Cell quantities measured at day 9 showed the efficiency of cell seeding on porous PHEMA–PMMA. Two structures of each porous PHEMA–PMMA type, with and without collagen, were measured three times.

2.6. Statistical analysis

MATLAB R2012a was used to conduct two sample t-tests at an alpha value of 0.05. Data are reported using mean ± standard error.

3. Results

3.1. In vitro cell response to KPro

Biocompatibility of the gas-foamed KPro was first established before we pursued other characterization such as pore structures, mechanical and optical properties of the scaffold. After seeding HCFs on the surface of collagen-coated KPros, cell growth was monitored at days 4 and 7 in the porous KPro skirt (Fig. 2A and B). Live cells, stained green by calcein AM fluorophore, exhibited the typical long spindle-like morphology that would be expected of cells seeded in a 3D scaffold [19,20]. The majority of cells (≥90%) were found to be viable. The fluorophore ethidium homodimer synthesized to stain dead cells showed very few non-viable cells; rounded cell morphology and strong red fluorescence signal would be expected from dead cells. We also noticed that ethidium homodimer stained the polymer structure; fluorescence images show the pores created by the gas-foaming technique. The collagen coating should enhance cell retention in the porous skirt of the KPro, since collagen is an extracellular matrix protein that provides binding sites for integrins for cell adhesion [21]. In order to validate this, the same number of cells was seeded in the PHEMA–PMMA scaffolds with or without collagen coating. Following 9 days after initial cell seeding, virtually no cells were detectable when collagen coating was not applied. In contrast, when coated with collagen, cells were found to be attached to the scaffold (Fig. 2C). Porous PHEMA–PMMA scaffolds were seeded with 174 cells/mm² to evaluate the cell seeding efficiency. Cells were not detected on the collagen-free porous PHEMA–PMMA because the seeded cells likely fell through the pores and the lack of cell adhesion. While cell–cell adhesion cannot be readily ruled out, cell–substrate adhesion is not favored. However, 16 cells/mm² were found on collagen coated porous PHEMA–PMMA at day 9. Providing a collagen network appears to facilitate cell retention.
Confocal microscopy was therefore used to assess the depth of cell growth into the collagen-coated porous scaffold. Positive immunofluorescent staining for collagen type I confirmed that a collagen network may have been established throughout the porous skirt (Fig. 3D). Non-gas foamed PHEMA–PMMA, without collagen coating, permitted shallow depths of HCF growth at days 4 (Fig. 3E) and 7 (Fig. 3F). Not only less viable cells were recorded in this scaffold, but also average depths of cell penetration remained unchanged from 35 ± 4 μm at day 4 to 38 ± 3 μm at day 7, suggesting no cell penetration into the collagen-free, non-gas foamed PHEMA–PMMA (Fig. 3G).

3.2. Structural and optical characterization

Motivated by encouraging results regarding cell viability and growth, the physical properties of the gas-foamed KPro were characterized next. The pore structure in the skirt and optical transparency of the core are expected to regulate the functionality of the gas-foamed KPro. First, SEM imaging shows that gas foaming with nitrogen created a high density of interconnected pores to the PHEMA–PMMA skirt (Fig. 4A), which was designed to encourage large scale cell ingrowth. During the gas foaming process, monomers polymerized to form an interconnected or open pore structure around nitrogen gas bubbles as the bubbles moved through the monomer solution. Without gas foaming however, PHEMA–PMMA has a mostly closed pore structure and no pore interconnectivity was noticeable (Fig. 4B). Closed pore structures are not expected to promote tissue ingrowth throughout the body of a polymer. For the gas-foamed polymer, referred to as porous PHEMA–PMMA, average pore size was 70 ± 8 μm in diameter, and the range was from 10 μm to >1000 μm in diameter. MicroCT data (images not shown) suggest that approximately 68 ± 1% of the porous scaffold was occupied by pores. Furthermore, optical transmittance data shows that the PHEMA (70% v/v) core of the KPro transmits most visible light (Fig. 5A). In the wavelength range from 650 to 700 nm, >85% transmittance was achieved, while the transmittance was as low as 70% below 500 nm. The PHEMA 70% v/v core used in the gas-foamed KPro appears to be optically transparent enough to permit vision. In the wavelength range between 650 and 700 nm, the addition of HCFs to PHEMA 70% v/v core (PHEMA 70% v/v + HCFs; Fig. 5B) had a negligible effect on transmittance compared to the control (PHEMA 70% v/v without cells). Phenol red in the cell culture media used as a pH indicator caused a significant loss in the light transmittance.

3.3. Mechanical characterization

Mechanical properties of the skirt alone and gas-foamed KPro were quantified. The KPro device and the skirt alone were found to have statistically equivalent elastic modulus (E) (p = 0.61) and ultimate tensile strength (UTS) (p = 0.90) values (Fig. 6A – B). However, strain at rupture for the KPro device was significantly greater than the porous skirt (p = 0.01) (Fig. 6C). For the KPro, E, UTS, and strain at rupture were 3557 ± 536 kPa, 273 ± 31 kPa, and 139 ± 18%, respectively. For the porous skirt alone, E, UTS, and strain at rupture were 3403 ± 340 kPa, 263 ± 66 kPa, and 64 ± 9%, respectively. The stress response of gas-foamed KPros and porous skirts was recorded until the samples ruptured (Fig. 6D). The materials displayed both hardness and strength. Prior to applying tensile force, the core was securely attached to the edge of the skirt. The partial attachment of the core to the skirt following device rupture showed that the gas-foamed KPro can maintain its structure under stresses that exceed the forces expected in the ocular environment (Fig. 7A). Following the tensile rupture of the skirt, the zigzag fracture pattern at the midsection of the sample was similar to that found in the rupture of full gas-foamed KPro (Fig. 7B). Taken together, the novel artificial cornea composed of copolymers was deemed biologically and mechanically suitable for corneal implantation.
Fig. 3. Side projections of live HCFs, in green, show HCF growth inside of porous PHEMA–PMMA at days 4 (A) and 7 (B). Again, ethidium homodimer in red color stained and identified the polymer structure. The depth of HCF growth into porous PHEMA–PMMA increased significantly ($p < 0.001$) from day 4 to 7, $n = 10$ (C). The presence of the collagen in the PHEMA–PMMA scaffold was verified using anti-collagen type I antibodies. The collagen fibers are shown and indicated by arrows (D). Non-gas foamed PHEMA–PMMA and without collagen coating allowed shallow depths of HCF growth at days 4 (E) and 7 (F). The depth of HCF growth remained virtually unchanged in the collagen-free, non-porous polymer (G; $n = 10$).

Fig. 4. SEM images show that gas foaming with nitrogen added a high density of interconnected or open pores to PHEMA–PMMA (A). The porous gas-foamed PHEMA–PMMA serves as the skirt of the KPro. Without gas foaming, PHEMA–PMMA has a predominately closed pore structure (B); inset, an enlarged view of the pores in the non-gas foamed polymer.
4. Discussion

The gas-foamed KPro was designed to resist adverse events including rupture or core-skirt separation, while permitting vision and ocular tissue ingrowth into the KPro skirt. Visible light transmittance through the KPro core (see Fig. 5) approximates that of natural cornea, 90 to 95% in the 400 to 550 nm wavelength range [22]. Transmittance (> 90%) through the PHEMA 70% v/v core at the wavelength range > 500 nm is consistent with similar measurements reported by Gulsen et al. for transparent PHEMA [23]. Since the commercially available AlphaCor KPro includes a PHEMA core made with a high fraction of HEMA, 70 – 90% by weight [24], it is expected to demonstrate similar transmittance. In addition, visual acuity following AlphaCor implantation demonstrates that a transparent PHEMA core can restore vision in patients who cannot receive donor cornea. Following device implantation, best corrected visual acuity ranged from light perception to 20/20; results were taken at a variety of time points following AlphaCor implantation [25]. Clinical studies with transparent PHEMA suggest that it can be used as the core to restore vision in a core-skirt model KPro.

Mechanical tensile data indicates that the KPro can comfortably maintain its structure in the ocular environment (Fig. 6). Intraocular pressure and eyelid movement are major forces that any corneal implant encounters. Average intraocular pressure is only up to 2–4 kPa [26,27], which falls well below the UTS of the gas-foamed KPro. High elastic modulus and UTS values for the gas-foamed KPro suggest that the device can resist rupture during implantation. Similar to other KPro models [3,28], our gas-foamed KPro does not perfectly match the mechanical properties of natural human cornea [29–31]. However, results from previously published KPro designs indicate that corneal tissues can integrate structures that possess a range of mechanical properties [3,9,13,14]. Functionally, the natural tear film is expected to minimize shear forces between the eyelid and the PHEMA optic of the KPro. It is worth noting that PHEMA is used in contact lenses because of its favorable tear film wettability [32]. In addition, the AlphaCor KPro which contains a PHEMA core or optic was FDA approved for patients with a satisfactory tear film [3].

Following KPro implantation, ocular tissues that can potentially grow into the porous skirt of the gas-foamed KPro are expected facilitate nutrient and gas exchange. The size of the optic, ~ 3.5 mm in diameter, will likely limit the effects of its non-physiological gas and nutrient exchange. Studies with contact lenses suggest that the low water content of the PHEMA 70% v/v optic, 24 ± 1%, will yield low oxygen permeability [33]. Experiments with poly (ethylene glycol) diacrylate (PEGDA) – poly (acrylic acid) hydrogels showed that nutrient exchange, particularly glucose flux, increased with the increased water content of the polymer structure [34]. The ocular tissues surrounding the small

![Fig. 5. Light transmittance of the PHEMA 70% v/v core in the visible wavelength range. Polymer samples were embedded in PBS during measurements; therefore, transmittance data were subtracted from using the PBS solution. Addition of HCFs to the polymer (PHEMA 70% v/v core + HCFs) had a negligible effect on transmittance compared to the control (PHEMA 70% v/v core). Phenol red in the cell culture medium, which was added to detect pH, reduced transmittance in the 400 – 600 nm ran, however. A representative image of HCFs (green color) on the PHEMA 70% v/v core at day 7 shows sparse cell attachment (B).](image1)

![Fig. 6. Mechanical characterization. The KPro device and the skirt alone were found to have statistically equivalent elastic modulus (E) (p = 0.61) and ultimate tensile strength (UTS) (p = 0.90) values (A and B). However, strain at rupture for the KPro device was significantly greater than the porous skirt alone (p < 0.01) (C; n = 4). The stress response of the KPros and porous skirts were measured until the samples ruptured. “X” marks the point of rupture for the samples (D).](image2)
PHEMA optic, including those integrated into the KPro, are expected to compensate for the limited mass transport of the optic. Given the volume and interconnectivity of pores in the skirt, the development of functional tissue in the skirt is anticipated in vivo. Studies with gas foamed PEGDA show that the gas foaming processes create an interconnected pore structure that facilitates large scale in vivo tissue ingrowth [4]. Cornea receives its oxygen and nutrients from the tear film and aqueous humor, respectively [35]. If vascularization occurs, mass transport in the skirt would likely resemble that of vascularized ocular tissue. Clinical data from the Boston KPro shows that a device with highly effective host integration in the skirt can achieve long-term stability in the absence of physiologically equivalent mass transport in the core [1].

The in vivo response to other KPros containing PHEMA or PMMA indicates that the gas-foamed KPro can potentially allow ocular tissue ingrowth while permitting vision. Cell migration, a prerequisite to tissue development, favors non-toxic and cell adhesive surfaces. Cell growth and viability data show that the gas-foamed KPro is non-toxic (Figs. 2 and 3). The addition of collagen was required to facilitate in vitro cell growth on porous or gas foamed PHEMA–PMMA. However, in vivo studies indicate that a porous PHEMA material can allow cell ingrowth without the addition of cell adhesion molecules. For example, ocular cells migrated into porous PHEMA in the AlphaCor KPro [9]. However, minimal cell growth was observed on the non-void porous PHEMA optic of AlphaCor [10]. This highlights an advantage of using non-porous, transparent PHEMA as the KPro core. Limiting uncontrolled cell growth on the optic aids the proper function of the KPro, as uncontrolled cell grow can opacify the optic. While low levels of in vitro HCF growth do not impact visible light transmittance (Fig. 5), large scale cell growth that covers the optic could reduce vision. Rather than PMMA optics that have been used in several KPro models [3], a PHEMA optic we have chosen for the gas-foamed KPro may potentially reduce the incident of retroprosthetic membrane (i.e., cell mediated opacification of the KPro optic). Higher incidents of retroprosthetic membrane have been reported with PMMA optics compared to PHEMA optics. [9,10,36], attributing this unwanted effect to its greater hydrophobicity compared to PHEMA. Surface hydrophobicity favors protein adsorption which aids cell attachment in vivo [37]. Ocular tissue ingrowth observed in porous PHEMA [11] suggests that a porous PHEMA–PMMA, having greater hydrophobicity, would also permit ocular tissue ingrowth. Based on the expected cell response to the polymers and the device structure, the gas-foamed KPro can potentially promote tissue ingrowth into the skirt and maintain an optically transparent core by deterring cell adhesion to the core.

5. Conclusions

We engineered a novel artificial cornea that is composed of PHEMA and PMMA, referred to as the gas-foamed KPro. Experimental results demonstrate that the KPro may be biologically, mechanically, and structurally compatible for full thickness corneal replacement. Mechanical data indicates that the device can maintain its structure in the ocular environment and resist rupture during implantation. The KPro core, which is securely attached to the skirt, is optically transparent. Given the device’s structure and known ocular compatibility of the polymers, the gas-foamed KPro may offer a cornea replacement option that generates fewer incidents of corneal melting and therefore achieve long-term stability in the ocular environment.

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