

Sphere Templated Angiogenic Regeneration (STAR) Biomaterials for Ophthalmic Applications

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We applied the favorable healing properties of STAR[®] biomaterial (Ratner BD. Polymer Intl. 2007;56:1183-1185) to advance treatments for two leading causes of blindness: corneal blindness and glaucoma.

Corneal Replacement: Opacified corneas require surgical replacement, but available replacement options are unsatisfactory. Donor corneas can only meet a small fraction of global demand, and rejection is a frequent issue. Risks of infection and extrusion due to poor tissue integration have prevented currently available artificial cornea designs from gaining widespread adoption (Chirila TV et al. Prog Polym Sci. 1998;23:447-473). Our design for a synthetic cornea uses a porous silicone STAR scaffold as a skirt surrounding the clear optic center. The pore geometry of the skirt maximizes bioavailable surface area to promote cell ingrowth and firmly anchor the device to the sclera. We have demonstrated successful anchoring and tissue integration of the porous skirt material in a rabbit model.

Glaucoma Treatment: Drugs to reduce intraocular pressure currently represent the standard of care for all but the most severe of glaucoma cases; but these are expensive, they frequently have problematic side effects, and they are often ineffective for controlling the progression of the disease. Surgical interventions such as lasers and glaucoma drainage devices (GDDs) suffer from serious limitations. The foreign body response to these implants generates fibrous tissue that clogs the drainage pathways (Market Scope. 2008). Our new GDD approach, which takes advantage of STAR biomaterial's ability to resist fibrosis, has demonstrated successful long-term patency in a canine model. The device (TR-ClarifEYE[™]) is now available on the veterinary market.

Methods:

Implant Fabrication: Sphere-templated porous silicone implants were fabricated from NuSil MED-6215 silicone with a previously described method (US Patent Appl. 2008/0075752). Corneal test implants had 36- μ m pores connected by 15- μ m throats, while GDDs had 27- μ m pores and 11- μ m throats. The GDDs were punched to a shape 11mm x 6mm x 0.3mm comprising a body, a narrowed neck, and a widened foot as shown in Fig. 1, while cornea test implants were punched to disks 4mm in diameter x 0.5-mm thickness.

Corneal implant study: The implant disks were treated with aminopropyl triethoxysilane followed by carbonyldiimidazole to covalently couple collagen type I and fibronectin to the silicone surface. A 4-mm diameter lamellar dissection was performed at the sclera-corneal

junction, and the implant disk was sutured onto the lamellar bed. Conjunctiva was then repositioned over the implanted disk. The animals were monitored with regular examinations to observe signs of infection or inflammation around the implant.

Glaucoma implant surgery: GDDs were implanted under the sclera of glaucomatous canine eyes (in pets) to shunt the fluid from the anterior chamber to the choroid. A limbal based conjunctival flap was created, and the foot of the implant was inserted through a 3-3.5mm opening into the anterior chamber through the filtration angle. The body of the implant was positioned over the choroid, the sclera flap closed, and the edges sutured. The patients received post-operative anti-inflammatories, antibiotics, and other medications as deemed necessary by the veterinarian.

Results:

Cornea test implants: Three of four surface treated cornea test implants remained well-anchored in the tissue until the rabbits were sacrificed at 32, 74, and 82 days. All four untreated silicone implants and the other treated implant survived the first month but were extruded shortly thereafter. Analysis by SEM (see Fig. 2) and by histological staining showed thorough cellular integration into the scaffold.

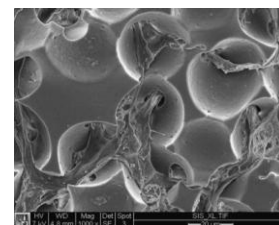


Fig. 2. SEM image of scleral tissue integration into silicone STAR at 1 month (scale bar: 20 μ m).

Glaucoma drainage devices: The glaucoma implants have been implanted into 10 canine eyes with the majority providing long-term success in reducing intraocular pressure. Two of the earliest implants continue to function beyond 23 months.

Conclusions:

STAR biomaterial has exhibited promise in two ophthalmic applications where previous implanted device approaches have shown limited success.

Preliminary results suggest that the STAR pore structure, when surface treated to enhance cell adhesion, is well-suited to provide tissue integration and anchoring of a silicone artificial cornea device. Our next step is to test a complete cornea implant with the skirt integrated with the transparent optic center.

The early success of the TR-ClarifEYE[™] canine glaucoma drainage shunt in maintaining healthy intraocular pressure demonstrates the functional effectiveness of STAR biomaterial in reducing fibrosis around implanted devices. We believe that this veterinary device can be successfully translated to human clinical use.



Fig. 1. TR-ClarifEYE[™] glaucoma implant.