

# Minimally Invasive Glaucoma Surgery and CyPass® Micro-Stent—A New Era in Glaucoma Surgery

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In the largest randomized clinical trial to date on a minimally invasive glaucoma surgery device, the CyPass® Micro-Stent was able to lower intraocular pressure (IOP) more than was modern cataract surgery (phacoemulsification and intraocular lens implantation) alone, and should be considered for patients with mild to moderate glaucoma already scheduled to undergo phacoemulsification surgery. The two-year outcomes of the COMPASS study found mean IOP reductions of 7.4 mmHg in the CyPass Micro-Stent group and no vision-threatening adverse events; more than 98% of subjects in the CyPass Micro-Stent group achieved 20/40 or better best-corrected visual acuity.

## Keywords

Glaucoma, MIGS, Cypass, Suprachoroidal stent, COMPASS

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Glaucoma is a degenerative disease that, if left untreated, will eventually cause irreversible damage to the optic disc, and loss of vision. This progressive optic neuropathy is estimated to affect 3 million people in the US.<sup>1</sup> Current treatment options are limited to lowering intraocular pressure (IOP), with medical therapy in the form of topical drops as the first-line treatment.<sup>2</sup> Unfortunately, topical medication use may not be sufficient for long-term IOP control in all patients.

It is not uncommon for patients with glaucoma to have other ocular comorbidities. For example, in the US about 20% of patients undergoing cataract surgery have concomitant glaucoma,<sup>3</sup> but combined phacoemulsification and glaucoma surgery are infrequently performed.

Traditional surgical options for glaucoma (trabeculectomy and tube shunt implantation) have a substantial number of potential complications, including hypotony, hyphema, bleb leakage, bleb infection, and endophthalmitis.<sup>4</sup> The potential for these complications have led to most cataract surgeons referring moderate-to-severe cases of glaucoma to specialists for medical and/or surgical management. This, in turn, means that patients undergoing traditional surgery tend to have more advanced stages of disease. It has long been a goal of glaucoma researchers/clinicians to perform less-invasive procedures that result in fewer complications while providing the same efficacy and reduction in the dependence upon medications as traditional filtration surgery. These types of procedures are likely to be incorporated more readily into cataract surgeons' practices.

## What is minimally invasive glaucoma surgery?

Minimally invasive glaucoma surgery (MIGS) aims to provide a conjunctival-sparing, ab interno approach to IOP reduction for patients with mild-to-moderate glaucoma that has a better safety profile than traditional incisional glaucoma surgery.<sup>5</sup> These devices and procedures are often combined with cataract surgery.

To date, MIGS can be performed using any of the following approaches: increasing trabecular outflow by bypassing the trabecular meshwork (TM), creating a subconjunctival drainage pathway, or increasing outflow via suprachoroidal pathways.<sup>5</sup> MIGS were developed to address the gap between topical medications and conventional glaucoma surgery, with the knowledge that efficacy would be less than trabeculectomy or shunts, but without the major complications associated with those more invasive glaucoma surgical procedures.

MIGS devices have been commercially available in the US since 2006, with the introduction of the trabectome.<sup>6</sup> Several devices are now available, and others are in late-stage development. Both the trabectome and the iStent® (Glaukos, California, US) bypass the TM, and are designed to give aqueous direct access from the anterior chamber into Schlemm's canal and the downstream collector channels.<sup>5</sup> The trabectome is commonly performed with cataract surgery, but can be performed alone; the iStent is approved for use only with concurrent cataract surgery in the US, and as both a stand-alone and combined procedure in Europe. Generally speaking, these devices/procedures are not recommended for patients with IOP targets below the episcleral venous pressure, or for those with Grave's disease or Sturge-Weber syndrome, or for those with very tight scleral buckles.<sup>5</sup> A third trabecular bypass device, the Hydrus™ (Ivantus Inc., Irvine, California, US), has not yet been approved but is in late-stage trials in combination with cataract surgery.

Supraciliary devices increase outflow by diverting it to the suprachoroidal space.<sup>5</sup> To date, only the CyPass® Micro-Stent (Alcon, Fort Worth, Texas, US) has been approved in this category of MIGS. The CyPass Micro-Stent was granted the Conformité Européenne (CE) mark in 2008, and was approved in the US in 2016. In the US, approval was based on results from the COMPASS study.<sup>7</sup> The remainder of this article will discuss the CyPass device and the pivotal trial data that led to its approval.

### CyPass Micro-Stent

In the US, the CyPass Micro-Stent is indicated for use only in conjunction with cataract surgery for the reduction of intraocular pressure in adult patients with mild-to-moderate primary open-angle glaucoma.<sup>8</sup> The device is a fenestrated micro-stent comprised of biocompatible polyimide material designed to be inserted into the supraciliary space, thereby creating a permanent conduit between the anterior chamber and the supraciliary space. By doing so, the device enables aqueous drainage through the uveoscleral pathway.<sup>8-9</sup> This mechanism of action is similar to commonly used topical medications for IOP control—specifically, the prostaglandin analogs. Prostaglandins are well known to lower IOP by remodeling the extracellular matrix in the ciliary muscle, thereby increasing the uveoscleral outflow.<sup>10-12</sup>

In the late 1980s, Emi et al. suggested that a negative pressure gradient between the suprachoroidal space and anterior chamber may be preferable for directing aqueous.<sup>13</sup> The CyPass Micro-Stent utilizes this platform; its implantation is *ab interno* and uses the same clear corneal incision as the cataract surgery. The device's proximal rings are visible under a goniolens, which provides guidance for proper insertion and depth.

The device is typically inserted following the cataract extraction and intraocular lens implantation. The patient's head is rotated away from the surgeon, the microscope is tilted away from the surgeon, and the goniolens is placed on the cornea using the non-dominant hand. Once clear visualization of the angle structures is obtained, the inserter is passed across the anterior chamber that is kept inflated with viscoelastic. Once the tip of the inserter is introduced just posterior to the scleral spur at the iris root, the curvature of the guidewire ensures that the distal aspect will end up in the supraciliary space when the device is fully advanced to the hub. When properly implanted, insertion of the device does not require any force and does not distort the globe or impart any collateral damage to adjacent structures.<sup>8</sup>

### Clinical trial data

The US approval of the CyPass Micro-Stent was based upon data from the two-year pivotal COMPASS Study. The study investigators used strict medication protocols to reduce any inherent bias.<sup>7</sup> Not only was the COMPASS study the largest to date for any MIGS procedure (enrolling more than 500 subjects), it was the first study to conform to US Food and Drug Administration (FDA) guidance and American National Standards Institute (ANSI) standards for MIGS. All told, the COMPASS study enrolled 131 subjects in the phaco-alone arm and 374 in the CyPass Micro-Stent plus phaco arm.<sup>7</sup> The primary endpoints were the proportion of patients with at least a 20% reduction in unmedicated, diurnal IOP; the mean change in unmedicated, diurnal IOP; and the proportion of eyes with unmedicated, diurnal IOP  $\geq 6$  mmHg and  $\leq 18$  mmHg.<sup>7</sup> Baseline demographics between the phaco-only group and the CyPass-phaco group were similar, with the overwhelming majority of patients in both groups were Caucasian and on one to two medications.<sup>7</sup>

The results in the intent-to-treat group were statistically significant. More CyPass patients (73%) than control (58%) achieved a 20% or higher reduction in unmedicated diurnal IOP at 24 months ( $p=0.002$ ).<sup>7</sup> In addition, postoperative IOP was reduced from baseline in the CyPass-phaco and phaco-only groups by a mean of  $7.9\pm 4.1$  mmHg and  $6.2\pm 3.8$  mmHg at 12 months, representing a 32% and 26% decline, respectively. At 24 months, the CyPass-phaco group had a  $7.4\pm 4.4$  mmHg (30%) reduction in IOP from baseline, and the control group had a  $5.4\pm 3.9$  mmHg (21%) reduction in IOP from baseline.<sup>7</sup>

Study results also suggested ongoing longevity of outcomes, with 61.2% of eyes in the CyPass group and 43.5% of the eyes in the control group maintaining an unmedicated diurnal IOP range between 6 mmHg and 18 mmHg at 24 months.<sup>8</sup> Of patients who obtained an unmedicated diurnal IOP reduction of 20% or more from baseline, 93% in the CyPass group were medication-free at 24 months compared with 72.4% of the control group.<sup>8</sup>

### Safety

Outcomes of the COMPASS study indicate the CyPass showed comparable safety compared with cataract surgery alone. Adverse events (AEs) in both groups were similar: 39% of the CyPass-phaco group and 36% of the phaco-only group patients reported an AE postoperatively.<sup>7</sup> The majority of AEs were considered generally manageable and transient and did not affect visual acuity outcomes.<sup>7</sup> There has been concern with the MIGS devices regarding postoperative hyphema. There were 10 patients in the CyPass-phaco group (2.7%) who experienced hyphema during the procedure, but this was not considered a serious intraoperative AE, and it resolved within the first week.<sup>7</sup> In the CyPass-phaco group, 11 subjects (2.9%) developed hypotony within the first month of implantation, but these also resolved without long-term sequelae.<sup>7</sup> Three of these (0.8%) had hypotony maculopathy, one which was due to an additional procedure; all of which resolved by month 24. Aside from hypotony maculopathy, there were no cases of flat anterior chamber requiring reformation, corneal folds, choroidal effusion requiring drainage, or suprachoroidal hemorrhage associated with any patients who had hypotony throughout the study. It is important to differentiate between numerical hypotony (IOP  $>$  three standard deviations below mean IOP corresponding to  $<6.5$  mmHg) and clinical hypotony (when IOP is low enough to result in vision loss). In the COMPASS study, among 374 patients, 11 had numerical

hypotony but only three had clinical hypotony, one of which was due to an additional procedure; all of which had resolved by month 24.<sup>7</sup>

## CyPass observations

The clinical studies found safety outcomes of the CyPass-phaco surgery to be comparable to phaco alone and to other MIGS interventions.<sup>7,14</sup> An earlier CyPass study<sup>15</sup> found subjects with baseline IOP of <21 mmHg (n=102) had a higher percentage of hypotony (IOP <6 mmHg in that study) within the first month after surgery (18.6%) than those with a baseline IOP ≥21 mmHg (n=65; 6.2%). In that study, all cases of hypotony resolved by one month without any visual sequelae.<sup>15</sup> That same study emphasized the importance of device position, as placement too far anteriorly resulted in corneal endothelial contact in 1.2% of subjects. Surgical advancement of the CyPass too far into the supraciliary space created an obstruction in seven cases (4.2%).<sup>15</sup> In the COMPASS study, however, there were only two cases of device malpositioning and eight cases of stent obstruction (2.1%).<sup>7</sup> In the CyPass Micro-Stent studies, the efficacy benefits over phacoemulsification alone were sustained over the 24-month study in both IOP and reduced glaucoma medication use.<sup>7</sup> The COMPASS study did acknowledge that the small percentage of Latino/Hispanic subjects (4%) may be underrepresented.<sup>7</sup>

MIGS provides cataract surgeons with an opportunity to improve patients' IOP and maintain vision by taking advantage of the surgical access granted by the clear corneal incisions used for the cataract surgery. In the case of the CyPass Micro-Stent, the device is conjunctiva-sparing, meaning that it will not preclude the possibility of a future trabeculectomy or tube shunt if necessary. Further, the implantation of the device is well within cataract surgeons' skill sets. CyPass Micro-Stent placement is intuitive for most surgeons, with only a minimal learning curve.

Although the overall MIGS category is in its infancy, and researchers and clinicians are still learning about the various devices, the CyPass Micro-Stent represents an option with strong evidence supporting its safety and efficacy. With more cataract patients having concomitant mild to moderate glaucoma, combined phaco-MIGS procedures are likely to become more commonplace.<sup>14</sup> As with any novel technique, clinicians are still determining which patients may or may not benefit from any one particular MIGS device. The FDA drafted guidelines for future MIGS studies to clearly specify the standard any new study should uphold;<sup>16</sup> it is hoped that these guidelines will better enable clinicians to compare the devices to one another and to determine the optimum timing and delivery of these treatments along the spectrum of glaucoma severity. □

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