MicroShunt for Open-Angle Glaucoma

Subjects: Ophthalmology

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For moderate-to-severe glaucoma, trabeculectomy remains the “gold standard” intraocular pressure (IOP)-lowering treatment; nonetheless, this method requires extensive post-operative maintenance. Microinvasive glaucoma surgery (MIGS) treatments are designed to lessen intra- and post-operative care burden while offering an acceptable IOP decrease for individuals with mild to moderate glaucoma. The PreserFlo® MicroShunt (previously InnFocus MicroShunt) is an 8.5 mm glaucoma drainage device manufactured from poly(styrene-block-isobutylene-block-styrene) (SIBS), an extremely biocompatible and bioinert material. The lumen is narrow enough to prevent hypotony, but big enough to avoid being obstructed by sloughed cells or pigment. The device is implanted ab externo, as a stand-alone procedure or in conjunction with cataract surgery, with intraoperative mitomycin C, and a bleb is produced under the conjunctiva and Tenon’s capsule. The MicroShunt was CE-marked in 2012 and designed for primary open-angle glaucoma, the IOP of which remains uncontrolled after maximally tolerated topical treatment. Several clinical trials evaluating the MicroShunt’s long-term safety and effectiveness have been conducted, highlighting the effectiveness of the device over time, along with a tolerable safety profile.

glaucoma micro-invasive glaucoma surgery MicroShunt mitomycin C SIBS polymer glaucoma drainage devices InnFocus MicroShunt PreserFlo PreserFlo MicroShunt XEN Gel Stent

1. Introduction

Glaucoma is a neurodegenerative disorder marked by the death of retinal ganglion cells and cupping of the optic nerve head, both of which cause vision field loss [1][2]. The most prevalent kind of glaucoma is primary open-angle glaucoma (POAG). The only well-established modifiable risk factor is intraocular pressure (IOP), and medicinal therapy is often used to reduce IOP in the treatment of glaucoma. Patient adherence to medicine, on the other hand, might be poor. In order to improve long-term IOP reduction, laser and incisional surgical techniques, including trabeculectomy and tube shunt surgery, have been introduced [3][4][5][6]. Both trabeculectomy and tube shunt surgery are invasive operations that need a significant amount of postoperative care [3][4][5].

Micro-invasive glaucoma surgery (MIGS), known also as minimally invasive glaucoma surgery (MIGS), defines a growing number of surgical techniques for glaucoma [7]. MIGS operations attempt to minimize intraoperative and postoperative management, as well as provide a less intrusive method of lowering IOP than standard glaucoma surgery, with the objective of minimizing reliance on topical drugs [8]. MIGS are able to reduce IOP exploiting different anatomical pathways: (1) boosting trabecular outflow by bypassing the trabecular meshwork and directly

involving Schlemm's canal, (2) lowering ciliary body aqueous production; (3) increasing uveo-scleral outflow through suprachoroidal routes, or (4) creating a link between the anterior chamber and the subconjunctival space to improve aqueous humor drainage and forming a bleb. [7][8] Although MIGS procedures have been claimed to have a better safety profile than traditional surgery, the variability among devices, with differences in the outflow pathway, ab interno versus ab externo approach, and whether a bleb is created, reflects a diverse target glaucomatous population, efficacy, and device- or procedure-related adverse events (AEs) [7][8][9].

On one side, most MIGS treatments without bleb formation have only been linked with minor decreases in IOP and are therefore focused on patients with mild-to-moderate glaucoma, thus indicating an unmet need for minimally invasive treatment of moderate-to-severe and refractory glaucoma [8][10]. MIGS devices that result in the formation of a bleb, on the other hand, have been linked to significant IOP reductions. Despite this, postsurgical management of the bleb, such as early needling with or without the concomitant injection of mitomycin C (MMC) to mitigate fibrosis, has a crucial role in the success rate of these devices [11][12]. Nevertheless, concerning these new devices, long-term IOP data are still lacking [10].

The discovery of a novel synthetic thermoplastic elastomeric biomaterial (poly(styrene-block-isobutylene-block-styrene); SIBS) lead to the introduction of a SIBS-based glaucoma device named PreserFlo MicroShunt (MicroShunt, formerly known as the InnFocus MicroShunt) [13][14]. This product received Conformité Européenne marking in 2012, Health Canada and Therapeutic Goods Administration of Australia approval in 2021, and a US Investigational Device Exemption (IDE) to initiate a Phase 3 clinical study was granted by the US Food and Drug Administration (FDA) in May 2013. At the moment, the PreserFlo is still an investigational device not yet approved by the Food and Drug Administration.

Structurally speaking, SIBS has the advantage to resist biodegradation in the body, along with the necessity for a safe and efficient means of treating glaucoma. The PreserFlo MicroShunt is an 8.5-mm-long glaucoma filtration surgical device with a 350-µm outer diameter and a 70-µm lumen that is implanted through an ab externo technique. The device's proximal tip rests in the anterior chamber, parallel to the iris, while the distal tip sits under the conjunctiva and Tenon's capsule, about 6 mm beyond the limbus, enabling aqueous humor to pass through the lumen to produce a posterior bleb after implantation [14][15].

2. History of PreserFlo MicroShunt

An iterative 20-year study was needed to give birth to SIBS material and, later, to the PreserFlo MicroShunt [16]. Pinchuk was the first to introduce SIBS at the University of Miami's Miller School of Medicine, Bascom Palmer Eye Institute, Optical Biophysics Center, sometime around 2003 [13][14].

In those years Parel et al. implanted 3 mm diameter, 1 mm-thick SIBS disks in the corneal stroma, as well as beneath the conjunctiva and Tenon's capsule of white rabbits' eyes. In the control group, silicone rubber (polydimethylsiloxane) disks were implanted alongside the SIBS disks. The biocompatility of this material was evaluated at the 2-month control, and no myofibroblasts or angiogenesis in the region of the SIBS disks, as well as

no integral capsules around the disks was described [17]. Few years after, Acosta and colleagues presented similar findings, proving in conclusion that SIBS was completely harmless to the eyes [18] (**Figure 1**).

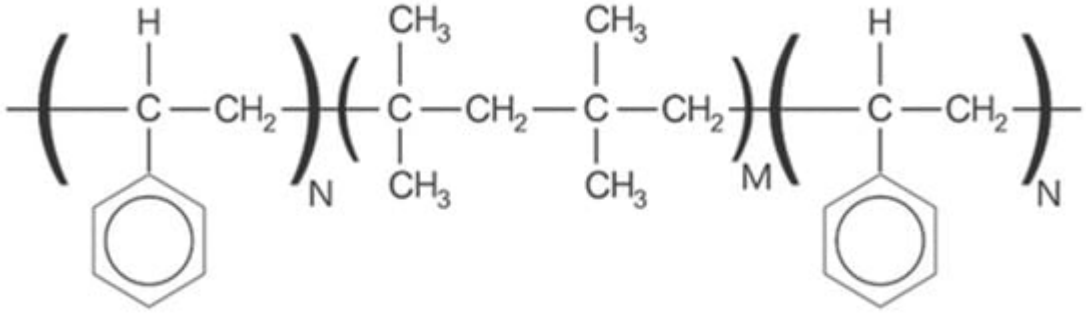

Figure 1. Simplified chemical structure of SIBS. M = number of isobutylene units; N = number of styrene units; SIBS = poly(styrene-block-isobutylene-block-styrene).

These researchers claimed that SIBS material could be used for a glaucoma drainage device, but optimal constructive features were necessary. To avoid clogging, the lumen needed to be greater than the diameter of a sloughed endothelial cell, which is about 40–50 um, while remaining small enough to avoid eye trauma and hypotony. The Hagen–Poiseuille equation was used to estimate the lumen size, and Arrieta et al., in a series of rabbit eye implants, demonstrated that a lumen diameter of 70 µm would meet these parameters [19][20]. Moreover, Pinchuk et al. highlighted that device drainage to a flap beneath the conjunctiva and Tenon's capsule, comparable to the trabeculectomy bleb, was the best approach [14][21]. These good preclinical results in ophthalmology were consistent with SIBS experience, previously adopted in cardiology. In fact, the SIBS coated TAXUS® (Boston Scientific Corporation, Natick, MA, USA) was a cardiac stent that minimizes restenosis by releasing the antiproliferative medication paclitaxel in the coronary artery [22]. TAXUS® has been implanted in over a million patients throughout the globe and has a proven safety record, showing negligible biodegradation and low inflammation in vitro and in vivo experiments, demonstrating SIBS' flexibility as a biocompatible polymer [14][22][23].

Before arriving at the present MicroShunt concept, three significant variations in the design were studied, with the first two to be investigated in acute and chronic rabbit eye biocompatibility studies [13][14]. The first approach was the Miami InnFocus Drainage Implant (MIDI)-Tube, an 11 mm SIBS tube with a 1 mm SIBS tab, firstly evaluated in two studies at the Bascom Palmer Eye Institute Ophthalmic Biophysics Center (OBC) (Miami, FL, USA), and then confirmed in a good laboratory practice (GLP) study at the North American Science Associates contract facility (Northwood, OH, USA) [14][21]. The second variation was named MIDI-Ray (a 350 µm diameter, 100 µm lumen, SIBS tube with a 7 mm diameter SIBS plate) and then studied in chronic, non-GLP animal research at the Bascom Palmer Eye Institute OBC [14].

These SIBS-based devices were subsequently put through clinical testing after receiving good findings from biocompatibility tests. Four human pilot feasibility studies (Bordeaux I and II, and Dominican Republic I and II) were needed in the successive 4 years to determine the optimum design, implantation procedures, and whether mitomycin C (MMC) use was necessary or not [14]. The MicroShunt technique along with MMC injection (0.4 mg/mL

for 3 min using sponges), was claimed to be successful in 95% of cases in the Dominican Republic II research, and was chosen for further clinical testing [14][15]. The final design, known as the InnFocus MicroShunt, was made up of an 8.5 mm-long SIBS tube with a 350 um outer diameter and a 70 µm lumen diameter.

3. Surgical Technique

The MicroShunt is implanted through an ab externo route, and the surgical process is minimally invasive when compared with trabeculectomy [13][24]. Aqueous humor drained from the anterior chamber is directed via the MicroShunt to a bleb produced under the conjunctiva and Tenon's capsule. The reabsorption of the subconjunctival fluid collected inside the bleb follows different pathways: (1) the episcleral venous system [13]; (2) the tear film through microcysts, which are naturally occurring conjunctival channels [13][25]; and (3) via orbital lymphatics [26][27]. The MicroShunt thus overcomes the significant resistance of the trabecular meshwork, Schlemm's canal, collecting channels, and scleral venous plexus by draining aqueous humor down this pathway [13][24].

At the nasal or temporal superior quadrants, a fornix-based subconjunctival and sub-flap Tenon's is dissected throughout a circle of 90 to 120 degrees, to at least 8 to 10 mm posterior to the limbus [24]. After this, mitomycin C (MMC)-soaked sponges are placed in the flap for 2 to 3 min of exposure. In minimally invasive devices, such as the MicroShunt, intraoperative application of MMC has been proven to lower the chance of surgical failure and raise the surgical success rate [13]. Various concentrations and application durations of MMC during MicroShunt implantation have been described, mostly focusing on concentrations of 0.2–0.4 mg/mL and application periods of 2–3 min [13][15][28].

Successively, after an abundant rinsing with saline solution, a marker is used to indicate a position 3 mm from the middle border of the surgical limbus in the blue-gray zone. A 1 mm knife is used to incise a shallow triangular pocket in the sclera (big enough to host the MicroShunt fins) at the distally marked position. The apex of the scleral pocket is then punctured with a needle in order to create a transscleral tunnel into the anterior chamber. The MicroShunt is finally inserted into the transscleral tube with forceps, bevel up and fins flat [24] (**Figure 2**).

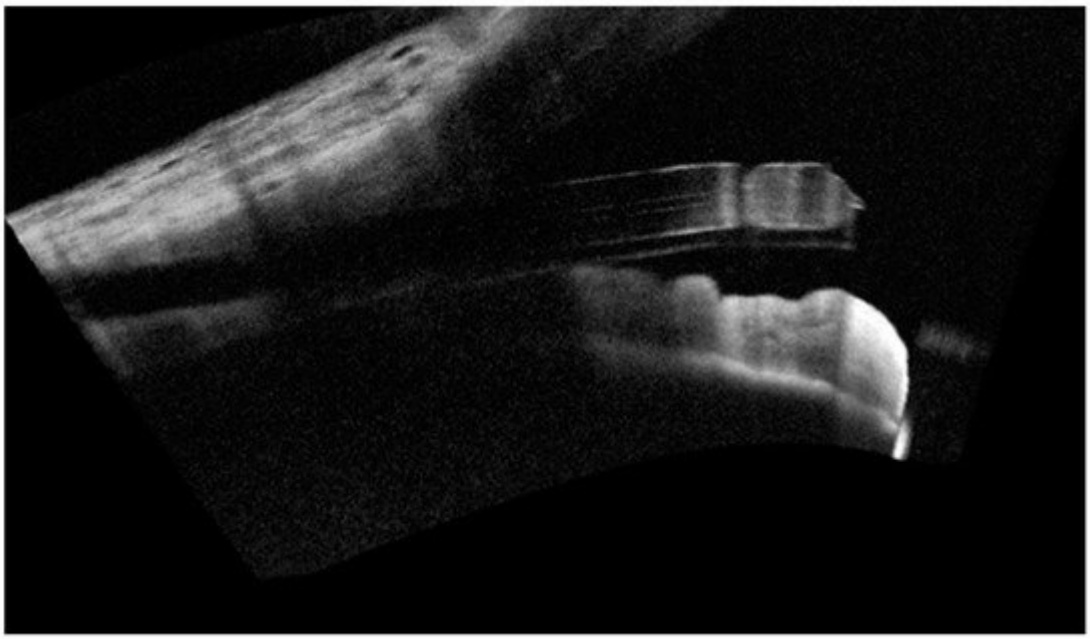

Figure 2. Anterior segment—optical coherence tomography (AS-OCT) showing successfully implanted PreserFlo MicroShunt, piercing the trabecular meshwork and positioned bevel up in the anterior chamber.

After that, the fins are squeezed into the scleral pocket. Prior to Tenon's capsule and conjunctiva closure, it is critical to evaluate flow via the MicroShunt. Successful flow is visually established by first seeing a percolation of aqueous humor from the device's distal end, just after air purge from the lumen. Flow may seem to decrease as the volume of the drop grows; nevertheless, volume increases to the third power of flow, making flow difficult to measure when the drop is too great. In that case, it may be useful to wipe the drop away with a sponge now and then and imagine a little drip to ensure flow [24]. The target IOP in that moment should reach about 6 mmHg or less at equilibrium flow, which may be achieved by depressing the central cornea using a 30 g cannula or using a Schiötz tonometer.

Different approaches can be applied, whether flow is seen through the lumen or not. Firstly, it is crucial to ensure that the MicroShunt's entry is clean of debris and not trapped in the iris or cornea. After this, a BSS injection in the anterior chamber may increase IOP to assure MicroShunt percolation functionality. If still not working, a 30 g cannula may be used to inject BSS into the MicroShunt's lumen to release air and prime the device. It is also important to check whether the fins are properly installed, because fluid flow around the MicroShunt may indicate that the path of minor fluid resistance may be around the device rather than into the lumen. Device withdrawal, if the fins are wedged too tightly, or new tunnel creation may be needed for troubleshooting when the aforementioned precautions are shown to be ineffective [24]. Following flow confirmation, the MicroShunt's distal end is tucked under Tenon's capsule and conjunctiva. After ensuring that the device is straight and free of tissue, sutures are necessary to reattach Tenon's capsule and conjunctiva over the device and to the limbus [13][15] (**Figure 3**).

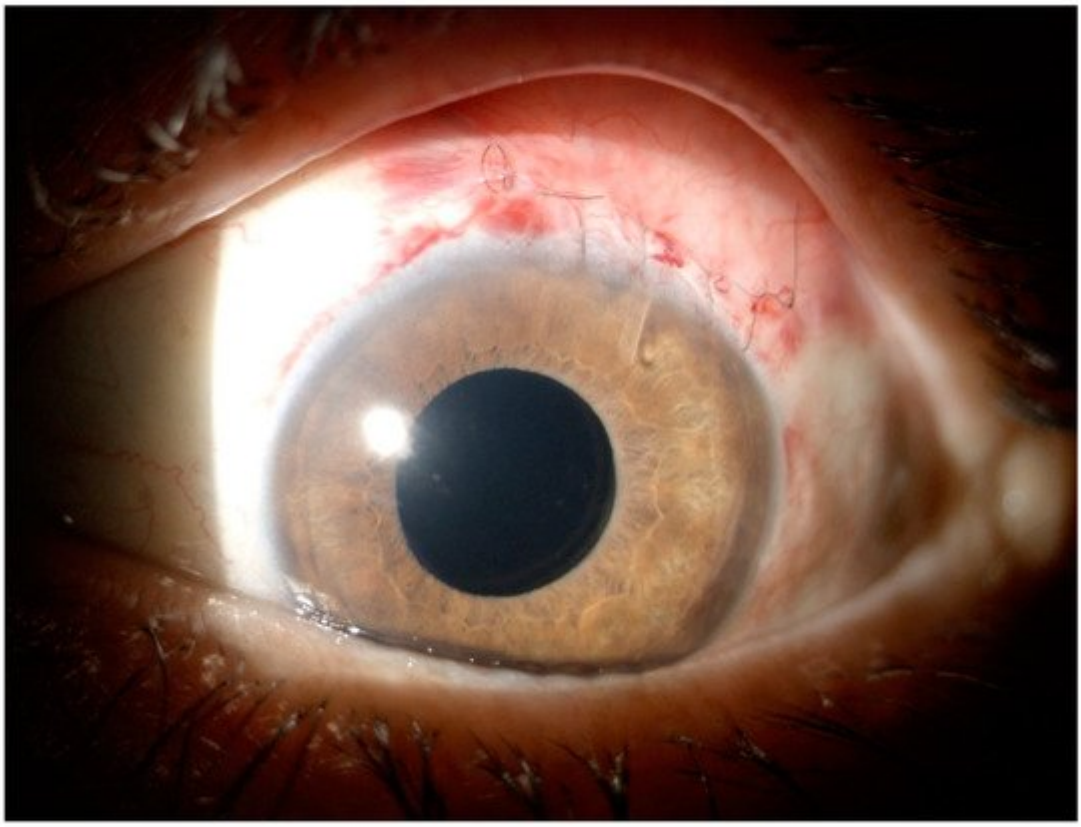

Figure 3. PreserFlo MicroShunt the day after surgical implant. Pretty visible tube in the anterior chamber, sutures over the conjunctiva and the forming filtering bleb.

PreserFlo MicroShunt may be implanted in conjunction with cataract surgery or as a stand-alone treatment. Everywhere, its minimally invasive approach highlights no need for intraoperative gonioscopy, sclerotomy, or iridectomy [29][30][31].

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