A closer look at the new wave of glaucoma surgery – radical or old school?

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Glaucoma is a challenging condition to treat because the exact pathophysiology remains unclear and the only readily modifiable factor is the intraocular pressure (IOP). Additionally, most glaucoma patients are completely asymptomatic, yet are often subjected to lifelong medical therapy. The problems of adherence, persistence and side-effects of glaucoma drops are well recognised clinically and well published academically [1]. Conventional surgical treatment for glaucoma has been proven to be highly effective over the long-term [2], but results vary significantly and the complication rate remains a concern for clinicians and patients. It is therefore not surprising to find a growing amount of interest in recent years to seek alternative surgical treatments that are effective in lowering IOP and reducing medication burden, but which are accompanied by a better safety profile.

Minimally invasive glaucoma surgery (MIGS) has been the ‘hot topic’ in glaucoma over the last decade. Procedures classified as MIGS are quick, performed through a micro-corneal incision without disruption of the sclera and conjunctiva (ab-internally), have fast surgical recovery and no postoperative manipulation. Trabectome (Neomedix Corporation, Tustin, California, USA) was first developed to remove trabecular meshwork (TM) over three to four clock hours exposing the underlying Schlemm’s canal and collector channels. The iStent (Glaukos Corporation, Laguna Hills, CA, USA) was designed to be implanted at the angle to bypass trabecular meshwork, allowing a better point of access to the canal. This concept was then further expanded by the Hydrus Microstent (Ivantis Inc, Irvine, CA), which not only bypasses the trabecular meshwork, but also scaffolds the canal over three clock hours. Clinical results of Trabectome and iStent have been well published and the adoption of these procedures has been worldwide. Hydrus data is slowly emerging but it is not yet a commercial product. Overall these procedures offer similar efficacy with significant IOP reduction to the mid to high teens, even with a reduction of one to two medications [3,4]. They are also often combined with cataract surgery for the extra IOP lowering effect phacoemulsification offers [5].

While the previously mentioned procedures were designed to enhance physiological aqueous outflow, other forms of MIGS are gaining popularity by exploring the traditional subconjunctival drainage concept. The XEN45 gel implant (Allergan PLC, Dublin, Ireland) and InnFocus Microshunt (Santen Pharmaceutical Co., Osaka, Japan) are drainage implants that form a fistula between the anterior chamber and subconjunctival / sub-Tenon’s space (Figure 1). While the XEN45 is implanted ab-internally, the InnFocus is implanted ab-externally after conjunctival dissection. The more invasive implantation technique, especially the latter, combined with the use of antifibrotics and the need for postoperative bleb management, has taken these devices slightly out of the MIGS arena, albeit with a favourably low complication rate. The efficacy of both of these implants appears to be superior to iStent, Hydrus and Trabectome and may approach the IOP lowering effect trabeculectomy [6,7], with potentially less attendant medication and follow-up burden, but data remains limited.

While the glaucoma community is still

Figure 1: Xen45 gel implant is 6mm long with an internal lumen of 45um and designed to create an external drainage bleb.
Figure 2: Kahook dual blade is designed to remove trabecular meshwork ab-internally under gonioscopic guidance.

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two medications to 13.3 mmHg on one medication at 12 months, with combined cataract surgery not significantly affecting the outcome [20].

**Supra-choroidal drainage**

There have been attempts in the past to divert aqueous into the suprachoroidal space, the SOLX Gold Shunt (SOLX Inc, MA, USA) being the most well known of these previously being the most well known of these. Its efficacy has not been well reproduced and device blockage by ingrowing fibrotic tissue has been demonstrated [21]. Two other devices with a similar design, also designed to be implanted ab-interno, the STARFlo Glaucoma Implant (iSTAR Medical SA) and the Aquashunt (previously OPKO Health Miami, USA) have been developed, although the Aquashunt no longer has any active clinical trials.

In recent years there is a resurgence of interest in this space in the form of two micro-stents: CyPass (Transcend Medical, Inc., Menlo Park, CA) and iStent supra (Glaukos Corporation, Laguna Hills, CA, USA). Both devices share similar design features and are both implanted ab-internally in an almost identical manner. The recently published COMPASS Study compared cataract surgery with concomitant CyPass insertion with cataract surgery alone [22]. Mean IOP reduction was 7.4 mmHg for the microstent group (from 24.5 mmHg) versus a 5.4 mmHg in controls (P < 0.001). Importantly, 85% of microstent subjects versus 59% of controls were medication free. There were no vision threatening adverse events.

The procedure has been developed further by combining stent insertion with injection of ophthalmic viscosurgical device to help maintain the suprachoroidal aqueous lake (termed Viscopass). A clinical trial comparing cataract surgery with concomitant Cypass insertion with cataract surgery alone [22]. Mean IOP reduction was 7.4 mmHg for the microstent group (from 24.5 mmHg) versus a 5.4 mmHg in controls (P < 0.001). Importantly, 85% of microstent subjects versus 59% of controls were medication free. There were no vision threatening adverse events.

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**In-flow procedure**

Although raised IOP in glaucoma is not thought to be an inflow issue, treatment to the ciliary body processes to reduce aqueous production, both pharmacologically and surgically, has served an invaluable role. Conventional cyclodiode laser has a proven track record in IOP reduction, especially in complicated and refractory glaucoma [23]. More recently, the adoption of endoscopic cyclophotocoagulation, especially combined with phacoemulsification, has shown significant IOP and medication reduction of a similar magnitude to current MIGS devices [24]. Unfortunately, cyclodestruction procedures are often associated with a higher rate of complications such as persistent inflammation, hypotony and cystoid macular oedema.

Efforts have therefore been made to explore safer methods of ciliary body treatment. High-intensity focused ultrasound (HIFU) is a technology used successfully in the treatment of uterine fibroid and prostate disease. It has been adopted for glaucoma use by EyeTechCare, France using a device consisting of a ring-shaped probe embedded with six piezo-electric crystals that sits directly on the eye (Figure 4). Focused ultrasound is used to target the ciliary body and histological studies have demonstrated ciliary epithelium destruction and potentially an increase in ciliary outflow [25]. HIFU was originally licensed and marketed to treat refractory glaucoma. There has been a series of prospective trials under the acronym Eyemust sponsored by the manufacturer. The pilot study in patients with refractory glaucoma, with at least one glaucoma procedure previously, showed a substantial reduction in IOP from 37.9 mmHg at baseline to 24.7 mmHg at up to one year [26]. The most recent study was conducted in POAG patients who had not had previous surgery. This showed a reduction in IOP from 28.2 mmHg to 19.6 mmHg at 12 months [27]. However, as with the previous studies, the final IOP was achieved on 3.1 medications, (compared to 3.6 at baseline) which is greater than many of the other procedures described here and is in contrast to the majority of published results on photocyclocoagulation. Complications included persistent anterior chamber flare at one month in 33% of patients, corneal ulceration in 17% of patients and corneal thinning in one patient. Studies are ongoing and its efficacy and safety, especially in pre-surgical eyes, remains to be proven. A further drawback of this procedure is that anterior segment measurements are required preoperatively to accurately locate the ciliary body so that a probe of the correct size can be used.

An alternative cyclodiode modality, termed Micropulse cyclophotocoagulation (Iridex, USA), is currently available commercially. The technology allows a continuous-wave laser beam to be divided into a train of shorter, repetitive, low energy pulses separated by a brief rest period. This allows the tissue to cool and is intended to reduce thermal tissue damage. A study from the National University Hospital, Singapore on 38 patients demonstrated a reduction in IOP from 40.1 mmHg to 24.6 mmHg at final follow-up [28]. IOP lowering medications were reduced from 2.1 before micropulse to 1.3 at final follow-up. There were no serious complications, although larger series would be required to demonstrate improved safety over trans-scleral diode. Similarly to HIFU, its efficacy in mild to moderate glaucoma is yet to be proven. More importantly, the safety profile of a ciliary body based treatment requires careful evaluation. Although these treatments are not truly
marketed as MIGS, low complication rate and high patient satisfaction are important criteria that all new procedures should fulfill.

**Conclusion**

In order for medical treatment to advance there has to be a close collaboration between clinicians and industry. Those clinicians involved in such innovations are ultimately grateful for the vast amount of interest and investment into this field, yet are fully aware of the effect of any potential commercial pressure. It is our view that all clinicians interested in the early adoption of these new procedures should have an open but critical approach, proceed cautiously and have a robust self-auditing and reporting process in place. While we eagerly await longer-term data from our ‘first wave’ of MIGS devices, the second wave is already fast approaching. Although some of the newest additions appear to be modifications to some tried and tested existing operations, their efficacy is yet to be proven and a lot more work is required to guide us through this maze.

**References**


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- The complexity, complications and follow-up burden of conventional glaucoma surgery has lead to a search for alternatives.
- The early success of some MIGS procedures has encouraged a rapid expansion of new techniques.
- All of these techniques are based on the principles of already existing operations.
- Much work remains to be done in establishing their efficacy and safety, as well as the best candidates for surgery.