Ocular Biocompatibility of a SIBS-based Glaucoma Drainage Tube

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Statement of Purpose: Glaucoma is the second leading cause of adult irreversible blindness next to untreated cataracts. It is estimated that over 7 million people go blind due to progression of glaucoma each year and an estimated 46 million people suffer from the disease worldwide. The last line of defense is large-plate glaucoma drainage devices (GDD) which are time consuming to implant and suffer from a myriad of adverse events that include double vision and erosion.[1] InnFocus has developed a new glaucoma treatment device called the InnFocus MicroShunt™ (IMS also known as the MIDI Arrow) (**Figure 1**) made from a highly biocompatible biomaterial called poly(styrene-*block*-isobutylene-*block*-styrene) or "SIBS" (**Figure 2**).[2] The first use of SIBS was as the carrier for the drug paclitaxel on Boston Scientific Corporation's TAXUS™ drug-eluting coronary stent. It has been used successfully in human coronary arteries for over 12 years. This abstract reviews the safety and efficacy of this device in relation to the biocompatibility of SIBS in the rabbit & human eye.

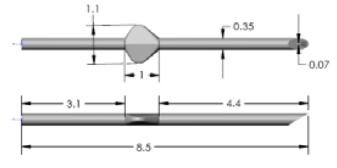

Figure 1: Schematic of the InnFocus MicroShunt™

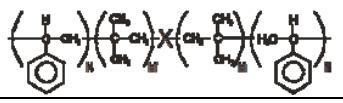

Figure 2: SIBS, where X is a hindered dicumylether and N/(N+M) = 0.3

Methods: SIBS was prepared in a solvent system using living cationic polymerization in two steps by first polymerizing isobutylene in the presence of a proton trap under a blanket of dry nitrogen at -80C. When the central polyisobutylene block reached the desired molecular weight, styrene was added and the polymerization was continued until the outer polystyrene blocks reached a predetermined length. The process was quenched with methanol, purified and the solvent flashed off. SIBS was then extruded into tubes and compression molded. The IMS is comprised entirely of SIBS of durometer Shore 40A. The lumen of the device serves as a flow restrictor to drop intraocular pressure (IOP) and was determined by the Hagen Poiseuille equation and confirmed *in vivo* to be approximately 70 microns.[4] Sixteen New Zealand rabbits were implanted with the IMS for up to 6 month follow up and silicone (Sil) tubes were used in 8 control animals.[3] Flow patency and immunoflourescence assessments were made. Twenty three IMS were later implanted in patients at the Centro Laser, Santo Domingo, Dominican Republic and followed for a period up to 27 months. Patient selection was restricted to those who had failed maximum tolerated glaucoma medication. All used the antiproliferative drug Mitomycin C (0.4 mg/mL applied for 3 min) as is practiced in trabeculectomy.

Results: Flow was confirmed in all 16 IMS rabbit implants and only 2 of 6 Sil controls using 0.01% fluorescein. Surprisingly, myofibroblasts in tissue around the IMS tube were not observed, in contrast to Sil tubes (**Figure 3**). In patients, the one and two-year success rates, as measured by dropping IOP by ≥20% without surgical intervention, was 96%. The percent of patients totally off of glaucoma medication at one and two years was 87%. The average IOP was 10.7 ± 2.8 mmHg at 12 months (n=23) and 10.3 ± 2.0 mmHg at 27 months (n=11), which represents a 55% and 57% drop in IOP, respectively. There were no long-term sight-threatening adverse events. **Figure 4** shows a typical rabbit and human eye showing no encapsulation of the SIBS tube in the anterior chamber and a healthy eye. There was no clinically significant inflammation or cataract formation observed in any of the eyes.

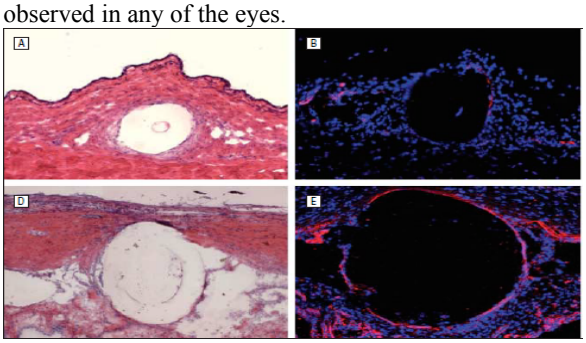

Figure 3: A, B SIBS tube; D, E Sil tube. Smooth muscle actin was expressed in Sil tubes shown in red (E), not in IMS tube (B). Left H&E; Right Immunofluorescence.

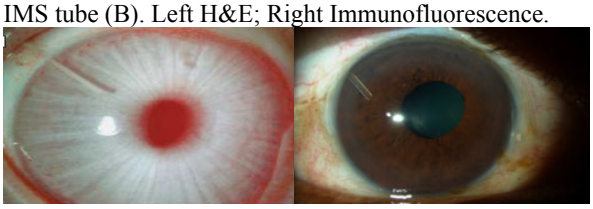

Figure 4: Six month in rabbit and one year in human implant of the InnFocus MicroShunt showing no encapsulation of the tube.

Conclusions: The InnFocus MicroShunt™ made from SIBS exhibits an insignificant inflammatory reaction with no long-term adverse events supporting safe use in the eye. Control of IOP was excellent in all patients with 87% of patients off of glaucoma medication. A prospective randomized clinical study with a larger patient population will determine if this SIBS-based glaucoma device will meet the requirement for the ideal treatment of glaucoma.

References: 1) Gedde S, Am J Ophthalmology, 2012:153(5): 789–803. 2) Pinchuk L, Biomaterials; 2008; 29(4); 448-460. 3) Acosta AC, Arch Ophthalmol 2006:124:1742-1749. 4) Arrieta -Quintero E, Ophthalmic Surg, Laser, Imaging 2011:42(4):338-45.

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