

Minimally Invasive Glaucoma Surgery (MIGS)-An Update on MIGS Implants

Ejaz Ansari*

Consultant Ophthalmic Surgeon, Maidstone & Tunbridge Wells NHS Trust, UK

***Corresponding author:** Ejaz Ansari, Consultant Ophthalmic Surgeon, Maidstone & Tunbridge Wells NHS Trust, UK, Tel/Fax: 01622 226275; Email: e.ansari@nhs.net

Published Date: September 04, 2017

ABSTRACT

For several years, the gold standard for surgical treatment of glaucoma has been trabeculectomy. Although very successful in reducing intraocular pressure (**IOP**), there are several potential complications, including sight-threatening problems. This has stimulated much research in the development of new and effective procedures to lower IOP with an enhanced safety profile. Minimally invasive glaucoma surgery (**MIGS**) procedures prioritise patient safety, but also demonstrate efficacy in reducing IOP. We performed an online search of peer-reviewed literature using PubMed, entering keywords relevant to this clinical discipline. In summary, there is a lack of long-term safety and efficacy data, a lack of comparative data and a lack of data on standalone (i.e. without simultaneous cataract surgery) procedures. Most implants are not yet FDA approved. Although not exhaustive, this article summarizes the range of different MIGS implants that are available to the ophthalmic surgeon.

Keywords: CyPass; Glaucoma; Hydrus; Implant; iStent; Microshunt; MIGS; Phaco; Stent; XEN; Innfocus

INTRODUCTION

Glaucoma remains the leading cause of irreversible blindness worldwide. It is estimated that 64.3 million people have glaucoma [1]. The only modifiable risk factor is raised intraocular pressure (**IOP**), with therapy aimed at reducing this by various means [2]. This includes topical hypotensive agents, laser trabeculoplasty and glaucoma drainage surgery. Adherence to drops and their multiple side-effects limit their use and efficacy, whereas laser trabeculoplasty effects wear off over time requiring multiple repeat procedures [3,4]. Drainage surgery, e.g. trabeculectomy and aqueous shunts demonstrate excellent efficacy but have less than ideal risk profiles [5]. Despite their efficacy, tube and trabeculectomy patients have similar rates of vision-threatening complications such as endophthalmitis, or choroidal haemorrhage; ocular surface scarring and ocular surface disease can lead to poor quality of life for patients [6].

MIGS offer a safer, less invasive means of reducing IOP than traditional surgery, with the goal of reducing dependency on topical agents. MIGS can usually be combined with cataract surgery and most clinical studies have analysed results of combined surgery. With MIGS there is a trade-off between enhanced safety with less efficacy compared to traditional surgery. MIGS procedures are currently targeted at patients with mild-to-moderate glaucoma.

Generally speaking, MIGS procedures are ab interno, microincisional and conjunctiva-sparing. They share the common approach of minimal tissue trauma and minimal disruption of normal anatomy and physiology [7]. For the patient, MIGS provide IOP control in the mid to low-teens with rapid visual rehabilitation and less dependence on topical treatment. This article summarises the current literature on the range of MIGS implants available.

There are three main groups of implants. These include implants that increase trabecular outflow by bypassing the juxtacanalicular trabecular meshwork (**TM**), increasing uveoscleral outflow via suprachoroidal pathways, or by creating a subconjunctival drainage pathway. (Table 1) summarises the different implants and their mechanisms of action; the ones highlighted in bold print are discussed in this review.

Table 1: A summary of MIGS implants (highlighted ones are discussed in this article).

TRABECULAR	Implant	Material	Dimensions	
	i-Stent i-Stent inject	heparin-coated, non-ferromagnetic, titanium	1mmx0.3mm 230mcm x 360mcm	Glaukos Corp., Laguna Hills, CA, USA
	Hydrus	nitinol (nickel–titanium alloy)	8mm length	Ivantis Inc., Irvine, CA, USA
UVEOSCLERAL	Cypass	Polyamide	6.35 mm length, 510 µm external diameter	Alcon, Fort Worth, TX, USA
	i-Stent Supra			Glaukos Corp.,
SUBCONJUNCTIVAL				
Ab interno	XEN	gelatin crosslinked with glutaraldehyde	6mm length, 45 µm internal diameter	Allergan, Dublin, Ireland Santen
Ab externo	Innfocus	SIBS (Poly Styrene block- IsoButylene-block- Styrene)	8.5mm length, 70 µm internal diameter	Pharmaceutical Company Ltd, Osaka, Japan

TRABECULAR MESHWORK BYPASS STENTS

iSTENT (Glaukos Corp., Laguna Hills, CA, USA)-this heparin-coated, non-ferromagnetic titanium device has a snorkel shape, which is used for implantation into Schlemm's Canal (**SC**). It can be implanted solo (single or multiple), or in combination with cataract surgery (Figure 1a).

The iStent Study Group [8] randomised controlled trial (**RCT**) compared cataract surgery alone to combined surgery with one iStent (n=240). In the study group (combined surgery group), 72% had IOP<21mmHg at 12 months and 61% at 24 months, which was statistically significant. In the cataract surgery group, success rate was 50% at 12 and 24 months. Mean IOP reduction was 8.4mmHg+/-3.6 (33%) at 12 and 24 months in the study group. There was a mean decrease of medications, 1.4+/-0.8, in the study group (87%) and 1.0+/-0.8 in the controls (73%) (p=0.005) at 12 months. In the study group, 15% were taking glaucoma medications at 12 months compared to 35% in the cataract group (p=0.001).

Further evidence that the reduction of IOP is not the result of cataract surgery alone was provided by another RCT [9]. At 16 months (p=0.042) and 48 months (p=0.02) there was a significantly lower IOP in the combined surgery group compared to the cataract only group. This also demonstrated a beneficial effect in IOP reduction for a long period of time with a reduction in medications.

Although there is more emphasis in using MIGS for earlier stages of glaucoma, iStent has been studied in more advanced cases of glaucoma including post-drainage surgery eyes [10]. At 36 months, the mean IOP in the cases without previous surgery was 15.4 +/- 2.2mmHg, with 13% on topical treatment. The mean IOP in the group with previous surgery was 14.2 +/- 2.3mmHg, with 44% taking medications.

There is evidence of enhanced IOP reduction with multiple implants. In a prospective study (n=119) of solo cases, at 18 months off topical treatment, The IOP was 15.9+/-0.9mmHg with one

stent, 14.1+/-1.0mmHg with two stents and 12.2+/-1.1mmHg with three stents [11]. Implantation of each additional stent realized a significant further reduction of IOP (p=0.001).

This has led to the development of a 2nd generation iStent, the iStent Inject/ model GST400. This is preloaded with two stents (Figure 1b).

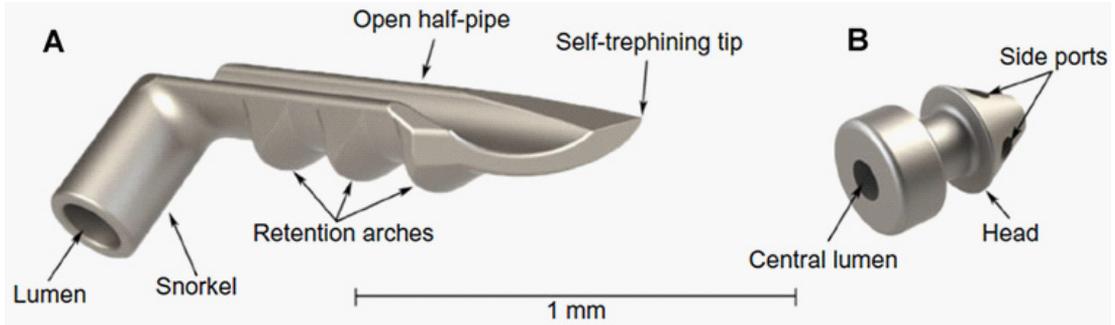


Figure 1: iStent (Glaukos Corporation, Laguna Hills, CA, USA) (a) and iStent Inject (Glaukos Corporation) (b). Figure used courtesy of Glaukos Corporation.

iStent Inject-Standalone Studies

The Synergy Trial was a European multicenter prospective, unmasked study (n=99) with OAG on at least two topical ocular hypotensive medications, who underwent implantation of two GTS400 stents in a standalone procedure [12]. Followup was for 12 months. 66% achieved IOP ≤18 mmHg at 12 months without medication, and 81% of subjects achieved IOP ≤ 18 mmHg with either a single medication or no medication. Mean baseline washout IOP values decreased by 10.2 mmHg/ 39.7%. Mean IOP at 12 months was 14.7 (SD 3.1) mmHg in subjects not using ocular hypotensive medications. Reduction in the number of drops taken occurred in 86.9% of patients.

Eighteen ocular adverse events were reported. Ten were of elevated IOP, which resolved in 4 subjects after topical treatment, and in 6 subjects after surgical intervention- two trabeculectomies and one gonio-trephation. In 13 cases, one of the stents was not visible, one case of goniosynechia (treated with laser), and one case of lens-iris synechia, which resolved uneventfully [12].

In another prospective, open label, single arm study, 57 phakic eyes underwent a standalone procedure of two GTS400 trabecular micro-bypass stents. At 12 months post-operatively, 100% of eyes achieved an IOP of >= 20% without medication compared to pre-operative unmedicated IOP; 75% had IOP reduction of >=20% without medication compared to pre-operative medicated IOP. There was a 42% IOP reduction post-operatively at 12 months, which was maintained at 18 months with a very good safety profile [13].

Two studies have explored the concept of possible synergy between increasing conventional aqueous outflow via trabecular micro-bypass stenting and uveoscleral outflow via a prostaglandin analogue:

A prospective, nonrandomized, open-label study with standalone implantation of two GTS400 stents + postoperative topical prostaglandin (**Travaprost**) was conducted in OAG eyes uncontrolled on two preoperative drops (n=53). At 12 months, 91% of eyes achieved IOP reduction $\geq 20\%$ with reduction of one medication. 100% had intraocular pressure ≤ 18 mmHg with reduction of one medication, and 87% had intraocular pressure ≤ 15 mmHg. Mean IOP on one medication was ≤ 13.0 mmHg ($\geq 34\%$ reduction) at 18 months with no adverse events recorded [14].

In a similar prospective, single-arm, unmasked study (GTS400 stents + postoperative topical prostaglandin [Travaprost]), of 39 phakic eyes with OAG, at 36 months postoperative, 97% of eyes had achieved an IOP reduction of $\geq 20\%$ from baseline with a reduction of 1 medication. 86% of eyes had IOP of ≤ 18 mmHg with a reduction of 1 medication. Mean IOP decreased to 14.0 ± 2.6 mmHg on 1 medication versus 22.4 ± 2.3 mmHg on 2 medications preoperatively. The mean unmedicated IOP decreased to 17.7 ± 1.7 mmHg at 37 months from 25.3 ± 1.9 mmHg preoperatively. Adverse events included CE in 3 eyes and trabeculectomy in 1 eye. No intraoperative or device-related adverse events occurred [15].

iStent Inject + Cataract Extraction and Lens Implant (CE+IOL)

A prospective, uncontrolled, nonrandomized, interventional study was conducted in phakic eyes with mild or moderate open-angle glaucoma/ OHT. Patients underwent CE+IOL+ implantation of two iStent inject (**G2**) devices.

20 patients were followed up for a mean of 47.4 ± 18.46 months. Mean end follow-up IOP was $16.25 \text{ mmHg} \pm 1.99 \text{ mmHg}$, i.e. an IOP decrease of $36.92\% \pm 9.74\% \pm 3.14 \text{ mmHg}$ ($p < 0.001$), from baseline washout IOP. The mean number of medications was significantly reduced from 1.3 ± 0.66 to 0.75 ± 0.79 ($p = 0.017$). 45% of patients were medication-free by the end of follow-up. Mean best corrected log MAR visual acuity (**BCVA**) improved significantly from 0.42 ± 0.16 to 0.18 ± 0.16 ($p < 0.001$). There were no peri-operative complications [16].

iStent Inject-Comparative Study

A retrospective intraindividual eye study of 27 patients/ 54 eyes was conducted, comparing CE+IOL+ ab interno trabeculectomy (group 1) with CE+IOL+ GTS400 (group 2). Mean preoperative IOP decreased from 22.3 ± 3.7 mmHg in group 1 and 21.3 ± 4.1 mmHg in group 2 to 15.6 ± 3.6 mmHg for ab interno trabeculectomy ($p < 0.001$) and 14.0 ± 2.3 mmHg for GTS400 (i-Stent inject) ($p < 0.001$) at 12 months, with no significant difference between the groups ($p > 0.05$). There were no vision-threatening complications. In each group trabeculectomy had to be performed in two eyes due to insufficient efficacy [17].

HYDRUS (Ivantis Inc, Irvine, CA, USA)-this is crescent shaped trabecular bypass device made of nitinol (an alloy of nickel and titanium), a shape memory alloy. This means that when deformed, it returns to its original shape after being heated. Being 8mm long it straddles 3 clock hours of SC,

with the aim of accessing more collector channels and dilating the SC, acting as a scaffold so that it does not block the collector channel ostia.

A RCT of 100 cases randomised to cataract surgery alone or combined cataract surgery with Hydrus, has been completed [18]. At 24 months, a significantly greater proportion of combined surgery cases reached the endpoint of 20% reduction in washed out diurnal IOP (80% versus 46%, $p=0.0008$). The IOP was also significantly lower in the combined surgery group ($16.9\pm 3.3\text{mmHg}$ versus $19.2\pm 4.7\text{mmHg}$, $p=0.0093$). There was also a significant reduction in cases without ocular hypotensive medications in the combined surgery group (73% versus 38%, $p=0.0008$).

The safety in the Hydrus group was similar to the control. Six of 50 (12%) Hydrus patients had focal peripheral anterior synechiae, but this did not affect device efficacy adversely. The Hydrus stent would have the same indications and relative contraindications as the iStent in theory, but more data are needed to support this.

SUPRACHOROIDAL IMPLANTS

The CyPass (Alcon, Fort Worth, TX, USA) is a suprachoroidal shunt, reviewed below. The iStent supra is another one under investigation, but there are no peer-reviewed studies to date. Finally, the SOLX Gold microshunt (SOLX, Waltham, MA, USA) is a suprachoroidal shunt implanted via an ab externo conjunctival and scleral dissection and thus will not be discussed here. It is worth noting that while there are no published clinical trials on the SOLX Gold, it may be an alternative for a patient with corneal opacities preventing a clear view on gonioscopy.

The CyPass is a polyamide implant, 6.35 mm in length and 510 μm in external diameter that creates a permanent conduit between the anterior chamber and the supraciliary space. Along the length of the stent are microholes that allow for circumferential egress of aqueous into the suprachoroidal space, and the distal end of the stent allows longitudinal egress of fluid. The collar of the device rests in the anterior chamber angle (Figure 2). The procedure is visualized using gonioscopy. Implant positioning is confirmed by postoperative gonioscopy and/or anterior segment OCT [19].

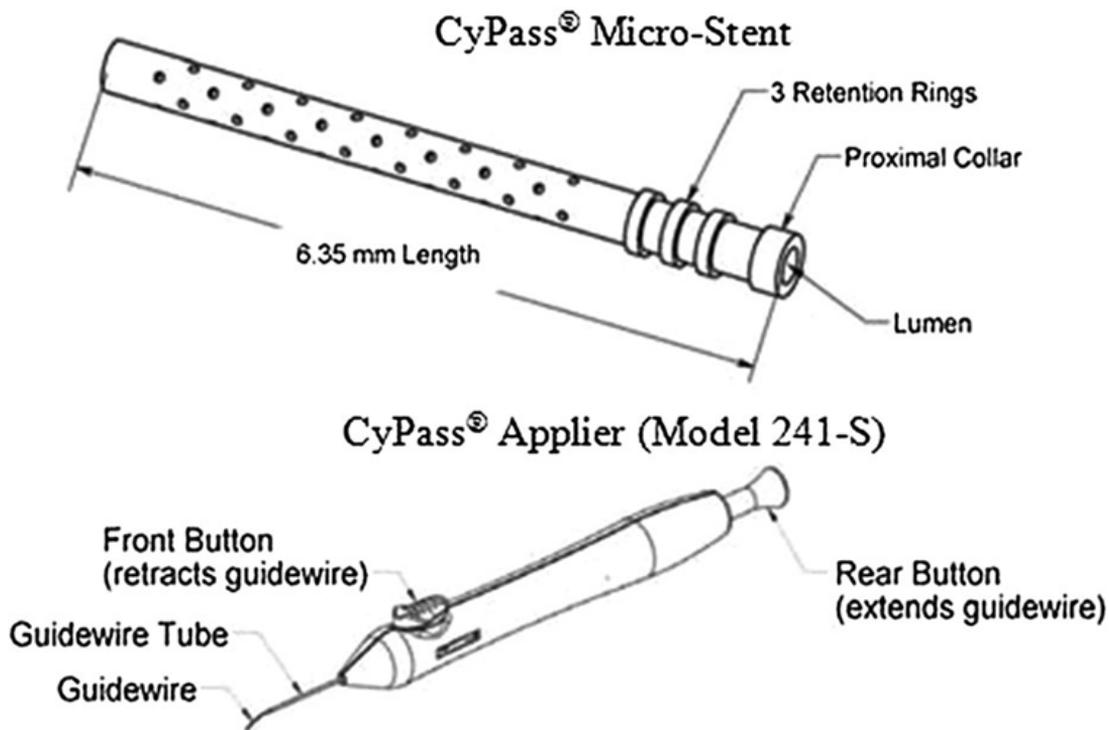


Figure 2: CyPass implant. Sourced from the FDA website on 1/06/2017.

CyPass with Cataract Extraction and Intraocular Lens Implant (CE/IOL)

In 2013, Hoeh et al reported the results of a multicenter prospective series of 57 uncontrolled (≥ 21 mmHg) POAG patients and 41 IOP-controlled (< 21 mmHg) POAG patients undergoing CyPass implantation combined with cataract surgery. They demonstrated a favorable safety profile. The mean medicated IOP in both groups combined was 21.1 ± 5.91 mmHg (baseline IOP for each group was not stated). The resulting IOP at 6 months was 15.6 ± 0.53 mmHg on 0.9 ± 0.15 medications in the uncontrolled group; this was a 37% decrease in IOP ($P < 0.001$) and a 50% reduction in glaucoma medications ($P < 0.001$). The resulting IOP in IOP-controlled patients was 15.6 ± 0.68 mmHg on 0.6 ± 0.07 medications; this was a 71.4% reduction in glaucoma medications ($P < 0.001$) [20].

CyPass Implantation Alone

The COMPASS Trial was a two-year RCT of 505 subjects randomized to CE/IOL+ CyPass or CE/IOL alone [21]. The treatment group demonstrated IOP lowering of 7.4 mmHg compared to 5.4 mmHg in the control group ($p < 0.001$), with 85% of treated patients being drop-free at 24 months. There were no vision-threatening AEs in the CyPass group and visual acuity was at least 20/40 in 98% of all cases studied.

In contrast to the COMPASS Trial, the DUETTE study followed patients (n=65) for 1 year after stand-alone CyPass implantation. This was a multicentre, single-arm interventional study of 65 eyes with OAG and IOP uncontrolled at >21 mmHg on topical therapy. Baseline IOP was reduced from 24.5 ± 2.8 mmHg with 2.2 ± 1.1 medications to 16.4 ± 5.5 mmHg with 1.4 ± 1.3 medications at 12 months, i.e. a 34.7% reduction in IOP. IOP spikes to >30 mmHg lasted beyond 1 month in 11% of cases; 12.2% had cataract progression at 12 months; four eyes had hyphaema that resolved by month 1. 17% of patients went on to require a trabeculectomy; 6% exited the study by choice, and 4.6% were lost to follow-up [22].

Viscopass is a term used to describe CyPass implantation combined with the injection of 60mL of ophthalmic viscosurgical device (**OVD**) at the end of the lumen to increase the size of the aqueous drainage area created by the CyPassMicro-Stent. A clinical trial comparing this with CyPass alone is underway.

SUBCONJUNCTIVAL FILTRATION

XEN Gel Stent

Subconjunctival filtration creates a nonphysiologic route for aqueous outflow and is the basis of the traditional trabeculectomy and aqueous shunt glaucoma surgeries. The XEN gel stent (Allergan, Dublin, Ireland) is an ab interno gelatin stent under investigation that would be implanted via a clear corneal incision without conjunctival dissection. The stent is 6 mm in length and composed of porcine gelatin crosslinked with glutaraldehyde. There are three models being evaluated that have inner diameters of 45 μm , 63 μm , and 140 μm [23]. With the 45 μm being the recommended device by the manufacturer (Figure 3). The stent follows Poiseuille's law of laminar flow where the length of the tube and inner diameter of the tube manage the rate of flow. Hypotony is avoided by the flow resistance determined by the length and inner diameter of the tube. Preclinical tests established that the implant does not occlude inside the lumen and the implant material does not cause a tissue reaction in the eye [23].

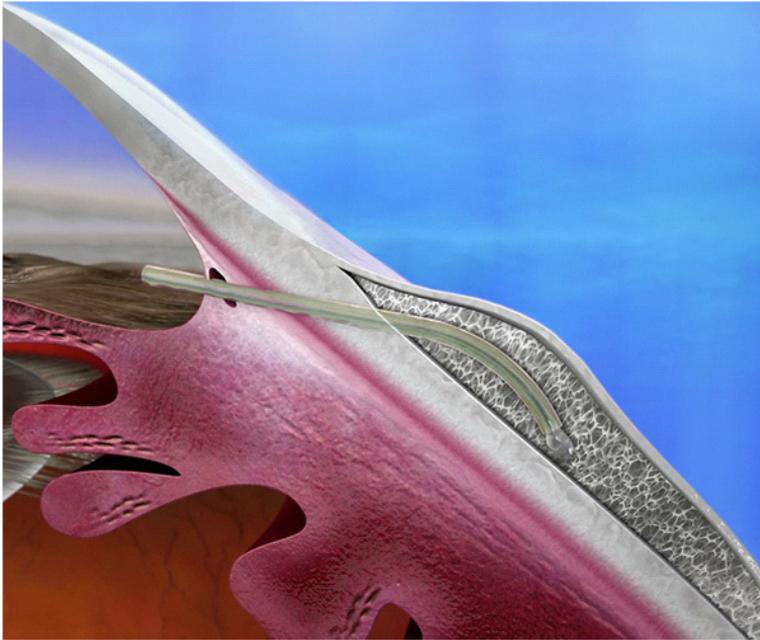


Figure 3: XEN implant. Image courtesy of Allergan.

There are few published studies on the XEN 45 implant. Two pilot studies [24, 25] have been published. One study investigated combined XEN implant (63 and 140) with cataract surgery, and demonstrated a reduction of IOP from 22.4 (+/-4.2) mmHg to 15.4 (+/-3.0) mmHg at 12 months; there was a reduction in glaucoma medications from 2.5 +/-1.4 to 0.9+/-1.0 [24].

In another pilot study using XEN implantation alone (n=49 eyes), 40% had unqualified success at 12 months (IOP<=18mmHg and >=20% reduction in IOP). 89% had qualified success, and most cases were of previously failed trabeculectomy [25].

In these studies, there were no serious adverse events such as tube erosion or prolonged hypotony, but some patients did require injection of ophthalmic viscosurgical device into the anterior chamber, particularly in the XEN 140 group.

In a small prospective interventional study (n=13, XEN 45+Mitomycin C), mostly combined procedures (n=10), the IOP reduced by 25% and mean number of medications reduced by 84% at 12 months [26]. There was choroidal detachment in 2 eyes, implant extrusion in one eye and 2 eyes required trabeculectomy.

A retrospective, multi-centre comparative study between XEN gel stent standalone implantation (n=189) versus trabeculectomy (n=169) has been reported recently. The adjusted hazard ratio (HR) of failure of the microstent relative to trabeculectomy was 1.2 (95% confidence interval [CI], 0.7-2.0) for complete success and 1.3 (95% CI, 0.6-2.8) for qualified success. Time to 25% failure was 11.2 months versus 10.6 months for complete success and 30.3 months versus 33.3

months for qualified success. 43% versus 31% underwent needling, and 50% of trabeculectomy eyes had laser suture lysis. Most reported complications were transient. Ten percent and 5% underwent reoperation (P = 0.11) [27].

Results of the phase 4 APEX trial using XEN 45 will be available later this year.

INNFOCUS

The Innfocusmicroshunt (Santen Pharm Ltd, Osaka, Japan) is an ab externo drainage device it involves more steps akin to trabeculectomy compared to other MIGS. The material is SIBS (Poly Styrene block- IsoButylene-block- Styrene) which has been developed specifically for medical implants. It is a biocompatible and biostable thermoplastic elastomer.

In one study (n=23 eyes), 80% had IOP<=14mmHg at 3 years, but some cases were standalone and others were combined procedures. The mean IOP for the entire group was 10.7 +/-1.5 mmHg at 3 years; qualified success rate was 95% with a reduction in medications from 2.6+/-0.9 to 0.8+/-1.2 [28].

Transient hypotony and transient choroidal effusion occurred in 13% and 8.7% respectively, but with spontaneous resolution. There were no serious long-term adverse events, leaks, erosions, migrations or infections.

DISCUSSION

MIGS implants targeting different aqueous outflow pathways offer an improved safety profile for glaucoma surgery while preserving modest efficacy (Table 2). An important advantage for patients in addition to the safety element is that comorbid cataract can be treated simultaneously with MIGS implants. The procedures targeting the subconjunctival space appear to be more efficacious in terms of IOPreduction. However, there is a lack of comparative studies between the different implants.

Table 2: Summary of efficacy and safety data.

	Phaco/iStent (8)	Phaco/iStent inject (16)	Phaco/Hydrus (13)	Phaco/CyPass (17)	Phaco/XEN 45 (26)	InnFocus (28)
Pre-op IOP (mmHg)	18.6	26.0	26.3	24.4	16.0	23.8
Post-op IOP (mmHg)	17.0	16.25	16.9	17.0	12.0	10.7
% IOP drop; % medication reduction	33%; 87% (versus 32.5%; 73% in controls)	36.92%; 42%	50%; 73% (versus 28%; 38% in controls)	30.3%; 85.7% (versus 22%; 53.9% in controls)		55%; 69.2%
AEs	0.85% endothelial touch; 6% iris touch; 4.2% secondary surgery		12% focal peripheral anterior synechiae		Transient choroidal detachment=2, tube extrusion=1, trabeculectomy=2	Transient hypotony=13% transient choroidal effusion=8%

Although RCTs have been conducted for some of the implants discussed, well-designed randomised clinical trials with an extended follow-up are required to evaluate the long-term efficacy and late complications of these implants.

MIGS technology has potential advantages that could improve the management of glaucoma. These include reducing the medication burden, which enhances patient quality of life, bypassing or delaying the need for more invasive surgery and preserving the conjunctiva if a more-invasive intervention were to be required later on. There are limited data on the cost-effectiveness of MIGS, but one study showed the cost-effectiveness of iStent compared to branded medications [29]. More studies like this are required for a wider range of MIGSs to demonstrate their cost-effectiveness compared to medical treatment.

However, there are several limitations to the current state of MIGS. There is a lack of high-quality data, a lack of study standardization, a lack of cost-effectiveness data, a lack of long-term data and incomplete knowledge of ideal patient selection. Furthermore, many studies have been performed for cases combined with cataract surgery, meaning that they lack robust evidence for the effect of MIGS alone [30]. It is also unclear which established procedures should be compared to the MIGS devices. Standardization and improvements in the quality of future MIGS studies will help clinicians to negotiate this ever-expanding area more knowledgeably and help them to optimize the selection of the appropriate device for the right patient. With the correct approach to investigating and evaluating new technologies, there is much potential for future generations of MIGS to improve the quality of care for glaucoma patients.

ACKNOWLEDGEMENTS

No funding or sponsorship was received for this study or publication of this article. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published.

References

1. Tham YC, Li X, Wong TY, Quigley HA, Aung T, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*. 2014; 121: 2081-2090.
2. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, et al. Early Manifest Glaucoma Trial Group. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. *Arch Ophthalmol*. 2002; 120: 1268-1279.
3. Lemij HG, Hoevenaars JG, van der Windt C, Baudouin C. Patient satisfaction with glaucoma therapy: reality or myth? *ClinOphthalmol*. 2015; 9: 785-793.
4. Leahy KE, White AJ. Selective laser trabeculoplasty: current perspectives. *ClinOphthalmol*. 2015; 9: 833-841.
5. Gedde SJ, Herndon LW, Brandt JD, Budenz DL, Feuer WJ, et al. Tube Versus Trabeculectomy Study Group. Postoperative complications in the Tube Versus Trabeculectomy (TVT) study during five years of follow-up. *Am J Ophthalmol*. 2012; 153: 804-814.
6. Gedde SJ, Schiffman JC, Feuer WJ, Herndon LW, Brandt JD, et al. Tube versus Trabeculectomy Study Group. Treatment outcomes in the Tube Versus Trabeculectomy (TVT) study after five years of follow-up. *Am J Ophthalmol*. 2012; 153: 789-803.
7. Saheb H, Ahmed IK. Micro-invasive glaucoma surgery: current perspectives and future directions. *Curr Opin Ophthalmol*. 2012; 23: 96-104.

8. Craven R, Katz LF, Wells JM, Giamporcaro JE, iStent Study Group. Cataract surgery with trabecular micro-bypass stent implantation in patients with mild to moderate open angle glaucoma and acataract: Two year follow-up. *J Cat Ref Surg* 2012; 38: 1339-1345.
9. Fea AM. Phacoemulsification versus phacoemulsification with micro-bypass stent implantation in primary open-angle glaucoma: randomized double-masked clinical trial. *J Cataract Refract Surg.* 2010; 36: 407-412.
10. Neuhann TH. Trabecular micro-bypass stent implantation during small incision cataract surgery for open angle glaucoma or ocular hypertension: long term results. *J Cat Ref Surg.* 2015; 41: 2664-2671.
11. Katz LJ, Erb C, Carceller GA, Fea AM, Voskanyan L et al. Prospective randomised study of one, two, or three trabecular bypass stents in open angle glaucoma subjects on topical hypotensive medication. *ClinOphthalmolAuckl NZ.* 2015; 9: 2313-2320.
12. Voskanyan L, Garcia-Feijoo J, Belda JI, Fea A, Jünemann A, et al. Prospective masked evaluation of the iStent inject system for open-angle glaucoma: synergy trial. *AdvTher.* 2014; 31: 189-201.
13. Lindstrom R, Lewis R, DM Hornbeak, Voskanyan L, Giamporcaro JE, et al. Outcomes following implantation of two second generation Trabecular Micro-Bypass Stents in Patients with POAG. *Adv Therapeutics.* 2016; 33: 2082-2090.
14. Berdahl J, Voskanyan L, Myers JS, Hornbeak DM, Giamporcaro JE, et al. Implantation of two second-generation trabecular micro-bypass stents and topical travoprost in open-angle glaucoma not controlled on two preoperative medications: 18-month follow-up. *ClinExp Ophthalmol.* 2017; 6: 12958.
15. Chang DF, Donnenfeld ED, Katz LJ, Voskanyan L, Ahmed IIK, et al. Efficacy of two trabecular micro-bypass stents combined with topical travoprost in open-angle glaucoma not controlled on two preoperative medications: 3-year follow-up. *Clinical Ophthalmology.* 2017; 11: 523-528.
16. Arriola-Villalobos P, Martinez-de-la-Casa JM, Diaz-Valle D, Morales-Fernandez L, Fernandez-Perez C, et al. Glaukos iStent inject® Trabecular Micro-Bypass Implantation Associated with Cataract Surgery in Patients with Coexisting Cataract and Open-Angle Glaucoma or Ocular Hypertension: A Long-Term Study. *J Ophthalmol.* 2016; 1056573.
17. Gonnermann J, Bertelmann E, Pahlitzsch M, Maier-Wenzel AKB, Torun N, et al. Contralateral eye comparison study in MICS & MIGS: Trabectome® vs. iStent inject®. *Graefes Arch ClinExpOphthalmol.* 2017; 255: 359-365.
18. Pfeiffer N, Garcia-Feijoo J, Martinez-de-la-Casa JM, Larrosa JM, Fea A, et al. A randomized trial of a Schlemm's canal microstent with phacoemulsification for reducing intraocular pressure in open-angle glaucoma. *Ophthalmology.* 2015; 122: 1283-1293.
19. Saheb H, Ianchulev T, Ahmed II. Optical coherence tomography of the suprachoroid after CyPass Micro-Stent implantation for the treatment of open-angle glaucoma. *Br J Ophthalmol.* 2014; 98: 19-23.
20. Hoeh H, Ahmed IK, Grisanti S, Grabner G, Nguyen QH, et al. Early postoperative safety and surgical outcomes after implantation of a suprachoroidal micro-stent for the treatment of open-angle glaucoma concomitant with cataract surgery. *J Cataract Refract Surg.* 2013; 39: 431-437.
21. Vold S, Ahmed IIK, Craven ER, Mattox C, Stamper R, et al. Two-Year COMPASS Results: Supraciliary Microstenting with Phacoemulsification in Patients with Open-Angle Glaucoma and Cataracts. *Ophthalmology.* 2016; 123: 2103-2111.
22. Garcia-Feijoo J, Rau M, Grisanti S, Hüh H, Erb C, et al. Supraciliary micro-stent implantation for open-angle glaucoma failing topical therapy: 1-year results of a multicenter study. *Am J Ophthalmol.* 2015; 159: 1075-1081.
23. Lewis RA. Ab interno approach to the subconjunctival space using a collagen glaucoma stent. *J Cataract Refract Surg.* 2014; 40: 1301-1306.
24. Sheybani A, Lenzhofer M, Hohensinn M, Reitsamer H, Ahmed II, et al. Phacoemulsification combined with a new ab interno gel stent to treat open-angle glaucoma: pilot study. *J Cat Ref Surg.* 2015; 41: 1905-1909.
25. Sheybani A, Dick HB, Ahmed II. Early clinical results of a novel ab interno gel stent for the surgical treatment of open-angle glaucoma. *J Glaucoma* 2016; 25: e691-e696.
26. Galal A, Bilgic A, Eltanamly R, Osman A. XEN glaucoma implant with mitomycin C 1 year follow-up: result and complications. *J Ophthalmol.* 2017: 5457246.
27. Schlenker MB, Gulamhusein H, Conrad-Hengerer, Somers A, Lenzhofer M, et al. Efficacy, Safety, and Risk Factors for Failure of Standalone Ab Interno Gelatin Microstent Implantation versus Standalone Trabeculectomy. *Ophthalmology.* 2017; S0161-6420: 30464-30465.
28. Battle JF, Fantes F, Riss I, Pinchuk L, Albuquerque R, et al. Three year follow-up of a novel aqueous humor microshunt. *J Glaucoma.* 2016; 25: e58-e65.
29. Tan SZ, Au L. Manchester iStent study: 3-year results and cost analysis. *Eye (Lond).* 2016; 30: 1365-1370.
30. Chen PP, Lin SC, Junk AK, Radhakrishnan S, Singh K, et al. The effect of phacoemulsification on intraocular pressure in glaucoma patients: a report by the American Academy of Ophthalmology. *Ophthalmology.* 2015; 122: 1294-1307.