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focus

Minimally Invasive Glaucoma Surgery: MIGS

Gus Gazzard MBBChir MA MD FRCOphth
Consultant Ophthalmic Surgeon, Moorfields Eye Hospital & UCL
Reader in Ophthalmology (Glaucoma Studies)

Introduction

Minimally Invasive Glaucoma Surgery or 'MIGS' is a term applied, more or less appropriately, to the widening range of implants, devices and techniques (see table) that seek to lower intra-ocular pressure with less surgical risk than the more established procedures (of trabeculectomy, non-penetrating procedures (deep sclerectomy, canaloplasty, viscocanulostomy etc.) and tube drainage devices (Baerveldt, Ahmed or Molteno)).

A rapid expansion of options has out-paced robust randomised controlled trial evidence to guide their use. Into that gap have stepped enthusiastic early adopters who frequently perform only one or two of the available techniques. 'Conflicts of enthusiasm' (many procedures are avidly performed privately) and industry-led innovation (in a devices market with less regulation than governs new drug development) has made unbiased information even more difficult to obtain. Nonetheless, many of these techniques seem to hold the promise of drop-free IOP lowering with less surgical risk than accompanies existing surgical techniques.

Definitions: what is MIGS?

MIGS has been defined as IOP-lowering surgery with the following characteristics that distinguish it from traditional glaucoma surgery:

- 'Minimally traumatic'
- Via an ab-interno conjunctiva-preserving approach
- High safety profile
- Rapid recovery
- Frequently combined with cataract extraction
- Provides more modest IOP lowering than trabeculectomy

It is generally (though not universally) accepted that MIGS uses an ab-interno approach that leaves the conjunctiva intact for potential later trabeculectomy or non-penetrating surgery. Some surgeons (and companies) have more inclusively used the term 'MIGS' to include surgery that does affect the conjunctiva, most notably the Aquesys Xen implant which is widely performed with peri-operative sub-conjunctival MMC and frequently requires needle-revision of sub-conjunctival scar formation. The alternative, but confusing, term '*Moderately* Invasive Glaucoma Surgery' has been suggested for these.

MIGS procedures form a heterogeneous group of techniques: they may bypass trabecular meshwork (TM) resistance to aqueous flow with stents into Schlemm's canal (iStent, Hydrus), via drainage into the suprachoroidal space (Cypass, iStent Supra) or by excision of TM itself (Trabectome); whereas endo-cylodiode uses directly observed ablation of ciliary processes under endoscopic control to reduce aqueous production and ABiC visco-dissects the existing outflow channels. Each of these may present different challenges: supra-choroidal routes have historically failed due to later fibrosis limiting flow; Schlemm's canal routes seem to have a physiological 'floor' of around 16mmHg due to downstream resistance to flow [OVERBY][1] ; targeting aqueous production raises concerns about long-term hypotony risks, and it remains unclear what lasting benefit visco-dissection of existing channels will achieve (ABiC). The more invasive sub-conjunctival drainage techniques (Xen, Microshunt) bypass physiological flow routes entirely but are subject to the same risk of scar formation by tenon's and conjunctival fibroblasts that bedevil traditional *ab externo* surgery.

MIGS should be distinguished from other surgical innovations of the last few years have sought to improve upon existing *ab externo* techniques and as such are not truly minimally invasive. Such 'augmented incisional surgeries' include a wide variety of techniques that have all found advocates: device-augmented trabeculectomy using e.g. Express shunts; iTrack-guided *ab externo* visco-canulostomy and canaloplasty, and solid or gel spacers for augmented deep sclerectomy (e.g. Healaflow). However these would seem to sit at a similar level in the surgical hierarchy as traditional trabeculectomy, albeit sharing with MIGS a similar paucity of randomized controlled-trial (RCT) evidence.

Classification and choice: which MIGS? (see table)

Current ab-interno procedures may be classified into:

- Conjunctiva-sparing vs conjunctiva-involving
- Physiological outflow (Schlemm's canal) vs. non-physiological routes (via the supra-choroidal or sub-conjunctival spaces)
- Inflow procedures: reduction of aqueous production

Some techniques are not yet generally available, while extensive industry marketing heavily supports others. Not only do few robust RCTs exist, but there is minimal evidence that compares different techniques head-to-head. Currently the choice of which technique to learn is dictated as much by availability as evidence.

Angle surgery, however, whether trabectome TM excision, Hydrus, iStent or iTrack insertion into Schlemm's canal or Cypass injection into the supra-choroidal space, all use similar transferrable surgical techniques: transfer from one to another is relatively simple.

Risk and Benefit: MIGS when?

All clinical decisions balance risks of intervention with potential benefits. Glaucoma surgery is traditionally offered when topical medications and laser trabeculoplasty have failed to control IOP at safe levels. The significant risks of traditional surgeries restricted them to cases of confirmed deterioration or very high IOP. It is rare to offer *non*-MIGS surgery merely to achieve independence from eye-drops that are working well without allergy. (Although the current NIHR TAGS trial comparing drops with primary trabeculectomy for advanced glaucoma might alter that). But while trabeculectomy and tube surgery are highly successful in experienced hands [KIRWAN][2] they remain a source of patient discomfort [BARTON][3] and significant surgical risk [GEDDES][4] [BUDENZ][5].

Surgery that truly is safer could be offered with a similar risk/benefit balance even if it gives a smaller average reduction in IOP or lower frequency of success.

MIGS is frequently combined with cataract surgery ('PhacoPlus'). This carries a different Risk-Benefit assessment to stand-alone MIGS ('Solo-MIGS'): the additional risk and costs of adding a five-minute procedure to an existing intra-ocular case are less than those incurred by a separate admission, anaesthetic and intra-ocular surgery. Phaco-Plus may therefore further lower the threshold for MIGS procedures.

Is MIGS Better? Compared to what?

Many detractors of MIGS have compared the IOP lowering unfavourably to trabeculectomy surgery and ignore the apparent greater safety and higher patient acceptance of MIGS over trabeculectomy. However, the true comparator for MIGS may be continued drop therapy, rather than incisional surgery. Ophthalmologists markedly underestimate patients' extreme dislike of eye-drops and their non-compliance rates with treatments: patients hate drops more and use them less than we think. In a recent focus group of glaucoma patients (unpublished) 95% of participants would accept a significant risk from surgery to achieve not just complete drop-freedom but even simply a reduction in drop-frequency. Moreover, more invasive surgeries are still possible if necessary later, seemingly without compromising success rates.

Robust RCT evidence however is sparse however and little, if any, reliable evidence exists comparing the claims about one technique over another. Much of what is published is seriously limited by a lack of randomisation (single surgeon case series), small sample sizes, conflicts of interest (industry funded trials), lack of detailed reporting or over reliance on surrogate outcomes.

Several trials have looked at the iStent, showing modest single device IOP lowering but greater effects with more than one stent [MALVANKAR][6,7]. The Hydrus has been supported by several studies with a randomized controlled trail suggesting a clinically significant effect at two years [PFEIFFER][8], and studies of limited quality report good results for Trabectome [KAPLOWITZ][9], whereas only very limited data yet exist on the ABiC viscocanaloplasty technique or the InnFocus Microshunt [BATLLE][10].

Cost Effectiveness & Quality of Life: can we afford MIGS?

Modern clinical choices are increasingly patient-driven with wider use of patient reported outcome measures (PROMS & POEMS [SUMNER][11]). Patients seem to dislike eye-drops more than we realize and may value drop-freedom more than we allow. Safer surgery that targets not additional IOP lowering per se but aims for reduced drop-dependence is likely to be increasingly demanded by informed patients.

Drop-sparing surgery earlier in the disease may reduce total lifetime drop exposure thus protecting the conjunctiva from the well described harmful effects of long-term drop exposure [BROADWAY][12]) or, alternatively, defer loss of IOP control to such a time as surgery is no longer indicated or newer safer alternatives are available.

Whether our healthcare systems can afford this will require detailed data about what each technique offers: how much IOP reduction, with how great an independence from medications, for how long (not to mention effect on visual field loss and preservation in *clinically relevant* visual function) and ultimately with what impact on health-related quality of life. Balanced against this are the financial costs to patient, hospital and society, the opportunity costs of treatment and the of treatment burden to patient and family.

The Future: whither MIGS?

The 'New Paradigm' of glaucoma therapy will aspire to a much-reduced dependence on topical medication. I foresee a stepwise approach for mild to moderate disease that begins with early (often primary) selective laser trabeculoplasty, followed by preservative-free topical or injectable therapies and leads on to true *ab interno* MIGS procedures, with or without lens surgery. More invasive conjunctiva-involving stents might then be used for more severe disease or those who fail initial efforts. Alongside this, traditional mitomycin or anti-VEGF augmented trabeculectomies will still be necessary for those needing near-10 or below-10mmHg IOPs or presenting with advanced disease, while Tube surgery will likely remain the mainstay of surgical intervention for complex, secondary glaucomas and failed previous surgery.

MIGS procedures clearly hold great promise – it is our moral duty to use them responsibly and to investigate objectively their risks and benefits.

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Technique / Device	Drainage Route & Mechanism of IOP Reduction	Conjunctiva Involved?	Published Randomised Controlled Trial Evidence?
Trabectome (NeoMedix)	Via Schlemm's canal: excision of trabecular meshwork	No	No
iStent (Glaukos)	Via Schlemm's canal: bypass of trabecular meshwork	No	Yes
iStent Inject (Glaukos)	Via Schlemm's canal: bypass of trabecular meshwork	No	No
Hydrus (Ivantis)	Via Schlemm's canal: bypass of trabecular meshwork	No	Yes
AbIC: Ab Interno Canaloplasty with iTrack (Ellex)	Via Schlemm's canal: dilatation of trabecular meshwork	No	No
Cypass (Transcend)	Via supra-choroidal space	No	No
iStent Supra (Glaukos)	Via supra-choroidal space	No	No
Endo-cyclophotocoagulation 'Endo-Diode'	Cyclo-destructive:	No	No
Microshunt (Innfocus)	To sub-tenons / sun-conjunctival space	Yes	No
Xen (Aquesys / Allergan)	To sub-tenons / sun-conjunctival space	Yes	No