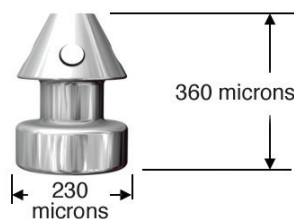


## MIGS roundtable

# Treatment algorithms for glaucoma are shifting dramatically with an increasing number of ophthalmologists taking advantage of micro invasive glaucoma surgery (MIGS) options to achieve intraocular pressure reduction.

The World Health Organization estimates the number of persons blind as a result of primary glaucoma to be 4.5 million, or 12 per cent of all global blindness.<sup>1</sup> Through appropriate treatment, sight may be maintained; otherwise the progression of the condition leads eventually to severe restriction of the visual field and irreversible blindness.

MIGS procedures have been developed in recent years to reduce some of the complications of traditional glaucoma surgery, by using microscopic-sized devices. The Glaukos iStent *inject*<sup>®</sup>, for example, with dimensions 360 microns by 230 microns, is the smallest known implantable medical device approved for use in humans.



While MIGS devices dramatically reduce the incidence of complications, the trade-off may be slightly less efficacy in lowering intraocular pressure compared to more invasive procedures such as trabeculectomy. However, the safety profiles of these procedures make them an attractive option for ophthalmologists treating mild to moderate glaucoma patients.

Undoubtedly, glaucoma treatment will continue to evolve as surgeons gain experience with MIGS. Indeed, MIGS is “eroding away” the gold standard of treatment via trabeculectomy, according to participants of an ophthalmology roundtable discussion.

All ophthalmologists, the roundtable agreed, have a duty of care to inform patients about the option of MIGS upon first diagnosis of glaucoma, to facilitate informed consent about treatment options.

The roundtable discussion, held in Sydney in February, was hosted by Glaukos

and chaired by Dr Colin Clement. Other participants included Dr Nathan Kerr, Dr David Manning, Dr Frank Howes and Dr Smita Agarwal.

Dr Colin Clement said Australian ophthalmologists are in the unusual position of having access to four MIGS devices. “Not many other countries in the world are in that position and we’ve had quite substantial experience with them clinically so we’re able to balance our clinical experience with what the clinical trials are telling us.”

### Safety First

For all participants at the roundtable, safety was the number one reason for including MIGS in the treatment paradigm.

“For me, the most important things are safety, efficacy and clinical evidence,” Dr Kerr said, “and the balance of those three depends very much on the individual patient... I think it is important to personalise the type of device and procedure to the patient we are treating.”

*In a five-year study, no adverse events related to iStent inject<sup>®</sup> implantation were reported.<sup>2</sup>*

While most of the participants were glaucoma specialists, with extensive experience with different MIGS devices, Dr Agarwal is primarily a cataract and refractive surgeon. She treats mild to moderate glaucoma and refers more advanced cases to glaucoma specialists.

“For me, the most important thing would be the safety, the predictability and the learning curve,” she said.

Dr Agarwal said newer devices, such as those implanted subconjunctivally or in the suprachoroidal space (Xen<sup>®</sup> and CyPass<sup>®</sup>), she had used only in model eyes but has

used the iStent *inject* regularly to treat mild to moderate glaucoma.

“It is straightforward; it is predictable. I can get good results. There are no additional side effects,” said Dr Agarwal. As a refractive surgeon, Dr Agarwal aims to give her patients good vision without glasses. In order to support this goal for her glaucoma patients, she uses Glaukos iStent *inject* to reduce the use of glaucoma drops and therefore the side effects of ocular dry eye from long term use of the drops.

Dr Kerr said “the most important thing” was to inform people with both cataract and glaucoma about the options of MIGS so that they are aware of all the options available to them “in terms of not only treating their cataracts but also treating their glaucoma, potentially providing better intraocular pressure control and reducing their need for glaucoma medications.”

“For patients with cataract and mild to moderate glaucoma, my preference is definitely for a bleb-less technique.”

Dr Howes has inserted more than 500 MIGS devices and believes the iStent *inject* “sits at the pinnacle of safety for MIGS devices.”

Dr Howes said he has used the iStent *inject* on significant numbers of patients, with no complications.

“Micro-hyphemas are commonly seen during surgery, and is a sign of correct iStent *inject* placement, but I have yet to see hyphaema at day 1 postop.

“Hyphema is very, very uncommon. We just don’t see it so it is not a refractive concern in those patients. We are all after refractive accuracy in cataract surgery. iStent *inject* is the glaucoma procedure that is least likely to disturb any refractive outcome when combined with the cataract extraction. There is undoubtedly a learning curve with iStent *inject* insertion but once that challenge is achieved, it really is very safe. So for me, it sits at the pinnacle of safety for MIGS devices. Yes, we have some cases when the desired efficacy is not achieved, but at least it is not accompanied by other complications and that, too, is important.”

## Not all MIGS are equal

MIGS have been defined by the presence of five criteria: a micro-invasive approach, minimal tissue trauma, at least modest efficacy, rapid recovery, and a high safety profile.<sup>3</sup>

But Dr Clement said one had to be careful in using MIGS as an umbrella term.

“From the point of view of someone who has a glaucoma practice – and I have patients who range from mild to very severe glaucoma – I think one of the issues here is the use of the term ‘MIGS’, which is an umbrella term with connotations that the devices are very safe, and they have a degree of efficacy that is beneficial to the patient.

“But not all MIGS are equal,” Dr Clement stated.

“So, the trabecular bypass (for example, iStent *inject*<sup>®</sup>, Hydrus<sup>™</sup>) is very different from suprachoroidal (CyPass<sup>®</sup>), which is very different to subconjunctival (Xen<sup>®</sup>, InnFocus<sup>®</sup>) – both in terms of efficacy and safety.

“I tend to use the trans-trabecular stents earlier in the disease process. These are your mild to moderate glaucomas that you’re trying to get off medication and a pressure reduction to the mid or possibly low teens would be ideal,” Dr Clement said.

“The subconjunctival devices are more of a trabeculectomy replacement for me, so these are patients who... in the past had a trabeculectomy or a non-penetrating glaucoma surgery but there’s the option to do the subconjunctival MIGS now, which are bleb dependent. They are a quicker

operation (than traditional trabeculectomy); they are a safer operation; they provide the potential for a quicker recovery, but they do still carry some of the same risks as any other bleb-dependent surgery. So that population tends to be a more moderate or advanced type of glaucoma for me. I certainly wouldn’t be using that in mild to moderate with a little bit of cataract.

“And then the suprachoroidal shunts – even though the clinical trials are, again, in mild to moderate combined with cataract, for me at the moment, these provide an opportunity to treat someone in whom you are desperately trying to avoid a subconjunctival based procedure.

They’ve likely had trabeculectomy or tube or something else before. Further interventions in that space are not likely to work; you need to get their pressure down. It seems to be the perfect opportunity to try to do it by the suprachoroidal space.

“Using it as a treatment for mild to moderate glaucoma in combination with cataracts when trabecular bypass stents are also available currently, for me, doesn’t sit right – that may change in the future, but it just doesn’t seem to make sense to me at the moment,” Dr Clement said.

Dr Manning also pointed out that, like MIGS,

glaucoma was being used as an “umbrella term” when, in actual fact, it is not a single disease. “We need to tailor our MIGS and our treatment to the type of glaucoma.”

“These (MIGS) devices won’t reduce the pressure to (an adequate) level for the really advanced, progressive glaucomas. I think

there is still a place for trabeculectomies, tubes and those sorts of things.

“If we are looking at mild to moderate glaucomas... undoubtedly the trabecular meshwork or trabecular bypass devices are what we need to use, from a risk-benefit point of view.

“But if I’m looking for a really low, low pressure, I’m going

to use a trabeculectomy rather than a Xen device. The suprachoroidal (MIGS device, CyPass) – I’m still trying to work out where that fits because I don’t think we have good evidence to show it works well in those refractory glaucomas that have had multiple trabs, multiple tubes.”

Dr Manning said while there was evidence that the CyPass works in mild to moderate glaucomas, he has found “early myopic shifts as well, which take a month to resolve, which is concerning from a cataract surgeon’s point of view.”

“And I also have big reservations about

*“It is straightforward; it is predictable. I can get good results. There are no additional side effects.”*

*“... not all MIGS are equal.”*

*“Every single ophthalmologist who is coming into contact with glaucoma patients should be talking to them... (MIGS) as an option... I think it is clear cut.”*

## Clinical Data Summary – iStent *inject*<sup>®</sup>

Surgery	Glaucoma Type	Follow-Up (Years)	IOP Reduction*	Medication Reduction**	Pre-Op Washout
2 iStent <i>inject</i> + Phaco <sup>4</sup>	POAG, PXG, OHT	1.0	9 mmHg, 36%	1.0	Yes
2 iStent <i>inject</i> <sup>5</sup>	POAG, PG, PXG	1.0	10 mmHg, 40%	2.0, 72%	Yes
2 iStent <i>inject</i> <sup>6</sup>	OAG	1.0	12 mmHg, 48%	1.0, 93%	Yes
2 iStent <i>inject</i> <sup>7</sup>	POAG, PG, PXG	0.5	7 mmHg, 33% 8.42 mmHg, 35%	1.3	No
2 iStent <i>inject</i> + Phaco <sup>8</sup>	OAG	1.0	7 mmHg, 34%	0.8	No
2 iStent <i>inject</i> <sup>9</sup>	OAG	1.5	10 mmHg, 41%	1.0	Yes
2 iStent <i>inject</i> + Phaco <sup>2</sup>	POAG, PXG, OHT	5.0	10 mmHg, 37%	0.1	Yes
2 iStent <i>inject</i> <sup>10</sup>	OHT	1.5	12 mmHg, 48%	1.0	Yes

\*Compared to Baseline, where appropriate after Washout  
\*\*Compared to Screening, where appropriate before Washout

Key: POAG=Primary Open-Angle Glaucoma; OAG=Open Angle Glaucoma; PXG=Pseudoexfoliative Glaucoma; OHT=Ocular Hypertension; PG=Pigmentary Glaucoma

leaving something that large in that space for a long period of time. So, I'm not quite sure where the suprachoroidal shunt really sits..."

The question of what was left behind by MIGS devices, also troubled Dr Howes.

"I do have a little bit of concern about the quantity of foreign material in relation to Hydrus™ that is going to be in place for a long time. There is therefore an element of the unknown in the predictability that is yet to be understood"

Hydrus is made of a unique, biocompatible alloy called "nitinol," which has two components, nickel and titanium.

Dr Howes said nitinol "lasts a long time as a cardiac stent so may do the same as a Schlemm stent, but the length and thickness, in the long term, may cause disruption of canal physiology and possible foreign body reaction."

"So, I have continued preferentially with the iStent *inject*® which has given us pretty good results. When you're talking about clinical evidence, the iStent *inject* and Hydrus seem to be paralleling each other so if we have less material but parallel results, it would appear to be sensible to err on the side of the lesser quantum of material," Dr Howes said.

"I am now using MIGS frequently in practice. Obviously trabeculectomy remains the gold standard and is the go to procedure when sustained low pressure results are really needed, but the MIGS procedures are eroding away at these principles all the time."

Dr Kerr agreed MIGS is "greatly changing the way we manage our glaucoma patients."

"In terms of the devices... the most logical way to classify them is by their target – the trabecular meshwork (iStent *inject* or the Hydrus), the suprachoroidal space, like the CyPass® or soon to be iStent SUPRA®, or the subconjunctival space like the Xen®."

Dr Kerr said he performs "all of those procedures" and there is a distinct pathway.

For people who have predominantly cataract with controlled glaucoma, Dr Kerr said he offers a bleb-less device, such as a trabecular meshwork device like the iStent *inject*, "particularly where people are intolerant to medications, adherence is an issue, or where medications are not controlling intraocular pressure as well as needed."

"It adds a little bit of time to their cataract surgery, gives them a predictable post-operative recovery with the benefit, potentially, of improvement in their IOP and the ability to reduce their glaucoma medications.

"The big advantages are that the procedures are bleb-less, they add no significant increase in the number of post-operative visits over their cataract surgery and then,

## MIGS devices in Australia

### MIGS devices can be categorised as falling into three distinct spaces.

#### The trabecular meshwork

**iStent *inject*®** (Glaukos Corp., Laguna Hills, CA, USA) is inserted through the trabecular meshwork into Schlemm's canal, usually at the time of cataract surgery. It is a heparin-coated non-ferromagnetic, titanium stent with dimensions 360 microns in length and 230 microns in width. The iStent *inject* is the smallest implantable medical device approved for use in humans.

**The Hydrus™ Microstent**, (Ivantis Inc., Irvine, CA, USA), is an implant that holds Schlemm's canal open to allow more fluid out. Like the iStent *inject*, this is usually inserted during cataract surgery. Hydrus Microstent is an 8mm-long crescent-shaped nickel-titanium (Nitinol) device.

#### The suprachoroidal space

**The CyPass® Microstent**, (Alcon, Fort Worth, TX, USA) is a fenestrated polyimide shunt that enhances uveoscleral outflow via insertion into the suprachoroidal space, essentially creating a controlled cyclodialysis cleft. The implant is 6.35mm long.

**iStent SUPRA®** (Glaukos Corp., Laguna Hills, CA, USA). This is a suprachoroidal Micro-Bypass Stent which in February 2017 announced completion of patient enrolment in the pivotal phase of its US Food and Drug Administration (FDA) Investigational Device Exemption (IDE) trial. It will not be available in Australia for some time.

#### The subconjunctival space

The **Xen® 45 Gel Stent** (Allergan Plc, Dublin, Ireland) creates a low-lying, ab-interno bleb in refractory glaucoma, creating a new pathway for aqueous flow from the anterior chamber to the subconjunctival space. Six millimetres long, it is composed of a gelatin derived from porcine dermis, formed into a tube, and then cross-linked with glutaraldehyde.

The **InnFocus MicroShunt®** Glaucoma Drainage System (Santen Pharmaceutical Co. Miami, Florida, USA) is an implant consisting of a micro-tube (about twice the size of an eyelash) that shunts aqueous fluid from the anterior chamber of the eye to a sub-conjunctival/sub-Tenon flap. The device is made of SIBS, a thermoplastic elastomeric material. The InnFocus MicroShunt has yet to receive TGA approval for use in Australia.

hopefully, if these devices provide better pressure control, then we will see – with time and more ongoing studies – whether that relates to better control of glaucoma.

"For people who have more refractory glaucoma, where we are aiming to prevent vision loss from glaucoma and we need to achieve the lowest possible IOP levels... the devices draining to the subconjunctival space provide the greatest level of intraocular pressure reduction of all of the MIGS devices at present. But with that comes a bleb and the associated long-term risks and so it again comes down to risk management.

"We need to balance the goal of lowering intraocular pressure and preventing vision loss from glaucoma against the small but potentially serious risks that can come with subconjunctival filtration," Dr Kerr said.

### Moving into MIGS

For ophthalmologists looking to offer MIGS for the first time, Dr Argawal has some simple, common-sense advice: choose your patient wisely and understand your limitations.

She said she found iStent *inject* "pretty easy to learn, but you have to experiment and learn the right positioning."

All the ophthalmologists at the round-table suggested observing or being trained by colleagues who had performed multiple MIGS, attending wet lab training where possible and even watching YouTube.

"If someone is not going to do MIGS, it is not through a lack of training opportunity," Dr Clement noted.

Dr Howes recommended ophthalmologists wanting to incorporate MIGS in their practice start with the iStent *inject*<sup>®</sup>, before considering Xen<sup>®</sup>.

"I certainly think the iStent *inject* is the one to start with," Dr Howes suggested, although he acknowledged that there is undoubtedly a learning curve.

**MIGS procedures share the following:**

- Ab interno microincisional approach
- Minimally traumatic to the target tissue
- Efficacious
- Favorable safety profile
- Rapid recovery with minimal safety risk

"From a practical point of view, it is then worth learning the technique of Xen Gel Implant filtering surgery then returning to picking up the skills of Hydrus<sup>™</sup>. Once the evidence base of suprachoroidal shunting increases, we can then consider the use of Cypass<sup>®</sup>" Dr Howes said.

## The Duty of Care

Dr Clement said ophthalmologists had a clear duty of care to inform patients of MIGS treatment.

"MIGS has a very strong evidence base for mild to moderate glaucoma. It has a proven safety record and there's emerging data now showing that it is cost effective. So, patients need to be aware that it is available and it's a treatment option and it does fill a previously unmet need and a void in the treatment algorithm."

Dr Agarwal stressed the importance of informing patients about MIGS at the first opportunity. "Being a cataract refractive surgeon, just as the toric lens brought the 'wow' factor in cataract surgery, MIGS has revolutionised the treatment of glaucoma... we should be telling the patients at the first diagnosis of glaucoma that these are the options available and we should be offering the treatment options available, whether we do it ourselves or we send the patients away."

"At the end of the day," Dr Agarwal said, "it is patients' choice whether they are happy to continue to use eye drops for life, whether they want laser (SLT) or whether they want MIGS."

She said if patients did not want to adhere to the regime of glaucoma drops several times a day with the associated side effects, MIGS is an option that could help lower IOP and ensure significantly less conjunctival scarring.

"If they are happy to have MIGS done, why not?"

Dr Kerr noted that patients were increasingly well-informed about MIGS.

"Now many of my patients... are often referred to me specifically for whether this patient is suitable for MIGS by their optometrist. My optometry colleagues are now very good at identifying those patients who may be suitable for these procedures. They often have talked to the patient before the patient has seen me and that really helps our discussion."

Dr Manning agreed: "Do we have a duty of care to offer it (MIGS) to our glaucoma patients? I'm not sure we have a duty of care to offer it, but we certainly have a duty of care to inform our patients of it.

"And... whose role is it? Every single ophthalmologist who is coming into contact with glaucoma patients should be talking to them about... (MIGS) as an option... I think it is clear cut," Dr Manning said.

### Roundtable Participants



**Dr Colin Clement**

Dr Clement is a Sydney-based ophthalmologist with expertise in the diagnosis and management of glaucoma and cataract. His special interests include glaucoma surgery and ophthalmic teaching. Clinical research interests include mechanisms, outcomes and complications of glaucoma surgery. As Staff Specialist at the Glaucoma Unit at the Sydney Eye Hospital, he has pioneered non-penetrating glaucoma surgery and has established a glaucoma surgery wet lab course.



**Dr David Manning**

Dr Manning is a comprehensive ophthalmologist with interests in cataract and refractive surgery as well as glaucoma surgery. He is the founder and principal of Hunter Cataract and Eye Centre in Charlestown, New South Wales. He is also a Visiting Medical Officer for The Hunter New England Health Network as well as a conjoint lecturer at The University of Newcastle.



**Dr Frank Howes**

Dr Howes is a cataract, refractive and glaucoma surgeon based at the Eye & Laser Centre on Queensland's Gold Coast. With extensive experience in Canada and the UK – he introduced SLT to the UK in 1998 – his interest in MIGS developed in 2012. He has inserted more than 500 MIGS devices (iStent and iStent *inject* and Xen) since that time. He was responsible for the first iStent insertion in Australia in 2015.



**Dr Nathan M. Kerr**

Dr Kerr is a fellowship-trained glaucoma sub-specialist in Melbourne, Australia. A recipient of the Bayer Scholarship, he completed a prestigious fellowship at Moorfields Eye Hospital in London where he trained in minimally invasive glaucoma surgery. He serves as a glaucoma section editor for Clinical and Experimental Ophthalmology and is the clinical lead for glaucoma trials at the Centre for Eye Research Australia. Dr Kerr specialises in cataract and glaucoma surgery.



**Dr Smita Agarwal**

Dr Agarwal is a comprehensive ophthalmologist with a special interest in refractive cataract surgery, glaucoma, diabetes and anterior segment eye diseases. She is currently Head of Ophthalmology at Wollongong and Shellharbour Hospitals and a visiting medical officer at various private hospitals in the Illawarra and Shoalhaven region. Dr Agarwal does refractive work at Vision Eye Institute, Hurstville and operates a private clinic in Wollongong, Nowra and Shellharbour. She is a Senior Clinical Lecturer in Ophthalmology at the University of Wollongong and University of Sydney.

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**To see videos on iStent *inject*<sup>®</sup> and other videos from Glaukos, go to: [eyetube.net/collections/glaukos](http://eyetube.net/collections/glaukos)**

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