Engineered Synthetic Cornea with Controlled Porosity Edge Region for Biological Integration

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Introduction:

Degradation of the cornea, affecting millions of people globally is a significant cause of treatable blindness [1]. While corneal transplantation using fresh human donor corneas has been successful in some developed countries, the majority of people worldwide with corneal blindness today remain untreated. The goal of this project is the development of an implantable synthetic device biologically integrated into the sclera of an eye as a replacement for a degraded natural cornea.

Approaches and Methods:

Our approach is built on using the advantages of current artificial corneal implants, the Boston-keratoprosthesis [2] and the AlphaCor [3], while addressing significant concerns with these devices [4]. To address concerns of cellular integration with existing devices, novel controlled porosity silicone devices have been developed possessing excellent strength and transparency along with enhanced biointegration. The polymeric composition is injected into a mold and crosslinked *in situ* forming an optic centered core that displays precise rigid optical structure, and may be customized to refractive requirements of individual patients. The well-defined porous structure was co-molded using a sphere-templating technique [5] that imparts interconnected pores forming a flexible skirt that is intended to encourage cell ingrowth and integration.

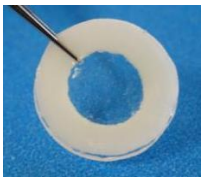

Fig. 1. The synthetic cornea device with opaque porous skirt and transparent optic core.

Several analyses were conducted including i*n vitro* cytotoxicity assays. Then *in vivo* implantation into rabbit eyes was performed to demonstrate that the designed interconnected pores of the skirt region of the device was integrated into the scleral tissue sufficiently for practical application. In addition, mechanical peel tests of integrated interfaces was conducted.

Results and Discussion:

The corneal replacement device was designed to mimic the essential functions of the human cornea (refractive function, oxygen permeability and strong mechanical barrier), Healing and biointegration of the implanted skirt-scaffold were encouraged by optimizing the pore size to 30-38μm.

The mechanical peel test results post 120-days implantation are compared to comparable natural tissues from control eyes.

The porous skirt material integration into the sclara was examined using histology stains (H & E, trichrome and IHC for AE3 and AM5), and both optical and electron microscopy.

Overall, the subjects' high retention rate of the implanted device for periods of up to seven months indicated sufficient fixation of the device-tissue interface.

These results have shown that the structural integration of the skirt region of the device is sufficient for further development of the device to proceed.

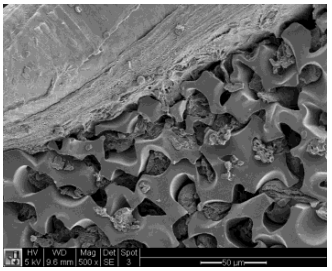

Fig. 2. SEM examination of the interface shows cell attachment and infiltration into the interconnected porous skirt material of the device.

Conclusions:

Preliminary results obtained have indicated that materials tested are well-tolerated *in vitro* using cytotoxicity assays and *in vivo* as shown in the rabbit eye model. These findings are supported by histology and morphological examination.

Acknowledgements:

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References:

1 Whitcher JP. *et al. Bull World Health Organ* 2001;79(3):214-21.
2 Duan D. *et al. Expet Rev Med Dev.* 2006; 3(1):59-72.
3 Chirila TV. *et al. Prog Polym Sci.*1998; 23,3:447-473.
4 Dudenhoefer EJ *et al. Cornea* 2003; 22(5):424-428.
5 Ratner BD. *et al. US Pat Appl* 20080075752