The suprachoroidal space has been explored as a target for IOP reduction for the past 100 years. In 1900, Ernst Fuchs, MD, PhD, described the relationship between ciliary body detachment and low IOP after cataract surgery.1 Five years later, Leopold Heine, MD, devised the cyclodialysis spatula to reproducibly create a cyclodialysis cleft to lower IOP.2 Although early IOP reductions were obtained with this approach, the results were complicated by prolonged hypotony, hemorrhage, and profound IOP spikes following spontaneous closure of the cleft. Thus, the procedure was not widely adopted. Although it had become clear that accessing the suprachoroidal space via cyclodialysis clefts was a powerful way to lower IOP,3,4 a safe and reliable surgical approach remained elusive.

After decades without significant advances in this space, in 1966, James Gills, MD, developed a Teflon implant that was placed ab externo within the cleft to prevent spontaneous closure. However, this device ultimately failed due to difficulty of implantation, profound inflammation, and IOP spikes.5,6 Again, interest in this space waned in favor of more traditional subconjunctival approaches to glaucoma surgery.

Fast forward to 2005, when the Solx 24-karat gold suprachoroidal microshunt (Solx) received the CE Mark with promising results.7 This device was designed to be placed via an ab externo approach that required some degree of conjunctival manipulation. It contained 19 channels to provide flow from the anterior chamber to the suprachoroidal space. Despite its early success—including a reported mean IOP reduction of 9 mm Hg7—the Solx microshunt never received FDA approval due to high rates of failure (upwards of 97%) caused by significant scarring around the device and in its micropores.8

Several other devices are undergoing clinical evaluation as an ab externo means of utilizing the suprachoroidal space; these include the
Aquashunt (Opko Health), the Starflo (iStar Medical), and the Esnoper-Clip implant (AJL Ophthalmics). Although safety and efficacy data for these devices seem promising,9-11 clinical trial enrollment has been relatively low (ranging from 15 to 41 patients), and none of these devices has been approved by the FDA to date. Although the long-term issues inherent to subconjunctival filtering surgery are avoided, the major drawback of these devices is that they involve conjunctival manipulation during ab externo implantation, which may limit future surgical options.

**CyPass Rise and Fall**

As the first ab interno supraciliary microstent to receive FDA approval in 2017, the CyPass (Alcon; no longer available) enjoyed widespread adoption among glaucoma specialists. The CyPass was constructed of a biocompatible polyimide material and measured 6.35 mm in length with a 300-µm lumen (Figure 1). It was designed to be placed at the time of cataract surgery.

The COMPASS trial of the CyPass (n = 505) revealed compelling efficacy data at 2 years, with a mean IOP reduction of 7.4 mm Hg and 85% of patients off IOP-lowering medications.12 Overall, adverse events were low and consisted most commonly of transient hyphema, iritis, and hypotony.12 In August 2018, however, Alcon voluntarily withdrew the device from the market based on preliminary results of the COMPASS-XT trial, which suggested that patients in the CyPass group had a higher incidence of significant endothelial cell loss at 5 years compared with patients in the standalone cataract surgery group.13 The FDA officially recalled the device shortly thereafter. The future of CyPass and whether it will be released with different labeling remain uncertain.

**iStent Supra**

The iStent Supra (Glaukos) is another supraciliary microstent designed for ab interno placement, similar to the CyPass. The iStent Supra measures 4 mm in length, and it is constructed from polyethersulfone and titanium, with a 165-µm heparin-coated lumen (Figure 2).14 Early reports employed postoperative travoprost and demonstrated a 30% to 50% IOP reduction at 12 months. No major adverse events were reported. The most common
adverse events were transient hypotony and self-limited choroideal effusions.15,16 The iStent Supra received the CE Mark in 2010, and it is currently being evaluated in a randomized clinical trial in pursuit of FDA approval, with an anticipated 2020 completion date.17

MINIJECT

Another suprachoroidal device under investigation is the Miniject (iStar Medical). This device is made from the company’s proprietary Star material, a biocompatible silicon containing a geometric porous microstructure that reportedly promotes integration with surrounding tissues and reduces fibrosis to preserve flow (Figure 3).18 The Miniject is implanted via an ab interno approach, and only a very small part of the device is exposed to the anterior chamber to reduce corneal endothelial cell injury.

The STAR-I trial enrolled 25 patients with mild to moderate primary open-angle glaucoma who underwent Miniject implantation. At 1 year, the device showed a mean IOP reduction of 32.6%, with 75% of patients remaining medication-free. Importantly, no serious ocular adverse events were reported.19

ADDITIONAL APPLICATIONS

In addition to a powerful alternative pathway for IOP reduction, the suprachoroidal space provides an opportunity for novel drug delivery systems. Delivery of corticosteroids to the suprachoroidal space in animal studies has shown similar efficacy to intravitreal instillation, with a longer half-life and a lower incidence of IOP increase.20

To access this space for drug delivery, microneedles, which have a length of less than 1,000 µm, are being engineered to penetrate only the sclera, allowing medication to be delivered into the suprachoroidal space without entering the vitreous cavity. One promising study (Tanzanite) employed suprachoroidal triamcinolone plus intravitreal aflibercept (Eylea, Regeneron) for the treatment of macular edema from retinal vein occlusion.21 The investigators found that this combination significantly reduced the need for additional intravitreal aflibercept injections and provided better control of macular edema.

Additionally, Clearside Biomedical has targeted the suprachoroidal space as a site for delivery of DNA nanoparticles as a novel approach to ocular gene therapy.22 This could potentially provide a safer and more efficient alternative to subretinal injection as a means to produce gene transfection.

CONCLUSION

Despite a historically underwhelming track record as a route to lower IOP, the suprachoroidal space has resurfaced as a target for potentially powerful glaucoma treatments. The ability to reliably and safely exploit it to lower IOP now seems within reach. In addition to these developments in the glaucoma sphere, potential applications of the suprachoroidal space are being explored for vitreoretinal disorders. Innovation in eye care over the next few years is almost certainly going to involve utilization of this space to treat an increasingly wide array of diseases.


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